ISSN:1305-9319 | E-ISSN:1305-9327 | Cilt / Volume 16 | Sayı / Issue 2 | Yıl / Year 2020

MEDICAL JOURNAL OF BAKIRKÖY TIP DERGİSİ

www.bakirkoytip.org

ISSN: 1305-9319 | E-ISSN 1305-9327 | Year: 2020 | Volume: 16 | Issue: 2

MEDICAL JOURNAL OF BAKIRKÖY TIP DERGİSİ

www.bakirkoytip.org

Owner
SBÜ. İstanbul Bakırköy Dr. Sadi Konuk Research and Training Hospital

Administrative Office
SBÜ. İstanbul Bakırköy Dr. Sadi Konuk Research and Training Hospital
Tevfik Sağlam Cad. No: 11 Zuhuratbaba
İstanbul - Turkey
Tel: +90 212 414 71 59 / 90 212 241 68 20
mail: info@bakirkoytip.org

Language Editors
Gürkan KAZANCI
Ümit ÖZKAN

Statistics Editors
Emire Bor

Graphics
Arzu Deniz ÖLMEZ
Ayfer ERYEŞİL

Publication Coordinator
Hira Gizem FİDAN

Publication Type: Local Periodicals

Publisher
LOGOS YAYINCILIK TİC. A.Ş.
Yıldız Posta Cad. Sinan Apt. No. 36 D. 63/64 34349
Gayrettepe-İstanbul

Tel : (0212) 288 05 41
Faks : (0212) 211 61 85
E-mail : logos@logos.com.tr
web : www.logosyayincilik.com

Bakirkoy Medical Journal of is an official scientific Journal of SBÜ. Dr. Sadi Konuk Research and Training Hospital (BMJ)

It is published quarterly as 4 issues every year (March, June, September, December).

BMJ is an open Access, free and peer-reviewed journal and indexed in ESCI, EMBASE, Scopus, EBSCO and ULAKBİM TR Dizin.

Instructions for Authors and publication policy is available on our website.
www.bakirkoytip.org

www.bakirkoytip.org

Advisory Board

www.bakirkoytip.org

Advisory Board

www.bakirkoytip.org

Advisory Board

www.bakirkoytip.org

Advisory Board

www.bakirkoytip.org

ISSN 1305-9319
E-ISSN 1305-9327

Contents

www.bakirkoytip.org

Contents

www.bakirkoytip.org

ISSN 1305-9319
E-ISSN 1305-9327

Editorial

Dear Colleagues;

Medical Journal of Bakırköy (BMJ) has been a periodical publication of Sadi Konuk Research and Training Hospital for 16 years. We are honoured to publish the second issue of 2020 with high quality papers.

Medical Journal of Bakırköy is currently within the scope of ESCI as well as many other major indexes and our ultimate goal is to meet the Science Citation Index (SCI) criteria and be listed in that database. In order to increase the visibility and usability of published papers, the language of the journal is English. After the renewal of website and journal managament system, with your valuable contributions to the Journal, we are able to publish the submitted articles within a short period of time. I would like to thank our reviewers who voluntarily reviewed the submitted articles and put their best effort to edit.

We are very excited by the number and the quality of papers that have been submitted. With the momentum we receive from you, we will continue to work.

Prof. Dr. Esra Şevketoğlu
Chief Editor

Original Article

Med J Bakirkoy 2020;16(2):95-102
doi: 10.5222/BMJ.2020.46330

Medical Journal of Bakirkoy

Comparison of CA 125, CA 72-4, Risk of Malignancy Index and DePriest Scoring System in the Differentiation Between Benign and Malignant Adnexal Masses

Benign ve Malign Adneksiyal Kitle Ayrımında CA 125, CA 72-4, Malignite Risk İndeksi ve DePriest Skorlama Sisteminin Karşılaştırması

Haydar Kaya[1], Kemal Sandal[2], Ahmet Gocmen[3], İbrahim Yilmaz[4]

[1] *Department of Gynecology and Obstetrics, Saruhanlı State Hospital, Manisa, Turkey*
[2] *Department of Gynecology and Obstetrics, Saglik Bilimleri Üniversity Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, Istanbul, Turkey*
[3] *Department of Gynecology and Obstetrics, Memorial Hospital, Istanbul, Turkey*
[4] *Medical Biochemistry Laboratory, Haseki Training and Research Hospital, Istanbul, Turkey*

Received: 10 December 2019 / **Accepted:** 21 March 2020 / **Publication date:** 26 June 2020

Cite as: Kaya H, Sandal K, Gocmen A, Yilmaz İ. Comparison of CA 125, CA 72-4, risk of malignancy index and DePriest scoring system in the differentiation between benign and malignant adnexal masses. Med J Bakirkoy 2020;16(2):95-102.

ABSTRACT

Objective: *The aim of this study is to compare prospectively CA 125, CA72-4, risk of malignancy index (RMI) and DePriest morphological scoring system in differentiation between benign and malignant adnexal masses.*
Method: *Data of 116 cases operated due to adnexal mass were analyzed. Blood samples were taken from the patients for CA 125 and CA 72-4 before the operation. In ultrasonographic examination, risk of malignancy index (RMI) and DePriest morphological scoring system were used. SPSS 22.0 (Statistical Package for Social Sciences) for Windows program was used for analyses.*
Results: *The mean age was 53.8±5.4 years in malignant group which was significantly higher than the mean age of benign group (43.3±5.5 years). However, the weight, body mass index (BMI), gravidity and parity rates were similar and not statistically significant. CA 125, CA 72-4, RMI and DePriest morphological scoring system were significantly higher in malignant group than benign group (p<0,05). Pelvic pain was the most common admission complaint (56%: n=65) followed by referral from another hospital (32.7%: n=38). Benign masses were reported in 88 (75,9%), and malignant masses in 28 (24,1%) of 116 patients. Endometrioma (n=19, 16,3%) and serous cystadenoma (n=19, 16,3%) were the most common pathological entities in the benign group, while serous cystadenocarcinoma (n=13 11,2%) was the most common pathological entity in the malignant group.*
Conclusion: *CA72-4 did not have enough effectivity to predict the results of pathology in adnexal masses because of its low sensitivity. Significant efficiency of RMI and CA 125 were monitored. DePriest morphological scoring system was found to be more effective than CA 125, CA 72-4 and RMI in differentiation between benign, and malignanat adnexal masses.*

Keywords: *CA 125, CA 72-4, risk of malignancy index, adnexal mass*

ÖZ

Amaç: *Bu çalışmada CA 125, CA 72-4, malignite risk indeksi (RMI) ve DePriest morfolojik skorlama sisteminin benign-malign adneksiyal kitle ayrımında prospektif olarak karşılaştırılması amaçlanmıştır.*
Yöntem: *Adneksiyel kitle nedeniyle opere olan 116 hastanın verileri incelendi. Operasyon öncesi hastalardan CA 125 ve CA 72-4 için kan alındı. USG değerlendirmesinde malignite risk indeksi (RMI) ve DePriest morfolojik skorlama sistemi kullanıldı. Analizlerde SPSS 22.0 (Statistical Package for Social Sciences) programından yararlanıldı.*
Bulgular: *Malign hasta grubunda yaş ortalaması 53,8±5,4 saptandı ve benign gruptaki hastaların yaş ortalamasına (43,3±5,5) göre istatistiksel olarak anlamlı yüksekti. Ancak her iki grubun da kilo, VKİ, gravida ve parite oranları benzerdi ve istatistiksel olarak anlamlı değildi. Malign olan grupta CA 125 ve CA 72-4 değerleri, RMI ve DePriest skoru benign olan gruptan anlamlı (p<0,05) olarak daha yüksekti. Hastaneye geliş şikayetlerinde %56 (n=65) ile ilk sırada pelvik ağrı gelirken onu %32,7 (n=38) ile başka merkezden referans ile yönlendirilme izlemekteydi. Hastaların %75,9'unda (n=88) histopatolojik değerlendirmede sonuçların benign, %24,1'inde (n=28) ise malign olduğu görüldü. Benign grupta en sık (n=19 %16,3) endometrioma ve (n=19 %16,3) seröz kistadenom görülürken, malign grupta ise seröz adenokarsinom en sık (n=13 %11,2) saptanan over tümörü oldu.*
Sonuç: *Sensitivitesinin düşük olması sebebiyle CA72-4 adneksiyel kitlelerde patoloji sonucunu öngörmede yeterli bulunmamıştır. RMI ve CA 125'in anlamlı etkinliği gözlenmiştir. Çalışma sonucunda malignite öngörüsünde tek başına değerlendirildiğinde Depriest skorlama sisteminin CA 125, CA 72-4 ve RMI skorlama sisteminden daha etkin olduğu izlenmiştir.*

Anahtar kelimeler: *CA 125, CA 72-4, malignite risk indeksi, adneksiyal kitle*

Corresponding Author:
✉ haydartip@gmail.com

H. Kaya 0000-0001-9021-5125
K. Sandal 0000-0002-3736-0523
A. Gocmen 0000-0002-0839-7490
İ. Yilmaz 0000-0003-4719-0246

INTRODUCTION

Adnexal masses develop from the uterus, ovary, tuba or surrounding tissue. They are benign., and largely ovarian neoplasms. Surgery is applied to 5-10% of women throughout their life due to ovarian neoplasia. Malignancy is detected in 13-21% of these women [1]. According to the United States (USA) data, approximately 300,000 women are hospitalized each year due to adnexal masses [2]. The most important preoperative issue is to evaluate the possibility of ovarian cancer, except for patients who come with emergency findings. Ovarian cancer is the leading cause of gynecological cancer-related deaths. Most of the patients are in their postmenopausal period. The incidence of ovarian cancer in women aged 20-49 is 1.6-16 / 100000 and 0.7-14 / 100000 in adolescents under 20 years of age [3]. Ovarian cancer is the seventh most common cancer and the fifth most common cause of death among all cancers in women, according to USA data [4].

Many laboratory examinations, imaging methods or their combined use have been determined or are currently being studied in order to evaluate patients with adnexal masses in terms of presence of malignancy. In the embedding method, tumor diameter (>50 mm), thick septa, wall thickness, solid component, contrast enhancement, invasion, acid and bilaterality are used in the distinction of malignancy, and the presence of 3 or more criteria is considered significant [5]. CA 125, a glycoprotein antigen, is found in the celilomic epithelium, amniotic fluid, pleura, peritoneum, pericardium, bronchial and cervical secretion of normal adults. While it is not found in normal adult ovarian tissue, it is detected in 80% of epithelial ovarian cancers [6]. CA 72-4 is a glycoprotein surface antigen found in colon, gastric and ovarian cancers. It increases in 67% of ovarian cancers and its sensitivity is higher for mucinous tumors [7]. The malignancy risk index (RMI) published by Jacobs et al. in 1990 is known as a model used in the differentiation between malignant, and benign adnexal masses and in which ultrasound, RMI score, serum CA 125 and menopausal status are evaluated in combination [8]. Another scoring system is DePriest's 3-criteria morphological scoring system. In this system, by recording the ovarian volume, cyst wall structure and septa structure, a prediction can be made without using additional laboratory methods [9]. In our study, we aimed to compare CA 125, CA 72-4, malignancy risk index (RMI) and DePriest morphological scoring systems prospectively.

MATERIAL and METHOD

Ethics committee approval was obtained from the Ethics Committee of Medeniyet University Göztepe Training and Research Hospital. In this study, 126 patients who were scheduled for an operation with a diagnosis of adnexal mass between September 2014 and December 2015 in the Obstetrics and Gynecology Clinic were evaluated. The study was designed as a prospective cohort study. The non-pregnant patients without a biopsy history from the adnexal mass, or undergoing ovulation induction process and voluntarily giving consent to the study were included in the study . Patients with a history of malignancy were excluded. Voluntary informed consent was obtained from a total of 126 patients. Ten patients were excluded from the study. Blood tests of 4 patients were taken inappropriately, 4 patients refused to undergo surgery, 1 patient had a history of colon cancer, 1 patient had a history of rectal cancer. Age, body mass index (BMI), pregnancy and number of births (parities) CA 125 and CA 72-4 values and ultrasonography findings of 116 patients were recorded in accordance with RMI and DePriest scoring systems.

Technical data

In the ultrasonographic evaluation, 5-2 Mhz convex abdominal and 9-5 Mhz endovaginal probes were used with Sonoscape S11 3D ultrasound device. All ultrasonographic evaluation was done by a single clinician. RMI score; The ultrasound score (U), menopause score (M) and serum CA 125 values were recorded and calculated with the formula [U] x [M] x [CA 125] (Table 1). Two hundred or more values were interpreted in favor of malignant mass. DePriest score was determined by evaluating ovarian volume, cyst wall structure and septa structure (Table 2). Ovarian volume was calculated with the ellipsoid formula (length x height x width x 0.523). If total score calculated for volume + cyst wall + septa structure score was ≥ 5, then the results were evaluated in favor of a malignant mass. After 8-12 hours of fasting, blood samples were drawn into anticoagulant-

Table 1. Risk of malignancy index (RMI).

	RMI 1*
Menopausal condition (M)	Premenopausal: 1 Postmenopausal: 3
Ultrasonography findings (U)	
Multilocular cyst	
Solid field	No feature: 0
Bilaterality	1 feature: 1
Ascites	>1 feature: 3
Metastasis	
Serum CA 125	Serum CA 125 level

**RMI 1: The risk of malignancy index, Jacobs et al. published in 1990.*

free gel tubes. After waiting for no more than 1 hour at room temperature, their serums were separated by centrifugation at 2500 rpm for 10 minutes.

The obtained serums were portioned into 1.5 mL Eppendorf tubes and stored at -80°C until analysis.

All analyzes were performed simultaneously. The laboratory team conducting the studies were blinded about patient information. Serum CA 125 and CA 72-4 measurements were made using the Modular E170 analyzer (Roche Diagnostics GmbH, Germany) by electrochemiluminescence method. Normal values for CA 125 (<35 U/ml), CA 72-4: (0-4 U/mL) were taken into consideration during assessments.. The pathology results of the patients after surgery were compared to the measurements of CA 125, CA 72-4 in blood samples stored at -80 degrees, with the RMI and DePriest scoring system.

Statistics

Mean, standard deviation, median lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The normality of distribution of variables was evlauated by Kolmogorov -Smirnov test. In the analysis of quantitative data, Mann-Whitney U test was used. Chi-square test was used in the analysis of qualitative data. SPSS 22.0 (Statistical Package for Social Sciences) program was used in the analysis. The level of statistical significance was set at $p<0.05$.

RESULTS

In the evaluation of data of 116 patients, the mean age was 45.9±11.9 years (min 21-max 70). The mean age of the malignant group was 53.8±5.4 years which was statistically significantly higher than the mean age of the patients in the benign group (43.3±5.5 years). However, the weight, BMI, gravida and parity ratios of both groups were similar and were not statistically significant. CA 125, CA 72-4, RMI and DePriest scores in the malignant group were significantly higher ($p<0.05$) than the benign group. Demographic characteristics, CA 125, CA 72-4 values, RMI and DePriest scores of the patients according to benign and malignant groups are given in Table 3.

Pelvic pain was the most frequent admission complaint (56%:=65) followed by referral from another center (32.7%:n=38). Adnexal mass was detected incidentally in 6 patients (5.1%) in routine gynecological examination. Mass, amenorrhea and vaginal bleeding were less likely causes of application to the hospital. In histopathological evaluation in 75.9% (n=88) of the patients, benign, and in 24.1% (n=28) patients malignant (borderline ovarian tumor was included in the malignant group) masses were detected. In the benign group (n=19 16.3%), endometrioma and (n=19 16.3%) serous cystadenoma were the most common pathologies, while in the malignant group, serous adenocarcinoma was the most common (n=13 11.2%) ovarian tumor. The patients in the malignant group were in Stages 1 (n=18: 15.5%), 3 (n=9: 7.8%), and 4 (n=1: 0.9%). Other benign pathological diagnoses were mature cystic teratoma, follicle cyst, corpus luteum cyst, mucinous cystadenoma, leiomyoma, struma ovarii,

Table 2. DePriest morphological scoring system.

Parameters	0	1	2	3	4
Volume	<10 cm^3	10-50 cm^3	50-200 cm^3	200-500 cm^3	>500 cm^3
Cyst wall (thickness)	Smooth <3 mm	Smooth ≥3 mm	Papillary bulge <3 mm	Papillary bulge ≥3 mm	dominant solid
Septa structure (thickness)	No septa	Thin septa <3 mm	Thick septa 3-10 mm	Solid septa ≥10 mm	dominant solid

**RMI 1: The risk of malignancy index, Jacobs et al. published in 1990.*

Table 3. Demographic characteristics, CA 125, CA 72-4 values, risk of malignancy index (RMI) and DePriest scores of patients in benign and malignant groups.

	Benign		Malignant	
	Mean±s.d	Med (min-max)	Mean±s.d	Med (min-max)
Weight	63,8±8,8	65 50-82	67±6	66 53-108
BMI*	25,4±3,8	25 18,4-35,6	26±3,7	26 20-39,7
Age	43,3±5,5	45 21-68	53,8±5,4	57 36-70
Gravida	3,1±3,2	2 0-17	3±2,6	2 0-12
Parity	2±2,7	1 0-10	2,2±2,1	3 0-7
CA 125	59,1±134,3	20 5,8-901	261,4±407	77,7 6,5-1719
CA 72-4	2,1±2,8	1,1 0,7 -17,1	15,5±56,1	2,0 0,8-299,8
DePriest score	3,2±2,4	2,0 0,0-10,0	7,3±1,8	8,0 5,0-10,0
RMI†	123±291	43 0-2303	1502±2446	380 27-10764
Menopausal condition				
Premenopausal	64 72,7%		10 35,7%	
Postmenopausal	24 27,3%		18 64,3%	

**BMI: Body mass index, †RMI: Risk of malignancy index*

Table 4. Comparison of CA 125, CA 72-4, risk of malignancy index and DePriest scores.

	Benign	Malignant	Sensitivity	PPV*	Specificity	NPV†	Kappa	p
CA 125								
(-)	63	8	71,4%	44,4%	71,5%	88,7%	0,088	0,002
(+)	25	20						
CA 72-4								
(-)	79	20	28,6%	47,1%	89,8%	79,8%	0,212	0,017
(+)	9	8						
RMI‡								
<200	78	10	64,3%	64,3%	88,6%	88,6%	0,529	0,000
≥200	10	18						
DePriest score								
<5	68	0	100%	58,3%	77,3%	100%	0,621	0,000
≥5	20	28						

**PPV: Positive predictive value. †NPV: Negative predictive value, ‡RMI: Risk of malignancy index*

fibrotechoma, tuboovarian abscess, hemorrhagic cyst and ovarian torsion. Other malignant diagnoses were endometrioid adenocarcinoma, mucinous adenocarcinoma, borderline serous tumor, borderline mucinous tumor, granulosa cell tumor, Sertoli-Leydig cell tumor, Brenner tumor. Although diagnostic sensitivity of CA 125 was 71.4%, its diagnostic specificity, and the positive predictive values were 44.4% and 71.5%, respectively (p=0.002). The positive, and negative predictive values of CA 72-4 were 47.1% and 79.8%, respectively (p=0.017). Significant (p=0,000) and strong efficacy of cut- off values of ≥ 200 for RMI scores in the prediction of malignant and benign group of patients were observed. As cut-off value, De Priest score of 5 points was found to be statistically significant and the highest index in the differential diagnosis of malignancy with 100% sensitivity, 77.3% specificity, 58.3% PPV and 100% NPV (p=0,000). The results are given comparatively in Table 4.

Forty women (36.2%) were in the postmenopausal period, while 57.1% of patients with RMI score of ≥ 200 and 52% of patients with DePriest score of ≥ 5 were in the postmenopausal period. These rates were found to be 60% and 64% in patients with CA 125 ≥ 35 and CA 72-4 ≥ 4, respectively. As a statistically significant finding, 64.7% of malignant group of patients consisted of postmenopausal women. Comparison of benign and malignant groups by menopausal status is given in Table 5.

Eight patients with CA 125 false negative results had

Table 5. Comparison of benign and malignant groups by menopausal status.

	Benign		Malignant	
	Premenopausal	Postmenopausal	Premenopausal	Postmenopausal
CA 125				
(-)	53	10	3	5
(+)	15	10	3	17
CA 72-4				
(-)	60	19	8	12
(+)	4	5	2	6
RMI‡				
<200	58	20	4	6
≥200	6	4	6	12
DePriest score				
<5	51	17	0	0
≥5	13	7	10	18

**RMI: Risk of malignancy index*

Table 6. Comparison of false positives and false negatives by menopausal status.

	False	Positivity	False	Negativity
	Premenopausal	Postmenopausal	Premenopausal	Postmenopausal
CA 125	23	2	4	4
CA 72-4	8	1	7	13
RMI*	6	4	4	6
DePriest	13	7	0	0

**RMI: Risk of malignancy index*

borderline serous tumors (n=3), serous carcinoma (n=2), granulosa cell tumors (n=2), and Sertoli-Leydig cell tumor (n=1), while 17 of 25 patients with false positivie results were detected to have endometriomas. Eight of 20 patients with CA 72-4 with false negative results were serous carcinoma and in 5 of 9 patients who gave false positive results, had received the diagnosis of endometrioma. Serous carcinoma was seen in 3 of 10 patients with false negative RMI results, and in 7 of 10 patients with false positive results were diagnosed as endometrioma. While the DePriest scoring system did not give false negative results, the most common diagnoses of 20 patients with false positive results were leiomyoma in 5, serous cystadenoma in 4, and mucinous cystadenoma in 4 patients. Twenty-three of 25 patients with false positive CA 125, 8 of 9 patients with false positive CA 72-4, 6 of 10 patients with alse positive RMI, and 13 of 20 patients with false positive DePriest scores were observed in premenopausal period. Comparison of false positivity and false negativity rates according to menopausal status is given in Table 6.

While 16 of 19 patients diagnosed with endometrioma were found CA 125 positive, RMI was positive in 6 patients. DePriest scoring system was found positive in 8 of 8 patients diagnosed with borderline tumor. CA 125 and RMI were positive in 5 patients. The results are given in Table 7.

Table 7. Methods used in the diagnosis of endometrioma and borderline ovarian tumors.

Method	Endometrioma (n:19)	Borderline ovarian tumor (n:8)
CA 125	16	5
CA 72-4	5	1
RMI*	6	5
DePriest score	0	8

**RMI: Risk of malignancy index*

In our study, for the diagnosis of endometrioma, CA 125, and for the diagnosis of borderline tumor, DePriest scoring system come to the fore. If the four methods are combined, the lowest positive predictive value was 38.8% and the negative predictive value was 100% if any method is positive. Considering that 100% negative predictive value was determined when the DePriest scoring system was used, the combination of four methods does not provide an extra diagnostic advantage.

DISCUSSION

Being able to make differential diagnosis of adnexal masses preoperatively is very important for the effectiveness of the treatment to be applied. In the patient group included in the study, a correlation was observed between age and menopausal status and the possibility of malignancy which is consistent with the literature. There was no significant difference between BMI, gravida and parity values. The reason for this is that the patient distribution cannot be homogenized due to the limited sample size and our center being a tertiary oncology center as well as accepting reference patients as an advanced center for pelvic pain and endometriosis. While pelvic pain (56%, n=65) and referral from another center (32.7%, n=38) were the most common causes of admission to our clinic, in the another study the most common reasons for admission were pelvic pain and vaginal bleeding or menstrual irregularity [10].

The lowest, highest, and mean RMI scores for were 0, 10764, and 456±1349, respectively. RMI scores below, and above were 200 were estimated for 88 (75.9%), and 28 (24.1%) patients, respectively.While the mean RMI score was 123±291 in the benign group, it was 1502±2446 in the malignant group (p=0.000). In our study, we also determined the sensitivity (64.3%), specificity (88.6%), positive (64.3%) and negative (88.6%) predictive values of RMI scores. In 2004, in a case series consisting of 100 patients, Obeidat et al., found the sensitivity, specificity, positive and negative predictive values of RMI as 90, 89, 96 and 78 % respectively [11]. In the study of Andersen et al. performed with 180 patients in 2003, the sensitivity (70.6 %), specificity (87.7%), positive (66.1%) and negative (89.8%) predictive values for RMI were stated as indicated [12]. In the study of Tingulstad et al. performed with 365 patients, sensitivity specificity positive and negative predictive values were detected as 71, 92, 69, and 92%, respectively [13]. In our study, we found that our data were compatible with the literature.

In our study, the DePriest scores ranged from 0 to 10 (mean: 4.2±2.9, median: 4.0). In the study, 68 (58.6%) patients had <5, and 48 (41.4%) patients had > 5 points. While the mean DePriest score was 3.2±2.4 in the benign patient group, it was 7.3±1.8 in the malignant group. In the malignant group, the DePriest score was significantly higher (p=0,000) than the benign group. The sensitivity (100%), specificity (77.3%), positive (58.3%), and negative (100%). predictive values for the DePriest cut-off score of 5 points in predicting the pathology results were as indicated in parentheses. There was a significant (Kappa: 0.621/p=0.000) agreement between DePriest scores and pathology results. In a study with premenopausal patients, Osmers et al. found that the risk of malignancy increases with increasing mass size in simple cysts [14]. Although we determined the sensitivity of cut-off value of DePriest score of 5 points for the differential diagnosis of malignancy as 100%, the scores were higher in 20 patients with benign pathology. This indicates that a different cut-off value needs to be investigated with further studies in order to reduce the false positivity rate.

In our study, the minimum (5.8), maximum (1719), median (26.1), and mean (108±245) values for CA 125 were also determined. While in the benign group (n:88), the mean value for CA 125 was 59.1±134.3, and in the malignant group (n: 28) it was 261.4±407. In the malignant group, the CA 125 value was significantly higher (p=0.002) than the benign group. In a study conducted by Tuxen, CA 125 was found to be normal in 10-20% of patients diagnosed with Stage 1 ovarian cancer. For this reason, CA 125 alone is not considered sufficient in screening for ovarian cancer, and it is recommended to evaluate the patient with physical examination and ultrasonographic findings [15]. In the study with 158 patients in 2003, Torres et al. foundi ts sensitivity as 51 and its specificity as 88 percent. Positive and negative predictive values were not specified in the study [16]. In a study with 140 patients in 2003 Ma et al. determined the sensitivity, spcificity, positive, and negative pre-

dictive values for CA-125 test as 73, 85.7, 80.7 and 79.5 %, respectively [17]. In a study by Morgante et al. sensitivity, specificity, positive and negative predictive values of CA-125 test were found as 74, 95, 82 and 92 %, respectively [18]. In their study with 152 patients in 2000, Manjunath et al. found the sensitivity, specificity positive and negative predictive values of CA-125 test as 77, 87, 91, and 70 %, respectivelyt [19]. In the study of Jacobs et al. with 143 patients in 1990, sensitivity, and specificity of CA-125 test were reported as 78.6 and 53.5%, respectivelyt. Positive and negative predictive values were not specified in the report [20]. In our study, for CA 125 we found sensitivity (71.4%), specificity (71.5%), positive (44.4%), and negative (88.7 %) predictive values, as indicated. Except for the low sensitivity rate found by Torres et al. the data of our study are compatible with the literature data.

In the malignant group, the CA 125 value was significantly higher (p=0.002) relative to the benign group. In a study by Anastasi et al comparing 50 healthy women, and patients with benign ovarian tumors (n=17), ovarian endometriomas (n= 57) and ovarian cancer (n=39), serum CA 125 concentrations were found to be higher in patients with endometriomas and ovarian cancer, whille they were within normal limits in patients with benign ovarian masses [21]. In our study, higher CA 125 levels were detected in 16 of 19 patients with endometriomas. Therefore, it was concluded that CA 125 alone was not sufficient to predict malignancy in ovarian cancer. Endometrioma is an important disease that makes us look for another method or molecule to be used in the differential diagnosis of ovarian cancer. The blood tests of a patient who had a borderline seromucnous tumor as a result of pathology were sent to the laboratory twice on two different days and a significant difference was observed between CA125 values (231→49). Likewise, although the blood tests of two other patients diagnosed with serous cystadenoma and leiomyoma were sent to the laboratory twice on two different days, the results were close to each other (6→5,8 and 12→10). This shows us that there may be different underlying mechanisms in malignant masses.

In 1995 study of Guadagni et al., the specificity of CA 72-4 for ovarian cancer was found to be > 95% and when it was combined with CA 125, it was stated that its sensitivity increased without any change in its specificity [22]. In the study by Steven J. Skates et al., preoperative sensitivity rates for early stage disease were 45% for CA 125, 67% for CA 125 and CA72-4, 70% for CA 125, CA72-4 and M-CSF, and for all four parameters, including sonography a sensitivity rate of 68% was determined. It was reported that the preoperative combination of CA 125, CA72-4 and M-CSF increases the sensitivity rate from 45% to 70% in early-stage disease. Evaluation of CA72-4 together with pelvic examination, USG and serum CA 125 has been reported to be beneficial in distinguishing between malignant and benign pelvic masses [23]. In our study, we found the sensitivity (28.6%), specificity (89.8%), positive (47.1%), and negative (79.8%). predictive values of CA72-4, as indicated In a study conducted by Anastasi et al., sensitivity, specificity, positive and negative predictive values for CA72-4 were reported as 84, 89, 67, and 96%, respectively [21]. It was also stated that there was a significant difference in CA72-4 values between ovarian cancer and endometioma patients. In our study, we detected CA72-4 above the cut -off value in 5 of 19 patients who had endometrioma. The low sensitivity of CA72-4 can be explained by the higher number of endometrioma cases in our study. Although the sensitivity, and specificity of CA72-4 were 28.6% and 89.8% which appears to be statistically significant (p=0.017), in malignant-benign distinction of adnexal masses it is not sufficient for screening alone. When combined with CA 125, there is no change in sensitivity and only some increase in specificity was noted.

CONCLUSION

Due to its low sensitivity, CA72-4 was not sufficient to predict the pathology outcome in adnexal masses. Significant efficacy of RMI and CA 125 has been observed. As a result of the study, it was observed that DePriest scoring system has gtreater diagnostic efficacy than CA 125, CA 72-4 and RMI scoring system when it was evaluated alone in the prediction of malignancy. However, further studies are needed to be more effective in our clinical practice in predicting pathology results by using them alone or in combination.

Acknowledgement
I would like to thank to Assoc. Dr. Banu İŞBİLEN BAŞOK and Dr. Emre YALÇINKAYA for their guidance in biochemical tests, and the Editorial Board of The Medical Journal of Bakırköy thet will evaluate my manuscript for publication.

Ethics Committee Approval: All authors have not declared any conflict of interest.S.B. Approval was obtained from the Clinical Research Ethics Committee of Istanbul Medeniyet University Göztepe Training and Research Hospital (23.09.2014 / 2014/0142).
Conflict of interests: All authors have not declared any conflict of interest.
Funding: Two thousand one hundred and thirty- four Turkish Liras were granted from Istanbul Medeniyet University Scientific Research Projects Coordination Unit as a financial support to purchase CA 125 and CA72-4 laboratory kits.
Informed Consent: Since it was a prospective study, enlightened voluntary consent form was signed by all patients.

REFERENCES

1. DiSaia PJ, Creasman WT. Clinical gynecologic oncology. 6th ed. 2002. p. 259. https://doi.org/10.1016/B0-32-301089-X/50013-1
2. Ayhan A, Durukan T, Günalp S. Temel kadın hastalıkları ve doğum bilgisi. 2008. p. 987.
3. Ayhan A, Gültekin M, Dursun P. Tekxtbook of gynecological oncology. Ankara: Güneş Publishing; 2009. p. 312.
4. Berek SJ. Berek and Novak's gynecology. 2007. p. 1457-9.
5. Oztoprak B, Karakus S. Value of multiple computed tomography criteria for prediction of malignancy in patients with ovarian mass. Gynecology Obstetrics & Reproductive Medicine. 2018;24(1):42-6. Available from: http://gorm.com.tr/index.php/GORM/article/view/706/666 https://doi.org/10.21613/GORM.2017.706
6. Kabawat SE, Bast RC Jr, Welch WR, Knapp RC, Colvin RB. Immunopathologic characterisation of a monoclonal antibody that recognizes common surface antigens of human ovarian tumors of serous, endometrioid and clear cell types. Am J Clin Pathol. 1983;79(1):98-104. https://doi.org/10.1093/ajcp/79.1.98
7. Hasholzner U, Baumgartner L, Stieber P, et al. Clinical significance of the tumour markers CA 125II and CA 72-4 in ovarian carcinoma. Int J Cancer. 1996;69(4):329-34. https://doi.org/10.1002/(SICI)1097-0215(19960822)69:4<329::AID-IJC16>3.0.CO;2-0
8. Yamamoto Y, Yamada R, Oguri H, et al. Comparison of four malignancy indices in the preoperative evaluation of patients with pelvic masses. Eur J Obstet Gynecol Reprod Biol. 2009;144(2):163-7. https://doi.org/10.1016/j.ejogrb.2009.02.048
9. Lerner JP, Timor-Tritsch IE, Federman A, Abramovich G. Transvaginal ultrasonographic characterization of ovarian masses with an improved, weighted scoring system. Am J Obstet Gynecol. 1994;170(1 Pt 1):81-5. https://doi.org/10.1016/S0002-9378(94)70388-4
10. Deregözü A, Uzun I, Karahasanoğlu A, Yücel O. Bir eğitim ve araştırma hastanesinde opere edilen benign adneksiyal kitleli olguların analizi. Bakırköy Tıp Dergisi. 2018;14:40-3. Available from: http://cms.galenos.com.tr/Uploads/Article_20005/BTD-14-40.pdf https://doi.org/10.5350/BTDMJB.20151223113440
11. Obeidat BR, Amarin ZO, Latimer JA, Crawford RA. Risk of malignancy index in the preoperative evaluation of pelvic masses. Int J Gynaecol Obstet. 2004;85(3):255-8. https://doi.org/10.1016/j.ijgo.2003.10.009
12. Andersen ES, Knudsen A, Rix P, Johansen B. Risk of malignancy index in the preoperative evaluation of patients with adnexal masses. Gynecol Oncol. 2003;90(1):109-12. https://doi.org/10.1016/S0090-8258(03)00192-6
13. Tingulstad S, Hagen B, Skjeldestad FE, Onsrud M, Kiserud T, Halvorsen T, Nustad K. Evaluation of a risk of malignancy index based on serum CA 125, ultrasound findings and menopausal status in the pre-operative diagnosis of pelvic masses. Br J Obstet Gynaecol. 1996;103(8):826-31. https://doi.org/10.1111/j.1471-0528.1996.tb09882.x
14. Osmers RG, Osmers M, von Maydell B, Wagner B, Kuhn W. Preoperavite evaluation of ovarian tumors in the premenopouse by transvaginosonography. Am J Obstet Gynecol. 1996;175(2):428-34. https://doi.org/10.1016/S0002-9378(96)70157-6
15. Tuxen MK, Soletormos G, Dombernowsky P. Tumor markers in the menagement of patients with ovarian cancer. Cancer Treat Rev. 1995;21(3):215-45. https://doi.org/10.1016/0305-7372(95)90002-0
16. Torres JCC, Derchain SFM, Faundes A, Gontijo RC, Martinez EZ, Andrade LA. Risk of malignancy index in preoperative evaluation of clinically restricted ovarian cancer. Sao Paulo Med J. 2002;120(3):72-6. https://doi.org/10.1590/S1516-31802002000300003
17. Ma S, Shen K, Lang J. A risk of malignancy index in preoperative diagnosis of ovarian cancer. Chin Med J (Engl). 2003;116(3):396-9. PMID: 12781045.
18. Morgante G, la Marca A, Ditto A, De Leo V. Comparison of two malignancy risk indices based on serum CA 125, ultrasound score and menopausal status in the diagnosis of ovarian masses. Br J Obstet Gynaecol. 1999;106(6):524-7. https://doi.org/10.1111/j.1471-0528.1999.tb08318.x
19. Manjunath AP, Pratapkumar, Sujatha K, Vani R. Comparison of three risk of malignancy indices in evaluation of pelvic masses. Gynecol Oncol. 2001;81(2):225-9. https://doi.org/10.1006/gyno.2001.6122
20. Jacobs IJ, Oram D, Fairbanks J, Turner J, Frost C, Grudzinskas JG. A risk of malignancy index incorporating CA 125, ultrasound and menopausal status for the accurate preoperative diagnosis of ovarian cancer. Br J Obstet Gynaecol. 1990;97(10):922-9. https://doi.org/10.1111/j.1471-0528.1990.tb02448.x
21. Anastasi E, Granato T, Falzarano R, et al. The use of HE4, CA 125 and CA72-4 biomarkers for differential diagnosis between ovarian endometrioma and epithelial ovarian cancer. J Ovarian Res. 2013;6(1):44. https://doi.org/10.1186/1757-2215-6-44
22. Guadagni F, Roselli M, Cosimelli M, et al. CA72-4 serum marker-a new tool in the management of carcinoma patients. Cancer Invest. 1995;13(2):227-38. https://doi.org/10.3109/07357909509011692
23. Skates SJ, Horick N, Yu Y, et al. Preoperative sensitivity and specificity for early-stage ovarian cancer when combining cancer antigen CA-125II, CA 15-3, CA 72-4, and macrophage colony-stimulating factor using mixtures of multivariate normal distributions. J Clin Oncol. 2004;22(20):4059-66. https://doi.org/10.1200/JCO.2004.03.091

Original Article

Med J Bakirkoy 2020;16(2):103-7
doi: 10.5222/BMJ.2020.30502

Medical Journal of Bakirkoy

Low *Bordetella pertussis* Antibody Seroprevalence Among Mothers and Infants

Annelerde ve Bebeklerde Düşük Bordetella pertussis Antikor Seroprevalansı

Bahar Kural[1], Perran Boran[2], Esra Devecioglu Karapinar[3], Gulbin Gokcay[4], Tijen Eren[5] Selim Badur[6], Gonca Yilmaz[7]

[1] *Department of Pediatrics, Bakirköy Dr. Sadi Konuk Research and Training Hospital, Istanbul, Turkey*
[2] *Department of Pediatrics, Division of Social Pediatrics, Marmara University Faculty of Medicine, Istanbul, Turkey*
[3] *Department of Social Pediatrics, Istanbul University Institute of Child Health, Istanbul, Turkey*
[4] *Department of Pediatrics, Istanbul University Istanbul Medical School, Istanbul, Turkey*
[5] *Department of Pediatrics, Koç University Faculty of Medicine, Istanbul, Turkey*
[6] *Emeritus from Istanbul Faculty of Medicine, Department of Medical Microbiology, Istanbul, Turkey*
[7] *Department of Pediatrics, Dr. Sami Ulus Childrens' Hospital, Ankara, Turkey*

Received: 4 April 2020 / **Accepted:** 11 May 2020 / **Publication date:** 26 June 2020

Cite as: Kural B, Boran P, Devecioglu Karapinar E, Gokcay G, Eren T, Badur S, Yilmaz G. Low *Bordetella pertussis* antibody seroprevalence among mothers and infants. Med J Bakirkoy 2020;16(2):103-7.

ABSTRACT

Objective: *The greatest risk of morbidity and mortality from pertussis infection is observed among infants who are 6 months and younger. Therefore protection from pertussis infection is very important during the first 6 months of life. The aim of the study is to assess Bordetella pertussis antibody titers among infants after two doses of pertussis vaccination at 6 months of age.*
Method: *This was a prospective, multicentered cohort study. Paired maternal and infant serum samples were obtained during the first month after delivery and only infant serum samples were again taken at 6 months of age. Serum samples were tested for Bordetella pertussis-IgG by the enzyme-linked immunosorbent assay (ELISA).*
Results: *The study enrolled 209 mother-infant pairs. At one month after delivery 49.7% of mothers and 32.1% of infants had detectable Bordetella pertussis-IgG antibodies. After two doses of DTaP-IPV-Hib vaccine, at 6th months of age, Bordetella pertussis-IgG seroprevalence among infants increased to 43.3%.*
Conclusion: *After 2 doses of DTaP-IPV-Hib, more than half of the infants at 6 months of age had undetectable Bordetella pertussis-IgG and presumed unprotected against pertussis disease. A new strategy of protecting infants from pertussis must be implemented.*

Keywords: *pertussis, maternal antibody, infant antibody, seroconversion*

ÖZ

Amaç: *Altı aylık ve daha küçük bebekler boğmaca enfeksiyonundan en yüksek morbidite ve mortalite riskine sahiptirler. Bu nedenle boğmaca enfeksiyonundan korunma, yaşamın ilk 6 ayında çok önemlidir. Bu çalışmanın amacı, bebeklerde Bordetella pertussis antikor titrelerini 6 aylıkken iki doz boğmaca aşılamasından sonra değerlendirmektir.*
Yöntem: *Bu bir prospektif, çok merkezli kohort çalışmasıdır. Doğumdan sonraki ilk ayda anne ve bebek çiftlerinden serum örnekleri alındı ve yine sadece bebek serum örnekleri 6 aylıkken alındı. Serum numuneleri, enzime bağlı immünosorban analizi (ELISA) ile Bordetella pertussis-IgG için test edildi.*
Bulgular: *Çalışmaya 209 anne-bebek çifti alındı. Doğumdan bir ay sonra annelerin % 49,7'si ve bebeklerin % 32,1'i saptanabilir Bordetella pertussis-IgG antikorlarına sahipti. İki doz DTaP-IPV-Hib aşısından sonra, 6. aylıkken, bebeklerde Bordetella pertussis-IgG seroprevalansı % 43,3'e yükseldi.*
Sonuç: *İki doz DTaP-IPV-Hib aşısı sonrasında, 6 aylık bebeklerin yarısından fazlasında Bordetella pertussis-IgG saptanmadı ve bunların boğmaca hastalığına karşı korumasız olduğu varsayıldı. Bebekleri boğmacadan korumak için yeni bir strateji uygulanmalıdır.*

Anahtar kelimeler: *boğmaca, anneye ait antikor, bebeğe ait antikor, serokonversiyon*

Corresponding Author:
✉ drbahsal@yahoo.com

B. Kural 0000-0001-9528-1009
P. Boran 0000-0002-9885-7656
E. D. Karapinar 0000-0003-4679-7513
G. Gokcay 0000-0003-1042-0407
T. Eren 0000-0001-9650-3734
S. Badur 0000-0002-1316-6259
G. Yilmaz 0000-0003-2242-5416

INTRODUCTION

Pertussis is especially most hazardous for infants under 6 months of age, which account for nearly all pertussis-related hospitalizations and deaths. On the other hand it was recognized that pertussis is grossly underreported. Global vaccination coverage with 3 doses of pertussis-containing vaccine was estimated to be 86% in 2016 [1,2]. In Turkey this rate of coverage was 96% in 2017 [3]. Infants whose vaccination schedule is not completed, contract the infection from their mothers and other family members [4]. In Turkey, whole cell vaccine was introduced in 1968 whereas acellular pertussis vaccine in 2008 to the Expanded Programme for Immunisation. Infants are vaccinated at 2, 4, and 6 months of age. Booster acellular pertussis vaccine is administered at the age of 18 months and 6 years [5]. The routine pertussis vaccination programme is not yet implemented for pregnant women and adults. The Global Pertussis Initiative emphasized the importance and effectiveness of maternal immunization [6]. Some countries have introduced maternal vaccination programs [7,8]. Studies are needed about the pertussis serologic status of newly delivered mothers and their infants under 6 months of age in developing countries [9].

The aim of this study was to assess pertussis seroprevalence in mothers and their infants at 1 month after delivery and in 6-month-old infants before they received the third dose of pertussis-containing vaccine.

MATERIAL and METHODS

This prospective, multi-centered clinical study was carried out at Well Child Outpatient Clinics of 4 hospitals between October 2013 and October 2014. Infants brought for routine well child visits were consecutively enrolled. Paired maternal and infant blood samples were obtained at the first well child visit during the first month after delivery. All women reported that they had been vaccinated against pertussis during childhood but this was not confirmed by any documentation.

The qualitative immunoenzymatic determination of Ig G-class antibodies against *Bordetella pertussis* was carried out by the Enzyme-Linked Immunosorbent Assay (ELISA) technique according to the instructions of the manufacturer (GenWay Biotech, Inc, San Diego, CA, USA). The investigation covered the determination of Ig G-Class antibodies against *Bordetella pertussis* and *Bordetella pertussis* toxin. The samples were tested in duplicate. Diagnostic specificity was reported as 93.02% (95% CI: 80.94%-98.54%), and sensitivity as 98.31% (95% CI: 90.91%-99.96%). Inclusion criteria for the study were maternal age between 18 and 45 years and infant gestational age of 37 to 42 weeks. The exclusion criteria included history of premature or low birth weight, acute or chronic illness, transfusion of blood and/or blood product(s). Demographic characteristics such as maternal age, infant gestational age, birth weight, mode of delivery, gender of the study participants were recorded.

Blood was drawn from 209 mother-infant pairs during the first month after delivery and from 164 infants at 6 months of age before the administration of the third dose of DTaP-IPV-Hib vaccine (Figure 1). The vaccines were all administered at the Well Child Clinic. The samples were centrifuged and stored at -20 C until analyzed at Istanbul University Virology and Immunology Department Laboratory. The results were classified as negative and positive based on the cut-off values of the manufacturer's kit. *Bordetella pertussis*-IgG titers of positive serum samples were recorded. Mother-infant pairs were categorized into seronegative versus seropositive groups based on their antibody titers. Vaccine-associated seroconversion was defined as the change from seronegative to seropositive.

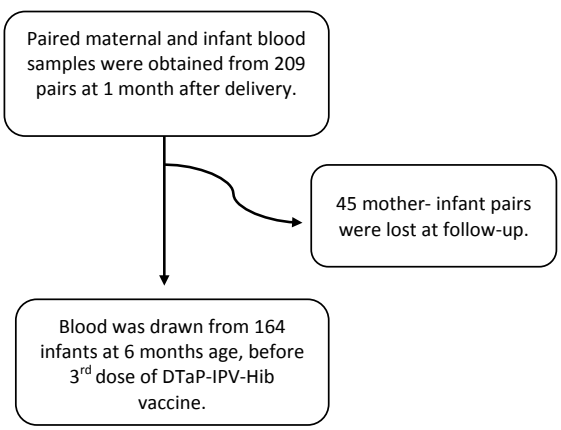


Figure 1. Flowchart of the study population.

Ethical approval and necessary institutional permissions were obtained for the study (05/24/2013 No:10). All mothers provided written informed consent prior to enrollment.

Statistical analyses were performed using the SPSS software version 21. The univariate analyses to identify variables associated with immune response were performed using Chi-square, Fisher exact, Student's t and Mann-Whitney U tests, where appropriate. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analyses to determine independent predictors of immune response. Continuous variables were presented as means with standard deviations or confidence intervals where applicable. Categorical variables were presented as numbers with corresponding percentages. Pearson correlation coefficient was used to assess the relationship between maternal and infant serum Bordetella pertussis-IgG concentrations.

RESULTS

Two hundred and nine mother-infant pairs were eligible for the study. None of the mothers were vaccinated against pertussis either during pregnancy or within the previous 5 years. No participants reported a recent history of pertussis disease, or known pertussis exposure at the beginning or during the follow-up period. Of all deliveries, 44.5 % were normal vaginal delivery and 50.2% of infants were female. Mean (± SD) birth weight of infants were 3337±375 grams. The mean (± SD) gestational age of infants was 38.7±1 weeks and maternal age was 29.6±6.2 years.

Seroprevalence rates of *Bordetella pertussis*-IgG up to 1 month postpartum were 49.7% (104/209) in mothers and 32.1% (67/209) in infants. Of babies born to seropositive mothers, 46.2% (48/104) were Bordetella pertussis-IgG seronegative. A significant positive correlation was observed between maternal and infant Bordetella pertussis-IgG status at 1 month postpartum (p<0.001, r=0.600).

Forty-five infants were lost at follow-up and serum samples of 164 infants were evaluated at 6 months of age (Figure 1). At Table 1, the distribution of seropositivity rates of mother-infant pairs at one month after delivery is given in Table 1.

After receiving 2 documented doses of pertussis-containing-vaccines at 2 and 4 months of age, 56.7% (71/164) of the infants were seropositive for Bordetella pertussis-IgG (Table 1). Out of total seropositive 71 infants, twenty-two (13.4 %) continued their prevaccination immunity. When we exclude the cases that were lost at follow-up; seronegative infants showed seroconversion after the vaccination. This difference between seronegative and seropositive infants was statistically significant (p<0.001). Of 113 seronegative infants at one month 49 became seropositive after two doses of pertussis-containing vaccine. According to the definition used in this study, vaccine-associated response after two doses of pertussis vaccine was 43.4%. This figure could be slightly underestimated because we could not identify the seroconverted babies among 22 infants who were seropositive at the beginning and also at the end of the study after administration of two doses of vaccine. Some of these infants might also be converters after the vaccination.

Table 1. Serology of mother-infant pairs followed until 6 months (n=164).

		Seronegative (%)	Seropositive n (%)	Total n (%)
One month after delivery	Mother	77 (47)	87 (53)	164 (100)
	Infant	113 (68.9)	51 (31.1)	164 (100)
At 6 months	Infant	93 (56.7)	71 (43.3)	164 (100)

When we compared the vaccine-associated seropositivity in babies at 6 months according to maternal serology, seroconversion was observed in 48.3% (42/87) of babies who were born to seropositive mothers and this rate was 37.7% (29/77) in babies born to seronegative mothers. The difference was not statistically significant (p=0.170).

At 6 months, vaccine-associated seroprevalence was 2 times higher in boys (OR 2.1, 95% CI: 1.09-4.12). This difference was statistically significant (p<0.026). Gender was entered into logistic regression for vaccine-associated response at 6 months and remained statistically significant (p=0.019; RR:2.2 with 95% CI: 1.07-4.55).

DISCUSSION

In our study, *Bordetella pertussis*-IgG seroprevalence rates were 49.7% in mothers and 32.1% in infants up to one month after delivery. After two doses of pertussis vaccine, 56.7% of the infants were still seronegative at 6 months. When vaccine-associated seroprevalence was considered, only 43.4% of infants had seropositivity after two doses of TDaP-IPV-Hib vaccination. The study demonstrated a low level of seropositivity against *B. pertussis* in mothers, which may increase the risk of pertussis in very young infants. Thus the greatest risk of morbidity and mortality from pertussis infection is among infants who are below 6 months of age and yet more than half of the babies in our study were susceptible to pertussis [1]. It is suggested that maternal pertussis antibodies protect the infants from pertussis by passive immunity. In a study of Turkish mothers where maternal and cord blood levels of anti-pertussis toxin were detected, only 34,6 % of infants had protective levels of antigens against pertussis [10]. Similarly, our results showed that only 32% of the infants have been protected, leaving the majority of infants unprotected to pertussis infection.

Either vaccination of the mothers during pregnancy or accelerated immunization of the infants for pertussis is a proposed strategy in preventing infant pertussis. Pertussis vaccination during pregnancy has already been shown to be effective in achieving higher pertussis antibody concentrations in infants and it has been introduced in several countries. However due to economic costs; universal vaccination of mothers during pregnancy cannot be covered at the moment. So, accelerated vaccination of infants for pertussis may be beneficial. One possible strategy to address this might be revisiting the current infant TDaP-IPV-Hib primary immunization schedule in Turkey. In the United Kingdom, pertussis vaccine is given when infants are 8, 12 and 16 weeks old [11]. In Netherlands, TDaP-IPV-Hib vaccine is administered at 3,5 and 11 months of age. If the mother was not vaccinated against pertussis during pregnancy then her infant receives an extra vaccination at the age of 2 months [12]. Current TDaP-IPV-Hib vaccine administrations are at 2,4,6 months in Turkey and may be that regimen needs to be changed to 2,3,4 or 2,3,5 months in order to immunize against pertussis at an earlier age. If one assumes that acceptable level of immunity is reached 1 month after the third injection, then infants younger than 5–7 months become at least partly susceptible to pertussis [7].

It is suggested that the effectiveness of the first dose of vaccine varies between 62% to 68% in infants under 6 months of age, and effectiveness increases with subsequent doses [13-15]. However, our study results showed that seropositivity is achieved in only 43.3% of the infants after two doses of the vaccine. The lower efficacy of the vaccine observed in our study should be explored in future studies.

Maternal passive immunity may affect infants' immune response to vaccination. Maternal antibodies can interfere with the immune response to vaccination, a phenomenon known as "blunting" [16]. In this study, seroconversion rate among babies at 6 months of age was not statistically significant according to maternal serology. Yet, we can assume that maternal immunity did not affect immune response to vaccination in our study.

Conflicting findings are reported about gender difference for pertussis seropositivity [17,18]. In the current study, we found out that vaccine immune response positivity was seen 2 times more in boys in univariate analysis. In a study conducted in Turkey, geometric mean titers were also statistically higher in boys [19]. Underlying immunological differences between gender may also result in differential immune responses to vaccination. In a Dutch study, pertussis vaccine immunity did not reportedly differ between genders [20]. Fischinger et al. stated that sex differences have been noted in quality of vaccine-induced immune response to MMR and DTP across the sexes [21]. This finding should be explored in future studies.

Limitations of the study

There are some limitations of our study. Cord blood samples of infants were not available. The pertussis serology was measured by the determination of Ig G-Class antibodies against *Bordetella pertussis* and *Bordetella pertussis* toxin. Antibodies for filamentous hemagglutinin, pertactin, and fimbriae were not measured. On the other hand, our findings shed light for future studies and changes in immunization schedule of infants.

CONCLUSION

Maternal pertussis seropositivity and infant protection by passive immunity was low suggesting maternal pertussis immunization should be considered in addition to the existing tetanus maternal immunization programme in Turkey [12,22]. Cocooning strategy may be suggested to parents who cannot receive pertussis vaccine during pregnancy [23].

After 2 doses of DTaP-IPV-Hib more than half of the infants at 6 months of age were found to be *Bordetella pertussis*-Ig G seronegative. An alternative accelerated vaccine strategy, changing the immunization timeline for DTaP-IPV-Hib vaccination may be an option for protection of infants against pertussis.

Ethics Committee Approval: Approval was obtained from the Istanbul Medical Faculty Clinical Research Ethics Committee (05/24/2013 No: 10).

Conflict of Interest: The authors declared no conflict of interest.

Funding: The study was funded by Istanbul University, Scientific Research Projects Committee (number 35513).

Informed Consent: All mothers provided written informed consent prior to enrollment.

REFERENCES

1. World Health Organization. Pertussis vaccines: WHO position paper. Wkly Epidemiol Rec. 2015;90:433-58.
2. World Health Organization. Immunization, Vaccines and Biologicals. Pertussis. 2018. Available from: http://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/pertussis/en/ (Accessed April 12, 2020.)
3. Bora Başara B, Soytutan Çağlar I, Aygün A, Özdemir TA, (editors). Prevention of disease and protection of health. Health statistics yearbook 2017. General Directorate of Health Information Systems, Turkey Ministry of Health, Ankara, Turkey: Kuban Matbaacılık Yayıncılık; 2018. p. 77. Available from: https://www.saglik.gov.tr/TR,52696/saglik-istatistikleri-yilligi-2017-yayinlanmistir.html (English edition is avaliable. Accessed April 12, 2020.)
4. Wiley KE, Zuo Y, Macartney KK, McIntyre PB. Sources of pertussis infection in young infants: a review of key evidence informing targeting of the cocoon strategy. Vaccine. 2013;31(4):618-25. https://doi.org/10.1016/j.vaccine.2012.11.052
5. Özbek ÖA, Öktem İMA, Hekimoğlu CH, Sekreter Ö, Emek M, et al. Seroprevalence of pertussis toxin antibody in Manisa province of Turkey, after six years implementation of acellular pertussis vaccine. Mikrobiyol Bul. 2018;52(2):180-9. https://doi.org/10.5578/mb.57534
6. Forsyth K, Plotkin S, Tan T, Wirsing von König CH. Strategies to decrease pertussis transmission to infants. Pediatrics. 2015;135(6):e1475-82. https://doi.org/10.1542/peds.2014-3925
7. Amirthalingam G, Campbell H, Ribeiro S, Fry NK, Ramsay M, et al. Sustained Effectiveness of the Maternal Pertussis Immunization Program in England 3 Years Following Introduction. Clin Infect Dis. 2016;63(Suppl. 4):S236-S243. https://doi.org/10.1093/cid/ciw559
8. Gkentzi D, Katsakiori P, Marangos M, Hsia Y, Amirthalingam G, et al. Maternal vaccination against pertussis: a systematic review of the recent literature. Arch Dis Child Fetal Neonatal Ed. 2017;102(5):F456-63. https://doi.org/10.1136/archdischild-2016-312341
9. Fallo AA, Neyro SE, Manonelles GV, Lara C, Hozbor D, et al. Prevalence of pertussis antibodies in maternal blood, cord serum, and ınfants from mothers with and those without tdap booster vaccination during pregnancy in Argentina. J Pediatric Infect Dis Soc. 2018;7(1):11-7. https://doi.org/10.1093/jpids/piw069
10. Türkoğlu E, Sönmez C, Özer E, Çöplü N, Kurugöl Z. Low pertussis antibody levels in maternal and umbilical cord blood samples in Turkey. Turk J Pediatr. 2016;58(6):573-8. https://doi.org/10.24953/turkjped.2016.06.001
11. United Kingdom National Health Services. NHS Vaccinations. 6-in-1 vaccine overview. Available from: https://www.nhs.uk/conditions/vaccinations/6-in-1-infant-vaccine/ (Accessed April 12, 2020.)
12. Dutch National Immunisation Programme. Available from: https://rijksvaccinatieprogramma.nl/english (Accessed April 12, 2020.)
13. Campbell H, Amirthalingam G, Andrews N, Fry NK, George RC, et al. Accelerating control of pertussis in England and Wales. Emerg Infect Dis. 2012;18(1):38-47. https://doi.org/10.3201/eid1801.110784
14. Juretzko P, von Kries R, Hermann M, Wirsing von König CH, Weil J, et al. Effectiveness of acellular pertussis vaccine assessed by hospital-based active surveillance in Germany. Clin Infect Dis. 2002;35(2):162-7. https://doi.org/10.1086/341027
15. Quinn HE, Snelling TL, Macartney KK, McIntyre PB. Duration of protection after first dose of acellular pertussis vaccine in infants. Pediatrics 2014;133(3):e513-9. https://doi.org/10.1542/peds.2013-3181
16. Bento AI, Rohani P. Forecasting epidemiological consequences of maternal immunization. Clin Infect Dis. 2016;63(Suppl. 4):S205-S212. https://doi.org/10.1093/cid/ciw557
17. Mattoo S, Cherry JD. Molecular pathogenesis, epidemiology, and clinical manifestations of respiratory infections due to Bordetella pertussis and other Bordetella subspecies. Clin Microbiol Rev. 2005;18(2):326-82. https://doi.org/10.1128/CMR.18.2.326-382.2005
18. Kilgore PE, Salim AM, Zervos MJ, Schmitt HJ. Pertussis: Microbiology, disease, treatment, and prevention. Clin Microbiol Rev. 2016;29(3):449-86. https://doi.org/10.1128/CMR.00083-15
19. Inandi T, Guraksin A, Hacialioglu N. Seroprevalence of pertussis among children in Eastern Turkey. Public Health. 2005;119(6):550-5. https://doi.org/10.1016/j.puhe.2004.08.018
20. Boef AGC, van der Klis FRM, Berbers GAM, Buisman AM, Sanders EAM, et al. Differences by sex in IgG levels following infant and childhood vaccinations: An individual participant data meta-analysis of vaccination studies. Vaccine. 2018;36(3):400-7. https://doi.org/10.1016/j.vaccine.2017.11.070
21. Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. Semin Immunopathol. 2019;41(2):239-249. doi: 10.1007/s00281-018-0726-5. https://doi.org/10.1007/s00281-018-0726-5
22. Türkiye Cumhuriyeti Sağlık Bakanlığı, Halk Sağlığı Genel Müdürlüğü. Aşı Portalı. Yetişkin Aşılama. Available from: https://hsgm.saglik.gov.tr/depo/mevzuat/genelge/1117gbpgenelge2008pdf.pdf (Accessed April 12, 2020.)
23. Rowe SL, Tay EL, Franklin LJ, Stephens N, Ware RS, et al. Effectiveness of parental cocooning as a vaccination strategy to prevent pertussis infection in infants: A case-control study. Vaccine. 2018;36(15):2012-2019. https://doi.org/10.1016/j.vaccine.2018.02.094

Original Article

Med J Bakirkoy 2020;16(2):108-13
doi: 10.5222/BMJ.2020.52824

Medical Journal of Bakirkoy

The Truth We Cannot See; Hypothermia in Patients Under Spinal Anesthesia

Göremediğimiz Gerçek; Spinal Anestezi Altındaki Hastalarda Hipotermi

Ahmet Yuksek, Gamze Talih

Yozgat Bozok University, Department of Anesthesiology and Reanimation, Yozgat, Turkey

Received: 24 March 2020 / **Accepted:** 5 May 2020 / **Publication date:** 26 June 2020

Cite as: Yuksek A, Talih G. The truth we cannot see; hypothermia in patients under spinal anesthesia. Med J Bakirkoy 2020;16(2):108-13.

ABSTRACT

Objective: *The frequency of using a temperature monitor in patients under spinal anesthesia is lower than desired. Besides, it is open to debate how and from where temperature monitoring should be done most practically in awake patients. In this study, we investigated the incidence of hypothermia in geriatric patients under spinal anesthesia and compared the temperature measurement methods.*
Method: *Preoperative and postoperative temperature monitoring were compared with three different measurement methods in elderly patients undergoing spinal anesthesia. The success of methods and the factors that may cause loss of temperature were examined.*
Results: *The incidence of hypothermia in geriatric patients was found to be 46 percent. One-third of hypothermic cases were seen in surgeries lasting less than one hour. External auditory canal measurements using an infrared method were correlated with thermocouple measurements. However, axillary skin temperature measurements were significantly erroneous. Low hemoglobin values were related to loss of temperature.*
Conclusion: *Old age is a special situation contributiing to hypothermia and creating a vulnerable population in terms of its results. In cases where the core temperature cannot be measured, infrared measurements of the external auditory canal can be used. Axillary skin temperature is misleading but may at least contribute to the information. But a measurement that has not been done is still the worst. With the most appropriate technique within the possibilities available, temperature monitoring should be used regardless of the operation time in geriatric patients. Because undiagnosed hypothermia cannot be treated.*

Keywords: *geriatrics, spinal anesthesia, hypothermia, intraoperative monitoring*

ÖZ

Amaç: *Spinal anestezi altındaki hastalarda sıcaklık monitörizasyonunun kullanımı beklenenden daha azdır. Ayrıca, uyanık hastalarda sıcaklık izleminin en pratik olarak nasıl ve nereden yapılması gerektiği tartışmaya açıktır. Bu çalışmada spinal anestezi altında geriatrik hastalarda hipotermi insidansını araştırdık ve sıcaklık ölçüm yöntemlerini karşılaştırdık.*
Yöntem: *Spinal anestezi uygulanan yaşlı hastalarda ameliyat öncesi ve sonrası sıcaklık izlemleri üç farklı ölçüm yöntemi kullanılarak karşılaştırıldı. Yöntemlerin başarısı ve sıcaklık kaybına neden olabilecek faktörler incelendi.*
Bulgular: *Geriatrik hastalarda hipotermi insidansı% 46 olarak bulundu. Hipotermik vakaların üçte biri 1 saatten kısa süren operasyonlarda görüldü. Infrared yöntem ile dış kulak yolu ölçümleri termokupl ölçümleri ile korele idi. Bununla birlikte, aksiller cilt sıcaklığı ölçümleri önemli ölçüde yanlıştı. Düşük hemoglobin değeri sıcaklık kaybıyla ilişkiliydi.*
Sonuç: *Yaşlılık, hipotermiye katkıda bulunan ve sonuçları açısından hassas bir populasyon yaratan özel bir durumdur. Core sıcaklığının ölçülemediği durumlarda, dış kulak yolunun infrared yöntem ile ölçümleri kullanılabilir. Aksiller cilt sıcaklığı yanıltıcıdır, ama en azından fikir sahibi olmaya katkıda bulunabilir. Ancak henüz yapılmayan bir ölçüm en kötüsüdür. Mevcut olasılıklar dahilinde en uygun teknikle, geriatrik hastalarda ameliyat süresine bakılmaksızın sıcaklık monitörizasyonu kullanılmalıdır. Çünkü teşhis edilmemiş hipotermi tedavi edilemez.*

Anahtar kelimeler: *geriatri, spinal anestezi, hipotermi, intraoperatif monitörizasyon*

Corresponding Author:
✉ mdayuksek@hotmail.com

A. Yuksek 0000-0002-7529-2971
G. Talih 0000-0003-4743-9734

INTRODUCTION

Unintended perioperative hypothermia is defined as a fall in the patient's core temperature below 36°C. Hypothermia is frequently observed in patients whose surgery lasted for a long time under general anesthesia without the application of any heating methods [(1)]. The known complications include increased incidence of wound site infection, perioperative bleeding, delayed recovery from anesthesia, prolonged hospital stay, increased mortality and morbidity rates and higher cost [(2)]. Even in mild hypothermia, the risk of cardiac complications is increased [(3)]. Redistribution is the most effective mechanism in heat loss and vasodilation caused by spinal anesthesia (SA) leading to increased redistribution of anesthetic material [(4)].

Thermoregulation by vasoconstriction and shivering is less effective in the elderly, both in the presence and absence of anesthesia [(1)]. Decreased adipose tissue and sometimes decreased levels of communication to express the perception of feeling cold also contribute to the development of hypothermia, Based on these reasons, both national and international guidelines emphasize that geriatric patients are at greater risk of hypothermia [(5-7)]. It is now an indisputable issue that it is necessary to monitor the perioperative temperature in these patients. But the question is how to do it. According to the studies performed so far, thermocouple core temperature measurement has been the most appropriate and true method for perioperative temperature monitoring in patients undergoing surgery [(4)]. However, using the thermocouple method under spinal anesthesia can be difficult for the awake patient. Temperature monitoring with skin temperature measurement is practical for the awake patient, but it may differ from the core temperature. Therefore, skin temperature measurement can only be used for informational purposes.

Our study aimed to determine the incidence of hypothermia in geriatric patients under spinal anesthesia and compare the success of different measurement methods.

MATERIAL and METHOD

Ethical approval for this study was obtained from the local ethics committee (decision number; 2017-KAEK- 189_2019.03.13_03). One hundred and twenty patients over 65 years of age who underwent orthopedic surgery under SA were included in this study. Patients with American Society of Anesthesiologists Classification (ASA) status of 1-3 were included in the study . On the other hand; preoperative fever (38°C), thyroid disorders, autonomic neuropathy, peripheral vascular diseases, uncontrolled hypertension, vasoactive drug use, contraindications for spinal anesthesia and the patient's refusal to participate in the study were determined as exclusion criteria. In cases where we have to switch to general anesthesia (GA) during the operation were not included in the study.

Study protocol

The ambient temperature of the operating room was kept constant, between 20-22°C. Patients with a measured body temperature above 36°C in the preoperative waiting room were taken to the operation room. Preoperative heart rate, preoperative systolic arterial blood pressure values of the patients were recorded for the study after standard anesthesia monitoring and a 5- minute rest. Demographic data such as age, gender, body mass index (BMI), comorbidities and hemoglobin values obtained using standard pre-anesthesia tests were recorded. SA was performed with 10-15 mg of hyperbaric bupivacaine (Marcaine Spinal Heavy %0.5, Zentiva, Kırklareli) injected targeting the T10 level. After standard anesthesia monitoring, patients were treated with Ringer's lactate solution at 37°C at an initial IV infusion rate of 100 ml/hr, then infusion rate was adjusted, and maintained in consideration of their fluid, and electrolyte losses.

A soft tip thermocouple probe (M1024247 General purpose probe GE, USA) was inserted into the right auditory canal and secured with cotton and a bandage. The patient's core temperature was measured from the tympanic membrane using this thermocouple probe. An infrared thermometer was used to measure the tympanic membrane temperature of the left ear. At the same time, the axillary skin temperature was also measured and recorded using the same infrared thermometer (Thermoscan 5-IRT6020; Braun, Hessen, Germany).

The first minute after spinal anesthesia was considered to be time zero recorded as T1. The final measurement taken in the operation room was recorded as T2. Besides, the patients' heart rate, oxygen saturation, and blood pressure values were recorded with noninvasive monitoring methods during the study. The ambient temperature, duration of surgery, fluids applied, transfused blood units in milliliters, estimated blood loss and preoperative hemoglobin values also recorded as predictors of hypothermia. Measurement of the temperature of the tympanic membrane with a thermocouple probe is one of our measurement methods, and accepted as the actual core temperature value in this study. Classification and comparison of hypothermic (Group H) and normothermic (Group N) patients were made according to this value. Patients with a core temperature below 36 degrees were defined as hypothermic. Preoperative and postoperative temperature measurements, reasons for temperature loss were compared, and the concordance between the three different measurements was determined.

Statistical analysis

According to the power analysis made based on the previous study on the subject; it was deemed appropriate to take at least 50 patients with 0.8 power and 0.5 alpha ratio to determine the incidence of hypothermia in geriatric patients [8]. The data were analyzed using the IBM SPSS Statistics for Windows, version 18 package program (SPSS IBM Inc., Chicago, IL, USA). Data with a normal distribution were presented as the mean±standard deviation. The conformity of data to a normal distribution was assessed using the Kolmogorov-Smirnov test. The independent samples t-test was used to analyze normally distributed quantitative data. The chi-square (χ^2) test was used to analyze qualitative data. A p-value of <0.05 was accepted as statistically significant.

RESULTS

A total of 113 patients were included in our study. The mean age of the participants was 73.15±5.87 (min-max; 65-87) years. Three patients who required GA during surgery were excluded from the study. Other three patients were excluded because the first temperature measurement was not within the target temperature range (36-38 degrees). Also, one patient was unable to complete the study because she was disturbed by the temperature probe in her ear during the operation.

In normothermic patients, preoperative hemoglobin value was higher (p<0.001), the amount of bleeding (p=0.001) and the number of blood products infused were significantly less (p=0.003). There was no difference between the groups regarding the amount of fluid administered, BMI, and age. Operation times of hypothermic and normothermic patients were similar. A comparison of hypothermic and normothermic patients is presented in Table 1.

The temperatures before and after the operation were measured in three different ways. A total of 52 patients (46%) were found to be hypothermic based on the measurement of tympanic temperature using a thermocouple probe at the end of the operation, while the infrared tympanic temperature measurement identified hypothermia in 59 patients (52%). There was no difference between the two measurements in detecting hypothermia (p=0.458). Seventy

Table 1. Comparison of hypothermic and normothermic patients.

Parameters	Group H (n=52)	Group N (n=61)	p
Age (years)	74.49±5.77	71.59±5.66	0.593
BMI	28.73±3.96	26.93±3.05	0.229
Operation time (min)	82.57±34.47	79.78±37.43	0.90
Estimated blood loss (ml)	187.70±247.59	143.26±132.85	0.001
Blood products (ml)	35.24±98.88	11.53±61.52	0.003
IV fluids (ml)	1103.27 ±459.51	1049.03 ±365.21	0.70
Preoperative hemoglobin (g/dl)	12.10±1.19	13.13±1.86	<0.001
Preoperative Heart rate (bpm)	81.73±13.18	81.90±13.99	0.804
Preoperative systolic arterial pressure (mmHg)	130.44±15.93	122.09±13.74	0.134

** BMI; body mass index, IV fluids; total IV fluids administered during surgery;*
Statistical analysis was performed by independent samples t-test. Data are presented as mean ± standard deviation.

Table 2. Comparison of measurement techniques.

	Tcore (T1-T2)	T tympanic (T1-T2)	T axillary (T1-T2)	p
Temperature loss (degree)	0.76±0.61[a]	0.71±0.64[b]	1.03±0.92	<0.05
Hypothermic patients (n)	52[a]	59	70	<0.05*

Tcore, the difference between preoperative and postoperative core temperature
T tympanic, the difference between preoperative and postoperative tympanic membrane temperature
Taxillary, the difference between preoperative and postoperative axillary skin temperature.
[a] Tcore was significantly lower compared to Taxillary
[b] T tympanic was significantly lower compared to Taxillary.
*Statistical analysis was performed by independent samples t-test and *chi-square test.*

patients (61%) were found to be hypothermic according to the axillary temperature measurements, but this number of hypothermic patients was incorrectly high (p=0.027; Table 2). Considering the temperature losses according to the different measurement techniques; the decrease in temperature detected by the measurement with a thermocouple probe was similar to that of the tympanic temperature measurement using an infrared sensor (p=0.854). However, the magnitude of temperature loss according to the axillary measurement was significantly different from the measurement using a thermocouple probe (p=0.007) and tympanic temperature measurement wtih an infrared sensor (p=0.004; Table 2).

In eight of the 55 hypothermic patients (15.3 %), the operation time was less than 30 minutes, and in 10 hypothermic patients (19.2 %) the operation time was between 30 minutes and 1 hour. Therefore, in one-third (18/55, 32 %).of the hypothermic patients, the operation time was less than one hour.

DISCUSSION

Geriatric patients are more tend to the development of hypothermia due to decreased heat production, decreased muscle mass and adipose tissue, and inefficient autonomic vasodilatory and vasoconstrictory responses. Furthermore, even mild hypothermia causes an increase in risks of complication, especially cardiac complications in elderly patients [9].

According to a study examining the risk factors for the development of hypothermia, the riskiest patient groups were determined as those operated at low operating room temperature, newborns, burn patients, and those operated under a combination of GA and SA [1].

The first and the most important phase in the development of hypothermia is redistribution [4]. In a study that compared patients receiving GA and those receiving GA combined with regional anesthesia, it was found that regional anesthesia had a great effect on the redistribution phase and increased heat loss [10].

Turkish, European and American anesthesia associations recommend perioperative routine temperature monitoring. Particularly, for newborns and elderly patients temperature monitoring should be performed regardless of the duration of the operation [5,6]. However, studies have shown that the rate of heat monitoring are rarely performed in surgeries realized under regional anesthesia. Frank et al. reported a rate of 33% for these surgeries, while rates of 27% were reported in a study by Arkilic et al. and in a study of obstetric patients in the UK [11-13]. Limited access to the measurement sites in awake patients and work intensity were revealed to be the reasons for this low monitoring rate [12].

The pulmonary artery, tympanic membrane, nasopharynx, rectum and urinary bladder are appropriate sites for core temperature monitoring [11]. The most accessible of these areas for core temperature measurement in awake patients under SA is tympanic membrane approached through external auditory canal However, the measurement must be performed with an appropriate technique, as infrared temperature readings may not produce accurate results [10]. For an adequate measurement, thermocouple thermometers or thermistors should be used. This type of measurement device should be counted as one of the standard anesthesia monitoring tools and used routinely. However, the appropriate measuring device may not be available in all operating rooms. A more striking situation; the question of

where to place this temperature probe on the awake patient, poses a problem. Sessler et al. [10] inserted cotton wrapped probe into the external auditory canal and fixed with a bandage. In our study, this method was applied. One patient wanted to leave the study because she was uncomfortable with the heat probe used in this way. This factor makes performing the measurement difficult and therefore restricts routine temperature monitoring [11].

If the appropriate measurement areas for the measurement of the core temperature cannot be found, or if there is not enough equipment, the tympanic membrane appears to be superior to the axillary skin for temperature monitoring. However, it is important to know the appropriate measurement technique for both core temperature measurements and skin temperature measurement [10].

In our study, the mean temperature loss and hypothermia rates were not significantly different between infrared and thermocouple measurements of the tympanic membrane. Axillary skin temperature measurement was ineffective for detecting hypothermia in geriatric patients which may be due to the fact that axillary skin temperature is affected by many factors, including ambient temperature. According to our results, infrared tympanic temperature measurement can be used to predict hypothermia in patients for whom core temperature cannot be measured with thermocouple or thermistors, or when there are no other acceptable measurement sites.

When the overall study group is considered, 46% of patients developed hypothermia, which is very high. This is consistent with a study by Arkilic et al. [12], who reported an even higher rate of 77 percent. One of our study aims was to determine the incidence of hypothermia in geriatric patients. However, it may also be important to determine the incidence in our younger patients who were operated under spinal anesthesia in the same period. This subject may be a limitation of our study or it may be a new study subject.

Frank et al. [11] have shown that the risk and magnitude of hypothermia increases in proportion to age in patients under regional anesthesia. In this case, temperature monitoring becomes more important in the elderly. Even in our patients who were all over 65 years of age, the temperature loss increased with age. The temperature of the operating room, the patient's body mass index, block-level, blood loss, and fluid therapy may affect temperature loss, in addition to the age [14].

In our study, we tried to keep the block level standard and block-level did not rise in any patient .The ambient temperature in the operating room was maintained at the same level. BMI, the amount of fluid given did not differ between patient groups. Preoperative hemoglobin values were higher in normothermic patients, the amount of bleeding and the number of blood products administered were lower.

An important finding of our study was there was no significant difference in duration of operation between hypothermic and normothermic patients, and hypothermia has seen in short-term operations too. This fact emphasizes the effect and importance of redistribution, which occurs in the first half-hour of the operation, in the development of hypothermia in patients under SA. To emphasize again; hypothermia was observed in 46% of geriatric patients under SA and in one-third of the hypothermic patients, the operation time was less than one hour (18/55, 32%).

Considering the low rate of temperature monitoring shown in studies, the diagnosis of hypothermia is often overlooked, which means that treatment cannot be performed without making a diagnosis [2,4]. It is important to note that geriatric patients are sensitive to the negative effects of hypothermia, and even mild hypothermia increases the complication rate.

Conclusion

The risk of hypothermia is high in geriatric patients under SA. However, hypothermia cannot be diagnosed unless temperature monitoring is performed. Therefore, more attention should be paid to temperature monitoring. Infrared temperature measurements of the tympanic membrane can be used for perioperative temperature monitoring if core temperature monitoring cannot be performed.

Ethics Commitee Approval: For this study ethics committee approval was received from the local ethics committee of Yozgat Bozok University Faculty of Medicine. (decision number; 2017-KAEK-189_2019.03.13_03).

Conflict of interest: Authors have no conflict of interest.

Funding: There are no financial supports.

Informed Consent: Patient consent was obtained for his study.

REFERENCES

1. Macario A, Dexter F. What are the most important risk factors for a patient's developing intraoperative hypothermia? Anesth Analg. 2002;94(1):215-20. https://doi.org/10.1213/00000539-200201000-00042
2. Allen TK, Habib AS. Inadvertent perioperative hypothermia induced by spinal anesthesia for cesarean delivery might be more significant than we think: are we doing enough to warm our parturients? Anesth Analg. 2018;126(1):7-9. https://doi.org/10.1213/ANE.0000000000002604
3. Díaz M, Becker DE. Thermoregulation: physiological and clinical considerations during sedation and general anesthesia. Anesth Prog. 2010;57(1):25-32; quiz 33-4. https://doi.org/10.2344/0003-3006-57.1.25
4. Sessler DI. Perioperative thermoregulation. Geriatr Anesthesiol. 2016;6736(15):107-22. https://doi.org/10.1007/978-0-387-72527-7_8
5. Turkish Society of Anaesthesiology and Reanimation (TSAR). Practice Guideline for Prevention of Unintentional Perioperative Hypothermia. Turk J Anaesthesiol Reanim. 2013;41:188-90. https://doi.org/10.5152/TJAR.2013.64
6. National Institute for Care and Health Excellence. Hypothermia: prevention and management in adults having surgery-clinical guideline [CG65]. 2008;April 2008:1-18. Available from: https://www.nice.org.uk/guidance/cg65. (accessed on 01.12.2019)
7. American Society Of Anesthesiologists. Standards for basic anesthetic monitoring. 2015. Available from: https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring (accessed on 31.03.2020).
8. Emmert A, Gries G, Wand S, et al. Association between perioperative hypothermia and patient outcomes after thoracic surgery: A single center retrospective analysis. Medicine (Baltimore). 2018;97(17):e0528. https://doi.org/10.1097/MD.0000000000010528
9. Connor EL, Wren KR. Detrimental effects of hypothermia: a systems analysis. J Perianesth Nurs. 2000;15(3):151-5. https://doi.org/10.1053/jpan.2000.7508
10. Sessler D. Temperature monitoring and perioperative thermoregulation. Anesthesiology. 2008;109(2):318-38. https://doi.org/10.1097/ALN.0b013e31817f6d76
11. Frank SM, Nguyen JM, Garcia CM, Barnes RA. Temperature monitoring practices during regional anesthesia. Anesth Analg. 1999;88(2):373-7. https://doi.org/10.1097/00000539-199902000-00028
12. Arkiliç CF, Akça O, Taguchi A, Sessler DI, Kurz A. Temperature monitoring and management during neuraxial anesthesia: an observational study. Anesth Analg. 2000;91(3):662-6. https://doi.org/10.1213/00000539-200009000-00031
13. Aluri S, Wrench IJ. Enhanced recovery from obstetric surgery: a UK survey of practice. Int J Obstet Anesth. 2014;23(2):157-60. https://doi.org/10.1016/j.ijoa.2013.11.006
14. Frank SM, El-Rahmany HK, Cattaneo CG BR. Predictors of hypothermia during spinal anesthesia. Anesthesiology. 2000;92(5):1330-4. https://doi.org/10.1097/00000542-199809200-00054

Original Article

Med J Bakirkoy 2020;16(2):114-9
doi: 10.5222/BMJ.2020.66487

Medical Journal of Bakirkoy

Natural Course of Branch Retinal Vein Occlusion up to 3 Months for Early Referral Cases §

Erken Başvuran Retina Ven Dal Tıkanıklığı Olgularının İlk 3 Aylık Doğal Seyri

Emir Volkan Altan, Ismail Umut Onur, Ozge Pinar Akarsu Acar, Fadime Ulviye Yigit

Department of Ophthalmology, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Received: 6 July 2019 / **Accepted:** 27 December 2019 / **Publication date:** 26 June 2020

Cite as: Altan EV, Onur İU, Akarsu Acar OP, Yigit FU. Natural course of branch retinal vein occlusion up to 3 months for early referral cases. Med J Bakirkoy 2020;16(2):114-9.

ABSTRACT

Objective: *To evaluate functional and anatomical changes in branch retinal vein occlusion (BRVO) up to 3 months in early referral BCVA cases.*
Method: *Twenty-three eyes of 23 consecutive BRVO patients diagnosed within 4 weeks of symptom onset were enrolled in this prospective, observational study. Eyes were followed up without treatment. Measurements in best corrected visual acuity (BCVA) and central macular thickness (CMT) at the baseline, 2 weeks, 1 month and 3 months were evaluated.*
Results: *The improvement in mean BCVA from the baseline to 2 weeks (p=0.043), 1 month (p=0.012) and 3 months was found statistically significant (p=0.001). Despite a decrease in central macular thickness (CMT) was observed, the change in CMT from the baseline to 3 months did not reach a clinical significance (p=0.068).*
Conclusion: *Considering the natural course in BRVO, follow-up without treatment may also be acceptable up to the first 3 months. Our results indicate that delaying treatment up to 3 months is not associated with increased CMT or deteriorated BCVA for recent onset early referral BRVO cases.*

Keywords: *natural course, branch retinal vein occlusion, best corrected visual acuity, central macular thickness*

ÖZ

Amaç: *Erken başvuran retina ven dal tıkanıklığı (RVDT) olgularında ilk 3 aydaki işlevsel ve anatomik değişiklikleri incelemek.*
Yöntem: *Semptomların ortaya çıkışıyla ilk 4 hafta içerisinde RVDT tanısı alan ardışık 23 hastanın 23 gözü prospektif, gözlemsel çalışmaya dahil edildi. Gözler sadece tedavisiz takip edildi. Başlangıçta alınan en iyi düzeltilmiş görme keskinliği (EİDGK) ve santral makula kalınlığı (SMK) ölçümleri 2. haftada, 1. ayda ve 3. ayda tekrarlandı. Bu parametrelerdeki değişimler analiz edildi.*
Bulgular: *Ortalama EİDGK'de başlangıca göre 2. haftada, 1. ayda, 3. ayda istatistiksel olarak anlamlı düzelme kaydedildi (sırasıyla p=0,043, p=0,012, p=0,001). Ortalama SMK'da ise başlangıca göre 3. ayda azalma izlenmiş olsa da fark istatistiksel olarak anlamlı bulunmadı (p=0.068).*
Sonuç: *RVDT'nin doğal seyri ile birlikte düşünüldüğünde ilk 3 aya kadar tedavisiz gözlem, bir seçenek olarak değerlendirilebilir. Çalışmamızın sonuçları, erken başvuran olgularda tedavinin 3 aya kadar bekletilmesinin EİDGK ve SMK parametreleri üzerinde olumsuz bir etki ilişkili olduğunu göstermemiştir.*

Anahtar kelimeler: *doğal seyir, retina ven dal tıkanıklığı, en iyi düzeltilmiş görme keskinliği, santral makula kalınlığı*

Corresponding Author:
✉ umuton@gmail.com

E. V. Altan 0000-0001-9293-9143
İ. U. Onur 0000-0002-9028-2421
O. P. Akarsu Acar 0000-0003-4424-2215
F. U. Yigit 0000-0003-0176-1509

§ Derived from the thesis of E. Volkan Altan 2014- Istanbul

INTRODUCTION

Retinal vein occlusion (RVO) is the second most common retinal vascular disorder after diabetic retinopathy, and causes visual loss commonly associated with macular edema and retinal ischemia [1,2]. Current options for the treatment of RVO complications include applications of argon laser photocoagulation, intravitreal corticosteroids and anti-vascular endotelial growth factors (anti-VEGFs) [3,4]. However, several attempts have been made to perform anastomoses using surgery and laser or relieve the obstruction pharmacologically by thrombolytics and bypass the congestion via optic nerve sheathotomy, which all proved ineffective [5].

A number of multicenter trials have evaluated the efficacy of argon laser photocoagulation, intravitreal corticosteroids and anti-VEGFs in RVO. Nevertheless, a common aspect of all these studies was the relatively long duration between symptom onset and treatment, which generally exceeded 3 months [6-11]. In systematic reviews and meta-analyses on the natural course of ocular complications in patients with untreated symptomatic branch retinal vein occlusion (BRVO), it has been reported that the best corrected visual acuity (BCVA) generally improves up to 2 lines or by 1 letter at 3 months and up to 15 letters over 18 months in one third to three quarters of eyes [5-8]. Current data on the timing of treatment for recent onset BRVO is not clear and evidence is not strong on this issue. The aim of this study was to observe the functional and anatomical changes in early referral BRVO patients without any treatment up to 3 months.

MATERIALS and METHODS

The study was conducted in accordance with the tenets of the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study with the approval of the institutional ethical review board (Approval number: 2014/61).

Twenty-three eyes of consecutive 23 BRVO patients diagnosed within 4 weeks of symptom onset between September 2011 and March 2014 were enrolled in this prospective, observational study conducted at our tertiary eye department. At first visit, a questionnaire on medical history, family background and drug use was applied to all patients requiring specifically for personal or family history of hypertension, diabetes mellitus, thrombophilia, spontaneous abortion, pulmonary embolism or deep venous thrombosis and use of oral contraceptive drugs. Hematology and cardiology consultations were requested for the evaluation of cardiovascular and hematologic risk factors including hypertension, hyperlipidemia, hyperhomocysteinemia, presence of factor V Leiden mutation and thrombophilic disorders. Detailed ophthalmic examinations were carried out. BCVA was expressed as decimal units and was converted to the logarithm of the minimal angle of resolution (log MAR) for statistical analyses. Intraocular pressure (IOP) measurement with non-contact tonometer (Topcon CT-80, Tokyo, Japan), and assessments using slit-lamp biomicroscopy, dilated fundus examination, optical coherence tomography (OCT) and colored fundus photography imaging were performed. These examinations were repeated at 2 weeks, 1 month and 3 months. Patients with a history of intraocular surgery, diagnosed or suspected glaucoma or mature cataracts preventing OCT examination were excluded from the study. A technician performed the OCT examinations with RTVue-100 OCT device (Optovue Inc., Fremont, US), which had a 5 µm axial image resolution with a speed of 27.000 scans per second for all macular measurements. All eyes were assessed 30 minutes after topical tropicamide 1% administration for signal strength enhancement. Segmental division in MM5 protocol outputs (5x5 mm^2 grid of 11 horizontal and 11 vertical lines with 668 A-scans each and 3x3 mm^2 inner grid of 6 horizontal and 6 vertical lines with 400 A scans each) with retinal thickness of 1 mm diameter central ring (CMT-central macular thickness retinal thickness) on thickness map was recorded.

Fundus photography and fundus fluorescein angiography (FFA) were performed by an experienced physician using Kowa VX-10i retinal camera (Kowa Optimed Europe Ltd., Berkshire, UK). Fundus photographs were taken at the baseline, second week, first and third months and then reevaluated by two physicians. Reduction in the bleeding area and the number of punctate hemorrhages, disappearance of the exudates, recovery of venous tortuosity and distension were accepted as recovery criteria. Because

fresh retinal hemorrhages generally preclude the examination of retinal capillaries and the macula in the acute phase, FFA examinations were not performed at presentation, but later within the first 3 months of BRVO. Location of BRVO, existence of ischemia and neovascularization were analysed with FFA. The retinal ischemia was defined as the presence of capillary non-perfused areas after the hemorrhages cleared up.

Statistics

In the descriptive summary of the data, mean, standard deviation (SD), median (med), first quarter-third quarter (Q1-Q3), frequency and ratio values were used whenever appropriate. The distribution of the variables was assessed by the Kolmogorov-Smirnov test. Mann-Whitney U test and chi-square test were used in the analysis of qualitative and quantitative data, respectively. Wilcoxon test and Mc Nemar's test were used in the repetitive measurements. Analyses were performed with SPSS 22.0 (IBM Corporation, New York, US) software.

RESULTS

In this study 23 eyes of 23 patients, 16 (69.6%) male and 7 (30.4%) female with early referral BRVO were analysed. None of the patients declared hypertension and any cardiovascular or hematologic risk factors were not detected in the study group at presentation. The demographic characteristics of the patients included in the study are summarized in Table 1.

At the baseline visit, the mean BCVA (log MAR) was 0.57 ± 0.40 (Med =0.52). Only 6 (26.09%) eyes had a BCVA higher than 0.4 decimal units and 17 (73.91%) eyes had a BCVA lower than 0.5 decimal units (Table 2). At 2 weeks of follow up, BCVA improved 1 line or more in 12 (57.1%) of the eyes. BCVA did not change in 5 (23.8%) of the eyes and a 1 line loss in BCVA was detected only in 4 (19.1%) eyes. In comparison with baseline at 1 month, an improvement of 1 line or more in BCVA was seen in 13 (65%) of the eyes. BCVA did not change in 4 (20%) eyes and 1 line loss was detected in 3 (15%) eyes. At 3 months, in 16 (69.6%) eyes, BCVA improved 1 line or more. BCVA did not change in 6 (26.1%) of the eyes and a 1 line loss was detected in 1 eye (4.3%) (Table 2 and Figure 1). At 3 months, the mean BCVA (log MAR) was 0.34±0.39 (Med =0.04). Fourteen (61%) eyes had a BCVA higher than 0.4 decimal units and 9 (39%) eyes had a BCVA lower than 0.5 decimal units (Table 2). The change in BCVA from baseline to 2 weeks (P=0.043), 1 month (P=0.012) and 3 months was found statistically significant (P=0.001).

The mean central macular thickness (CMT) measured with OCT at the baseline, 2 weeks, 1 month and 3 months were 437 µm±158 µm (Med=451 µm), 423 µm±181 µm (Med=385 µm), 423 µm±193 µm (Med= 359µm) and 363 µm±116 µm (Med=315 µm), respectively. Although the change in CMT from the baseline to 3 months was not statistically significant (p= 0.068) an improvement in macular edema and a decrease in the central macular thickness were detected (Figure 2).

Table 1. Demographics.

	Med	Q1-Q3	Mean±SD	n	%
Age (years)	52	43-60	53.7±13.2		
Gender					
Female				7	30.4%
Male				16	69.6%
Duration of symptoms at referral (day)	15	4-25	14.6±9.8		
Eye					
Right				12	52.2%
Left				11	47.8%
Refraction (Diopters) (SE)	0.12	-0.50-0.62	0.20±2.10		
Location of BRVO					
Inferior Temporal				5	21.7%
Superior Temporal				18	78.3%

Q1-Q3: First quadrile to 3rd quadrile, SE: spherical equivalent

Table 2. BCVA (Log Mar).

Case	Baseline	2 weeks	1 month	3 Months
1	0.39	0.04	0.04	0
2	0.69	0.22	0.04	0.04
3	0	0	0	0
4	1	1.3	0.82	0.69
5	1.52	1.52	1.3	0.69
6	0.69	1	1	0.69
7	0.39	0.3	0.22	0.22
8	0.69	0,3	0.22	0.3
9	0.09	0.15	0.15	0.04
10	1	0,52	0.15	0.04
11	1	1	1	1
12	0.39	0.3	NA	0.04
13	1	1	1	1.3
14	0.3	0,22	0.09	0.04
15	0.04	0.15	0.22	0.04
16	0.52	0.52	0.52	0.52
17	0,82	0.52	0.69	0.69
18	0.15	0.09	0.04	0
19	0.09	0	0	0
20	0.15	0	0.04	0.04
21	0.69	NA	NA	0.69
22	0.39	NA	NA	0.04
23	1	0.52	0.52	0.69

Data of 23 patients with recent onset BRVO showing relationship to the location of the occlusion and best corrected visual acuity (BCVA).

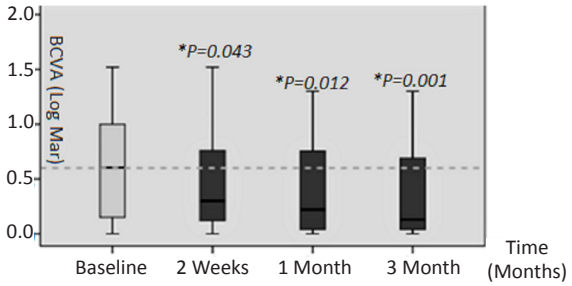


Figure 1. Change in mean BCVA (Log MAR).
**The changes in BCVA from baseline to 2 weeks (p=0.043), 1 month (p=0.012) and 3 months (p=0.001) were found to be statistically significant.*

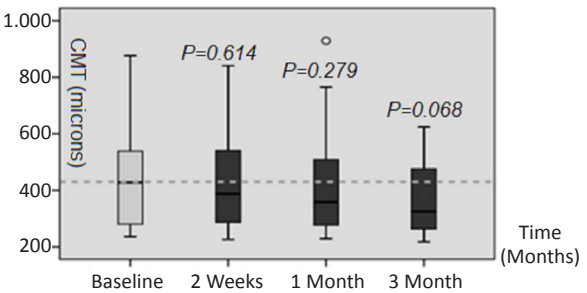


Figure 2. Change in mean CMT (microns).

The change in hemorrhage size, number of punctate hemorrhages, exudates, venous tortuosity and distension in fundus photographs were evaluated and a significant improvement was found at 1 month and 3 months compared to the baseline. FFA examinations revealed no macular ischemia or neovascularization in the study group. Peripheral capillary non-perfusion was detected in 13% of the patients. However, none of the patients developed retinal neovascularization, abnormal rise in IOP, involvement of the other eye or systemic cardiovascular pathologies such as myocardial infarction or cerebrovascular occlusion within the 3 months of follow-up period.

DISCUSSION

Our results indicate that in eyes with recent onset early referral BRVO, delaying treatment up to 3 months may not be associated with increased CMT or deteriorated BCVA. Indeed, we have observed a slow and limited recovery in the affected eyes in the 3 -month follow up period.

A number of pivotal multicenter randomized trials have investigated the management and treatment of complications in BRVO. However, cases enrolled in these studies display a heterogeneous duration of symptoms from the onset of the disease dispersed over a wide range. The multicenter, randomized laser trial [Branch Vein Occlusion Study (BVOS)] included the BRVO patients with symptom duration between 3 to 19 months [7,8], while The Standard Care versus Corticosteroid for Retinal Vein Occlusion (SCORE) trial included the patients with a mean symptom duration of 4 months (range,1-24 months) [9]. However, anti VEGF-ranibizumab (BRAVO) trial enrolled patients with a relatively uniform symptom duration, ranging between 3.3 months to 3.7 months (10). In the dexamethasone intravitreal implant (GENEVA) trial, the average time interval between symptom onset and treatment was 153 (49-944) days [11]. Compared to these multicenter, randomized studies mentioned above, the average duration of symptoms for the patients in our study was significantly shorter with 14.6 days (range: 1-30 days).

Regarding natural course, Shroff et al. studied 20 patients with recent onset BRVO with duration of symptoms less than 6 weeks and reported an average improvement of 19.6% from the baseline in

BCVA at 6 months [12]. BRAVO study reported that the patients in the sham group gained an average of 7.3 (5.1-9.5) letters at 6 months [10]. The multicenter, randomized, sham-controlled GENEVA study reported that BCVA improved 3 lines or more in the 18% of the patients in the sham group and 22% of the patients in the 0.7 mg dexamethasone implant group at month 6 and the difference between the groups remained statistically insignificant [11]. Kwon et al. studied BRVO patients in 3 groups which received intravitreal triamcinolone injections, intravitreal bevacizumab injections or intravitreal sham treatment. At 6 months, statistically significant BCVA improvement from the baseline was only detected in the sham treatment group which reached 0.3 or more log MAR units of improvement in 55.2% of the patients at month 12 [13]. Of note, improvement from the baseline in mean BCVA was significant in our study at all visits.

On the other hand, a functional and an anatomical threshold for starting up treatment have been adopted in all randomized trials. BCVA, less than 0.5 decimal units with detection of macular edema by OCT was accepted as treatment criteria in the previous studies [7,9-11]. In the laser era, BVOS recommended performing grid laser photocoagulation after 3 months of presentation when BCVA is lower than 0.5 decimal units and persistent macular edema is present, since BCVA and macular edema may improve spontaneously in the first 3 months after onset of symptoms [7,8].

The OCT examinations are important to detect macular edema; but increase in CMT currently is not accepted as an indication for treatment independent of BCVA. Relevantly, the GENEVA study reported that the change in CMT between the sham, 0.35 mg dexamethasone implant and 0.7 mg dexamethasone treatment groups to be statistically insignificant at 6 months [11]. Similarly, Kwon et al. reported that the changes in mean CMT between sham, intravitreal triamcinolone injection and intravitreal bevacizumab injection groups to be statistically insignificant at 12 months [13]. Furthermore, Shroff et al studied the natural course of CMT in early onset (<6 weeks) BRVO patients and found the mean baseline CMT of 398.9 µm reducing to 346.8 µm at 3 months. This change was statistically insignificant, but a gradual decline was highlighted in CMT up to month 7 [12] .The change in CMT from baseline values was similarly statistically insignificant at 2 weeks, 1 month and 3 months in our study and we also observed a gradual decline in CMT like Shroff et al.

It has been proposed in the consensus document of RVO Guidelines Development Group, that the prognosis is favorable and follow-up without any treatment may be reasonable in BRVO patients with a perfused periphery and preserved BCVA above a predetermined threshold as long as monthly follow-ups for the first three months are possible [3,6]. FFA should be performed to detect the location of retinal vein occlusion and nonperfused areas. The size of peripheral or macular nonperfusion and the existence of neovascularization should be evaluated as well, because the natural course of BRVO is associated with the location of occlusion, arterial perfusion at the BRVO area, and the efficiency of collateral circulation on nonperfused retina [14,15]. Monthly monitorization for the first three months is advised in case of a decrease in BCVA and development of macular edema [3]. On the contrary, a recent prospective, multicenter clinical trial has reported that the improvement in BCVA over 6 months in BRVO or CRVO patients with recent onset macular edema was found to be better in the early (< 90 days) dexamethasone intravitreal implant treatment group. However, this study included patients who had been previously treated for RVO [16], whereas in our study all eyes were treatment- naive. In addition, Pacella et al. compared the effects of early (within 7 days of diagnosis) and delayed (>7 day after diagnosis) dexamethasone implant treatment on 35 BRVO and 46 CRVO patients without a history of a previous laser treatment or intravitreal injection and found no significant differences in therapeutic response [17]. According to an another recent, prospective, multicenter clinical trial (BRIGHTER study) patients with a shorter BRVO duration until treatment has a better BCVA gain than those with a longer BRVO duration. However, the mean time between symptom onset and treatment was 9.9 months and the median time between symptom onset and treatment was 2.9 months in this study [18].

STUDY LIMITATIONS

The major limitations of this study are the limited number of patients and 3 months of follow-up time.

However, early referral of treatment naïve eyes with BRVO to a tertiary ophthalmology department is not common. We also ended follow-up without treatment at month 3 according to the results that multicentered, randomized studies indicated in favor of treatment thereafter.

CONCLUSION

In conclusion, there is a trend for very early intervention for the patients with BRVO regardless of natural course, even in cases with preserved BCVA. However, follow-up without intervention for a while may also be acceptable given the natural course of BRVO. Subgroup analysis of outcomes stratified according to the duration and onset of symptoms in the pivotal randomized studies will aid in identifying the optimal approach based on patient characteristics.

ACKNOWLEDGEMENTS

Authors thank to Murat Icen, MD for English proofreading.

Ethics Committee Approval: Bakırköy Dr. Approval was obtained from Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (2014/61, 14.03.2014).

Conflict of interests: None of the authors have disclosed financial interest related to this study.

Funding: No grants or funding have been received for this study.

Informed Consent: Informed consent was obtained from all individual participants included in the study with the approval of the institutional ethical review board (Approval number: 2014/61).

REFERENCES

1. Frangieh GT, Green WR, Barraquer-Somers E, et al. Histopathologic study of nine branch retinal vein occlusions. Arch Ophthalmol. 1982;100(7):1132-40. https://doi.org/10.1001/archopht.1982.01030040110020
2. Bandello F, Querques G. Medical Retina. 2012 ESASO Course Series. Basel, Karger. Vol 1. p. 111-8. https://doi.org/10.1159/isbn.978-3-8055-9991-7
3. Coscas G, Loewenstein A, Augustin A, et al. Management of Retinal Vein Occlusion - Consensus Document. Ophthalmologica. 2011;226(1):4-28. https://doi.org/10.1159/000327391
4. Laouri M, Chen E, Looman M, et al. The burden of disease of retinal vein occlusion: review of the literature. Eye. 2011;25:981-8. doi: 10.1038/eye.2011.92. https://doi.org/10.1038/eye.2011.92
5. Ip M, Hendrick A. Retinal Vein Occlusion Review. Asia-Pac J Ophthalmol. 2018;7:40-5. https://doi.org/10.22608/APO.2017442
6. Rogers SL, McIntosh RL, Lim L, et al. Natural history of branch retinal vein occlusion: an evidence-based systematic review. Ophthalmology. 2010;117(6):1094-1101.e5. https://doi.org/10.1016/j.ophtha.2010.01.058
7. Branch Vein Occlusion Study Group. Argon laser photocoagulation for macular edema in branch vein occlusion. Am J Ophthalmol. 1984;98(3):271-82. https://doi.org/10.1016/0002-9394(84)90316-7
8. BVOS Group. Argon laser scatter photocoagulation for prevention of neovascularization and vitreous hemorrhage in branch vein occlusion. A randomized clinical trial. Branch Vein Occlusion Study Group. Arch Ophthalmol. 1986;104(1):34-41. https://doi.org/10.1001/archopht.1986.01050130044017
9. Scott IU, VanVeldhuisen PC, Oden NL, et al. The Standard Care vs Corticosteroid for Retinal Vein Occlusion (SCORE) Study Study Report 1: Baseline Associations between Central Retinal Thickness and Visual Acuity in Patients with Retinal Vein Occlusion. Ophthalmology. 2009;116(3):504-12. https://doi.org/10.1016/j.ophtha.2008.10.017
10. Campochiaro PA, Jeffrey S, Heier JS, et al. BRAVO Investigators. Ranibizumab for macular edema following branch retinal vein occlusion: six month primary end point results of a phase III study. Ophthalmology. 2010;117(6):1102-1112.e1. https://doi.org/10.1016/j.ophtha.2010.02.021
11. Haller J, Bandello F, Belfort R Jr, et al. OZURDEX GENEVA Study Group. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology. 2010;117(6):1134-1146.e3. https://doi.org/10.1016/j.ophtha.2010.03.032
12. Shroff D, Mehta DK, Arora R, et al. Natural history of macular status in recent-onset branch retinal vein occlusion: an optical coherence tomography study. Int Ophthalmol. 2008;28(4):261-8. https://doi.org/10.1007/s10792-007-9123-0
13. Kwon SI, Kim YW, Bang YW, et al. Comparison of natural course, intravitreal triamcinolene, and intravitreal bevacizumab for treatment of macular edema secondary to branch retinal vein occlusion. J Ocul Pharmacol Ther. 2013;29(1):5-9. https://doi.org/10.1089/jop.2011.0249
14. Michels RG, Gass JDM. Natural course of temporal retinal branch occlusion. Trans Am Acad Ophthalmol Otolaryngol. 1974;78:166-77.
15. Rehak J, Rehak M. Branch Retinal Vein Occlusion: Pathogenesis, Visual Prognosis, and Treatment Modalities. Curr Eye Res. 2008;33(2):111-31. https://doi.org/10.1080/02713680701851902
16. Eter N, Mohr A, Wachtlin J, et al. Dexamethasone intravitreal implant in retinal vein occlusion: real-life data from a prospective, multicenter clinical trial. Graefes Arch Clin Exp Ophthalmol. 2017;255(1):77-87. https://doi.org/10.1007/s00417-016-3431-x
17. Pacella F, La Torre G, Basili S, et al. Comparison between early or late intravitreal injection of dexamethasone implant in branch (BRVO) or central (CRVO) retinal vein occlusion: six-months follow-up. Cutan Ocul Toxicol. 2017;36(3):224-30. https://doi.org/10.1080/15569527.2016.1254648q
18. Tadayoni R, Waldstein SM, Boscia F, et al. Individualized stabilization criteria-driven ranibizumab versus laser in branch retinal vein occlusion: six months results of BRIGHTER. Ophthalmology. 2016;123(6):1332-44. https://doi.org/10.1016/j.ophtha.2016.02.030

Original Article

Med J Bakirkoy 2020;16(2):120-4
doi: 10.5222/BMJ.2020.03522

Medical Journal of Bakirkoy

Vitamin B12 Status in Children with *Helicobacter pylori* Gastritis

Helicobacter pylori Gastriti Tanılı Çocuklarda Vitamin B12 Düzeyi

Hasret Ayyildiz Civan

Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Received: 20 December 2019 / **Accepted:** 10 March 2020 / **Publication date:** 26 June 2020

Cite as: Ayyildiz Civan H. Vitamin B12 status in children with Helicobacter pylori gastritis. Med J Bakirkoy 2020;16(2):120-4.

ABSTRACT

Objective: *Helicobacter pylori is rdescribed as the major etiological factor for gastritis and also associated with gastroesophageal reflux disease, and vitamin B12 deficiencies. Therefore, we aimed to evaluate the relationship between Helicobacter pylori gastritis and vitamin B12 status as well as to determine prevalence of esophagitis in children with H.pylori infections.*
Method: *A total number of 556 children who underwent eso-gastro-duodenoscopy were evaluated retrospectively. Diagnosis of H pylori infection, esophagitis, and gastritis was performed with histopathologic examination. Patients were divided into H.pylori (+) and (-) groups. Patients' demographic characteristics, physical examination, imaging and laboratory findings were recorded and evaluated.*
Results: *Patients included in the study consisted of 310 (55.8%) females, and 246 (44.2%) males. The mean age was significantly lower in males (9.43±5.69) than females (11.10±5.32) (p<0.001). The most common symptom was abdominal pain (41,5%). According to the histopathological examination H.pylori was positive in 24.5% (n=136) of our patients. Of the patients 28.6% (n=159) were diagnosed with esophagitis and 55.4% (n=308) with chronic gastritis. Esophagitis was detected in 30.1% of patients diagnosed with H.pylori and all chronic gastritis patients were found to be positive for H.pylori (p<0.001). There were no statistically significant differences found in mean levels of vitamin B12 between H.pylori negative and positive groups of patients with chronic gastritis. But the mean serum levels of vitamin B12 measured in the H.pylori positive group (382.93±245.50 pg/mL) was statistically significantly lower than H.pylori-negative group (467.90±305.36 pg/mL) (p=0.028). There were also no significant differences found in mean levels of iron between H.pylori-negative and positive groups.*
Conclusion: *Although all children with chronic gastritis were positive for H.pylori, our findings provide no evidence for a link between esophagitis, iron deficiency and H.pylori infection. In addition, H.pylori infection has been demonstrated to be a risk factor for vitamin B12 deficiency.*

Keywords: *bacterial meningitis, aseptic meningitis, mortality, pediatric intensive care unit*

ÖZ

Amaç: *Helicobacter pylori gastritin ana etiyolojik faktörü olarak tanımlanmakta, ayrıca gastroözofageal reflü hastalığı ve B12 vitamini eksiklikleri ile de ilişkilendirilmektedir. Bu nedenle, bizde H.pylori gastriti ve B12 vitamin statüsü arasındaki ilişki yanında H.pylori enfeksiyonu olan çocuklarda özofajit prevalansının değerlendirmeyi amaçladık.*
Yöntem: *Özogastroduodenoskopi yapılan toplam 556 çocuk retrospektif olarak değerlendirildi. H pylori enfeksiyonu, özofajit ve gastrit tanıları histopatolojik inceleme ile konuldu. Hastalar H.pylori pozitif ve negatif gruplara ayrıldı. Hastaların demografik özellikleri, fizik muayene, görüntüleme ve laboratuvar bulguları kaydedildi ve değerlendirildi.*
Bulgular: *Çalışmaya dahil edilen hastalar 310'u (%55,8) kız ve 246'sı (%44,2) erkek idi. Erkek hastalarda ortalama yaş (9,43±5,69) kızlardan (11,10±5,32) anlamlı şekilde düşüktü (p <0,001). Hastalarımızda en sık bildirilen semptom karın ağrısıydı (%41,5). Histopatolojik incelemeye göre H.pylori hastalarımızın % 24.5'inde (n=136) pozitifti. Hastaların % 28.6'sı (n=159) özofajit ve % 55.4'ü (n=308) kronik gastrit tanısı aldı. H.pylori tanısı alan hastaların % 30.1'inde özofajit saptandı ve tüm kronik gastrit hastalarının H.pylori için pozitif olduğu belirlendi (p<0,001). H.pylori negatif ve pozitif kronik gastritli hasta grupları arasında ortalama B12 vitamini düzeyleri açısından istatistiksel olarak anlamlı bir fark bulunmadı. Ancak H.pylori pozitif grupta (382,93±245,50 pg/mL) ölçülen ortalama B12 vitamin düzeyi istatistiksel olarak anlamlı şekilde H.pylori negatif gruptan (467,90±305,36 pg/mL) düşük olduğu belirlendi (p=0,028). Bununla beraber H.pylori negatif ve pozitif gruplar arasında ortalama demir düzeyleri açısıdan anlamlı bir fark bulunmadı.*
Sonuç: *Her ne kadar kronik gastritli tüm çocuklar H.pylori için pozitif olsa da, çalışmamızda H.pylori enfeksiyonu ile özofajit ve demir eksikliği arasında ilişki kurulamamıştır. Bunlara ek olarak, H.pylori enfeksiyonunun B12 vitamini eksikliği için bir risk faktörü olduğu gösterilmiştir.*

Anahtar kelimeler: *Helicobacter pylori, gastrit, Vitamin B12, özofajit*

Corresponding Author:
✉ hasretayyildiz@yahoo.com

H. Ayyildiz Civan 0000-0002-5604-9722

INTRODUCTION

H.pylori is a spiral-shaped, microaerophilic, noninvasive and gram-negative bacteria that colonize gastric epithelial cells with facilitation of flagellum-associated proteins, adhesins, and chemotactic activities [1]. It is the most common chronic bacterial infection worldwide particularly in developing countries (75-90%) [2]. *H.pylori* infection is generally acquired in early infancy particularly before the age of 10 years and persists throughout entire life without treatment [3]. The colonization of bacteria in stomach triggers gastric inflammation. Production of heat shock protein, urease and antigen presented by bacteria lead to activation of T-cells and increase in the levels of certain proinflammatory cytokines which results in gastric mucosal damage [4]. Thus, local and systemic immune responses of the host against *H.pylori* is related with chronic gastritis, peptic ulcer, mucosa-associated tissue lymphoid lymphoma and gastric cancer [5].

H.pylori is widely accepted as the major etiological factor for gastritis and peptic ulcer [6]. Although *H.pylori* infections are mostly asymptomatic, majority of patients develop acute gastritis which alters into chronic gastritis. In addition, childhood *H.pylori* infections are frequently associated with antral gastritis [7].

Recently, childhood *H.pylori* infections have been also associated with other digestive disorders such as gastroesophageal reflux disease. Moreover limited number of published data with controversial results, have indicated the presence of an inversely relation of *H.pylori* with esophagitis severity [8,9]. Besides, *Helicobacter pylori* gastritis has been linked to malabsorption and has been demonstrated as the potential causative agent of vitamin B12 deficiency in numerous studies [10,11]. Therefore, we aimed to evaluate the relationship between *Helicobacter pylori* gastritis and vitamin B12 status as well as to determine the prevalence of esophagitis in children with *H.pylori* infections.

MATERIALS and METHODS

This study was performed with the Institutional Review Board protocol approval date 18/02/2019 and number 2019/13 in Istanbul Dr. Sadi Konuk Training and Research Hospital, Department of Pediatric Gastroenterology, Hepatology and Nutrition, between January 2017 and June 2018. A total number of 556 children, aged between 0-18 years, who underwent eso-gastro-duodenoscopy were evaluated retrospectively. The diagnosis of *H.pylori inf*ection, esophagitis, and gastritis was made based on histopathologic examination. Patients were divided into *H.pylori* (+) and *H.pylori* (-) groups. Patients' demographic characteristics, physical examination, imaging and laboratory findings were recorded.

Blood cell count analysis was performed using patients' venous blood samples. Haematological parameters were analysed using a hematology analyser (Cell-Dyne 3700, Abbott, Abbott Park, IL, USA). Biochemical analysis was performed with serum samples using electro-chemiluminescence immunoassay on Beckman Coulter Unicel DXI 800 analyzer. Serum vitamin B12 analysis was performed using an immunodiagnostic system (Siemens, Advia Centaur xp, Germany) at a normality level of 220 pg/ml.

Statistical analysis

All the data were analysed with SPSS (Statistical Package for the Social Sciences) software for Windows (v21.0; IBM, Armonk, NY, USA). Individual and aggregate data were summarized using descriptive statistics including mean, standard deviations, medians (min-max), frequency distributions and percentages. Normality of data distribution was verified by Kolmogorov-Smirnov test. Comparison of the variables with normal distribution was made using Student t test. For the intergroup comparisons of variables which were not normally distributed, the Mann Whitney and Kruskal Wallis tests were performed. Evaluation of categorical variables was performed using chi-square test. P-Values of <0.05 were considered statistically significant.

RESULTS

Patients included in this study consisted of 310 (55.8%) females, and 246 (44.2%) males. Mean age of all patients (n=556) was 10.22±4.87 months (range: 0-18 years). In addition, the mean age was significantly lower in male patients (9.43±5.69) than

Table 1. Comparison of hronic gastritis and esophagitis rates in patients with *H.pylori*.

	Clinical Variables	*H.pylori* Negative n (%)	*H.pylori* Positive n (%)	p-value
Esophagitis	Absent	302 (71.9%)	95 (69.9%)	0.645
	Present	118 (28.1%)	41 (30.1%)	
Chronic gastritis	Absent	248 (59.6 %)	0 (0.0%)	0.000*
	Present	172 (41.0%)	136 (100.0)	

** = p<0.05 statistically significant.*

Table 2. Comparison of laboratory findings between *H.pylori* negative and positive groups in patients diagnosed with chronic gastritis.

Laboratory results	*H.pylori* Negative (Mean±SD)	*H.pylori* Positive (Mean±SD)	P-value
Iron (ug/dL)	64.83±48.75	68.62±35.75	0.230
Hemoglobin (g/dL)	12.46±1.32	12.74±1.54	0.050*
MCV (fL)	85.46±53.38	80.81±5.41	0.860
RDW (%)	13.64±1.98	13.52±1.60	0.848
PLT ($x10^9$/L)	303.8±897.5	332.4±985.0	0.058
Vitamin B12 (pg/mL)	431.7±263.4	382.9±245.5	0.171

** = p<0.05 statistically significant.*

Table 3. The comparison of laboratory findings between esophagitis- negative and positive groups in *H.pylori* positive cases.

Laboratory results	Esophagitis Negative (Mean±SD)	Esophagitis Positive (Mean±SD)	P-value
Iron (ug/dL)	66.44±33.96	73.71±40.19	0.606
Hemoglobin (g/dL)	12.54±1.56	13.19±1.40	0.121
MCV (fL)	80.41±5.39	81.70±5.45	0.496
RDW (%)	13.58±1.70	13.39±1.39	0.734
PLT ($x10^9$/L)	332.0±973.0	333.1±102.8	0.697
Vitamin B12 (pg/mL)	389.38±261.74	361.27±187.36	0.877

female patients (11.10±5.32) (p<0.001).

The most common symptom reported in our patients was abdominal pain seen in 41.5 % (n=220) of the cases, followed by abdominal pain + nausea (n=118, 22.3%), vomiting (n=57, 10.8%), and weight loss + sour liquid rushing into the mouth + puffiness + dysphagia (n=45, 8.5%) respectively. According to the histopathological examination *H.pylori* was positive in 24.5% (n=136) of our patients. In addition, 28.6% (n=159) of the patients were histopathologically diagnosed with esophagitis and 55.4% (n=308) of them with chronic gastritis. In our study, esophagitis was detected in 30.1% of patients diagnosed with *H.pylori*-positive and 28.1% of *H.pylori* -negative patients (p=0,645). Moreover, all of our patients with chronic gastritis were found to be positive for *H.pylori* (p<0,001) (Table 1).

According to the evaluation of laboratory findings; the mean values of: iron, hemoglobin, MCV, RDW, vitamin B12 and PLT in the study population were 70.67±42.40 ug/dl, 12.62±1.39 g/dL, 82.48±30.85 fL, 13.50±1.75 %, 448.11±294.28 pg/mL, and 315.8±103,8 $x10^9$/L, respectively. The comparison of laboratory findings between *H.pylori* -negative and positive groups in patients diagnosed with chronic gastritis is presented in Table 2. Mean level of hemoglobin was found to be statistically higher in *H.pylori* -positive group (12,74±1,54) than *H.pylori* -negative group (12,46±1,32) (p=0.05). Additionally, there were no statistically significant differences in mean serum levels of iron, MCV, RDW, vitamin B12 and POLİTİKA between *H.pylori* -negative and positive groups (p>0,05) (Table 2).

Furthermore, the comparison of laboratory findings between esophagitis- negative and positive groups in *H.pylori* -positive cases is presented in Table 3. Any statistically significant differences were found in mean serum levels of iron, hemoglobin, MCV, RDW, vitamin B12 and PLT between esophagitis -negative and positive groups (p>0,05) (Table 3).

Additionally, only *H.pylori*- positive and negative cases were compared according to the laboratory findings; the mean serum levels of vitamin B12 measured in the *H.pylori* -positive group (382,93±245,50 pg/mL) was statistically lower than the *H.pylori* -negative group (467,90±305,36 pg/mL) (p=0,028) (Table 4).

Table 4. Comparison of laboratory findings according to H.pylori diagnosis.

Laboratory results	*H.pylori* Negative (Mean±SD)	*H.pylori* Positive (Mean±SD)	P-value
Iron (ug/dL)	71.28±44.24	68.62±35.75	0.996
Hemoglobin (g/dL)	12.58±1.34	12.74±1.54	0.120
MCV (fL)	82.94±34.75	80.81±5.41	0.929
RDW (%)	13.50±1.79	13.52±1.60	0.515
PLT ($x10^9$/L)	311.1±104.0	332.4±985.0	0.064
Vitamin B12 (pg/mL)	467.90±305.36	382.93±245.50	0.028*

** = p<0.05 statistically significant.*

DISCUSSION

Helicobacter pylori infection is the most common infection worldwide and it is estimated that approximately half of the world's population is infected with Helicobacter pylori. Since majority of the infected patients are asymptomatic, it seems difficult to eradicate *H.pylori* infection. Moreover, *H.pylori* is commonly responsible for etiology of gastritis [7]. Development of chronic gastritis depends on bacterial virulence factors, host and environmental factors [3]. In a meta analysis, Weck et al. concluded that a very strong association existed between *H.pylori* infection and chronic gastritis by evaluating 66 relevant articles [12]. Similarly, Langner et al. reported chronic active gastritis in all children with *H.pylori* infection in their study investigating 132 gastric biopsies [13]. In accordance with these published data, in our study all of our patients with chronic gastritis were found to be positive for *H.pylori.*

Although a link has been identified between decreased serum iron status and childhood *H.pylori* infection, it is debated in published data whether *H.pylori* infection causes iron deficiency or iron deficiency anemia [14]. In a study, Vendt et al. found no relationship between *H.pylori* infection and iron deficiency in 363 children with *H.pylori* infection [15]. In addition, older age is documented to be more responsible for iron deficiency [15,16]. Supportively in our study, no statistically significant differences were found between *H.pylori* -negative and positive groups according to the mean serum iron levels.

It is appears to be controversy in the limited number of published data whether *Helicobacter pylori* infection is protective or triggering factor for gastroesophageal reflux disease. Prevalence of gastroesophageal reflux disease reported to be increased as a result of decrease in the *Helicobacter pylori* incidence [9]. Daugule et al. reported a higher prevalence of *H.pylori* in patients with reflux oesophagitis among 130 children [17]. Similarly, Moon et al. concluded that *Helicobacter pylori* infection is a risk factor for reflux oesophagitis development [18]. On the contrary, Emiroglu et al. found no significant association between the prevalence of *H.pylori* infection and reflux oesophagitis or the oesophagitis severity in 206 children [19]. Supportively, Zagorski et al. compared 308 children with reflux esophagitis and 418 patients with chronic gastritis without reflux esophagitis. *Helicobacter pylori* infection was detected in 44.5% of children with reflux esophagitis and it was not significantly differed in patients without reflux esophagitis. Researchers concluded that the development of reflux esophagitis was not associated with *Helicobacter pylori* infection [9]. In accordance with these data, 28.6% (n=159) of our patients were histopathologically diagnosed with esophagitis. Esophagitis was detected in 30.1% of patients diagnosed with *H.pylori* and 28.1% in *H.pylori* negative patients. Thus, *Helicobacter pylori* infection was not significantly effected prevalence of esophagitis in our study.

Although various conditions may lead to vitamin B12 deficiency, it is frequently caused by chronic gastritis. *H.pylori*-induced gastritis damages the parietal cells which are essential for vitamin B12 absorption. Kaptan et al. reported *Helicobacter pylori* infection in 56% of patients with pernicious anemia. Researchers demonstrated a post-treatment improvement of vitamin B12 in 40% of the patients [20]. In a study by Sarari et al. which, compared *H.pylori* -infected and non-infected patients consisting of 60 children, mean levels of vitamin B12 were 207.7+21.9 and 419.7+39.8, respectively (p=0,000). Vitamin B12 was found to be lower than 200 pg/ml in 67.4% of patients with *H.pylori* infection [21]. Similarly, Akcam et al. reported mean levels of vitamin B12 as 303±135 pg/mL in *Helicobacter pylori* positive and 393±166 pg/mL *Helicobacter pylori* -negative groups in a study included 50 children aged 5-18 years [22]. In accordance with these data, the mean serum level of vitamin B12 measured in the *H.pylori* -positive group

(382,93±245,50 pg/mL) was statistically lower than the *H.pylori* -negative group (467,90±305,36 pg/mL) in present study.

In conclusion, although all children with chronic gastritis were positive for *H.pylori*, our findings have not provided any evidence for a link between esophagitis, iron deficiency and *H.pylori* infection. In addition, *H.pylori* infection has been demonstrated to be a risk factor for vitamin B12 deficiency. In this respect a rapid, accurate diagnosis and an effective treatment approach are crucial to achieve appropriate management of *H.pylori* infection in children.

Acknowledgements
Author declare that there is no conflict of interest. Any specific grant was not received for this research from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics Committee Approval: This study was performed with the Institutional Review Board protocol approval date 18/02/2019 and number 2019/13 in Istanbul Dr. Sadi Konuk Training and Research Hospital, Department of Pediatric Gastroenterology, Hepatology and Nutrition, between January 2017 and June 2018.
Conflict of Interest: None
Funding: None
Informed Consent: Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Windsor HM, O'Rouke J. Bacteriology and taxonomy of Helicobacter pylori. Gastroenterol Clin North Am. 2000;29(3):633-48. https://doi.org/10.1016/S0889-8553(05)70135-7
2. Paul B, Adimoolam S, Qureshi MJ. A Review of Helicobacter pylori infection diseases, antibiotic resistance and diagnosis. Asian J Pharm Clin Res. 2018;11(12):566-71. https://doi.org/10.22159/ajpcr.2018.v11i12.24745
3. Sýkora J, Rowland M. Helicobacter pylori in pediatrics. Helicobacter. 2011;16:59-64. https://doi.org/10.1111/j.1523-5378.2011.00882.x
4. Testerman TL, Morris J. Beyond the stomach: an updated view of Helicobacter pylori pathogenesis, diagnosis, and treatment. World J Gastroenterol. 2014;20(36):12781-808. https://doi.org/10.3748/wjg.v20.i36.12781
5. McColl KE. Helicobacter pylori infection. N Engl J Med. 2010;362(17):1597-604. https://doi.org/10.1056/NEJMcp1001110
6. Pacifico L, Anania C, Osborn JF, Ferraro F, Chiesa C. Consequences of Helicobacter pylori infection in children. World J Gastroenterol. 2010;16(41):5181-94. https://doi.org/10.3748/wjg.v16.i41.5181
7. Watari J, Chen N, Amenta PS, Fukui H, Oshima T, Tomita T, et al. Helicobacter pylori associated chronic gastritis, clinical syndromes, precancerous lesions, and pathogenesis of gastric cancer development. World J Gastroenterol. 2014;20(18): 5461-73. https://doi.org/10.3748/wjg.v20.i18.5461
8. Richter JE. Effect of Helicobacter pylori eradication on the treatment of gastro-oesophageal reflux disease. Gut. 2004;53(2):310-1. https://doi.org/10.1136/gut.2003.019844
9. Zagorski SE, Nazarenko ON. Reflux esophagitis and Helicobacter pylori: Is there an association in children?. Progress in Health Sciences. 2014;4(1):41-6.
10. Nizami MA, Mirza SA, Khan FA. Frequency of Vitamin B12 Deficiency in patients with Helicobacter pylori gastritis. Pak Armed Forces Med J. 2012;62(2):203-5. Available from: https://www.pafmj.org/index.php/PAFMJ/article/view/1663/1432
11. Kadhim G, Shikh M, Omar H, Ismail A. Vitamin B12 Deficiency in Helicobacter pylori Infected Patients. Open Access Library Journal. 2018;5(3):1-4. https://doi.org/10.4236/oalib.1104172
12. Weck MN, Brenner H. Association of Helicobacter pylori infection with chronic atrophic gastritis: Meta-analyses according to type of disease definition. Int J Cancer. 2008;123(4):874-81. https://doi.org/10.1002/ijc.23539
13. Langner M, Machado RS, Patrício FR, Kawakami E. Evaluation of gastric histology in children and adolescents with Helicobacter pylori gastritis using the Update Sydney System. Arq Gastroenterol. 2009;46(4):328-32. https://doi.org/10.1590/S0004-28032009000400015
14. Ashorn M, Ruuska T, Mäkipernaa A. Helicobacter pylori and iron deficiency anaemia in children. Scand J Gastroenterol. 2001;36(7):701-5. https://doi.org/10.1080/003655201300191950
15. Vendt N, Kool P, Teesalu K, Lillemäe K, Maaroos HI, Oona M. Iron deficiency and Helicobacter pylori infection in children. Acta Paediatr. 2011;100(9):1239-43. https://doi.org/10.1111/j.1651-2227.2011.02281.x
16. Huang SC, Yang YJ, Cheng CN, Chen JS, Lin CH. The etiology and treatment outcome of iron deficiency and iron deficiency anemia in children. J Pediatr Hematol Oncol. 2010;32(4):282-5. https://doi.org/10.1097/MPH.0b013e3181d69b2b
17. Daugule I, Rumba I, Alksnis J, Ejderhamn J. Helicobacter pylori infection among children with gastrointestinal symptoms: a high prevalence of infection among patients with reflux oesophagitis. Acta Paediatr. 2007;96(7):1047-9. https://doi.org/10.1111/j.1651-2227.2007.00329.x
18. Moon A, Solomon A, Beneck D, Cunningham-Rundles S. Positive association between Helicobacter pylori and gastroesophageal reflux disease in children. J Pediatr Gastroenterol Nutr. 2009;49(3):283-8. ttps://doi.org/10.1097/MPG.0b013e31818eb8de
19. Emiroglu HH, Sokucu S, Suoglu OD, Gulluoglu M, Gokce S. Is there a relationship between Helicobacter pylori infection and erosive reflux disease in children?. Acta Paediatr. 2010;99(1):121-5. https://doi.org/10.1111/j.1651-2227.2009.01512.x
20. Kaptan K, Beyan C, Ural AU, Cetin T, Aycu F, Gulsen M, et al. Helicobacter pylori: is it a novel causative agent in Vitamin B12 deficiency? Arch Intern Med. 2000;160(9):1349-53. https://doi.org/10.1001/archinte.160.9.1349
21. Sarari AS, Farraj MA, Hamoudi W, Essawi TA. Helicobacter pylori, a causative agent of vitamin B12 deficiency. J Infect Dev Ctries. 2008;2(5):346-9. https://doi.org/10.3855/jidc.194
22. Akcam M, Ozdem S, Yilmaz A, Gultekin M, Artan R. Serum ferritin, vitamin B 12, folate, and zinc levels in children infected with Helicobacter pylori. Dig Dis Sci. 2007;52(2):405-10. https://doi.org/10.1007/s10620-006-9422-8.

Original Article

Med J Bakirkoy 2020;16(2):125-31
doi: 10.5222/BMJ.2020.70299

Medical Journal of Bakirkoy

Carpal Tunnel Release with a Minimally Invasive Surgical Approach at the Proximal of the Distal Wrist Crease: The Evaluation of the Efficacy of the Technique with Clinical and Magnetic Resonance Imaging

Minimal İnvaziv Cerrahi Yaklaşım ile Distal El Bilek Kırışıklığının Proksimalinde Karpal Tünel Gevşetmesi: Tekniğin Etkinliğinin Klinik ve Manyetik Rezonans Görüntüleme ile Değerlendirilmesi

Ahmet Yilmaz

Department of Orthopedics and Traumatology, Adana City Training and Research Hospital, University of Health Sciences, Adana, Turkey

Received: 02 February 2019 / **Accepted:** 20 June 2019 / **Publication date:** 26 June 2020

Cite as: Yilmaz A. Carpal tunnel release with a minimally invasive surgical approach at the proximal of the distal wrist crease: The evaluation of the efficacy of the technique with clinical and magnetic resonance imaging. Med J Bakirkoy 2020;16(2):125-31.

ABSTRACT

Objective: *In this prospective study, we aimed to evaluate the efficacy of minimally invasive surgical technique at the proximal of the distal wrist crease for carpal tunnel release with clinical and pre- and postoperative magnetic resonance imaging (MRI) findings.*
Method: *Carpal tunnel release was performed on 102 wrists of 65 patients with a mini-incision at the proximal of the distal wrist crease. Clinical assessment of the patients was made with the Boston Carpal Tunnel Questionnaire. Preoperative and postoperative third month MRIs were examined.*
Results: *There was a clinically significant difference between the preoperative and postoperative third month results (p<0.001). The findings from the preoperative MRIs have significantly decreased in number in the postoperative MRIs (p<0.001). None of the patients experienced pillar pain or scar tissue sensitivity. No resurgery was required.*
Conclusion: *Carpal tunnel release with a minimally invasive approach performed at the proximal of the distal wrist crease is an efficient method. Early return to physiological activities has increased the patient comfort.*

Keywords: *carpal tunnel syndrome, decompression, minimally invasive surgical procedures, wrist, magnetic resonance imaging*

ÖZ

Amaç: *Bu prospektif çalışmada, karpal tünel gevşetmesi için distal el bileği kırışıklığı proksimalinde minimal invasiv cerrahi tekniğin etkinliğini klinik ve pre- ve postoperatif manyetik resonans görüntüleme (MRG) bulguları ile değerlendirmeyi amaçladık.*
Yöntem: *65 hastanın 102 eline, distal el bileği kırışıklığı proksimalinde yapılan mini insizyon ile karpal tünel gevşetmesi uygulandı. Olguların klinik değerlendirilmesi Boston Karpal Tünel Anketi ile yapıldı. Preoperatif ve postoperatif 3. ayda MRG incelendi.*
Bulgular: *Klinik değerlendirmede ameliyat öncesi ve ameliyat sonrası 3. ay değerleri arasında anlamlı fark vardı (p<0.001). Preoperatif MRG'de tesbit edilen bulgular postoperatif MRG'de anlamlı oranda azaldı (p<0.001). Hiçbir hastada pillar ağrısı ve skar dokusu hassasiyeti görülmedi. Yeniden ameliyat gerekmedi.*
Sonuç: *Distal el bileği kırışıklığı proksimalinde, mini invasiv yaklaşımla uygulanan karpal tünel gevşetmesi etkin bir yöntemdir. Hastaların fizyolojik aktivitelerini erken başarmaları yaşam konforlarını artırmıştır.*

Anahtar kelimeler: *karpal tünel sendomu, dekompresyon, minimal invasiv cerrahi işlemler, el bileği, manyetik rezonans görüntüleme*

Corresponding Author:
✉ ahmetyilmaz-dr@hotmail.com

A. Yilmaz 0000-0002-4015-5045

INTRODUCTION

Carpal tunnel syndrome (CTS) is the entrapment neuropathy of the median nerve due to the increased pressure in the carpal tunnel. It is the most common chronic compression neuropathy of the peripheral nerves, with a prevalence of 4% in the general population [1]. Increasing pain at nights and paraesthesia on the area of the hand innervated by the median nerve are the most characteristic complaints [2]. If the etiology of CTS cannot be identified, then it has been defined as primary (idiopathic) CTS in vast majority of the cases [3].

Conventional surgical treatment of CTS is usually performed with standard open technique, limited incision and endoscopic procedures [4]. Surgical decompression of the carpal tunnel with a longitudinal incision results in a minimal rate of complications [1]. However, carpal tunnel release via standard open surgery has been reported to result in delayed wound healing, scar tissue sensitivity, pillar pain and late return to work [1,5-7]. Mini open palmar incisions, mini open transverse wrist incisions and endoscopic procedures allow for faster wound healing and return to work whereas scar tissue sensitivity and pillar pain will be still present [5,7-9] and endoscopic procedures have led to incomplete release of the flexor retinaculum and iatrogenic nerve injuries [10-14]. On the other hand, carpal tunnel release via a mini longitudinal incision made to the proximal of the wrist crease has been discussed in a limited number of studies [15,16]. We performed decompression of the carpal tunnel with a mini-incision at the proximal of the distal wrist crease, in an attempt to avoid the pillar pain and scar tissue sensitivity seen following CTS surgery and to achieve patients' early return to their daily activities. We evaluated the efficacy of our method with clinical and pre- and postoperative magnetic resonance imaging (MRI) findings.

MATERIALS and METHODS

In this prospective study, 65 consecutive patients (63 females, 2 males; median age: 49.1 years, range: 37 to 68 years) with CTS who had undergone carpal tunnel decompression at the orthopedics clinic of our tertiary research and training hospital between October 2010 and December 2016 and followed up for 12 months were evaluated. Approval from the local research ethics committee was obtained before the study. For a total of 102 hands carpal tunnel surgeries were performed; 37 patients (56.9%) underwent bilateral and 28 patients (43.1%) unilateral releases. Patients with diabetes mellitus, osteoarthritis, autoimmune disease, space occupying lesion on the wrist, cervical radiculopathy, tuberculosis tenosynovitis, or those who were pregnant or had a history of wrist trauma or carpal tunnel surgery were excluded. Existence of recurring or persistent paresthesia at the innervation area of the median nerve, history of pain, and disturbed sleep due to paresthetic complaints or pain were investigated for clinical diagnosis. Positive physical examination findings (Tinel's sign, Phalen test, carpal compression test, thumb abduction and opposition weakness and thenar atrophy) were investigated. Clinical diagnosis was made in existence of the combination of three or more of these symptoms and findings [5]. In clinical staging of the CTS; cases with subjective symptoms alone were considered to be in the 'early stage', cases with combination of subjective symptoms and positive diagnostic test results for CTS were considered to be in the 'intermediary stage', and cases with weakness in abduction and opposition of the thumb and thenar atrophy in addition to the symptoms and positive diagnostic test results for CTS were considered to be in the 'advanced stage'. Nerve conduction studies (NCS) for all hands clinically diagnosed with CTS were performed. NCS grading was done according to Bland's criteria from "very mild" through "extremely severe" [17]. Electrophysiological studies were repeated in cases initially diagnosed as early stage of CTS but without any response to three months-of conservative treatment. Among these cases, patients whose disease proceeded to the advanced stage during clinical evaluation and nerve conduction studies, those in the intermediary stage who did not respond to three months-of conservative treatment and cases with an initial diagnosis of 'advanced stage CTS ' were included in the study.

All patients scheduled for surgery were evaluated using the Boston Carpal Tunnel Questionnaire (BCTQ), defined by Levine et al. [18], which included the symptom severity and functional capacity scales. MRIs of all hands diagnosed with CTS were obtained within one week before surgery and checked for the

presence of an increase in the signal intensity of the median nerve, palmar bowing of the flexor retinaculum or nerve flattening. All patients gave written informed consent before surgery. The surgery was performed under local anesthesia in 93 and general anesthesia in 9 hands, with a pneumatic tourniquet wrapped around the arms. A curved incision on the ulnar side of the thenar crease, starting from 2 cm proximal to the distal wrist crease and ending at the same crease, was made on the medial aspect of the palmaris longus (Figure 1). After observing the fusion of the palmaris longus muscle with the flexor retinaculum, the elevators were placed in a fashion that the palmaris longus muscle would be on the ulnar side. The proximal aspect of the transverse carpal ligament and the entry of the median nerve into the tunnel were exposed through the palmaris longus and flexor carpi radialis tendons. With a blunt dissection, using scissors and a periosteal elevator with a 4 mm-wide blunt tip, the carpal ligament was released on the volar and dorsal sides and along the line thought to pass through the radial aspect of the fourth finger. The elevators were placed accordingly and the carpal ligament was fully exposed in a proximal to distal orientation (Figure 2). The distal aspect of the carpal ligament was clearly exposed. Using a right angle clamp, the distal part of the carpal ligament was released from the palmar aponeurosis with a blunt dissection. The periosteal elevator was inserted through the carpal tunnel entrance and advanced distally and adjacent to the carpal ligament. Thus, the periosteal elevator was placed in a fashion to protect the median nerve. Attention was paid not to position the median nerve and palmar artery at the distal aspect of the carpal ligament incision to be made. Using a curved Mayo scissors and keeping the curved shanks on the ulnar side, the transverse carpal ligament was cut off the ulnar side (Figure 3). The skin was closed and the hand and the wrist were bandaged (Figure 4). For bilateral CTS cases the same procedure was applied. The patients were discharged the same day.

The patients were instructed to use their hands for eating, dressing, and combing their hair the same day and were asked to meet their hygienic needs after putting on big gloves with assistance. In patients that underwent unilateral and bilateral carpal tunnel decompression time intervals elapsed till they used their hands actively were recorded and the difference between the two groups was compared using the chi-square (X^2) test ($p<0.05$). The BCTQ was applied to all patients on the postoperative third month and their wrist MRIs were taken. Pre-, and postoperatve BCTQ scores and MRI findings were compared. The BCTQ was repeated at the postoperative 6th and 12th month follow-ups. The repeated measures ANOVA was performed to determine the presence of any differences among the preoperative and postoperative 3rd, 6th and 12th month BCTQ scores in terms of symptom severity and functional capacity scales ($p<0.05$). Hands with an increase in

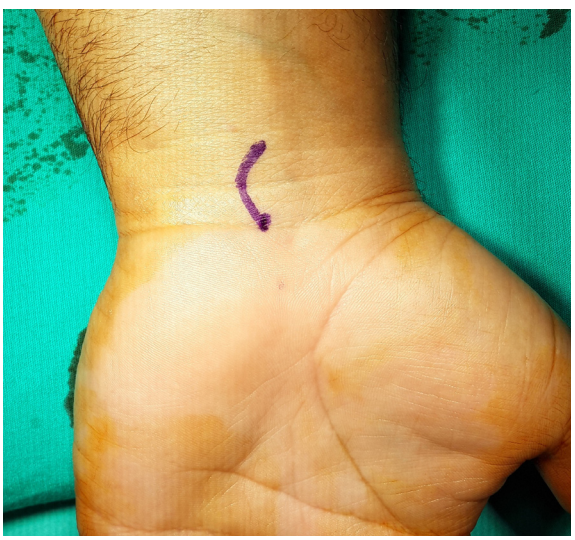


Figure 1. Mini-incision line over the wrist, with ulnarly curved.

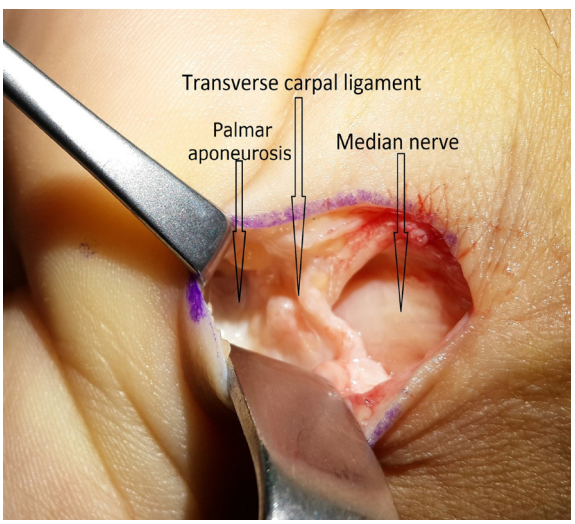


Figure 2. The picture shows the fully exposed transverse carpal ligament and the entry of the median nerve into the carpal tunnel.

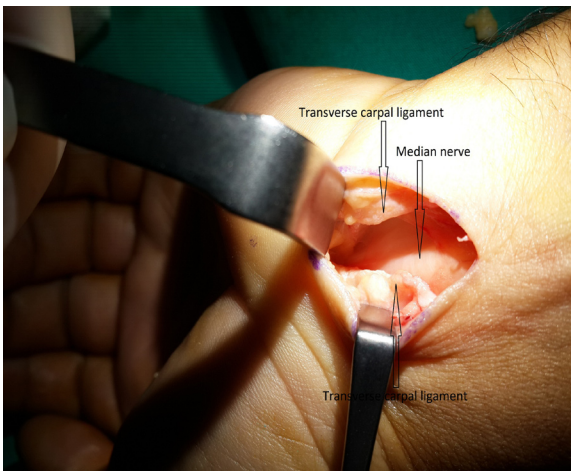


Figure 3. Decompression of the carpal tunnel following the release of the transverse carpal ligament.

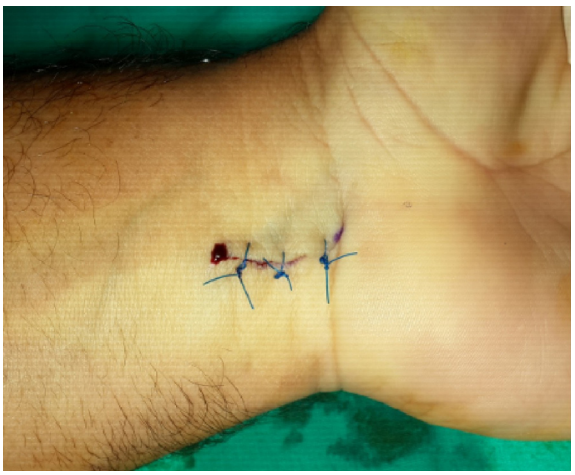


Figure 4. Postoperative appearance .

the signal intensity of the median nerve and with persistence of palmar bowing of the flexor retinaculum and flattening of the median nerve revealed in the MR images obtained at the third month, were noted. Differences between the preoperative and postoperative MRI findings were compared using the chi-square (X^2) test ($p<0.05$).

RESULTS

All patients had nocturnal pain and paresthetic complaints before surgery. In clinical examination, the Phalen test was positive in 91 (89.2%), Tinel's test in 82 (80.4%) and carpal tunnel compression test in 84 (82.4%) hands. Thenar atrophy was observed in 11 (10.8%) hands. Intermediary stage CTS in 76 (74.5%) and advanced stage CTS in 26 (25.5%) hands were diagnosed following preoperative clinical and electrophysiological staging of the patients. The outcomes of the preoperative clinical staging and electrophysiological staging were the same in all patients. Pain and paresthetic complaints were completely resolved in 97 of the 102 hands (95.1%) at the postoperative third month follow-up. There was a statistically significant difference between the preoperative and postoperative third month results of the Boston carpal tunnel symptom severity and functional capacity scale scores ($p<0.001$). Postoperative 6th and 12th month BCTQ scores were even lower (Table 1).

All unilateral carpal tunnel decompression cases were able to eat, dress, meet their hygienic needs, and wear gloves on the day of surgery. Of the 37 bilateral CTS cases, 26 (70.3%) were able to eat, dress, meet their hygienic needs and wear gloves with assistance on the day of surgery and the remaining 11 patients could achieve the same functions on

Table 1. Boston carpal tunnel symptom severity and functional capacity scale scores (Mean±SD).

Operated wrist (n=102)	± Standard deviation	Test statistic	p	Test	Difference
Preoperative and postoperative follow-up symptom severity scales					
Preoperative symptom severity scale	3.685±0.302	F=8.327	<0,001	Repeated measures	1-2, 1-3, 1-4
Symptom severity scale at the postoperative 3rd month	1.180±0.130				
Symptom severity scale at the postoperative 6th month	1.128±0.103			ANOVA	
Symptom severity scale at the postoperative 12th month	1.099±0.085				
Preoperative and postoperative functional capacity scales					
Preoperative functional capacity scale	3.497±0.458	F=3.239	<0,001	Repeated measures	1-2, 1-3, 1-4
Functional capacity scale at the postoperative 3rd month	1.266±0.153				
Functional capacity scale at the postoperative 6th month	1.83±0.131			ANOVA	
Functional capacity scale at the postoperative 12th month	0.125±0.118				

Table 2. MRI findings before surgery and at the postoperative third month (%).

Operated wrist (n=102)	Number	Percentage	Test Statistic	p	Test
Increase in signal intensity of the median nerve					
Preoperative	96	94.1%	X^2=13,32	<0,000	Chi-square test
Postoperative	4	3.90%			
Bowing of the median nerve					
Preoperative	64	62.7%	X^2=36,02	<0,000	Chi-square test
Postoperative	0	0%			
Flattening of the median nerve					
Preoperative	54	52.9%	X^2=13,24	<0,000	Chi-square test
Postoperative	13	12.7%			

the second postoperative day. Patients who underwent unilateral carpal tunnel release could use their hands actively after a median period of 12.7 (range: 11 to 23) days while bilateral cases could actively use their hands after a median period of 13.1 (range: 11 to 34) days. The difference between the unilateral and bilateral groups in terms of time to using their hands actively was statistically insignificant (p>0.05). The improvement in the postoperative third month MRI results of all three symptoms were statistically significant (p<0.001) (Table 2). None of the patients had pillar pain or scar tissue sensitivity. No neurological or vascular complications were observed in any patient. No resurgery was required.

DISCUSSION

Conservative treatment has been necessitated for the early and intermediary stage CTS patients. In CTS cases initially diagnosed as advanced stage and where conservative treatment yields no results, surgical release of the transverse carpal ligament is consensually recommended. Mini palmar incision and endoscopic procedures have gained popularity with time over the standard open surgical carpal tunnel release [5,7]. The leading reason for a revision surgery is irresolution of the complaints due to incomplete release of the flexor carpal ligament during primary surgery [7,11.12].

The efficacy of the surgical treatment of CTS was evaluated with clinical symptoms and findings in some studies [18,19]. In some other studies, radiological examinations such as MRI [20] or ultrasonography [21,22] were utilized to support the clinical findings. MRI has been defined as a reliable technique in validating the incomplete release of the flexor retinaculum in postoperative assessments [23]. Electrophysiological studies have been employed to assist with the clinical evaluations during postoperative follow-up [24,25]. In clinical evaluation of the response to treatment in CTS, the American Academy of Orthopaedic Surgeons (AAOS) have recommended the use of the BCTQ, defined by Levine et al. [18] which includes the symptom severity and functional capacity scales [26]. Levine et al. performed the clinical evaluation of 38 CTS patients, followed up for a median period of 14 months using the BCTQ scoring system [18]. In their study, the mean preoperative symptom severity score of 3.4 and functional capacity score of 3 were recorded as 1.9 and 2, respectively, in the postoperative period. In another study, the postoperative BCTQ scale scores were found significantly lower [19]. In a comparison of the clinical results of carpal tunnel release performed with standard open surgery versus mini open surgery, postoperative 6th and 12th month results of the mini open surgery were significantly better [7]. With our significantly better postoperative third month results in comparison to the preoperative BCTQ scores, we can assert that clinical recovery in CTS is possible within the first three months. In our opinion, clinical evaluation should suffice in postoperative follow-up. The significant difference between our pre- and postoperative MRI findings can be considered important since it indicates the efficacy of our technique.

The release of the flexor retinaculum with the standard incision technique results in a longer incision line, pillar pain and scar tissue sensitivity that might last up to two years or a delayed return to daily activities [1]. The prevalence of scar tissue sensitivity

was reported as 10%, pillar pain as 5% and recurrence as 3.6% in the postoperative period [7]. Recently, mini open palmar incisions [5,8,24] and endoscopic release procedures [5,19] have been employed to avoid the unfavorable results of the standard open carpal tunnel surgery and a decrease was observed in the postoperative morbidity rates and in the time to return to work [1,7]. The time to return to work reportedly vary from three to six weeks after standard open carpal tunnel surgery, however it is merely 10 to 21 days following mini open and endoscopic surgery [5,7,14]. Carpal tunnel release procedures using both endoscopic technique, and mini palmar incision were reported to decrease the morbidity rate whereas pillar pain and scar tissue sensitivity rates ranging from 3.1 to 33% were reported with the same procedures [5,7,8]. In addition, incomplete release of the carpal ligament in 0.5 to 1.2% [10-12], iatrogenic nerve injuries in 0.007 to 10% [10-14] and converting to open surgery due to failure in distinguishing the anatomical structures in 0.5 to 3.4% of the cases [10,12] were reported following endoscopic carpal decompression in various studies. Practicing the technique is challenging and has a long learning curve [27].

In some studies, carpal tunnel release was performed via transverse incisions performed at the wrist level [9,28]. In a study comparing limited open carpal release with mini open transverse incision at the distal wrist crease, there was no difference between both groups in terms of functional recovery, scar tissue sensitivity, pillar pain and recurrence rates [9]. In another study where conventional longitudinal incision and transverse mini incision made at 1 cm proximal to the wrist crease were compared, less pillar pain and scar tissue sensitivity was reported after carpal ligament release performed via transverse incision. The authors attributed the low incidence of pillar pain following the transverse incision performed at the proximal part of the flexor ligament to making the incision outside the pressure area of the hand [28]. Carpal tunnel surgery via a mini longitudinal incision made to the proximal of the distal wrist crease has been discussed in a limited number of studies [15,16]. In a study where a 1-cm incision at the proximal of the distal wrist flexion crease was performed using a surgical microscope, no pillar pain or scar tissue sensitivity was reported which is related to the fact that the skin at the proximal of the wrist crease is thinner than the skin of the wrist and the palmar region was highlighted better using this approach. Recurrence was reported in three cases. The authors stated that, in their technique, the proximal portion of the carpal ligament was dissected after it was exposed with a scalpel and subsequently the distal portion was dissected using surgical scissors. No information was provided regarding the total exposure of the carpal ligament [15]. In another study comparing the carpal tunnel release via incisions performed to the 2 cm proximal and 2 cm distal of the wrist crease, the pillar pain and scar tissue sensitivity following the carpal ligament release via proximal incision was significantly low. It was asserted that the mini incision made at the proximal of the wrist reduced the scar tissue formation due to decreased possibility of tissue damage. No recurrence was observed in either of the groups [16].

The time to using hands actively in our study conforms to the literature data on endoscopic and mini open carpal tunnel release procedures. However, our unilateral CTS cases were able to eat, dress and meet their hygienic needs, and wear gloves on the day of surgery and bilateral cases could achieve the same functions on the first or second postoperative day which was a significant finding in assessing the patient comfort. We believe that our minimally invasive surgical approach at the proximal of the transverse carpal ligament, in the thin dermis layer, was an important factor in not observing any pillar pain or scar tissue sensitivity. In carpal tunnel surgery, both the volar and dorsal side of the carpal ligament should be completely released and the proximal and distal of the ligament should be well exposed. Ample exposure of the transverse carpal ligament could be achieved with our surgical approach. The lack of a comparison group is a limitation of our study.

In conclusion, minimally invasive surgical technique applied at the proximal of the distal wrist crease for carpal tunnel release is an efficient method. No pillar pain or scar tissue sensitivity develops after surgery. Early return to physiological activities increases the patient comfort.

Ethics Commitee Approval: Approval was obtained from Adana Numune Training and Research Hospital Ethics Committee (08.09.2010, decision no. 34).
Conflict of interest: The author declares that there is no conflict of interest.
Funding: No financial support was received.
Informed Consent: Informed consent was obtained from all individual participants included in the study.

REFERENCES

1. Raja S, Carlos AJ. Carpal tunnel syndrome - current controversies. Orthopaedics and Trauma. 2015;29:273-7. https://doi.org/10.1016/j.mporth.2015.08.001
2. Sucher BM, Schreiber AL. Carpal tunnel syndrome diagnosis. Phys Med Rehabil Clin N Am. 2014;25(2):229-47. https://doi.org/10.1016/j.pmr.2014.01.004
3. Thurston A. Carpal tunnel syndrome. Orthopaedics and Trauma. 2013;27:332-41. https://doi.org/10.1016/j.mporth.2013.08.003
4. Huisstede BM, Randsdorp MS, Coert JH, Glerum S, van Middelkoop M, Koes BW. Carpal Tunnel Syndrome. Part II: Effectiveness of surgical treatments-A systematic review. Arch Phys Med Rehabil. 2010;91(7):1005-24. https://doi.org/10.1016/j.apmr.2010.03.023
5. Aslani HR, Alizadeh K, Eajazi A, Karimi A, Karimi MH, Zaferani Z, et al. Comparison of carpal tunnel release with three different techniques. Clin Neurol Neurosurg. 2012;114(7):965-8. https://doi.org/10.1016/j.clineuro.2012.02.017
6. Boya H, Ozcan O, Oztekin HH. Long-term complications of open carpal tunnel release. Muscle Nerve. 2008;38(5):1443-6. https://doi.org/10.1002/mus.21068
7. Tarallo M, Fino P, Sorvillo V, Parisi P, Scuderi N. Comparative analysis between minimal access versus traditional accesses in carpal tunnel syndrome: a perspective randomised study. J Plast Reconstr Aesthet Surg. 2014;67(2):237-43. https://doi.org/10.1016/j.bjps.2013.10.033
8. Osei DA, Calfee RP, Stepan JG, Boyer MI, Goldfarb CA, Gelberman RH. Simultaneous bilateral or unilateral carpal tunnel release? A prospective cohort study of early outcomes and limitations. J Bone Joint Surg Am. 2014;96(11):889-96. https://doi.org/10.2106/JBJS.M.00822
9. Cho YJ, Lee JH, Shin DJ, Park KH. Comparison of short wrist transverse open and limited open techniques for carpal tunnel release: a randomized controlled trial of two incisions. J Hand Surg Eur Vol. 2016;41(2):143-7. https://doi.org/10.1177/1753193415603968
10. Pajardi G, Pegoli L, Pivato G, Zerbinati P. Endoscopic carpal tunnel release: our experience with 12,702 cases. Hand Surg. 2008;13(1):21-6. https://doi.org/10.1142/S0218810408003815
11. Agee JM, McCarroll HR Jr, Tortosa RD, Berry DA, Szabo RM, Peimer CA. Endoscopic release of the carpal tunnel: a randomized prospective multicenter study. J Hand Surg Am. 1992;17(6):987-95. https://doi.org/10.1016/S0363-5023(09)91044-9
12. Müller LP, Rudig L, Degreif J, Rommens PM. Endoscopic carpal tunnel release: results with special consideration to possible complications. Knee Surg Sports Traumatol Arthrosc. 2000;8(3):166-72. https://doi.org/10.1007/s001670050209
13. Hankins CL, Brown MG, Lopez RA, Lee AK, Dang J, Harper RD. A 12-year experience using the brown two-portal endoscopic procedure of transverse carpal ligament release in 14,722 patients: Defining a new paradigm in the treatment of carpal tunnel syndrome. Plast Reconstr Surg. 2007;120(7):1911-21. https://doi.org/10.1097/01.prs.0000287287.85044.87
14. Brown RA, Gelberman RH, Seiler JG, Abrahamsson SO, Weiland AJ, Urbaniak JR, et al. Carpal tunnel release. A prospective, randomized assessment of open and endoscopic methods. J Bone Joint Surg Am. 1993;75(9):1265-75. https://doi.org/10.2106/00004623-199309000-00002
15. Isik HS, Bostanci U. Experience of Carpal Tunnel Syndrome that operated using a limited uni skin incision. Turk Neurosurg. 2011;21(2):177-80. https://doi.org/10.5137/1019-5149.JTN.3246-10.2
16. Uçar BY, Demirtaş A, Bulut M, Azboy I, Uçar D. Carpal tunnel decompression: two different mini-incision techniques. Eur Rev Med Pharmacol Sci. 2012;16(4):533-8. PMID: 22696883.
17. Bland JD. A neurophysiological grading scale for carpal tunnel syndrome. Muscle Nerve. 2000;23(8):1280-3. https://doi.org/10.1002/1097-4598(200008)23:8<1280::AID-MUS20>3.0.CO;2-Y
18. Levine DW, Simmons BP, Koris MJ, Daltroy LH, Hohl GG, Fossel AH, et al. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. J Bone Joint Surg Am. 1993;75(11):1585-92. https://doi.org/10.2106/00004623-199311000-00002
19. Beck JD, Wingert NC, Rutter MR, Irgit KS, Tang X, Klena JC. Clinical outcomes of endoscopic carpal tunnel release in patients 65 and over. J Hand Surg Am. 2013;38(8):1524-9. https://doi.org/10.1016/j.jhsa.2013.05.016
20. Momose T, Uchiyama S, Kobayashi S, Nakagawa H, Kato H. Structural changes of the carpal tunnel, median nerve and flexor tendons in MRI before and after endoscopic carpal tunnel release. Hand Surg. 2014;19(2):193-8. https://doi.org/10.1142/S0218810414500191
21. Abicalaf CA, de Barros N, Sernik RA, Pimentel BF, Braga-Baiak A, Braga L, et al. Ultrasound evaluation of patients with carpal tunnel syndrome before and after endoscopic release of the transverse carpal ligament. Clin Radiol. 2007;62(9):891-4. https://doi.org/10.1016/j.crad.2007.01.029
22. Karabay N, Kayalar M, Ada S. Sonographic assessment of transverse carpal ligament after open surgical release of the carpal tunnel. Acta Orthop Traumatol Turc. 2013;47(2):73-8. https://doi.org/10.3944/AOTT.2013.2890
23. Mesgarzadeh M, Triolo J, Schneck CD. Carpal tunnel syndrome. MR imaging diagnosis. Magn Reson Imaging Clin N Am. 1995;3(2):249-64. PMID: 7553021.
24. Kanatani T, Nagura I, Kurosaka M, Kokubu T, Sumi M. Electrophysiological assessment of carpal tunnel syndrome in elderly patients: one-year follow-up study. J Hand Surg Am. 2014;39(11):2188-91. https://doi.org/10.1016/j.jhsa.2014.08.011
25. Gaba S, Bhogesha S, Singh O. Limited incision carpal tunnel release. Indian J Orthop. 2017;51(2):192-8. https://doi.org/10.4103/0019-5413.201700
26. Keith MW, Masear V, Chung KC, Amadio PC, Andary M, Barth RW, et al. American Academy of Orthopaedic Surgeons Clinical Practice Guideline on The Treatment of Carpal Tunnel Syndrome. J Bone Joint Surg Am. 2010;92(1):218-9. https://doi.org/10.2106/JBJS.I.00642
27. Uchiyama S, Nakamura K, Itsubo T, Murakami H, Hayashi M, Imaeda T, et al. Technical difficulties and their prediction in 2-portal endoscopic carpal tunnel release for idiopathic carpal tunnel syndrome. Arthroscopy. 2013;29(5):860-9. https://doi.org/10.1016/j.arthro.2013.01.027
28. Teixeira Alves Mde P. Prospective comparative study between proximal transverse incision and the conventional longitudinal incisions for carpal tunnel release. Rev Bras Ortop. 2015;45(5):437-44. https://doi.org/10.1016/S2255-4971(15)30433-X

Original Article

Med J Bakirkoy 2020;16(2):132-7
doi: 10.5222/BMJ.2020.27247

Medical Journal of Bakirkoy

Comparison of Emergency and Elective Cesarean Sections in the Breech Presentation: A Case-Control Study

Makat Prezentasyonunda Acil ve Elektif Sezaryenlerin Karşılaştırılması: Vaka Kontrol Çalışması

Bugra Coskun[1], Ramazan Erda Pay[2], Bora Coskun[1], Coskun Simsir[1], Rıza Dur[3]
Eser Colak[4], Kazim Emre Karasahin[2]

[1] *Yüksek İhtisas University, Department of Obstetrics and Gynecology, Ankara, Turkey*
[2] *Health Science University, Gülhane Training and Research Hospital, Department of Obstetrics and Gynecology, Ankara, Turkey*
[3] *Health Science University, Etlik Zübeyde Hanım Women Health Training and Research Hospital, Department of Obstetrics and Gynecology, Ankara, Turkey*
[4] *Başkent University, Konya Application and Research Hospital, Department of Obstetrics and Gynecology, Konya, Turkey*

Received: 23 November 2019 / **Accepted:** 25 March 2020 / **Publication date:** 26 June 2020

Cite as: Coskun B, Pay RE, Coskun B, Simsir C, Dur R, Colak E, Karasahin KE. Comparison of emergency and elective cesarean sections in the breech presentation: a case-control study. Med J Bakirkoy 2020;16(2):132-7.

ABSTRACT

Objective: *In this study, we aimed to compare the characteristics and outcomes between the patients who underwent emergency or elective cesarean section (CS) with the indication of breech presentation (BP).*
Method: *All the patients who underwent cesarean delivery with the indication of BP between January 2016-December 2018 were included in this retrospective study. BP Patients with any other indication for CS were excluded from the study. Group I; consisting of patients with BP who underwent emergency CS due to progression of cervical dilation and/or effacement, pain or membrane rupture, presence of ≥ 3 contractions at regular intervals over 25 mmHg within 10 minutes, and Group II; consisting of term pregnant patients without any additional problem who underwent elective CS following 38. gestational weeks between 08:00 AM to 05:00 PM were compared statistically. Also, subgroups were compared according to BP subtypes and cervical opening measurements.*
Results: *APGAR scores at the 1st / 5th minutes and postoperative hemoglobin values were significantly lower in the emergency CS group than the elective CS group. Also we found that the decreases in hemoglobin values before and after the cesarean section, and APGAR scores at 1., and 5. min, were significantly higher, the operation time was significantly longer in the emergency CS group. Also, the median value of the week of emergency cesarean section was 37 gestational weeks, and we found that when the cervical dilation was 2 cm and above before operation, the drop in hemoglobin value, need for blood transfusion and neonatal intensive care increased significantly. No significant difference was found between BP subtypes.*
Conclusion: *Postoperative parameters may tend to be unfavourable in patients with BP who underwent emergency CS due to pain or progression of cervical dilation. Therefore, clinicians who prefer cesarean delivery in patients with BP, should be very cautious against possible emergency operation until the time of the elective operation and also avoid iatrogenic preterm labor.*

Keywords: *emergency cesarean, elective cesarean, breech presentation*

ÖZ

Amaç: *Çalışmamızda makat prezentasyonu (MP) endikasyonuyla acil ya da elektif sezaryen (CS) olan hastaların özelliklerini karşılaştırıp, ne gibi klinik yansımaları olduğunu ortaya koymayı amaçlandı.*
Yöntem: *Şubat 2017-Temmuz 2019 tarihleri arasında hastanemize uterin fibroide yani miyoma bağlı semptomları nedeniyle başvurup UAE tedavi işlemi uygulanan hastaları retrospektif olarak inceledik. Çalışmaya yaşam kalitesini bozacak şekilde miyoma bağlı miktar olarak fazla, uzun süreli, sık ve düzensiz aralıklarla olan uterin kanamalar, anemi, karın ağrısı, ele gelen kitle ve sık idrara çıkma şikayetleri olan hastalar dahil edildi. Tüm hastalarda UAE öncesi ve UAE sonrası 6. ayda, manyetik rezonans görüntüleme (MRG) ile klinik semptomları kaydedildi.*
Bulgular: *Çalışmamızda acil sezaryan olan MP gebelerde anlamlı olarak 1. ve 5. dakika APGAR skorları ile postoperatif hemoglobin değerinin daha düşük, sezaryen öncesine göre hemoglobin değerindeki düşüşün daha fazla, ve ayrıca operasyon süresinin daha uzun olduğunu buldundu. Ayrıca acil sezaryen ihtiyacı haftasının median değeri 37. hafta olup, CS öncesi servikal dilatasyon 2 cm ve üstünde olduğunda hemoglobin değerindeki düşüşün arttığını ve ES transfüzyonu ile yenidoğan yoğun bakım ihtiyacının artmakta olduğunu gördük. MP subtipleri arasında fark izlenmedi.*
Sonuç: *Sancı ya da servikal açılma şüphesi nedeniyle acil sezaryen olan MP gebelerde postoperatif parametreler daha olumsuz yönde olabilmektedir. Bu yüzden MP gebeliklerde elektif CS doğumu tercih eden klinisyenlerin bir yandan elektif operasyon zamanına kadar olası acil bir operasyon hakkında dikkatli olması gerekirken bir yandan da iatrojenik preterm doğumdan kaçınmanın önemli olduğunu düşünmekteyiz.*

Anahtar kelimeler: *acil sezaryen, elektif sezaryen, makat prezentasyonu*

Corresponding Author:
✉ drbugracoskun@gmail.com

B. Coşkun 0000-0003-1938-3833
R. E. Pay 0000-0001-7183-4246
B. Coşkun 0000-0002-2338-7186
C. Simsir 0000-0003-1825-6584
R. Dur 0000-0002-9225-9030
E. Colak 0000-0002-8184-7531
K. E. Karasahin 0000-0002-4624-4874

INTRODUCTION

The mortality associated with hemorrhage and infection caused mainly by cesarean section (CS) has dramatically declined with the development of infection control measures, blood transfusions, and anesthesia techniques [1]. Today, cesarean delivery is considered a safe operation [2] with increasing prevalence around the world [3]. It is estimated that around 750,000 CS operations are performed annually in Turkey [4]. Although there is no clear consensus on the ideal method of delivery in the breech presentation (BP), which is seen in 3-4% of all term pregnancies [5], elective CS is recommended at weeks 39-41. The prevalence of BP among all CS cases is around 8-12% [6,7].

Emergency surgeries are associated with greater number of surgical complications than elective surgeries [8]. Similarly, emergency CS is likely associated with an increased risk of complications when compared to elective CS. In this study, we aimed to compare the characteristics of BP patients that underwent emergency or elective cesarean delivery and to determine the clinical outcomes.

MATERIAL and METHOD

This study was granted ethical approval by the relevant Ethics Committee (Health Science University, Gulhane Medical School Local Ethical Committee, Date: 09.25. 2018, Decision Number: 18/230). We retrospectively evaluated data of BP patients that underwent CS between December 2016 and December 2018. We recorded the demographic characteristics of the patients, the preoperative vaginal examination findings, the pre- and postoperative hemogram parameters, neonatal findings, and adverse clinical events. The patients who underwent CS for any indication other than BP (multiple pregnancies, previous uterine surgery, previous cesarean section, intrauterine development retardation, pregnancy cholestasis, maternal systemic and metabolic diseases, preeclampsia, fetal distress, macrosomia, fetal anomaly, antenatal hemorrhage, etc.) were excluded from the study. None of our subjects tried for vaginal delivery. We considered the suspected start of labor (effacement and/or advanced dilation, three and more contractions of 25 mmHg and higher every 10 minutes at regular intervals observed in cardiotocography) or membrane rupture as an indication of emergency C-section without waiting for active labor. We compared the data of Group I (29 BP patients that underwent an emergency cesarean section) and Group II (patients that underwent elective cesarean section after week 38 without any additional medical conditions).

Elective C-sections were performed during the day within working hours (08:00-16:00) on a predetermined date, where patients had been fasting for an adequate duration of time and had received the required consultations. Emergency CS was not performed on a predetermined date or time but at any time of the day as soon as possible when surgery was indicated by the determined conditions, and under conditions that were available at that time.

Also, subgroups were compared according to BP subtypes and cervical opening measurement subgroups.

Statistical Analysis

The data were analyzed using SPSS version 23. We used Kruskal-Wallis and Mann- Whitney U-tests to compare non-normally distributed data. We used the chi-square test to evaluate the distribution of qualitative data according to groups. Qualitative data were expressed as frequency (percent), and quantitative data as mean (minimum-maximum). Level of statistical ignificance was set at $p<0.05$.

RESULTS

Total number of births was 3216 within the determined time frame. The CS rate was 29.91%, the primary CS rate was 13.08% and the BP-related CS rate was 4.12%.

There were no statistically significant differences in age, parity, the gender of the baby, birth weight, or median preoperative hemoglobin values of Groups I and II ($p > 0.05$). The median time of delivery was 37 gestational weeks for Group I and gestational 38.1 weeks for Group II ($p<0.001$). The median cervical dilation in the last examination before cesarean delivery was 3 cm in Group I and 0 cm in Group II ($p<0.001$). The median 1- and 5-minute Apgar scores

of the newborns were similar in both groups; however, the point distributions were significantly different (pq<0.05). In Group I, the median postoperative hemoglobin value was lower, the postoperative decrease in hemoglobin values was higher, and also the duration of the operation was longer (p<0.05). The median operating time in Groups I and II were 75 and 60 minutes, respectively. There was no statistical difference between the groups in terms of BP subtypes (p=0.181). The incidence of adverse clinical events [erythrocyte suspension (ES) transfusion, neonatal intensive care, cord prolapse] was significantly higher in Group I. Four patients in Group I and one patient in Group II required ES transfusions. Five infants in Group I and one infant in Group II required neonatal intensive care. Cord prolapse was observed in 2 emergency C-section patients, both of which were in an incomplete breech position (Table 1).

We found that BP subtypes (complete breech, incomplete breech, frank breech) were not associated with parity, gestation time, cervical dilation, gender of the newborn, birth weight, 1- and 5-minute-scores, postoperative hemoglobin values, postoperative decrease in hemoglobin, and operation time (Table 2).

Table 2. Comparison of parameters according to breech position.

	Frank Breech*	Complete Breech*	Incomplete Breech*	p
Apgar 1-minute	7 (4-7)	7 (5-7)	7 (4-7)	0.722
Apgar 5-minute	9 (7-9)	9 (8-9)	9 (6-9)	0.728
Delta Hemoglobin (g/dL)	1 (0-4.7)	0.9 (0.2-1.5)	1.1 (0.1-2.4)	0.382
Operation time (minutes)	60 (45-115)	75 (50-110)	60 (45-90)	0.419
Emergency Cesarean Section	22/100 (%22)	3/15 (%20)	4/42 (%9.5)	0.181

Median (minimum-maximum)
Delta Hemoglobin = [postoperative hemoglobin] – [preoperative hemoglobin]

When patients were grouped according to cervical dilation masurements; In the group where cervical dilation was 0-1 cm, newborn 1 and 5 minute APGAR scores were better, postoperative drop in hemoglobin was lesser and duration of the operation was

Table 1. Comparison of parameters by groups.

	Group I Emergency Cesarean Section (n = 29)	Group II Elective Cesarean Section (n = 124) *	p
Age* (years)	28 (22-34)	29 (20-36)	0.09
Parity*	1 (1-3)	1 (1-4)	0.905
Gestational Week*	37 (35.1-38.2)	38.1 (37-40)	< 0.001
Delivery position**			
Frank breech	22 (75.9)	78 (59.7)	0.181
Complete breech	3 (10.3)	12 (9.7)	
Incomplete breech	4 (13.8)	38 (30.6)	
Dilation (cm) *	3 (1-8)	0 (0-2)	< 0.001
Gender**			
Male	15 (20)	60 (80.0)	0.907
Female	14 (17.9)	64 (82.1)	
Weight (g) *	2890 (1480-3660)	3085 (630-4990)	0.058
1-minute Apgar score*	7 (4-7)	7 (5-7)	< 0.001
5-minute Apgar score*	9 (6-9)	9 (8-9)	< 0.001
Preoperative Hemoglobin (g/dL) *	11.8 (8.9-14.5)	11.5 (9.1-14.4)	0.25
Postoperative Hemoglobin (g/dL) *	10.1 (7.1-13.6)	10.6 (7.8-13.3)	0.045
Delta Hemoglobin (g/dL) *	1.7 (0.5-4.7)	0.9 (0-2.2)	< 0.001
Adverse clinical events**			
None	18 (62.1)	122 (98.4)	----
ES transfusion	4 (13.8)	1 (0.8)	
Neonatal intensive care	5 (17.2)	1 (0.8)	
Cord prolapse	2 (6.9)	---	
Operation duration (minutes) *	75 (55-115)	60 (45-95)	< 0.001

**Median (minimum-maximum)*
***Frequency (percentage)*
Delta Hemoglobin = [postoperative hemoglobin] – [preoperative hemoglobin]

Table 3. Comparison of parameters according to cervical dilatation.

	Group 1 (0-1 cm cervical dilation) (n=119)	Group 2 (2-3 cm cervical dilation) (n=23)	Group 3 (4 cm and more) (n=11)	p
Apgar 1	7 (5 -7) [a]	7 (4-7) [b]	7 (4-7) [b]	<0.001
Apgar 5	9 (8 -9) [a]	9 (7-9) [b]	9 (6-9) [b]	<0.001
Delta Hemoglobin	0.9 (0-2.5) [a]	1.4 (0.4-3.1) [b]	1.7 (0.5-4.7) [b]	0.001
Operation time	60 (45-95) [a]	75 (45-110) [b]	75 (65-115) [b]	<0.001
Adverse clinical events*				
No	117 (98.3)	17 (73.9)	6 (54.5)	<0.001
Yes	2 (1.7)	6 (26.1)	5 (45.5)	
Operation type *				
Emergency	2 (1.7)	16 (69.6)	11 (100)	<0.001
Elective	117 (98.3)	7 (30.4)	---	

[a, b]: The results of the cervical dilation groups marked with the same latter are not statistically different
**frequency (percentage)*
Delta Hemoglobin = [postoperative hemoglobin] – [preoperative hemoglobin]

shorter which was statistically different from other groups (p<0.001).

Adverse clinical events (ES transfusion, neonatal intensive care, cord prolapse) were found to be affected by cervical dilation (p<0.001). Cervical dilation was positively correlated with the incidence of adverse clinical events (Table 3).

DISCUSSION

We found that in the emergency CS group, 1- and 5-minute Apgar scores and postoperative hemoglobin values were lower, the postoperative decrease in hemoglobin values was higher, and also the duration of the operation was longer. The median time of emergency CS was 37. gestational week. We found that a cervical dilation of 2 cm and more at the operation time was associated with decreased postoperative hemoglobin value, increased need for neonatal intensive care, and ES transfusion. We did not observe any difference between BP subtypes in terms of the parameters mentioned above.

A total of 153 CSs were performed with the indication of BP. As the standard protocol of our clinic vaginal delivery is not performed for BP, so our CS rate was 100% for BP patients. The BP rate within all cesarean deliveries was 4.12%. Studies from Turkey indicate the rate of BP among all cases of CS to be 6-12% [9-11]. Our clinic is a referral center, and thus, the rate of complicated pregnancies and the incidence of CS are comparatively high. Hence, the rate of BP within all cases of CS is comparatively low.

Today, there is still no ideal method of delivery for BP. The first possible option is an external cephalic version (ECV), where delivery is completed vaginally if successful, and surgically, if not. The literature indicates that ECV and its potential complications must be described to the expecting mother in detail, and performed only after their consent [12]. Another option is to try vaginal delivery in a breech presentation if ECV fails. Another possible option is a planned CS. The final decision of the delivery method will depend on the experience of the physician, the available facilities and the preference of the expecting mother [13].

ACOG states that vaginal delivery is an option for babies delivered at ≥37. gestational week in an incomplete or complete breech position, that weigh 2500-4000 g, and have not have any fetal abnormalities [13]. However, the multicenter randomized 'Term Breech Trial' study published in Lancet in 2000 found that perinatal and neonatal mortality and severe neonatal morbidity were significantly lower in planned CS when compared to planned vaginal delivery [14]. Later studies also evaluated the perspectives of the physician and found that they were more likely to prefer CS for BP [15].

Elective or emergency CS will have different morbidity and mortality outcomes for the mother and the

baby. There are many studies comparing emergency and elective CS procedures [16-18]. The literature defines an elective cesarean section as an operation performed within working hours (typically between 08:00 and 17:00) with an anesthesia team, the neonatal care team and the entire operation team ready at the scheduled time [19]. We have based our definition of elective C-section on these criteria. However, there is no consensus both on the delivery method in breech presentation and definitiive criteria for an emergency cesarean section.

Some medical centers prefer to try the external cephalic version in BP and resort to a cesarean section only if it fails, whereas others directly try vaginal birth in BP and switch to emergency cesarean delivery if required due to any indication (non-progressive labor, etc.). Some other medical centers plan CS in BP in the appropriate gestational week and plan an emergency operation in case of pain and dilation, which are considered to indicate a need for CS. Another option is to perform a CS with the start of the first labor contractions and cervical dilation, without planning beforehand. In this case, BP itself has not been considered as an indication for CS until the patient is called a post-term. There are not enough studies on the different forms of management for BP.

However, majorly of physicians prefer cesarean delivery for breech presentations all over the world and in Turkey. Vaginal birth is virtually abondoned due to medicolegal concerns [20]. Hence, it becomes harder and harder to find physicians that are experienced in vaginal birth in cases with BP.

Physicians tend to plan CS directly without trying vaginal birth in BP. Studies in the literature compare vaginal birth and CS in BP, but only include patients that were operated when vaginal birth was tried but failed [21]. Our study is the first to compare elective CS with emergency CS that is performed at the onset of the first contraction or cervical dilation (considered as indications for emergency CS) in BP pregnancies.

The median gestation week of the emergency CS patients was 37, whereas it was 38.1 weeks for elective CS patients with BP. This shows that some pregnant women that are waiting for their scheduled elective CS can undergo emergency CS due to early labor. Preterm and even late preterm births are associated with poor outcomes compared to term births [22]. In Turkish medical practice, physicians schedule BP patients a CS before the start of labor. However, false labor pains and cervical dilation that is actually not progressive can lead to an unnecessary preterm birth and bring along the risks associated with emergency CS. If the physician will schedule the CS before the start of labor, they must carefully evaluate cervical dilation and false labor pains to avoid unnecessary preterm birth.

Although there are some studies comparing elective CS and emergency CS performed after complications of vaginal births in the case of BP, our study is the first study to compare elective CS with emergency CS performed due to indication of the onset of contractions and/or cervical dilation in term pregnancies.

The fact that suspicion of the start of the labor is based on subjective evaluation by the physician is the most important limitation of our study. Another significant limitation is not having tried vaginal delivery in BP, and not being able to compare the relevant outcomes.

CONCLUSION

Postoperative parameters of BP patients can be negatively affected if they undergo emergency CS only because of pain and findings of cervical dilation. We conclude that clinicians should closely follow-up BP patients up until the scheduled elective CS and be prepared for a possible emergency operation while avoiding iatrogenic preterm birth, if possible.

Ethics Committee Approval: This study was granted ethical approval by the relevant Ethics Committee (Health Science University, Gulhane Medical School Local Ethical Committee, Date: 09.25. 2018, Decision Number: 18/230).
Conflict of Interest: None.
Funding: None.
Informed Consent: None due to the retrospective design of the study.

REFERENCES

1. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, et al. Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. N Engl J Med. 2004;351(25):2581-9. https://doi.org/10.1056/NEJMoa040405
2. Notzon FC, Cnattingius S, Bergsjø P, Cole S, Taffel S, Irgens L, et al. Cesarean section delivery in the 1980's: International comparison by indication. Am J Obstet Gynecol. 1994;170(2):495-504. https://doi.org/10.1016/S0002-9378(94)70217-9
3. Menacker F, Declercq E, Macdorman MF, editors. Cesarean delivery: background, trends, and epidemiology. Semin Perinatol. 2006;30(5):235-41. https://doi.org/10.1053/j.semperi.2006.07.002
4. Ulubay M, Öztürk M, Fidan U, Keskin U, Fıratlıgil FB, Kıncı MF, et al. Skin incision lengths in caesarean section. Cukurova Medical Journal. 2016;41(1):82-6. https://doi.org/10.17826/cutf.147190
5. Güney G, İnan N, Tokmak A, Doğan M. A different tecnique for head stuck in breech delivery. Gynecology Obstetrics & Reproductive Medicine. 2015;21(2):109-11. Available from: http://gorm.com.tr/index.php/GORM/article/view/31/26
6. Hofmeyr GJ, Lockwood C, Barss V. Delivery of the fetus in breech presentation. Waltham, MA: UpToDate; 2013.
7. Kolås T, Hofoss D, Daltveit AK, Nilsen ST, Henriksen T, Häger R, et al. Indications for cesarean deliveries in Norway. Am J Obstet Gynecol. 2003;188(4):864-70. https://doi.org/10.1067/mob.2003.217
8. Elveđi-Gašparović V, Klepac-Pulanić T, Peter B. Maternal and fetal outcome in elective versus emergency caesarean section in a developing country. Coll Antropol. 2006;30(1):113-8. PMID: 16617584.
9. Yıldız A, Köksal A, Çukurova K, Keklik A, Çelik N, İvit H. Bir obstetrik kliniğinde 15 yıllık period süresince sezaryen oranları ve endikasyonlarının yıllara göre dağılımı. Evaluation. 2010;39:44.
10. Tekirdağ Aİ, Cebeci R. Eğitim hastanesinde sezaryen oranları. İstanbul Kanuni Sultan Süleyman Tıp Dergisi (IKSST). 2010;2(1):21-6.
11. Aksoy H, Özyurt S, Aksoy Ü, Açmaz G, Karadağ Öİ, Babayiğit MA. Hastanemizdeki sezaryen hızı ve endikasyon dağılımları ışığında Türkiye'de sezaryen ile doğuma genel bakış. Kocaeli Tıp Dergisi. 2014;3(3):1-7.
12. Hofmeyr GJ, Kulier R, West HM. External cephalic version for breech presentation at term. Cochrane Database Syst Rev. 2015;2015(4):CD000083. https://doi.org/10.1002/14651858.CD000083.pub3
13. ACOG Committee on Obstetric Practice. ACOG Committee Opinion No. 745: Mode of term singleton breech delivery. Obstet Gynecol. 2018;132(2):e60-e63. https://doi.org/10.1097/AOG.0000000000002755
14. Hannah ME, Hannah WJ, Hewson SA, Hodnett ED, Saigal S, Willan AR, et al. Planned caesarean section versus planned vaginal birth for breech presentation at term: a randomised multicentre trial. Lancet. 2000;356(9239):1375-83. https://doi.org/10.1016/S0140-6736(00)02840-3
15. Rietberg CCT, Elferink-Stinkens PM, Visser GH. The effect of the Term Breech Trial on medical intervention behaviour and neonatal outcome in The Netherlands: an analysis of 35,453 term breech infants. BJOG. 2005;112(2):205-9. https://doi.org/10.1111/j.1471-0528.2004.00317.x
16. Suwal A, Shrivastava VR, Giri A. Maternal and fetal outcome in elective versus emergency cesarean section. JNMA J Nepal Med Assoc. 2013;52(192):563-6. PMID: 25327227. https://doi.org/10.31729/jnma.2426
17. Benzouina S, Boubkraoui ME-m, Mrabet M, Chahid N, Kharbach A, Elhassani A, et al. Fetal outcome in emergency versus elective cesarean sections at Souissi Maternity Hospital, Rabat, Morocco. Pan Afr Med J. 2016;23:197. https://doi.org/10.11604/pamj.2016.23.197.7401
18. Raees M, Yasmeen S, Jabeen S, Utman N, Karim R. Maternal morbidity associated with emergency versus elective caesarean section. Journal of Postgraduate Medical Institute. 2012;27(1):55-62. Available from: https://www.researchgate.net/publication/282744910
19. Daniel S, Viswanathan M, Simi B, Nazeema A. Comparison of fetal outcomes of emergency and elective caesarean sections in a teaching hospital in Kerala. Academic Medical Journal of India. 2014;2(1):32-6. Available from: https://api.semanticscholar.org/CorpusID:44182723
20. Karabel MP, Demirbaş M, İnci MB. Türkiye'de ve Dünya'da değişen sezaryen sıklığı ve olası nedenleri. Sakarya Med J. 2017;7(4):158-63. Available from: https://dergipark.org.tr/tr/download/article-file/398631 https://doi.org/10.31832/smj.368600
21. Roman J, Bakos O, Cnattingius S. Pregnancy outcomes by mode of delivery among term breech births: Swedish experience 1987-1993. Obstet Gynecol. 1998;92(6):945-50. https://doi.org/10.1016/S0029-7844(98)00326-3
22. De Luca R, Boulvain M, Irion O, Berner M, Pfister RE. Incidence of early neonatal mortality and morbidity after late-preterm and term cesarean delivery. Pediatrics. 2009;123(6):e1064-71. https://doi.org/10.1542/peds.2008-2407

Original Article

Med J Bakirkoy 2020;16(2):138-42
doi: 10.5222/BMJ.2020.77487

Medical Journal of Bakirkoy

In Patients with ST-Elevated Myocardial Infarction The Relationship Between Complications Developed and Age

ST-Elevasyonlu Miyokard Enfarktüs Olgularında Gelişen Komplikasyonların Yaş ile İlişkisi

Nursel Kocamaz[1], Gulcin Sahingoz Erdal[1], Pinar Kasapoglu[2], Nilgun Isiksacan[2]

[1] Health Science University, Bakirkoy Dr Sadi Konuk Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey
[2] Health Science University, Bakirkoy Dr Sadi Konuk Training and Research Hospital, Department of Biochemistry Istanbul, Turkey

Received: 22 December 2019 / **Accepted:** 04 April 2020 / **Publication date:** 26 June 2020

Cite as: Kocamaz N, Sahingoz Erdal G, Kasapoglu P, Isiksacan N. in Patients with ST-elevated myocardial infarction the relationship between complications developed and age. Med J Bakirkoy 2020;16(2):138-42.

ABSTRACT

Objective: *Coronary artery diseases (CADs) are the most common causes of death worldwide. Every year more than 7 million people die of CAD which accounts for 12.8% of all –cause deaths. Generally, while a part of the patients recovered without any complication during the 3-4 week course of acute myocardial infarction, various complications may occur in the majority of patients.*
Method: *In our study, we compared the relationship between the age and the early complications of the 488 ST- elevated acute myocardial infarction patients in the coronary intensive care unit in Hamidiye Şişli Etfal Hospital Coronary Intensive Care Unit between January 1988 and June 1991.*
Conclusion: *In our study, although there was no significant difference in terms of myocardial infarction complications between the two groups under 60 years old and above, heart failure, cardiogenic shock, premature death and cerebrovascular diseases were more frequent in the group over 60 years of age. However, no complication was observed in a total of 129 patients (26.4%). It is generally found that young patients with myocardial infarction have low mortality and better prognosis; which may be related to their better health status or smaller area of myocardial infarction, it should also be taken into consideration that collateral vessels may develop in time. In the elderly, so they can overcome the infarction more easily which increases the possibility of surviving their post-infarction life.*

Keywords: *acute myocardial infarction, ST-elevation, age*

ÖZ

Amaç: *Koroner arter hastalıkları (KAH) tüm dünyada ölümün en sık nedenidir. Her yıl 7 milyondan fazla kişi KAH nedeniyle ölmektedir ve tüm ölümlerin %12,8'sini oluşturmaktadır. Genel olarak akut miyokard inlarktüsünün 3-4 haftalık seyrinde hastaların bir bölümü komplikasyonsuz olarak iyileşirken hastaların büyük çoğunluğunda, değişik önemde çeşitli komplikasyonlar ortaya çıkabilir.*
Yöntem: *Çalışmamızda, Hamidiye Şişli Etfal Hastanesi Koroner Yoğun Bakım Ünitesinde 1988 Ocak-1991 Haziran ayları arasında koroner yoğun bakım ünitesinde takip ettiğimiz 488 ST elevasyonlu akut miyokard infarktüsü hastasında gelişen erken komplikasyonların yaş ile ilişkilerini karşılaştırdık.*
Sonuç: *Yaptığımız çalışmada 60 yaş altı ve üstü her iki grup arasında miyokard infarktüsü komplikasyonları yönünden genelde anlamlı fark olmamakla birlikte, kalp yetmezliği, kardiyojenik şok, erken ölüm, serebrovasküler hastalıklar 60 yaş üstü grupta daha sıktı. Bununla birlikte toplam 129 hastada (% 26.4) hiç bir komplikasyon görülmedi. Çalışmalarda genellikle genç miyokard infarktüslülerin mortalitesinin düşük, prognozunun daha iyi bulunması genç hastaların sağlık durumu veya miyokard infarktüs alanının daha elverişli olmasına bağlı olabileceği düşünülse de, yaşlılarda zamanla kolleteral damarların gelişebileceği, infarktı daha kolay atlatabilecekleri ve infarkt sonrası yaşamlarını sürdürebilme olasılığını arttıracağı da göz önünde bulundurulmalıdır.*

Anahtar kelimeler: *akut miyokart enfarktüs, ST elevasyonu, yaş*

Corresponding Author:
✉ nurselkocamaz@hotmail.com

N. Kocamaz 0000-0003-3489-2329
G. Sahingoz Erdal 0000-0001-5815-5847
P. Kasapoglu 0000-0003-1703-2204
N. Isiksacan 0000-0002-0230-6500

INTRODUCTION

Coronary artery diseases (CADs) are the most common causes of death worldwide. More than 7 million people die every year due to CAD which accounts for 12.8% of all –cause deaths [1].

Myocardial infarction (MI) is defined as myocardial cell death due to prolonged ischemia in pathology. Electrocardiography (ECG) and measurement of cardiac biomarkers are the current diagnostic cornerstones that complement the clinical assessment [2]. Clinical manifestations of ischemic heart disease are silent ischemia, stable angina pectoris, unstable angina, MI, heart failure and sudden death [3].

In Turkey, according to the data of the TEKHARF (Heart Disease and Risk Factors in Turkish Adults) study, it is estimated that approximately 2 million people have CAD, and annually 90-100 thousand new cases occur, and 130,000 people die due to CAD [4,5].

Generally, in the 3-4 week course of acute myocardial infarction, some of the patients recover without compilications. But in the vast majority of patients, various complications of different significance may occur. Dysrhythmias (bradyarrhythmia, fascicular block, tachyarrhythmia, ventricular tachycardia, ventricular fibrillation), left ventricular failure, cardiogenic shock, myocardial rupture, ventricular aneurysm, left ventricular thrombus and arterial embolism, pulmonary embolism, pericardial effusion, pericarditis, Dressler syndrome, sudden death are some of these complications. The occurrence of these complications depends on the size of the infarction, its localization, age, gender, risk factors carried by the person, whetherthe patient has had an infarction before, and patient's timely transport to the hospital and coronary units [6]. In our study, in patients with ST-elevated acute myocardial infarction that we followed up in the coronary intensive care unit; we aimed to investigate the relationship between early complications and age.

MATERIAL and METHOD

Four hundred and eighty-eight patients who were hospitalized in the Hamidiye Şişli Etfal Hospital Coronary Intensive Care Unit with the diagnosis of ST –elevated myocardial infarction (STEMI) between January 1988 and June 1991 were included in the study. In patients included in the study and diagnosed with STEMI; an anamnesis of ischemic chest pain lasting more than 20 minutes, newly emerged pathological Q wave changes, ST and T wave changes in ECG, and typically increasing and decreasing serum enzyme activities were elicited. Since all patients firstly applied to our emergency outpatient clinic of internal medicine, their first echocardiographic examinations (ECG) were performed there, and then repeated every day during their stay in the intensive care unit.

ECGs were taken at a rate of 25/sec and a total of 12 leads were examined including 3 standard, 3 unipolar extremity, and 6 precordial leads. Meanwhile, electrocardiographic traces and D2 and V1 derivations were recorded and examined for a long time to better recognize the rhythm disturbances. Complications as rhythm and conduction disorders were detected during continuous follow-up, and evaluated in line with changing and developing symptoms and signs. For this purpose, fever, arterial blood pressure, pulse rate, and heart rate were measured, and frequent physical examinations were performed.

Complete blood count, erythrocyte sedimentation rate, complete urinalysis, serum glutamic oxalacetic transaminase (SGOT), lactate dehydrogenase (LDH), creatine kinase (CK), CK-MB, blood sugar, creatinine, blood urea nitrogen, blood electrolytes were evaluated in each patient These tests were performed in biochemistry and bacteriology laboratory of our hospital. Meanwhile, SGOT, LDH, CK, CK-MB analyses were repeated every day in terms of progression of acute myocardial infarction. Echocardiographic and angiographic procedures were also performed in patients in case of need, and cranial imaging was also performed if necessary.

RESULTS

Four hundred and eighty-eight patients who applied to our clinic between 1988 and 1991 and followed up in the Coronary Intensive Care Unit with the diagnosis of ST -Elevated Acute Myocardial Infarction; were divided into two age groups as those aged ≤ 60 (Group 1; n=254)) , and > 60 years (Group 2: n=234)). Complications of myocardial infarction in the coronary

Table 1. Comparison of complications in both groups.

Complications	Group 1 n:255	Group 2 n:234	Total	p
Dysrhythmia	104 (40.9%)	73 (31.2%)	177 (36.3%)	<0.3
Heart failure	25 (9.8%)	62 (26.5%)	87 (17.8%)	<0.001
Cardiogenic shock	14 (5.5%)	26 (1.1%)	40 (8.2%)	<0.05
Pericarditis	13 (5.1%)	5 (2.1%)	18 (3.7%)	<0.1
Ventricular fibrillation	12 (4.7%)	21 (9%)	33 (6.8%)	<0.1
Sudden death	1 (0.4%)	3 (1.3%)	4 (0.8%)	<0.3
Uncomplicated	85 (33.4%)	44 (18.8%)	129 (26.4%)	<0.001

intensive care unit in Groups 1, and 2 were compared.

Three hundred and seventy-three (76.4%) patients were men and 118 (24.1%) of them were women. The ages of the patients ranged between 21, and 96 years, (mean: 57.38 years), the ages of women ranged between 35, and 87 years (mean: 63.87 years). Complications evaluated in both groups were dysrhythmias, congestive heart failure (CHF), severe rhythm disorder (ventricular tachycardia and fibrillation), pericarditis, sudden death, and cardiogenic shock. These complications were monitored while patients were hospitalized in the coronary intensive care unit. However, no complications were observed in 129 patients (26.4%) (Table 1).

There was no significant difference in terms of ventricular fibrillation in both groups (p<0.1). However, 8 of 12 patients aged 60 and under responded to defibrillation, but 4 patients died (33.3%). In Group 2 16 patients (76.1%) died. Ventricular fibrillation was seen in the group aged over 60, and led to more mortal consequences.

Cerebral hemorrhage, embolism and ischemic attacks were evaluated as cerebrovascular disease (CVD). CVD was observed in a total of 12 patients (2.4%), 2 of them were under the age of 60 and 10 were over the age of 60. There was a significant difference between the two groups (p<0.01).

Seventy-six of 488 patients in the study were lost while being followed up in the coronary intensive care unit, and 75% of deaths occurred in the first day. Twenty-three (9.05%) patients aged ≤ 60 years, and 53 patients over 60 years of age (22.6%) exited These two mortality rates were found to be highly statistically significant (p<0.001) (Table 2).

Table 2. Mortality of patients followed in coronary intensive care unit.

	Group 1	Group 2	Total	p
Surviving	254	234	488	<0.001
Deceased	23 (9.05%)	53 (22.6%)	76 (45.5%)	

DISCUSSION

We investigated the distribution of the complications developed in 488 patients diagnosed with ST-elevated acute myocardial infarction in the coronary intensive care unit of our hospital between 1988 and 1991, by age groups and compared our results with the literature. The frequency of rhythm and conduction disorders without ventricular fibrillation was largely in line with studies on this subject [7-9]. In our study, ventricular fibrillation developed in a total of 33 patients, and there was no significant difference in terms of frequency of ventricular fibrillation between the two age groups. This result was compatible with the studies in the literature [7-9].

A total of 87 patients had various levels of heart failure, and a statistically significant difference was found in terms of heart failure in the group aged over 60 years (p<0.001). Some studies published similar results, [10-12]; while in some other studies any significant difference could not be detected in terms of heart failure among age groups [13].

Cardiogenic shock developed in 40 of the patients we followed and these patients were more commonly over the age of 60. Some studies in the literature supported our data [10-12], while others revealed different results [8,9,14]. Early deaths in our coronary intensive care patients were found to be significantly more common over 60 years of age, and this result is com-

patible with similar studies in the literature [12,13].

Eighteen of the patients we followed developed pericarditis, and although not statistically significant, pericarditis were more frequently seen under the age of 60. Findings of Farrell et al. and also James et al. were compatible with the findings in our study [12,13].

In our study, although there is no significant difference in terms of complications of myocardial infarction between both groups under and over 60 years of age; heart failure, cardiogenic shock, early death, cerebrovascular diseases were more common in the group over 60 years of age.

Although the infarct size was smaller in the elderly compared to the younger ones, left ventricular ejection fraction was lower, and congestive heart failure and cardiogenic shock developed more frequently. Thus, acute myocardial infarction became less lethal in young patients than in the elderly. However, tolerance to heart failure, arrhythmia and hypotension was significantly lower in the elderly. Opinions stating that the significant difference in mortality between the two groups can be explained by the more frequently seen multisystem diseases in elderly patients are generally supported.

Other predisposing causes to heart failure in the elderly are cardiovascular diseases such as age-related left ventricular hypertrophy, decreased ventricular compliance, and concomitant hypertension.

Mortality and morbidity rates in our elderly patients were similar to mortality and morbidity rates in other studies. All over the world, the incidence of myocardial infarction increases with age. Although mortality and morbidity rates are higher in the elderly after acute myocardial infarction, specific factors responsible for higher complication rates have not been clearly identified [12].

It has been generally reported that young patients with myocardial infarction have low mortality rates,and better prognosis; may be due to their better health status or smaller area infarct area. In the elderly it should also be taken into consideration that collateral vessels may develop in time, so they can overcome the infarction more easily which increases their post-infarction survival rates.

Ethics Committee Approval: Bakırköy Dr. Approval was obtained from the Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (218/33, 13.09.2018).
Conflict of interests: There is no conflict of interest.
Funding: There is no funding.
Informed Consent: Informed consent of the patients was obtained.

REFERENCES

1. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2012;33(20):2569-619.
https://doi.org/10.1093/eurheartj/ehs215
2. Alpert JS, Thygesen K. A new global definition of myocardial infarction for the 21st century. Pol Arch Med Wewn. 2007;117(11-12):485-6.
PMID: 18363245.
https://doi.org/10.20452/pamw.232
3. Bassand JP, Hamm CW, Ardissino D, Boersma E, Budaj A, Fernández-Avilés F, et al. ST segment yükselmesi olmayan akut koroner sendromların tanı ve tedavi kılavuzu. Eur Heart J. 2007;28(13):1598-660.
https://doi.org/10.1093/eurheartj/ehm161
4. Enar R. Temel kardiyoloji semiyoloji ve kardiyovasküler hastalıklar. İstanbul: Nobel Tıp Kitabevleri; 2007. p. 557-9.
5. Onat A, Uğur M, Çiçek G, et al. TEKHARF 2009 taraması: Kırsal kesim ve kentlerde benzer kardiyovasküler ölüm riski. Türk Kardiyol Dern Arş. 2010;38(3):159-63.
6. Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, et al. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64(24):e139-e228.
Erratum in: J Am Coll Cardiol. 2014;64(24):2713-4. Dosage error in article text. PMID: 25260718.
https://doi.org/10.1016/j.jacc.2014.09.017
7. Davia JE, Hallal FJ, Cheitlin MD, Gregoratos G, McCarty R, Foote W. Coronary artery disease in young patients: arteriographic and clinical review of 40 cases aged 35 and under. Am Heart J. 1974;87(6):689-96. PMID: 4828802.
https://doi.org/10.1016/0002-8703(74)90412-8
8. Dolder MA, Oliver MF. Myocardial infarction in young men. Study of risk factors in nine countries. Br Heart J. 1975;37(5):493-503.
PMID: 1137658; PMCID: PMC482827.
https://doi.org/10.1136/hrt.37.5.493
9. Bergstrand R, Vedin A, Wilhelmsson C, Wallin J, Wedel H, Wilhelmsen L. Myocardial infarction among men below age 40. Br Heart J. 1978;40(7):783-8.
PMID: 687475; PMCID: PMC483484.
https://doi.org/10.1136/hrt.40.7.783
10. Harris R, Piracha AR. Acute myocardial infarction in the aged: prognosis and management. J Am Geriatr Soc. 1970;18(11):893-904.
PMID: 5471846.
https://doi.org/10.1111/j.1532-5415.1970.tb02841.x
11. Yang XS, Nillems JL, DeGest H.Acute myocardial infarction in the aged: prognosis and manegment. J Am Geriatr Soc18:893-

4,1970.
https://doi.org/10.1111/j.1532-5415.1970.tb02841.x
12. Tofler GH, Muller JE, Stone PH, et al. Factors leading to shorter survival after acute myocardial infarction in patients ages 65 to 75 years compared with younger patients. Am J Cardiol. 1988;62(13):860-7.
PMID: 3177233.
https://doi.org/10.1016/0002-9149(88)90882-X
13. Uhl GS, Farrell PW. Myocardial infarction in young adults: risk factors and natural history. Am Heart J. 1983;105(4):548-53.
PMID: 6837409.
https://doi.org/10.1016/0002-8703(83)90476-3
14. Walker WJ, Gregoratos G. Myocardial infarction in young men. Am J Cardiol. 1967;19(3):339-43.
PMID: 6020303.
https://doi.org/10.1016/0002-9149(67)90445-6

Original Article

Med J Bakirkoy 2020;16(2):143-7
doi: 10.5222/BMJ.2020.14633

Medical Journal of Bakirkoy

Hypercalcemia in the Emergency Department: Prevalence, Etiology, and Mortality Rate

Acil Serviste Hiperkalsemi; Prevalans, Etiyoloji ve Mortalite Oranı

Semih Korkut[1], Ozlem Polat[2], Mehmet Hanifi Kazanci[3], Halil Dogan[1], Deniz Tural[4]

[1]Department of Emergency Medicine, University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey
[2]Department of Family Medicine, University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey
[3]Department of Internal Medicine, University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey
[4]Department of Medical Oncology, University of Health Sciences Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Istanbul, Turkey

Received: 08 February 2020 / **Accepted:** 16 May 2020 / **Publication date:** 26 June 2020

Cite as: Korkut S, Polat Ö, Kazancı MH, Doğan H, Tural D. Hypercalcemia in the emergency department: prevalence, etiology, and mortality rate. Med J Bakirkoy 2020;16(2):143-7.

ABSTRACT

Objective: *The aim of the study was to describe the prevalence, clinical characteristics of hypercalcemia and the impacts on renal function and survival in emergency department (ED) patients.*
Method: *We conducted a retrospective cross sectional descriptive study, all patient admitted between January 1, 2017, and January 1, 2018 to the ED of University of Health Sciences Bakirkoy TAR, were screened for the presence of hypercalcemia, defined as a serum calcium level greater than 10.3 mg/dL. Demographic, laboratory and outcome data were collected.*
Results: *During the study period, 1.246 of 318.527 patients (120.418 patients received a measurement of serum calcium) (0.01%) were found to have hypercalcemia (Serum calcium 11.0±0.8 mg/dL) Mild hypercalcemia seen more frequently (calcium level <12 mg/dL, 94.3%). Renal fuction was normal in 995 (79.8%) of all patients with hypercalcemia. The total mortality rate was 0.01%, and death was associated with higher age, higher calcium level, lower albumin, lower hemoglobin, higher creatinine and higher white blood cells (all p<0.05).*
Conclusions: *Although hypercalcemia is common in ED, severe hypercalcemia is rare and fatal. Therefore we recommend measuring the serum calcium level in at-risk patients in the ED and treatment should be initiated to detected underlying disease.*

Keywords: *hypecalcemia, electrolyte disturbance, emergency department*

ÖZ

Amaç: *Bu çalışmayla acil servise başvuran hastalarda hiperkalsemi prevelansını, klinik özelliklerini, böbrek fonksiyonu üzerine etkilerini ve mortalite oranını belirlemeyi amaçladık.*
Yöntem: *Retrospektif kesitsel tanımlayıcı olarak 1 Ocak 2017 ve 1 Ocak 2018 tarihleri arasında Sağlık Bilimleri Üniversitesi Bakırköy Dr. Sadi Konuk Eğitim ve Araştırma Hastanesi Acil Servisine başvuran hastalarda, kalsiyum seviyesi 10,3 mg/dL'den daha yüksek olanlar belirlendi. Bu hastaların demografik, laboratuvar ve klinik verileri toplandı.*
Bulgular: *Bir yıllık süreçte başvuran 318.527 hasta içinden 120.418 hastada kalsiyum seviyesi tetkik edildi ve hastaların 1.246'sında (%0,01) hiperkalsemi saptandı. (Serum kalsiyum 11,0±0,8 mg/dL). Hastaların %94,3'ünde hafif hiperkalsemi vardı (kalsiyum seviyesi <12 mg/dL, %94,3). Hastaların %79,8'inde renal fonksiyonları normaldi. Mortalite oranı %0,01 idi. İleri yaş, ağır hiperkalsemi, kreatinin yüksekliği ve lökositoz durumları mortalite ile ilişkili saptandı (p<0,05). Ek olarak albumin ve hemoglobin değerleri daha düşük olan hastalarda mortalite oranının arttığı görüldü (p<0,05).*
Sonuç: *Şiddetli hiperkalsemi nadir görülmesine rağmen ölümcül olabilmektedir. Bu nedenle acil servise başvuran risk altındaki hastalarda serum kalsiyum düzeyini ölçmeyi ve zaman kaybetmeden altta yatan hastalığı tedavi etmeyi öneriyoruz.*

Anahtar kelimeler: *hiperkalsemi, elektrolit bozuklukları, acil servis*

Corresponding Author:
✉ m.kazanci@saglik.gov.tr

S. Korkut 0000-0002-5409-3586
O. Polat 0000-0002-7512-1283
M.H. Kazanci 0000-0001-9129-6393
H. Dogan 0000-0003-4751-030X
D. Tural 0000-0003-2144-6469

INTRODUCTION

Electrolyte disorders are commonly observed in the ED. Deterioration of calcium levels is very important issue. The clinical range of hypocalcemia and hypercalcemia is wide and can cause death. Although many patients are diagnosed as asymptomatic in practice, it is common in patients applying for ED with different symptoms. There was a few studies on electrolyte disorders in ED. Two of them retrospective study on the epidemiology of hypercalcemia in the ED has been published [1,2]. Also a study on hospitalized patients from Hong Kong confirmed hypercalcemia. (Incidence 1%) [3]. A <5% incidence was found in hospital admission patients and less than 1.0% in outpatients [4,5]. The clinical range of hypercalcemia is wide. It also cause neurologic symptoms such as weakness, lethargy, and even coma. On the other hand, it causes gastrointestinal signs such as vomiting, nausea [6].

Most patients with hypercalcemia are asymptomatic; but symtoms of hypercalcemia usually proportional to calcium elevation. Symptoms may be rapid onset because of calcium serum level variability and the underlying disease. When serum calcium level exceeds 14.0 mg/dL, hypercalcemia crisis occurs. This is associated with mortality. In this case severe complications may occur. Therefore, it is necessary to measure the serum calcium level in patients admitted to ED. In addition, Hypercalcemia can be seen in conjunction with other electrolyte should be noted. Especially magnesium and sodium homeostasis should be looked at when evaluating patients [7].

We evaluated patients who admitted to the ED with symptoms of hypercalcemia. We investigate the prevalence of hypercalcemia, survival of ED patients and hypercalcemia association with renal failure.

MATERIAL AND METHODS

In this retrospective descriptive study , the database of the central laboratory of University of Health Sciences Bakirkoy TAR was scanned for elevated serum calcium levels from the Department of ED. All patients admitted between January 1, 2017, and January 1, 2018. In our hospital, the level of serum calcium is 8.6 to 10.3 mg/dL is normal range. We defined hypercalcemia was serum total calcium concentration greater than 10.3 mg/dL. In addition; serum albumin level affects serum calcium level. Therefore, we perform a correction formula was used to calculate exact calcium level: [1] Corrected total serum calcium level (mg/dL) = measured total calcium level (mg/dL) + 0.8 × [4.0 - albumin concentration (g/dL)].

Patients were divided into three parts depending on serum calcium levels. Mild hypercalcemia (10.3-11.9 mg/dL), moderate hypercalcemia (12.0-14.0 mg/dL), and severe hypercalcemia (>14.0 mg/dL). Demographic data (all identified patientes, namely, age and gender) were recorded. Biochemical data including sodium, magnesium, creatine, albumin concentration, renal function test results and hemogram results were also recorded. All patients followed from the duration of in-hospital to until his or her discharge and in-hospital mortality.

Statistical analysis was performed by use of SPSS 19.0. Data are presented as mean±SD. Student's t-test, Mann Whitney U test was used to compare demographic and biochemical data between survivor and nonsurvivor groups. X^2 test used for the statistical significance of the effect of various degrees of hypercalcemia on mortality rate, renal failure, and other variables. In additon, independent variables was selected on factors that showed significant changes between survivors and nonsurvivors. A P-value less than 0.05 was statistically significant.

RESULTS

During in this study, 318527 patients (all admitted patients) were admitted to our ED, of which 120418 (37%) received a measurement of serum calcium levels. Among them, 1246 patients (0.01%) presented with hypercalcemia. 635 (51%) patients were female and 611 (49%) patients were male. Median serum calcium was 10.77 mg/dL, with 21 mg/dL being the highest serum calcium value observed. Reference calcium level was 8.6-10.3 mg/dL. Mild hypercalcemia was defined as serum calcium level 10.3-11.9 mg/dL, moderate hypercalcemia was defined as 12-14 mg/dL and severe hypercalcemia was defined as 14 mg/dL. Most of patients had mild hypercalcemia (calcium level 10.3-12 mg/dL, 94.37%)

The level of hypercalcemia in respect to the age distribution of the patients participated in our study which was split into 7 groups (20 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years,70 years) is investigated. Mild hypercalcemia found to be significantly (p=0.003) in 20-29 years (17.14%) and 50-59 years (17.32%) among all the other age groups. Moderate hypercalcemia found to be significantly (p=0.000) in 50-59 years (25.0%), 60-69 years (25.0%) and 70 years (38.46%). There was no significant difference in the age distribution of groups with severe hypercalcemia (p=0.198) (Table 2).

In order to track seasonal variation of serum calcium levels, the serum calcium levels of the study samples in respect to each month were investigated. Mild hypercalcemia, the case numbers were significantly (p=0.000) elevated in September (24.02%) and October (23.66%). Moderate/severe hypercalcemia wasn't found to be significantly in respect to each months. Overall, the cases of mild hypercalcemia found to be significantly (p=0.0001) elevated among all the other hypercalcemia groups screened during the whole year.

The major determinants of renal failure are serum urea and creatinine values in respect to plasma calcium levels were investigated. As compared to mild hypercalcemia, serum creatinine levels were significantly (p=0.000) elevated in severe hypercalcemia. With increasing calcium level, the incidence of concurrent renal failure also increased after the uremic group is excluded. Also, urea levels found to be decreased in mild hypercalcemia as compared to severe hypercalcemia.

Since anemia is common in advanced renal failure, hemoglobin levels were also investigated in respect to plasma calcium levels. As compared to severe or moderate hypercalcemia serum hemoglobin is ele-

Table 1. Characteristics of Hypercalcemic Patients.

Female gender, n (%)	635 (50.96)
Male gender, n (%)	611 (49.04)

Table 2. The level of hypercalcemia in respect to the age distribution of the patients.

	Mild (10.3-11.9 mg/dL)	Moderate (11.9-14.0 mg/dL)	Severe (Camg/dL)	P value*
Patients, n (%)	1174 (94.37)	52 (4.18)	18 (1.45)	
Age Groups				
20 years	148 (99.33)	1 (0.67)	0 (0.00)	0.000
20-29 years	197 (98.99)	2 (1.01)	0 (0.00)	0.000
30-39 years	152 (99.35)	1 (0.65)	0 (0.00)	0.000
40-49 years	155 (98.1)	2 (1.27)	1 (0.63)	0.000
50-59 years	200 (92.17)	13 (5.99)	4 (1.84)	0.000
60-69 years	155 (88.57)	13 (7.43)	7 (4.00)	0.000
70 years	167 (89.53)	20 (10.36)	6 (3.11)	0.000
P value	0.003	0.000	0.198	

Table 3. Serum calcium levels stratified for the laboratory finding.

	Mild hypercalcemia Mean+SD Med. (Min.-Max.)	Moderate hypercalcemia Mean+SD Med. (Min.-Max.)	Severe hypercalcemia Mean+SD Med. (Min.-Max.)	p
Calcium	10.84±0.29 10.75- (10.3-11.94)	12.72±0.59 12.58- (12-13.94)	15.65±1.33 15.32- (14.01-19.35)	0.000
Creatinine	1.09±1.16 0.86- (0.21-19.04)	1.77±1.79 0.95- (0.52-8.18)	2.95±2.14 2.98- (0.53-9.13)	0.000
Urea	40.02±28.96 32- (10-276)	74.46±55.71 58.5- (17-264)	118.88±63.42 100- (24-223)	0.000
Albumin	4.82±0.63 4.9- (0.1-6.8)	3.54±0.86 3.6- (2-5.2)	3.29±0.61 3.5- (2.2-4.1)	0.000
WBC	10.89±4.28 9.93- (0-38.5)	14.53±8.49 11- (4.23-37.39)	19.53±10.56 15.69- (7.29-42.1)	0.000
Hemoglobin	13.88±2.19 14- (0-20.9)	11.26±2.61 11.54- (6.63-15.3)	10.38±2.82 10.3- (5.02-14.7)	0.000
Trombocyte	298.44±110.63 289- (1.52-2166)	287.78±165.69 251- (26.7-744)	222.27±95.6 236.5- (55.09-353)	0.005

vated in mild hypercalcemia. Serum albumin level found to be significantly (p=0.000) elevated in mild hypercalcemia compared to moderate or severe hypercalcemia. Also compared to mild hypercalcemia white blood count is elevated in severe hypercalcemia (p=0.001). Hemoglobin levels found to be significantly higher in mild hypercalcemia rather than moderate or severe hypercalcemia (Table 3).

Survival among the study samples is significantly (P=0.002) higher in 20 years 20-29 years of age. Mortality is significantly (P=0.005) higher in70 years of age. The mortality rate increased significantly as the hypercalcemia progressed. Patients with severe hypercalcemia had the highest mortality rate (11,1% p=0.002) (Table 5). Patients who died had significantly higher calcium, higher white blood count, and lower albumin levels, whereas gender, hemoglobin levels and platelet counts were similar in both survivors and non-survivors (Table 4).

Table 4. Comparison between hypercalcemic patients who survived and those who died.

	Survivors Mean+SD Med. (Min.-Max.)	Non-survivors Mean+SD Med. (Min.-Max.)	p
Calcium	10.93±0.8 10.75- (7.92-19.35)	12.13±1.76 11.75- (8.57-15.76)	0.001
Creatinine	1.13±1.21 0.87- (0.21-19.04)	2.92±2.19 2.28- (0.92-9.13)	0.000
Urea	42.6±32.39 33- (10-262)	110.24±80.24 93- (24-276)	0.000
Albumin	4.74±0.71 4.9- (0.1-6.8)	3.76±0.87 3.6- (2.1-5.5)	0.000
WBC	11.18±4.79 10.06- (0-48.41)	18.11±10.59 13.5- (3.61-42.1)	0.001
Hemoglobin	13.74±2.29 13.9- (0-20.9)	12.41±2.99 12.94- (6.76-16.5)	0.093
Trombocyte	296.08±112.14 288- (1.52-2166)	269.84±160.31 283- (51-536.2)	0.606

** Mann Whitney U test*

Table 5. Comparison between level of hypercalcemia in patients who survived and those who died.

	Survivors N (%)	Non survivors N (%)
Mild hypercalcemia	1160 (98.80)	14 (1.20)
Moderate hypercalcemia	51 (98.08)	1 (1.92)
Severe hypercalcemia	16 (88.89)	2 (11.11)*
p		0.002*

**x^2 test*

Table 6. Genders of hypercalcemic patients who survived and those who died.

	Survivors N (%)	Non survivors N (%)
Female	625 (98.58)	9 (1.42)
Male	603 (98.69)	8 (1.31)
p	0.530	0.808

** x^2 test*

DISCUSSION

We have presented although hypercalcemia was common electrolyte disturbance in patients in the ED but severe hypercalcemia was rare and fatal. The incidence was much lower in our study than in other studies [4,5]. In one of the other studies, the incidence of hypercalcemia was detected 7.5% [1]. Some studies similar to our study, the prevalence of hypercalcemia is low [2]. Also the low prevalence of hypercalcemia was detected in hospitalized patients in some studies [12,13].

In our study on more than 120 000 ED patients, 0.01% were identified to have hypercalcemia defined as a serum calcium exceeding 10.3 mg/dL after correction for serum albumin. Hypercalcemia can be seen in conjunction with other electrolyte should be noted. Especially magnesium and sodium homeostasis should be looked at when evaluating patients [7]. The vast majority of our patients had previously been diagnosed with hyperparathyroidism and malignancy. Hyperparathyroidism and malignancy most common cause of hypercalcemia. Similar results have been shown in the etiology of hypercalcemia in many previous studies [4,5,8,9]. High incidence of hypercalcemia in patients diagnosed with malignancy is explained by several different mechanisms. These mechanisms depend on type and degree of malignancy. Hypercalcemia is common, especially in cases of advanced cancer or terminal stage. These conditions are considered bad prognosis. The average survival expectancy is usually very short in these patients.

Increased bone resorption, calcium absorption from the intestine and reduction of renal tubular reabsorbion are some of the mechanisms of hypercalcemia in the head. Hypercalcemia is also seen in cases such

as severe systemic infections, increased cytokine release, diabetic ketoacidosis, liver abscess [1]. In some studies, uremia has also shown that hypercalcemia is a common cause. Reduction of renal tubular reabsorbion of calcium, reduced glomerular filtration, hypovolemia, nephrotoxic agents are also effected renal failure. Therefore, hypercalcemia can often occur with acute renal failure due to all these mechanisms. This may explain the high incidence of acute renal failure with hypercalcemia. In other studies, acute renal failure with hypercalcemia is commonly reported [1,10,11].

The clinical range of hypercalcemia is very wide. While not symptoms in the asymptomatic period, symptoms become noticeable as serum calcium levels rise [1,2,14]. Depending on the underlying diseases and complications, the increase in serum calcium levels may vary. Therefore, serum calcium levels are very important in patients at risk. Patients with severe hypercalcemia had the highest mortality rate in our study. Patients who died had significantly higher calcium and lower albumin levels, whereas hemoglobin levels, white blood count and platelet counts were similar in both survivors and non-survivors. Similar results to our study have been shown in previous studies [1,2,4].

Our study is limited due to its retrospective. Restrictions such as not documenting all symptoms and symptoms in patients with hypercalcemia, not working with each patient of important data such as Vitamin PTH and Vitamin D, and giving ambulatuar treatment without detecting the underlying disease are in the missing aspects of the study.

Consequently, hypercalcemia is seldom electrolyte disorder in the ED but severe hypercalcemia is rare and harmful. In our study, we found that the mortality rate was higher as hypercalcemia was more severe. Also our results show that in patients with higher hypercalcemia, lower albumin levels, higher age had the highest mortality. Therefore we recommend measuring the serum calcium level in all patients diagnosed with malignancy, both gastrointestinal and neurological symptoms and in at-risk patients in the ED. In at-risk patients, it is important to find the underlying disease starting early in treatment.

Ethics Committee Approval: Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee approval was received (2020/185).
Conflict of Interest: None.
Funding: No financial support was received.
Informed Consent: Consent was obtained from patients.

REFERENCES

1. Lee CT, Yang CC, Lam KK, Kung CT, Tsai CJ, Chen HC. Hypercalcemia in the emergency department. Am J Med Sci. 2006;331(3):119-23. https://doi.org/10.1097/00000441-200603000-00002
2. Lindner G, Felber R, Schwarz C, Marti G, Leichtle AB, Fiedler GM, Zimmermann H, Arampatzis S, Exadaktylos AK. Hypercalcemia in the emergency department: prevalence, etiology, and outcome: Am J Emerg Med. 2013 Apr;31(4):657-60 https://doi.org/10.1016/j.ajem.2012.11.010
3. Shek CC, Natkunam A, Tsang V, Cockram CS, Swaminathan R. Incidence, causes and mechanism of hypercalcaemia in a hospital population in Hong Kong. QJ Med. 1990;77(284):1277-85. https://doi.org/10.1093/qjmed/77.3.1277
4. Fisken RA, Heath DA, Somers S, et al. Hypercalcaemia in hospital patients: clinical and diagnostic aspects. Lancet. 1981;1:202-7. https://doi.org/10.1016/S0140-6736(81)90071-4
5. Shek CC, Natkunam A, Tsang V, et al. Incidence, causes and mechanism of hypercalcaemia in a hospital population in Hong Kong. Q J Med. 1990;77:1277-85. https://doi.org/10.1093/qjmed/77.3.1277
6. Bushinsky DA, Monk RD. Electrolyte quintet: calcium. Lancet. 1998;352(9124): 306-11. https://doi.org/10.1016/S0140-6736(97)12331-5
7. Milionis HJ, Rizos E, Liamis G, et al. Acid-base and electrolyte disturbances in patients with hypercalcemia. South Med J. 2002;95:1280-7. https://doi.org/10.1097/00007611-200295110-00011
8. Diamond TH, Botha JR, Vermaak WJ, Kalk WJ. Hypercalcaemia in the Johannesburg Hospital. Differential diagnosis and physician awareness of primary hyperpara- thyroidism. S Afr Med J. 1987;72(2):113-5.
9. Rajathurai A, Cove-Smith R. Hypercalcaemia in Cleveland: a hospital-based survey. J R Soc Med. 1984;77(9):742-6. https://doi.org/10.1177/014107688407700906
10. Levi M, Ellis MA, Berl T. Control of renal hemodynamics and glomerular filtration rate in chronic hypercalcemia: role of prostaglandins, renin-angiotensin system, and calcium. J Clin Invest. 1983;71:1624-32. https://doi.org/10.1172/JCI110918
11. Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. Am J Kidney Dis. 2002;39:930-6. https://doi.org/10.1053/ajkd.2002.32766
12. Dent DM, Miller JL, Klaff L, Barron J. The incidence and causes of hypercalcaemia. Postgrad Med J. 1987;63(743):745-50. https://doi.org/10.1136/pgmj.63.743.745
13. McLellan G, Baird CW, Melick R. Hypercalcaemia in an Australian hospital adult population. Med J Aust. 1968;2(8):354-6 https://doi.org/10.5694/j.1326-5377.1968.tb82823.x
14. Ziegler R. Hypercalcemic crisis. J Am Soc Nephrol. 2001;12(Suppl):S3-9.

Original Article

Med J Bakirkoy 2020;16(2):148-51
doi: 10.5222/BMJ.2020.97269

Medical Journal of Bakirkoy

Evaluation of Clinical and Operative Characteristics of Patients Undergoing Laparoscopic and Open Simple Nephrectomy

Laparoskopik ve Açık Basit Nefrektomi Yapılan Hastaların Klinik ve Operatif Özelliklerinin Değerlendirilmesi

Ekrem Guner, Yusuf Arikan

Health Science University, Bakirkoy Dr. Sadi Konuk Training and Research Hospital, Department of Urology, Istanbul, Turkey

Received: 1 April 2019 / **Accepted:** 4 January 2020 / **Publication date:** 26 June 2020

Cite as: Guner E, Arikan Y. Evaluation of clinical and operative characteristics of patients undergoing laparoscopic and open simple nephrectomy. Med J Bakirkoy 2020;16(2):148-51.

ABSTRACT

Objective: *We aimed to raise awareness of patient management by examining the clinical and operative characteristics of patients undergoing simple nephrectomy for benign pathologies.*
Method: *Data of patients who underwent simple nephrectomy for benign pathologies in our clinic between 2008-2019 were reviewed retrospectively. Demographic data, nephrectomy indications, renal scintigraphy results and operative characteristics of the patients were analyzed.*
Results: *A total of 90 patients (51 female and 39 male) were included in the study. The mean age of the patients was 45.1 ± 14.6 years. Fourty-eight of the nephrectomized kidneys were right kidney and 42 were left kidneys. Laparoscopic nephrectomy was performed in 47 (52.2%) patients and open nephrectomy was performed in 43 (47.8%) patients. A total of 6 patients (6.6%) had peroperative complications. There was no difference in peroperative complications in patients undergoing laparoscopic and open nephrectomy (p = 0.14). Patient ages, BMIs and operative times were similar; p = 0.535, p = 0.337 and p = 0.074, respectively.*
Conclusion: *Laparoscopic and open surgery provides similar surgical results in simple nephrectomies due to benign pathologies compared to the surgeon experience.*

Keywords: *simple nephrectomy, laparoscopic nephrectomy, non-functional kidney*

ÖZ

Amaç: *Benign patolojiler sebebi ile basit nefrektomi yapılan hastaların klinik ve operatif özelliklerini incelemek sureti ile hasta yönetiminde farkındalık yaratmayı amaçladık.*
Yöntem: *2008-2019 yılları arasında kliniğimizde benign patolojiler nedeniyle basit nefrektomi yapılan hastaların verileri geriye dönük olarak tarandı. Hastaların demografik verileri, nefrektomi endikasyonları, renal sintigrafi sonuçları, operatif özellikleri incelendi.*
Bulgular: *Çalışmaya 39'u kadın ve 51'i erkek olmak üzere toplam 90 hasta dahil edildi. Hastaların ortalama yaşı 45.1±14.6 yıl idi. Nefrektomi yapılan böbreklerin 48'i sağ böbrek iken 42 tanesi sol böbrek idi. Hastaların 47'sine (%52.2) laparoskopik nefrektomi yapılırken 43'üne (%47.8) açık nefrektomi yapıldı. Toplam 6 hastada (%6,6) peroperatif komplikasyon izlendi. Laparoskopik ve açık nefrektomi yapılan hastalarda peroperatif komplikasyon açısından farklılık izlenmezken (p=0.14), hasta yaşları, VKİ'leri ve operasyon süreleri benzer idi; sırasıyla p=0.535, p=0.337 ve p=0.074.*
Sonuç: *Laparoskopik ve açık cerrahi benign nedenler dolayısı ile yapılan basit nefrektomilerde cerrah deneyimine göre benzer cerrahi sonuçlar sunmaktadır.*

Anahtar kelimeler: *ebasit nefrektomi, laparoskopik nefrektomi, non-fonksiyone böbrek*

Corresponding Author:
dryusufarikan@gmail.com

E. Guner 0000-0002-4770-7535
Y. Arikan 0000-0003-0823-7400

INTRODUCTION

While simple nephrectomy is generally used to define nephrectomy done for benign pathologies, radical nephrectomy is a term used for nephrectomy done for malign diseases. This terminology actually causes misunderstandings. Although nephrectomy can be considered as an easier technique with less complications compared to radical nephrectomy based on this term, this is not the actual condition as accepted by many experienced surgeons. Especially nephrectomies related to severe pyelonephritis and stone disease can be more difficult and have complications compared to its radical conjugate [1,2]. Simple nephrectomy can be done in many different ways such as retroperitoneal, transperitoneal, open, laparoscopic, robot-assited [3,4,5]. Underlying pathology affects the operation characteristics.

Our aim in this study was to create awareness in patient management by examining clinical and operative characteristics of patients who had simple nephrectomy due to benign pathologies.

MATERIAL and METHOD

After taking the consent of local ethics board of our hospital, data of patients who had simple nephrectomy due to benign pathologies in our clinic between 2008 and 2019 were retrospectively scanned. Demographic data, nephrectomy indications, renal scintigraphy results and operative characteristics of the patients were examined. Male and female patients between the ages of 18 and 80 who had nephrectomy due to benign pathologies were included in the study. Patients who were under 18 years of age, had nephrectomy secondary to trauma and whose data were unreachable were excluded from the study. Patients were separated into two groups based on the operation type as open and laparoscopic.

Statistical Analysis

SPSS statistics package program version 21 was used for data analysis. While constant variables were given in mean ± standard deviation, categorical variables were given in percentages. Mann-Whitney U test was used for the comparison of the two groups. $P<0.05$ was regarded as statistically significant.

RESULTS

A total of 90 patients including 39 male and 51 female patients were included in the study. The mean age of the patients was 45.1±14.6 years. Nephrectomy was made on the right side in 48 and left side on 42 of the kidneys. 24 of the patients who had nephrectomy had urinary system intervention story. When the etiologies of the pathologies causing nephrectomy are examined, 66 (73%) patients had obstruction-causing stone, 15 (16.6%) had ureteropelvic junction obstruction, 4 (4,4%) had vesico-ureteral reflux, 3,3 (3,3%) had preparation before kidney transplantation, 2 (2,2%) had trauma. No function was observed in the kidney based on the scintigraphic examination made on 70 patients. When DMSA evaluations of all patients were examined, average kidney function was found as 4.3±9.6. While laparoscopic nephrectomy was made in 47 of the patients (52,2%), open nephrectomy was made in 43 (47,8%). Average operation duration was 120±28.2 min. While intraoperative difficulty of dissection was observed in hilus in 45 (50%) patients and kidney parts other than hilus in 35 (38,8%) patients, no difficulty of dissection was observed in 10 patients. Peroperative complication was observed in a total of 6 patients (6,6%). While difference was observed in peroperative complications in the patients who had laparoscopic and open nephrectomy ($p=0.14$), the patient ages, BMIs and operation durations were similar; $p=0.535$, $p=0.337$ and $p=0.074$ in order. Length of hospital stay was significantly shorter in the laparoscopic group (3.6 days vs. 1.7 days; $p<0.0001$). Mean postoperative pain score on postoperative first day after surgery was significantly lower laparoscopic group between 2 groups on the visual analog pain scale ($p<0.005$). Non-steroidal anti-inflammatory drug (NSAID) and narcotic use was decreased in the laparoscopic group on postoperative first day ($p=0.008$) (Table 1).

Based on the examination of final pathology specimens, chronic pyelonephritis was observed in 42 patients (46,6%), tubulo-interstitial nephritis in 23 patients (25,5%), atrophic kidney in 22 patients (24.4%) and other pathologies in 3 patients (3,3%).

Table 1. Evaluation of patients undergoing open and laparoscopic nephrectomy.

Variables		Laparoscopic Simple Nephrectomy (n=47)	Open Simple Nephrectomy (n=43)	P value
Age		44.5±14.6	47.3±15	0.53
Gender	Man Woman	26 (55.3%) 21 (44.7%)	13 (30.2%) 30 (69.7%)	0.2
Body-Mass Index (kg/m^2)		26.03±1.32	26.4±1.9	0.33
Operation Time		143.4±26.4	127.6±31.3	0.74
Complication		4 (8.5%)	2 (4.6%)	0.14
		Bleeding=2 Bowel Injury =1 Pneumothorax=1	Bleeding=1 Bowel Injury=1	
Hospital Stay (day)		1.7±0.6	3.6±2.2	0.001
VAS score		3.1±2.1	6.6±3.2	0.005
NSAID and Narcotic Drug Use (n,%)		20 (42.5%)	35 (81.3%)	0.008

DISCUSSION

Nephrectomies to be made due to benign pathologies can be laparoscopic or open. Less postoperative pain, shorter hospitalization duration, early returning to daily life and better cosmetic results are the superiorities of laparoscopic surgery. Laparoscopic and open surgery has difficulties in obese patients. While retraction of fatty tissue may create problem in open surgery, trocar places may need to be changed due to the increasing distance in laparoscopic surgery [6].

It was considered that etiologies indicating benign nephrectomy may have effects on the operation results. In a study made by Kurt et al [7], patients who had laparoscopic simple nephrectomy were separated into two groups as those with and without inflammatory etiology and the surgery results were compared. In this small-scale study including 49 patients, no difference was detected in operation duration, peroperative bleeding, hospitalization duration, postoperative hemoglobin and creatinine change among the two groups [7]. In another study made by Manohar et al [8], operation results of the patients who had laparoscopic and open surgery and simple nephrectomy due to inflammatory etiologies were compared. While pleura injury was observed significantly more in open nephrectomy group, visceral organ injury was observed more in laparoscopic nephrectomy group. Hospitalization duration and analgesic need were observed to be significantly high in open nephrectomy group again in this study, 4.3±0.8 days vs 8.07±1.8 days and 165±71.2 gr diclofenac sodium vs 284±81 gr in order. In our study, no difference was detected in the peroperative complications of the patients who had laparoscopic and open nephrectomy.

In a study made by Shah et al [9], factors which may predicate intraoperative difficulty in laparoscopic simple nephrectomy were investigated. As a result, presence of pyonephrosis in preoperative imagings in multi-variate analysis and BMI under 25 kg/m^2 were found as the most important factors predicating intraoperative difficulty in laparoscopic simple nephrectomy. In addition, kidney intervention story in uni-variate analysis was found as a factor predicating intraoperative difficulty [9]. Ages and BMIs of the patients who had laparoscopic and open nephrectomy were similar in our current study.

In a study made by Zelhof et al, the most common intraoperative complications in open surgery were

reported as adjacent organ injury (intestine, spleen, liver, and pancreas), bleeding and pneumothorax. The most common postoperative complications were wound and lung infections. While intraoperative bleeding more than 500 mL was reported in 6.8% of the patients, blood transfusion was made for 4.8% of the patients. Intraoperative and postoperative complications, blood loss and returning to open were observed more than other indications in nephrectomies due to urinary system stone disease [(1)]. While bleeding and intestinal injury were observed in our study, bleeding, intestinal injury and pneumothorax were observed in laparoscopic surgery.

One of the advantages of laparoscopy versus open surgery is that it reduces the length of hospital stay and the need for postoperative NSAID and narcotic drugs is decreased. The fact that the incision is much smaller in laparoscopic surgery reduces the need for medication for pain control and shortens the postoperative time to mobilization. It was observed that the early mobilization of the patient also reduced the length of hospital stay [(10)]. In our study, it was found that the hospitalization stay and the need for postoperative pain medication was statistically lower in the laparoscopic surgery group.

CONCLUSION

Depending on the experience of the surgeon, laparoscopic and open surgery presents similar surgical results in simple nephrectomies made due to surgical benign causes. Recovery speed, cosmetic results and less pain in postoperative period may support laparoscopic surgery.

Ethics Committee Approval: Bakırköy Dr. Approval was obtained from the Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (2019/325, 02.09.2019).

Conflict of Interest: The author declares that he has no conflict of interest.

Funding: No financial support was received.

Informed Consent: Informed consent was not obtained since the study is retrospective.

REFERENCES

1. Zelhof B, McIntyre IG, Fowler SM, Napier-Hemy RD, Burke DM, Grey BR, British Association of Urological S. Nephrectomy for benign disease in the UK: results from the British Association of Urological Surgeons nephrectomy database. BJU Int 2016;117(1):138-44. https://doi.org/10.1111/bju.13141
2. Connolly SS, O'Brien MF, Kunni IM, Phelan E, Conroy R, Thornhill JA, Grainger R. Is simple nephrectomy truly simple? Comparison with the radical alternative. Ir J Med Sci 2011;180 (1):177-9. https://doi.org/10.1007/s11845-010-0651-7
3. McDougall EM, Clayman RV. Laparoscopic nephrectomy for benign disease: comparison of the transperitoneal and retroperitoneal approaches. J Endourol 1996;10 (1):45-9. https://doi.org/10.1089/end.1996.10.45
4. EAU Guidelines on Renal Cell Carcinoma, 2019
5. Malignant Renal Tumors. Steven C. Campell MD, PhD and Brian R. Lane MD, PhD Campell Walsh Urology, 57, 1314-1364.e14.
6. Gupta NP, Gautam G. Laparoscopic nephrectomy for benign non functioning kidneys. J Minim Access Surg. 2005;1 (4):149-54. https://doi.org/10.4103/0972-9941.19261
7. Kurt O, Buldu I, Turan C, Yazici CM. Does laparoscopic transperitoneal simple nephrectomy for inflammatory and non-inflammatory kidneys differ? Springerplus 2016;5(1):1358. https://doi.org/10.1186/s40064-016-2945-3
8. Manohar T, Desai M, Desai M. Laparoscopic nephrectomy for benign and inflammatory conditions. J Endourol 2007;21 (11):1323-8. https://doi.org/10.1089/end.2007.9883
9. Shah P, Ganpule A, Mishra S, Sabnis R, Desai MR. Prospective study of preoperative factors predicting intraoperative difficulty during laparoscopic transperitoneal simple nephrectomy. Urol Ann 2015;7(4):448-53. https://doi.org/10.4103/0974-7796.152045
10. Shuford MD, McDougall EM, Chang SS, LaFleur BJ et al. Complications of Contemporary Radical Nephrectomy: Comparison of Open vs. Laparoscopic Approach. Urol Oncol, 2004;22(2):121-6. https://doi.org/10.1016/S1078-1439(03)00137-6

Original Article

Med J Bakirkoy 2020;16(2):152-9
doi: 10.5222/BMJ.2020.14622

Medical Journal of Bakirkoy

Our Magnetic Resonance Imaging Findings in Symptomatic Uterine Fibroid Patients Who Underwent Uterine Artery Embolization

Uterin Arter Embolizasyon Tedavisi Yapılan Semptomatik Uterin Miyomu Olan Hasta Grubunda Klinik ve Manyetik Rezonans Görüntüleme Bulgularımız

Caglayan Cakir, Fatih Kilinç, Aysun Erbahceci Salik, Hakan Selcuk

University of Health Sciences, Radiology Depertment of Bakirkoy Dr Sadi Konuk Training and Resarch Hospital, Istanbul, Turkey

Received: 11 September 2019 / **Accepted:** 13 January 2020 / **Publication date:** 26 June 2020

Cite as: Cakir C, Kilinç F, Erbahceci Salik A, Selcuk H. Our magnetic resonance imaging findings in symptomatic uterine fibroid patients who underwent uterine artery embolization. Med J Bakirkoy 2020;16(2):152-9.

ABSTRACT

Objective: *We aimed to examine the technical success, early-stage clinical results and radiological follow up findings of uterine artery embolization (UAE) treatment for symptomatic uterine fibroids in patients.*
Method: *In the present study, we retrospectively evaluated the patients who were admitted to our hospital. Between February 2017 and July 2019 with symptoms due to uterine fibroids namely myomas and underwent endovascular embolization treatment. Patients with complaints of excessive, prolonged, irregular, and frequent episodes of uterine bleeding, anemia, abdominal pain, palpable mass, and pollakiuria associated with uterine myoma which impaired quality life of the patients were included in this study. In addition, Magnetic Resonance Imaging (MRI) findings, and clinical symptoms of all patients before UAE, and 6th months after UAE were recorded.*
Results: *In our study, a total of 40 patients aged between 23-50 years (mean 41.3), one of whom had a history of hysterectomy underwent UAE procedure in our hospital. In our series, clinical symptoms, MRI and digital subtraction angiography (DSA) findings were presented. Uterine fibroid volumes as estimated based on MRI images obtained before - and 6 months after UAE were recorded (234,47±76,48 vs 17,27±43,53 (p=0,001). Embolization was cancelled due to intense atherosclerotic causes in one patient, and embolization of unilateral uterine artery could be achieved. The remaining 39 patients underwent successful UAE procedure bilaterally. There were no complications associated with endovascular procedure. After the procedure, all of these 39 patients were discharged on the same day following bed rest and one patient could be discharged one week later due to the development of urosepsis.*
Conclusion: *UAE is a novel treatment modality which is being increasingly used in patients with symptomatic uterine fibroids, and it is an important and effective treatment option since it is much less invasive compared to hysterectomy, does not require hospitalization after the procedure and can be performed under simple sedation or spinal anesthesia.*

Keywords: *uterine fibroids, uterine artery, embolization, magnetic resonance imaging*

ÖZ

Amaç: *Çalışmamızda miyom nedeniyle semptomları olan hasta grubunda Uterin Arter Embolizasyon (UAE) tedavisinin teknik başarı, erken dönem klinik sonuçları ve radyolojik takip bulgularını gözden geçirmeyi amaçladık.*
Yöntem: *Şubat 2017-Temmuz 2019 tarihleri arasında hastanemize uterin fibroide yani miyoma bağlı semptomları nedeniyle başvurup UAE tedavi işlemi uygulanan hastaları retrospektif olarak inceledik. Çalışmaya yaşam kalitesini bozacak şekilde miyoma bağlı miktar olarak fazla, uzun süreli, sık ve düzensiz aralıklarla olan uterin kanamalar,anemi, karın ağrısı, ele gelen kitle ve sık idrara çıkma şikayetleri olan hastalar dahil edildi. Tüm hastalarda UAE öncesi ve UAE sonrası 6. ayda, manyetik rezonans görüntüleme (MRG) ile klinik semptomları kaydedildi.*
Bulgular: *Çalışmamızda uterin fibroide bağlı semptomları olan 23-50 yaş arası (ort. 41,3) daha önce bir tanesi histerektomi operasyonu geçirmiş olmak üzere toplam kırk hastaya UAE işlemi yapıldı. Serimizde hastaların klinik semptomları, MR ve dijital subtraksiyon anjiyografi (DSA) bulguları sunulmuştur. UAE öncesi ve 6. ayda total, MR Uterin fiboid hacmi; 234,47±76,48 ve 117,27±43,53 (p=0,001) olup UAE öncesi ve 6. aydaki değerleri kayıt altına alındı. Bir hastada yoğun aterosklerotik sebeplerden dolayı işlem iptal edilmiş olup tek taraflı uterin arter embolize edilebilmiştir. Otuz dokuz hastada çift taraflı olarak başarılı bir şekilde UAE işlemi uygulanmıştır. Hastalarda endovasküler işlemle ilişkili herhengi bir komplikasyon gelişmedi. Toplam 39 hasta işlemin ertesi günü yatak istirahatini takiben aynı gün taburcu edilmiş olup 1 hastada ürosepsis gelişmesi nedeniyle 1 hafta sonra tabucu edilebilmiştir.*
Sonuç: *UAE miyomu olan hastalarda giderek artar sıklıkta kullanılmakta olan öncelikle tercih edilmesi gereken alternatif bir tedavi yöntemi olup histerektomiye göre çok daha az invaziv olması, işlem sonrası hastanede yatış gerektirmemesi ve basit sedasyon ya da spinal anestezi altında yapılabilir olması ile önemli alternatif bir seçenektir.*

Anahtar kelimeler: *miyom, embolizasyon, uterin arter, manyetik rezonans*

Corresponding Author:
drcakir1983@gmail.com

C. Cakir 0000-0001-8030-6795
F. Kilinç 0000-0002-7224-7737
A. Erbahçeci Salik 0000-0001-5344-560X
H. Selcuk 0000-0001-5606-4423

INTRODUCTION

Uterine fibroids which are known as leiomyomas are the most common gynecological benign neoplasias of the reproductive age, affecting 20-30% of women in this period [1]. Uterine fibroids do not pose a vital threat, but it reduces the quality of life of the patient due to the symptoms patients encountered.

Ultrasonography (US) is the first-line imaging modality for uterine myomas, although it often fails to detect lesions smaller than 1 cm in diameter. Transvaginal US has greater sensitivity than transabdominal US in detecting uterine leiomyomas. Today computed tomography (CT) is not indicated for imaging uterine fibroids. In consideration of the advantages of magnetic resonance (MR) imaging with regard to detection of myomas, MR can be used to determine number and localization of myomas and even perform volumetric calculations; thus, it is regarded as the best imaging method for uterine leiomyomas. Uterine leiomyosarcoma. uterine contractions, adenomyosis, adnexal masses are pathologies to be considered in differential diagnosis.

The aim of treatment is to prevent complications that may occur due to fibroids, and to improve the patient's quality of life. Medical treatment, hysterectomy, myomectomy and embolization are methods used in the treatment of fibroids. Uterine artery embolization (UAE), which is a minimally invasive method, can be performed with intravenous sedation, spinal anesthesia or local anesthesia. Many studies have shown that UAE has become an important option in relieving the symptoms that occur by decreasing the fibroid volume and thereby increasing the quality of life of patients [2]. UAE is a safe treatment method that can be applied by invasive radiologists during angiography, and the aim of this study was to evaluate the effectiveness of uterine artery embolization.

MATERIALS and METHODS

The study was planned as a single-center retrospective study and included 40 patients who had undergone UAE procedure, and presented to our clinic between February 2017 and July 2019 due to symptoms (less frequent urination, bleeding, anemia, abdominal pain and palpable mass) associated with uterine leiomyoma.

Patients who had uterine leiomyoma but did not have complaints associated with myoma such as bleeding, anemia, frequent urination, and abdominal pain and a asymptomatic course were not included in the study.

In addition, intracavitary myoma, broad-ligament myoma and cervical myoma, determined on MRI were not deemed to be suitable localizations for UAE, and therefore patients with myoma in these localizations were excluded from the study. In the current study patient group, the myomas were in intramural, subserous, submucous or multiple localizations.

All patients provided informed consent for UAE procedure. For all patients, MR images, clinical symptoms experienced were scanned before UAE procedure and at the 6th month after the procedure and digital subtraction angiography (DSA) images were obtained retrospectively from patient files, computerized recording systems, and imaging archives.

MRI scans were performed using pelvic superficial coils in a 3T (Tesla) MRI device (Siemens Verio, Malvern, PA, US). Pelvic MR scans included T2W sagittal and axial; T1W sagittal, axial, and coronal; and post-i.v. 15 cc Gadobutrol injection T1W sagittal, axial, and coronal sequences. Volumes of leiomyomas were calculated based on sagittal and axial images with the formula: height x width x length x $\pi/6$. In cases having multiple myomas, total myoma volume was calculated by adding the volume of each myoma.

For the embolization procedure, 8 cases received spinal anesthesia and 32 cases sedatives as perioperative analgesia. Foley catheter was inserted in all patients before the procedure, and the foley catheter was filled with 3/4 iodine contrast material and 1/4 saline solution. In addition, IV hydration was applied during procedure to ensure the elimination of the contrast agent.

Afterwards UAE procedures were performed under fluoroscopic (Allura FD 20/20, PhilipsMedicalSystem, Best, Netherlands) guidance. For the procedure, a 5

French (Fr) arterial sheath was placed in the right common femoral artery under ultrasonographic guidance. Then, internal iliac arteries were selectively catheterized using Kobra diagnostic catheter (5 Fr) [Cordis, Johnson and Johnson, USA] for the left uterine artery and Simmon 1 diagnostic catheter (5 Fr) [Cordis, Johnson and Johnson, USA] for the right uterine artery. Distal embolization was achieved using microsphere agents (Embosphere Microspheres; MeritMedical, USA) with sizes varying between 500-700 microns and 700-900 microns and with super selective catheterization of central and peripheral branches of uterine artery by inserting 2.8 Fr Rebar 27 (Medtronic, Irvine [CL], USA) or 2.8 Fr EmboCath Plus (BiosphereMedical, France) microcatheter through the existing diagnostic catheter in ipsilateral oblique projection. Dyeing for myoma disappeared in control angiograms after embolization, and this was accepted as complete embolization. None of the patients developed any complications associated with the endovascular procedure.

Foley catheter was removed following the procedure, and patients received i.v. analgesics until the 6th post-op hour. All patients received ciprofloxacin 500 mg peroral twice daily and nonsteroid anti-inflammatory medication and proton pump inhibitors for 10 days.

Statistical Analysis

Frequency and percentage values were given for categorical variables. Mean, standard deviation, median, minimum and maximum values were given for continuous variables. The normal distribution of continuous variables was tested by the Kolmogorov-Smirnov test. Mann-Whitney U test was used for comparison of two independent groups and Kruskal-Wallis H test for comparisons of more than two groups. For intergroup comparisons of independent variables that could not show normal distribution, Wilcox's sign rank test was used. A p value of $p<0.05$ was considered statistically significant. Statistical analyses of the data obtained in the study were performed using NCSS 11 software (Number Cruncher Statistical System, 2017 Statistical Software).

RESULTS

In the present study, a total of 40 patients underwent UAE procedure due to symptoms associated with uterine fibroids. One of the patients had a history of hysterectomy. Patient ages ranged between 23–50 years (mean: 41.23).

All the patients included in the study were symptomatic and the most common symptom was uterine bleeding lasting longer than 7 days, i.e. menorrhagia (80%), or excessive, long-term bleeding at frequent and irregular intervals, leading to secondary anemia (60%). Other symptoms included complaints of abdominal pain, palpable mass, and frequent urination in several patients. All patients were offered hysterectomy by the gynecology clinics before referral to our unit, or they were told that hysterectomy may be required during myomectomy.

Medical treatment (GNRH analog) had been previously taken by 12 patients and 1 patient had undergone a myomectomy operation. In the patient histories, there was multiparity in 30, primaparity in 9, and nulliparity in 1. case Although myomectomy is known to be recommended when the patient wishes to preserve fertility, there was no expectation of pregnancy in any of the study group patients and no pregnancy was observed during the follow-up period.

The largest myoma in our series had a volume of 1020 cc, and the smallest one had a volume of 17 cc. In our series, clinical symptoms, MRI and digital subtraction angiography (DSA) findings were presented. Based on MRI findings mean volumes of uterine fibroids before UAE and 6 months after UAE were 234.47±76.48 ccand 117.27±43.53 cc, respectively (p=0,001) and also all parameters were statistically significant (Table 1).

Table 1. MRI findings mean volumes of uterine fibroids before UAE and 6 months after UAE.

	Pre UAE (n)	Post UAE (n)	P-value
	Ort.+SS Med. (Min.-Maks.) (n=40)	Ort.+SS Med. (Min.-Maks.) (n=40)	
MRI	234,47±76,48 193- (17-1020)	117,27±43,53 90- (4-810)	0,001

MRI (p=0.001, p<0.05), the pre-median value was found to be statistically significantly higher than the post value.

Examination of mean and median values estimated before and after UAE procedure showed that the procedure resulted in reduction in the volume of myoma (Graphic 1). In addition to changes in myoma volume, decreased signal intensity on T2A images, and changes in contrast enhancement in myoma on pelvic MRI.were also analyzed. A successful procedure was accepted as presence of 50% or greater volumetric regression of the size of myoma and decrease in signal intensity of myoma in T2A images with loss or decrease of contrast enhancement in fibroids at the 6-month follow-up MRI. When all these MR parameters were evaluated before and at 6th months after the UAE procedure, the desired result was seen to have been achieved and the procedure was accepted as successful in all 39 patients.

Embolization was performed unilaterally due to intense atherosclerotic lesions in one patient, so, an unsuccessful procedure was accepted as presence of 50% smaller volumetric regression of the myoma at the 6-month follow-up MRI. The remaining 39 patients underwent successful bilateral UAE procedure. There were no complications associated with endovascular procedure. After the procedure a total of 39 patients were discharged on the same day following bed rest and 1 patients could be discharged 1 week later due to developmentn of urosepsis. The procedure was not repeated in any patient. In the examinations the patient's bleeding and anemia and other described symptoms completely regressed after 6 months.

DISCUSSION

Myomas are well-circumscribed, benign tumors, which are mainly formed of smooth muscle cells and pseudocapsules with different amounts of fibroconnective tissue. Myomas can be single or multiple, with size varying from just a few millimeters to a volume sufficient to fill the abdomen. As the size increases, urinary incontinence may occur due to bladder compression, and its posterior localisation may cause constipation in the rectosigmoid region [1,3]. In literature, the most common complication of fibroids has been reported to be abnormal uterine bleeding [1]. Generally, myomas with a submucosal location cause ulceration and degeneration in the endometrium [4].

All the patients in the current series had uterine bleeding, i.e. menometrorrhagia, which is defined in literature as menorrhagia or excessive bleeding at long, frequent and irregular intervals which resulted in chronic anemia in 2 cases, that did not improve despite medical treatment. Hysterectomy and myomectomy are traditional treatment methods for symptomatic myomas [5]. In addition to abnormal menstrual bleeding, UAE can be preferred to hysterectomy in cases with evident pain and pressure symptoms, and in patients who did not expect to become pregnant. The standard imaging method of contrast-enhanced pelvic MRI was used in the current study as it shows the uterine zonal anatomy perfectly during evaluation of patients who are to undergo fibroid embolization before the procedure and at the 6-month follow-up examination [6]. Myomas are observed on MRI as well-defined masses. On high-resolution, fat-free T2A images taken in three planes they are observed with a significantly lower signal intensity compared to the myometrium and these imaging modalities are therefore the most reliable imaging sequences for the detection of fibroids [7,8]. Accompanying pathologies and their amount can also be determined and volumetric calculation can be made. As the sizes increase in myomas, different types of degeneration develop in the process of progression with arterial feeding, and significant deterioration is seen especially in the central section. Non-degenerated myomas consist of smooth muscle cells as well as collagen in different proportions. The reason for the high signal intensity detected on T2A images is that myomas consist of compact smooth muscle cells, and do not contain collagen. They also show marked contrast enhancement due to increased vascularity and intense cellularity, and thus give the best response to UAE treatment [9].

Degenerated myomas have mostly irregularly defined contours, and they are observed with a low signal intensity on T2A images if they contain hyaline and areas of calcifications depending on the content, and may show different signal intensities. In addition, T1A images may show different ratios of contrast enhancement Although degenerated cystic myomas show a high signal on T2A images, they do not uptake contrast material. Myomas with myxoid degeneration show a very high T2A signal intensity with minimal contrast uptake [1]. In addition to num-

ber and signal intensity, intracavitary myoma, broad-ligament myomas and cervical myomas observed on MRI are not suitable localizations for UAE, and such patients with myoma were excluded from the study. The patient group of the current study comprised patients with myomas located in intramural, subserous, submucous or multiple localizations. Although the submucosal type is less common (approximately 5%), they are largely symptomatic, as in the current series, and frequently cause dysmenorrhea, menorrhagia and infertility [10]. The UAE procedure, which is performed by selective catheterization of the uterine artery, aims to prevent the blood supply of central and peripheral sections by blocking arterioles feeding the myoma with the use of an ideal size embolizing agent. Embolization agents include non-spherical polyvinyl alcohol (PVA) particles, trisacryl gelatin microspheres, and embozene microspheres, all of which have been shown to provide a successful and safe shedding embolization process in fibroids [6,11].

Microspheric microparticles produced from various

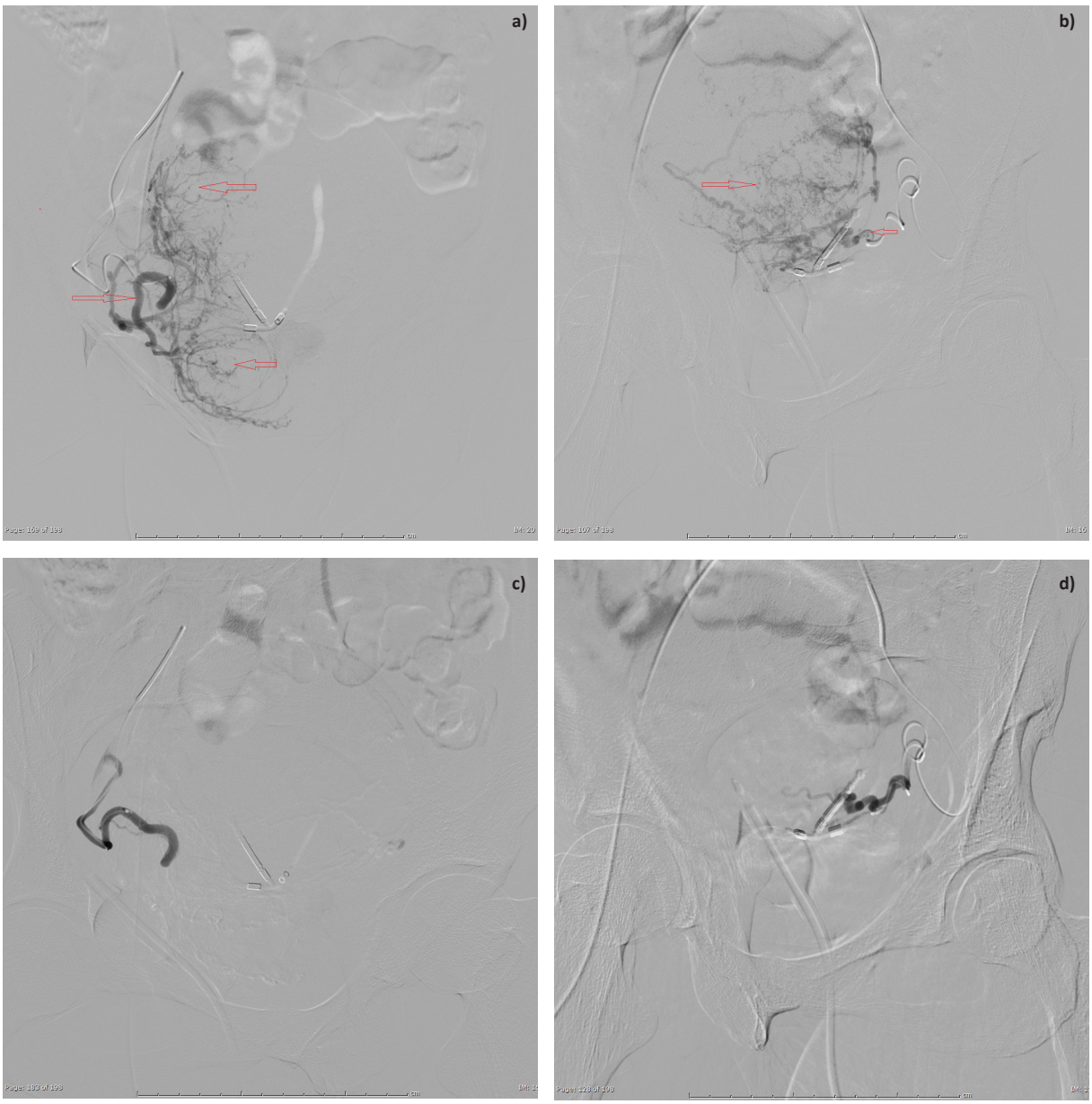


Figure 1. Digital subtraction angiography showing (a) the branches of myomas fed from the right uterine artery (red arrows), (b) the branches of myomas fed from the left uterine artery (red arrows), (c, d) after successful embolization of the uterin artery..

materials are the current first choice embolization agents, and these were used in the present series. Distal embolization was achieved in uterine arteries in this study with the use of microspheric agents ranging in size from 500-700 microns to 700-900 microns. The UAE procedure was terminated when the myoma stopped bleeding completely and the blood flow was observed to in the uterine artery. All the fibroids had a prominent hypointense signal on T2A contrast images and necrosis was observed on contrast T1A images after successful embolization of the uterine fibroid [9] (Figure 2).

In this series, almost all necrosis was observed with T1A contrast images, and that the persistence of partial contrast enhancement indicates that the procedure had failed and embolization was required in the myomas. A review of the related literature shows varying volumetric reduction rates between 42–83% following UAE. This rate was 50% in ur series. Previous studies reported reduction in uterine size by 43–58% after the procedure. This rate was 51% in our series [12-15]. İn the examinations the patient's menorrhagia, menometrotagy and other described symptoms completely regressed after 6 months.

Complications related to the treatment of endovascular embolization in UAE; especially pseudoaneurysm due to vascular injury at the intraducer access site, arterial dissection and arteriovenous fistulas with contrast nephropathy. In addition, off-target embolization should be carefully avoided by preserving the abdominal aorta and cervicovaginal artery branches during the procedure.

Infection, uterine necrosis, pulmonary embolism,

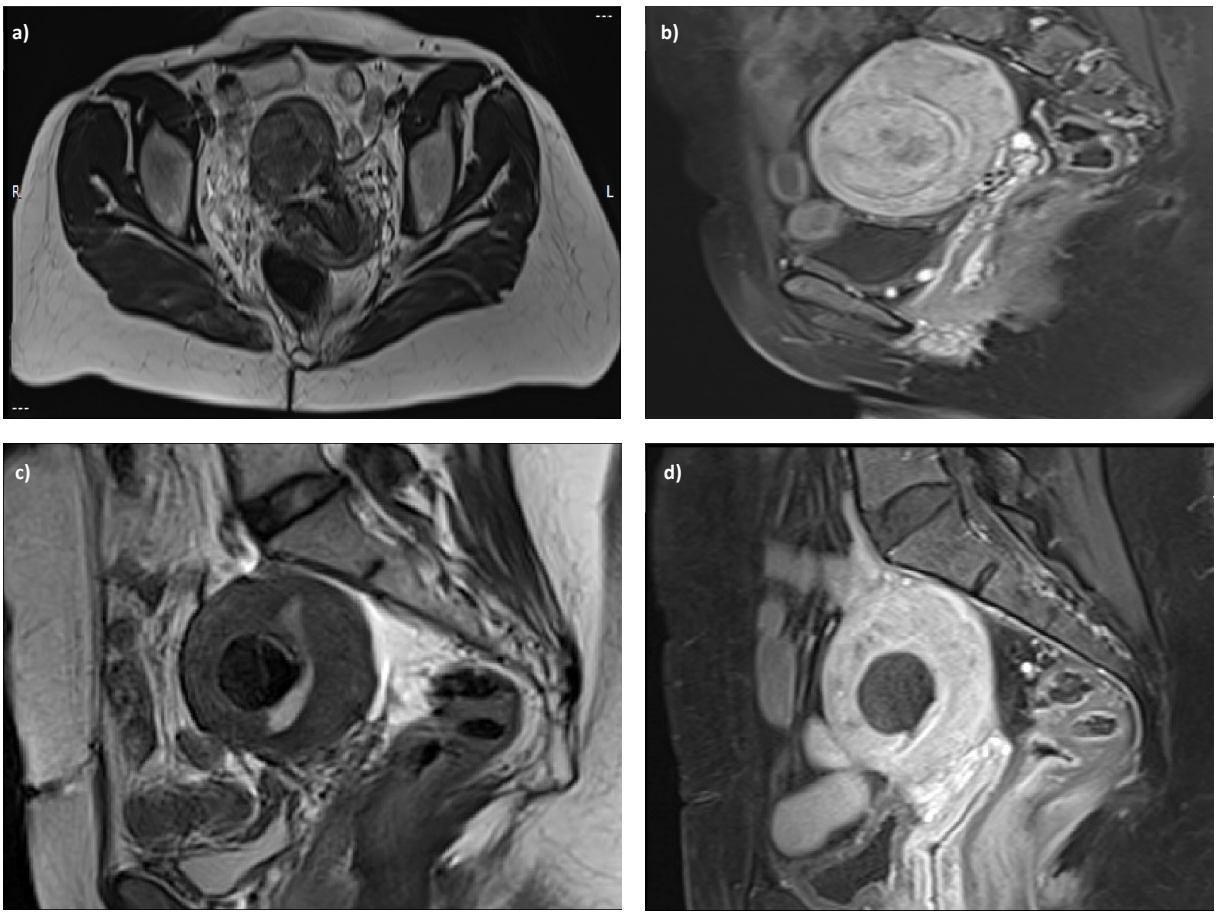
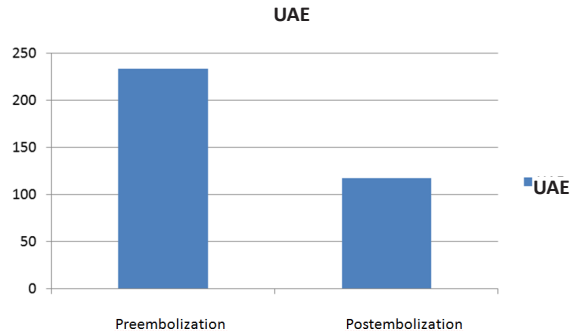


Figure 2. In this case, (a) 58 cc intramural myoma in T2-weighted pelvic MRI in axial viev before embolization of the uterin artery, (b) Fibroid like contrast heterogeneous myometrium in T1-weighted pelvic MRI in axial viev before embolization of the uterin artery and after (c) UAE. T2-weighted pelvic MRI in sagittal Note the significant volumetric reduction of the myoma (22 cc). T1-weighted contrast sagital image (d) with left infarcted areas in the myoma after UAE.



Graphic 1. Uterine Artery Embolization (UAE) procedure showed that the procedure resulted in reduction in the volume of myoma.

and ovarian failure are among the major UAE complications [16-18]. In the current study, no major or minor complications were observed in the patient group treated. "Postembolization syndrome", presenting with signs of pelvic pain (uterine cramping), fever, nausea and vomiting was observed ias an an early phase clinical condition after the uterine artery embolization. This clinical condition was tolerated with the administration of IV analgesia, which lasted for up to twenty-four hours postoperatively. The rate of surgical complications of hysterectomy increases especially as the fibroid volume increases. Compared to the high morbidity rate of open hysterectomy, which causes a very high amount of bleeding during surgery and requires intensive care after the procedure, UAE is a less invasive method. UAE is a technically easy procedure, and if applied by experienced centers, it may be considered as a safe treatment method for a young patient group with variations in pelvic vascular anatomy, as in the current series. Superselective catheterization and embolization of bilateral uterine artery with DSA in patients with symptomatic myomas is a minimally invasive, successful and effective method, and the technical success and early follow-up findings of the currrent study are similar to those of previous reports in literature.

Ethics Committee Approval: Bakırköy Dr. Approval was obtained from Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (2019/400, 02.09.2019).

Conflict of interests: The authors declare that they have no conflict interests.

Funding: We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support and funding for this work that could have influenced its outcome.

Informed Consent: Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

REFERENCES

1. Murase E, Siegelman ES, Outwater EK, Perez-Jaffe LA, Tureck RW. Uterine leiomyomas: histopathologic faeatures, MR imaging fndings, differential diagnosis, and treatment. Radiographics. 1999;19(5):1179-97. https://doi.org/10.1148/radiographics.19.5.g99se131179
2. Lohle PN, Voogt MJ, De Vries J, et al. Long-term outcome of uterine artery embolization for symptomatic uterine leiomyomas. J Vasc Interv Radiol. 2008;19(3):319-26. https://doi.org/10.1016/j.jvir.2007.10.011
3. Buttram VC Jr. Uterine leiomyomata-aetiology, symptomatology and management. Prog Clin Biol Res. 1986;225:275-96.
4. Creasman WT. Disorders of the uterine corpus. In: Scott JR, DiSaia PJ, Hammond CB, Spellacy WN, editors. Danforth's obstetrics and gynecology. Philadelphia: Lipincott; 1994. p. 925-55.
5. Tomislav S, Josip M, Liana CS, et al. Uterine artery embolization as nonsurgical treatment of uterine myomas. ISRN Obstet Gynecol. 2011;2011:489281. https://doi.org/10.5402/2011/489281
6. Voogt MJ, Arntz MJ, Lohle PNM, Mali WPM, Lampmann LEH. Uterine fibroid embolisation for symptomatic uterine fibroids: a survey of clinical practice in Europe. Cardiovasc Intervent Radiol. 2011;34(4):765-73. https://doi.org/10.1007/s00270-010-9978-8
7. Hamlin DJ, Pettersson H, Fitzsimmons J, Morgan LS. MR imaging of uterine leiomyomas and theircomplications. J Comput Assist Tomogr. 1985;9:902-7. https://doi.org/10.1097/00004728-198509000-00012
8. Riccio TJ, Adams HG, Munzing DE, Mattrey RF. Magnetic resonance imaging as an adjunct to sonography in the evaluation of the female pelvis. Magn Reson Imaging. 1990;8(6):699-704. https://doi.org/10.1016/0730-725X(90)90004-L
9. Chang S, Kim MD, Lee M, Lee MS, Park S, Won JY, et al. Uterine artery embolization for symptomatic fibroids with high signal intensity on T2-weighted MR imaging. Korean J Radiol. 2012;13(5):618-24. https://doi.org/10.3348/kjr.2012.13.5.618
10. Corson SL. Hysteroscopic diagnosis and operative therapy of submucous myoma. Obstet Gynecol Clin North Am. 1995;22(4):739-55.
11. Stampfl U, Radeleff B, Sommer C, et al. Midterm results of uterine artery embolization using narrow-size calibrated embozene microspheres. Cardiovasc Intervent Radiol. 2011;34(2):295-305. https://doi.org/10.1007/s00270-010-9986-8
12. Spielmann A, Keogh C, Forster B, Martin ML, Machan LS. Comparison of MRI and sonography in the preliminary evaluation for fbroid embolization. AJR Am J Roentgenol. 2006;187(6):1499-504. https://doi.org/10.2214/AJR.05.1476
13. Stewart EA, Rabinovici J, Tempany CM, Inbar Y, Regan L, Gostout B, et al. Clinical outcomes of focused ultrasound surgery for the treatment of uterine fibroids. Fertil Steril. 2006;85(1):22-9. https://doi.org/10.1016/j.fertnstert.2005.04.072
14. Helmberger T, Jakobs TF, Reiser MF. Embolization of uterine fibroids. Abdom Imaging. 2004;29(2):267-77. https://doi.org/10.1007/s00261-003-0075-1

15. Moss JG, Cooper KG, Khaund A, Murray LS, Murray GD, Wu O, et al. Randomised comparison of uterine artery embolization (UAE) with surgical treatment in patients with symptomatic uterine fibroids (REST trial): 5-year results. BJOG. 2011;118(8):936-44. https://doi.org/10.1111/j.1471-0528.2011.02952.x
16. Kitamura Y, Ascher SM, Cooper C, Allison SJ, Jha RC, Flick PA, et al. Imaging manifestations complications associated with uterine artery embolization. Radiographics. 2005;25 Suppl 1:S119-32. https://doi.org/10.1148/rg.25si055518
17. Torigian DA, Siegelman ES, Terhune KP, Butts SF, Blasco L, Shlansky-Goldberg RD. MRI of uterine necrosis After uterine artery embolization for treatment of uterine leiomyomata. AJR Am J Roentgenol. 2005;184(2):555-9. https://doi.org/10.2214/ajr.184.2.01840555
18. Dutton S, Hirst A, McPherson K, Nicholson T, Maresh M. A UK multicentre retrospective cohort study comparing hysterectomy and uterine artery embolisation for the treatment of symptomatic uterine fbroids (HOPEFUL study): main results on medium-term safety and effcacy. BJOG. 2007;114(11):1340-51. https://doi.org/10.1111/j.1471-0528.2007.01526.x

Original Article

Med J Bakirkoy 2020;16(2):160-4
doi: 10.5222/BMJ.2020.18189

Medical Journal of Bakirkoy

Incidental Appendiceal Mucinous Neoplasms in Patients Who Underwent Right Hemicolectomy

Sağ Hemikolektomi Hastalarında İnsidental Olarak Saptanan Apendiksin Müsinöz Neoplazmları

Salih Tosun[1], Oktay Yener[1], Ozgur Ekinci[1], Ihsan Metin Leblebici[1], Ahmet Yusuf Serdaroglu[1] Mehmet Acar[1], Tuce Soylemez[2], Orhan Alimoglu[1]

[1] Istanbul Medeniyet University, School of Medicine, Department of General Surgery, Istanbul, Turkey
[2] Istanbul Medeniyet University, School of Medicine, Department of Pathology, Istanbul, Turkey

Received: 24 March 2020 / **Accepted:** 16 April 2020 / **Publication date:** 26 June 2020

Cite as: Tosun S, Yener O, Ekinci O, Leblebici İM, Serdaroğlu AY, Acar M, Soylemez T, Alimoglu O. Incidental appendiceal mucinous neoplasms in patients who underwent right hemicolectomy. Med J Bakirkoy 2020;16(2):160-4.

ABSTRACT

Objective: *Subclinical appendiceal mucinous neoplasms (AMNs) may accompany abdominal malignancies which must be considered during colectomies. We aimed to evaluate the treatment and follow-up approach to the patients in whom incidentally appendiceal mucinous neoplasm detected following right hemicolectomy performed for abdominal malignancies.*
Method: *The records of the patients who underwent right hemicolectomy due to benign or malign conditions in our general surgery clinic between January 2016 and December 2019 were analyzed. After the exclusion of the patients who had undergone hemicolectomies due to benign causes and appendiceal pathologies detected before the operation, the records of remaining patients' were evaluated. The patient records who underwent right hemicolectomy for gastrointestinal or gynecologic malignanacies were analyzed. The patients whose pathology results were reported as AMNs were included in the study. The incidence of AMN was analyzed and compared with the literature.*
Results: *Hundred and sixty-seven of the 214 patients with gastrointestinal or gynecologic malignanacies were included in this study. Eighty patients were female and 87 were male. The mean age was 63 (23-95) years. The incidence of AMN was 2.9% in patients who underwent right hemicolectomy for malignity in three years period. According to the pathology reports; 3 patients (60%) had appendiceal mucinous neoplasia, one patient (20%) appendiceal mucinous cystadenocarcinoma and one (20%) appendiceal carcinoid tumor.*
Conclusions: *IIncidentally detected AMN is a rare entity and should be considered during the right hemicolectomy operations of different malignancies. Resections must follow principles for malignancy surgery. The preoperative evaluation of the patients needs attention, their postoperative treatment must be planned according to the pathology reports and the patients must be followed for any potential accompanying colorectal tumors.*

Keywords: *appendectomy, incidental, tumor, appendiceal neoplasm*

ÖZ

Amaç: *Subklinik apendiks müsinöz neoplazmları (AMN) abdominal malignitelere eşlik edebilir ve kolektomiler sırasında göz önünde bulundurulmalıdır. Çalışmamızda, abdominal maligniteler sebebiyle sağ hemikolektomi uygulanan hastalarda insidental apendiks müsinöz patoloji saptanması halinde tedavi ve takip yaklaşımını değerlendirmeyi amaçladık.*
Yöntem: *Ocak 2016 - Aralık 2019 yılları arasında genel cerrahi kliniğimizde benign ya da malign nedenler sebebiyle sağ hemikolektomi uygulanan hastaların kayıtları incelendi. Benign nedenlere bağlı yapılan hemikolektomiler ve operasyon öncesi appendiks patolojisi saptanan hastalar çalışma dışına alındıktan sonra kalan olgular incelendi. Gastrointestinal veya jinekolojik malignite için sağ hemikolektomi uygulanan hasta dosyaları değerlendirildi. Patoloji sonucu AMN olarak raporlananlar çalışmaya alındı. İnsidental olarak saptanan AMN'ler değerlendirilerek literatürle karşılaştırıldı.*
Bulgular: *214 hastanın gastrointestinal veya jinekolojik kaynakli malignite sebebi ile sağ hemikolektomi uygulanan 167' si calışmaya alındı. Hastaların 80'i kadın, 87'si erkek idi. Yaş ortalaması 63 (23-95) idi. Kliniğimizde üç yıllık sürede malignite sebebiyle sağ hemikolektomi operasyonu geçiren hastalarda AMN insidansı %2.9 idi. Patoloji raporlanmasinda 3 hastada (%60) musinoz neoplazi, 1 hastada (%20) musinoz kistadeno kanser saptandı. 1 hastada ise (%20) appendiks karsinoid tümörüyle karşılaşıldı.*
Sonuç: *AMN nadir görülen bir antitedir ve malignite nedenli sağ hemikolektomilerde akılda olmalıdır.Yapılacak rezeksiyonlar malignite cerrahisi prensipleri gözetilerek gerçekleştirilmelidir. Hastaların preoparatif değerlendirmeleri dikkatle yapılmalı, tedavileri postoperatif patoloji sonuçlarına göre yönlendirilmeli ve hastalar gelişebilecek kolorektal tümörler açısından takip edilmelidir.*

Anahtar kelimeler: *appendektomi, insidental, tümör, appendiks neoplazmı*

Corresponding Author:
✉ drsalihtosun@yahoo.com

S. Tosun 0000-0002-5033-4477
O. Yener 0000-0001-5488-4583
O. Ekinci 0000-0002-2020-1913
I.M. Leblebici 0000-0002-1403-7643
A.Y. Serdaroglu 0000-0001-5263-6252
M. Acar 0000-0002-6095-4522
T. Soylemez 0000-0003-3030-7030
O. Alimoglu 0000-0003-2130-2529

INTRODUCTION

Mucocele is a rare appendiceal pathology (0.2-0.7% of all appendectomy specimens) [1-3]. Appendiceal mucinous neoplasms (AMNs) are very rare with 1000 to 2000 cases diagnosed annually in the United States [4] and they are responsible about 1% of all cancers worldwide [5]. AMNs include a heterogeneous group of diseases and their malignancy potential varies as seen in different classification systems [6-8]. Different classifications with similar terminology were suggested to define lesions of variable biologic potential by several authors. Not only classification but also management of AMNs are also problematic for clinicians [7,8]. A remarkable part of the lesions is asymptomatic, and they are incidental findings at surgeries AMNs are usually diagnosed incidentally during surgery performed for suspiect cases of appendicitis [9]. Advanced stage of AMN is observed with abdominal distension related to the accumulation of mucin in the peritoneal cavity. These tumors may disseminate throughout the peritoneal cavity in the form of gelatinous deposits; the worst complication of AMNs called peritoneal pseudomyxoma, caused by spontaneous or iatrogenic appendix perforation with high rate of morbidity and mortality [10,11]. Also, there are no clear guidelines on the extent of surgical resection; therefore, many reports on surgical procedures have been published [3,12]. Considering uncertain potential malignant progression, an early and accurate preoperative identification of AMNs confined to the appendix is crucial for prediction of prognosis and decision on treatment strategy [13].

In our study we aimed to evaluate the treatment and follow-up approach to the patients who had incidentally detected appendiceal mucinous pathology following right hemicolectomy performed for abdominal malignancies.

MATERIAL and METHODS

Patients, inclusion and exclusion criteria:
We have analyzed the records of the patients who underwent right hemicolectomy performed due to benign or malign conditions in our general surgery clinic between January 2016 and December 2019. The records were analyzed for demographics, surgery reports, pathology results and long-term outcomes.

Patients with a history of a previous operation for benign conditions, such as acute appendicitis or with a radiographically or pathologically confirmed appendicitis before the primary surgery were excluded from the study. After exclusion of patients who had undergone hemicolectomies due to benign causes and appendiceal pathologies detected before the operation, records of remaining patients were evaluated.

We have identified the cases matching the inclusion criteria that was pre-described as malignancy. Physical examination notes, operation, and the pathology records as well as clinical data of all included patients were carefully reviewed.

The patients with a final pathological diagnosis of appendiceal mucinous neoplasm were also included in the study. The incidence of appendiceal mucinous pathology was analyzed and compared with the literature. The AMN cases were re-examined and evaluated based on pathology reports recorded during the study.

Pathologic evaluation:
Appendiceal mucinous pathology (intracytoplasmic mucine containing nuclear atypia) was identified in histological specimens (Figure 1).

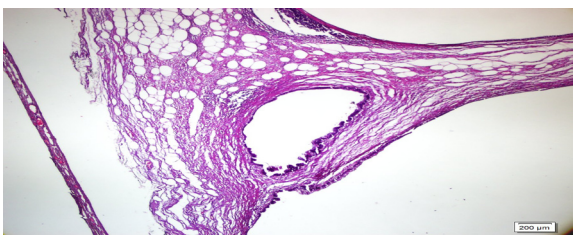


Figure 1. Neoplastic columnar cells with mild intracytoplasmic mucine containing nuclear atypia (HE X40, X200).

Ethics committee approval was obtained. All patients were evaluated in follow-up visits after surgery.

RESULTS

There were 214 patients who underwent right hemicolectomy due to benign or malign conditions in our general surgery clinic in three years period. A total of

167 (78%) patients were included in the study who had medical history of a gastrointestinal or gynecologic malignancy and underwent primary surgery.

A total of 167 cases who underwent right hemicolectomy due to malignancy; consisted of 80 (47.9%) female and 87 (52.1%) male patients. The mean age of the patients was 63 (23-95) years.

In the present study, 5 of the 167 cases evaluated were diagnosed with appendiceal mucinous neoplasms by histomorphological and architectural findings and two of them had lesions of >2 cm in diameter. The study population consisted of four women and one man. The median age of these patients was 52 (23-63) years. The incidence of appendiceal mucinous neoplasm was 2.9% in patients who underwent right hemicolectomy for gastrointestinal or gynecologic malignanacies from January 2016 to December 2019 in surgery department (Figure 2).

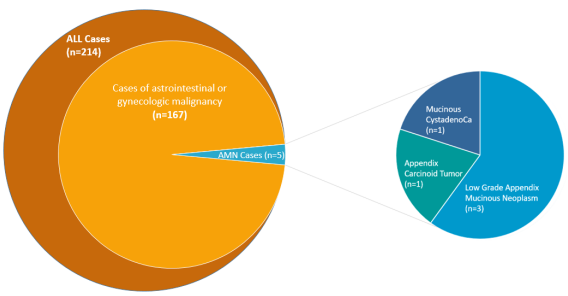


Figure 2. Distrubition of appendiceal mucinous pathology among patient s who underwent right hemicolectomy.

Three out of five cases (60%) had been diagnosed with low-grade appendiceal mucinous neoplasms according to pathological reports of specimens during the study. One out of five patients (20%) was diagnosed with mucinous cystadeno cancer and one out of five patients (20%) was diagnosed with an appendiceal carcinoid tumor.

DISCUSSION

Primary neoplasms of appendix are rarely seen (less than 2% of surgical appendectomy specimens) and their major categories include epithelial tumors, mesenchymal tumors, and lymphomas. AMNs is a complex, diverse group of epithelial neoplasms often causing cystic dilation of the appendix due to the accumulation of gelatinous material, morphologically referred to as mucoceles [14].

AMN is an infrequently seen adenoma which can either be in the appendix or the surrounding appendiceal mucosa wall. Mucoceles are also very rare seen (0.2% and 0.7%) among all appendectomy specimens. They affect women 4 times more than men. Appendiceal mucinous lesions (both benign and neoplastic) have also a slight female predominance [15,16]. In our study, 80% of the cases were female. AMNs are usually diagnosed in patients in their 50s and 60s [15,16]. In our case series the medan age of these patients was 52 years.

Patients with AMN can present with intussusception, abdominal pain and obstruction. However, these neoplasms are often found incidentally in asymptomatic patients. AMNs are requentlymis diagnosed as acute appendicitis, retroperitoneal tumors of the right iliac fossa, or an adnexal mass of [17]. Ultrasound and CT (the most commonly used radiographic interpretation for preoperative diagnosis) are the main imaging techniques in terms of diagnosis [13,18]. Cystic dilation of appendiceal lumen, calcifications of appendiceal wall and irregular appendiceal wall thickening are common abdominal CT findings.

In pathological examination; appendiceal wall hyalinization and fibrosis with a grossly swollen appendix secondary to mucinous accumulation [19] can be seen. Histological characteristics of AMNs usually present as atypical glandular cells and epithelial cells with “pushing invasion” of malignant cells creeping into the appendiceal wall with possible diverticular formation. Mucinous cells, goblet cells among colon cells are frequently identified within AMNs [20]. AMNs of <2 cm diameter are rarely malignant and usually classified as benign simple or retention mucoceles. AMNs of >6 cm represent high risk of malignancy, appendiceal perforation, and development of pseudomyxoma peritonei [21]. Two of our cases had lesions of >2 cm in diameter. One of them was diagnosed with mucinous cystadenocancer while the other patient was diagnosed with appendiceal carcinoid tumor.

Controversies remain as to the best surgical approach (laparoscopic vs open), adjuvant therapy, duration of

follow-up, and imaging technique. The goal of the AMN management includes the prevention from rupture, seeding, and pseudomyxoma peritonei [22]. Right hemicolectomy in the absence of lymph node metastasis has been replaced by appendectomy which is the only approach used for the treatment of benign appendiceal mucoceles. Upon the discovery of submucosal malignancy, infiltration or lymph node metastasis, right hemicolectomy with or without omentectomy may be performed.

In our study, incidentally discovered appendiceal mucinous pathologies were evaluated in right hemicolectomy operations of the patients who underwent surgery for gastrointestinal or gynecologic malignanacies. Incidentally detected appendiceal mucinous pathology is a rare entity.

AMNs can mimick appendicitis and be diagnosed pathologically in less than 2% of surgical appendectomy specimens [14]. The incidence of AMN in colon resection operations is not well defined. In our study, the AMN incidence in right hemicolectomy malignancies was 2.9 percent.

AMNs of > 2 cm are considered to have malignancy potential and right hemicolectomy is the recommended surgical treatment in such cases [23]. Any appendiceal abnormality was not detected before surgery in our patients. We identified 5 AMN cases for whom we performed right hemicolectomy for gastrointestinal or gynecologic malignancies in our records.

Pathology reports revealed appendiceal mucinous pathologies in these patients. Thus, any further surgical and adjuvant therapies were not required in these cases.

CONCLUSIONS

Overall, further studies are needed to identify the best diagnostic method and treatment approach for appendiceal mucinous pathology. There remains a lack of standardization for post-treatment surveillance. AMNs should be considered during the colectomy operations of different malignancies and resections must follow principles for malignancy surgery We recommend exploring the appendix for any potential AMNs while performing colectomies due to any reason.

Ethics Commitee Approval: S. B. Istanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee (2020 / 0120, 19.02.2020).
Conflict of interest: The authors declare no conflict of interest.
Funding: No financial support was received.
Informed Consent: Not obtained since the study is retrospective.

REFERENCES

1. Honnef I, Moschopulos M, Roeren T. Appendiceal mucinous cystadenoma. Radiographics. 2008;28(5):1524-7. https://doi.org/10.1148/rg.285075160
2. Karakaya K, Barut F, Emre AU, et al. Appendiceal mucocele: case reports and review of current literature. World J Gastroenterol. 2008;14(14):2280-3. https://doi.org/10.3748/wjg.14.2280
3. de Abreu Filho JG, de Lira EF. Mucocele of the appendix - appendectomy or colectomy? J Coloproctol. 2011;31(3):276-84. https://doi.org/10.1590/S2237-93632011000300008
4. Choudry HA, Pai RK. Management of mucinous appendiceal tumors. Ann Surg Oncol. 2018;25(8):2135-2144. https://doi.org/10.1245/s10434-018-6488-4
5. Pai RK, Longacre TA. Appendiceal mucinous tumors and pseudomyxoma peritonei: histologic features, diagnostic problems, and proposed classification. Adv Anat Pathol. 2005;12(6):291-311. https://doi.org/10.1097/01.pap.0000194625.05137.51
6. Dixit A, Robertson JH, Mudan SS, Akle C. Appendiceal mucoceles and pseudomyxoma peritonei. World J Gastroenterol. 2007;13(16):2381-4. https://doi.org/10.3748/wjg.v13.i16.2381
7. Panarelli NC, Yantiss RK. Mucinous neoplasms of the appendix and peritoneum. Arch Pathol Lab Med. 2011;135(10):1261-8. https://doi.org/10.5858/arpa.2011-0034-RA
8. Carr NJ, Cecil TD, Mohamed F, et al. A consensus for classification and pathologic reporting of pseudomyxoma peritonei and associated appendiceal neoplasia: The results of the Peritoneal Surface Oncology Group International (PSOGI) modified delphi process. Am J Surg Pathol. 2016;40(1):14-26. https://doi.org/10.1097/PAS.0000000000000535
9. Isaacs KL, Warshauer DM. Mucocele of the appendix: computed tomographic, endoscopic, and pathologic correlation. Am J Gastroenterol. 1992;87(6):787-9. PMID: 1590322.
10. Que Y, Tao C, Wang X, Zhang Y, Chen B. Pseudomyxoma peritonei: some different sonographic findings. Abdom Imaging. 2012;37(5):843-8. https://doi.org/10.1007/s00261-012-9843-0
11. Yantiss RK, Shia J, Klimstra DS, Hahn HP, Odze RD, Misdraji J. Prognostic significance of localized extra-appendiceal mucin deposition in appendiceal mucinous neoplasms. Am J Surg Pathol. 2009;33(2):248-55. https://doi.org/10.1097/PAS.0b013e31817ec31e
12. Kwak HD, Ju JK. A prospective study of discrepancy between clinical and pathological diagnosis of appendiceal mucinous

neoplasm. Ann Surg Treat Res. 2020;98(3):124-9. https://doi.org/10.4174/astr.2020.98.3.124
13. Yu X, Mao J, Tang W, et al. Low-grade appendiceal mucinous neoplasms confined to the appendix: clinical manifestations and CT findings. J Investig Med. 2020;68(1):75-81. https://doi.org/10.1136/jim-2018-000975
14. Foster JM, Gupta PK, Carreau JH, et al. Right hemicolectomy is not routinely indicated in pseudomyxoma peritonei. Am Surg. 2012;78(2):171-7. PMID: 22369825. https://doi.org/10.1177/000313481207800234
15. Jarvinen P, Jarvinen HJ, Lepisto A. Survival of patients with pseudomyxoma peritonei treated by serial debulking. Colorectal Dis. 2010;12(9):868-72. https://doi.org/10.1111/j.1463-1318.2009.01947.x
16. Landen S, Bertrand C, Maddern GJ, et al. Appendiceal mucoceles and pseudomyxoma peritonei. Surg Gynecol Obstet. 1992;175(5):401-4. PMID: 1440166.
17. Pai RK, Beck AH, Norton JA, et al. Appendiceal mucinous neoplasms: clinicopathologic study of 116 cases with analysis of factors predicting recurrence. Am J Surg Pathol. 2009;33(10):1425-39. https://doi.org/10.1097/PAS.0b013e3181af6067
18. Shaib WL, Assi R, Shamseddine A, et al. Appendiceal mucinous neoplasms: diagnosis and management. Oncologist. 2017;22(9):1107-16. https://doi.org/10.1634/theoncologist.2017-0081
19. Ashrafi M, Joshi V, Zammit M, et al. Intussusception of the appendix secondary to mucinous cystadenoma: A rare cause of abdominal pain. Int J Surg Case Rep. 2011;2(2):26-7. https://doi.org/10.1016/j.ijscr.2010.11.004
20. Caspi B, Cassif E, Auslender R, Herman A, Hagay Z, Appelman Z. The onion skin sign. a specific sonographic marker of appendiceal mucocele. J Ultrasound Med. 2004;23(1):117-21. https://doi.org/10.7863/jum.2004.23.1.117
21. Hoeffel C, Crema MD, Belkacem A, et al. Multi-detector row CT: spectrum of diseases involving the ileocecal area. Radiographics. 2006;26(5):1373-90. https://doi.org/10.1148/rg.265045191
22. Ronnett BM, Yan H, Kurman RJ, Shmookler BM, Wu L, Sugarbaker PH. Patients with pseudomyxoma peritonei associated with disseminated peritoneal adenomucinosis have a significantly more favorable prognosis than patients with peritoneal mucinous carcinomatosis. Cancer. 2001;92(1):85-91. https://doi.org/10.1002/1097-0142(20010701)92:1<85::AID-CNCR1295>3.0.CO;2-R
23. Glasgow SC, Gaertner W, Stewart D, et al. The American Society of Colon and Rectal Surgeons, Clinical Practice Guidelines for the Management of Appendiceal Neoplasms. Dis Colon Rectum. 2019;62(12):1425-38. https://doi.org/10.1097/DCR.0000000000001530

Original Article

Med J Bakirkoy 2020;16(2):165-73
doi: 10.5222/BMJ.2020.32032

Medical Journal of Bakirkoy

Comparison of Triglyceride/Glucose Index with the FINDRISC Diabetes Risk Questionnaire in Determining Diabetes Risk in Individuals Attending Periodic Health Examinations

Periyodik Sağlık Muayenesi için Başvuran Bireylerde Diyabet Riskini Belirlemede Trigliserit/Glikoz İndeksinin "FINDRISK" Diyabet Risk Anketi ile Karşılaştırılması

Nur Demirbas, Ruhuşen Kutlu

Necmettin Erbakan University Meram Medical Faculty Department of Family Medicine, Konya, Turkey

Received: 27 December 2019 / **Accepted:** 14 March 2020 / **Publication date:** 26 June 2020

Cite as: Demirbas N, Kutlu R. Comparison of triglyceride/glucose index with the FINDRISC diabetes risk questionnaire in determining diabetes risk in individuals attending periodic health examinations. Med J Bakirkoy 2020;16(2):165-73.

ABSTRACT

Objective: *In this study, we aimed to compare the FINDRISC questionnaire and the triglyceride/glucose index, used to determine the risk of diabetes in healthy individuals, and to investigate their relationships with obesity.*
Method: *This study was planned as a retrospective review of the files of healthy individuals who had applied to a family medicine polyclinic for a periodic health examination. Sociodemographic characteristics, anthropometric measurements, routine laboratory results from the same period, and the FINDRISC diabetes risk score found in the participants' files were recorded in a separate file. The triglyceride/glucose (TyG) index was calculated using the appropriate formula. After the files meeting the exclusion criteria were removed, the study was completed with 879 people.*
Results: *Of the participants, 66.7% (n=586) were male and the mean age was 37.20±11.8 years. The mean diabetes risk score calculated by FINDRISC for women was 10.92±4.9 points and the mean TyG index score was 8.56±0.5 points, while the mean diabetes risk score of men was 8.75±4.7 points and the mean TyG index score was 8.77±0.5. There was a statistically significant association between gender and both mean diabetes risk score and TyG index (p<0.001). Of the participants, 17.1% were found to be at high risk of developing diabetes within 10 years by the FINDRISC survey. There was a moderately significant positive correlation between the diabetes risk score and TyG index and body mass index.*
Conclusion: *The FINDRISC questionnaire and TyG index are easy, practical, and cost-effective methods that can be used in primary health care centers in order to determine the risk of developing diabetes in the early period and inform individuals about this issue.*

Keywords: *healthy individual, diabetes risk, FINDRISC questionnaire, triglyceride/glucose index*

ÖZ

Amaç: *Bu çalışmada sağlıklı bireylerde diyabet riskini belirlemek için kullanılan FINDRISK anketi ile trigliserit/glikoz indeksini karşılaştırmayı ve obezite ile ilişkilerini araştırmayı amaçladık.*
Yöntem: *Bu çalışma aile hekimliği polikliniğine periyodik sağlık muayenesi için başvurmuş sağlıklı bireylerin dosyalarının retrospektif taraması olarak planlandı. Katılımcıların dosyalarında bulunan sosyodemografik özellikleri, antropometrik ölçümleri, aynı dönemde yapılmış rutin laboratuvar sonuçları ile FINDRISK diyabet risk puanı ayrı bir dosyaya kaydedildi. Uygun formül kullanılarak trigliserit/glikoz (TyG) indeksi hesaplandı. Dışlama kriterlerine uyan dosyalar çıkarıldıktan sonra araştırma 879 kişi ile tamamlandı.*
Bulgular: *Çalışmaya dahil edilenlerin %66,7'si (n=586) erkek ve yaş ortalaması 37,20±11,8 yıl idi. Kadınların FINDRISK ile hesaplanan diyabet risk puanı ortalaması 10,92±4,9 puan, TyG indeksi ortalaması 8,56±0,5 ve erkeklerin diyabet risk puanı ortalaması 8,75±4,7 puan, TyG indeksi ortalaması 8,77±0,5 idi. Diyabet risk puanı ortalaması ve TyG indeksi ile cinsiyetler arasında istatistiksel olarak anlamlı bir ilişki bulundu (p<0,001). Katılımcıların %17, 1'inde FINDRISK anketi ile 10 yıl içinde diyabet gelişme riski yüksek olarak bulundu. Diyabet risk puanı ve TyG indeksi ile beden kitle indeksi arasında pozitif yönde orta derecede anlamlı bir korelasyon vardı.*
Sonuç: *FINDRISK anketi ve trigliserit/glikoz indeksi sağlıklı görünen bireylerde diyabet gelişim riskini erken dönemde tespit etmek ve bireyleri bu konuda bilgilendirebilmek için birinci basamakta kullanılabilecek kolay, pratik ve uygun maliyetli yöntemlerdir.*

Anahtar kelimeler: *sağlıklı birey, diyabet riski, FINDRISK anketi, trigliserit/glikoz indeksi*

Corresponding Author:
ndemirbas76@hotmail.com

N. Demirbas 0000-0002-4038-9386
R. Kutlu 0000-0002-8502-0232

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease and a serious public health problem that requires continuous medical care because the body cannot make sufficient use of carbohydrates, fats, and proteins due to insulin deficiency or impairments in the effects of insulin. There has been a worldwide increase in the prevalence of DM due to many factors such as increasing obesity and sedentary lifestyle. This creates an important burden for the health economy due to both illness and complications [1]. The prevalence of DM is 8.8% worldwide and 14.7% in Turkey [1,2].

Type 2 DM is a disease with an asymptomatic period and accounts for about 90-95% of all cases of DM [2]. Community-based studies show that nearly half of DM patients in Turkey are not yet aware of their disease [3]. It is possible to detect DM during this asymptomatic period, to detect and regulate risk factors, and to stop or delay the onset of the disease [4]. Simple, effective, reliable, and widely applicable tools are being developed to ensure diabetes awareness. In recent years, researchers have proposed several risk factors, predictive models, and inflammatory biomarkers for identifying people at high risk for type 2 diabetes in the future [5-7]. However, data on the role of inflammatory biomarkers such as high-sensitivity C-reactive protein, tumor necrosis factor-alpha, or interleukin-6 are limited. Furthermore, these new markers are impractical and expensive for use in primary health care [8]. Insulin resistance (IR), the main indicator used in the diagnosis of DM, is defined as a decrease of cells' glucose uptake even at certain insulin concentrations. There are several methods for the diagnosis of IR. In clinical practice, the hyperinsulinemic-euglycemic clamp method is considered the gold standard, but it is expensive and difficult to apply [9]. The homeostasis model assessment of insulin resistance (HOMA-IR) is one of the most widely used methods for assessing IR in healthy people [10]. However, it is necessary to measure serum insulin levels to calculate HOMA-IR, and this measurement is not a part of routine evaluation in health care services.

The relationship between fasting blood glucose (FBS) and triglyceride (TG) levels with the development of type 2 diabetes has been reported in the literature [11,12]. The triglyceride/glucose (TyG) index is a new index proposed as an indicator of IR [13-15]. A number of recent studies have shown a significant correlation between the clamp method and HOMA-IR and the TyG index [16,17]. Although many studies have been conducted on the TyG index as a predictor of type 2 diabetes in many countries of the world, the number of studies on this subject is limited in Turkey.

Today, survey studies are also conducted to evaluate the risk of diabetes in adults. One of these tools is the Finnish Diabetes Risk Score (FINDRISC). The FINDRISC questionnaire identifies the risk of the development of diabetes in adults over the next decade and allows for early diagnosis of high-risk individuals.

In this study, we aimed to compare the TyG index and FINDRISC questionnaire, used as predictors of diabetes, to determine the risk of diabetes in healthy individuals and their relationship with obesity.

MATERIALS AND METHODS

Place, type, and universe of the study

This study was planned as a retrospective review of the files of healthy individuals over 18 years old who attended a family medicine outpatient clinic between January 1, 2014 and December 31, 2016 for periodic health examinations. In this period, the files of individuals who applied to our outpatient clinic were examined and sociodemographic characteristics such as age, gender, marital status, educational status, and smoking status; anthropometric measurements such as height, weight, and waist circumference; systolic and diastolic blood pressures; and fasting blood glucose and lipid parameter results were recorded in a separate program for analysis. The participants' health habits and scores from the FINDRISC diabetes risk questionnaire were recorded.

The following individuals were excluded from the study: those with incomplete information; those with congenital or subsequent body abnormalities; patients with cancer; patients with diseases that would affect blood sugar and lipid parameters and those using drugs for this; patients with bone, endocrine, and metabolic diseases; pregnant women and those in puerperium; those receiving medical or

surgical obesity treatment; diabetes patients; those receiving treatment for hypertension; and those under 18 years of age. Considering the exclusion criteria, the study was completed with 879 individuals.

Ethics committee approval: Before starting the study, approval of the Necmettin Erbakan University Meram Medical Faculty's Non-Interventional Clinical Research Ethics Committee (2019/2172) was obtained.

Data collection: Weight, height, and waist circumference were recorded as anthropometric measurements from the study participants' files and body mass index (BMI) was calculated as BMI=weight (kg)/height (m^2). BMIs of 18.50-24.99 were evaluated as normal weight, 25.0-29.99 as overweight, and ≥30.0 as obese. BMIs of <18.5 were not included in the study because of the small number of people. Fasting blood glucose (FBS), total cholesterol (T-Chol), triglyceride (TG), high-density lipoprotein (HDL-c), and low-density lipoprotein (LDL-c) values were recorded from patients' files. The TyG index was calculated according to the following formula:

Triglyceride/Glucose (TyG) Index: ln[triglyceride (mg/dL) × fasting glucose (mg/dL) /2] [18].

Diabetes Risk Questionnaire (FINDRISC): The FINDRISC questionnaire [19], developed by the Finnish Diabetes Association within the scope of the Finnish Type 2 Diabetes Prevention Programme, is also widely used in our country and is recommended by the Turkish Society of Endocrinology and Metabolism (TEMD). This questionnaire determines the risk of developing diabetes in the next decade [2]. The FINDRISC questionnaire consists of 8 questions: age, BMI, waist circumference, physical activity, fruit and vegetable consumption, history of antihypertensive medication, high blood sugar, and family history of diabetes. The scores corresponding to the answers are summed and the total diabetes risk score, ranging from 0 to 26, is calculated. If the total score is <7, the risk is low (1%), while 7-11 points signify mild risk (4%), 12-14 points moderate risk (16%), 15-19 points high risk (33%), and ≥20 points very high risk (50%).

Statistical Analysis: SPSS 20.0 for Windows was used for statistical analysis. Descriptive statistics of continuous variables are given as means and standard deviations, and descriptive statistics of categorical data are given in terms of frequency and percentage. Compliance with normal distribution was evaluated by the Kolmogorov-Smirnov test. Accordingly, one-way ANOVA was used to compare quantitative data showing normal distribution. The post hoc Tukey test was performed when there was a significant difference between groups. The chi-square test was used to compare categorical data. Pearson correlation analysis was used for correlations between parameters. Correlation coefficients (r) of 0.00-0.24 were evaluated as weak relationships, 0.25-0.49 as moderate, 0.50-0.74 as strong, and 0.75-1.00 as very strong. Linear regression analysis was performed between two variables and the regression coefficient was calculated. The results were evaluated with 95% confidence intervals and $p<0.05$ significance level.

RESULTS

A total of 879 participants who applied to the family medicine outpatient clinic for periodic health examinations were included in the study; 66.7% (n=586) were male, 33.3% (n=293) were female, and the mean age was 37.20±11.8 years (range: 18-76). The sociodemographic characteristics of the participants are shown in Table 1.

The mean BMI of the women participating in the study was 31.48±6.6 kg/m^2 and the mean waist circumference was 95.24±15.1 cm, while the mean BMI of the men was 28.62±5.2 kg/m^2 and the mean waist circumference was 99.33±14.3 cm. A statistically significant relationship was found between both waist circumference and BMI and gender ($p<0.001$). The mean BMI of women was greater than that of men, while the mean waist circumference of men was greater than that of women. The mean diabetes risk score calculated by FINDRISC for women was 10.92±4.9 points and the mean TyG index was 8.56±0.5, while for men, the mean diabetes risk score was 8.75±4.7 points and the mean TyG index was 8.77±0.5. There was a statistically significant relationship between the mean diabetes score and TyG index ($p<0.001$) (Table 2).

According to the FINDRISC questionnaire, participants were divided into 3 groups in terms of the risk

Table 1. Sociodemographic characteristics of the participants.

	Mean±SD	
Age (years)	37.20±11.8	(18-76)
	n	**%**
Gender		
Male	586	66.7
Female	293	33.3
Marital status		
Married	691	78.6
Single	188	21.4
Occupation		
Employed	374	42.5
Unemployed/retired	505	57.5
Education status		
Primary school or less	337	38.3
Secondary school	234	26.6
Higher education	308	35.1
Smoking status		
Smoker	251	28.6
Nonsmoker	628	71.4

of developing diabetes within 10 years. Those who scored 11 points or fewer from the questionnaire (n=552, 62.8%) were considered to be of low/mild risk, those who scored 12-14 (n=177, 20.1%) were of moderate risk, and those who scored 15 or above (n=150, 17.1%) were of high risk. The mean BMI, waist circumference, FBS, and TyG index of the participants in the group with a high risk of diabetes were higher than those with mild and moderate risk and the difference was statistically significant (p<0.001) (Table 3).

The TyG index was divided into 4 groups according to percentile values. Waist circumference, BMI, and FINDRISC diabetes risk scores of those with TyG index values of ≥8.97 were also higher than those of the other groups and this difference was statistically significant (p<0.001) (Table 4).

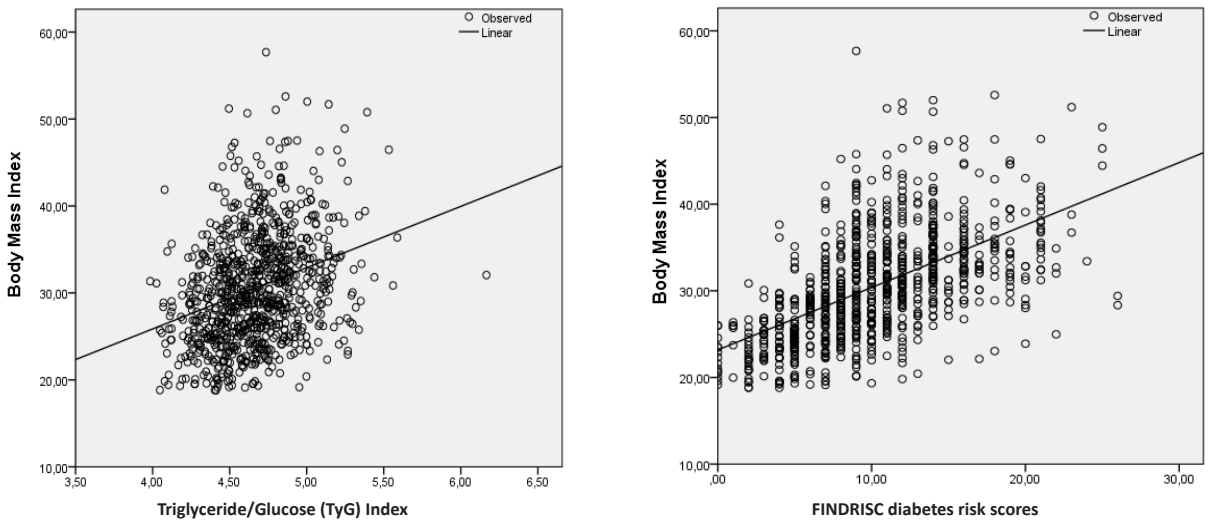


Figure 1. Linear regression graphs for TyG index and diabetes risk score and BMI.

Table 2. Comparison of some parameters with the genders of the participants.

	Female Mean±SD	Male Mean±SD	t	p
BMI (kg/m²)	31.48±6.6	28.62±5.2	6.946	**<0.001**
Waist circumference (cm)	95.24±15.1	99.33±14.3	-3.861	**<0.001**
Systolic BP (mmHg)	126.95±13.8	129.88±12.7	-3.117	**0.002**
Diastolic BP (mmHg)	77.44±10.1	77.44±9.44	0.012	0.990
Fasting blood glucose (mg/dL)	96.53±19.0	96.33±15.9	0.155	0.877
T-Chol (mg/dL)	190.16±39.4	190.63±44.5	-0.153	0.878
LDL-c (mg/dL)	117.19±32.2	122.60±38.5	-2.077	**0.038**
HDL-c (mg/dL)	48.07±10.1	39.73±8.6	12.680	**<0.001**
Triglyceride (mg/dL)	124.13±73.1	153.74±81.9	-5.231	**<0.001**
Diabetes risk score	10.92±4.9	8.75±4.7	6.184	**<0.001**
TyG index	8.56±0.5	8.77±0.5	-5.516	**<0.001**

Table 3. Comparison of some parameters with participants' diabetes risk status.

	Low/mild risk[a] (n=552) Mean±SD	Moderate risk[b] (n=177) Mean±SD	High-very high risk[c] (n=150) Mean±SD	F	p
BMI (kg/m²)	28.34±5.6	33.52±5.8	35.01±5.6	111.223	<0.001[ab] <0.001[ac]
Waist circumference (cm)	92.52±13.7	102.23±14.0	104.97±14.4	65.079	<0.001[ab] <0.001[ac]
Systolic BP (mmHg)	125.53±12.2	129.60±13.1	134.78±16.1	31.098	0.001[ab] <0.001[ac] 0.005[bc]
Diastolic BP (mmHg)	76.04±9.3	78.48±9.8	81.36±10.8	18.841	0.012[ab] <0.001[ac] 0.039[bc]
Fasting blood glucose (mg/dL)	92.95±12.5	97.29±14.2	108.42±29.9	48.340	0.001[ab] <0.001[ac] <0.001[bc]
T-Chol (mg/dL)	186.03±40.2	195.45±41.6	200.03±42.1	8.673	0.026[ab] 0.001[ac] <0.001[bc]
LDL-c (mg/dL)	115.63±34.1	123.45±35.2	126.10±33.2	7.397	0.030[ab] 0.002[ac]
HDL-c (mg/dL)	45.48±10.5	44.68±11.0	45.28±9.2	0.397	0.673
Triglyceride (mg/dL)	127.56±78.7	141.47±79.3	148.87±67.0	5.562	0.003[ac]
TyG index	8.54±0.5	8.70±0.5	8.87±0.51	24.685	0.001[ab] <0.001[ac] 0.011[bc]

When correlations of variables with the diabetes risk scores of the participants were examined, there was a moderate positive correlation with age, waist circumference, and FBS and a strong positive correlation with BMI (r=0.348, r=0.481, r=0.341, p<0.001). Also, there was a moderate positive correlation between age, BMI, waist circumference, and FBS and the TyG index (r=0.332, r=0.305, r=0.382, r=0.468, p<0.001). The correlations between diabetes risk score and TyG index and other parameters are shown in Table 5.

When linear regression analysis was performed, 32.0% of the increase in diabetes risk score and 9.3% of the increase in TyG index was attributed to increase in BMI (Figure 1).

DISCUSSION

The results of our study are important because this is one of the few studies conducted with the FINDRISC questionnaire and the TyG index, the predictor of insulin resistance, used to predict early diabetes development in our country.

According to FINDRISC, 17.1% of the participants were at high risk of developing DM within 10 years. In a study conducted to determine the risk of diabetes in hospital employees, 7.8% of the employees were found to be high-risk with the FINDRISC survey [20]. In another study conducted in healthy adults, the risk of diabetes was found to be high in 19.3% of the participants as a result of FINDRISC [21]. In a study conducted in our region, the frequency of those with high risk of diabetes was found to be 15.5%, similar to our present results [22]. In the study of İğci et al., applying the ADA diabetes risk questionnaire to 3138 people, the percentage of those with a high risk of diabetes was found to be 32% [23]. This difference may be due to the different number of partici-

Table 4. Comparison of some parameters with TyG index of participants.

	TyG ≤ 8.24[a] Mean±SD	TyG: 8.24-8.61[b] Mean±SD	TyG:8.61-8.97[c] Mean±SD	TyG ≥ 8.97[d] Mean±SD	p
Waist circumference (cm)	88.63±12.2	94.53±15.0	99.0±14.0	109.99±13.7	<0.001[ab] <0.001[ac] 0.004[bc]
BMI (kg/m²)	27.57±5.2	30.19±6.2	31.31±6.3	32.93±6.4	<0.001[ab] <0.001[ad] 0.026[cd]
Systolic BP (mmHg)	122.68±12.2	125.54±11.9	130.14±13.2	133.17±14.3	<0.001[ad] <0.001[ac] <0.001[bc]
Diastolic BP (mmHg)	74.33±10.0	76.53±9.7	79.41±9.2	79.43±9.8	<0.001[ad] <0.001[ac] <0.001[bc]
Fasting blood glucose (mg/dL)	89.07±7.3	93.53±10.3	95.67±10.0	107.28±29.0	<0.001[ac] <0.001[bc] 0.028[ab]
T-Chol (mg/dL)	168.96±35.1	181.89±35.0	196.87±36.8	212.83±43.6	<0.001[ac] 0.021[bc]
LDL-c (mg/dL)	103.73±30.1	116.92±31.1	126.49±33.5	128.47±36.9	0.014[bc] <0.001[ad]
HDL-c (mg/dL)	50.95±11.2	46.20±9.6	43.79±9.7	40.37±8.0	<0.001[ac] <0.001[bc]
Triglyceride (mg/dL)	66.32±13.9	98.59±13.7	137.18±18.4	231.07±87.7	<0.001[ac] <0.001[bc]
Diabetes risk score	8.12±4.0	9.73±4.5	10.72±5.1	12.16±5.3	<0.001[ab] <0.001[ac] <0.001[bc]

pants and the questionnaire used for risk assessment. According to 2017 International Diabetes Federation (IDF) data, the incidence of diabetes in Turkey is reported to be 14.7% and it is estimated that this rate will increase gradually in the next 15 years [(1)]. In the present study, a significant relationship was found between age and gender of the participants and their diabetes risk scores. The risk score was higher in older individuals and females, while it was higher in younger participants and males. Contrary to this study, no significant association between 10-year diabetes risk and gender was identified in some other studies of diabetes risk [(20-22)]. Although the community-based TURDEP-2 study to determine the prevalence of DM in Turkey found DM to be more common in women, no significant relationship between gender and DM frequency was found [(3)]. In our study, the reason for the higher risk of diabetes in females than males may be that the women living in our region have higher BMIs and waist circumferences due to a lack of physical activity and nutritional patterns, and this may increase the risk of diabetes. Obesity and high waist circumference are the most important factors that increase the risk of diabetes, as shown in many studies [(20-24)].

The TyG index is calculated based on the individual's measured triglyceride and fasting blood sugar using the formula ln[triglyceride(mg/dL)×fasting glucose (mg/dL)/2]. Many prospective studies in the literature in recent years have shown that the TyG index is associated with new-onset diabetes [(25)], hypertension [(26)], and cardiovascular events [(27,28)]. In a cohort study aimed to evaluate the role of the TyG index in predicting and mediating the development of cardiovascular disease (CVD), the TyG index of 6078 par-

Table 5. Correlation between TyG index and diabetes risk score and some parameters.

	Diabetes risk score		TyG index	
	r	p	r	p
Age	0.348**	p<0.001	0.322**	p<0,001
BMI (kg/m2)	0.566**	p<0.001	0.305**	p<0,001
Waist circumference (cm)	0.481**	p<0.001	0.382**	p<0,001
Systolic BP (mmHg)	0.286**	p<0.001	0.280**	p<0,001
Diastolic BP (mmHg)	0.261**	p<0.001	0.192**	p<0,001
Fasting blood glucose (mg/dL)	0.341**	p<0.001	0.468**	p<0,001
T-Chol (mg/dL)	0.176**	p<0.001	0.443**	p<0,001
LDL-c (mg/dL)	0.148**	p<0.001	0.267**	p<0,001
HDL-c (mg/dL)	-0.033**	p<0.001	-0.366**	p<0,001
Triglyceride (mg/dL)	0.152**	p<0.001	0.904**	p<0,001
Diabetes risk score	1		0.279**	p<0.001
TyG index	0.279**	p<0.001	1	

ticipants over 60 years of age was calculated and a significant relationship was shown between increasing TyG and CVD, which increased over time [29]. In this study, we found that systolic and diastolic blood pressures were higher in individuals with a high TyG index. A study in Chinese adults has been shown that a higher TyG index, regardless of obesity, synergistically increases the risk of prehypertension, and the TyG index has a higher predictability for HT compared to traditional indices [30]. In another study, the relationship between the Increasing TyG index and prehypertension and hypertension risk was determined [31].

In a study in which 617 adults without diabetes were followed for approximately 9 years, the TyG index was used to evaluate the risk of developing diabetes, and it was found that the frequency of diabetes development was higher in patients with high TyG index over time than in those with a low index. While there is no relationship between gender and diabetes development, it has been shown that the frequency of diabetes development increases with age and BMI [32]. In the present study, the TyG index was found to be significantly higher in women than in men. Although triglyceride levels were lower in female participants than in men, there was no difference between fasting blood glucose levels, and this may have caused the difference in the index.

In a comparative study that applied HOMA-IR and the TyG index to evaluate insulin resistance, the TyG index was found to be significantly higher in patients with high HOMA-IR values and the positive predictive value of the TyG index was calculated as 73.3% [33]. In a previous study to predict the development of diabetes and cardio-metabolic changes, the area under the curve (AUC) in ROC analysis was 0.790 for FBS and 0.640 for the TyG index, while the AUC was 0.802 for the TyG index in another study [30,31]. In their study, Unger et al determined the TyG index cut-off point as 8.8 for patients with metabolic syndrome [14]. According to our study, the frequency of those with the TyG index above 8.8 was found to be 35.4% (n=311). According to the results of the FINDRISC questionnaire, the frequency of those with medium and high risk was 37.2% (n=327). The two tests are compatible with each other. In a different study, the cut off value was used between 8.15-8.65 for different groups [34]. In our study, we found that those with a TyG value of 8.97 and above are at high risk.

In a comparative study using HbA1C and the TyG index as predictors of glycemic control in type 2 DM patients, in the linear regression analysis, a significant positive correlation was found between HbA1c level and TyG index even after BMI, age, sex, duration of diabetes, and smoking factors were fixed. As a result of the study, it was concluded that the TyG index may be useful as a predictor of glycemic control in overweight and obese patients with type 2 DM [35]. In the present study, correlation analysis of the FINDRISC diabetes risk score and TyG index showed a moderate positive correlation with age, BMI, and waist circumference. In overweight and obese individuals, the risk of developing diabetes and IR as calculated by the TyG index is higher than among indi-

viduals of normal weight. Diabetes can be prevented by lifestyle changes, adequate physical activity, and regulation of eating habits.

Limitations: The results of this study should be interpreted within the framework of its limitations. The present study does not explain the causality of the results, as it was planned to retrospectively scan patients' files. Our results cannot be generalized because the study was conducted with a limited number of participants in a particular community. Most importantly, we could not evaluate HOMA-IR, one of the gold-standard methods for IR measurement. Insulin level measurement is not a routine test in periodic health examinations. However, the utility of the TyG index in routine clinical practice has been proven in previous studies. It is recommended that future studies include cohort-type studies covering a long follow-up period and be conducted with larger numbers of participants.

CONCLUSION

According to the results of FINDRISC, 17.1% of the participants had a high risk of developing DM in 10 years. When correlations with the diabetes risk score were examined, there were significant positive correlations with age, waist circumference, and FBS and a strong positive correlation with BMI. For the TyG index, there was a moderately significant correlation with age, BMI, waist circumference, and FBS. After linear regression analysis, 32.0% of the increase in diabetes risk score and 9.3% of the increase in TyG index were attributed to increase in BMI.

To assess the risk of developing diabetes in healthy individuals, the FINDRISC questionnaire and the TyG index, which is a predictor of IR, are easy and simple to apply. Early detection of obesity as one of the most important risk factors for diabetes development, lifestyle changes, and regulation of nutrition are among the most important tasks of family physicians. It is recommended that primary care workers be supported with in-service training on risk identification and risk management issues.

Ethics Committee Approval: Before starting the study, approval of the Necmettin Erbakan University Meram Medical Faculty's Non-Interventional Clinical Research Ethics Committee (2019/2172) was obtained.

Conflict of Interest: All the authors declare that they have no conflicts of interest to disclose.

Funding: No funding used for the study.

Informed Consent: Consent was not obtained from the patients since it was a retrospective study.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 8th ed. 2017. Available from: https://www.idf.org/diabetesatlas (Date of access: 14.11.2019)
2. Turkey Endocrine and Metabolic Society (TEMS). Diagnosis, Treatment and Follow-up Guide of Diabetes Mellitus and Complications 2019. Available from: http://www.turkendokrin.org/files/15055_DIYABET_web(1).pdf. (Date of access: 14.11.2019)
3. Satman I, Ömer B, Tutuncu Y, et al. Twelve-year trends in the prevalence and risk factors of diabetes and pre- diabetes in Turkish adults. Eur J Epidemiol. 2013;28(2):169-80. https://doi.org/10.1007/s10654-013-9771-5
4. American Diabetes Association. Prevention or delay of type 2 diabetes. Sec. 5. In: Standards of Medical Care in Diabetes. 2015. Diabetes Care. 2015;38:31-2. https://doi.org/10.2337/dc15-S008
5. Abbasi A, Peelen LM, Corpeleijn E, et al. Prediction modelsfor risk of developing type 2 diabetes: systematic literaturesearch and independent external validation study. BMJ. 2012;18(345):e5900. https://doi.org/10.1136/bmj.e5900
6. Buijsse B, Simmons RK, Griffin SJ, Schulze MB. Risk assessment tools for identifying individuals at risk ofdeveloping type 2 diabetes. Epidemiol Rev. 2011;33:46-62. https://doi.org/10.1093/epirev/mxq019
7. Noble D, Mathur R, Dent T, Meads C, Greenhalgh T. Risk models and scores for type 2 diabetes: systematic review. BMJ. 2011;28;343:d7163. https://doi.org/10.1136/bmj.d7163
8. Liu S, Tinker L, Song Y. et al. A prospective study ofinflammatory cytokines and diabetes mellitus in amultiethnic cohort of postmenopausal women. Arch Intern Med. 2007;167(15):1676-85. https://doi.org/10.1001/archinte.167.15.1676
9. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979;237(3):E214-23. https://doi.org/10.1152/ajpendo.1979.237.3.E214
10. Matthews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9. https://doi.org/10.1007/BF00280883
11. Rhee SY, Woo JT. The prediabetic period: review of clinical aspects. Diabetes Metab J. 2011;35(2):107-16. https://doi.org/10.4093/dmj.2011.35.2.107
12. Janghorbani M, Amini M. Normal fasting plasma glucose and risk of prediabetes and type 2 diabetes: the Isfahan Diabetes Prevention Study. Rev Diabet Stud. 2011;8(4):490-8 https://doi.org/10.1900/RDS.2011.8.490
13. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metab Syndr Relat Disord. 2008;6(4):299-304. https://doi.org/10.1089/met.2008.0034
14. Unger G, Benozzi SF, Perruzza F, Pennacchiotti GL. Triglycerides and glucose index: a useful indicator of insulin resistance.

Endocrinol Nutr. 2014;61(10):533-40.
https://doi.org/10.1016/j.endonu.2014.06.009
15. Guerrero-Romero F, Simental-Mendía LE, González-Ortiz M, et al. The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparisonwith the euglycemichyperinsulinemic clamp. J Clin Endocrinol Metab. 2010;95(7):3347-51.
https://doi.org/10.1210/jc.2010-0288
16. Vasques AC, Novaes FS, de Oliveira MS, et al. TyG index performs better than HOMA in a Brazilian population: a hyperglycemic clamp validated study. Diabetes Res Clin Pract. 2011;93(3):e98-e100.
https://doi.org/10.1016/j.diabres.2011.05.030
17. Mohd Nor NS, Lee S, Bacha F, Tfayli H, Arslanian S. Triglyceride glucose index as a surrogate measure of insulin sensitivity in obese adolescents with normoglycemia,prediabetes,and type 2 diabetes mellitus: comparison with the hyperinsulinemic euglycemic clamp. Pediatr Diabetes. 2016;17:458e65.
https://doi.org/10.1111/pedi.12303
18. Mehran Hosseini S. Triglyceride-glucose index simulation. JCBR. 2017;1(1):11-6.
https://doi.org/10.18869/acadpub.jcbr.1.1.11
19. Finnish Diabetes Association, Programme for the Prevention of Type 2 Diabetes in Finland 2003-2010. Available from: https://www.diabetes.fi/files/1108/Programme_for_the_Prevention_of_Type_2_Diabetes_in_Finland_2003-2010.pdf
20. Arpacı I, Olgun N, Eren I. Assessment of diabetes risk in hospital employees. Diyabet, Obezite ve Hipertansiyonda Hemşirelik Forumu. 2019;11(1):7-11.
21. Kulak E, Berber B, Temel H, et al. Determination of type 2 diabetes risk levels in individuals applying to family medicine. Turk J of Fam Prac. 2019;23(1):20-30. Available from: http://www.turkailehekderg.org/articles/research-article/determination-of-type-2-diabetes-risk-levels-in-individuals-applying-to-family-medicine/
22. Kutlu R, Sayın S, Koçak A. Applicability of the Finnish Diabetes Risk (FINDRISC) as a Screening Tool for Type 2 Diabetes Mellitus. Konuralp Med J. 2016;8(3):158-66.
https://doi.org/10.18521/ktd.287466
23. Igci MA, Basat O. Determine type 2 diabetes development risk in adult patients presenting to family medicine department of Gaziosmanpaşa Taksim Training and Research Hospital using diabetes risk assessment test. Namık Kemal Med J. 2019;7(2):53-60.
24. Bayındır Cevik A, Karaaslan MM, Koçan S, et al. Prevalence and screening for risk factors of type 2 diabetes in Rize, Nourtheast Turkey: findings from a population-based study. Prim Care Diabetes. 2016;10(1):10-8.
https://doi.org/10.1016/j.pcd.2015.06.002
25. Zhang M, Wang B, Liu Y, et al. Cumulative increased risk of incident type 2 diabetes mellitus with increasing triglyceride glucose index in normal-weight people: The Rural Chinese Cohort Study. Cardiovasc Diabetol. 2017;16(1):30.
https://doi.org/10.1186/s12933-017-0514-x
26. Zheng R, Mao Y. Triglyceride and glucose (TyG) index as a predictor of incident hypertension: a 9-year longitudinal population-based study. Lipids Health Dis. 2017;16(1):7.
https://doi.org/10.1186/s12944-017-0410-0
27. Sanchez-Inigo L, Navarro-Gonzalez D, Fernandez-Montero A, Pastrana-Delgado J, Alfredo Martinez J. The TyG index may predict the development of cardiovascular events. Eur J Clin Invest. 2016;46(2):189-97.
https://doi.org/10.1111/eci.12583
28. Zhao S, Yu S, Chi C, et al. Association between macro- and microvascular damage and the triglyceride glucose index in community-dwelling elderly individuals: the Northern Shanghai Study. Cardiovasc Diabetol. 2019;18:95.
https://doi.org/10.1186/s12933-019-0898-x
29. Xie Y, Guo R, Li Z, et al. Temporal relationship between body mass index and triglyceride-glucose index and its impact on the incident of hypertension. Nutr Metab Cardiovasc Dis. 2019;29(11):1220-29.
https://doi.org/10.1016/j.numecd.2019.07.003
30. Xie H, Song J, Sun L, Xie X, Sun Y. Independent and combined effects of triglyceride-glucose index on prehypertension risk: a cross-sectional survey in China. J Hum Hypertens. 2020. doi: 10.1038/s41371-020-0321-9. [Epub ahead of print]
https://doi.org/10.1038/s41371-020-0321-9
31. Wang K, He G, Zhang Y, et al. Association of triglyceride-glucose index and its interaction with obesity on hypertension risk in Chinese: a population-based study. J Hum Hypertens. 2020. [Epub ahead of print]
https://doi.org/10.1038/s41371-020-0326-4
32. Chamroonkiadtikun P, Ananchaisarp T, Wanichanon W. The triglyceride-glucose index, a predictor of type 2 diabetes development: A retrospective cohort study. Prim Care Diabetes. 2020;14(2):161-7.
https://doi.org/10.1016/j.pcd.2019.08.004
33. García AG, Urbina Treviño MV, Villalpando Sánchez DC, Aguilar CA. Diagnostic accuracy of triglyceride/glucose and triglyceride/HDL index as predictors for insulin resistance in children with and without obesity. Diabetes Metab Syndr. 2019;13(4):2329-34.
https://doi.org/10.1016/j.dsx.2019.05.020
34. Moon S, Park JS, Ahn Y. The cut-off values of triglycerides and glucose ındex for metabolic syndrome in American and Korean adolescents. J Korean Med Sci. 2017;32(3):427-33.
https://doi.org/10.3346/jkms.2017.32.3.427
35. Babic N, Valjevac A, Zaciragic A, Avdagic N, Zukic S, Hasic S. The Triglyceride/HDL ratio and triglyceride glucose index as predictors of glycemic control in patients with diabetes mellitus type 2. Med Arch. 2019;73(3):163-8.
https://doi.org/10.5455/medarh.2019.73.163-168

Original Article

Med J Bakirkoy 2020;16(2):174-81
doi: 10.5222/BMJ.2020.57441

Medical Journal of Bakirkoy

Evaluation of Information and Practices About Breast Cancer Screening Performed in Women Presented to a University Hospital in Istanbul

İstanbul'da Bir Üniversite Hastanesine Başvuran Kadınlarda Meme Kanseri Taramalarına Yönelik Bilgi ve Uygulamaların Değerlendirilmesi

Aysegul Akdogan Gemici[1], Safiye Tokgoz Ozal[1], Ebru Sen[2], Elif Hocaoglu[1], Ercan Inci[1]

[1] *Health Science University, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Department of Radiology, Istanbul, Turkey*
[2] *Health Science University, Bakirkoy Dr Sadi Konuk Education and Research Hospital, Department of General Surgery, Istanbul, Turkey*

Received: 7 December 2019 / **Accepted:** 2 March 2020 / **Publication date:** 26 June 2020

Cite as: Gemici AA, Tokgoz Ozal S, Sen E, Hocaoglu E, Inci E. Evaluation of information and practices about breast cancer screening performed in women presented to a university hospital in Istanbul. Med J Bakirkoy 2020;16(2):174-81.

ABSTRACT

Objective: *The aim of this study was to determine the information and practices related to breast cancer screening performed in women who presented to the mammography unit of a university hospital in Istanbul.*
Method: *A questionnaire was prepared using the literature. It was performed with a face-to-face interview method in the patients who were referred to the mammography (MG) unit of our hospital. It consisted of questions about sociodemographic characteristics, breast self-examination (BSE), clinical breast examination (CBE) and information about MG and performing these methods.*
Results: *In 260 women with a mean age of 52.5 (36-81) years; while the rate of BSE was 69.2%, the rate of CBE was 77.7% and the rate of MG was 78.5%, these were higher than the literature. The mean level of knowledge of patients about breast cancer was 6.2/10 (62%) and it was higher than the literature. Breast cancer risk factors knowledge level scores were significantly higher in patients who underwent MG procedure and BSE ($p=0.031$; $p=0.001$; $p<0.05$). Contrary to the literature, no significant effect of income and education level on the rates of BSE, CBE, undergoing MG procedure was determined. There was a statistically significant difference between the level of knowledge of the patients according to the family history of breast cancer ($p=0.004$; $p<0.01$). However, there was no statistically significant difference in the rates of MG, CBE, and BSE in those ($p>0.05$).*
Conclusion: *The knowledge and practices about breast cancer screening are good in the women who presented to our hospital. However, in women who have a positive family history, although there is a high level of knowledge, it has been determined that there is no increase in participation in screening. In addition to the entire female population, this susceptible group needs health workers' support.*

Keywords: *breast cancer, screening, breast examination, mammography*

ÖZ

Amaç: *İstanbul'da bir üniversite hastanesi mamografi ünitesine gelen kadınlarda meme kanseri taramalarına yönelik bilgi ve uygulamaların belirlenmesi amaçlanmıştır.*
Yöntem: *Araştırmacılar tarafından literatür bilgisinden yararlanılarak hazırlanan 20 soruluk anket formu, hastanemiz mamografi (MG) ünitesine yönlendirilmiş hastalarda, çekim sonrasında, yüz yüze görüşme yöntemi doldurulmuştur. Anket sosyodemografik özellikler, kendi kendine meme muayenesi (KKMM), klinik meme muayenesi (KMM) ve MG hakkında bilgiler, bu yöntemleri yapma/yaptırma durumu hakkında sorulardan oluşmaktadır.*
Bulgular: *Yaş ortalaması 52,5 (36-81) olan 260 kadında; KKMM yapma oranı % 69,2, KMM yapma oranı % 77,7, MG çektirme oranı % 78,5 olup güncel ülke verilerimize göre yüksek bulunmuştur. Hastaların meme kanseri hakkında ortalama bilgi düzeyi 6.2/10 (% 62) olup literatür ile kıyaslandığında yüksektir. MG çektirenler ve KKMM yapanların meme kanseri risk faktörleri bilgi düzeyi puanları, istatistiksel olarak yüksek saptanmıştır ($p=0.031$; $p=0.001$; $p<0.05$). Literatürün aksine, gelir ve eğitim düzeyinin KKMM, KMM, MG yaptırma oranlarında anlamlı etkisi tespit edilmemiştir. Ailede meme kanseri öyküsü varlığına göre olguların bilgi düzeyi puanları arasında istatistiksel olarak anlamlı farklılık saptanmıştır ($p=0.004$; $p<0.01$). Ancak bu olguların MG çektirme, KMM ve KKMM yapma oranları istatistiksel olarak anlamlı farklılık göstermemektedir ($p>0.05$).*
Sonuç: *Yapılan anket sonucunda, hastanemize başvuran kadınlarda, meme kanseri taramalarına yönelik bilgi ve uygulamaların iyi olduğu görülmektedir. Son yıllarda Kanser Erken Teşhis, Tarama ve Eğitim Merkezleri (KETEM) ile yaygınlaşmaya başlayan MG taramalarının bunda etkin olduğunu düşünmekteyiz. Ancak aile öyküsü pozitifliğinde, bilgi düzeyi yüksek olmasına rağmen taramalara katılımda artış olmadığı tespit edilmiş olup genel kadın nüfusa ek olarak bu hassas grupta sağlık çalışanlarının desteğine ihtiyaç mevcuttur.*

Anahtar kelimeler: *meme kanseri, tarama, meme muayene, mamografi*

Corresponding Author:
✉ aysegulakdogan@yahoo.com

A. Akdogan Gemici 0000-0002-7707-1849
S. Tokgoz Ozal 0000-0003-1690-4744
E. Sen 0000-0002-0121-4540
E. Hocaoglu 0000-0002-2506-4794
E. Inci 0000-0002-3791-2471

INTRODUCTION

Breast cancer is the leading cause of death among women worldwide [1]. Women in 140 of 180 countries in the world were most frequently diagnosed with breast cancer. Currently, breast cancer accounts for one quarter of all cancers in women. As it is worldwide, breast cancer is one of the most common types of cancer in women also in Turkey [2]. Breast cancer is the leading one among some cancers most commonly seen in women across all age groups with a rate of 24.6% in this group [3,4].

Early diagnosis and treatment are important to reduce breast cancer mortality [5,6]. In breast cancer, making an early diagnosis favorably affects the prognosis, reduces mortality and enables to perform breast preservation surgery in suitably selected patients [5]. Going to doctors' visits for breast examination, undergoing mammography procedure and breast self-examination (BSE), clinical breast examination (CBE) within the scope of screening program has an important place in the early diagnosis of breast cancer [7,8]. According to the guidelines for breast cancer screening defined by the Ministry of Health, the following is recommended: BSE annually and CBE every two years in women between 20-40 years of age, routine annual BSE and MG every two years in women between 40-69 years of age [9].

The most important screening method for reducing breast cancer mortality is mammography. It is known that reductions by up to 30% occur in breast cancer mortality due to making an early diagnosis in screenings performed with mammography [10]. American Cancer Society and American Cancer Institute recommend mammography as a screening method for breast cancer in women older than 40 years of age even though they have no symptoms [11,12]. It is known that BSE and CBE are useful to raise the awareness of breast cancer among women [11,13,14]. Although the cancer mortality reduction effect of BSE is controversial, it is a recommended method for creating awareness of breast among women. In the literature, it is reported that approximately 80% of the masses in the breast are discovered for the first time by women themselves [13]. Therefore, it is important for women to practice BSE regularly in order to be able to present to health institutions by recognizing their own breast tissues and detecting the possible changes earlier.

The frequency of early diagnostic methods for breast cancer shows differences depending on many factors. These factors are socio-demographic features and culture. Health beliefs of women are reported to be among the most important factors affecting breast cancer screening [15,16].

In addition to early diagnosis and screening of cancer, raising the awareness about cancer in the society regarding its reasons, risk factors and symptoms and creating behavior change is quite important [17]. In this regard, it is considered that the determination of information, judgement and behaviors related to cancer and screenings is quite important in order to understand the education requirements of women regarding breast cancers. The aim of this study planned based on the aforementioned idea was to determine the information and practices related to breast cancer screening performed among women who presented to the mammography unit of a university hospital in Istanbul.

MATERIAL and METHODS

This descriptive and cross-sectional study was approved by the Ethics Committee of Health Sciences University, Bakirkoy Dr. Sadi Konuk Training and Research Hospital. The study data were collected by using a questionnaire. The research questionnaire was filled out by the researchers using a face-to-face interview method with the participants.

The research questionnaire form was comprised of questions about sociodemographic characteristics, information about breast self-examination (BSE), clinical breast examination (CBE) and mammography and questions determining these states and conditions of practicing/having these methods. A face-to-face interview was conducted with 260 women participating in the study. Informed Consent Form and written volunteer consent were obtained by explaining the purpose of this study orally. Participation in the study was based on voluntariness.

The questionnaire form prepared using the literature knowledge by the researchers and comprising of 20

questions were applied to the patients referred to the MG unit of our hospital by MG technician after the mammography procedure.

There were 4 questions for determining some sociodemographic characteristics (age, education level, marital status, income level) of women in the first part of the data collection form. There were 8 questions for determining the risk factors for breast cancer such as age of menarche, the numbers of their pregnancies and alive births, oral contraceptive use, family history of breast cancer, menopausal status, menopausal age, use of hormone replacement therapy (HRT) of women in the first part of data collection form. There were 8 questions consisting of information and practices related to BSE and CBE in the last part of the data collection form.

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for the statistical analysis of the data obtained from the study. During the evaluation of the study data, the Student t test was used for the intergroup comparisons of descriptive statistical methods (mean, standard deviation, median, frequency, and ratio, minimum, maximum) as well as quantitative data with normal distribution and Mann-Whitney U test was used for the intergroup comparisons of parameters without normal distribution. Pearson's Chi-Square test and Fisher's Exact test were used regarding the comparisons of qualitative data. Significance was evaluated at a level of $p<0.05$.

RESULTS

The study was performed with 260 women referred to the Radiology Department of our hospital for the mammography procedure between January 2018 and May 2018. When the participation in the screening program was evaluated, BSE, CBE, and MG were performed with rates of 69.2%, 77.7%, 78.5%; respectively. The distribution of demographic characteristics and risk factors examined was shown in Table 1.

The distribution of information regarding MG and BSE was shown in Table 2. No statistically significant difference was determined between the ages of patients according to the condition of undergoing MG procedure ($p=0.001$; $p<0.01$). The ages of patients undergoing MG procedure were higher than the ages of patients not undergoing MG procedure. No statistically significant difference was determined between the rates of patients undergoing MG procedure according to the presence of menopausal status ($p=0.001$; $p<0.01$). The rate of undergoing MG procedure was higher in patients with the menopausal status. There was no statistically significant difference between the rates of patients undergoing MG procedure according to ages of menarche, breastfeeding conditions, education levels, income levels and conditions of use of agent delaying the menopause ($p>0.05$). A statistically significant difference was determined between breast cancer risk factors knowledge level scores of patients according to the condition of undergoing MG procedure ($p=0.031$; $p<0.05$). Knowledge level scores of patients undergoing MG procedures were higher.

A statistically significant difference was determined between breast cancer risk factors knowledge level scores of patients according to the presence of a family history of breast cancer ($p=0.004$; $p<0.01$). Knowledge level scores of patients with a family history of breast cancer were higher. There was no statistically significant difference between the rates of undergoing mammography procedure, going to doctors' examinations and breast self-examination of patients according to the presence of a family history of breast cancer ($p>0.05$) (Table 3).

There was no statistically significant difference between the rates of going to doctors' examinations of patients according to ages of menarche, breastfeeding conditions, education levels, income levels, the presence of menopausal status and conditions of use of agent delaying the menopause ($p>0.05$). No statistically significant difference was determined between breast cancer risk factors knowledge level scores of patients according to conditions of going to doctors' examinations ($p>0.05$) (Table 4).

There was no statistically significant difference between the rates of practicing BSE of patients according to ages, ages of menarche, breastfeeding conditions, education levels, income levels, presence of menopausal status and conditions of use of agent delaying the menopause ($p>0.05$). A statistically significant difference was determined between breast

Table 1. Distribution of demographic characteristics.

		n (%)
Age (year)	***Min-Max (Median)***	36-86 (51)
	Mean±SD	52.50±9.56
Educational status	**Illiterate/Literate**	22 (8.5)
	Primary school	126 (48.5)
	Secondary school	24 (9.2)
	High School	56 (21.5)
	University	32 (12.3)
Occupation	**Not working**	187 (71.9)
	Working	55 (21.2)
	Retired	18 (6.9)
Income level	**Low**	64 (24.6)
	Medium	193 (74.2)
	High	3 (1.2)
Marital status	**Married**	213 (81.9)
	Single	13 (5.0)
	Divorced	15 (5.8)
	Widowed	19 (7.3)
Having a child	**Absent**	23 (8.8)
	Present	237 (91.2)
Number of children (n=237)	***Min-Max (Median)***	1-10 (2)
	Mean±SD	2.64±1.36
Number of children (n=260)	**No child**	23 (8.8)
	1 child	30 (11.5)
	2 children	103 (39.6)
	3 children	69 (26.5)
	≥ 4 children	35 (13.5)
Breastfeeding (n=237)	**Absent**	6 (2.5)
	Present	231 (97.5)
First menarche age (year)	***Min-Max (Median)***	11-18 (13)
	Mean±SD	13.46±1.32
Age of menarche	**≤ 11 years (early)**	14 (5.4)
	12-14 years (normal)	186 (71.5)
	> 14 years (late)	60 (23.1)
Menopause	**Yes**	175 (67.3)
	No	85 (32.7)
Menopause age (n=175)	**Early (≤ 40 years)**	26 (14.9)
	Normal (41-54 years)	137 (78.2)
	Late (≥ 55 years)	12 (6.9)
Use of agent delaying the menopause	**Yes**	19 (7.3)
	No	241 (92.7)
Family history of breast cancer	**Absent**	193 (74.2)
	Present	67 (25.8)

Table 2. Distribution of information related to mammography and breast self-examination.

	n (%)
Undergoing mammography procedure	
Yes	204 (78.5)
No	56 (21.5)
Knowing that mammography should be undergone periodically	
Yes	212 (81.5)
No	48 (18.5)
Going to doctor examination	
Yes	202 (77.7)
No	58 (22.3)
Knowing breast self-examination	
I have no information, I do not practice	45 (17.3)
I have information, I practice	35 (13.5)
I have information, I practice incidentally	101 (38.8)
I have information, I practice monthly	12 (4.6)
I have information, I practice after each bathing	58 (22.3)
I have information, I practice after the end of each menstrual period	9 (3.5)
Condition of practicing breast self-examination	
Yes	180 (69.2)
No	80 (30.8)
•Where did she receive information about breast self-examination	
TV	124 (47.7)
Book, Magazine, Brochure, Newspaper	12 (4.6)
Internet	12 (4.6)
Close friend - Neighbour	21 (8.1)
Allied Health Personnel	19 (7.3)
Doctor	130 (50.0)
•Where did she receive information about mammography	
TV	34 (13.1)
Book, Magazine, Brochure, Newspaper	7 (2.7)
Internet	13 (5.0)
A close friend - Neighbour	7 (2.7)
Allied Health Personnel	17 (6.5)
Doctor	223 (85.8)
Undergoing Pap smear test	
Yes	195 (75.0)
No	65 (25.0)

cancer risk factors knowledge level scores of patients according to conditions of practicing BSE (p=0.001; p<0.01). Knowledge level scores of patients practicing BSE were higher (Table 5).

Table 3. Evaluation of level of knowledge about risk factors for breast cancer according to the presence of family history of breast cancer.

		Family history of breast cancer		
		Absent (n=193)	**Present (n=67)**	**p**
Level of knowledge about risk factors for breast cancer	***Min-Max (Median)*** ***Mean±SD***	1-10 (6) 6.12±2.08	3-10 (7) 6.97±1.64	[a]0.004**
Number of correct answer for risk factors for breast cancer; n (%)	**9-10 correct answers** **7-8 correct answers** **5-6 correct answers** **≤ 4 correct answers**	26 (13.5) 68 (35.2) 54 (28.0) 45 (23.3)	10 (14.9) 30 (44.8) 22 (32.8) 5 (7.5)	
Undergoing mammography procedure	**Yes** **No**	148 (76.7) 45 (23.3)	56 (83.6) 11 (16.4)	[b]0.237
Going to doctor examination	**Yes** **No**	145 (75.1) 48 (24.9)	57 (85.1) 10 (14.9)	[b]0.092
Condition of practicing breast self-examination	**Yes** **No**	133 (68.9) 60 (31.1)	47 (70.1) 20 (29.9)	[b]0.850

[a] Mann Whitney U Test,
*[b] Pearson's Chi-square Test, **p<0.01*

Table 4. Evaluation of condition of going to doctor examination according to descriptive characteristics.

		Condition of going to doctor examination		
		Yes (n=202) n (%)	**No (n=58) n (%)**	**p**
Age (year)	***Min-Max (Median)*** ***Mean±SD***	36-86 (52) 52.93±9.67	39-79 (50.5) 51.02±9.10	[c]0.181
Age of menarche	**≤ 11 years (early)** **12-14 years (normal)** **> 14 years (late)**	12 (5.9) 149 (73.8) 41 (20.3)	2 (3.4) 37 (63.8) 19 (32.8)	b0.124
Breastfeeding (n=237)	**Absent** **Present**	5 (2.7) 180 (97.3)	1 (1.9) 51 (98.1)	[d]1.000
Educational status	**Illiterate/literate** **Primary school** **Secondary school** **High School** **University**	13 (6.4) 95 (47) 21 (10.4) 47 (23.3) 26 (12.9)	9 (15.5) 31 (53.4) 3 (5.2) 9 (15.5) 6 (10.3)	[b]0.107
Income level	**Low** **Middle/high**	51 (25.2) 151 (74.8)	13 (22.4) 45 (77.6)	
Menopause	**Yes** **No**	136 (67.3) 66 (32.7)	39 (67.2) 19 (32.8)	[b]0.990
Use of agent delaying the menopause	**Yes** **No**	13 (6.4) 189 (93.6)	6 (10.3) 52 (89.7)	[b]0.659
Level of knowledge about risk factors for breast cancer	***Min-Max (Median)*** ***Mean±SD***	2-10 (7) 6.36±2.06	1-10 (7) 6.26±1.81	[a]0.650
Number of the correct answer for risk factors for breast cancer	**9-10 correct answers** **7-8 correct answers** **5-6 correct answers** **≤ 4 correct answers**	31 (15.3) 73 (36.1) 58 (28.7) 40 (19.8)	5 (8.6) 25 (43.1) 18 (31) 10 (17.2)	

[a] Mann Whitney U Test
[b] Pearson's Chi-square Test
[c] Student t Test
*[d] Fisher's Exact Test, **p<0.01, *p<0.05*

Table 5. Evaluation of condition of practicing breast self-examination according to descriptive characteristics.

		Condition of practicing breast self-examination		
		Not practicing (n=80) n (%)	Practicing (n=180) n (%)	p
Age (year)	***Min-Max (Median)*** ***Mean±SD***	39-86 (52.5) 54.14±9.78	36-86 (51) 51.77±9.40	[c]0.066
Age of menarche	**≤ 11 years (early)** **12-14 years (normal)** **> 14 years (late)**	4 (5,0) 57 (71,3) 19 (23.8)	10 (5,6) 129 (71,7) 41 (22.8)	[b]0,972
Breastfeeding (n=237)	**Absent** **Present**	2 (2.9) 67 (97.1)	4 (2.4) 164 (97.6)	[d]1.000
Educational status	**Illiterate/literate** **Primary school** **Secondary school** **High School** **University**	12 (15) 39 (48.8) 4 (5.0) 18 (22.5) 7 (8.8)	10 (5.6) 87 (48.3) 20 (11.1) 38 (21.1) 25 (13.9)	[b]0.054
Income level	**Low** **Middle/high**	22 (27.5) 58 (72.5)	42 (23.3) 138 (76.7)	[b]0.472
Menopause	**Yes** **No**	60 (75.0) 20 (25.0)	115 (63.9) 65 (36.1)	[b]0.078
Use of agent delaying the menopause	**Yes** **No**	9 (11.3) 71 (88.8)	10 (5.6) 170 (94.4)	[b]0.103
Level of knowledge about risk factors for breast cancer	***Min-Max (Median)*** ***Mean±SD***	1-10 (6) 5.70±2.06	2-10 (7) 6.62±1.92	[a]0.001**
Number of the correct answer for risk factors for breast cancer	**9-10 correct answers** **7-8 correct answers** **5-6 correct answers** **≤ 4 correct answers**	6 (7.5) 23 (28.8) 27 (33.8) 24 (30)	30 (16.7) 75 (41.7) 49 (27.2) 26 (14.4)	

[a] *Mann Whitney U Test* [c] *Student t Test* **p<0.05*
[b] *Pearson's Chi-square Test* [d] *Fisher's Exact Test* ***p<0.01*

DISCUSSION

Awareness of breast cancer, BSE, CBE, and MG will improve survival by accelerating progression from symptom to diagnosis. If the awareness and compliance with breast cancer screenings are less, then mortality increases with late diagnosis. In our study, we aimed to learn the levels of knowledge of women about breast cancer and their approaches related to CBE, BSE, and MG procedure who were referred to the mammography unit among ones presenting to our hospital. The mean level of knowledge of patients about breast cancer was 6.2/10 (62%) and this rate was found to be higher than the literature [18,19]. Again, similarly, BSE, CBE, and MG were performed with rates of 69.2%, 77.7%, 78.5%; respectively and these levels were good. According to data of the Ministry of Health, the rates of BSE and undergoing MG procedures performed on a monthly base are 22.9% and 13.6%; respectively. Our results are markedly better than these rates. We think that these better results occur due to the study group comprising of patients routinely undergoing mammography with higher levels of awareness about breast cancer.

When we evaluated conditions of BSE, CBE and undergoing MG procedure, CBE; it was determined that only age factor and menopausal status were associated with MG procedure. The rate of undergoing MG procedure was higher in women with advanced age and menopausal status than the women without advanced age and menopausal status.

Contrary to the literature, no significant effect of income and education level on the rates of undergoing MG procedure was determined and this condition was due to the selection of the participants [19,20,21]. Seventy-four point two percent of women were at a middle income level and only 24.6% of women stated that they were at a low income level. We think that the group participating in the questionnaire does not reflect the general population with this characteristic. Only 9 of women practicing BSE performed the examination at proper time namely after the end of the menstrual period. While the rate of practicing BSE was found to be better in our study, it was determined that practicing BSE was not performed at proper time. Also, it was thought that there could be uncertainty regarding if it was performed with proper technique. It has been considered that the level of knowledge about the BSE technique should be increased. Also in the literature, it was emphasized that there was a lack of performing BSE at proper time with proper technique [19,22]. In some of the countries in which regular cancer screening is performed by the government, BSE is not recommended and presentation of patients with false positive findings to the hospital is tried to be prevented. Despite MG scans which have become widespread with Cancer Early Diagnosis, Screening and Training Centers (KETEM) in recent years, BSE maintains its importance yet for our country [23].

In the study performed by Gocgeldi et al. (2008), the authors determined that health providers (37.3%) and television/newspapers (34.3%) constituted the first two ranks of sources of information of women regarding BSE [24]. In the study performed by Aslan and Sahin, the sources of information of women related to BSE were reported to be health providers (32.0%) and television programs (21.5%) [25]. In our study, 47.7% and 50% of women stated that they learned BSE information from television programs and female doctors; respectively. This condition indicates the extensiveness of television which is the most readily accessible mass medium on this subject. Again, consistent with the literature, it was seen that BSE was learned mainly from the doctor. This condition shows the importance of reaching the large masses of women by health providers who can be in close contact with especially women.

Additionally, when the approach regarding the practice of breast screening in women with a family history of breast cancer is evaluated, there is no statistically significant difference between the rates of undergoing MG procedure, CBE and BSE. However, when knowledge level scores of patients are evaluated, knowledge level scores of patients with a family history of breast cancer were higher. In our study, it was observed that the presence of a family history of breast cancer caused an awareness on this subject but did not cause a difference in taking an action. In the recent study performed by Brum et al., it was shown that the practice of breast cancer screening was better in women with a family history of breast cancer [26]. But, in the study performed by Lerman et al. in 1993, it was reported that breast cancer worries might pose a barrier to mammography adherence among high-risk women, particularly those with a lower level of education in case of presence of a family history of breast cancer [27]. Also in our study group, we thought that a similar mechanism might pose a barrier to taking an action in screening.

The main limitation of our study is the application of the questionnaire in a single center to a group considered to have a relatively higher level of awareness than the population means who presented to the hospital for undergoing MG procedure. Study results should be evaluated considering these characteristics of the study group. Moreover, since breast cancer was a delicate subject for women, some participants might have refrained from answering the questions in the questionnaire correctly. In order to decrease this limitation, our female mammography technician selected to conduct the questionnaire applied it in a proper environment after the mammography procedure. Patients were ensured to answer the questions related to BSE, CBE, and MG procedure by themselves.

CONCLUSION

While performing our study in a single center and obtaining the results after conduction the questionnaire to a group presenting to the hospital by itself is a limitation, we understand from the data obtained that practices of BSE, CBE and MG procedures and levels of knowledge about breast cancer are high. We think that MG scans which have become widesp-

read with KETEM in recent years are effective on this subject. But it has been determined that there was no increase in participation in screening despite a higher level of knowledge in women who had a positive family history of breast cancer. Health workers' support is required in this susceptible group together with the entire female population.

Ethics Committee Approval: Approval was obtained from the Bakirkoy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (2019/57).

Conflict of Interest: No potential conflict of interest relevant to this article was reported.

Funding: None

Informed Consent: Obtained.

REFERENCES

1. Drageset S, Lindstrom TC, Giske T, Underlid K. Being in suspense: Women's experiences awaiting breast cancer surgery. J Adv Nurs. 2011 Sep; 67(9):1941-51. https://doi.org/10.1111/j.1365-2648.2011.05638.x
2. Erkin Ö, Ardahan M. Meme kanseri ve kendi kendine meme muayenesinin pullardaki tarihi. Lokman Hekim Journal 2014. 4(3): 22-8.
3. Kanserle Savaş Daire Başkanlığı: http://kanser.gov.tr/Dosya/2016 Haberler/kanser insidanslari 2013 kisa rapor.pdf
4. Alpteker H, Gümüş D, Doğan S, Bilir S, Önal M. Kız öğrencilerin meme kanseri ve kendi kendine meme muayenesi bilgi ve uygulamalarının incelenmesi. The Journal of Breast Health 2011;7(3):176-81.
5. Topuz E, Aydıner A, Dinçer M. Meme Kanseri. İstanbul. Nobel Tıp Kitapevi, 2003, s.113-23.
6. Taşkın L. Üreme Sistemleri Kanserleri. Doğum ve Kadın Sağlığı Hemşireliği. 4. baskı. Sistem Ofset Matbaacılık, 2000, s.529-32.
7. Erkoç A, Oran F, Yorulmaz H. Hemşirelik öğrencilerinin kendi kendine meme muayenesi (KKMM) ile ilgili bilgi durumlarına eğitimin etkisi. Meme Sağlığı Dergisi 2011;7(2):101-5.
8. Karadağ M. Bir sağlık yüksekokulundaki öğrencilerin kendi kendine meme muayenesi davranış ve inançlarının belirlenmesi. Türkiye Klinikleri J Nurs Sci. 2010;2(1):1-10.
9. Health Ministry [database on the Internet]. Turkish Public Health Institution. Available from: http://www.thsk.gov.tr/dosya/birimler/ah_egitim_gelis_db/dokumanlar/rehberler/30062015.pdf.
10. Thompson PA, Lopez AM, Stopeck A. Breast Cancer Prevention. Springer, 2005;3(2):255-76. https://doi.org/10.1007/3-540-26337-3_12
11. Breast Cancer: Can Breast Cancer Be Found Early? American Cancer Society.http://www.cancer.org/cancer/breastcancer/detailedguide/breastcancer- detection?rnav=cri (Access date: June 02, 2014).
12. National Cancer Institute. Breast cancer screening.http://www.cancer.gov/cancertopics/pdq/screening/breast/health-professional (Access date: June 02, 2014).
13. Akyolcu N, Altun Uğraş G. Breast self examination: how important in early diagnosis? J Breast Health 2011;7:10-4.
14. Özmen V. Breast Cancer Screening: current controversies. J Breast Health. 2011;7:1-4.
15. Jironjwong S, McLennan R. Health beliefs, perceived self-efficacy, and selfexamination among Thai migrants in Brisbane. Journal of Advanced Nursing 2002;41(3):241-9. https://doi.org/10.1046/j.1365-2648.2003.02552.x
16. Petro-Nustas W, Mikhail B. Factors associated with breast self-examination among Jordanian women. Public Health Nursing. 19(4):263-71. https://doi.org/10.1046/j.1525-1446.2002.19406.x
17. Arslan M, Şahin DA. Kadınların meme kanseri ve kendi kendine meme muayenesi ile ilgili bilgi durumlarına planlı eğitimin etkisi. Yıldırım Beyazıt Üniversitesi Hemşirelik E-Dergisi 2013; 1(1):8-16.
18. Secginli S, Nahcivan NO. Factors associated with breast cancer screening behaviours in a sample of Turkish women: a questionnaire survey. Int J Nurs Stud. 2006;43(2):161-71. https://doi.org/10.1016/j.ijnurstu.2005.02.004
19. Dahiya N, Basu S, Singh MC, Garg S, Kumar R, Kohli C. Knowledge and practices related to screening for breast cancer among women in Delhi, India. Asian Pac J Cancer Prev. 2018;19(1):155-9.
20. Anwar SL, Tampubolon G, Van Hemelrijck M, Hutajulu SH, Watkins J, Wulaningsih W. Determinants of cancer screening awareness and participation among Indonesian women. BMC Cancer. 2018 Mar 6; 18(1):208. https://doi.org/10.1186/s12885-018-4125-z
21. Özaydın AN, Güllüoğlu B, Ünalan P et al. Bahçeşehir'de oturan kadınların meme kanseri bilgi düzeyleri, bilgi kaynakları ve meme sağlığı ile ilgili uygulamaları. The Journal of Breast Health 2009;5:4-9.
22. Puri S, Mangat C, Bhatia V, Kalia M, Sehgal A, Kaur A. Awareness of Risk factors and aspects of breast cancer among North Indian women. The Internet Journal of Health. 8;2.
23. http://ketem.org.
24. Göçgeldi E, Açıkel C H, Hasde M, et al. Ankara-Gölbaşı ilçesinde bir grup kadının kendi kendine meme muayenesi yapma konusundaki tutum ve davranışlarının belirlenmesi. Fırat Tıp Dergisi 2008;13(4):261-5.
25. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi Araştırma Makalesi GUSBD 2017;6(4):113-21.
26. Brum IV, Rodrigues T, Laporte E, Aarestrup F, Farinazzo G, Laporte B. Does Knowing Someone with Breast Cancer Influence the Prevalence of Adherence to Breast and Cervical Cancer Screening? Rev. Bras. Ginecol. Obstet. 2018 Apr 40(4):203-8. https://doi.org/10.1055/s-0038-1623512
27. Lerman C, Daly M, Sands C, et al. Mammography adherence and psychological distress among women at risk for breast cancer. J Natl Cancer Inst.1993 Jul 7;85(13):1074-80. https://doi.org/10.1093/jnci/85.13.1074

Original Article

Med J Bakirkoy 2020;16(2):182-9
doi: 10.5222/BMJ.2020.94830

Medical Journal of Bakirkoy

Early Weight Loss Percentile Charts in Exclusively Breastfed Infants According to Mode of Delivery

Sadece Anne Sütü ile Beslenen Bebeklerde Doğum Şekline Göre Erken Kilo Kaybı Persentil Eğrileri

Bahar Kural[1], Tijen Eren[2], Gulbin Gokcay[3]

[1] *Istanbul University Institute of Health Sciences and Institute of Child Health Social Pediatrics Doctoral Programme, Istanbul, Turkey*
[2] *Department of Pediatrics, Koç University Faculty of Medicine, Istanbul, Turkey*
[3] *Istanbul University Institute of Child Health, Department of Social Pediatrics, Istanbul, Turkey*

Received: 8 May 2020 / **Accepted:** 8 June 2020 / **Publication date:** 26 June 2020

Cite as: Kural B, Eren T, Gokcay G. Early weight loss percentile charts in exclusively breastfed infants according to mode of delivery. Med J Bakirkoy 2020;16(2):182-9.

ABSTRACT

Objective: *Early weight loss percentile charts can be used to determine the expected weight loss of newborns. Mode of delivery has a marked effect on weight loss in the immediate postpartum period. The aim in the present study was to construct weight loss percentile charts according to mode of delivery in exclusively breastfed, healthy term infants during hospital stay.*
Method: *Weight loss in a large Turkish cohort of infants, born between January 1, 2011 and December 31, 2014, was evaluated retrospectively. Data on healthy, term and exclusively breastfed neonates during the immediate postpartum hospital stay were collected. Weight change percentile charts were plotted according to mode of delivery.*
Results: *The study encompassed 3247 exclusively breastfed neonates. Of infants 48.1% were girls. Mean gestational age was 38.94±0.84 (range 37-41) weeks and birth weight of infants was 3381.1±380.9 (range 2150-5190) grams. The rate of caesarean delivery was 69.3%. The time of hospital stay of infants born by caesarean delivery was significantly longer than infants born vaginally. The frequency of weight measurements of infants showed a statistically significant difference according to the type of delivery. Weight loss as a percentage of birthweight for infants born by caesarean delivery were significantly greater at 24, 48, 72 and 84 hours after birth compared to those born via vaginal delivery.*
Conclusion: *Plotted percentile charts according to mode of delivery will enable prediction of early weight loss immediately post-partum. In addition, these percentile charts will help to reassure mothers and encourage breastfeeding exclusivity.*

Keywords: *early weight loss, percentile charts, exclusive breastfeeding*

ÖZ

Amaç: *Erken kilo kaybı persentil eğrileri, yenidoğanlarda beklenen kilo kaybını belirlemek için kullanılabilir. Doğum şekli, hemen doğum sonrası dönemde kilo kaybı üzerinde belirgin bir etkiye sahiptir. Bu çalışmada amaç, sadece anne sütü ile beslenen, sağlıklı, term bebeklerde hastanede kalış sırasında doğum şekline göre kilo kaybı persentil eğrilerini oluşturmaktır.*
Yöntem: *Geniş bir Türk bebek kohortunda, 1 Ocak 2011 - 31 Aralık 2014 tarihleri arasında doğanların kilo kaybı geriye dönük olarak değerlendirilmiştir. Doğum sonrası hastanede kalış süresi boyunca sağlıklı, term ve sadece anne sütü ile beslenen yenidoğanlara ilişkin veriler toplanmıştır. Ağırlık değişim persentil eğrileri doğum şekline göre çizilmiştir.*
Bulgular: *Çalışma sadece anne sütü ile beslenen 3247 yenidoğanı kapsamaktadır. Bebeklerin % 48,1'i kızdır. Ortalama gebelik süresi 38,94 ± 0,84 (37-41) hafta ve bebeklerin doğum ağırlığı 3381,1 ± 380,9 (2150-5190) gramdır. Sezaryenle doğum oranı % 69,3'tür. Sezaryen ile doğmuş bebeklerin hastanede kalış süresi vajinal doğum ile doğan bebeklere göre anlamlı olarak daha uzundur. Bebeklerin ağırlık ölçümlerinin sıklığı, doğum şekline göre istatistiksel olarak anlamlı bir farklılık göstermiştir. Sezaryen ile doğmuş bebekler için doğum ağırlığına oranla yüzdesel olarak kilo kaybı, doğumdan 24, 48, 72 ve 84 saat sonra, vajinal doğumla doğanlara göre anlamlı olarak daha yüksektir.*
Sonuç: *Doğum şekline göre çizilen persentil eğrileri, doğumdan hemen sonra erken kilo kaybının tahmin edilmesini sağlayacaktır. Ek olarak, bu persentil eğrileri anneleri rahatlatmaya ve bebeklerini sadece anne sütü ile beslemeye teşvik etmeye yardımcı olacaktır.*

Anahtar kelimeler: *erken ağırlık kaybı, persentil eğrileri, sadece anne sütü ile beslenme*

Corresponding Author:
✉ drbahsal@yahoo.com

B. Kural 0000-0001-9528-1009
T. Eren 0000-0001-9650-3734
G. Gokcay 0000-0003-1042-0407

INTRODUCTION

The World Health Organization (WHO), United Nations International Children's Fund (UNICEF) and various health organisations dealing with children's health, all advocate infants be exclusively breastfed for the first six months of life to achieve optimal growth, development and health [1]. Normal post-partum physiologic weight loss is defined as 5-7% loss of the birth weight [2]. Various early weight loss limits have been described in healthy infants such that losing 7-10% of birth weight is seen as common [3,4]. There are also known morbidities related to early weight loss, such as hypoglycaemia, hyperbilirubinemia and hypernatremic dehydration [5,6,7].

In an earlier study from this center, the risk factors for early weight loss in infants was investigated in the same cohort presented here and mode of delivery was identified as a significant factor [8]. Delayed lactogenesis, delayed time of feeding initiation, post-operative pain, and maternal comorbidities leading to emergency caesarean delivery may cause breastfeeding difficulties and increase weight loss in newborns [9]. During caesarean delivery, it is normal to use intravenous fluids which will affect the birth weight and subsequent weight loss of the neonate [4]. Excessive weight loss after birth may cause anxiety and reduced breastfeeding success [10,11,12]. Early supplementation with formula will lead to failure to achieve an exclusive breastfeeding target for the first six months of life [13].

The first early weight loss nomograms were published by Flaherman et al. [14]. The study encompassed nearly 109,000 infants in the USA. One study from Turkey, examined the relationship between gender, ethnicity and early weight loss of breastfed and term infants up to 72 hours after birth [15]. Management plans for infants with excess weight loss generally focus on promoting weight gain but do not always focus on promotion of consistent, evidence-based infant feeding support to parents [9]. By using percentiles, clinicians may estimate weight loss patterns on a time-interval basis and identify infants who are at risk for excessive early weight loss [14]. In addition, parents can be shown the pattern and estimated weight loss of their babies according to mode of delivery during hospital stay. Parents can thus be reassured about weight change patterns and this information can be useful for promoting exclusive breastfeeding.

The aim of this study was to develop early weight loss percentile charts according to delivery mode in a cohort of exclusively breastfed healthy infants in the immediate post-partum hospital stay in Turkey.

MATERIALS and METHODS

This retrospective, cohort study was based on the evaluation of postnatal hospital records of newborns. Changes in weight for healthy, term, exclusively breastfed newborns after delivery and during hospital stay were analysed.

Infants delivered in a private hospital between 1 January 2011 and 31 October 2014 were eligible for inclusion in the study. Hospital patients belonged to high and very-high income level groups. All mothers were offered antenatal (30-36 weeks of gestation) 'breastfeeding education' during pregnancy. All neonates were evaluated by a paediatrician immediately after birth. Skin-to-skin contact and breastfeeding within one hour after delivery were early goals. A family medicine specialist, who was also an International Board-Certified Lactation Consultant (IBCLC), evaluated all mother-infant pairs during hospital stay in order to achieve breastfeeding exclusivity.

A total of 3247 term, singleton neonates with uneventful perinatal periods were eligible for inclusion in the study. Exclusion criteria were: infants who were non-breastfed; any formula use; gestational age <37 weeks or ≥42 weeks; presence of any metabolic or congenital disease; Neonatal Intensive Care Unit (NICU) admittance and/or APGAR score lower than 7; and multiple births (twins or triplets). Birth weight was not considered as an exclusion criterion. Flowchart of the study was given in Figure 1. Routine weight measurements were performed until discharge, the first one being immediately in the delivery room (birth weight) and daily thereafter. All weight measurements were done by a trained nurse when infants were naked. The electronic digital platform scales accurate to 5 grams were used. The scales were calibrated in accordance with hospital policy. All infants were visited by a paediatrician and IBCLC daily.

When weight loss reached or exceeded 7% of birth weight, measurements were taken at least every 12 hours and re-evaluation of breastfeeding technique and additional breastfeeding consultancy was provided. If latch was not successful, manually expressed milk was given by cup feeding. For the purpose of this study, those babies who were given expressed mother's own milk (MOM) were still assumed to be exclusively breastfed.

Retrospective data were collected from postnatal hospital records of neonates. Infants were grouped according to mode of delivery. Ethical and institutional approvals were obtained.

Number Cruncher Statistical System 2007 (NCSS, Kaysville, UT, USA) was used for statistical analysis. In analysis descriptive statistical methods including mean, standard deviation, median, range (minimum and maximum), frequency and ratio were used. Quantitative data were investigated using visual (graph plots) and analytical methods (Shapiro-Wilk's test) to determine whether or not they were normally distributed. Student's t test was used for comparing two groups of normally distributed variables, and Mann Whitney U test was used for comparing groups when one or both were non-parametric. Pearson Chi-Square test and Fisher's Exact test were employed for comparison of qualitative data. All results were evaluated at the 95% confidence interval, and $p<0.05$ was assumed to indicate significance.

RESULTS

Hospital records of 3247 healthy, term neonates were evaluated for this study. The proportion of males was 51.9% (n=1684). Maternal age varied between 19 and 52 , median was 34 years. Mean gestational age and birth weight of infants were 38.94±0.84 (range 37-41) weeks and 3381.1±380.9 (range 2150-5190) grams respectively. All neonates were exclusively breastfed after delivery for the duration of hospital stay. Maternal age, gestational week and birth weight distributions are given in Table 1.

Mother/baby pairs were divided into two groups by mode of delivery (caesarean delivery n=2249 and normal vaginal delivery n=998) and the rate of caesarean delivery was 69.3%. There was a statistical significance between maternal age and mode of delivery ($p<0.01$); mothers who delivered by caesarean delivery were significantly older than women in the vaginal delivery group (34.2 vs 32.8 years, $p=0.001$). Baby gender by mode of delivery did not yield statistical significance ($p>0.05$). The gestational age of infants born vaginally was significantly higher than infants born via caesarean delivery ($p=0.001$). There was a statistically significant difference between birth weights according to mode of delivery ($p=0.003$); infants born by caesarean delivery were heavier than those born vaginally.

The mean duration of hospital stay was 63.25±15.95 hours in the whole cohort. The time of hospital stay of infants born by caesarean delivery was significantly longer than infants born vaginally ($p=0.001$).

The number of weight measurements of neonates included in the study are given in Table 2. The frequency of weight measurements of infants showed a statistically significant difference according to the type of delivery ($p=0.001$). Excluding birth weight measurement, infants born by vaginal delivery were more likely to have their weight measured ≤3 times while infants born by caesarean delivery were more likely to be weighed ≥4 times.

Time intervals and early weight loss percentages of newborns are given in Table 3. Weight loss proportions for infants born by caesarean delivery compared to infants born via vaginal delivery were significantly higher at 24^{th} hour ($p=0.001$), 48^{th} hour ($p=0.001$), 72^{nd} hour ($p=0.001$) and 84^{th} hour ($p=0.011$).

In all cases, for caesarean and vaginal deliveries; 95%, 90%, 75% and 50% weight loss percentile values over time (24, 48, 72 and 84 hours after delivery) are given in Table 4. Using this data early weight loss percentages were plotted and weight loss percentile charts were created. The charts for weight loss percentile for exclusively breastfed infants delivered by caesarean delivery and normal vaginal delivery are shown in Figures 2 and 3, respectively.

Table 1. Demographic and clinical characteristics of the mothers and infants by mode of delivery

		Total n (%)	Caesarean (n=2249) n (%)	Vaginal (n=998) n (%)	p
Maternal age	*Median (range)*	34 (19-52)	34 (20-52)	33 (19-46)	[a]***0.001****
	Mean ± SD	33.75±4.0	34.17±4.1	32.82±3.8	
	≤30	664 (20.4)	401 (17.8)	263 (26.4)	
	31-35	1536 (47.3)	1033 (45.9)	503 (50.4)	
	36-40	895 (27.6)	686 (30.5)	209 (20.9)	
	≥41	152 (4.7)	129 (5.7)	23 (2.3)	
Infant gender	**Boy**	1684 (51.9)	1178 (52.4)	506 (50.7)	[c]***0.377***
	Girl	1563 (48.1)	1071 (47.6)	492 (49.3)	
Gestation al age (weeks)	*Median (range)*	39 (37-41)	38.7 (37-41)	39.3 (37-41)	[a]***0.001****
	Mean ± SD	38.9±0.8	38.8±0.8	39.3±0.9	
	37-38	1609 (49.6)	1289 (57.3)	320 (32.1)	
	≥39	1638 (50.4)	960 (42.7)	678 (67.9)	
Birth weight (grams)	*Median (range)*	3370 (2150-5190)	3380 (2150-5190)	3350 (2330-4700)	[a]***0.003****
	Mean ± SD	3381.1±380.9	3394.2±385.3	3351.5±369.1	
	2000-2500	17 (0.5)	9 (0.4)	8 (0.8)	
	2501-2999	472 (14.5)	309 (13.7)	163 (16.3)	
	3000-3999	2572 (79.2)	1783 (79.3)	789 (79.1)	
	≥4000	186 (5.7)	148 (6.6)	38 (3.8)	
Duration of hospital stay (hours)	*Median (range)*	72 (12-84)	72 (24-84)	48 (12-84)	[a]***0.001****
	Mean ± SD	63.25±15.95	71.03±7.66	45.71±15.87	

[a] *Student t Test*
[b] *Mann Whitney U Test*
[c] *Pearson Chi-Square Test*
**p<0.05, **p<0.01*

Table 2. Number of weight measurements by mode of delivery.

Number of weights recorded after birth weight	Caesarean (n=2249) n (%)	Vaginal (n=998) n (%)	*p*
1	0 (0)	5 (0.5)	[d]***0.001****
2	10 (0.4)	255 (25.6)	
3	152 (6.8)	578 (57.9)	
4	1924 (85.5)	145 (14.5)	
5	163 (7.2)	15 (1.5)	

[d] *Fisher Freeman Halton Test*
***p<0,01*

DISCUSSION

The study showed that infants born by caesarean delivery and exclusively breastfed, had significantly higher early weight loss in the immediate post-partum period compared to vaginally delivered infants. Weight loss percentiles during the first days of life according to mode of delivery were developed using the collected data (Figures 2 and 3). It was demonstrated that expected weight loss differences between type of delivery mode continued over the first few days of life.

There has been a worldwide increase in the rates of caesarean deliveries [16]. The latest caesarean delivery rate reported by the Turkish Demographic and Health Survey of 2018 was 52% [17]. The WHO has stated that no robust evidence existed for ideal caesarean delivery rates [16]. In another study from Turkey, where early weight loss in infants was investigated, the caesarean delivery rate was 47% in the setting of a teaching hospital of the Turkish Ministry of Health [15]. A recent study from Brazil showed that the caesarean delivery in the private sector was more than twice the rate in the public sector (87.9% versus 42.9%, respectively) [18]. Saki *et al.* showed that 80% of mothers who lived in high income families had caesarean delivery and this study has reinforced the view that women from wealthier families tend to opt for caesarean delivery [19]. The rate of caesarean delivery in our study was quite high

Table 3. Weight loss proportions of the study group by mode of delivery during hospital stay.

Time (hours)	Mode of delivery	n	Median (Min-Max)	Mean±SD	*[a]p*
24	**Caesarean**	2249	4.1 (0-10.3)	-4.06±1.54	***0.001****
	Vaginal	993	3.1 (0-9.5)	-3.24±2.03	
48	**Caesarean**	2239	7.3 (0.4-13.4)	-7.22±1.49	***0.001****
	Vaginal	738	5.8 (0-11.6)	-5.78±1.65	
72	**Caesarean**	2087	7.6 (0.3-13.1)	-7.54±2.06	***0.001****
	Vaginal	160	6.8 (1.2-11.9)	-6.71±1.98	
84	**Caesarean**	163	6.9 (0.9-11.1)	-6.71±2.29	***0.011****
	Vaginal	15	5.3 (0-8.1)	-5.13±2.38	

[a] Student t Test
**p<0.05, **p<0.01*

Table 4. Weight loss percentiles of study group and by mode of delivery.

		Weight loss (%)				
Mode of delivery	**Time (h)**	**n**	**95 %**	**90 %**	**75 %**	**50 %**
Whole cohort	24.	3242	-6.53	-5.92	-4.97	-3.91
	48.	2977	-9.42	-8.87	-8.00	-6.97
	72.	2247	-10.75	-10.03	-8.92	-7.58
	84.	178	-10.04	-9.51	-8.28	-6.88
Caesarean	24.	2249	-6.46	-5.90	-5.03	-4.12
	48.	2239	-9.56	-9.04	-8.24	-7.29
	72.	2087	-10.77	-10.07	-8.97	-7.64
	84.	163	-10.11	-9.57	-8.38	-6.94
Vaginal	24.	993	-6.71	-5.95	-4.72	-3.08
	48.	738	-8.28	-7.74	-6.94	-5.79
	72.	160	-9.83	-9.15	-8.02	-6.83
	84.	15	-7.98	-7.68	-7.17	-5.29

Table 5. Studies on early weight loss in exclusively breastfed infants.

	Falherman et al. [14] 2009-2013		**Samayan et al. [23] Aug-Oct 2012**		**Hamilcıkan et al [15] Jan-Aug 2016**		**Kural et al. Jan 2011-Dec 2014**	
Data period Delivery type	**V (n= 83433)**	**CS (n=25474)**	**V (n=55)**	**CS (n=49)**	**V (n=670)**	**CS (n=758)**	**V (n=998)**	**CS (n=2249)**
Hours	**Median percentage loss (%)**							
24	4.2	4.9	2.2	3.2	3.88	4.59	3.1	4.1
48	7.1	8.0	--	-	5.80	6.00	5.8	7.3
72	6.4	8.6	4.7	5.9	5.1	6.95	6.8	7.6
84	-	-	-	-	-	-	5.3	6.9
96	-	5.8	-	-	-	-	-	-

(69.3%). Our study setting was a private hospital and only private insurances were accepted.

When breastfed infants lose too much weight after birth, healthcare providers may become concerned that there is a problem with breastfeeding [20]. Studies concerning breastfeeding difficulties after birth have stated that special attention and follow-up are required during hospital stay [21]. Besides counselling for breastfeeding techniques, the use of

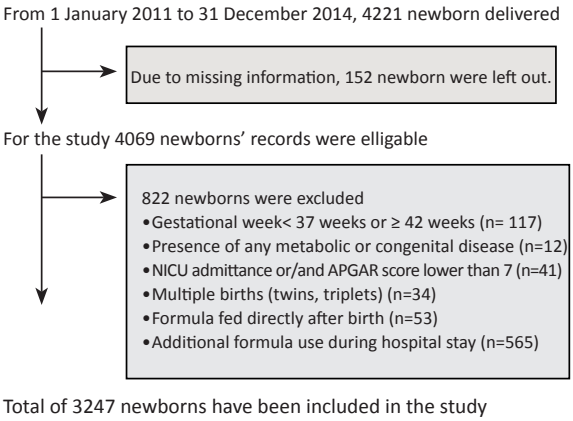


Figure 1. Flowchart of the enrolled participants.

early weight loss percentiles can provide mothers an insight with a visual representation of how their infants are compared according to mode of delivery. This can provide reassurance that exclusive breastfeeding is perfectly adequate for nourishment.

Hourly weight loss percentiles would help clinicians to foresee expected early weight loss of infants and thus allow a personalized approach and management. Flaherman *et al.* attempted to identify the trajectories of breastfeeding outcomes by using early weight-loss nomograms, and concluded that the use of such nomograms might help identify infants at higher risk of cessation of exclusive breastfeeding [22].

Samayan *et al.* studied early weight loss among 104 exclusively breastfed newborns prospectively in Bangalore, India. The median percentage weight loss of infants born vaginally at 24 and 72 hours was 2.2% and 4.7% respectively, while the mean weight loss for infants born by caesarean delivery was 3.2 % and 5.9% at the same time points [23]. The mean weight loss percentages reported by Samayan *et al.* were lowest in both delivery types when compared with other studies whilst those reported by Flaherman *et al.* were the highest (Table 5) [14,23]. When the early weight loss studies were compared, in vaginal deliveries the highest median weight losses occurred at 48 hours, whereas in our study it occurred at 72 hours (see Table 5). The maximum mean weight loss percentages were observed at 48 hours in caesarean deliveries in our study as well as two other studies. [14,15].

Studies have shown that the length of hospital stay following caesarean delivery is higher than those following vaginal delivery [18]. The mean lengths of hospital stay were 71.0 hours for caesarean and 45.7 hours for vaginal deliveries and this difference

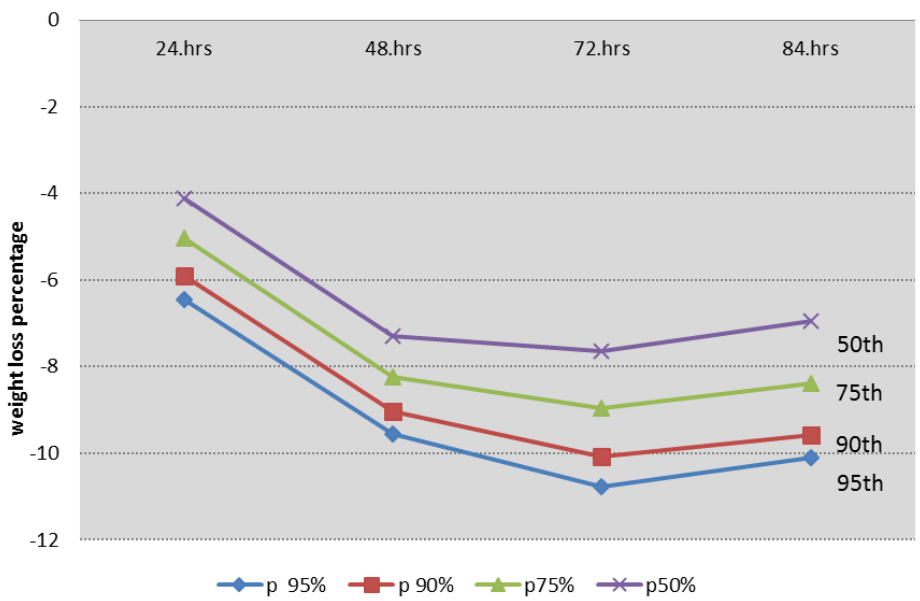


Figure 2. Weight loss percentages of exclusively breastfed infants who were born via caesarean delivery.

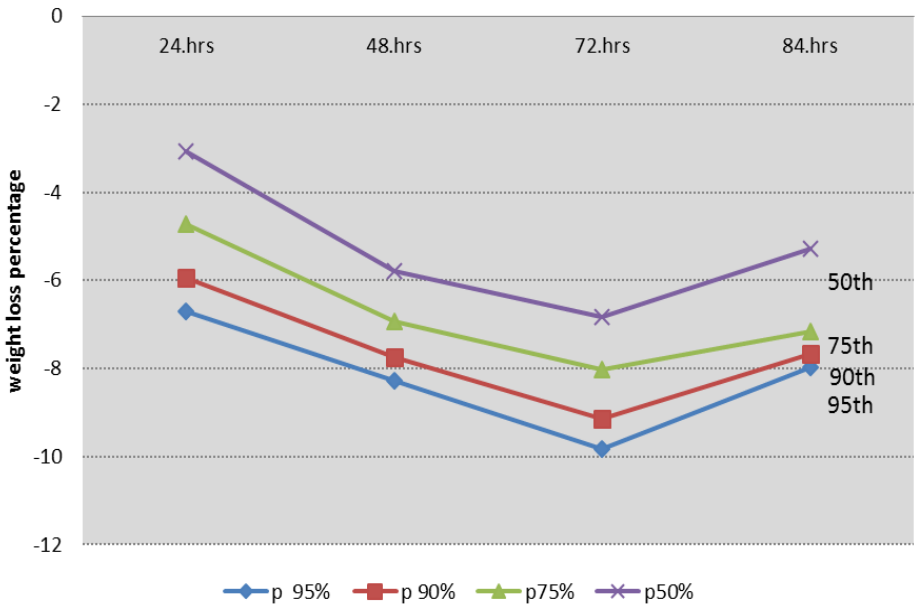


Figure 3. Weight loss percentages of exclusively breastfed infants who were born vaginally.

was statistically significant (p=0.001). It has been suggested that for the establishment of successful breastfeeding, infants should be followed up for 72-96 hours after birth and that may lead to longer hospital stay after caesarean deliveries [21]. Weight measurements were continued as long as weight loss persisted. Flaherman *et al.* reported that 71.9% of infants born via vaginal delivery had one further weight measurement, following birthweight whereas 48.8% of infants born by caesarean deliveries had two weight measurements taken [14]. In our study 57.9% of infants born via vaginal deliveries had three further weight measurements while 85.5% of infants born via caesarean deliveries had four weight measurments. This may be due to the difference between delivery modes in the mean length of stay. Mothers and infants in Flaherman's study stayed in hospital for slightly shorter periods (2.6 and 1.6 days for caesarean and vaginal deliveries, respectively) than in our study. A prospective study to investigate the benefit of using early weight loss percentile charts in terms of breastfeeding success is planned.

Limitations of the study: As only healthy term neonates were included in the study, birth weight of infants was mostly above 3000 grams. Information about the indication for caesarean delivery (elective or emergency) was not evaluated. Generalizability of the study may be limited, it was conducted at a private hospital where most of the infants were from high income families. One of the key strengths of the present study was the large sample size. Although the study was retrospective in nature, data was extracted precisely from hospital records.

CONCLUSION

Vaginal birth should be promoted in order to protect both maternal and neonatal health. The likely greater post-partum weight loss following caesarean delivery must be explained to those mothers who are planning to choose this delivery method. Early weight loss percentiles will have the dual benefit of predicting the expected weight loss in infants and thus reassuring mothers which, in turn, will encourage breastfeeding exclusivity.

Ethics Committee Approval: Approval was obtained from the Koç University Ethics Committee (2015.058. IRB2.024).
Conflict of Interest: The authors declared no conflict of interest.
Funding: No financial support was received.
Informed Consent: Informed consent was not obtained since the study is retrospective.

REFERENCES

1. UNICEF/WHO. Baby-Friendly Hospital Initiative: Revised, Updated and Expanded for Integrated Care, Section 1, Background and Implementation, Preliminary version. 2009. https://apps.who.int/iris/bitstream/handle/10665/43593/9789241594967_eng.pdf;jsessionid=62D44EC8221A7324A9488561160A2B17?sequence=1 (Last Accessed date:22.02.2020).
2. Boies E, Vaucher YE, and the Academy of Breastfeeding Medicine. ABM Clinical Protocol #10: Breastfeeding the late preterm (34-36 6/7 weeks of gestation) and early term infants (37-38 6/7 weeks of gestation) Second Revision 2016. Breastfeed Med. 2016;11(10):494-500. https://doi.org/10.1089/bfm.2016.29031.egb
3. Chantry CJ, Nommsen-Rivers LA, Peerson JM, et al. Excess weight loss in first-born breastfed newborns relates to maternal intrapartum fluid balance. Pediatrics 2011;127(1):e171-9. https://doi.org/10.1542/peds.2009-2663
4. Lawrence RA, Lawrence RM. Breastfeeding: A Guide For The Medical Profession. Breastfeeding Support Groups and Community Resources. 8th Ed. W.B. Saunders, Mosby, Churchill:Elsevier; 2016.
5. Taylor JA, Impson EA. Categorizing weight loss in breastfed infants: A good first step. Pediatrics 2015; 135(1);e174-e175. https://doi.org/10.1542/peds.2014-3354
6. Fonseca MJ, Severo M, Barros H, et al. Determinants of weight changes during the first 96 hours of life in full-term newborns. Birth 2014;41(2):160-8. https://doi.org/10.1111/birt.12087
7. Castilho S, Miranda AM, Fernandes CA, et al. Excess weight loss and hypernatremia in exclusively breastfed infants. J Pediatr Neonat Individual Med. 2018; 7(2):e070212.
8. Eren T. Follow-up of the weight loss in exclusively breastfed newborns before hospital discharge. PhD Thesis, Istanbul University Institute of Health Sciences and Institute of Child Health Social Pediatrics Doctoral Programme, 2018.
9. Kelly NM, Keane JV, Gallimore RB, et al. Neonatal weight loss and gain patterns in caesarean section born infants: integrative systematic review. Matern Child Nutr. 2020; 16(2):e12914. https://doi.org/10.1111/mcn.12914
10. Lewallen LP, Dick MJ, Flowers J, et al. Breastfeeding support and early cessation. J Obstet Gynecol Neonatal Nurs. 2006;35(2):166-72. https://doi.org/10.1111/j.1552-6909.2006.00031.x
11. Chen YJ, Chen WC, Chen CM. Risk factors for hyperbilirubinemia in breastfed term neonates. Eur J Pediatr. 2012; 171(1):167-71. https://doi.org/10.1007/s00431-011-1512-8
12. Livingstone VH, Willis CE, Abdel-Wareth LO, et al. Neonatal hypernatremic dehydration associated with breast-feeding malnutrition: a retrospective survey. CMAJ. 2000;162(5):647-652.
13. Holmes AV, Auinger P, Howard CR. Combination feeding of breast milk and formula: Evidence for shorter breast-feeding duration from the National Health and Nutrition Examination Survey. J Pediatr. 2011;159(2):186-191. https://doi.org/10.1016/j.jpeds.2011.02.006
14. Flaherman VJ, Schaefer EW, Kuzniewicz MW,et al. Early weight loss nomograms for exclusively breastfed newborns. Pediatrics 2015;135(1):e16-23. https://doi.org/10.1542/peds.2014-1532
15. Hamilcikan Ş, Gok V, Bent S, et al. Early Weight Loss in Exclusively Breastfed Term Neonates. Iran J Pediatr. 2017;27(2):e9497. https://doi.org/10.5812/ijp.9497
16. Vogel JP, Betrán AP, Vindevoghel N, et al. WHO Multi-Country Survey on Maternal and Newborn Health Research Network. Use of the Robson classification to assess caesarean section trends in 21 countries: a secondary analysis of two WHO multicountry surveys. Lancet Glob Health. 2015;3(5):e260-70. https://doi.org/10.1016/S2214-109X(15)70094-X
17. Hacettepe University Institute of Population Studies "2018 Turkey Demographic and Health Survey". Hacettepe University Institute of Population Studies, T.R. Ministry of Development and TÜBİTAK,2019, Ankara, Turkey.
18. Silva TPR, Carmo AS, Novaes TG,et al. Hospital-acquired conditions and length of stay in the pregnancy and puerperal cycle. Rev Saude Publica. 2019;53:64. https://doi.org/10.11606/s1518-8787.2019053000688
19. Saki A, Eshraghian MR, Mohammad K, et al. A prospective study of the effect of delivery type on neonatal weight gain pattern in exclusively breastfed neonates born in Shiraz, Iran. Int Breastfeed J. 2010;5:1. https://doi.org/10.1186/1746-4358-5-1
20. Breastfeeding and the Use of Human Milk. Section On Breastfeeding. Pediatrics 2012,129(3):e827-e841; https://doi.org/10.1542/peds.2011-3552
21. Dewey KG. Risk Factors for suboptimal infant breastfeeding behavior, delayed onset of lactation and excess neonatal weight loss. Pediatrics 2003;112(3):607-19. https://doi.org/10.1542/peds.112.3.607
22. Flaherman VJ, Schaefer EW, Kuzniewicz MK, et al. Newborn Weight Loss During Birth Hospitalization and Breastfeeding Outcomes Through Age 1 Month. J Hum Lact. 2017;33(1):225-30. https://doi.org/10.1177/0890334416680181
23. Samayam P, Ranganathan PK, Balasundaram R. Study of Weight Patterns in Exclusively Breast Fed Neonates- Does the Route of Delivery have an Impact? J Clin Diagn Res. 2016; 10(1):SC01-SC3. https://doi.org/10.7860/JCDR/2016/17889.7025

Original Article

Med J Bakirkoy 2020;16(2):190-6
doi: 10.5222/BMJ.2020.58076

Medical Journal of Bakirkoy

Evaluation of Partner Violence in Female Patients with Fibromyalgia Syndrome

Kadın Fibromyalji Hastalarında Eş Şiddetinin Değerlendirilmesi

Ozge Sahmelikoglu Onur[1], Ender Cesur[1], Fadime Gizem Donmezler[1], Filiz Yildiz Aydin[2], Meltem Vural[2], Meltem Guru[3]

[1]*Bakirkoy Research and Training Hospital for Psychiatry Neurology and Neurosurgery, Department of Psychiatry, Istanbul, Turkey*
[2]*Bakirkoy Dr. Sadi Konuk Research and Training Hospital, Department of Physical Medicine and Rehabilitation, Istanbul, Turkey*
[3]*Gazi University Health Care Center, Department of Psychiatry, Ankara, Turkey*

Received: 13 July 2019 / **Accepted:** 15 December 2019 / **Publication date:** 26 June 2020

Cite as: Sahmelikoglu Onur Ö, Cesur E, Dönmezler FG, Yıldız Aydın F, Vural M, Guru M. Evaluation of partner violence in female patients with fibromyalgia syndrome. Med J Bakirkoy 2020;16(2):190-6.

ABSTRACT

Objective: *Fibromyalgia syndrome (FMS) is a disorder that causes chronic extensive musculoskeletal pain. Although there has been great debate in recent investigations regarding the risk factors of FMS, no agreement has been reached about the pathophysiology of the syndrome. In recent studies, it has been suggested that there is an abnormal response to stress factors in this syndrome due to the neuro-endocrine system perturbation as a result of stress experiences such as abuse during childhood, adolescence or adulthood. In this context, this study aims to evaluate the differences of all types of partner violence experienced by patients with FMS and healthy controls.*
Method: *Forty-three consecutive married women aged between 18-65 years who were recently diagnosed as having FMS were recruited from Bakirkoy Dr. Sadi Konuk Research Hospital Outpatient Clinic. The diagnosis of FMS was made by experienced physical medicine and rehabilitation physicians according to the American College of Rheumatology (ACR) FMS diagnostic criteria . Patients who were referred to the Bakırköy Psychiatric Research and Training Hospital were evaluated by an experienced psychiatrist. 43 female patients with FMS and 45 female (non-FMS) controls were evaluated with a questionnaire about previous physical, sexual, emotional, social and economic partner violence, the Hamilton Depression and Anxiety Inventories (HAM-D and HAM-A, respectively), and a Visual Analogue Scale (VAS).*
Results: *The FMS group and healthy control group showed no statistically significant difference in terms of age and the presence of psychiatric administration ($p>0.05$); however, the sample showed a significant difference with regards to education, occupation status, and history of suicide attempts. Significantly higher scores were observed for partner physical violence (27.9% vs. 11.1%), economic violence (48.8% vs. 13.3%), social violence (83.7% vs. 22.3%), and emotional violence (62.8% vs. 28.9%) in FMS patients than in controls ($p<0.05$). Higher HAM-A and HAM-D inventory and VAS scores were observed in the FMS group than controls ($p<0.05$). A statistically significant positive correlation was observed between VAS and HAM-A, HAM-D scores ($p<0.05$).*
Conclusion: *Our results may have implications to show the effect of partner violence on the clinic and course of FMS.*

Keywords: *anxiety, depression, fibromyalgia, pain severity, partner violence*

ÖZ

Amaç: *Fibromiyalji sendromu (FMS), kas iskelet sisteminde yaygın ağrıya neden olan kronik bir hastalıktır. FMS'nin risk faktörleri ile ilgili büyük araştırmalar yapılmasına rağmen, sendromun patofizyolojisi konusunda bir uzlaşmaya varılmamıştır. Yapılan son çalışmalarda, çocukluk, ergenlik veya erişkinlik döneminde suistimal, istismar gibi stres deneyimlerinin bir sonucu olarak nöro-endokrin sistemde bir bozulma olduğu ve bu sebeple stres faktörlerine anormal bir yanıt olduğu öne sürülmüştür. Bu çalışmada FMS olan kadınlarla sağlıklı kontroller arasında eş şiddetinin tüm tipleri açısından farklılıkların araştırılması amaçlanmıştır.*
Yöntem: *Bakırköy Dr. Sadi Konuk Eğitim Araştırma Hastanesi Polikliniği'nde FMS tanısı konan 18-65 yaşları arasındaki kırk üç evli kadın çalışmaya alındı. FMS tanısı Amerikan Romatoloji Derneği (ACR) FMS tanı kriterlerine göre fizik tedavi ve rehabilitasyon uzman doktorları tarafından konuldu. Bakırköy Prof. Dr. Mazhar Osman Ruh ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi psikiyatri polikliniğine yönlendirilen hastalar deneyimli bir psikiyatrist tarafından değerlendirildi. FMS tanısı konan 43 kadın hasta grubuna ve 45 kadın (FMS tanısı olmayan) sağlıklı kontrol grubuna, sosyodemografik veri formu, önceki cinsel, fiziksel, duygusal, sosyal ve ekonomik eş şiddetini ölçen bir şiddet değerlendirme formu, Hamilton Depresyon ve Anksiyete ölçekleri (HAM-D ve HAM-A) uygulandı. Ağrı şiddetini değerlendirmek için Vizüel Analog Skala (VAS) kullanıldı.*
Bulgular: *FMS grubu ve sağlıklı kontrol grubu, yaş ortalaması ve daha önce psikiyatri başvurusu varlığı açısından istatistiksel olarak farklılık göstermedi ($p>0.05$). Bununla birlikte iki grup arasında eğitim durumu, meslek ve intihar girişimlerinin geçmişi açısından önemli farklılıklar tespit edildi. Eşinden fiziksel şiddet görme (%27,9-%11,1), ekonomik şiddet (%48,8-%13,3), sosyal şiddet (%83,7-%22,3) ve duygusal şiddete maruz kalma (%62,8-%28,9) FMS'li hasta grubunda kontrol grubundan daha fazla idi ($p<0.05$). FMS grubunda HAM-D, HAM-A ve VAS skorları kontrol grubundan daha yüksekti ($p<0.05$). VAS ve HAM-A, HAM-D skorları arasında istatistiki açıdan anlamlı korelasyon gözlendi ($p<0.05$).*
Sonuç: *Bu sonuçlar, eş şiddetinin FMS'nin ortaya çıkışı ve sürekliliği üzerinde bir etkisi olabileceği ihtimalini artırmaktadır. Ayrıca, bu çalışmadan elde edilen sonuçların sadece tıbbi bakım almak isteyen FMS'li hastalara ait olduğu ve FMS'li tüm hastalara genellenemeyeceği göz önünde bulundurulmalıdır. Kadına yönelik şiddet ve FMS arasındaki ilişki konusunda daha fazla araştırma yapılmalıdır.*

Anahtar kelimeler: *anksiyete, depresyon, fibromyalji, ağrı şiddeti, eş şiddeti*

Corresponding Author:
✉ meltemguru@gmail.com

Ö. Sahmelikoglu Onur 0000-0003-0447-4636
E. Cesur 0000-0002-8982-8626
F.G. Donmezler 0000-0002-0902-6982
F. Yildiz Aydin 0000-0003-4763-7538
M. Vural 0000-0003-4360-8318
M. Guru 0000-0001-8751-6453

INTRODUCTION

Fibromyalgia syndrome (FMS) is a disorder that causes chronic extensive musculoskeletal pain and multiple tender points that are painful to palpation [1]. FMS, with a 0.7-3.2% worldwide prevalence, is less prevalent in men than women [2]. Although there has been great debate in recent investigations regarding the risk factors of FMS, the theories about the pathophysiology of the FMS have been contraversial [3-6]. In recent studies, a vulnerability to stress factors has been suggested in this syndrome due to the neuroendocrine system perturbation as a result of stress experiences such as abuse during childhood, adolescence or adulthood [7]. In a study FMS patients, with a history of past sexual abuse had worser experience of the illness than patients without abuse. However, in that study FMS was not significantly more likely among adult survivors of sexual violence than that of non-abused counterparts [8]. Moreover, a combination of reported physical and sexual abuse is significantly more likely during child or adulthood among patients with FMS than in those without FMS [9].

Violence against women varies in the literature according to the cultural factors, the description used, the age range of population studied, and the duration of the observation period [10-14]. Depression, anxiety, and posttraumatic stress disorder are proposed to be more common in women having violence exposure than in women with no history of violence [15,16].

Although previous studies have focused on the health implications of physical and sexual violence exposure, there is a limited number of studies about psychological, economic, and social violence. The main difference observed is the type of violence that is more closely related to the syndrome and age of violence exposure. Some studies have claimed a greater association between physical abuse in adulthood. Moreover, a combination of reported physical and sexual abuse is significantly more likely during childhood or adulthood among patients with FMS than in those without FMS [17], while others find emotional abuse [18,19] or sexual abuse during childhood [20]. Also in a study it was suggested that the experience of child abuse might be related with FMS symptom severity and may result polysymptomatic distress and pain [21].

The first aim of our study was to evaluate the differences of partner violence including economic violence and social violence experienced by patients with FMS and healthy controls. The second aim of our study was to investigate the effect of violence severity on the severity of depression and anxiety.

MATERIALS AND METHODS

The study sample consisted of 43 FMS patients who were reffered from Bakirkoy Dr. Sadi Konuk Research Hospital Physical Medicine and Rehabilitation Outpatient Clinic to the outpatient treatment unit of Bakirkoy Research & Training Hospital for Psychiatry, Neurology and Neurosurgery between January 2016 and August 2017. Forty-three consecutive married women aged between 18-65 years who were recently diagnosed as having FMS were recruited from Bakirkoy Dr. Sadi Konuk Research Hospital Physical Medicine and Rehabilitation Outpatient Clinic. The diagnosis of FMS was made by experienced physical medicine and rehabilitation physicians according to the American College of Rheumatology (ACR) FMS diagnostic criteria [1]. Patients who were referred to the Bakırköy Psychiatric Research and Training Hospital were evaluated by an experienced psychiatrist. Subjects without a sufficient mental capacity for verbal communication and patients with neurologic or physical illnesses those with a history of psychosurgery or other brain surgery, alcohol/drug addiction, head trauma, comorbid psychiatric disease other than specific phobia, presenting psychotic symptoms, having electroconvulsive therapy in the last 6 months, were excluded. Women accompanied by their husbands were excluded from the study. The same researchers invited the relatives of hospital workers to participate in the research. Physical medicine and rehabilitation physician and psychiatrist interviewed with the ones who accepted. Fortyfive married women aged between 18-65 years were included in the study after being confirmed to not have FMS as control group. Written informed consent was obtained from both the patients with FMS and controls prior to participation. The Ethics Committee of Bakırköy Education and Research Hospital approved the study (Protocol No: 495, Date:3rd November 2015). A Socio-demographic Data Form, the Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HAM-D), and the Partner Violence Data

Form were administered to both the control and FMS groups. In an attempt to measure the severity of pain symptoms, a visual analogue scale (VAS) was referred to the FMS group.

Sociodemographic Data Form
This form was composed of questions about demographic variables such as occupation, age, education level, sex, and other characteristics. Both control and patient groups were evaluated with this data form.

Hamilton Depression Rating Scale (HAM-D)
The HAM-D test measures is administered by a physician to individuals to evaluate the severity of depression symptoms. It was developed by Hamilton [22]. The validity and reliability of the Turkish version was performed by Akdemir et al. [23].

Hamilton Anxiety Rating Scale (HAM-A)
The HAM-A was used to measure anxiety levels and symptom distribution [24]. In 1998, the validity and reliability of the Turkish version of the scale was confirmed [25].

Visual Analogue Scale (VAS)
The VAS is a continuous line from which the patient chooses the point that indicates their pain intensity. Patients give a score to the intensity of pain (for pain intensity, 10 represents the worst possible pain and 0 represents absence of pain) [26].

Partner Violence Data Form
The presence of partner violence and type was evaluated with this semi-structured form prepared by the authors. The Conflict Tactics Scale [27] and a scale which is used to evaluate domestic violence in Turkey in a prior study were used to define the violence type [28]. The questionnaire including questions about five types of violence (social, physical, emotional, economic and sexual) was referred to participants by a semi-structured interview. The physical violence questions were adapted: "Have you ever been slapped, kicked, hit, or hurt otherwise physically by your husband?" (yes/no). The sexual violence questions were as follows: "Have you ever been forced into sexual activities by your husband?" (yes/no).

The database was analyzed using the SPSS Statistics, version 18.0 software package (SPSS, Chicago, IL). In addition to descriptive statistical methods like frequency, mean, standard deviation, the independent sample t-test and Chi-square test were used in comparison of two groups. Spearman's correlation analysis was used to investigate the relationship between the two variables. A value of $p<0.05$ was considered to be statistically significant.

RESULTS

We assessed 70 FMS. Participants accompanied by their husbands (n=14), with insufficient mental capacity for verbal communication (n=5), presenting psychotic symptoms (n=2), drug/alcohol use (n=2), Bipolar Disorder (n=2), neurologic disease (n=12) were excluded as seen in the Figure 1. This resulted in a sample of 43 patients with FMS available for the study (Figure 1).

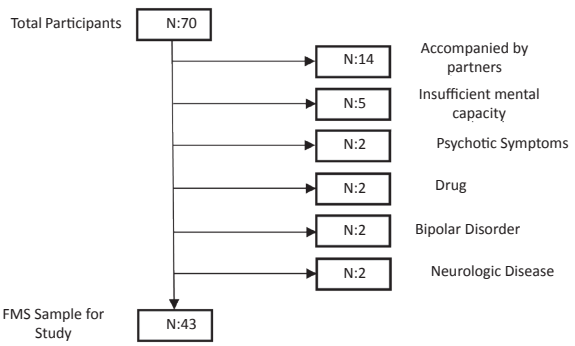


Figure 1. Assesment of patient group for inclusion.

Description of the study population.70 patients with FMS were interviewed. 14 were accompanied with their husbands. 5 were with insufficient mental capacity for verbal communication, 2 had psychotic symptoms (1 had auditory hallucinations and other had persecution delusions), 2 were drug use (alcohol abuse), 2 had a diagnoses of Bipolar Disorder Type 1, 2 had Epilepsy. These patients were excluded from the study. As a result, 43 patients with FMS were available for the study.

The FMS group and healthy control group showed no statistically significant difference in terms of age and the presence of psychiatric administration ($p>0.05$); however, the sample showed a significant difference with regards to education, occupation status, and history of suicide attempts ($p<0.05$). As shown on Table 1, the results revealed that education level and occupation status were less among the FMS group compared with the controls.

When the groups were compared by the means of violence subscales, patients with FMS showed grea-

Table 1. Clinical and sociodemographic variables of the groups.

		FMS Mean±SD (%)	Control Mean±SD (%)	t/x²	p
Age		44.77±7.69	44.30±10.92	0.237	0.813[1]
Education	None	1 (2.3%)	0 (0%)	15.61	0.000[2]
	Elementary	25 (58.1%)	18 (40.0%)		
	Middle	7 (16.3%)	5 (11.1%)		
	High	7 (16.3%)	5 (11.1%)		
	University	3 (7%)	17(37.8%)		
Occupation	Housewife	35 (81.4%)	11 (24.4%)	37.24	0.008[2]
	Seasonal employee	0 (0%)	1 (2.2%)		
	Regular employee	1 (2.3%)	8 (17.8%)		
	Civil Servant	3 (7%)	21 (46.7%)		
	Employer	1 (2.3%)	4 (8.9%)		
	Student	3 (7%)	0 (0%)		
Psychiatric Administration	Present	4 (9.3%)	3 (6.7%)	0.209	0.710[2]
	Absent	39 (90.7%)	42 (93.3%)		
Suicide Attempt	Present	4 (9.3%)	0 (0%)	4.385	0.050[2]
	Absent	39 (90.7%)	45 (100%)		

FMS: Fibromyalgia Syndrome; SD: standard deviation
[1]Independent sample t-test
[2]Chi-square test
**p<0.05*

Table 3. Comparison of anxiety and depression scores between the groups.

		FMS Mean±SD	Control Mean±SD	t	p
Hamilton Depression		21.8±11.1	3.8±4.82	-9.89	0.000
Hamilton Anxiety	Psychic Anxiety	11.8±5.9	2.82±3.64	-9.57	0.000
	Somatic Anxiety	20.13±8.48	2.66±4.68	-12.03	0.000
	Total	32.0±12.50	5.48±8.10	-11.85	0.000

FMS: Fibromyalgia syndrome
Independent t-test
**p<0.05*

ter presence of economic, physical, social, and emotional violence than controls (p<0.05). A comparison of the presence of sexual violence yielded no statistical difference (p>0.05) (Table 2).

A comparison of the groups by the means of the HAM-A and HAM-D subscales, patients with FMS had higher scores than the controls in all subscales (p<0.05) (Table 3).

In the FMS group a positive significant correlation was found between VAS score and HAM-A and HAM-D scores (p<0.05) (Table 4).

Table 2. Comparison of groups in terms of types of violence.

		FMS n (%)	Control n (%)	x²	p
Physical Violence	Present	12 (27.9%)	5 (11.1%)	3.980	0.040*
	Absent	31 (72.1%)	40 (88.9%)		
Sexual Violence	Present	4 (9.3%)	1 (2.2%)	2.057	0.150
	Absent	39 (90.7%)	44 (97.8%)		
Emotional Violence	Present	27 (62.8%)	13 (28.9%)	10.193	0.010*
	Absent	16 (37.2%)	32 (71.1%)		
Economic Violence	Present	21 (48.8%)	6 (13.3%)	13.032	0.010*
	Absent	22 (51.2%)	39 (86.7%)		
Social Violence	Present	36 (83.7%)	10 (22.2%)	33.334	0.010*
	Absent	7 (10.3%)	35 (77.8%)		

FMS: Fibromyalgia syndrome
Chi-square test
**p<0.05*

Table 4. Correlation of VAS score with hamilton anxiety and hamilton depression scores.

	Hamilton Anxiety Psychic		Hamilton Anxiety Somatic		Hamilton Anxiety Total		Hamilton Depression	
	r	p	r	p	r	p	r	p
VAS	0.369	0.015*	0.467	0.002*	0.466	0.002*	0.465	0.002*

VAS: Visual Analogue Scale
Spearman Correlation
** p<0.05*

DISCUSSION

We found that patients with FMS were exposed to more partner violence than control subjects. In addition, subjects with FMS demonstrated increased levels of pain severity, anxiety, and depression compared with the control group. In the FMS group, the level of pain severity was positively correlated with anxiety and depression levels. What distinguishes our study from the others is the investigation of all types of violence.

Much research has been conducted on the relationship between violence against women and somatic symptoms. In a study, it was suggested that exposure to violence had a negative effect on physical health independent from the effect on mental health due to increased vulnerability to disease and illness as a result of it being a 'stressful event' [29]. Eberhard-Gran et al. [30] found high correlations between levels of sexual and physical violence and the amount of somatic symptoms and diseases including FMS. In our study, we also found a statistically positive correlation between pain severity and anxiety and depression levels.

The focus in recent research has been on the relationship between life-time exposure to physical and sexual violence and FMS. Since children's brain are more vulnerable than adults' brains, it may be suggested that there can be differences according to the time of violence exposure [31]. More damage may be expected if exposure to violence occurs during childhood because children's brains are still developing. However, due to higher resilience of children's brains, another possibility is that damage is minimized in a way to 're-wire' themselves [32]. Some studies reported that physical abuse in adulthood gave rise to the greatest symptoms in patients with FMS [18], whereas others claimed a greater association between emotional [17] or sexual abuse during childhood [18,20,33-35]. Hauser et al. [36] found a higher frequency of retrospectively reported childhood adversities and of lifetime traumatic events in FMS patients than control group. Also in another study it was suggested that the onset of FMS was perceived as an ineluctable result of mental or physical trauma [37]. In our study, only partner violence during adulthood was investigated and the physical, emotional, economic, and social violence were found to be higher in the patients with FMS cases than in the control group. Violence during adulthood may also be greater in patients with FMS, as with childhood violence.

Taylor et al. [8] noted a higher prevalence of sexual violence experienced by FMS patients. Another study found that, in cases of sexual violence, the severity and number of symptoms were found higher in healthcare institutions in addition to the use of pain medication [8,17]. Boisset-Pioro et al. [9] found more life-time physical and sexual violence among women with FMS than in their control group, but there was no statistically significant difference in the type of sexual violence. Similarly, there was no statistically significant difference in sexual partner violence between the FMS and control groups in our study. The fact that different outcomes have been achieved in terms of sexual violence may be due to differences in the questions asked. The questions we used to identify violence were those used in a recent study of violence against women in our country [28]. This may have led to a change in the questions asked in the studies according to cultures.

Although several studies have investigated physical and sexual violence in FMS, little attention has been paid to social and emotional violence. Aaron et al. [38] also underlined the emotional abuse experienced by FMS patients. The high prevalence of emotional abuse among the patients with FMS in our study also contributes a new aspect because previous studies have not investigated emotional violence as much as physical and sexual violence.

As far as we know, there are limited number of studies in which all types of violence were investigated in women with FMS in our country. Another significant strength of our study was that the sample comprised patients with FMS who had not been treated before. However, there are some limitations of our study. First, since participants accompanied by their husbands were excluded remove a possible form of man's control over woman, the frequency of violence in these women might be higher. Furthermore, self-reporting bias of a socially unacceptable, intimate subject of this study should also be kept in mind. Finally, it should also be considered that subjects in this study were help-seeking members of the FMS population and and the results may not be generalizable to the whole group.

CONCLUSIONS

Although our study is cross-sectional and does not suggest a causal relationship, our findings suggest that domestic violence in marriage may play a role in pain severity and accompanying symptoms of depression and anxiety in FMS. It is also noteworthy that depression and anxiety levels are associated with pain severity. Therefore, it may be beneficial to investigate domestic violence during the treatment and follow-up period of patients with FMS, to evaluate the symptoms of anxiety and depression, to take precautions for such patients, and to develop appropriate treatment approaches. The physical and mental results of violence in different types may be carried by the individual. Understanding any exposure to violence may give information about individual's health behavior and any possible reluctance to undergo treatment in patients with FMS.

Acknowledgement: This paper was given as an oral presentation at the Congress of Clinical Child and Adult Psychiatry held in Istanbul on 23-25 September 2016.

Ethics Committee Approval: T. C. Ministry of Health, Public Hospitals Authority Turkey in Istanbul Bakirkoy Region Association of Public Hospitals Secretary General Prof. Bakirkoy Dr. Mazhar Osman Mental Health and Neurological Diseases Training and Research Hospital Ethics Committee approval was received (03.11.2015/495).

Conflict of Interest: The authors declare no conflict of interest.

Funding: This research did not receive any specific grant from funding agencies in the public,commercial or not-for-profit sectors.

Informed Consent: Was optained.

REFERENCES

1. Wolfe F, Smythe HA, Yunnus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis & Rheumatism. 1990;33:160-72. https://doi.org/10.1002/art.1780330203
2. Lorentzen F. Fibromyalgia: a clinical challenge. Journal of intern medicine. 1994;235:199-203. https://doi.org/10.1111/j.1365-2796.1994.tb01060.x
3. Leza JC. Fibromyalgia: a challenge for neuroscience. Revista de Neurologia. 2003;36:1165-75. https://doi.org/10.33588/rn.3612.2003154
4. Panerai AE, Vecchiet J, Panzeri P, Meroni P, Scarone S, Pizzigallo E, et al. Peripheral blood mononuclear cell Beta-endorphin concentration is decreased in chronic fatigue syndrome and fibromyalgia but not in depression: preliminary report. The Clinical Journal of Pain. 2002;18:270-3. https://doi.org/10.1097/00002508-200207000-00008
5. Klerman EB, Goldenberg DL, Brown EN, Maliszewski AM, Adler GK. Circandian Rhythms of women with fibromyalgia. The Journal of Clinic Endocrinology & Metabolism. 2001;86:1034-9. https://doi.org/10.1210/jc.86.3.1034
6. Gur A, Cevik R, Nas K, Colpan L, Sarac S. Cortisol and hypothalamic-pituitary-gonadal axis hormones in follicular-phase women with fibromyalgia and chronic fatigue syndrome and effect of depressive symptoms on these hormones. Arthritis Research & Therapy. 2004;6:232-8. https://doi.org/10.1186/ar1163
7. Neeck G, Crofford LJ. Neuroendocrine perturbations in fibromalgia and chronic fatigue syndrome. Rheumatic Disease Clinics of North America. 2000;26:989-1002. https://doi.org/10.1016/S0889-857X(05)70180-0
8. Taylor ML, Trotter DR, Csuka ME. The prevalence of sexual abuse in women with fibromyalgia. Arthritis & Rheumatism. 1995;38,229-34. https://doi.org/10.1002/art.1780380211
9. Boisset-Pioro MH, Esdaile JM, Fitzcharles MA. Sexual and physical abuse in women with fibromyalgia syndrome. Arthritis & Rheumatism. 1995;38:235-41. https://doi.org/10.1002/art.1780380212
10. McCauley J, Kern DE, Kolodner K, Dill L, Schroeder AF, DeChant HK et al. The "battering syndrome": prevalence and clinical charecteristics of domestic violence in primary care internal medicine practices.. Annals of Internal Medicine. 1995;123(10):737-46. https://doi.org/10.7326/0003-4819-123-10-199511150-00001
11. Campbell J, Jones AS, Dienemann J, Kub J, Schollenberger J, O'Campo P et al. Intimate partner violence and physical health consequences. Archives of Internal Medicine. 2002;162:1157-63. https://doi.org/10.1001/archinte.162.10.1157
12. Nicolaidis C, Curry MA, McFarland B, Gerrity M. Violence, mental health, and physical symptoms in an academic internal medicine practice. Journal of General Internal Medicine. 2004;19:819-27. https://doi.org/10.1111/j.1525-1497.2004.30382.x
13. Campbell JC. Health consequences of intimate partner violence. Lancet. 2002;359:1331-6. https://doi.org/10.1016/S0140-6736(02)08336-8
14. Krug EG, Mercy JA, Dahlberg LL, Zwi AB. The world report on violence and health. The Lancet. 2002, Volume 360, Issue 9339, Pages 1083-8. https://doi.org/10.1016/S0140-6736(02)11133-0
15. Golding JM. Intimate partner violence as a risk factor for mental disorders: a meta-analysis. Journal of Family Violence. 1999;14:99-132. https://doi.org/10.1023/A:1022079418229
16. Coker AL, Weston R, Creson DL, Justice B, Blakeney P. PTSD symptoms among men and women survivors of intimate partner violence: the role of risk and protective factors. Violence Victims. 2005;20:625-43. https://doi.org/10.1891/0886-6708.20.6.625
17. Alexander RW, Aaron LA, Alberts KR, Martin MY,Stewart KE, Bradley LA, et al. Sexual and physical abuse in women with fibromyalgia: association with outpatient health care utilization and pain medication usage. Arthritis & Rheumatology 2005;11:102-15. https://doi.org/10.1002/art.1790110206
18. Van Houdenhove B, Neerinckx E, Lysens R, Vertommen H, Van Houdenhove L, Onghena P, et al. Victimization in chronic fatigue syndrome and fibromyalgia in tertiary care: a controlled study on prevalence and characteristics. Psychosomatics. 2001;42:21-8. https://doi.org/10.1176/appi.psy.42.1.21
19. Varinen A, Kosunen E, Mattila K , Koskela T , Sumanen M. The relationship between childhood adversities and fibromyalgia in the general population. Journal of Psychosomatic Research. 2017;99:137-42. https://doi.org/10.1016/j.jpsychores.2017.06.011
20. Weisbecker I, Floyd A, Dedert E, Salmon P, Sephton S. Childhood trauma and diurnal cortisol disruption in fibromyalgia syndrome. Psychoneuroendocrinology. 2006;31:312-24. https://doi.org/10.1016/j.psyneuen.2005.08.009
21. Ortiz R, Ballard ED, Machado-Vieira R, Saligan LN, Walitt B. Quantifying the influence of child abuse history on the cardinal symptoms of fibromyalgia. Clin Exp Rheumatol. 2016;34(2 Suppl 96):S59-66.
22. Hamilton M. A rating scale for depression. Journal of Neurology, Neurosurgery, and Psychiatry. 1960;23:56-62. https://doi.org/10.1136/jnnp.23.1.56
23. Akdemir A, Dönbak Örsel S, Dağ İ, Türkçapar HM, İşcan N, Özbay H. Hamilton Depresyon Derecelendirme Ölçeği (HDDÖ)'nin geçerliği-güvenirliği ve klinikte kullanımı. 3P Dergisi. 1996;4:251-9.
24. Hamilton M. The assessment of anxiety states by rating. British Journal of Medical Psychology. 1959;32:50-5. https://doi.org/10.1111/j.2044-8341.1959.tb00467.x
25. Yazıcı MK, Demir B, Tanrıverdi N. Hamilton Anksiyete Değerlendirme Ölçeği, değerlendiriciler arası güvenirlilik ve geçerlilik çalışması. Türk Psikiyatri Dergisi. 1998;9:114-7.
26. Wewers ME, Lowe NK. A critical review of visual analogue

scales in the measurement of clinical phenomena. Research in nursing & health. 1990;13:227-36.
https://doi.org/10.1002/nur.4770130405
27. Straus MA. Measuring intrafamily conflict and violence: The Conflict Tactics Scales. Journal of Marriage and the Family. 1979;41:75-88.
https://doi.org/10.2307/351733
28. Akyazi S, Tabo A, Guveli H, İlnem MC, Oflaz S. Domestic Violence Victims in Shelters: What Do We Know About Their Mental Health? Community Mental Health Journal. 2018;54:361.
ttps://doi.org/10.1007/s10597-018-0240-1
29. McEwen BS. Protective and damaging effects of stress mediators. The New England Journal of Medicine. 1998;338:171-9.
https://doi.org/10.1056/NEJM199801153380307
30. Eberhard-Gran M, Schei B, Eskild A. Somatic symptoms and diseases are more common in women exposed to violence. Journal of General Internal Medicine. 2007;22(12):1668-73.
https://doi.org/10.1007/s11606-007-0389-8
31. Leserman J, Drossman D A, Li Z, Toomey TC, Nachman G, Glogau L. Sexual and physical abuse history in gastroenterology practice: How types of abuse impact health status. Psychosomatic Medicine. 1996;58:4-15.
https://doi.org/10.1097/00006842-199601000-00002
32. Kendall-Tackett K, Marshall R, Ness K. Chronic pain syndromes and violence against women. Women & therapy. 2003;26(1-2): 45-56.
https://doi.org/10.1300/J015v26n01_03
33. Martínez-Lavín M. Disrregulación autonómica en la fibromialgia: Implicaciones patogénicas y terapéuticas. XXXI Congreso Español de Reumatología. Las Palmas (España). 18-20 Mayo 2005.
34. Finestone HM, Stenn P, Davies F, Stalker C, Fry R, Koumanis J. Chronic pain and health care utilization in women with a history of childhood sexual abuse. Child Abuse & Neglect 2000;24:547-56.
https://doi.org/10.1016/S0145-2134(00)00112-5
35. Walker EA, Keegan D, Gardner G, Sullivan M, Bernstein D, Katon WJ. Psychosocial factors in fibromyalgia compared with rheumatoid arthritis: II. Sexual, physical, and emotional abuse and neglect. Psychosomatic Medicine. 1997;59:572-7.
https://doi.org/10.1097/00006842-199711000-00003
36. Häuser W, Hoffmann EM, Wolfe F, Worthing AB, Stahl N, Rothenberg R, et al. Self-reported childhood maltreatment, lifelong traumatic events and mental disorders in fibromyalgia syndrome: a comparison of US and German outpatients. Clinical and Experimental Rheumatology. 2015;33(1 0 88):86-92.
37. Sallinen M, Kukkurainen ML. 'I've Been Walking on Eggshells All My Life': Fibromyalgia Patients' Narratives About Experienced Violence and Abuse. Musculoskeleteal Care. 2015;13(3):160-8.
https://doi.org/10.1002/msc.1096
38. Aaron LA, Bradley LA, Alarcón GS, Triana-Alexander M, Alexander RW, Martín MY, et al. Perceived physical and emotional trauma as precipitating events in fibromyalgia. Arthritis & Rheumatism. 1997;40:453-60.
https://doi.org/10.1002/art.1780400311


T.C. SAĞLIK BAKANLIĞI İL SAĞLIK MÜDÜRLÜĞÜ SAĞLIK BİLİMLERİ ÜNİVERSİTESİ
BAKIRKÖY DR. SADİ KONUK EĞİTİM VE ARAŞTIRMA HASTANESİ