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EDITORIAL

Our Dear Readers,

First of all, I congratulate you all on your holiday. We are proud to publish the third issue of JOMPAC in 2023. As you know, our journal is publish 6 times per a year. We are getting closer to our scientific goals day by day. In near future, we want to contribute to international literature at an increasing level and to increase the success bar of our journal by entering valuable international indexes such as SCI-Expanded, ESCI and Pubmed, Scopus. We would like to thank all authors for submitting articles contributing to their comprehensive scientific article for publication in our journal. We would also like to thank everyone who contributed to the journal.

Kind Regards

Professor Aydın ÇİFCİ, MD
Editor in Chief

CONTENTS

Original Article

Original Article

MEDICINE PALLIATIVE CARE

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Evaluation of the relationship between insulin resistance and different phenotypes of polycystic ovary syndrome

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ABSTRACT

Aims: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women. Hyperinsulinemia and insulin resistance (IR) are the most important metabolic abnormalities that affect these patients. This study aimed to investigate the variables related to IR in patients with different PCOS phenotypes.

Methods: This retrospective study included 389 women diagnosed with PCOS in Bezmialem Hospital between november 2020 and september 2022. Information about patients was collected through their electronic records. PCOS was diagnosed based on the Rotterdam criteria, and four phenotypes of A (oligoovulation+ hyperandrogenism+PCO), B (oligoovulation+hyperandrogenism), C (hyperandrogenism +PCO), and D (oligoovulation+absent PCO) were considered for PCOS. The homeostatic model assessment for ınsulin resistance (HOMA-IR) was used to evaluate IR. The Mann-Whitney U test was performed to study the difference between the groups.

Results: The highest value of HOMA-IR was for the phenotype B group, and the lowest value was for the phenotype C group. However, the difference between the groups was not significant (p=0.221). Estradiol and free T4 were significantly higher in the phenotype A group (p≤0.001). Thyroid-stimulating hormone (TSH), prolactin, anti-mullerian hormone (AMH), fasting insulin, total testosterone, and red blood cell distribution width (RDW) were significantly higher in the phenotype B group (p≤0.001). Total cholesterol, high density lipoprotein (HDL), leukocyte, basophil, and monocyte were significantly higher in the phenotype C group (p≤0.001). Also, MPV values were significantly higher in the phenotype D group (p≤0.001).

Conclusion: The results showed that the variables related to IR in phenotypes A and B of PCOS are higher than in other phenotypes.

Keywords: Polycystic ovary syndrome, insulin resistance, HOMA-IR, RDW

INTRODUCTION

The absence of ovulation is a common complication with various clinical manifestations, including oligomenorrhea, amenorrhea, hirsutism, and abnormal uterine bleeding.[1] Also, this complication can cause potentially harmful results such as infertility, increased risk of endometrial hyperplasia and neoplasia, and breast cancer.[2] Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women, and the classic form of this syndrome is amenorrhea or completely irregular menstruation, infertility, hirsutism, obesity, and bilateral enlargement of the ovary full of cysts.[3] This complication is seen in reproductive age and affects about 5% of women at this age.[4] Today, studies have shown that various genetic and environmental factors cause PCOS, all of which are involved in the pathophysiology of this occurrence.[3] The definition of PCOS includes hyperandrogenism without a specific cause, such as an androgen-producing tumor, congenital adrenal hyperplasia with late-onset, lack of ovulation, the appearance of polycystic ovaries on ultrasound in the form of more than eight follicles with a size of 2 to 8 mm, and the increase of ovarian stroma. On the other hand, the sonographic appearance of polycystic ovaries can be seen in 16% of asymptomatic women.[5]

In addition to these symptoms, the prevalence of obesity, type 2 diabetes mellitus (DM), high blood pressure, and cardiovascular diseases in PCOS patients is higher than in the general population.[6] Hyperinsulinemia and insulin resistance (IR) are the most important metabolic abnormalities that affect these patients.[7] IR is when a lower-than-normal glucose decrease is achieved with a certain amount of insulin. First, the beta cells in the pancreas compensate for this resistance by increasing insulin production and keeping the blood glucose level normal. At this time, the patient only has IR with high

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amounts of this hormone. Over time, a person with IR goes from the stage of high levels of this hormone with normal levels of glucose to high and abnormal levels of glucose and finally develops type 2 DM.[8] High amounts of insulin produce large amounts of androgens by stimulating the ovaries. In addition, the high amount of insulin reduces the globulin binding to sex hormones, increasing the strength of androgens.[9]

It is possible that high amounts of insulin in the brain also increase the secretion of luteinizing hormone (LH), which stimulates androgen production from the ovary and stimulates appetite.[8] Therefore, factors such as increased secretion of LH, high levels of androgens, and obesity cause ovulation disorders.[9] With evidence of a relationship between PCOS and IR, and since IR is a crucial factor in type 2 DM occurrence, it is suggested that women with this syndrome are at a higher risk of developing type 2 DM.[8-10] This study aimed to investigate the variables related to IR in patients with PCOS with different phenotypes.

METHODS

In this retrospective study, which was conducted in Bezmialem University Hospital, 389 women in the age range of 18 to 37 years diagnosed with polycystic ovaries in an ultrasound between november 2020 and september 2022 were included. Information about patients was collected through their electronic records. The study was carried out with the permission of Bezmialem University Hospital Ethics Committee (Date: 22.11.2022, Decision No: 2022/321). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Inclusion criteria in the study group; 1) between the ages of 18-37 who cannot have children despite wanting a child for at least one year, 2) diagnosed with PCOS, provided that they have at least two of the 2003 Rotterdam Consensus criteria, 3) who are not diagnosed with DM, impaired glucose tolerance, thyroid dysfunction, hyperprolactinemia and hypercortisolism, 4) who were not given oral contraceptives or any medication known to alter hormone, lipid, or insulin metabolism 3 months prior to the study and non-smokers will be included.

Exclusion criteria in the study group; 1) smokers, 2) who diagnosed with hypertension, DM and any endocrinopathy, 3) who use oral contraceptives in the last 3 months for PCOS, those who use drugs that increase IR or those who use drugs for hyperlipidemia

Among the patients who applied to our routine obstetrics and gynecology outpatient clinic with menstrual irregularity and desire to have children, we look at the patients on the 3rd day of their menstruation after the examination; Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Estradiol (E2), Prolactin, Thyroid Stimulating Hormone (TSH), free T4, Anti-Mullerian Hormone (AMH), Hemogram, biochemistry (total cholesterol, LDL, HDL, Triglyceride), fasting blood glucose, fasting insulin, HOMA-IR values will be examined.

The Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) is also used to evaluate IR. HOMA-IR was calculated from the following formula using fasting serum glucose and insulin levels:

HOMA-IR=[Fasting Glucose (mg/dl) x Fasting Insulin (uU/ml)/22.5]

If subjects have a HOMA index greater than or equal to 2.38, they are considered insulin resistant.

In the present study, PCOS was diagnosed based on the Rotterdam criteria. Diagnostic criteria for PCOS is the presence of at least two of the following three symptoms:

1) Menstrual disorders (oligoovulation); 2) Clinical/laboratory hyperandrogenism; 3) Ovaries containing multiple cysts in ultrasound (PCO).

Accordingly, four phenotypes were considered for PCOS: (A) menstrual disorders, clinical/laboratory hyperandrogenism, and ovaries containing multiple cysts on ultrasound; (B) menstrual disorders and clinical/laboratory hyperandrogenism in the absence of ovaries containing multiple cysts on ultrasound; (C) clinical/laboratory hyperandrogenism and ovaries containing multiple cysts on ultrasound in the absence of menstrual disorders; (D) Menstrual disorders and ovaries containing multiple cysts on ultrasound in the absence of clinical/laboratory hyperandrogenism.

Table 1 shown the groups of phenotypes. Clinical hyperandrogenism (CH) was defined as hirsutism (hirsutism score ≤8 using the Freeman Galloway scale) as well as acne or androgenic hair loss. Biochemical hyperandrogenemia (BH) with free thyroxine (FT4), total testosterone (TT), and dehydroepiandrosterone (DHEAS) values above 95% was examined for those women who did not have evidence of Hyperandrogenism at the bedside, menstrual disorders, or taking hormonal drugs. Hyperandrogenism (HA) was diagnosed by the presence of CH and BH. Menstrual disorders were defined as menstrual cycles of more than 35 or less than 26 days or amenorrhea.

Table 1. Groups of phenotypes

Groups	Phenotypes
Group I	Phenotype A: Oligoovulation+hyperandrogenism+PCO
Group II	Phenotype B: Oligoovulation+hyperandrogenism
Group III	Phenotype C: Hyperandrogenism +PCO
Group IV	Phenotype D: Oligoovulation +PCO

Statistical Analysis

In order to examine the normality, the Kolmogorov-Smirnov test was performed. Considering the groups' non-normality, the nonparametric tests were performed before the statistical analyses. For each continuous variable, mean and standard deviations (SD) were measured. The Mann-Whitney U test was performed to study the difference between the groups. SPSS v22 was used for statistical analyses. A value of $p < 0.05$ was accepted as statistically significant. The GPower 3.1 program was used to calculate the sample size. Four groups' total mean was measured based on the Kruskal Wallis H test with a power of 95%, effect size of 90%, and 0.05 type 1 error for at least 389 patients.

RESULTS

This study included 389 women aged 18 to 37 diagnosed with polycystic ovaries divided into four phenotypes. The descriptive statistics of participants are shown in Table 2.

Table 2. Descriptive statistics of participants

Study parameters	Median (range), mean±SD
Age (Years)	29 (18-37), 28.47±4.47
BMI (kg/m²)	25.6 (17.1-37.8), 25.51±3.19
Insulin resistance (HOMA-IR)	3.23 (0.59-12.24), 3.85±2.24
FSH (mIU/ml)	6.75 (1.34-12), 6.51±1.94
LH (mIU/ml)	6.45 (2.65-52.57), 7.28±4.39
Estradiol (pg/ml)	45 (6.98-330.9), 52.04±37.7
FT4 (ng/dL)	1.18 (0.31-4.01), 1.15±0.28
TSH (uIU/ml)	2 (0.46-7.98), 2.19±1.28
Prolactin (µg/L)	18.2 (0.13-143), 20.71±13.34
AMH (ng/ml)	5 (0.08-20.52), 5.62±2.48
Fasting blood sugar (mg/dL)	95 (73-121), 95.19±8.9
Fasting insulin (pmol/L)	12.3 (3.42-81.42), 14.85±9.43
Total cholesterol (mg/dL)	174 (20-352), 180.1±46.32
LDL (mg/dL)	101.4 (-48.8-243.8), 104.05±36.62
HDL (mg/dL)	51 (12-154), 54.17±15.6
Triglyceride (mmol/L)	92 (31-341), 106.31±52.74
Total testosterone (ng/dl)	27 (0.03-317.9), 37.68±52.98
DHEAS (µg/dL)	262 (33.8-677.3), 280.97±114.31
Leukocyte (10^3/L)	7.34 (2.94-13.5), 7.56±2.15
Neutrophil (10^3/L)	4.37 (1.66-11), 4.79±1.68
Basophil (10^3/µL)	0.3 (0-2.47), 0.7±0.23
Lymphocyte (10^3/µL)	2.23 (0.03-4.89), 2.32±0.76
Monocyte (10^3/µL)	0.46 (0.03-1.36), 0.49±0.18
Hemoglobin (g/dl)	13.2 (9.6-24.5), 13.15±1.24
Hematocrit (g/dl)	39.5 (30.7-45.2), 39.28±2.92
PLT (mm^3)	273 (116-419), 261.56±50.39
PCT (ng/ml)	0.237 (0-1), 0.24±0.11
RDW (ng/ml)	13 (10.9-18.4), 13.2±1.22
MPV (μm^3)	9.7 (6.9-12.8), 9.67±0.87
MCV (μm^3)	85.8 (69.9-98.2), 85.07±4.73

SD, standard deviation, BMI, body mass index; HOMA-IR, homeostatic model assessment for ınsulin resistance;FSH, follicle-stimulating hormone; LH, luteinizing hormone; FT4, Free thyroxine; TSH, thyroid-stimulating hormone; AMH,anti mullerian hormone; LDL,low density lipoprotein; HDL,high density lipoprotein; DHEAS, dehydroepiandrosterone sulfate; PLT, platelet; PCT, procalcitonin; RDW, red cell distribution width; MPV, mean platelet volume; MCV, mean corpuscular volume.

Table 3 shows the comparison of phenotype groups on the study parameters. As shown in, there is no significant difference between the age and body mass index (BMI) of different phenotypic groups (p=0.981 and 0.963, respectively). The highest value of HOMA-IR was for the second group (phenotype B), and the lowest value was for the third group (phenotype C). However, the difference between the groups was not significant (p=0.221). FSH was significantly different between groups; phenotypes B and C had the highest values and phenotypes A and D had the lowest values (p=<0.001).

The values of LH, fasting blood sugar, LDL, triglyceride, DHEAS, Neutrophil, Lymphocyte, Hemoglobin, platelet (PLT), procalcitonin (PCT), and mean corpuscular volume (MCV) did not have any significant differences between different phenotypic groups ($p \geq 0.05$).

Estradiol and free thyroxine (FT4) were significantly higher in the first group (phenotype A) ($p \leq 0.001$). TSH, Prolactin, AMH, Fasting Insulin, total testosterone (TT), and red blood cell distribution width (RDW) were significantly higher in the second group (phenotype B) ($p \leq 0.001$). Total cholesterol, HDL, leukocyte, basophil, and monocyte were significantly higher in the third group (phenotype C) ($p \leq 0.001$). Also, mean platelet volume (MPV) values were significantly higher in the fourth group (phenotype D) ($p \leq 0.001$).

DISCUSSION

The results showed that IR-related variables were more in patients with A (oligoovulation+ hyperandrogenism+ PCO) and B (oligoovulation+hyperandrogenism) phenotypes than in C (hyperandrogenism +PCO) and D (oligoovulation+absent PCO) phenotypes groups. These results were consistent with some previous studies.[10-13]

In a similar study, Eftekhar et al.[14] investigated the prevalence and clinical characteristics of IR in Pakistan's different phenotypic young women with PCOS. This research reported the number of IR-related variables in phenotypes A and B higher than in other phenotypes. The average age of these people was 18 to 39 years old, which is close to the average age of our study.

Another study was conducted by Cutler et al.[15] to investigate IR and obesity in different PCOS phenotypes. In this study, the variables related to IR in two phenotypes, A and C, were higher than in other phenotypes. In this study, IR was evaluated and calculated with the HOMA-IR, and most women were obese. Researchers found that increased body fat may play a pathogenic role in developing this syndrome in susceptible individuals. The reason for the discrepancy between the results of this

research and the data obtained from our work can be the high weight of the participants in this study. The mean BMI of subjects in our study was 25.5, while it was 27.3 in their study.

The average BMI of the patients in the present study was classified as overweight. The prevalence of obesity in the general population is 30-40%, while this rate is more than 50% in people with PCOS, where fat is usually accumulated centrally. About 50-70% of women with PCOS have varying degrees of IR, a risk factor for developing type 2 DM. Even in non-obese women with PCOS, a slight increase in this risk can be seen.[16,17] Kim et al.[18] showed a high level of IR in PCOS patients independent of obesity or phenotypes. This study determined lower levels of high molecular weight adiponectin in obese PCOS subjects. Although IR is common in PCOS patients, it is not a universal feature for any particular phenotype. Mumusoglu et al.[19] studied the IR prevalence in PCOS of different phenotypes using the HOMA-IR model. According to the model, the IR prevalence in patients with PCOS was 64.4%, and no significant difference was observed between phenotypes, which is inconsistent with our results. They concluded that patients with IR were more clinically affected and showed that race, BMI, and age were determinants, especially when diagnosing IR.

Regardless of the criteria used to diagnose PCOS, phenotypes differences can be caused by different genetic factors, lifestyles, and nutritional habits.[20] In addition, the method of using samples can seriously affect the prevalence estimate, which can be affected by selection bias in non-population research. Recent studies have shown that the inclusion of PCO criteria in the definition of PCOS can increase its prevalence to 25.[21] According to NIH,[22] about 90 % of the diagnosis of patients with PCOS are confirmed by the Rotterdam criteria, which indicates that most women with hyperandrogenism also have PCO. Recently, the NIH has recommended using the Rotterdam criteria because it includes all PCOS phenotypes and recommended that more extensive and controlled studies be conducted on the prevalence of PCOS.

Table 3. Comparison of phenotype groups

Study parameters	Group I (n=106) M±SD	Group II (n=111) M±SD	Group III (n=83) M±SD	Group IV (n=89) M±SD	p
Age (Years)	28.37±4.78	28.5±4.3	28.52±4.35	28.51±4.47	0.981
BMI (kg/m²)	25.95±4.91	25.38±1.93	25.32±1.46	25.35±3.04	0.963
Insulin resistance (HOMA-IR)	3.6±2.25	4.08±2.27	3.87±2.19	3.84±2.26	0.221
FSH (mIU/ml)	5.62±1.94	7.06±1.51	7.57±1.42	5.91±2.15	<0.001
LH (mIU/ml)	8.59±6.71	6.54±2.36	6.1±1.19	7.73±4.35	0.183
Estradiol (pg/ml)	69.97±60.54	40.95±8.43	43.59±5.47	52.41±34.18	<0.001
FT4 (ng/dL)	1.26±0.31	1.09±0.31	1.04±0.25	1.21±0.15	<0.001
TSH (uIU/ml)	2.72±1.42	1.71±0.84	1.48±0.52	2.82±1.49	<0.001
Prolactin (µg/L)	23.75±17.57	18.01±8.33	16.78±5.51	24.13±15.96	<0.001
AMH (ng/ml)	5.03±3.19	6.12±2.36	6.2±2.65	5.15±0.46	<0.001
Fasting blood sugar (mg/dL)	94.77±8.49	95.5±8.98	94.18±9.32	96.24±8.88	0.337
Fasting insulin (pmol/L)	15.28±9.02	16.67±9.12	10.11±5.08	16.47±11.78	<0.001
Total cholesterol (mg/dL)	176.35±40.96	171.12±48.04	201.43±49.2	175.87±41.87	<0.001
LDL (mg/dL)	102.64±35.88	100.43±39.01	112.11±35.97	102.73±34.46	0.128
HDL (mg/dL)	53.28±15.1	49.52±14.79	63.8±17	52.03±11.78	<0.001
Triglyceride (mmol/L)	102.48±54.86	110.31±52.28	105.45±45.33	106.67±57.48	0.334
Total testosterone (ng/dl)	37.5±22.95	72.21±82.95	31.75±14.77	37±0.23	<0.001
DHEAS (µg/dL)	276.92±122.54	283.65±121.18	289.76±82.24	274.25±122.05	0.158
Leukocyte (10^3/L)	7.35±1.91	7.44±1.83	8.58±2.27	7.01±2.4	<0.001
Neutrophil (10^3/L)	4.43±1.48	4.94±1.93	5.11±1.71	4.74±1.5	0.048
Basophil (10^3/µL)	0.5±0.24	0.7±0.24	0.1±0.27	0.7±0.19	<0.001
Lymphocyte (10^3/µL)	2.3±0.74	2.23±0.85	2.45±0.74	2.32±0.66	0.280
Monocyte (10^3/µL)	0.42±0.12	0.43±0.11	0.59±0.19	0.57±0.23	<0.001
Hemoglobin (g/dl)	13.07±1.18	13.01±1.07	13.36±1.07	13.24±1.6	0.131
Hematocrit (g/dl)	39.36±2.89	39.01±2.57	39.63±3.18	39.19±3.11	0.254
PLT (mm^3)	271047.17±54068.45	257209.91± 49794.29	265079.52± 43774.26	252786.52± 51574.19	0.160
PCT (ng/ml)	0.25±0.04	0.23±0.16	0.24±0.11	0.24±0.11	0.241
RDW (ng/ml)	13.47±1.24	13.33±0.99	12.83±1.32	13.07±1.26	<0.001
MPV (μm^3)	9.15±0.92	9.82±0.66	9.8±0.87	9.97±0.79	<0.001
MCV (μm^3)	85.82±5.25	84.67±4.76	85.13±4.3	84.6±4.37	0.056

M, Mean; N, number of subjects; BMI, body mass index; HOMA-IR, homeostatic model assessment for ınsulin resistance;FSH, follicle-stimulating hormone; LH, luteinizing hormone; FT4, Free thyroxine; TSH, thyroid-stimulating hormone; AMH,anti mullerian hormone; LDL,low density lipoprotein; HDL,high density lipoprotein; DHEAS, dehydroepiandrosterone sulfate; PLT, platelet; PCT, procalcitonin; RDW, red cell distribution width; MPV, mean platelet volume; MCV, mean corpuscular volume.

The pathophysiology of anovulation in many women with ovulation disorders and PCOS is IR. Considering that these patients are at increased risk of DM and cardiovascular diseases, infertility, hyperplasia, endometrial cancer, and possibly breast cancer,[23] timely diagnosis of treatment in these people is of particular importance. In addition, according to the studies, the families of people with PCOS constitute a high-risk group in which IR should be examined to prevent the occurrence and development of its complications.

This study's limitation can be the small population, and it is suggested to study more populations with PCOS of different phenotypes in future studies. Also, using only one method to assess IR can be considered another limitation. It is recommended to improve the interpretation and comparison of existing research based on the non-selective population on the relationship between PCOS phenotypes and IR in different ethnic groups.

CONCLUSION

The results showed that IR-related variables in phenotypes A and B of PCOS are higher than in other phenotypes. Due to the occurrence of ovulation disorders and the risk of diabetes in people with this syndrome, periodic screening and follow-up of these phenotypes regarding risk factors for glucose tolerance and IR are necessary.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bezmialem University Hospital Ethics Committee (Date: 22.11.2022, Decision No: 2022/321).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Comparison of laparoscopic versus open Burch colposuspension techniques for female stress or mixed urinary incontinence: a ten-year experience in a tertiary center

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ABSTRACT

Aims: To evaluate postoperative course, efficacy, and complication rates of Open Burch Colposuspension and Laparoscopic Burch Colposuspension techniques in stress or mixed urinary incontinence at a single training and research hospital for the last ten years in İstanbul, Turkey.

Methods: A retrospective cohort study was conducted in all Burch Colposuspension cases performed between January 2011 and May 2022 in the Department of Gynecology and Obstetrics of İstanbul Kanuni Sultan Süleyman Training and Resaerch Hospital. All patients' data were reviewed from the electronic medical records and analyzed who underwent Burch colposuspension surgery either with an open or laparoscopic approach. The primary outcome was a surgical success, whereas secondary outcomes were perioperative and postoperative data, including surgical type, operating time, duration of hospital stay, estimated blood loss, complications, subjective cure, and additional interventional procedure types.

Results: The demographic and clinical characteristics among the groups have no significant difference ($p > 0.05$). The major complication rate postoperatively was considerably higher in the OC group ($p<0.004$). There is a statistically significant difference in favor of LC in terms of pain score values (VAS) postoperatively at the 6th and 48th hours (6th hour, $p=0.036$, 48th hour, $p<0.0001$). There was no statistically significant difference between study groups regarding objective success (%15,5 and %16,9, respectively). Postoperatively, there was no statistically significant difference between groups regarding subjective cure rates (UDI-6 and IIQ-7).

Conclusions: Midurethral Sling procedures are the first-line treatment in SUI patients. However, their long-term effectiveness is similar to other SUI treatments and lower complication rates, so surgeons can prefer LC.

Keywords: Burch colposuspension, laparoscopy, urinary incontinence

INTRODUCTION

Stress urinary incontinence (SUI) is unintentional urinary leakage during strenuous work that increases intra-abdominal pressure, such as coughing, sneezing, or exertion without urethral sphincter weakness. SUI prevalence among women increases with aging and dramatically reduces the quality of women's lives.[1] Surgery is recommended for moderate/severe SUI cases if the conservative therapy has failed. Several surgery methods can be applied for SUI treatment; however, ongoing debates exist regarding the highest procedure effectiveness, cost-effectivity, and lowest morbidity. Burch colposuspension is one of those methods primarily described in 1961, which aims to support the ureterovesical junction.[2] The laparoscopic approach was performed in 1991 by Vancaille and Schuessler; similar to the conventional procedure, moreover has many potential advantages, including minimal blood loss, shortened hospitalization, speed recovery, and a better approach to the retropubic space.[3] In the 1990s, Burch colposuspension was accepted as a gold standard method for SUI, which later left in place its status to mid-urethral slings (MUS) in the 2000s due to the minimally invasive approach and having similar cure rates when compared with Burch colposuspension.[4] Although MUS gained popularity until then, the context of current safety concerns regarding using synthetic meshes for incontinence surgery has led governments such as Scotland (2014), Australia (2017), New Zealand (2017), and the UK (2018) to take precautions against further complications.

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Furthermore, the Food and Drug Administration (FDA) reclassified surgical mesh instrumentation from low risk to intermediate risk (Federal Register 2017), as well as European Parliament and the Council of the European Union suggested reclassifying mesh instrumentation from intermediate risk to high risk (Regulation (EU) 2017).[5,6] NICE guideline (NG123), published in April 2019, recommends colposuspension as a treatment option for SUI whether non-surgical management has failed.[7] Under those circumstances, as a treatment option for SUI patients, colposuspension procedures have flared up again. Our current study illustrates our surgical team's clinical experience with Burch colposuspension, either open or laparoscopic approach, in ten years for women having SUI.

METHODS

A retrospective cohort study was performed on 390 patients diagnosed with SUI or mixed urinary incontinence who underwent anti-incontinence surgery (urethropexy) between January 2011 to May 2022 in the Department of Obstetrics and Gynecology of İstanbul Kanuni Sultan Süleyman Training and Research Hospital. The study protocol was approved by the Bezmialem Vakıf University Ethics Committee (Date: 15.11.2022, Decision No: 2022/321), and registered at ClinicalTrials.gov (NCT05452811). All procedures were carried out under the ethical rules and the principles of the Declaration of Helsinki. Due to the character of our study, informed consent was not obtained from the patients included in the study.

An electronic medical database of the hospital was used to determine patients who carried out open (OC) or laparoscopic colposuspension surgery (LC) for SUI without sphincter weakness in the last ten years. The patient's preoperative evaluation comprises history, physical examination, complete blood count, urinalysis, and cough stress test (CST). Demographic charts, including age, parity, body mass index (BMI), menopausal status, hormonal replacement status, type of birth, incontinence type, concomitant pelvic organ prolapse type (descensus uteri, cystocele, rectocele or enterocele), and comorbidities were obtained from patients records. The perioperative data such as the surgical type (open or laparoscopic), operating time, duration of hospital stay, estimated blood loss, additional interventional procedure types, urinary retention after surgery (>100 ml residual volume on the first operative day), voiding dysfunction (prolonged indwelling catheter usage) and short-term postoperative minor and major complications like persistent SUI, surgical wound infection, urinary tract infections, bladder or bowel injury, blood transfusion, and vault infections were recorded. Besides, women having prolapse concomitant with stress urinary incontinence were assessed according to the Pelvic Organ Prolapse Quantification system.

Patients having SUI or mixed urinary incontinence were included for whom conservative therapy (Kegel's pelvic floor exercises, bladder training, electrical stimulation, or medication) failed, and a cough stress test had proved SUI. Also, patients with urethral hypermobility supported by a residual urinary volume of less than 100 ml were included. Exclusion criteria were as follows; history of SUI operation, intrinsic sphincter deficiency at SUI, urinary retention, neurogenic bladder, suspected malignancy, only urge incontinence, chronic cystitis, pelvic inflammatory diseases, urinary tract infection, anticoagulant medication, anti-psychiatric medicine consuming, coagulation disorders, physically and medically unsuitable for colposuspension surgery, pregnancy and loss to follow-up.

Determination of the type of urinary incontinence based on objective tests such as a positive cough stress test (at the supine position, patients requested to cough with a filled bladder of at least 300 ml of saline). Multichannel urodynamic studies (MUDs)were performed to differentiate mixed-type incontinence from SUI alone. Urinary retention is designated as bladder volume exceeding 100 ml after micturition.

Anti-incontinence surgery was performed either open or laparoscopic, depending on the operating team's choice. The same experienced surgical team carried out all the procedures. Among patients having mixed incontinence, surgery was performed for whom SUI was predominant.

The laparoscopic Burch colposuspension technique (transperitoneal approach) was performed with the same surgical steps as in the open procedure using No:2 Ethibond (Ethicon) curved needle. Extracorporeal knots were used to stabilize the sutures using an endoscopic knot pusher. Subsequently, we used methylene blue (up to 300 ml) to rule out bladder injury during the operation. Also, we performed cystoscopy in cases of suspicion of injury at the bladder or urethra or in cases having recurrent urinary tract infections or dysuria after the operation. A single dose of cefazolin (broad-spectrum cephalosporin) was administered 1 hour before surgery as antibiotic prophylaxis. The standard duration of postoperative catheterization was two days. The catheterization was extended in conditions with infection or intraoperative bladder perforation.

After removing the urinary catheter at 48th hours, we measured the residual urine volume (PVR). For diagnosis, the cut-off limit for PVR was established as 100 ml. We removed the urinary catheter and discharged the patients after two consecutive measurements of PVR less than 100 ml. If the PVR volume exceeds 100 ml, the patient received a permanent catheter for three days, then the PVR measurement was repeated as before.

A visual Analog Scale (VAS) was performed after the 6th and 48th hours of the procedure to evaluate postoperative pain. A validated 100 mm VAS scale was used for measuring patients' pain scores. The follow-up period of all patients was arranged with control visits on the 10th day and 1, 6, 12, 24 months postoperatively and annually after that. The clinical examination was conducted during control visits performing cough stress tests to assess an objective cure. The objective cure was a negative cough stress test after the procedure. In contrast, the subjective cure was analyzed by asking patients to fill out a validated Turkish version of the urinary distress inventory (UDI-6) and incontinence impact questionnaire (IIQ-7).

Data analysis was performed using SPSS v.21 (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean, standard deviation, and nominal variables were expressed in numbers and percentages (%). For the comparison of continuous data between two independent groups, the t-test was used. The Chi-square and Fisher's exact tests were performed to compare categorical data. A p-value of <0.05 was considered to indicate statistical significance.

RESULTS

A total of 390 colposuspension patients were included in our study. While 52 of these patients had LC, 338 of them underwent OC. There was no significant difference among groups in terms of demographic and clinical characteristics (age, BMI, parity, smoking, chronic diseases, type of birth, type of incontinence, instrumental vaginal delivery, and menopause) (p>0.05) (Table 1 and 2).

The study showed a statistically significant difference between LC and OC operation times (p=0.042). The operational time was significantly shorter in the OC method in comparison with the LC approach (56.3 min versus 105.2 min). LC approach was associated with less blood loss than OC (70.5 ml and 143.7 ml, respectively). Despite similar preoperative hemoglobin levels before surgery, mean postoperative hemoglobin levels were significantly higher in the LC group compared with the OC approach, which reflects the difference in the amount of bleeding (12.2 g/dL vs. 10.38 g/dL, p<0.013). A statistically significant difference was found when the length of stay (LOS) in the hospital was compared (Table 3). This difference reduced hospital stays in the LC group (2.3 days vs. 2.7 days, respectively). When questioned during the postoperative first month at the outpatient clinic controls, the recovery time for daily activities was compared between the two groups. Resumption to regular activity is not significantly different (16.2 days vs. 26 days, p<0,069). No significant difference was found between the groups regarding residual urine volume measured in the preoperative and postoperative periods. Postoperative pain score values (VAS) at the 6th and 48th hours were compared between both groups, and statistically significant results were determined in favor of LC (6th hour, p=0.036, 48th hour, p<0.0001).

Table 1. Demographic parameters of patients

	Laparoscopic Burch n: 52		Open Burch n:338		P value
	mean	Standard deviation	mean	Standard deviation	
AGE	50.58	6.60	50.75	6.67	0.912
PARITY	3.54	1.41	3.67	1.49	0.609
BMI	25.96	2.73	25.91	2.64	0.855

Table 2. Preoperative data of patients

	Laparoscopic BURCH		Open BURCH		P value
	n: 52	%	n:338	%	
Smoking					0.451
Yes	16	30.8	95	28.1	
No	36	69.2	243	71.9	
Menopause status					0.769
Yes	38	75	188	55.6	
No	14	25	150	44.4	
Chronic disease					0.856
Not present	24	46.2	150	44.4	
Hypertension	14	26.9	94	27.8	
Diabetes Mellitus	5	9.6	38	11.2	
Comorbidity	9	17.3	56	16.6	
Type of birth					0.211
NSVD	39	75	255	75.4	
C/S	13	25	83	24.6	
Type of incontinence					0.514
Stress type incontinence	33	63.5	207	61.2	
Mix type incontinence	19	36.5	131	38.8	
Instrumental vaginal delivery/prolonged birth history					0.514
No	40	77	258	76.3	
Yes	12	23	80	23.7	

Table 3. Preoperative and postoperative results of the patients

	Laparoscopic BURCH n: 52		Open BURCH n:338		P value
	Mean	Standard deviation	Mean	Standard deviation	
Operation time (min)	105.29	8.19	56.36	7.26	0.042*
Estimated blood loss (ml)	70.57	20.81	143.73	49.93	<0.0001*
Pre-operative hemoglobin level (g/dL)	13.20	0.76	13.32	0.62	0.128
Post-operative hemoglobin level (g/dL)	12.28	0.75	10.39	1.15	0.013*
Duration of hospital stay (day)	2.35	1.03	2.70	0.59	0.027*
Recovery time to normal activity (day)	16.23	2.69	26.09	3.19	0.069
Pre-operative residual amount (ml)	6.64	8.44	6.42	8.33	0.908
Post-operative residual amount (ml)	6.06	6.59	10.52	26.98139	0.113
Post-operative 6th-hour pain score (VAS)	5.23	0.88	7.02	1.21	0.036*
Post-operative 48-the hour pain score (VAS)	2.85	0.78	6.15	1.43	<0.0001*
Pre-operative UDI-6 scores	9.48	3.15	9.55	3.61	0.016*
Post-operative sixth-month UDI-6 scores	0.60	0.66	0.81	0.71	0.981
Post-operative first-year UDI-6 scores	0.67	0.68	0.78	0.74	0.443
Pre-operative IIQ-7 scores	9.61	3.05	9.84	3.37	0.138
Post-operative sixth-month IIQ-7 scores	0.52	0.64	0.57	0.64	0.838
Post-operative first-year IIQ-7 scores	0.38	0.57	0.46	0.57	0.293

Concomitant surgeries performed during the LC group included hysterectomy (n: 40 [76.9%]), prolapse surgery (n: 10 [19.2%)]), posterior colporrhaphy/perineoplasty/Gardner cyst excision (n: 1 [1.9%)]) and myomectomy (n: 1 [1.9%)]. Moreover, open abdominal surgeries performed simultaneously with the Burch procedure included; hysterectomy (n: 255 [76.4%]), prolapse surgery (n: 74 [21.9%)]), posterior colporrhaphy/perineoplasty/Gardner cyst excision (n: 7 [2.1%)]) and myomectomy (n: 2 [0.6%)]. Objective and subjective cure rates, minor complication rates, and outcomes were not affected by the concomitant surgeries performed during Burch colposuspension in both groups (Table 4).

The postoperative major complication rate was considerably higher in the open surgery group (p<0.004). In the LC group, only three bladder injuries were seen (5,8%), while in the OC group 3 blood transfusions (0,9%), four bladder injuries (1,2%), one relaparotomy (0,9%), and one bowel injury (0,9%) were reported.

The success rates of the OC and LC groups were similar according to the presence of postoperative incontinence (15,5% and 16,9%, respectively). The preoperative and postoperative UDI-6 and IIQ-7 scores were compared between the groups reflecting subjective cure rates. There was no statistically significant difference between groups except preoperatively in UDI-6 and IIQ-7 scores. In the preoperative period, UDI-6 scores were higher in the OC group. Both OC and LC groups had improvement in UDI-6 and IIQ-7 scores postoperatively.

Table 4. Additional procedures during operations and post-operative complications

	Laparoscopic BURCH		Open BURCH		P value
	n: 52	%	n:338	%	
Concomitant procedures					0.576
Laparoscopic hysterectomy / abdominal hysterectomy/ adnexectomy	40	76.9	255	75.4	
Prolapse surgery (sacrocolpopexy, pectopexy, lateral suspension, Halban, Moscovic)	10	19.2	74	21.9	
Posterior colporrhaphy, perineoplasty, Gardner cyst excision	1	1.9	7	2.1	
Myomectomy	1	1.9	2	0.6	
Post-operative early complications (within the first week of surgery)					0.159
None	46	88.5	314	92.9	
Vault infection	1	1.9	5	1.5	
Wound infection	0	0	8	2.4	
Urinary tract infection	2	3.8	3	0.9	
Indwelling urinary catheterization	3	5.8	8	2.4	
Urinary retention	0	0	3	0.9	
Intra-operative complications					0.004*
None	49	94.2	329	97.3	
Blood transfusion	0	0	3	0.9	
Bladder injury	3	5.8	4	1.2	
Re-laparotomy (to open sutures)	0	0	1	0.9	
Bowel injury	0	0	1	0.9	
Post-operative late complications (>1 week after surgery)					0.555
None	49	94.2	318	94.1	
Vaut prolapse	1	1.9	5	1.5	
Cystocele	1	1.9	7	2.1	
Rectocele	1	1.9	5	1.5	
Enterocele	0	0	1	0.3	
Voiding dysfunction	0	0	2	0.6	
De novo urgency	1	1.9	0	0	
Post-operative incontinence					0.589
Yes	44	84.6	281	83.1	
No	8	15.4	57	16.9	

DISCUSSION

SUI hurts women's daily lives, which affects their routine activities and has a psychological burden. There are various surgical options for SUI that clinicians can choose according to their experience. Burch colposuspension is one method used as a standard gold method in patients with urethral hypermobility and left its place to MUS in time. Despite shorter operative times, relatively comfortable insertion technique, and higher success rates in the long-term of MUS, subversive mesh-related complications led clinicians to demand alternative meshless methods.[8] Another heated debate is continued regarding the governance of patients with SUI after unsatisfactory MUS operations.[9] Retropubic interventions (LC or OC) can be used as an optional surgical treatment in recurrent SUI patients following MUS operation with a cure rate of 84.2% objectively.[10] LC can be a preferable surgical treatment in patients having different comorbidities, which can be treated in the same session. A recent retrospective study compared Burch colposuspension with the MUS technique during a total laparoscopic hysterectomy procedure performed within the same session.[11] Seckin et al.[11] stated that the laparoscopic approach is a preferable treatment option due to its similar success rate, shorter surgical time, no mesh usage, and less blood loss than the open technique. LC seems to be a minimally invasive approach in patients with additional laparoscopy indications, which has similar cure rates with other SUI surgical managements.

Burch colposuspension operation has been a highly effective and long-lasting SUI procedure used successfully by surgeons for a long time.[12] The laparoscopic approach gained more popularity for its advantages, such as shorter hospital stays, better aesthetic results, improved visualization of retrius space, lesser blood loss during operations, and less usage of analgesics postoperatively.[13-15] Additionally, a current Cochrane review about open retropubic colposuspension, including fifty-five studies with 5417 women involved, suggests OC is an effective treatment option for SUI with continence rates of approximately 85%-90% in the first year, furthermore 80% continence rate in 5 years period.[3] The literature comprises two randomized control studies (RCT) comparing open versus laparoscopic colposuspension techniques in SUI patients. Although longer operation times were observed laparoscopically, postoperative pain and blood loss during the operation were less.[16] In addition, at five years of follow-up, anatomical success rates and subjective evaluation between OC and LC groups were similar. We observed the same results in which the length of the LC procedure was statistically longer. In contrast, blood loss, postoperative hemoglobin level change, duration at the hospital, and postoperative VAS scores were lower than the OC group.

Another RCT supporting these findings, which compares colposuspension methods, reported that objective and subjective cure rates were similar when both procedures were performed by skilled surgeons.[17] As we look at our data, similar to the literature, the objective cure rates between OC and LC were similar for two years (LC, 84.6%; OC, 83%, respectively). In the subjective cure rates in our study, similar results have been found, such as 76.2% in LC and 75.5% in the OC group. Subjective cure rates of our study support the Cochrane review performed by Freites et al.[18] where evidence suggests that the short-term subjective cure rates of the LC and OC groups were similar. The literature is scarce, and there needs to be more evidence to compare OC and LC to determine whether both have any advantage over each other regarding subjective cure rates and quality of life.[3] Most published studies compared BC with other surgical procedures for SUI, showing diverse conclusions regarding subjective cure rates on the long-term follow-up period.[11,12,17,19] A systematic review and meta-analysis comparing data from different SUI procedures showed that in long-term follow-up, MUS and BC have equal subjective continence rates.[20] We found similar postoperative subjective cure rates at the first month, the sixth month, and 1st year, similar to Fusco et al.[20] However, preoperative UDI-6 scores were higher in the open BC group. This result might be due to the difference in the number of samples among groups.

In our study, although the rates of minor complications were similar between the LC and OC groups, the major complication rates were higher in the OC groups ($p<0.004$). Complication rates in the literature were similar in both groups. Bladder injuries were slightly higher in the LK group.[15] In one review, there were 21 (4.14%) bladder injuries in the laparoscopy group of 507 cases, while in another study, 10 (1.92%) of 521 open surgery cases had bladder injuries.[15] In our study, we had 3 (5.77%) bladder injuries in the laparoscopy group and 4 (1.18%) in the open surgery group, and we had similar results to the literature. In the same review, although perioperative complications, including major complications, were rare, vascular injury, one of the major complications, was almost the same in both groups. In our study, the open surgery group had higher rates of bladder or bowel injuries, relaparotomy (in one case), and massive blood transfusion. There was no difference between the study groups in terms of major complications such as bowel injury and relaparotomy among our statistically different results in the studies in the literature. We attributed this to the fact that the number of patients who underwent open surgery from the patient groups we included in the study was higher than the number of patients who underwent closed surgery. Long-term prospective multicenter and multi-participant studies are needed to clarify this issue.

A Cochrane review performed in 2017 reported that after open colposuspension surgeries, pelvic organ prolapse is more likely compared to MUS or anterior colporrhaphy procedures.[3] We performed Burch colposuspension concomitant with prolapse surgeries, but we did not study the postoperative pelvic organ prolapse rates between groups which is one of our study's limitations. Another limitation of our study is that it was designed retrospectively, and we observed patients and the outcomes of the surgeries for two years. The patient numbers in each group were varied, and we did not use validated questionnaires for SUI outcomes. However, the strengths of our study include an experienced surgical team with the same operators performing the surgeries, a large sample size, and similar demographic characteristics between the two groups.

CONCLUSION

The literature concludes that traditional minimal invasive slings (transobturatuar or mid-urethral) have better cure rates than Burch colposuspension.[3,21] Although the superiority of sling procedures, adverse event rates are higher such as urinary retention and voiding dysfunction. In contrast, laparoscopic Burch colposuspension has the same effect as the open technique.[3] This study supports the conclusions about the Burch colposuspension procedure in the literature, where both open and laparoscopic techniques show similar cure rates. Conversely, in the literature, major complication rates (bladder or bowel injury, relaparotomy, blood transfusion) were higher in the open colposuspension group. Those results show that if the patient has concomitant pathologies that can be done laparoscopically, the surgeon should choose the laparoscopic approach based on their experience. There is no consensus on surgery selection after failed MUS surgeries which shows that researchers should focus on this issue. Most studies in the literature comparing open or laparoscopic Burch colposuspension were designed retrospectively; moreover, there need to be randomized controlled prospective studies.

SUI is a common health problem and a burden to the healthcare system, especially in premenopausal and postmenopausal women. Its incidence increases with age, and surgery is the optimal option for the treatment. There are different surgical options for SUI. However, the appropriate patient selection, correct indication, and surgical team experience will affect the treatment efficacy. Additionally, recurrent or persistent SUI case management after failed MUS surgery remains unclear, whereas Burch colposuspension seems an optional complementary surgical treatment.[22] Surgeons can prefer Burch colposuspension over other SUI treatments, where concomitant abdominal surgeries are planned, a vaginal approach is limited, or mesh usage is contraindicated.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of the Bezmialem Vakıf University Ethics Committee (Date: 15.11.2022, Decision No: 2022/321).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Original Article

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Monocyte-to-HDL-cholesterol as a predictor of disease severity in acute pancreatitis

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ABSTRACT

Aims: Acute pancreatitis is an inflammatory process of the pancreas that can affect local tissues or distant organ systems. Recent studies have described the monocyte count to high density lipoprotein (HDL) cholesterol ratio (MHR) as a significant prognostic marker. The aim of this study was to investigate the relationship between the MHR and disease severity in patients diagnosed with AP.

Methods: One hundred sixty-six AP patients were enrolled in this study. MHR and inflammatory parameters were measured for all study participants. Disease severity was measured using the Ranson score on admission, and cases were classified as mild or severe AP. MHR was then compared between the groups.

Results: MHR values were significantly higher in severe AP patients (25.2, range 7.89-77.8) compared with mild AP patients (14.32, range 0.71-80) (P=0.006). Based on the Ranson criteria, the overall accuracy of MHR in determining severe AP was sensitivity 72.7% and specificity 69% (AUC: 0.762; P=0.006). The overall accuracy of MHR in predicting disease severity was superior to other inflammatory markers.

Conclusion: The study findings indicated that MHR values are significantly elevated and capable of use in determining disease severity in AP patients.

Keywords: Monocyte, HDL, MHR, ranson, inflammation

INTRODUCTION

Acute pancreatitis (AP) constitutes an acute inflammatory process of the pancreas with variable involvement of local tissues or distant organ systems.[1,2] The clinical course is very wide, from self-limiting mild inflammation to severe organ failure.[3] Diagnosis can be easily established with acute onset typical abdominal pain and enzyme elevation (amylase and lipase). However, amylase and lipase elevations exhibit no correlation with disease severity, and their levels can also rise in some conditions other than AP (gastrointestinal perforation, salivary gland pathologies, kidney failure, etc.).[4]

The ability to predict the severity and prognosis of AP provides important clinical clues in the approach to the patient. Various scoring systems, such as Ranson, Glasgow, APACHE II and Balthazar, are therefore employed for this purpose.[5,6] A score of '0-2' on the Ransom scale, widely used in clinical practice among these different systems, predicts a risk of mortality below 3%, while scores of '3-4' predict a 15% risk of mortality.[7] Various studies have also suggested that some easily accessible, practical, and inexpensive markers can predict the severity of AP as an alternative to these scoring systems.[8-11] Two of these are the neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR). Although it has been suggested that these two parameters can predict AP-related mortality and prognosis when used separately, the findings are inconsistent.

The monocyte count to high density lipoprotein (HDL) cholesterol ratio (MHR) has been described as a significant prognostic marker in recent studies. It has been reported that the ratio indicates the inflammatory process and disease exacerbation in many diseases such as cardiovascular diseases, obstructive sleep apnea syndrome, metabolic syndrome and acute intracranial hemorrhage.[12-16]

Furthermore, Paraoxonase-1 (PON1) is a HDL attached, extracellular esterase synthesized mainly in the liver. PON1 is believed to contribute to the anti-atherogenic and

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anti-inflammatory properties of HDL; it degrades lipid peroxides, decreases HDL susceptibility to peroxidation, glycation, and homocysteinylation, and increases cholesterol efflux from macrophages.[17] Franco-Pons et al.[18] have suggested that serum PON-1 undergoes inhibition and proteolysis during pancreatitis. In an another experimental study, Tvarijonaviciute et al.[19] have proposed that serum PON-1 activity is lower in dogs with AP.

However, despite the relationship between MHR and inflammation, the prognostic value of MHR in patients with AP has not previously been investigated. We think that MHR can represent an alternative to existing scoring systems in predicting the severity of AP.

The aim of this study was to investigate the relationship between MHR and AP severity in patients diagnosed with this condition.

METHODS

Ethics

The study was carried out with the permission of a Düzce University Medical Faculty Non-interventional Clinical Researches Ethics Committee (Date: 2022, Decision No: 64). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

One hundred sixty-six patients diagnosed with AP in our tertiary reference center in Turkey between April 2017 and January 2020 were included in this retrospective analysis. The diagnosis of AP was made with symptoms of severe typical abdominal pain, usually accompanied by vomiting, tenderness in the middle epigastrium, and serum amylase and lipase levels at least three times the upper threshold of normal.The diagnosis was also confirmed using transabdominal ultrasonography and computed tomography (CT). The etiology of AP, age, gender, medical history, radiological imaging and laboratory findings of the patients were taken from the medical files of the patients and all data were evaluated.

Individuals with conditions capable of causing pancreatic enzyme elevation other than AP (pancreatic cancer, chronic pancreatitis, gastrointestinal system perforations, and salivary gland diseases), or with chronic kidney failure, heart failure, liver failure, acute or chronic inflammation, cancer, or hematological disease, patients who take drugs that may affect lipid metabolism like thiazolidinedione, statin, and fibrates were excluded from the study.

Disease severity was measured using the Ranson score during admission. Five Ranson score variables were analyzed. Cases with scores <3 were classified as mild AP and those with scores ≥3 as severe AP.

The modified CT severity score (MCTSI) was developed based on the degree of necrosis and inflammation, and the presence of fluid collections. Under this system, a normal pancreas is scored 0, intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat are scored 2, pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis are scored 4, the extent of pancreatic necrosis less than 30% is scored 2 and pancreatic necrosis exceeding 30% is also scored 4. The severity of pancreatitis was categorized as mild (0-3 points), moderate (4-6 points), or severe (7-10 points).

Laboratory analysis

Blood samples were collected by venipuncture with minimal stasis. All patients' blood specimens were collected during an initial presentation to the hospital. Fasting blood specimens for lipid profile analysis were collected the day after admission. Sera were separated by centrifugation at 4000 rpm for 10 minutes and then decanted. Routine parameters were evaluated photometrically at the Biochemistry Laboratory Research Hospital using an IDS B0728 auto analyzer device. Complete blood count analyses were performed using the same analyzer within 2 hours after collection of blood samples on a Beckman Coulter (High Wycombe, UK) Gen-S automated analyzer.

Statistical Analysis

The study data were analyzed on SPSS version 20.0 software (IBM Corp., USA). Quantitative parametric data were expressed as mean plus standard deviation (SD), and quantitative non-parametric data as median values plus minimum and maximum. The Kolmogorov–Smirnov test was used to analyze the distribution of variables. For non-parametric data, comparisons between different groups were performed using the Mann-Whitney U test, while the independent-t test was used to compare parametric data between the groups. Receiver operating characteristic (ROC) curve analysis was used to identify optimal cut-off values for MHR and other inflammatory markers levels to identify AP severity with maximum sensitivity and specificity. p values below 0.05 were considered statistically significant.

RESULTS

One hundred sixty-six patients, 113 (70%) with biliary AP, and 53 (30%) with non-biliary AP were enrolled in the present study. Eighty-nine (53%) patients were men and 77 (47%) were women. The mean age of the patients was 62±19.6 years. There were no statistically significant differences between the groups in terms of clinical characteristics, laboratory values, or inflammatory markers (**Table 1**).

Table 1. Basic characteristics of patients with biliary and non-biliary acute pancreatitis

Parameters	Biliary Pancreatitis (n=113)	Non-biliary Pancreatitis (n=53)	P value
Age (year)	67±17	52±21	0.000
Gender (F/M)	48/65(42%/57%)	29/24(53%/46%)	0.264
WBC (mm³ ×10³)	10.5±4.5	10.6±3.7	0.952
Hemoglobin (g/dl)	13.7±1.7	14.2±1.2	0.972
Platelet (/mm³×10³)	214 (34-696)	203 (90-560)	0.613
Neutrophil (ml)	8.1±3.9	8.1±3.7	0.721
Lymphocyte (ml)	1.4±0.8	1.8±1.2	0.069
Monocyte (ml)	0.64 (0.03-8.5)	0.67 (0.27-1.54)	0.437
HDL (mg/dl)	45.8±18.3	46.7±19.5	0.810
LDL (mg/dl)	108±32	110±43	0.527
TG (mg/dl)	74 (33-170)	104 (41-412)	0.126
Urea (mg/dl)	37 (13-162)	29 (11-123)	0.847
Creatinine (mg/dl)	0.91 (0.16-591)	0.91 (0.44-6.91)	0.211
AST (U/L)	91 (19-1115)	44 (5-506)	0.000
Amylase (U/L)	846 (402-3141)	723 (404-3355)	0.304
Lipase (U/L)	1138 (28-1504)	849 (23-1469)	0.066
NLR	5.86 (0.16-31.4)	4.66 (0.33-27.1)	0.151
PLR	174 (26-1039)	119 (32-822)	0.059
MHR	14.4 (0.71-62.9)	16.1 (3.3-48)	0.792
Ranson, n(%)			0.146
0-3	102 (90)	41 (77)	
4-6	21 (10)	12 (23)	
MCTSI, n(%)	39	22	0.472
0-3	25 (50)	13 (59)	
4-6	10 (40)	7 (31)	
7-10	4 (10)	2 (10)	

WBC, white blood count; HDL, high density lipoprotein; LDL, low density lipoprotein; TG, triglyceride; AST, aspartate aminotransferase; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; MHR, monocyte HDL ratio; MCTSI, modified CT severity score.

WBC, NLR and MHR were significantly higher in the severe AP group than in the mild AP group (9.83±3.6 vs 13.9±5.9; 5.09 (0.16-31.4) vs 10.28 (2.1-31); and 14.32 (0.71-80) vs 25.2 (7.89-77.8), respectively p<0.005 for all). No difference was observed between the two groups in terms of monocyte or HDL parameters (p>0.05), MHR differed significantly between the two (Figure 1).

ROC curve analysis suggested that the optimum MHR level cut-off point for severe AP based on Ranson scores was 18.6, with sensitivity, specificity of 76%, 69%, respectively (AUC: 0.716; p=.006). The same ROC curve analysis for MHR and other inflammatory markers is also shown in Table 3 and Figure 2.

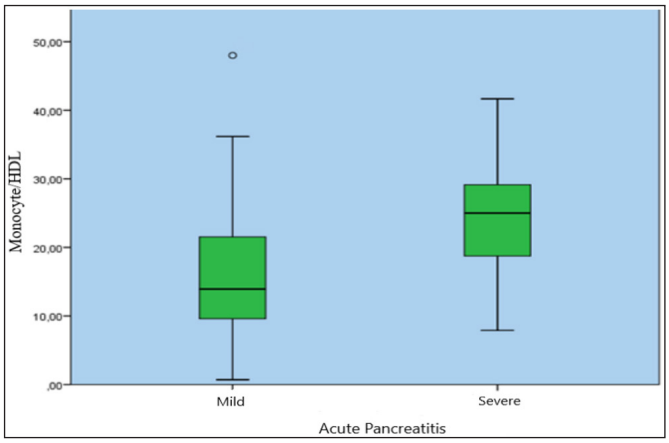

Figure 1. MHR levels between mild and severe pancreatitis

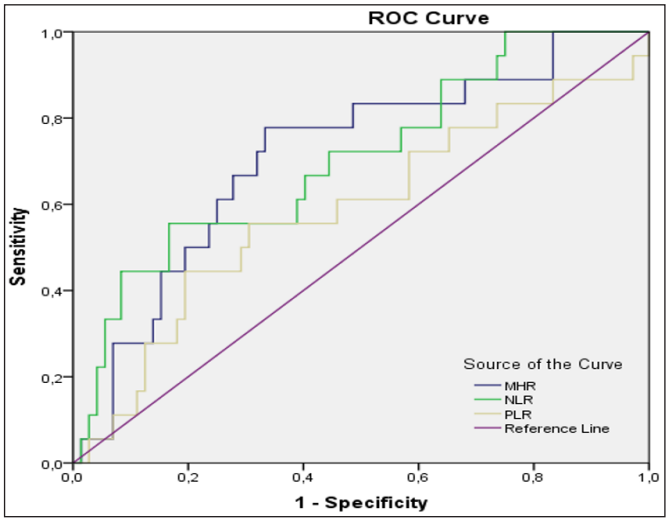

Figure 2. Overall accuracy and ROC analyses of MHR and other inflammatory markers in differentiating mild from severe AP according to the Ranson criteria

Table 2. A comparison of inflammation parameters in terms of severity of acute pancreatitis

Parameters	Mild pancreatitis (n=143)	Severe pancreatitis (n=33)	P value
WBC	9.83±3.6	13.9±5.9	0.003
Neutrophil (ml)	7.54±3.1	11.1±4.7	0.002
Lymphocyte (ml)	1.65±0.1	1.26±0.8	0.088
MCV	87±6	87±7	0.913
MPV	9±2	10±2	0.237
Monocyte (ml)	0.64 (0.30-8.5)	0.72 (0.2-4.67)	0.216
HDL	47.4±19.3	38.8±16	0.083
NLR	5.09 (0.16-31.4)	10.28 (2.1-31)	0.001
PLR	145 (31.4-1039)	220 (25-836)	0.065
MHR	14.32 (0.71-80)	25.2 (7.89-77.8)	0.006
CRP	7.3 (0.5-85)	10.2 (0.2—289)	0.134

WBC, white blood count; MCV, mean corpuscular volume; MPV, mean platelet volume; HDL, high density lipoprotein; NLR, neutrophil lymphocyte ratio; PLR, platelet lymphocyte ratio; MHR, monocyte HDL ratio.

Table 3: Overall accuracy and ROC analyses of MHR and other inflammatory markers in differentiating mild from severe AP according to the Ranson criteri

Parameters	AUC	Cut-Off	Sensitivity %	Specificity %	95% CI		p value
MHR	.716	18.6	76	69	.579	.006	.853
NLR	.691	5.66	64	60	.550	.015	.831
PLR	.570	119	64	42	.407	.374	.732

DISCUSSION

MHR was higher in severe AP than in mild AP in the present study. In addition, it was superior to previously investigated inflammatory markers such as NLR, PLR, and CRP in predicting the the severity of AP. To our knowledge, this is the first study to investigate MHR in predicting AP severity.

AP is an acute inflammatory disease arising from gallstone disease and capable of leading to significant morbidity and mortality. Although it is generally well-tolerated and self-limiting, it may sometimes be fatal due to the development of multi-organ failure.[20] Being able to predict the severity of AP might make it possible to reduce morbidity and mortality rates by modifying therapeutic and follow-up approaches. However, there is currently no ideal marker capable of predicting the severity of the disease.

CRP, an inflammatory marker frequently used alone, is not sufficiently capable of predicting the severity of AP. This is because the fact that it rises at least 24-48 h after the onset of symptoms and pancreatic inflammation limits its use in predicting AP severity.[21] Similarly in the present study, no statistically significant difference was observed in CRP values at the time of presentation between mild and severe AP.

The fact that NLR is characterized by a significant increase in inflammatory conditions has recently encouraged its clinical use. One recent study identified NLR as an independent predictor for the diagnosis of coronavirus 2019 (COVID-19).[22] Another study identified a link between NLR and malignancies.[23] NLR has also been shown to be useful as a prognostic factor in patients with AP.[24] A significant positive correlation was also found between NLR and Ranson score in another study.[25]

PLR, another of the parameters related to inflammation, has also been associated with the severity of AP and AP-related mortality Zhou et al.[10] Kaplan et al.[9] identified PLR as a significant predictor of prognosis in AP. Consistent with the previous literature, a significant relationship was determined between PLR and the severity of AP in the present study.

Recent publications have shown a particular association between MHR and cardiovascular events.[15,26] Monocytes and macrophages play an important role in atherosclerotic plaque formation. Monocyte count has been identified as an independent predictor of subsequent plaque formation.[27] In addition, proinflammatory cytokines such as interleukin (IL)-6, IL-1β and tumor necrosis factor-α (TNFα) are released from monocytes during the inflammatory process.[28] The monocyte count in peripheral blood increases in AP.[29] Increased monocyte activation has also been observed in mice with experimentally induced AP.[30]

The most important mission of high-density lipoprotein-cholesterol (HDL-C) is to transport cholesterol from cells and tissues to the liver. However, it also exhibits anti-atherosclerotic properties by eliminating the proinflammatory and pro-oxidant effects of monocytes through the inhibition of macrophage migration and LDL oxidation.[31] HDL has been shown to exhibit a negative response in the course of AP.[32] In light of the above, an increasing monocyte count and decreased HDL are thought to be capable of use as a marker in inflammatory conditions. One study recently investigated the value of the HDL/LDL ratio in predicting the severity of AP Wu et al.[33], and concluded that the ratio was significant in predicting the progression of the disease. An AUC of 0.533 was determined in that study at ROC analysis of the HDL/LDL ratio based on Ranson criteria used to calculate the severity of AP. The AUC for MHR in the present study was 0.716 (p=0.006).

The principal limitations of this study are its retrospective cross-sectional design, single center experience, and the low number of patients. Other limitations include the absence of other scoring systems used in predicting the severity of AP, other than the Ranson score, and the lack of follow-up data.

CONCLUSION

The present study demonstrated for the first time significantly elevated MHR levels capable of determining disease severity in AP patients. We, therefore, think that MHR is a valuable tool for providing a rapid overview as a simple and inexpensive test in the evaluation of AP disease activity and that the present research can serve as a guide for future prospective studies with larger patient numbers..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of a Düzce University Medical Faculty Non-interventional Clinical Researches Ethics Committee (Date: 2022, Decision No: 64).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Original Article

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Retrospective comparison of extrafamilial and intrafamilial incest abuse

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ABSTRACT

Aims: As per WHO data, one out of every three adult women and one out of every five adult men have been exposed to one or the other form of sexual abuse in their childhood or adolescence and the great majority of these abuses have been intrafamilial. In this context, the aim of the present study is to define the sociodemographic and clinical differences between two forms of incest, intra-familial and ekstra-familial, and evaluate the effect of these differences on the treatment and rehabilitation process.

Methods: Data from 113 cases of incest abuse presented to the Trabzon Child Monitoring Centre between 2015 and 2021 were examined and evaluated retrospectively; the results and differences were presented in tables and charts; and the values that satisfied $p<0.005$ were considered to be statistically significant.

Results: Of 113 cases, 98 were included in the study, and the female/male ratio was found to be 10.1. The mean age of the victims was 12.65+3.753 years, whereas that of males was 8.44+4.586 years, with that of the females being 13.07+3.418 years.

Conclusion: The duration of exposure to abuse and history of recurrent abuse in the intra-familial incest group was longer and more frequent when compared with the extra-familial incest group.

Keywords: Sexual abuse, incest, domestic violence

INTRODUCTION

The World Health Organization (WHO) defines child abuse, in its broadest sense, as all forms of treatment of a child by an adult in a specific period of time, which are unacceptable in that specific cultural context and have adverse effects on the physical and psychological development of the child.[1] Sexual abuse, on the other hand, is the "involvement of a child in sexual activity that he or she does not fully comprehend, is unable to give informed consent to, or for which the child is not developmentally prepared, or else that violates the laws or social taboos of society".[1] All kinds of behaviors toward a child exhibited by a person at least 6 years older than the child with the purpose of sexual stimulation are considered as child abuse.[2]

When abuses are evaluated in terms of the connection between the perpetrator and the victim, the cases in which the offender is a member of the family are classified as intra-familial sexual abuse and termed as incest.[3] The acts of sexual abuse against the child by those having parental authority are considered to be incest in line with the definition made by the US Department of Health, Education and Protection, whereas recent studies seemed to agree on the definition of incest as all kinds of erotic behaviors among the members of the family who are not married to each other.[4]

Extra-familial incest, on the other hand, is defined as incestuous acts perpetrated by the acquaintance, the family's friends, authority figures, or friends, usually in educational, daycare, entertainment, or religious settings or at the family's home.[5]

When the relationship between the victimized child and the perpetrator in cases of child abuse is examined, it has been reported in many studies that the perpetrator is an acquaintance of the child and that the perpetrator is frequently one of the members of the family in a broader sense. The biological or social closeness of the perpetrator in the family explains this frequency.[6]

Considering that 20% of females and 15% of males experience sexual abuse or attempted abuse at least once in their childhood according to WHO statistics, the incidence of incestuous abuse cases is above the limits that are termed dangerous.[7] Studies on incestuous sexual abuse have reported more serious psychosocial traumas in victims because of the recurring nature of incest cases, the extended duration of exposure to abuse, and social

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challenges in reporting such cases.[8] In addition, the experience of sexual abuse in childhood is considered to be the most serious risk factor for sexual problems that may arise in adulthood.[9]

The most frequent form of intrafamilial sexual abuse is father-daughter incest.[9] Yet, uncle-niece, brother-in-law-sister-in-law, and sibling incest cases have been also reported. If these forms are classified, then the cases of incest involving people having consanguinity with the victim such as father, uncle, or brother in a familial setting can be called intra-familial incest, whereas cases in which the perpetrator is a cousin, brother-in-law, stepfather or stepmother within a familial structure established by kinship and laws can be termed as extra-familial incest.[3]

Of course, this definition is not universal in nature. It would still provide guidance to experts in understanding incestuous abuse and organizing rehabilitation processes. The aim of the present study is three-pronged: to define the forensic and clinical differences between the two groups that were defined in this context, to propose solutions for the rehabilitation of emerging psychological and physical traumas, and to contribute to the literature in this regard.

METHODS

Approval was obtained from the parents of the victims, and the ethical approval was given by the Karadeniz Technical University Medical Faculty Scientific Researches Ethics Committee (Date: 30.05.2022, Decision No: 9). All procedures were carried out in accordance with the ethical rules and the principle of the Declaration of Helsinki.

In the present study, 113 cases of child abuse, reported to the Trabzon Child Monitoring Centre in Turkey between 01/01/2015 and 01/06/2021, in which the perpetrator was known to be a family member, were retrospectively screened using forensic interview forms, personal development cards, and forensic and psychiatric examination forms. The sociodemographic and clinical data of the victims and perpetrators were evaluated. As the age difference between the victim and the perpetrator was less than 6 years in 15 cases, these cases were excluded from the child abuse definition.

Thus, the study included 98 cases, which were classified as the intrafamilial group or the exrafamilial group depending on the victim's relationship with the perpetrator. Incestuous abuses involving those with first and second degree consanguinity were defined as the intrafamilial group, whereas the rest were designated as the exrafamilial group. The clinical and sociodemographic differences between the two groups were also evaluated.

The screened data were evaluated using the IBM SPSS Statistics software package (version 25). For statistical significance, Pearson Chi-Square test was used. $p < 0.05$ was considered to be statistically significant.

RESULTS

A hundred and thirteen cases in which the perpetrator was a member of the family reported to the Trabzon Child Monitoring Centre were screened retrospectively. As the age difference between the victim and the perpetrator was less than 6 years in 15 cases, these were excluded from the child abuse definition.

Of the 98 cases assessed, 89% (n=90) of the victims were female, and 9% (n=10) were male. The male/female ratio was calculated to be 0.099. The youngest victim was 4 years old, and the oldest victim was 17 years old. The median age was 14 years old. The mean age was 12.65+3.753 years. This value was 13.07+4.418 for the females and 8.44+4.586 for the males.

With regard to the identity of the perpetrator, 22.44% (n=22) were fathers; 7.14% (n=7) stepfathers; 16.32% (n=16) uncles; 20.4% (n=20) cousins; 18.36% (n=18) brothers-in-law; 5.1% (n=5) stepbrothers/stepsisters; 2.04% (n=2) brothers; 4.08% (n=4) grandfathers; 2.04% (n=2) step uncles; and 2.04% (n=2) aunts.

In the present study, the most prevalent form of incest was father-daughter incest, and cousins and brothers-in-law were the second most frequent perpetrators.

On the basis of the relationships between victims and perpetrators in 98 cases of child abuse, 46.93% (n=46) were placed in the intrafamilial group and 53.06% (n=52) were placed in the extrafamilial group (Table 1).

Table 1. Distribution of perpetrators

Intrafamilial	%	n	Extrafamilial	%	n
Father	22.44	23	Stepfather	7.14	7
Uncle	16.32	16	Step uncle	2.04	2
Grandfather	4.08	4	Step sibling	5.1	5
Sibling	2.04	2	Brother-in-law	18.36	20
Aunt	2.04	2	Cousin	20.4	19
Total	46.93	45	Total	53.06	53

On the basis of the nature of abuse, it was found that there were minor cases of abuse, such as fondling (34%) and verbal abuse (1%), as well as major cases of abuse, such as vaginal penetration (8%) and anal penetration (3%), in the intrafamilial group. On the other hand, there were cases of fondling (28%), verbal abuse (3%), vaginal penetration (16%), anal penetration (5%), and oral penetration (2%) in the extrafamilial group (Table 2).

Table 2. Distribution of the cases by nature

	Minor		Major		
	Fondling	Verbal Abuse	Vaginal penetration	Anal penetration	Oral penetration
Intrafamilial	34.0% n=34	1.0% n=1	8.0% n=8	3.0% n=3	-
Extrafamilial	28.0% n=28	3.0% n=3	16.0% n=16	5.0% n=5	2.0% n=2
Total	62.0% n=62	4.0% n=4	24.0% n=24	8.0% n=8	2.0% n=2

Pearson Chi-Square value: 3.862, df=1, p=0.049

Upon comparing the intrafamilial and exrafamilial groups in terms of the nature of abuse, it was determined that the minor offenses were statistically higher in the intrafamilial group, whereas the major offenses were statistically significantly higher in the ekstrafamilial group (Pearson Chi-Square value: 3.862, df=1, p=0.049).

In the evaluation of the genital examination findings of the cases, it was observed that 56 cases did not undergo genital examination by the forensic authorities as the victims refused to get examined, whereas in 44 cases in which genital examination was conducted, no medical finding was found in 32 cases; newly formed laceration in the hymen in 5 cases; ongoing pregnancy in 3 cases; chronic anal fissure in 2 cases; and erythema on labium minor in 2 cases.

In the present study, no statistical difference was observed in the comparison of genital findings between the two groups.

When the cases were examined in terms of history of recurrent abuse, it was determined that there was a history of recurrent abuse in 64 cases (36 in the intrafamilial vs. 28 in the extrafamilial group), whereas the victim experienced abuse only once in her/his lifetime in 36 cases (10 in the intrafamilial group vs. 26 in the extrafamilial group) (Table 3).

Table 3. Recurrence of abuse

	Recurring	Only once
Intrafamilial		
Count	36	10
Expected count	29.4	16.6
% of Total	36.0%	10.0%
Extrafamilial		
Count	28	26
Expected count	34.6	19.4
% of Total	28.0%	26.0%

Pearson Chi-Square value: 7.519, df=1, p=0.006

Upon comparing the two groups in terms of the recurrence of abuse, it was determined that the number of recurring offenses was statistically significantly higher in the intrafamilial group when compared with the extrafamilial group (Pearson Chi-Square value: 7.519a, df=1, p=0.006).

When the duration of exposure to abuse was examined, it was determined that the victim was exposed to abuse for more than 1 year in 58 cases, whereas the exposure time was less than 1 week in 9 cases (Table 4).

Table 4. Duration of exposure to abuse

	> 1 year	< 1 year
Intrafamilial		
Count	31	8
Expected count	26.6	12.4
% of Total	36.5%	9.4%
Extrafamilial		
Count	27	19
Expected count	31.4	14.6
% of Total	31.8%	22.4%

Pearson Chi-Square value: 4.209, df=1, p=0.04

When the duration of exposure to abuse was assessed, it was found that the duration of exposure to abuse was statistically significantly longer in the intrafamilial group (Pearson Chi-Square value: 4.209a, df=1, p=0.04).

Of the 98 cases included in the study, the victim did not undergo psychiatric assessment in 21, whereas in the 77 cases in which the victim was given psychiatric assessment, the victim was found to suffer from post-traumatic stress disorder (PTSD) in 15 cases; major depressive disorder in 10 cases; anxiety disorder in 3 cases; acute stress reaction in 3 cases; conduct disorder in 1 case; and mental retardation in 2 cases. Psychiatric examination produced no abnormality in 45 cases (Chart 1).

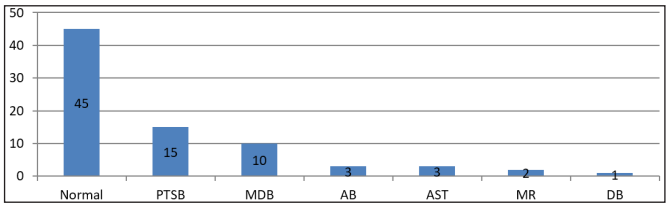

Chart 1. Psychiatric assessment of the cases

DISCUSSION

It is difficult to unveil cases of incest because they not only affect victims physically and psychologically over extended periods of time but also occur in closed settings. When they are uncovered, it is crucial that examination, medical assistance, and judicial process should be managed by experienced teams in the centers that are specialized in this area. The present study was conducted with the children presented to a center that was specialized with regard to child abuse cases through judicial reporting.

Sexual abuse affects children of all ages from all countries and cultures.[10,11] Girls and boys in all ages may be subject to incestuous relations.[12]

In many epidemiological studies, it has been reported that girls were 2–3 times more vulnerable to sexual assaults.[13,14] Of the 98 cases assessed, 89% (n=90) of the victims were female and 9% (n=9) were male. The male/female ratio was calculated to be 0.099. Similar ratios have been reported in the literature. In their study on 1,002 cases, Aydın et al.[15] reported 80.8% for females and 19.2% for males as gender distribution. Studying the judicial reporting of incest cases, Gündüz et al.[16] observed a gender distribution similar to the present study: 16.9% males and 83.1% females. Many other studies have reported similar results as well.

The youngest was aged 4 years and the oldest one was 17 years. The mean age was 12.65+3.753 years. In the studies including all age groups, too, the mean age has been reported to be 13±6.3 years.[17] Just as in the case of the female gender, younger ages constitute a risk factor for sexual abuse.

This value was 13.07+4.418 for the females and 8.44+4.586 for the males. In a study on incest, it was demonstrated that the mean age of females was greater than that of males (W: 15.3 - M: 8.5).[16]

In the present study, the most prevalent form of incest was father-daughter incest, and cousins and brothers-in-law were the second most frequent perpetrators. In a study on incest conducted at a university hospital, fathers have been reported as the most frequent perpetrators in a manner similar to that reported by the present study.[18] In a study with a small number of cases, however, the elder brother was reported as the most frequent perpetrator. Nevertheless, the rate of father-daughter incest cases reported in the same study could not be underrated.[19] It is known that father-daughter incest is the most frequent form of incest, and many studies have been conducted on its risk factors. In this form of incest, the father-daughter relationship is distorted from a developmental and structural perspective, leading to the highest level of public indignation. In terms of incidence, father-daughter incest is followed by brother-sister, sister-sister, and mother-son incest.[21,22]

In the present study, father-daughter incest was followed by cases of incest involving brothers-in-law and cousins from the extrafamilial group in terms of incidence. In a study conducted in our country, the most frequent cases of incest were indicated as those involving cousins, fathers, and brothers-in-law. Brothers-in-law (sister's husband or aunt's husband) become relatives by marriage, are included in the family, can establish direct contact with the victim, are trusted by the family, and have a chance to be alone with the victim—all these factors make it easier for them to perpetrate sexual abuse.[23]

On the basis of relationships between victims and perpetrators in 98 cases of child abuse, 46% (n=45) were placed in the intrafamilial group and 53% (n=54) were placed in the extrafamilial group. In what is similar to the findings reported by the present study, cases of extrafamilial abuse were reported to be more frequent in other studies as well.[6]

On the basis of the nature of abuse, it was found that there were minor cases of abuse, such as fondling (34%) and verbal abuse (1%), as well as major cases of abuse, such as vaginal penetration (8%) and anal penetration (3%), in the intrafamilial group. On the other hand, there were cases of fondling (28%), verbal abuse (3%), vaginal penetration (16%), anal penetration (5%), and oral penetration (2%) in the extrafamilial group. In sexual abuse and assaults, it is crucial to determine medical findings and align them with legal actions. Different ratios have been reported in studies on the matter. This is directly associated with the characteristics of the cases reported to the center where this examination is conducted as well as to the experience of the team performing the examination. Our center accepts reports from all provinces and regions concerning sexual abuse of children.

Upon comparing the intrafamilial and extrafamilial groups in terms of the nature of abuse, it was determined that the minor offenses were statistically higher in the intrafamilial group, whereas the major offenses were statistically significantly higher in the extrafamilial group. It was considered that the blood relation between the victim and the perpetrator could affect the nature of abuse in the intrafamilial group, whereas any secret and forbidden love affair between the victim and the perpetrator in the ektrafamilial group could affect the nature of abuse; however, this statistical difference should be reassessed in large-scale studies.

When the cases were examined in terms of recurring abuse history, it was determined that there was a history of recurrent abuse in 64 cases (36 in the intrafamilial group vs. 28 in the extrafamilial group). The possibility of recurrence in the intrafamilial group, which includes fathers, uncles, grandfathers, siblings, aunts, is higher because it is more difficult to discover or report the incidents, particularly sexual abuse, in this group.

Incest is the most severe form of sexual abuse, and as it tends to be kept a secret within the family, it can go on for extended periods, and this complicates diagnosis and prevention.[21]

Incest can be seen in all family types, from single-parent to extended families, but it is more widespread in elementary families, particularly introverted ones.[12] Upon comparing the intrafamilial and extrafamilial groups in terms of the recurrence of abuse, it was determined that the number of recurring offenses was statistically significantly higher in the intrafamilial group when compared with that in the extrafamilial group. This may be seen as the result of a closed structure that is attributable to the aforementioned biological affinity. In addition, considering that the incest perpetrator is a relative of the child, that the child trusts that relative, and that the incident tends to occur in a setting where the child feels safe, it becomes even more difficult for the victim to report the abuse, leading to the recurrence of abuse.[12]

In addition, the child may not readily perceive the incestuous behavior from his/her biological relative as abuse. Even if child perceives it, she/he may choose to keep it secret by normalizing it, feeling guilty, or succumbing to pressures, threats, or the perpetrator's authority. In the intrafamilial group, the approach by other members of the family to incest is decisive in reporting the incident or its becoming recurrent. Just as with the victim, they may choose to normalize the incident, blame themselves, and eventually keep the incident secret.

The duration of abuse is another major risk factor that may have adverse effects on the life of the victim. In the present study, it was determined that the victims were exposed to abuse for more than 1 year in 58 cases. In a study conducted in our country, exposure to abuse for more than 1 year was reported in 3 cases.[23] The high number of cases in the present study may be due to the fact that newly reported cases of abuse are referred to our center even if they occur in other cities. For the rehabilitation of the victimized children, it is critical for these cases to be evaluated, their forensic examination to be followed through, and psychiatric follow-ups to be conducted at a center that is specialized and experienced in dealing with sexual abuse cases of children.

Sensory, behavioral, and medical problems were reported in incest victims.[24] In the present study, the victim was found to suffer from post-traumatic stress disorder (PTSD) in 15 cases; major depressive disorder in 10 cases; anxiety disorder in 3 cases; acute stress reaction in 3 cases; conduct disorder in 1 case; and mental retardation in 2 cases. Likewise, PTSD, anxiety, and depressive disorders were reported as leading psychiatric conditions in another study.[23]

CONCLUSION

Incest is a social problem that must be acknowledged and prevented from being kept secret. Therefore, it is crucial for our country to expedite the determination of national policies for raising public awareness regarding the matter. The training and awareness-raising activities that are required to be conducted in the public sphere to encourage incest victims who conceal themselves with feelings of guilt, fault, or sin to report the offense may facilitate the disclosure of these bleeding wounds within the closed family motif..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval by the Karadeniz Technical University Medical Faculty Scientific Researches Ethics Committee (Date: 30.05.2022, Decision No: 9).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Factors affecting the progression of chronic kidney disease

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ABSTRACT

Aims: Chronic kidney disease (CKD) is characterized by irreversible and progressive loss of renal function. One of the most important goals in CKD management is to delay CKD progression. The aim of this study was to investigate the outcomes of non-dialysing CKD patients, rate of progression of disease and factors associated with CKD progression and mortality.

Methods: In this retrospective study, 245 non-dialysis CKD (stage 3-5) patients who presented to nephrology outpatient clinic between December 2013 and June 2015 were included. Patients' baseline demographic, clinical/laboratory data were obtained. Outcomes of the patients in terms of CKD progression (defined as the initiation of renal replacement therapy or death) between November 2022 and December 2022 were recorded.

Results: Patients' mean age (baseline) was 56±12 years; 116 patients (47.3%) were female. During median 46 months of follow-up period, 42.9% of the patients underwent renal replacement therapy and all-cause mortality rate was 9.8%. Baseline eGFR, proteinuria and having diabetes mellitus as a comorbidity were found to be associated with CKD progression, independently (the risk increases by 75% with each 1 ml/min decrease in eGFR, p<0.001; the risk increases approximately 1.8 times with each 1 gr/day increase in proteinuria, p=0.003; the risk increases approximately 3 times with diabetes mellitus, p=0.043).

Conclusion: Our findings showed that baseline eGFR level, having diabetes mellitus and baseline proteinuria values were independent risk factors associated with disease progression and mortality in non-dialysing CKD patients. Early diagnosis and close monitoring of CKD, applying interventions targeting risk factors associated with CKD progression should be considered to delay CKD progression.

Keywords: Chronic kidney disease, progression, renal replacement therapy, risk factors

INTRODUCTION

Chronic kidney disease (CKD) has a prevalence of 11-13% and in its course, there is irreversible and progressive loss of kidney function with increased morbidity, hospitalization, cardiovascular events and mortality.[1] CKD progresses gradually from stage 1, where the estimated glomerular filtration rate (eGFR) is within the normal range, to stage 5, where renal replacement therapy is required. Prevalence and progression of CKD vary between countries and also within countries by social determinants and ethnicity, possibly via epigenetic mechanisms.[2] CKD progression expresses cumulative loss of renal function over time (eventually leading to renal replacement therapy requirement).

The factors such as fibrosis, chronic inflammation, parenchymal cell loss, decreased regenerative capacity of kidney can contribute to progression of CKD.[3] Not all of the CKD patients progress to kidney failure; and prognosis of CKD and timing of adverse outcomes may vary between patients.[4] One of the most important goals in CKD management is to delay CKD progression and to reduce number of patients undergoing renal replacement therapy, by early diagnosis and close monitoring of CKD, by applying nephroprotective therapies and interventions targeting CKD progression and by modifying related risk factors. To delay CKD progression, effectiveness of current therapies are limited.[3] Interventions for specific symptoms, lifestyle recommendations or education considerations have beneficial effects.[2] Medical and non-medical interventions targeting glycol-metabolic control, hypertension, proteinuria and dyslipidemia can be useful. Previous studies showed that lowering sistolic blood pressure (≤130 mmHg) reduces cardiovascular risks and progression of CKD, but ideal sistolic blood pressure level in CKD patients has not yet been determined.[5] In a study, body mass index (BMI) in overweight range was found to be related with reduced risk for all-cause mortality and CKD progression.[6]

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There are limited number of study about long-term outcomes non-diaysing CKD patients and risk factors associated with CKD progression. In this study, we aimed to investigate the outcomes of CKD patients not requiring dialysis and independent risk factors affecting the CKD progression and mortality.

METHODS

All procedures performed in this study were in accordance with the ethical rules and with the principles of Helsinki Declaration and ethics committee permission was obtained from KTO Karatay University Faculty of Medicine Non-medicine and Non-medical Device Researches Ethics Committee (Date: 29.12.2022, Decision No: 2022/010). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this study with retrospective design, CKD patients (stage 3-5, aged ≥18 years) presented to the nephrology outpatient clinic between December 2013-June 2015 were included. The patients with cardiovascular disease, malignancy or with rapidly progressive glomerulonephritis or undergoing renal replacement therapy were excluded. The patients with missing baseline data were also excluded. Patients' demographic, clinical/laboratory parameters such as age, gender, comorbidities, smoking status, baseline BMI, sistolic and diastolic blood pressure values and initial laboratory parameters (hemoglobin, serum urea, creatinine, glucose, electrolites, calcium, magnesium, phosphorus, albumin, uric acid, C-reactive protein, lipids, parathormone, ferritin, eGFR, amount of proteinuria, venous blood gas) were all obtained from the patients' files. For eGFR calculation, Modification of Diet in Renal Disease Formula was used[7] and the CKD stage was classified as stage 3 (eGFR, 30–59 ml/min/1.73 m^2), stage 4 (eGFR, 15–29 ml/min/1.73 m^2) and stage 5 (eGFR, <15 ml/min/1.73 m^2).[8] For outcomes of the patients participated in this study, the patients' status between November 2022 and December 2022 were detected from the medical records of the hospital and the combined endpoint was defined as initiation of renal replacement therapy (dialysis or transplant) or death (whichever occurred first).

Statistical Analysis

For statistical analysis, SPSS 22.0 (IBM) software was used. To determine normally or non- normally distributed data Kolmogorov-Smirnov test was used. The results were shown as mean±SD (for variables distributed normally) and median (minimum-maximum) (for variables distributed non-normally). To compare variables, the T-test (for normal distributions) and the Mann Whitney-U test (for non-normal distributions) were used. The independent factors for primary outcomes were determined by performing Cox-regression analysis. A p value < 0.05 was considered statistically significant.

RESULTS

Data of 245 CKD patients were evaluated in this study: 116 (47.3%) were female and 129 (52.7%) were male; mean age (at baseline) was 56±12 years. CKD etiologies were diabetes mellitus (68 patients, 27.8%), hypertension (43 patients, 17.6%), glomerulonephritis (35 patients, 14.3%), polycystic kidney disease (31 patients,12.7%), urological causes (16 patients, 6.5%), amyloidosis (4 patients, 1.6%), unknown underlying etiologies (48 patients, 19.6%). Only 28 patient (11.4%) had smoking history. The median follow-up time was 46 months. During this period, regarding clinical outcome of the 245 patients, 64 (26.1%) had still non-dialysing CKD and were continiuing follow-up visits in nephrology outpatient clinic; 105 (42.9%) had required renal replacement therapy (85 patients (34.7%) were on dialysis and 20 patients (8.2%) underwent kidney transplantation); 24 patients (9.8%) died; and 52 (21.2%) patients were lost to follow-up (**Table 1**). In univariate correlation analysis, follow-up time (p<0.001), having diabetes mellitus as a comorbidity (p<0.001), baseline eGFR (p<0.001), calcium (p<0.001), phosphorus (p<0.001), albümin (p<0.001), potassium (p=0.025), hemoglobin (p<0.001), parathormone levels (p<0.001) and amount of proteinuria (p<0.001), baseline sistolic and diastolic blood pressure measurements (p<0.001 and p=0.002, respectively) were found to be related with CKD progression to end stage renal failure and all-cause mortality (**Table 1**). To determine the independant variables, Cox-regression analysis with the parameters found to be significant in univariate analysis were performed; and baseline eGFR (the risk increases by 75% with each 1 ml/min decrease in eGFR, p<0.001), baseline proteinuria (the risk increases approximately 1.8 times with each 1 gr/day increase in proteinuria, p=0.003) having diabetes mellitus as a comorbidity (the risk increases approximately 3 times with diabetes mellitus, p=0.043) were found to be associated with CKD progression, independently (**Table 2**).

DISCUSSION

CKD is the common and progressive result of various disease processes with different etiologies/pathogenesis rather than being one disease. The goal of nephrologists is to prevent or delay the progression of CKD as much as possible; and for this, knowing the risk factors affecting the progression of CKD is important. In our

study, the outcomes of non-diaysing CKD patients and the risk factors associated with CKD progression were investigated. During median 46 months of follow-up period, 42.9% of our patients underwent renal replacement therapy and all-cause mortality rate was 9.8%. In a previous study, of the 382 patients with non-dialysing CKD (stage 3-5), 190 patients progressed to renal replacement therapy requirement (dialysis or kidney transplant), (12.1%/year; mean follow-up, 4.1 years) and 150 died (6.5%/year; mean follow-up, 6.0 years).[9] In the study of Zhang et al.[10] rate of CKD progression (defined as initiation of dialysis) was 26.2% among 309 patients with CKD stage 3-4 (median follow-up time, 25.6 months). In another study from Sweden, included 26279 patients with CKD stage 3b-5, rate of CKD progression event (defined as initiation of renal replacement therapy or at least one CKD stage transition) was 19.6 patients /100 person-years; and 10.1 patients/100 person-years died.[11] These different CKD progression rates and mortality rates between studies may be attributed to the differences in sample size, CKD stage of study group, definition of CKD progression or follow-up time. In addition CKD progression time may vary between countries and even patient by patient.[4]

In our study, having diabetes mellitus as a comorbidity, baseline proteinuria and baseline eGFR values were found to be associated with CKD progression; the risk of CKD progression and mortality increased by 75% with each 1 ml/min decline in eGFR. In a previous study, each 30% decline in baseline eGFR was associated with 3-fold higher end stage renal failure rate and 1.3-fold higher death rate.[9] Similarly, previous other studies concluded that more baseline kidney impairment (CKD stage) is related with CKD progression and clinical events.[10,12,13] So, for the patients with more advanced stages of non-dialysing CKD, to develop strategies targeting improving dialysis provision and capacity of transplant services could be beneficial.[13] Regarding baseline proteinuria and having diabetes as a comorbidity, in our study, the risk of CKD progression increased approximately 1.8 times with each 1 gr/day increase in proteinuria; and it is increased 3 times in patients with diabetes mellitus. In concordance with our study, in the study of Zhang et al.[10] increased proteinuria associated with increased the risk for progression to initiation of dialysis by 2.592 fold and the patients with diabetes mellitus had 2.759 fold increase in CKD progression to renal replacement therapy compared to the patients without diabetes. In

Table 1. Baseline characteristics of the patients and univariate correlation analysis of chronic kidney disease progression with variables

Baseline characteristics	Overall* (n=245)	Non-dialysis during follow-up (n=64)	Underwent RRT or died during follow-up (n=129)	p
Age, year, mean±SD	56±12	54.4±11.4	56.7±12.4	0.220
Gender, female, n (%)	116 (47.3)	32 (50)	60 (46.5)	0.760
Presence of diabetes, n (%)	68 (27.8)	8 (12.5)	47 (36.4)	<0.001
Smoking history, n (%)	28 (11.4)	8 (12.5)	16 (12.4)	0.576
BMI, kg/m²	30.3±6.3	30.6±5.5	30.0±6.8	0.573
eGFR, ml/min/1.73 m²	30.1±13.1	56.0±13.5	33.4±14.8	<0.001
Serum creatinine, mg/dL	2.53 (1.14-6.35)	1.820.53	3.03±1.12	<0.001
Serum uric acid, mg/dl	7.1±1.7	6.95±1.79	7.17±1.67	0.402
Potassium (mmol/l)	4.7±0.5	4.67±0.55	4.86±0.55	0.025
Calcium, mg/dl	9.0±0.7	9.33±0.51	8.78±0.77	<0.001
Phosophorus, mg/dl	3.6±0.9	3.23±0.61	3.87±1.16	<0.001
Serum albumin , g/dl	3.9±0.4	4.11±0.29	3.81±0.49	<0.001
Systolic BP, mmHg	138±20	130.8±14.4	142.3±21.5	<0.001
Diastolic BP, mmHg	88±11	87.0 (47-115)	92 (52-141)	0.002
Hemoglobin, g/dl	12.8±1.9	13.7±2.1	12.3±1.8	<0.001
LDL- cholesterol, mg/dl	133 ±40	134.1±39.0	133.8±43.3	0.964
Triglyserides, mg/dl	186 (40-1191)	184±105	181±108	0.817
Bicarbonate (HCO_3^-), mmol/l	21.3±3.1	21.23±2.85	21.06±3.47	0.808
Parathormon, ng/l	82.85 (23-799)	82.85 (23-799)	172.8 (21-785)	<0.001
C-reactive protein, mg/l	3.44 (3-78)	3.44 (3-78)	3.7 (3-201)	0.077
Proteinuria (g/day)	2.16 (0.05-13.90)	0.87 (0.05-4.46)	3.17 (0.06-13.90)	<0.001
Follow-up time, month, median (range)	46 (2-108)	84 (62-91)	24 (2-84)	<0.001

*, 52 patients were lost to follow-up; RRT, renal replacement therapy; SD, standart deviation; BMI, bady mass index; eGFR, estimated glomerular filtration rate; BP, blood pressure; LDL-cholesterol, low-density lipoprotein cholesterol.

Table 2. Cox-regression analysis to determine independent variables

Variables	Step 1 Cox-Snell R2=0.321			Step 2 Cox-Snell R2=0.384			Step 3 Cox-Snell R2=0.399		
	p	Exp(β)	%95 CI	p	EExp(β)	%95 CI	p	Exp(β)	%95 CI
Baseline eGFR	<0.001	0.910	0.885-0.936	<0.001	0.926	0.899-0.954	<0.001	0.925	0.897-0.953
Baseline proteinuria				0.001	1.853	1.269-2.706	0.003	1.798	1.223-2643
Presence of diabetes							0.043	3.103	1.034-9314

eGFR, estimated glomerular filtration rate

another study, fast progression occurred in 23.0% of CKD patients with diabetes mellitus vs. 15.3% of CKD patients without diabetes during 24-month follow-up; and proteinuria was among the multivariable predictors of CKD progression.[14]

In our study, the factors including, baseline phosphorus, albümin, hemoglobin levels, baseline sistolic and diastolic blood pressure measurements were associated with CKD progression in univariate correlation analysis, but in multivariate analysis these factors could not retain their significance. Unlike our study, in some previous studies, the risk factors such as age,[13] male gender,[11] current smoker,[13] hypoalbuminemia,[10,13] increased low-density lipoprotein levels,[10] elevated blood pressure,[10,14] anemia,[13,14] higher serum phosphorus levels[13] were found to be associated with CKD progression. These different finding between studies can be atributed to the differences in study design, sample size or CKD stages of study group.

There are some limitations of this study: First, it is a retrospective study including patients from a single center; second we did not include data on the drugs used by the patients.

CONCLUSION

Our findings in this study showed that baseline eGFR level, having diabetes mellitus and baseline proteinuria values were independent risk factors affecting CKD progression and mortality in non-dialysing CKD patients. Early diagnosis and close monitoring of CKD, applying nephroprotective therapies and interventions targeting risk factors associated with CKD progression should be considered to delay CKD progression and to reduce number of patients requiring renal replacement therapy.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics Committee permission was obtained from KTO Karatay University Faculty of Medicine Non-medicine and Non-medical Device Researches Ethics Committee (Date: 29.12.2022, Decision No: 2022/010).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Morphometric analysis and clinical significance of the os sacrum

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ABSTRACT

Aims: The purpose of this study is to assess the architecture and clinical importance of the sacrum, which features the dorsal and pelvic nerves.

Methods: 32 os sacrum of adult Anatolians of undetermined gender were measured for this investigation. Sacrum maximum length, os sacrum maximum width, sacrum I vertebral body antero-posterior width, sacrum I vertebral body transverse width, sacral index, Auricular surface short arm, auricular surface long arm and auricular surface oblique arm, the measurements of pelvic surface linea transverse length and, the measurements of dorsal surface linea transverse length and the sacrum height from the dorsal surface are evaluated.

Results: Sacrum maximum length 103.30±10.03 mm, sacrum maximum width 108.40±6.10 mm, sacrum I vertebral body transverse width 47.00±5.00 mm, sacrum I vertebral body antero-posterior width 28.30±3.50 mm, sacral index 104.00±9.00, Auricular surface short arm 31.90±4.20 mm, Auricular surface long arm 39.40±4.80 mm, Auricular surface oblique arm 49.10±6.00 mm, the length measurements of dorsal surface distance respectively as mm; 36.72±0.37, 29.75±0.31, 26.53±0.33, 26.56±0.39, the length measurements of dorsal surface distance respectively as mm; 29.16±0.36, 27.16±0.33, 24.50±0.26, 24.38±0.24 and the sacrum height from the dorsal surface as 103.4±9.70 mm were calculated.

Conclusion: Clinically stated, understanding the architecture of the sacrum and taking morphometric measures of it are crucial to avoiding difficulties and the surgical intervention that will be used to treat disorders associated to the sacrum.

Keywords: Anatomy, morphometry, sacrum

This study was presented as a poster presentation at the "Anthropology, Radiology & Anatomy Congress" held in Ankara University, Ankara between 12-13 November 2015.

INTRODUCTION

The five sacral vertebrae come together to form the huge triangular bone known as the os sacrum, which is located in the posterior upper portion of the pelvic cavity (cavitas pelvis). Above is its base (basis ossis sacri), and below is its apex (apex ossis sacri). Facies pelvica and facies dorsalis are the names of the sacrum's anterior and rear surfaces, respectively.[1-5] The lateral side of the os sacrum forms a "L"-shaped joint with the facies auricularis of the ilium. The promontorium, or base of the sacrum, protrudes anteriorly. The union of the processus transversus additionally forms the crista sacralis lateralis. The ala ossis sacri, which resembles a pair of wings, is visible on the upper portion of the crista sacralis lateralis. Additionally, the sacrum's posterior surface is convex and its anterior surface is concave. There are four transverse lines, or linea transversae, on the face of the os sacrum, also known as the facies pelvica, which connect the corpus vertebrae. The foramina sacralia pelvica, eight holes on the right and left sides of these lines contain the anterior branches of the spinal nerves. Additionally, the aa. and vv. sacralis lateralis passes through these openings. The facies dorsalis refers to the dorsal surface of the os sacrum. There are eight foramina sacralia posteriora on the right and left posterior surfaces of the os sacrum, through which the posterior branches of the spinal nerves continue.[4,6] Through the foramen intervertebrales, these holes join the canalis sacralis.[7] In terms of protecting neural tissues during surgical interventions to this area and caudal anesthesia, foramina sacralia anteriora and foramina sacralia posteriora are clinically significant.[8]

The pelvic girdle has a solid joint system that allows weight to be transferred from the trunk to the lower extremities. The spine lumbalis transmits body weight to the os sacrum, which travels through the sacroiliac joint to the os coxae and os femoris.[5] The number of bones that make up the sacrum can change in some circumstances.[9] In the treatment of lumbosacral, sacral, and sacroiliac anomalies or injuries, the sacrum is a vital bone for

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stability and fusion. Therefore, it is crucial to understand the complicated anatomical nature of the os sacrum before performing any surgery there. The architecture of the os sacrum must be understood to provide adequate fixation and prevent neurovascular damage.[6,9-11]

This study, it is aimed to reveal the anatomical structure of the os sacrum with morphometric measurements and to emphasize its clinical importance. Thus, the results obtained in this study will guide clinical research and applications.

METHODS

Since the study was performed on dry bones, ethics committee approval is not required, institutional approval was obtained. All procedures were carried out in accordance with the ethical rules and the principles.

In this study, 32 pieces of dry bone os sacrum of unknown age and gender were measured. Partially broken, fragmented or damaged bones were excluded from the study. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. We measured maximum length of os sacrum, maximum width of os sacrum, anterior posterior width of os sacrum corpus vertebrae, transverse width of os sacrum corpus vertebrae, sacral index, facies auricularis short arm length, facies auricularis long arm length, facies auricularis oblique arm length, measurements of os sacrum facies pelvica, measurements of facies dorsalis and the height of the os sacrum on the dorsal (**Figure 1-5**). Measurements of os sacrum's includes facies pelvica length between foramina sacralia anteriora I, length between foramina sacralia anteriora II, length between foramina sacralia anteriora III, length between foramina sacralia anteriora IV parameters (**Figure 5**). In addition, the measurements of the facies dorsalis of the os sacrum are the length between foramina sacralia posteriora I, length between foramina sacralia posteriora II, length between foramina sacralia posteriora III, between foramina sacralia posteriora IV length parameters (**Figure 1**).

Measurement Design

Each bone was photographed from a distance of 100 cm under artificial light. The photographic system was set up by fixing the camera at a distance of 100 cm with an adjustable tripod. The tripod height was also positioned and fixed in accordance with the position of the bones. Photographs of dry bones were taken with a Digital SLR camera with fixed photo shooting settings (Canon EOS 80D; ISO 100 f/4.5) from the right-left, pelvic-dorsal side. The photos taken were transferred to the computer and uploaded to the Sketchup design program. The reference points of the parameters to be measured were determined and the length measurements were carried out by drawing lines between the two reference points.

Measurements Parameters

Measurements of the dorsal surface (facies dorsalis) of the os sacrum (FDL1-4): The length between the right foramina sacralia posteriora and the left foramina sacralia posteriora was measured (**Figure 1**).[11]

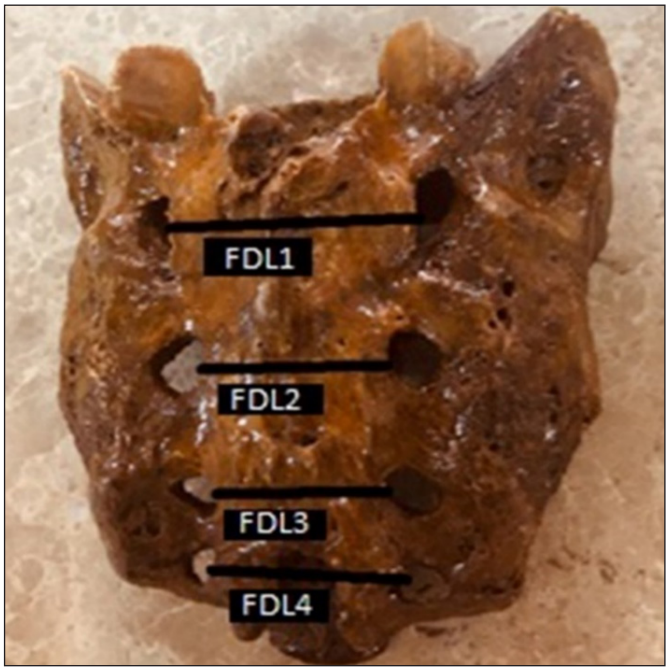

Figure 1. Measurements of os sacrum facies dorsalis (FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4).

Height of os sacrum (SH): The distance between the highest point of the crista sacralis media from the os sacrum facies dorsalis on the dorsal aspect and the cornu sacrale in the mid-sagittal plane was taken as reference.[11]

Anterior-posterior width of the os sacrum corpus vertebrae (CVAPW): The anterior-posterior width of the corpus vertebrae of the os sacrum was measured (**Figure 2**).[9]

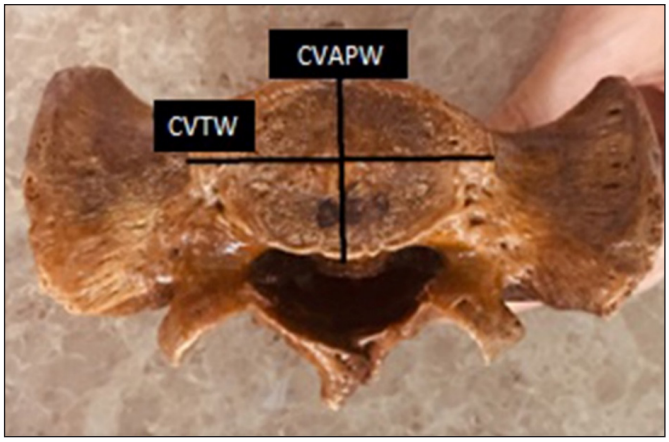

Figure 2. Measurements of os sacrum I corpus vertebrae (CVAPW; anterior posterior width of os sacrum corpus vertebrae, CVTW; transverse width of os sacrum corpus vertebrae).

Transverse width of the os sacrum corpus vertebrae (CVTW): The os sacrum corpus vertebrae was measured horizontally from right lateral to left lateral (Figure 2).[9]

Facies auricularis short arm length (SAL) of Os sacrum: Measurements were made from the right side and the distance from point A to point B was calculated (Figure 3).[11]

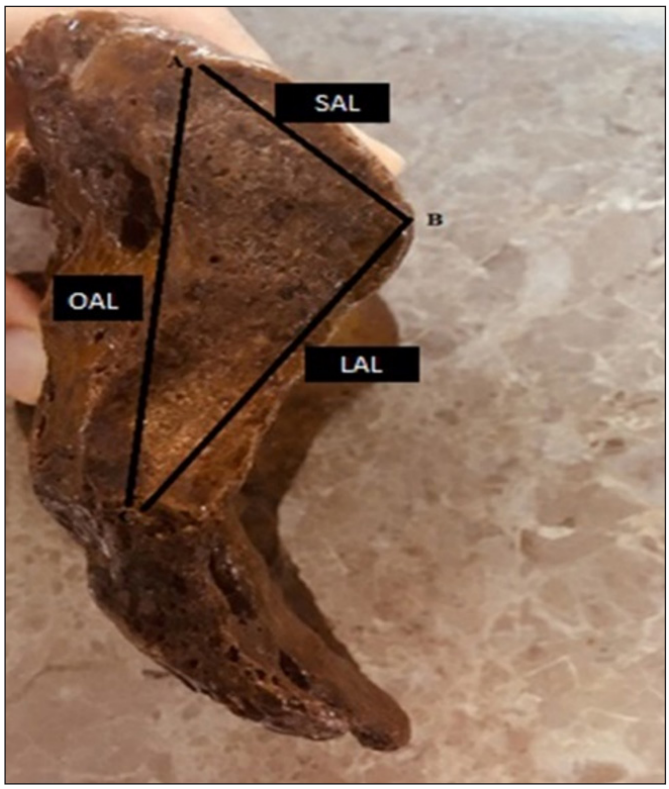

Figure 3. Measurements of facies auricularis of os sacrum (SAL; facies auricularis short arm length, LAL; facies auricularis long arm length, OAL; facies auricularis oblique arm length).

Facies auricularis long arm length (LAL) of Os sacrum: Measurements were taken from the right side and the distance from point B to point C was measured (Figure 3).[11]

Os sacrum's facies auricularis oblique arm length (OAL): Measurements were made from the right side and the distance from point A to point C was measured (Figure 3).[11]

Maximum length of the os sacrum (SL): The distance between the promontorium and the lowest point of the anterior edge of the os sacrum was calculated in the mid-sagittal plane (Figure 4).[12-14]

Maximum width of os sacrum (SW): The distance between the most lateral right and left parts of the ala ossis sacri on the most upper part of the os sacrum facies auricularis from the anterior facies was measured (Figure 4).[12-16]

Figure 4. Length and width measurements of the os sacrum (SL; maximum length of os sacrum, SW; maximum width of os sacrum).

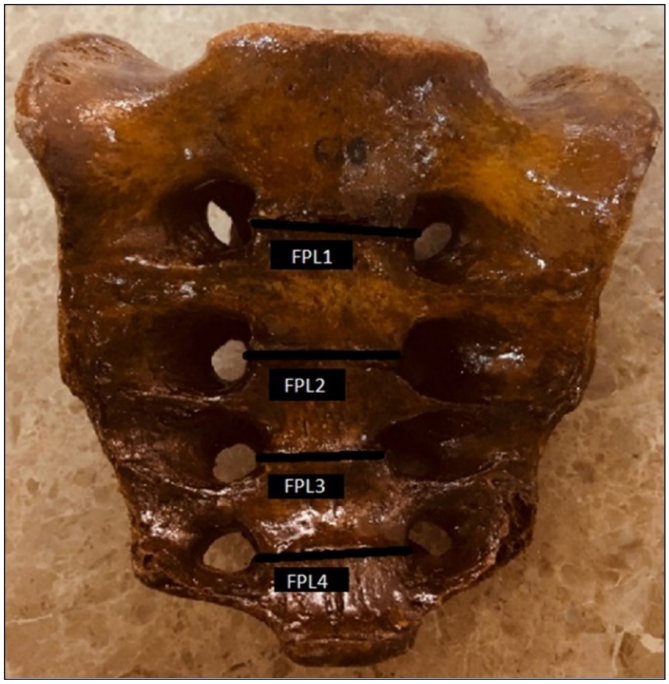

Figure 5. Measurements of os sacrum facies pelvica (FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora)

Sacral index (SI):[12-14] Maximum width of os sacrum × 100

Maximum length of the os sacrum

Measurements of the os sacrum facies pelvica (FPL1-4): The length of the linea transversa between the right foramina sacralia anteriora and the left foramina sacralia anteriora was measured (Figure 4).[11]

Statistical Analysis

The SPSS 22 package program was used for statistical analysis and statistically significant degree were considered as $p<0.05$. Also, the normal distribution of the data distribution were identified by Skewness and kurtosis statistics (between +1.5 and -1.5). After statistical evaluation of the measurement results, mean (μ), standard deviation (σ), minimum (min.) and maximum (max.) values were calculated.

RESULTS

Our study includes the following findings; width of os sacrum, length of os sacrum, transverse width of os sacrum corpus vertebrae, sacral index, anterior posterior width of os sacrum corpus vertebrae, facies auricularis short arm length, facies auricularis long arm length, facies auricularis oblique arm length, length between foramina sacralia posteriora 1, 2, 3, 4, length between foramina sacralia anteriora 1, 2, 3, 4 and facies dorsalis height of os sacrum. The minimum, maximum, mean and standard deviation values of the linear measurements of 32 dry bone os sacrum are shown in Table 1. In addition, we compared the results of these parameters in our study with the literature findings (Table 2, Table 3 and Table 4).

Table 1. Mean (μ), standard deviation (σ), minimum (min.) and maximum (max.) values of the measurements of os sacrum

Parameters (mm)	μ	σ	Minimum	Maximum
SW	108.40	6.10	91.50	120.00
SL	103.30	10.03	80.00	125.00
CVTW	47.00	5.00	37.00	56.00
CVAPW	28.30	3.50	21.50	35.00
SI	104.00	9.00	78.00	133.00
SAL	31.90	4.20	21.00	42.00
LAL	39.40	4.80	31.00	49.00
OAL	49.10	6.00	38.00	58.00
FDL1	36.72	0.37	28.0	40.3
FDL2	29.75	0.31	24.0	30.6
FDL3	26.53	0.33	22.0	30.3
FDL4	26.56	0.39	20.0	30.5
FPL1	29.16	0.36	23.0	30.6
FPL2	27.16	0.33	19.0	30.3
FPL3	24.50	0.26	20.0	30.0
FPL4	24.38	0.24	20.0	30.1
SH	103.40	9.70	82.0	126.0

SW; maximum width of os sacrum, SL; maximum length of os sacrum, CVTW; transverse width of os sacrum corpus vertebrae, CVAPW; anterior posterior width of os sacrum corpus vertebrae, SI; sacral index, SAL; facies auricularis short arm length, LAL; facies auricularis long arm length, OAL; facies auricularis oblique arm length, FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4, FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora 4, SH; Facies dorsalis height of os sacrum. μ; mean, σ: Standard deviation.

Table 2. Comparison of anterior and posterior surface measurements of the os sacrum with the literature

Parameters	μ±σ		Literature	Measurement type	Population/Year
FDL1	38.68±4.03 mm		Koç et al.[11]	Dry os	Turkey/2014
FDL2	31.45±4.13 mm				
FDL3	26.10±3.68 mm				
FDL4	26.04±3.31 mm				
FPL1	30.01±5.03 mm				
FPL2	28.33±4.48 mm				
FPL3	26.51±4.82 mm				
FPL4	24.81±3.93 mm				
FPL1	Erkek	Kadın	Duman.[6]	Computed Tomography	Turkey/2009
	31.1±3.6 mm	28.0±3.1 mm			
FPL2	28.8±3.4 mm	26.1±2 mm			
FPL3	26.5±2.3 mm	24.6±2.4 mm			
FPL4	24.6±2.4 mm	23.2±2.4 mm			
FDL1	36.72±0.37 mm		This study	Dry os	Turkey/2018
FDL2	29.75±0.31 mm				
FDL3	26.53±0.33 mm				
FDL4	26.56±0.39 mm				
FPL1	29.16±0.36 mm				
FPL2	27.16±0.33 mm				
FPL3	24.50±0.26 mm				
FPL4	24.38±0.24 mm				

FDL1; length between foramina sacralia posteriora 1, FDL2; length between foramina sacralia posteriora 2, FDL3; length between foramina sacralia posteriora 3, FDL4; length between foramina sacralia posteriora 4, FPL1; length between foramina sacralia anteriora 1, FPL2; length between foramina sacralia anteriora 2, FPL3; length between foramina sacralia anteriora 3, FPL4; length between foramina sacralia anteriora 4, μ; mean, σ: Standard deviation.

Table 3. Comparison of measurements of corpus vertebrae and facies auricularis of os sacrum with literature

Parameters (mm)	μ	Literature	Population/Year
CVAPW	29.71 mm	Koç et al.[11]	Turkey/2004
	31.10 mm (female) 29.50 mm (male)	Kothapalli et al.[12]	India/2012
	28.50 mm (female) 31.50 mm (male)	Sachdeva et al.[15]	India/2011
	29.40 mm	Singh et al.[16]	India/2017
	30.50 mm (female) 30.60 mm (male)	Kumar and Wishwakarma[17]	Oman /2015
	28.30 mm	This study	Turkey/2018
CVTW	49.33 mm	Koç et al.[11]	Turkey/2004
	47.20 mm (female) 44.60 mm (male)	Kothapalli et al.[12]	India/2012
	45.50 mm (female) 47.60 mm (male)	Sachdeva et al.[15]	India/2011
	48.00 mm	Singh et al.[16]	India/2017
	51.40 mm (female) 53.00 mm (male)	Kumar and Wishwakarma[17]	Oman/2015
	47.00 mm	This study	Turkey/2018
Facies auricularis lengths	32.08 mm (short arm) 52.47 mm (long arm) 59.60 mm (oblique arm)	Koç et al.[11]	Turkey/2004
	31.9 mm (short arm) 39.4 mm (long arm) 49.1 mm (oblique arm)	This study	Turkey/2018

CVAPW; Anterior-posterior width of the corpus vertebrae, CVTW: Transverse width of the corpus vertebrae, μ;mean

Table 4. Comparison of os sacrum length, width and index results with the literature...

Parameters (mm)	μ	Literature	Population/Year
SL	93.49 mm	Koç et al.[11]	Turkey/2014
	100.10 mm (female) 98.50 mm (male)	Kothapalli et al.[12]	India/2012
	100.10 mm (female) 98.50 mm (male)	Janipati et al.[13]	India/2014
	94.46 mm (female) 109.47 mm (male)	Patel et al.[14]	India/2014
	106.10 mm	Singh et al.[16]	India/2017
	91.80 mm (female) 104.10 mm (male)	Sachdeva et al.[15]	India/2011
	93.50 mm (female) 102.70 mm (male)	Kumar and Wishwakarma[17]	Oman/2015
	92.50 mm (female) 115.40 mm (male)	Mustafa et al.[18]	Egypt/2012
	90.58 mm (female) 107.53 mm (male)	Mishra et al.[19]	India/2003
	101.80 mm (female) 103.10 mm (male)	Sinha et al.[20]	India/2013
	103.30 mm	This study	Turkey/2018
SW	108.40 mm (female) 102.20 mm (male)	Başaoğlu et al.[9]	Turkey/2005
	111.67 mm	Koç et al.[11]	Turkey/2004
	108.20 (female) 101.10 (male)	Janipati et al.[13]	India/2014
	106.45 mm (female) 106.42 mm (male)	Patel et al.[14]	India/2014
	101.70 mm (female) 103.10 mm (male)	Sachdeva et al.[15]	India/2011
	103.10 mm	Singh et al.[16]	India/2017
	109.50 mm (female) 99.90 mm (male)	Kumar and Wishwakarma[17]	Oman/2015
	115.00 mm (female) 113.60 mm (male)	Mustafa et al.[18]	Egypt/2012
	105.79 mm (female) 105.34 mm (male)	Mishra et al.[19]	India/2003
	108.40 mm	This study	Turkey/2018
	108.20 mm (female) 101.10 mm (male)	Kothapalli et al.[12]	India/2012

Table 4. Comparison of os sacrum length, width and index results with the literature...(cont.)

Parameters (mm)	μ	Literature	Population/Year
SI	115.72 (female) 104.08 (male)	Kothapalli et al.[12]	India/2012
	115.72 (female) 104.08 (male)	Janipati et al.[13]	India/2014
	113.40 (female) 97.61 (male)	Patel et al.[14]	India/2014
	111.74 (female) 100.24 (male)	Sachdeva et al.[15]	India/2011
	117.35 (female) 97.51 (male)	Kumar and Wishwakarma[17]	Oman/2015
	121.70 (female) 100.20 (male)	Mustafa et al.[18]	Egypt/2012
	104	This study	Turkey/2018

SW; maximum width of os sacrum, SL; maximum length of os sacrum, SI; sacral index, μ: mean

DISCUSSION

The five sacral vertebrae fuse to form the triangle-shaped sacrum, which functions as the anterior border of the pelvic cavity.[1-5,21,22] The sacral vertebrae begin connecting after puberty. The development of the sacral canal and laminae is incomplete in the presence of any recognized formational defect. Spina bifida and cystitis are co-occurring conditions with this illness, and neurological issues might be seen in this scenario.[21] The median sacral crest is created when the spinous processes unite at the midlineOn either side of the median sacral crest lies the sacral groove. The sacral groove is made up of sacral laminae. The sacral groove serves as the origin of back muscles such the multifidi, sacrospinal muscle, and erector spinae. Without the formation of the second sacral lamina, these muscles won't be able to properly insert to the dorsal surface of the sacrum. Dorsal agenesis is brought on by the sacral lamina's failure to fuse, and hidden spina bifida is brought on by a defect in the sacral canal's posterior wall at the level of the second sacral vertebra.[21] Caudal anesthesia refers to the injection of the anesthetic into the sacral canal through the sacral hiatus during surgical procedures to be done to the uterine cervix and perineum after birth. Surgery can be done while under anesthesia if an anesthetic solution is applied to the roots of the sacral and coccygeal segments in the sacral canal. Knowing the sacrum morphometry inside and out is crucial in this regard.[7] Accordingly, it is claimed that effective caudal epidural anesthesia and analgesia require knowledge of the usual anatomical structure, morphometric values, and variations of the sacrum.[6,21,22] Additionally, the sacrum and coccyx are the vertebrae most frequently affected by malformations of the vertebrae connected to the number. A sixth lumbar vertebra, known as lumbarization, can be formed when the S1 vertebra separates from the sacrum and combines with the L5. On the other hand, sacralization and the fusion of L5 with the sacrum are both possible.[4,5,7,23] Spina bifida or concealed spina bifida, which emerge as a result of failure to fuse or develop that can be seen in the lamina vertebral arch of one or more vertebrae, may occur, as well as sacral hiatus variants, caudal agenesis, or developmental abnormalities.[7,23] On the other hand, since it is situated close to where the common iliac is divided into its terminal branches, the promontorium is a crucial point of reference in laparoscopic surgery.[7]

Clinicians such as anesthesiologists, radiologists, orthopaedists, and obstetricians should have an extensive knowledge of normal anatomy, morphometric measures, and variations of the sacrum. A structural difference in the sacrum helps in the analysis of sacral spina radiography by radiologists, the estimation of age, gender, and height by forensic scientists, the diagnosis of low back pain by orthopaedists, and the detection of spondylolisthesis by obstetricians.[6,21,22] Additionally, accurate diagnosis and administration of treatment in clinical disorders affecting the lumbosacral and sacrococcygeal regions depend on a detailed understanding of sacrum variations.[22]

Measurement results of the sacrum have been observed to vary between males and women in the literature.[6,15,23-25] In terms of gender, it is stated that the bones of men are heavier and larger. The reason why the SI value obtained as a result of dividing the width of the SW is lower in men is due to the fact that the sacrum is longer in men than in women. It has been reported that the sacrum is wider and shorter in women, while promontorium is smaller.[5,26] Differences in age, climatic conditions, race, and gender are thought to be the root causes of these sacral variations.[15,23,24] The fact that the ala of sacrum is wider in women is due to the increased pelvic volume and the need for a wider pelvic outlet during pregnancy, in addition to an increased sacrovertebral angle and the shifting of apex of sacrum to the posterior at delivery.[23] In addition, measurements such as sacral index and subpubic angle were found to be very useful measurements in determining gender differences due to the effect of sex hormones.[24,25] One of the bones

that is most frequently utilized to determine gender and that best demonstrates gender differences is the sacrum.[15] The sacrum morphometric data, according to Kumar and Viscwakarma, are valuable metrics for predicting gender in broken, incomplete, and damaged dry human bones.[17]

In our study, it was found that the FPL1-4 were higher than the FPL1-4. These values were found to be lower than the data in Koç et al.'s[11] study in all parameters, except for FDL3 and FDL4 parameters. When our FPL1-4 measurement values were compared with the results found in the study conducted by Duman T[6] by using computed tomography, it was found that all parameters except for FPL3 parameter were among the mean values found in female and male population. In our study, mean vertebral body anterior posterior diameter of the sacrum was found to be lower than that of Indian,[12,15,16] Oman[17] and Turkish[11] population. Mean of the CVTW was found to be lower than those found in studies by Koç et al.[11] Kumar and Viscwakarma[17] and Singh et al.[16]

Our mean auricular surface of the sacrum length measurements were found to be lower than those found in studies conducted in Turkey. On the other hand, the SL was found to be higher than the measurements in Turkish,[11] Oman[17] and Indian[12,13,20] populations. When the parameter of the SW was compared with the literature, it was found to be higher than the results found in studies conducted by Patel et al.[14] Mishra et al.[19], Sachdeva et al.[15] and Singh et al.[16]; similar to the results found in studies conducted by Janipati et al.[13] and Başaoğlu et al.[9] and lower than the results found in studies conducted by Mustafa et al.[18] and Koç et al.[11]

In addition, when we examine the current studies comparing CT and osteometry, Dubory et al. found that the thickness of the lower part of the Sacral 1 vertebrae body increased in male patients ($p<0.001$). While no significant difference was found between vertebral body width in men and women in this study, they found a significant difference ($p<0.001$) in both sexes in terms of vertebral body median diameter and vertebral body height parameters in both osteometry and CT scans.[27] In another study, the transverse and vertical diameters of the auricular surface had significant differences ($p<0.001$) in males and females in both osteometry and CT scans.[28]

The limitations of our study were the fact that 32 dry sacrum were used in the study since partly broken, fragmented and damaged bones were not included in the study and the study was conducted with only one department. We recommend such studies to be conducted by bringing together many departments or by using more sacrum.

CONCLUSION

It is thought that factors such as race, gender, age, nutritional status, geographical conditions and the measurement methods used are effective in differences between the data obtained from studies conducted in literature. In the present study, the relationship between vertebral column and pelvis and the sacrum and morphometric values of the sacrum were determined. It can be said that a good knowledge of the variations related with the sacrum, which is at a critical point, will increase the success of surgical interventions in this region in the future and prevent the emergence of future clinical complications. It is also clear that the data obtained as a result of the study will contribute to basic and clinical research that will be conducted on sacrum in the future.

ETHICAL DECLARATIONS

Ethics Committee Approval: Since the study was performed on dry bones, ethics committee approval is not required, institutional approval was obtained.

Informed Consent: Since the study was performed on dry bones, no written informed consent was obtained.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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The correlation between medical students' bowel habits and chronic constipation

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ABSTRACT

Aims: Constipation is one of the most common complaints of the digestive system. The prevalence of constipation in the general population is approximately 15%. The aim of this study was to investigate the frequency of constipation in medical students, their defecation habits and the correlation between the two.

Methods: The study was conducted between 1 January and 1 June 2019 through questionnaires. The relationship between individuals' defecation habits and chronic constipation was investigated within the scope of the study. Data on age, sex, constipation status, change in bowel habits within the last three months, defecation frequency, time of daily defecation, period spent in the toilet, reading in the toilet, and the type of toilet used were collected.

Results: 425 medical students were included in the study. 2.86% of the students reporting constipation were first year undergraduates in medical school, while 7.53% were third and 9.09% were sixth year students. Irregular defecation was higher in all groups. The rate of constipation was high in groups with irregular defecation. It was observed that those with regular defecation habits defecated more in the mornings. When the time spent for defecation was studied, it was seen that it was mostly less than 10 minutes.

Conclusion: In the younger population the incidence of constipation is lower compared to the elderly population. Bowel habits, however, vary according to societies and personal characteristics. Reading in the toilet has become a common habit among the younger population. Reading in the toilet elongates the time spent in the toilet.

Keywords: Bowel habits, constipation, defecation, medical student

INTRODUCTION

Bowel habits and constipation are closely correlated. Bowel habits vary according to societies and even to families (individuals). Bowel habits change depending on individuals' chronic diseases, medications they are on, their lifestyles and eating habits. Such variations affect frequency of constipation as well.[1]

Constipation is in fact a symptom, not a disease. It is one of the most common complaints of the digestive system.[2] Patients presenting with constipation may refer to different complaints. Some patients mention a decrease in defecation frequency, while some others refer to difficulty in defecation with hard to pass stools.[3] Yet 60% of patients complaining of constipation are those who defecate daily.[4] Such patients also complain of long-lasting defecation, straining taking up most of the time and a sensation of lingering discomfort. These complaints suggest functional constipation.[5]

The prevalence of constipation differ across societies, age groups and the characteristics of individuals questioned. Its overall prevalence in the general population is considered to be approximately 15% (12-19%).[6,7] It is, however, observed more in women and individuals over 60 years of age. Such frequency is affected by individuals' chronic diseases and lifestyles. Further, bowel habits cause defecation problems.

The aim of this study was, therefore, to investigate the frequency of constipation in medical students (healthy young individuals), their defecation habits, and the correlation between the two.

METHODS

The study was initiated with the approval of the Necmettin Erbakan University Meram Medical Faculty Clinical Researches Ethics Committee (Date:2018, Decision No:1603). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

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This study was planned as a survey study that was conducted on a volunteer basis. The questionnaire used comprised of 9 questions which were designed to investigate the participants' defecation habits and to collect data on the correlation between such habits and constipation. The study population was selected among the first, third and sixth year undergraduates studying at Necmettin Erbakan University Meram Faculty of Medicine. The reason why groups were allocated such population was that first year students were those who had not yet received medical training, thus, better reflecting the population. Third year students, on the other hand, were those who had completed their basic medical education but had not started clinical training yet. Sixth year students comprised the medical doctor group who had completed their medical training. These groups reflected three different stages in medical training. Further, the study was conducted between 1 January 2019 and 1 June 2019 through questionnaires.

The demographic data and bowel habits of all participants suggested to have affected constipation were questioned and studied. Bowel habits of the participants were also investigated. The screening parameters included age, sex, presence of constipation, change in bowel habits within the last three months, defecation frequency, time of daily defecation, time spent in the toilet, reading in the toilet (mini electronic device use), and the type of toilet used (sitting-squatting). Constipation is defined as less than 3 times stool discharge per week in epidemiological studies. However, more than half of the patients who stated that they defecated less than 3 times, they had bowel movements. Irregular defecation is called straining during defecation or incomplete defecation and fitful defecation periods.[8] The assessment of participants reporting constipation was conducted according to the Rome IV criteria.[9]

The exclusion criteria included individuals with a history of colorectal surgery and those who had inflammatory bowel disease, chronic metabolic diseases, endocrine and neurological disorders.

Statistical Analysis

Such descriptive statistics as the arithmetic mean, standard deviation, minimum and maximum values for the participants' age variable were put forth within the scope of data collected through questionnaires while cross tables were presented so as to include percentages and frequency figures for categorical data. The chi-square tests were used to investigate whether there were differences among the groups within the framework of cross table assessments. In addition, the calculations were made using Exact or Monte Carlo methods depending on the number of data and the type of table in the chi-square test. Statistical significance was determined as 5% and the analyses were conducted with the SPSS software version 22.

RESULTS

A total of 425 individuals were included in the study. Of these 140 were first year, while 186 were third year and 99 were sixth year medical students. Among the first year students 47 were male and 93 were female, while their mean age was 18.36. 88 of the third year students were male, while 98 were female and their mean age was 21.56. 55 of the sixth year students were male, while 44 were women and their mean age was 23.82.

2.86% of the students reporting constipation were first year students, 7.53% were third and 9.09% were sixth year students. Change in bowel habits within the last three years was 32.86%, 34.95% and 38.39% in first, third and sixth year students respectively.

When defecation frequency was investigated it was seen that a frequency of more than three times a week was dominant. While the third year students defecated every other day, first and sixth year students defecated rather daily. Most of the groups' defecation frequency was within normal limits.

When the time of daily defecation was investigated it was observed that this was more irregular. The rate of irregular defecation was high in all groups and this was statistically significant ($p<0.020$). The constipation rate was higher in groups with irregular defecation. While the rate of irregular defecation was 72.1% among the first year students, 2% of them were constipated. While the rate of irregular defecation was 55.4% among the third year students, 5.8% of them were constipated. While the rate of irregular defecation was 57.6% among the sixth year students, 10.5% of them were constipated. These results may have been affected by the intense physical activity of the 6th grade internship program and the stress factors that the exam prepared for postgraduate medical education may have caused in 6th grade students compared to other groups. It was also observed that those who had regular defecation did so more in the mornings.

When time spent for defecation was investigated, it was seen that it was mostly less than 10 minutes. The percentage of those who spent more than 30 minutes in the toilet was 2.1% among the first year students, 1.1% among the third and 1% among the sixth year students.

Reading in the toilet (mini electronic device use) rates were 32.86%, 34.95% and 38.39% for first, third and sixth year students respectively. The difference among the groups, however, was not statistically significant. The results of our study revealed no correlation between reading in the toilet and constipation.

When the types of toilet preferences were investigated, no significant difference was seen between the preference for alla turca and alla franca toilets. However more than half of the students preferred the former. Toilet preference had no effect on constipation. Those who used the alla franca toilets spent more time in the toilet. This was also found to be statistically significant. All the collected data has been summarized in Table 1.

DISCUSSION

It is not possible to classify bowel habits. In other words, normal bowel order is not uniform. Numerous factors and personal characteristics may affect bowel habits. Moreover there is only a limited number of studies on identifying bowel habits in literature. Yet such studies only reflect the characteristics of the society they were conducted in. Changes in bowel habits may also cause constipation.[10] Slowing down in bowel movements result in constipation. Constipation is usually defined as the slowing down of intestinal content in its movement from the proximal to the distal. Such slowing down is generally observed in the colon. It is more distinct in the distal part of the colon.[11] All these events are referred to as chronic constipation. Colorectal malignity; neurologic, metabolic and endocrine disorders and chronic medication play a significant role in chronic constipation occurring secondary to another reason. The overall prevalence of constipation in the general population is approximately 15%.[12] Age and sex are held responsible as the two important factors. The most significant step of treatment modalities for constipation is to fix bowel habits. The prevalence of constipation in the study groups was 6.35%. The results of our study also revealed that the frequency of constipation increased as the year in medical school advanced. Constipation rates in our study, however, were lower than those reported in literature. The most important reason why this rate was found to be lower than those of literature was that the study was conducted with young and healthy active individuals. Our results showed some increase as age went up. The most significant disadvantage of our study group was that they spent more time on the toilet.

Table 1. Toilet habits

	Year			p
	Year 1 (n: 140)	Year 3 (n: 186)	Year 6 (n: 99)	
Age: mean±s.d (min-max))	18.37±0.703 (17-21)	21.56±1.909 (20-43)	23.82±0.850 (22-27)	
Defecation frequency (n (%))				0.115
Daily	116 (82.9%)	141(75.8%)	68 (68.7%)	
Every other day	21 (15.0%)	33 (17.7%)	24 (24.2%)	
Every three days	1 (0.7%)	10 (5.4%)	6 (6.1%)	
Once a week	1 (0.7%)	2 (1.1%)	1(1.0%)	
More than seven days	1 (0.7%)	0 (0.0%)	0 (0.0%)	
Time of defecation (n (%))				0.020*
Morning	22 (15.7%)	49 (26.3%)	24 (24.2%)	
Noon	2 (1.4%)	6 (3.2%)	7 (7.01%)	
Evening	15 (10.7%)	28 (15.1%)	11 (11.1%)	
Irregular	101 (72.1%)	103 (55.4%)	57 (57.6%)	
Time spent in the toilet (n (%))				0.125
Less than 5 mins	72 (51.4%)	78 (41.9%)	38 (38.4%)	
5-10 mins	52 (37.1%)	93(50.0%)	47 (47.5%)	
10-20 mins	7 (5.0%)	9 (4.8%)	11 (11. %)	
20-30 mins	6 (4.3%)	4 (2.2%)	2 (2.0%)	
More than 30 mins	3 (2.1%)	2 (1.1%)	1 (1.0%)	
Change in bowel habits (n (%))				0.685
Yes	19 (13.6%)	31 (16.7%)	17 (17.2%)	
No	121 (86.4%)	155 (83.3%)	82 (82.8%)	
Reading in the toilet (n (%))				0.836
Yes	47 (33.6%)	65 (34.9%)	37 (37.4%)	
No	93 (66.4%)	121 (65.1%)	62 (62.6%)	
Which type of toilet do you use?				0.867
Alla turca	72 (51.4%)	101 (54.3%)	52 (52.5%)	
Alla franca	68 (48.6%)	85 (45.7%)	47 (47.5%)	
Sex (n (%))				0.002*
Male	47 (33.6%)	88 (47.3%)	55 (55.6%)	
Female	93 (66.4%)	98 (52.7%)	44 (44.4%)	
Are you consti- pated? (n (%))				0.103
Yes	4 (2.9%)	14 (7.5%)	9 (9.1%)	
No	136 (97.1%)	172 (92.5%)	90 (90.9%)	

*(p<0.05)

Defecation training is very important for patients with chronic constipation. Such individuals need to reorganize their lifestyles. A well-balanced diet with sufficient fibrous food and liquid is effective in preventing constipation.[13] Chronic diseases and medication to treat these trigger constipation. Abuse of laxatives have a negative effect on bowel habits. A well-balanced diet is important in fixing bowel habits. The gastrocolic reflex after eating, particularly after breakfast, facilitates defecation.[14] Defecation after eating is recommended to capitalize on this reflex. A great majority of our cases did not have defecation habits, on the contrary, they had irregular defecation habits. Most of our cases with regular defecation did so in the mornings. We believe that regular bowel habits would be challenging for groups involved in busy education and training schedules like those of medical schools. We, however, observed that medical training did not reduce the frequency of constipation. Chronic medication administration was very low in our age group.

Data on time spent in the toilet or restrooms are very limited in literature. Researchers have usually reported that it was less than 10 mins.[15] Yet there is no exactly accurate and widely accepted conception on time. It varies due to social and personal characteristics. Such time is affected by many factors such as constipation, perianal diseases, age, sex, lifestyle, chronic diseases and medication. Studies in literature have suggested that sitting on the toilet for a prolonged period of time rendered individuals to be more prone to contracting benign anorectal diseases like hemorrhoidal disease.[16] The results of such studies have also indicated that patients with hemorrhoids opted for spending more time in the restroom and their reading in the toilet rates were higher. Pelvic floor dyssynergia makes up about half of functional constipation cases. Pelvic floor dyssynergia is recognized as a behavioral problem that may be exacerbated in the presence of emotional stress.[17,18] The primary way to increase the quality of life for a significant part of the population affected by constipation is bowel habit training. The results of our study showed that 89% of the first year medical students, 92% of the third years and 86% of the sixth years spent less than 10 minutes in the toilet. These figures corresponded to those accepted for healthy individuals.

Studies on reading in the toilet has recently been on the rise in literature. Such behavior, however, goes as high as 40% particularly in western societies.[19] This rate is much higher in the male sex. Interestingly this rate is higher within the more educated and higher socio-economic classes and it affects the time spent in the toilet.[20] When we referred to reading in the toilet, we indicated telephone use, meaning the use of mini electronic devices rather than reading newspapers or magazines. This rate varied between 33.6% and 37.4% in our study.

Data on toilet use or bathroom behavior are quite limited in literature. Studies are usually on the results of defecation in squatting or sitting positions. Such studies report more positive results for defecation while squatting.[21] The results of our study revealed that alla turca toilets (squatting position) were preferred more by the participants. We believe that this result was brought about by the material conditions of toilets or social habits.

CONCLUSION

Constipation is seen less in the young population than the elderly population. Bowel habits vary according to societies and personal characteristics. Constipation was observed more in individuals with irregular bowel habits within the scope of our study. We think that more frequent irregular stools, especially in 1st and 6th grade medical students, may be due to seasonal factors. Reading books in the toilet or the use of telephone and mini electronic devices are becoming common among medical students in our country as well as all over the world. Its prevalence is similar to that of the developed countries. Reading in the toilet elongates the time spent in the toilet. The relationship between bowel habits and constipation in medical students is likely to be revealed by more comprehensive, multifactorial and multicenter studies..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Necmettin Erbakan University Meram Medical Faculty Clinical Researches Ethics Committee (Date: 2018, Decision No: 1603).

Informed Consent: Written consent was obtained from the patient participating in this study

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Profile of critically ill childrenin the pediatric intensive care unit: a tertiary-care single-center experience

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ABSTRACT

Aims: The aim of this study was to present a comprehensive overview of the clinical spectrum and outcomes of critically ill pediatric patients admitted to a tertiary-level pediatric intensive care unit (PICU). Furthermore, we aimed to assess potential factors that could influence the requirement for PICU admission. The findings of this study may aid in the prompt identification and management of critically ill pediatric patients, thereby reducing the likelihood of PICU admission.

Methods: This descriptive study investigated the presentation of critical illness among pediatric patients aged between 1 month-18 years old admitted to the PICU was conducted in Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital, from February 2022 to January 2023. Demographic data, clinical variables, and outcome data (alive/expired) were analyzed.

Results: A total of 456 patients were analyzed, of which 258 (56.6%) were males and 198 (43.4%) were females. The median length of stay in the PICU was 5 days (1-114). Respiratory diseases (43.2%) were the most common reasons for admission to the PICU, followed by sepsis (13.2%), and neurological diseases (13.8%). We observed a mortality rate of 6.1%, with no association with age or sex. Variables found to be risk factors for mortality were PRISM III score, presence of sepsis and acute renal failure, the requirement for mechanical ventilation, use of inotropic agents, continuous renal replacement therapy and therapeutic plasma exchange requirement, and length of stay ($p < 0.001$).

Conclusion: The profile of patients admitted to the PICU can serve as a basis for developing dedicated protocols for critical care and redistributing the PICUs' resources.

Keywords: Critical illness, intensive care unit, mechanical ventilation, mortality, sepsis

INTRODUCTION

Caring for critically ill children remains one of the most challenging and important issues all around the world, despite the ever-improving modern medical facilities. According to World Health Organization's global health observatory data, the global under-5 mortality rate reached 5 million in 2020, although it has decreased over the years.[1] Millions of children's lives can be saved each year by providing essential pediatric intensive care services such as fluid resuscitation, basic antibiotic support, oxygen, and mechanical ventilator support.[3] With the pediatric intensive care unit (PICU) first established in Goteborg Children's Hospital in Sweden in 1955, the history of pediatric intensive care has a very short history as a branch of medicine.[2] Since then, PICUs have expanded rapidly. It is a wise and practical method to benefit from old experiences when establishing new PICUs or developing existing PICUs.

In this study, we aimed to report the clinical spectrum, and outcomes of critically ill children admitted to a tertiary pediatric intensive care unit in Turkey, and to evaluate the factors that may be effective in the need for PICU, and accordingly to help early diagnosis and treatment response to reduce the possible need for PICU.

METHODS

This study was conducted in accordance with the Declaration of Helsinki. The study's protocol was approved by the Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (Date: 15.02.2023, Decision No: 2023/27), and all study-related anonymized data are available upon reasonable request.

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This retrospective study was conducted in the PICU at Sancaktepe Training and Research Hospital, Health Science University between February 2022 and January 2023. Healthcare provision for children aged from 1 month to 18 years is provided in our PICU, which is equipped with 12 beds, 12 ventilators, 5 Prismaflex™ hemofiltration machines (Baxter, USA), and 9 isolation rooms.

Demographic data (age, gender), clinical variables (admitting diagnosis, Pediatric Risk of Mortality III score, co-morbidity, length of PICU stay, presence of acute renal failure and sepsis, culture positivity, PICU therapies like mechanical ventilation, use of inotropes, extracorporeal therapy), and outcome data (alive/expired) were collected. Length of stay (LOS) in PICU is classified as ≤7 days, and >7 days. For age analysis, we adopted the following stratification: <1 year, 1-5 years, 5-10 years, and >10 years. Pediatric risk of mortality III (PRISM III) score corresponding to the first 24 hours of hospitalization were calculated according to the equation described by Pollack et al.[4]

Statistical Analysis

SPSS statistical software 20.0 for Windows was used for statistical analyses. Numbers, frequencies [%], ratios, medians, and ranges were used in the descriptive statistics of the data. Continuous variables were tested for normal distribution by Kolmogorov-Smirnov or Shapiro-Wilk test. For analyzes of continuous data, t-test or Mann–Whitney U test was performed to detect differences between the groups, depending on the distribution. Relationships between categorical variables were analyzed by Chi-square test. When Chi-square assumptions were not met, Fisher's exact test was used

RESULTS

During the study period, the total number of children admitted to our PICU was 456. The median age was 38.5 (1-272) months. The majority of the patients (32.2%) were aged 1-5 years, followed by children under the age of 1 (28.5%), and 56.6% were male. A total of 130 patients had co-morbid disease (28.5%), the most common neurological (39.2%), followed by respiratory (11.5%) and hemato-oncological diseases (9.2%). Respiratory diseases such as pneumonia (43.2%) and asthma attacks were the most common reasons for admission to the PICU, followed by sepsis (13.2%), and neurological diseases (13.8%) such as epilepsy and encephalitis. Given that we are in the pandemic period, only 6.1% of patients were Coronavirus disease (COVID-19) polymerase chain reaction (PCR) positive.

The median length of stay in PICU was 5 days, ranging from 1 to 114 days, and 28.5% had hospitalizations longer than 7 days. The median PRISM III score was 2 (0-40).

Table 1. Demographics of patients admitted to pediatric intensive care

	n (%)
Gender	
Male	258 (56.6)
Female	198 (43.4)
Age (month), median (range)	38.5 (1.0-272.0)
Age wisedistribution (month)	
1-12	130 (28.5)
13-60	147 (32.2)
61-120	70 (15.4)
>120	109 (23.9)
Weight, median (range)	15.0 (2.5-215.0)
Comorbiddiseases	
Neurologicaldiseases	51 (39.2)
Respiratorydiseases	15 (11.5)
Hematology-oncologicaldiseases	12 (9.2)
Immunodeficiency	10 (7.7)
Endocrinologicaldiseases	9 (6.9)
Geneticsyndromes	8 (6.2)
Cardiologicaldiseases	7 (5.4)
Metabolicdiseases	7 (5.4)
Chronicrenalfailure	7 (5.4)
Chronicliverfailure	3 (2.3)
Gastrointestinaldiseases	1 (0.8)
Etiologies of admission	
Respiratorydiseases	197 (43.2)
Neurologicaldiseases	63 (13.8)
Sepsis	60 (13.2)
Intoxication	39 (8.6)
Trauma	36 (7.9)
Endocrinologicaldiseases	21 (4.6)
Acuterenalfailure	9 (2.0)
Postoperativeadmissions	8 (1.8)
Cardiologicaldiseases	8 (1.8)
Hematology-oncologicaldiseases	6 (1.3)
Metabolicdiseases	2 (0.4)
Others	7 (1.5)
COVID-19 PCR positivity	28 (6.1)

COVID-19 :Coronavirus 19 PCR: polymerasechainreaction

Invasive mechanical ventilation (IMV) was required in 129 patients (28.3%), and the median duration of IMV was 6 (1-102) days. A total of 237 patients (52.1%) required non-invasive mechanical ventilation (NIMV) support during their stay in PICU. NIMV support was required after extubation in 21.2% of the patients. High-flow nasal oxygen therapy was given in 82.7% of the patients as NIMV support, followed by NIMV-pressure control in 10.5% and NIMV-pressure support in 6.8%. The median duration of NIMV was 3 (1-29) days.

Of the hospitalized patients, 25.7% had sepsis and 13.0% had acute renal failure. Inotropic drugs were used in 58 patients (12.7%). While therapeutic plasma exchange (TPE) was performed on 42 patients (9.2%), continuous renal replacement therapy (CRRT) was performed on 35 patients (7.7%).

Table 2. Clinical characteristics of patients admitted to pediatric intensive care

	n (%)
Length of stay (day), median (range)	5 (1-114)
Length of staywisedistribution	
≤7 days	326 (71.5)
>7 days	130 (28.5)
Sepsis	117 (25.7)
Development of acuterenalfailure	59 (13.0)
Requirement of IMV	129 (28.3)
Length of stay on IMV (day), median (range) (n=129)	6 (1-102)
Requirement of NIMV	
Yes	237 (52.1)
No	218 (47.9)
NIMV duration, median (range)	3 (1-29)
NIMV modality	
AIRVO	196 (82.7)
NIV-PCV	25 (10.5)
NIV-PSV	16 (6.8)
NIMV	
Inisial	186 (78.8)
Postextubation	50 (21.2)
Requirement of CRRT	35 (7.7)
Requirement of inotropicagents	58 (12.7)
Requirement of TPE	42 (9.2)
PRISM III score	2 (0-40)
Mortality	28 (6.1)

CRRT: Continuousrenalreplacementtherapy, IMV: Invasivemechanicalventilation, NIMV: Noninvasivemechanicalventilation, PRISM III: Pediatric Risk of Mortality, TPE: Therapeuticplasmaexchange

Table 3. Relationship between age groups and clinical characteristics

	Age groups (monthes)				p
	1-12	13-60	61-120	>120	
PRISM III score, median (range)	2 (0-22)	2 (0-39)	4 (0-28)	2 (0-40)	0.149
Length of stay>7 day, n (%)	40 (30.8)	43 (29.3)	24 (34.3)	23 (21.1)	0.218
Mortality, n (%)	6 (4.6)	9 (6.1)	5 (7.1)	8 (7.3)	0.821
ARF, n (%)	8 (6.2)	21 (14.3)	10 (14.5)	20 (18.3)	0.037
Requirement of CRRT, n (%)	4 (3.1)	13 (8.8)	8 (11.4)	10 (9.3)	0.115
Requirement of IMV, n (%)	32 (24.6)	42 (28.6)	25 (35.7)	30 (27.5)	0.423
Sepsis, n (%)	31 (23.8)	34 (23.3)	21 (30.0)	31 (28.4)	0.618
Requirement of inotropicagents, n (%)	10 (7.7)	20 (13.6)	13 (18.6)	15 (13.8)	0.149
Requirement of TPE, n (%)	1 (0.8)	14 (9.5)	12 (17.1)	15 (13.8)	<0.001

PRISM III: Pediatric Risk of Mortality, ARF: Acute renal failure, CRRT: Continuous renal replacement therapy IMV: Invasive mechanical ventilation TPE: Therapeutic plasma exchange

The mortality rate was 6.1% (n: 28) and was not associated with age or sex. Variables found to be risk factors for mortality were PRISM III score, presence of sepsis and acute renal failure, the requirement for mechanical ventilation, use of inotropic agents, CRRT and TPE requirement, and length of stay (p<0.001).

Table 4. Relationship between gender and clinical characteristics

	Gender		p
	Male	Female	
PRISM III score, median (range)	2 (0-30)	2 (0-40)	0.898
Length of stay>7 day, n (%)	73 (28.3)	57 (28.8)	0.908
Mortality, n (%)	14 (5.4)	14 (7.1)	0.468
ARY, n (%)	26 (10.1)	33 (16.7)	0.039
CRRT, n (%)	16 (6.2)	19 (9.6)	0.172
Requirement of IMV, n (%)	71 (27.5)	58 (29.3)	0.677
Sepsis, n (%)	62 (24.1)	55 (27.8)	0.377
Requirement of inotropicagents, n (%)	34 (13.2)	24 (12.1)	0.737
Requirement of TPE, n (%)	23 (8.9)	19 (9.6)	0.803

PRISM III: Pediatric risk of mortality, ARF: Acute renal failure, CRRT: Continuous renal replacement therapy IMV: Invasive mechanical ventilation TPE: Therapeutic plasmae xchange

In univariate analyzes for different age groups, there was a statistically significant relationship between the age group older than 120 months and the presence of acute renal failure and TPE requirement. However, in univariate analyzes for gender, only female gender and the presence of acute renal failure was found to be statistically significant. When the etiologies of PICU admission or co-morbid diseases and their relationship with the outcome were examined, no statistical significance could be found due to the low number of patient subgroups.

Table 5. Relationship between outcomes and clinical characteristics

	Outcome		p
	Mortality, n (%)	Survival, n (%)	
Length of stay			<0.001
≤7 day	9 (2,8)	317 (97,2)	
>7 day	19 (14,6)	111 (85,4)	
ARF			<0.001
Yes	15 (25,4)	44 (74,6)	
No	13 (3,3)	383 (96,7)	
Requirement of CRRT			<0.001
Yes	14 (40,0)	21 (60,0)	
No	13 (3,1)	407 (96,9)	
Requirement of IMV			<0.001
Yes	28 (21,7)	101 (78,3)	
No	0 (0,0)	327 (100,0)	
Sepsis			<0.001
Yes	24 (20,5)	93 (79,5)	
No	4 (1,2)	334 (98,8)	
Requirement of inotropicagents			<0.001
Yes	26 (44,8)	32 (55,2)	
No	2 (0,5)	396 (99,5)	
Requirement of TPE			<0.001
Yes	11 (26,2)	31 (73,8)	
No	17 (4,1)	397 (95,9)	
PRISM III score, median (range)	17,5 (3-40)	2 (0-30)	<0.001

PRISM III: Pediatric risk of mortality, ARF: Acute renal failure, CRRT: Continuous renal replacement therapy IMV: Invasive mechanical ventilation TPE: Therapeutic plasmae xchange

DISCUSSION

Care of critically ill patients requires broad-based knowledge to achieve good outcomes. Advances in pediatric critical care medicine have improved the survival rates of children in recent years. During the 12-month study period, 456 children, mostly aged 1-5 years, were admitted to our PICU, comparable to other tertiary PICUs in the country.[9] The median duration of stay in the PICU was found to be 5 days. Consistent with a study by Rady et al.[11] , 71.5% of patients were hospitalized for less than 7 days.

Respiratory diseases were the major causes of admission to our PICU, followed by sepsis and neurological diseases. Similarly, as a result of many studies, respiratory system diseases were reported as the most common reason for hospitalization in the intensive care unit.[3,5,6] However, Blessing et al.[7] reported cardiovascular disease (41.1%) as the most common cause of admission. In another study conducted in Pakistan, the most common hospitalization diagnosis was post-cardiac surgery (34%).[8] The reason for this difference can be explained by the lack of a fully equipped cardiovascular surgery team in different facilities. Therefore, clinicians should know the current conditions for the development of facilities and prepare treatment protocols accordingly.

Studies show that the presence of concomitant chronic disease in intensive care patients is effective on mortality and morbidity, and prolongs hospital stay. Poyrazoglu et al.[12] reported that the most common co-morbid disease in patients hospitalized in PICU was neurological disease (34.7%). We also found neurological diseases (39.2%) as the most common chronic disease in our patients. These results show that a significant proportion of intensive care hospitalizations are children with chronic diseases. For such patients, the opening of intermediate intensive care units in addition to the existing intensive care units in hospitals will allow more effective use of intensive care beds.

In previous studies, it has been reported that the requirement of IMV varies between 30-80%.[17,18] The frequency of IMV administration in our study was lower (29.4%) than in other studies. The findings in our study could be attributed to the development of NIMV technology, the frequency of its use, and the reduction in the requirement of IMV in recent years. Multiple NIMV modalities have been identified that could improve the prognosis of pediatric patients with respiratory failure. However, the effect of different modalities of NIMV on children's prognosis remains inconclusive. Many studies aimed to evaluate the efficacy of various NIMV strategies including high-flow nasal cannula (HFNC), bilevel-positive airway pressure, and standard oxygen therapy in children in need of respiratory support.[19,20] Boghi et al.[20] showed that in pediatric patients, NIMV can reduce the rate of intubation compared to standard oxygen therapy or HFNC. Nevertheless, no difference in mortality was observed between modalities. In our study, the requirement for NIMV was 52.1%. However, due to insufficient data on NIMV success, which limited our study, unsuccessful NIMV cases could not be evaluated.

Intensive care mortality is one of the important data in determining the success of PICU. Overall mortality in this study was 6.1%, regardless of age. Although some studies revealed a relationship between age groups and the outcomes of pediatric patients, no statistically significant difference was found between age groups in terms of mortality in our study.[10,11] Various factors and scoring systems are used to predict mortality in the PICU. In our study, PRISM III score, presence of sepsis and acute renal failure, the requirement for mechanical ventilation, use of inotropic agents, need for CRRT and TPE, and length of hospital stay were found to be factors affecting mortality. In many studies, it has been reported that mortality is statistically higher in patients with a high PRISM III score and that the requirement of inotropic agents and mechanical ventilation in the intensive care unit increases the mortality of patients.[13,14] They emphasized that it should be evaluated together with disseminated intravascular coagulation, multi-organ failure, and the need for mechanical ventilation, which are effective on mortality.[16]

CONCLUSION

Epidemiologic analysis of the profiles of patients admitted to PICU shows different etiologies for admission; however, it is seen that a significant portion of inpatients has chronic diseases. It has been concluded that the limited number of intensive care beds could be used more effectively for critically ill patients, through palliative rehabilitation centers that can be established in the near future for such patients.

In addition to the fact that the number of intensive care beds for children in our country should be increased; consideration should be targeted to intensive care units with a 24-hour accessible pediatric intensive care specialist, sufficient technical equipment and support staff, and easy access to other branches.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was approved by the Sancaktepe Sehit Prof. Dr. İlhan Varank Training and Research Hospital Ethics Committee (Date: 15.02.2023, Decision No: 2023/27).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Aortic valve regurgitation frequency following catheter ablation of premature ventricular complexes originating from coronary cusps

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ABSTRACT

Aims: There are conflicting results about the effect of radiofrequency catheter ablation (RFA) of aortic cusp premature ventricular complexes (PVCs) on aortic valve regurgitation (AR). We aimed to investigate the effect of aortic valve function and integrity of RFA of coronary cusp PVCs.

Methods: This cross-sectional study included 54 patients who underwent RFA of the aortic cusp region within the specified indications. Basal echocardiography was performed at baseline and 3 months after radiofrequency catheter ablation of aortic cusp PVCs. An increase of more than 1 degree in AR was considered significant.

Results: The mean age of the patients was 44.6±12.0 years and the male gender ratio was 42.6%. On 24-hour rhythm holter monitoring, the mean VES burden was 21.5%, of which 12.9% were right coronary cusp (RCC), 59.3% left coronary cusp (LCC), and 27.8% RCC-LCC junction. Total procedure time was 136.9±33.2 minutes and RFA time was 14.9±11.4 minutes. When pre- and post-ablation parameters were compared, left ventricular ejection fraction was found to be higher after the procedure than before the procedure ($p<0.001$). There was no statistically significant increase in the degree of AR before and after the procedure ($p>0.05$).

Conclusion: There was no increase in the degree of AR as a procedure-related complication and no significant AR was determined in patients who underwent RFA for PVCs in the aortic cusp region. Therefore, it can be concluded that VES ablations in the aortic cusp region are safe for the development of AR.

Keywords: Premature ventricular complexes, radiofrequency ablation, aortic cusp, aortic regurgitation

INTRODUCTION

Premature ventricular complexes (PVCs) are extremely common in general population. PVCs has a prevalence of 1-4% of the general population on standard electrocardiogram 12 leads, even it may reach 40-75% of subjects undergoing Holter monitoring.[1] PVCs may cause symptoms as palpitation, discomfort in chest or neck, strong heartbeat sensation, feeling of heart stopping, presyncope, dyspnea, fatigue. But the most feared complication of PVCs is PVC- induced cardiomyopathy (PVC-CMP). The treatment goal of the PVC s is not only decreasing the symptom burden of the patient but also preventing the PVC-CMP development or if exists reversing the CMP. Coronary cusp originated PVCs constitutes an important and common site for PVCs. Although different percentages are reported at different studies; 37% of PVCs originates from right ventricular outflow tract, 25% of from coronary cusp, 3% of from aortomitral continuity, 10% of from left ventricular (LV) summit/epicardial, 8% of from parahisian and 3% of from multiple foci.[2]

Treatment strategies for PVCs are radiofrequency catheter ablation (RFA) and medical treatment. Rarely seen complications of RFA are vascular access site hematoma, pericardial effusion, injury of coronary artery or veins, atrioventricular complete block. There are not many studies studying effect of RFA on aortic valve functions and integrity. Minich et al.[3] demonstrated a 30% increase in the incidence of aortic valve regurgitation (AR) after RFA of left-sided accessory connection. Edward et al.[4] reported that cusp ablation did not cause aortic valve dysfunction. Kis Z et al.[5] reported a case that aortic valve leaflet rupture following RFA of LV originated PVCs at a 72 years old man. Although studies have included ablations performed with conventional and 3D mapping, data on procedures performed in the 3D mapping era are limited.

We aimed to investigate the effect of aortic valve function and integrity of RFA of coronary cusp PVCs.

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METHODS

Ethics

The study protocol was approved by the Bursa High Specialization Training and Research Hospital Clinical Researches Ethics Committee (Date: 03.2020, Decision No: 2011-KAEK-25 2020/03-21). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Population

A total of 54 consecutive patients who underwent catheter ablation for PVCs were enrolled in this study at Bursa High Specialization Training and Research Hospital. Inclusion criteria were as follows: 1) patients with frequent PVCs as indicated by a total PVC count of >10000 beats during 24-h Holter electrocardiography monitoring, 2) patients having LV ejection fraction (LVEF) <50%, 3) patients who were resistant to antiarrhythmic drugs, beta blockers, or nondihydropyridine calcium channel blockers (for at least 6 months), 4) patients aged >18 years. The ablation procedure was considered to be successful when there was >80% decline in PVCs with the same morphology during 24-h electrocardiogram (ECG) holter monitorization at the 3-month follow-up. Exclusion criteria of this study were follows: 1) ischemic cardiomyopathy, severe valvular heart disease, LV hypertrophy and other cardiomyopathies 2) people referred to anti-arrhythmic drug treatment. Demographic, clinical, and laboratory characteristics of the study patients were recorded from patient files. Electrocardiography or 24-h ECG Holter recording electrocardiography data of the entire study population were also obtained. Details of the study were explained to patients and written informed consent was obtained before participation.

Echocardiography

Two-dimensional transthoracic echocardiography (Philips i33, Eindhoven, The Netherlands) was performed before and three months after the ablation procedure in accordance with the guidelines of the American Society of Echocardiography 6. A standard examination protocol was followed by a detailed assessment of the LV diastolic and systolic functions and left atrium (LA) functions. LVEF was determined by the biplane Simpson method. LV diastolic functions (LVDD) were assessed by pulsed-wave Doppler analysis of the diastolic mitral inflow and Tissue Doppler imaging of the LV wall at the basal segments of the lateral and septal walls. Conventional Doppler parameters along with LVDD grading were assessed, calculated, and recorded. Structure of the aortic valve, coaptation features, presence of AR and degree of regurgitation (classified as non-AR, mild-AR, moderate-AR, and severe-AR) were evaluated by echocardiography. One or more degree increase in the AR was accepted significant. These patients with significant increase in AR were evaluated by trans-esophageal echocardiography (TEE) after the patients' informed consent was taken.

Electrophysiological Study and Radiofrequency Catheter Ablation Procedure

All antiarrhythmic drugs, except amiodarone, were discontinued for five half-lives before the procedure. Endocardial signal and surface electrocardiography data were recorded using the EP Tracer device (Medtronic, Inc., USA). A 3D electro-anatomic map was plotted using the CARTO 3 D Mapping System (Biosense-Webster, CA, USA), NAVX (St Jude Medical, MN, USA) or by noncontact mapping (Ensite Array, St Jude Medical). All mapping was performed after heparin bolus, maintaining an activated clotting time ≥200 s. The aortic cusp sites were mapped via a retrograde aortic approach. If no PVCs were detected or in case of only rare PVCs, intravenous isoproterenol (1–3 μg/min) was administered to facilitate the detection of PVCs. Ablation was performed using an irrigated-tip catheter contact sense catheter (Thermo-cool-Smart Touch, Biosense-Webster, Inc., CA, USA), an open-irrigated noncontact sense catheter (3.5-mm tip Thermocool or Thermocool SF, Biosense-Webster), and a FlexAbility catheter (Endosense / Abbott, St. Paul, Minnesota, USA). The target site for the ablation was determined by the earliest bipolar electrogram preceding the QRS onset, the initial QS morphology for unipolar electrogram during PVCs and/or the excellent pace map (>11/ 12 leads). When the earliest ventricular activation site was recorded at the aortic cusp, selective angiography of the coronary artery and aorta was performed to assess the anatomical relationships between these structures and the location of the ablation catheter. Acute ablation success was defined as the absence of the clinical PVC at 30 min after the last RFA delivery.

Follow-Up

After three months following the ablation of PVCs two-dimensional transthoracic echocardiography was performed. One or more degree increase in the AR was accepted significant. These patients with significant increase in AR were evaluated by TEE.

Statistical Analysis

All statistical analyses were performed using the SPSS 23.0 software package for Windows, version 23.0 (IBM Corp., Armonk, New York, United States). Whether the distribution of continuous variables was normal or not was evaluated with the Kolmogorov–Smirnov test. Continuous variables were expressed as mean±SD or median (interquartile range). Categorical variables were expressed as numbers and percentages. Paired samples

t-test and Wilcoxon signed rank test were used to compare the variables in pre-ablation and post-ablation period. Relationship among post-ablation AR status and LVEF value, procedure time, total RFA duration and maximum RFA output were determined using correlation analysis and Spearman correlation coefficient was reported. P-value <0.05 was considered significant.

RESULTS

Fifty-four consecutive patients were enrolled in the study. The mean age of the patients was 44.6±12.0 years and the male gender ratio was 42.6%. The detailed demographic, clinical and laboratory characteristics of the study population are summarized in Table 1. PVCs originate from right coronary cusp (RCC) in %12.9 of patients, left coronary cusp (LCC) in %59.3 of patients, RCC-LCC commissure in % 27.8 of patients. Total procedure time was 136.9±33.2 minutes and RFA time was 14.9±11.4 minutes.

Changes in echocardiographic parameters after RFA were summarized in Table 2. Statistically significant increases were observed in the LVEF, mitral A wave after RFA. There is not a remarkable change in post-ablation AR degree when compared to pre-ablation values (p<0.05). In a patient with moderate AR before ablation, no worsening was observed three months after RFA and this was confirmed by TEE. Post-procedural complication rate was 1.9% with vascular access site hematoma at one patient.

DISCUSSION

This study revealed that there is not any increase at AR degree and presence after RFA of cusp PVCs.

RFA itself, through electrical heating, causes myocardial damage. Histologically, this damage results in coagulation necrosis of the myocardium, basophilic staining with evidence of intracellular calcium overload, contraction bands in the sarcomeres and nuclear pyknosis.[7] In the eighth week after ablation, the necrotic area is replaced by fibrotic tissue, adipose tissue, and cartilage tissue and may be enveloped by chronic inflammation.[8]

Table 1. Basal characteristics of study population

Variables	All population n=54
Age, years	44.6±12.0
Male gender n (%)	23 (42.6)
Body mass index, kg/m²	24.6±2.9
Risk factors, n (%)	
Diabetes mellitus	7 (12.9)
Hypertension	10 (18.5)
Hyperlipidemia	11 (20.4)
Smoking	16 (29.6)
Prior history of ablation, n (%)	5 (9.3)
ECG findings	
Heart rate, beats/min	69.0±18.0
Intrinsicoid deflection time, ms	71.5±11.6
Max deflection index, %	0.5±0.1
Maxium QRS duration, ms	136.5±9.2
Pseudo-delta, n (%)	7 (13.0)
Ventricular premature complex burden in 24-h Holter monitor, %	21,5 (9.0-33.0)
Cardiovascular drugs, n (%)	
Calcium channel blocker use	17 (31.5)
Beta blocker use	23 (42.60)
Amiodarone use	10 (18.5)
Propafenone use	21 (38.9)
Any antiarrhythmic	45 (83.3)
Anti-arrhythmic medication per patient	1.4±0.7
TSH levels, mIU/L	1.4 (0.5-3.9)
Potassium levels, mEq/L	4.5 (3.4-5.5)
Calcium leves, mg/dL	9.8 (9.0-10.4)
Catheter ablation techniques, n (%)	
Carto	36 (72.2)
Ensite presicion/Nav X	18 (27.8)
Contact force sensing catheter using, n (%)	
Yes	10 (18.5)
No	44 (81.5)
Ablation site, n (%)	
Right coronary cusp	7 (12.9)
Left coronary cusp	32 (59.3)
Right / left coronary cusp	15 (27.9)
Non coronary cusp	0
Procedural parameters	
Ablation success, n (%)	45 (83.3)
Radiofrequency time, min	14.9±11.4
Total procedure time, min	136.9±33.2
Fluoroscopy time, min	16.2±10.7
Average output, W	37.0±7.7
Cardiac tamponade, n (%)	0
Cerebrovascular events, n (%)	0
Hematoma, n (%)	1 (1.9)
Coronary damage, n (%)	0

Data presented as mean±SD or median (interquartile range) or number (%). Abbreviation: ECG, electrocardiogram; TSH, thyroid-stimulating hormone.

Table 2. Changes in systolic, diastolic, and left atrial functions following radiofrequency catheter ablation (RFA)

Variables	Pre-ablation	Post-ablation	p
Left ventricular ejection fraction, %	47.9±5.6	53,4±4,3	<0.001
Left atrium end-systolic antero- posterior diameter, mm	33.4±3.7	31.3±3.7	0.009
Mitral E velocity, cm/sec	81 (63-142)	89 (65-130)	0.079
Mitral A velocity, cm/sec	81 (62-110)	73.50 (55-110)	0.001
E/A ratio	1.1±0.2	1.2±0.3	0.027
DT, msec	188 (165-275)	185 (146-246)	0.069
Ea average, cm/sec	85.8 (70-116)	77 (65-112)	0.083
E/Ea ratio	1.0 (0.8-1.2)	1.1 (0.8-1.3)	0.047
Aortic velocity, m/sec	1.5±0.4	1.5±0.4	0.753

Data presented as mean±SD or median (interquartile range) or number (%). Abbreviation: DT, deceleration time.

There are conflicting results in the literature about the effect of RFA on aortic valve functions and integrity. Mainly two mechanisms are suggested for iatrogenic AR development. One explanation is that; mechanical compression and stretching of the aortic leaflets by the catheter tip and shaft. Catheter inserted into the LV through either the center of the aortic cusps or the non-coronary cusp-RCC commissure with the catheter bent in a "U" shape. This mechanism includes distortion of coaptation area of the aortic valve and results in especially central AR formation. The second explanation is that the RF energy given during ablation disrupts the valve functions based on the changes at the cellular level mentioned above.[9]

In a previous study by Edward et al.[4] assessing the effect of RFA on valves for VES of papillary muscle and valve origin, the presence of AR was evaluated in 84 cases of VES of aortic valve origin. An increase of two or more degrees of AR was considered significant. As a result, no significant change was found in AR levels before ablation and at least 6 months after ablation.[4] In the prospective multi-center AVATAR (Aortic Cusp Ventricular Arrhythmias: Long Term Safety and Outcome from a Multi-center Prospective Ablation Registry) study, 103 patients who underwent ablation of the aortic cusp region for ventricular arrhythmias were evaluated. In the study, "zero fluoroscopy" (using electro-anatomical mapping (EAM) and not using fluoroscopy), "EAM with fluoroscopy" and "conventional fluoroscopy" methods were applied. Aortic valve complications were divided into major (leaflet perforation, significant AR or stenosis) and minor (mild / moderate AR, stenosis, other valve abnormalities). Major complications were never seen, while 16% of patients had clinically non-significant aortic valve degeneration (usually valve margin thickening or fibrosis, less frequently mild AR). Mild/moderate aortic valve thickening and mild AR were not associated with the target ablation site and ablation details. In summary, it is concluded that ablation of the aortic valve area is safe.[10] Hoffmayer et al.[11] did not find any worsening of AR or aortic root complications in a group of patients who underwent ablation of the aortic cusp region under intracardiac echocardiography guidance for ventricular arrhythmia. In our study, similar to the findings of Edward et al.4 and Hoffmayer et al.[11] no clinically significant increase in AR related to the aortic valve was observed after ablation and at 3-month follow-up. In 1 patient, no increase in moderate AR was observed, confirmed by TEE. Minor complications reported in the AVATAR study were not found in our study.

Kis et al.[5] reported a case that aortic valve leaflet rupture following RFA of LV originated PVCs at a 72 years old man. This complication has been attributed to the mechanical effect of the catheter rather than the effect of RFA. In a study by Shinoda et al.[12] involving 32 patients who underwent ablation for idiopathic ventricular arrhythmia originating from the aortic cusp region and evaluating the presence of AR before and after the procedure, mild AR was observed in 6 patients, and there was no significant increase in the degree of AR in those who developed AR at a mean follow-up of 16.0±3.6 months. In addition, no AR was observed in patients who underwent RFA only above the valves.AR presence was found to be related to duration of the procedure and delivered energy amount during RF, with the highest risk with longer duration and highest power RF energy. In conclusion, the development of AR was found to be associated with concomitant and diffuse ablation above and below the valve, and also with mechanical damage due to catheter manipulation. In addition, AR was found to occur from the aortic valve center or the LCC-NCC junction.[12] In our study, we did not observe any degree of regurgitation of the aortic valve or any abnormality in the valve structure due to ablation or any other cause. The mean RFA time was 24.4±14.1 minutes in this study, whereas it was 14.9±11.4 minutes in our study. According to the data obtained from the study, since the development of AR was found to be associated with longer RFA duration, the shorter duration of RFA in our study may be related with the absence of AR development. Our study demonstrated that aortic cusp PVC ablation is a safe procedure with a very low incidence of complications and does not increase AR.

Study Limitations

Some limitations should be taken into cognizance before interpreting the results of the study. Firstly, our study is a single-center study and the number of patients is relatively small. Secondly, intracardiac echocardiography, which is used in some centers, was not used during our RFA procedures. Intra-procedural cardiac imaging may yield different results in the acute phase and procedure planning can be made accordingly. Third, in longer follow-up, it is not clear whether valvular pathology will develop and long-term follow-up results are required. Finally, transthoracic echocardiography or cardiac magnetic resonance imaging may detect newly developing valvular pathologies that are not visible on transthoracic echocardiography. Therefore, the use of these imaging modalities may be considered in selected patients.

CONCLUSION

In our study, no significant AR development was observed in aortic cusp-induced VES ablation. Thus, ablation of PVC originating from the aortic cusp region appears to be a safe procedure with a very low incidence of complications and does not increase AR.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bursa High Specialization Training and Research Hospital Clinical Research Ethics Committee (Date: 03.2020, No: 2011-KAEK-25 2020/03-21).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Original Article

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Comorbidity of lipedema and fibromyalgia; effects on disease severity, pain and health-related quality of life

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ABSTRACT

Aims: Both Fibromyalgia (FMS) and lipedema are characterized by pain in the soft tissue, and they have clinically similar aspects. The aims of this study were to determine how many of the patients with lipedema met the diagnostic criteria for FMS, the effect of the comorbidity of lipedema and FMS on pain and quality of life, and their relationship with extremity volumes, ultrasonographically measured soft tissue thickness and lipedema disease severity.

Methods: 53 women with lipedema and 32 patients with FMS without lipedema were included in the study. Symptom severity scale, widespread pain index, and FMS severity scale were calculated for the diagnosis of FMS. Pain intensity was determined by visual analog scale (VAS). The frequency of fibromyalgia was determined in the lipedema group. Lower extremity volumes of both groups were calculated by circumferential measurements and thigh and pretibial soft tissue thicknesses were measured ultrasonographically. Short form-36 quality of life scale was applied to both groups.

Results: The mean age of the 53 females with lipedema was 52±11.8 years, and for the 32 females with FMS it was 51.9±10.1 years ($p>0.05$). The extremity volumes and soft tissue thicknesses were higher in lipedema group than FMS group $p<0.001$).In lipedema group, 21(39.6%) patients have fulfilled the FMS criteria. FMS severity scores of Comorbid Lipedema and FMS group were similar with FMS patients ($p=0.199$). Bodily pain and VAS were more severe in Comorbid Lipedema and FMS group than lipedema group without FMS and FMS group ($p<0.001$). Generally, Short form-36 components were better in lipedema without FMS group than Comorbid FMS and FMS group ($p<0.05$)

Conclusion: The comorbidity of these two diseases in patients negatively affect their physical and mental functions. Investigation and treatment of comorbid FMS in lipedema patients may contribute to their quality of life and pain.

Keywords: Lipedema, fibromyalgia, soft tissue thickness, ultrasonography

INTRODUCTION

Lipedema is a disease that affects almost exclusively women and is characterized by a disproportionate distribution of abnormal adipose tissue between the extremities and trunk. Edema aggravated by orthostasis, easy bruising by minor trauma, increased sensitivity to pressure, and spontaneous pain are present in most patients. Its onset is usually during periods of hormonal changes such as puberty, pregnancy or menopause. There are no large epidemiological studies to determine the prevalence, but it is estimated to be about 0.1–9.7%.[1]

Fibromyalgia (FMS) is a syndrome that greatly affects quality of life and is characterized by chronic widespread pain, sleep disturbance, fatigue and cognitive impairment. Its estimated prevalence is 2.7%. It is the most important differential diagnosis of chronic soft tissue pain in clinical practice.[2]

FMS and lipedema have many demographic and clinical similarities including widespread pain and obesity.[2-4] Lipedema and FMS both have specific diagnostic criteria and although the diagnosis of lipoedema in stages 2 and 3 is not difficult, it may not be possible to distinguish stage 1 lipedema from FMS, because in stage 1 lipoedema, the skin surface is smooth and the subcutaneous fat tissue thickness is less.[4] These two chronic soft tissue pain syndromes may therefore coexist and be difficult to distinguish. However a few data are available on the frequency of FMS in lipedema patients. Angst et al.[4] showed that %34 lipedema patients have fulfilled American College of Rheumatology (ACR) 2016 FMS criteria.[5]

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Pain is the major complaint in lipoedema, impairing quality of life and correlated with depression. Reducing pain in lipoedema is one of the most important goals of treatment.[6] It is important to distinguish lipedema from FMS and from other chronic pain syndromes. Conservative treatment of lipedema pain is highly controversial, as there is no proven conservative treatment with long-term effectiveness.[6,7] There is no established curative gold standard treatment for lipoedema. Compression garments have some effect on mobility, but the effect on disease progression and pain has not been proven. Lipedema is more resistant to diet and exercise than obesity. Bariatric surgery and liposuction are useful in selected cases.[3] The effect of these treatments on lipedema pain is also unclear. It has been reported that the only effective treatment for lipoedema pain is microcannular tumescent liposuction.[6]

Both FMS and lipedema are diseases characterized by soft tissue pain seen in middle-aged women. Both diseases are chronic diseases with no curative treatment. Both diseases are seen in overweight people and together with depression. There are no abnormal imaging and laboratory findings that can be used in the differential diagnosis of these two conditions.[1-5] As far as we know, in the only study comparing these two chronic soft tissue pain conditions, it was reported that the clinical characteristics of FMS and lipedema were similar, and the perception of disease and comorbidities were more common in FMS patients than in lipedema patients.[4]

The aims of this study were to determine how many of the patients with lipedema meet the diagnostic criteria for FMS, the effect of the comorbidity of lipedema and FMS on pain and quality of life, and their relationship with extremity volumes, USG measured soft tissue thickness and lipedema disease severity. To the best of our knowledge, our study is the first in the literature to evaluate the pain and quality of life of patients with FMS and lipedema, and to investigate the relationship between dermal and subdermal ultrasonographic (USG) measurements and lipedema disease stage.

METHODS

We carried out a prospective cohort study. The protocol of our study approved by Ankara Training and Research Hospital Clinical Researches Ethics Committee (Date: 08.02.2023, Decision No: 1200/2023). The study have been conducted in accordance with the Helsinki Declaration of Principles. All patients included in the study signed the informed consent form.

The inclusion criteria for the study were a confirmed diagnosis of FMS according to ACR 2016 FMS criteria which consist of two anamnestic self-administered scores; The Widespread Pain Index (WPI) and the Symptom Severity Score (SSS) together subsumed in the Fibromyalgia Survey Questionnaire (FSQ). The WPI counts the number of painful body parts from 0 to 19. The SSS ranges from 0 to 12 and the sum of 3 dimensional items scaled 0=absent, 1=mild, 2=moderate, 3=severe/always and referring to: Daily fatigue, waking unrefreshed, cognitive symptoms plus 3 binary yes/no items regarding the presence (=1)/absence (=0) of headache, pain and cramps in the lower abdomen and depression. The diagnosis of FMS requires chronic pain (≥3 months) in 4 of 5 body regions (the 4 quadrants and the spine, assessed by the WPI) together with either (WPI ≥7 and SSS ≥5) or WPI 4-6 and SSS ≥9).[5] We included FMS patients with USG Thigh soft tissue thickness (sum of dermal and subdermal thickness) measurements less than 17.9 and pretibial soft tissue thickness measurements less than 11.7 mm.[8]

Lipedema stage 1- 3 were diagnosed according to S1 guidelines of the German Society of Phlebology. Summary of diagnostic criteria in lipedema; Onset during puberty, pregnancy, or menopause, disproportional proliferation of adipose tissue (extremities, trunk), cuffing around the joints, hands and feet are not affected, feelings of heaviness and tightness in the extremities affected, tenderness to palpation or spontaneous pain – increaising over the course of the day, Edema – increasing over the course of the day, easy bruising, Stemmer's sign negative.[1]

We included FMS patients with USG Thigh soft tissue thickness measurements greater than 17.9 and pretibial soft tissue thickness measurements greater than 11.7 mm.[8]

Exclusion criteria were other type of edema such as lymphedema, phleboedema, renal or hearth insufficiency, using any medication that could affect the body fluid and electrolyte balance, BMI>50, does not know Turkish well enough, low psycho-intellectual abilities, serious somatic disease.

Fifty three lipedema and 32 FMS patients were included in the study. The number of patients who completed the FMS diagnostic criteria in the lipedema group was determined. Demographic features of the patients were recorded. Classification of lipedema by morphological characteristics in arms and legs determined according to lipedema S1 guidelines. Stage 1: smooth skin; homogenous increase in subcotaneous tissue, Stage 2: irregular skin surface (indentations), nodular changes of the subcutaneous tissue, Stage 3: pronounced increase in circumference with loose skin/tissue ('dewlap') (**Figure 1**).[1]

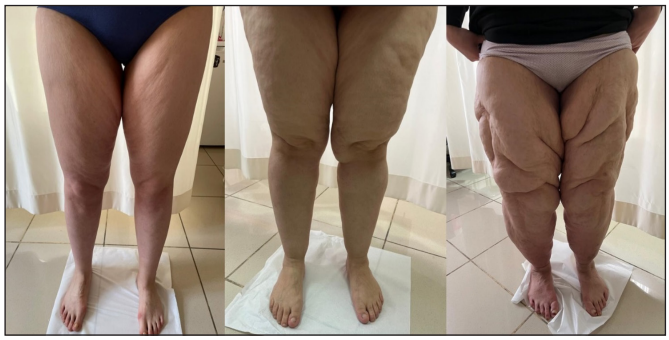

Figure 1. Lipedema stages

The truncated cone method was used to calculate the estimated volumes for the lower extremities in both groups. The right and left leg circumferences were measured at 4 cm. intervals starting from the ankle. The reliability and specificity of the calculated volume were previously reported.[9]

In addition to circumferential measurements and calculations, the dermal and subdermal thicknesses were measured by USG (7-12 MHz linear-array transducer, Logic P5, GE medical systems, Wisconsin, USA) at the same points on both limb by the same physician with more than 5 years' experience on musculoskeletal USG (BDÇ). USG gel was applied generously to the skin, and the probe was placed transversely on the leg. No pressure was applied during the USG measurements. Amato et al.[8] suggested a cut-off of 11.7 mm for more accurate pretibial soft tissue thickness measurements for the diagnosis of lipoedema, followed by a cut-off of 17.9 mm for the thigh. Anterior thigh measurements were made between the iliac crest and the lower patellar border. The pre-tibial measurements were made midpoint between anterior tibial tuberosity and medial malleolus.[8] Dermal and subdermal thicknesses were summed and recorded as a thigh and pre-tibial soft tissue thicknesses (**Figure 2**,**3**).

Health related quality of life was evaluated using the Short Form-36 (SF-36). SF-36 includes both physical and mental health parameters related to activities of daily living.[10]

Statistical Analysis

Statistical analysis was performed using SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). The normality of variances was tested with the Shapiro–Wilk test. Descriptive analyses were used for the demographic data and Spearman's rank correlation coefficient to determine the relationship between the variables. The Mann Whitney U test and Student t test were conducted to evaluate the mean difference between groups when appropriate. The level of statistical significance was set at p<.05.

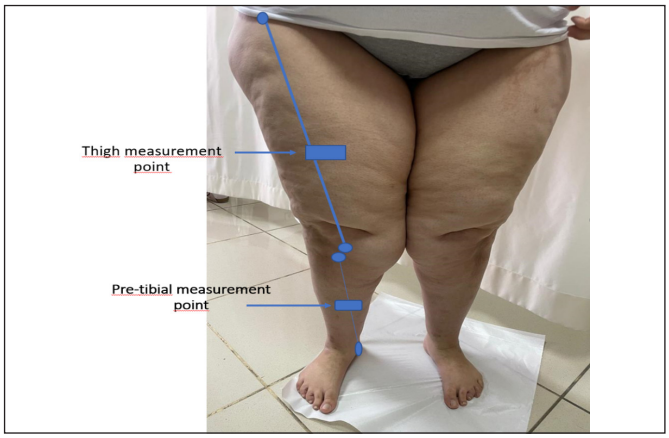

Figure 2. Thigh and pretibial measurement points where ultrasonographic soft tissue thicknesses are evaluated (Modified from Amato et al. 2021)

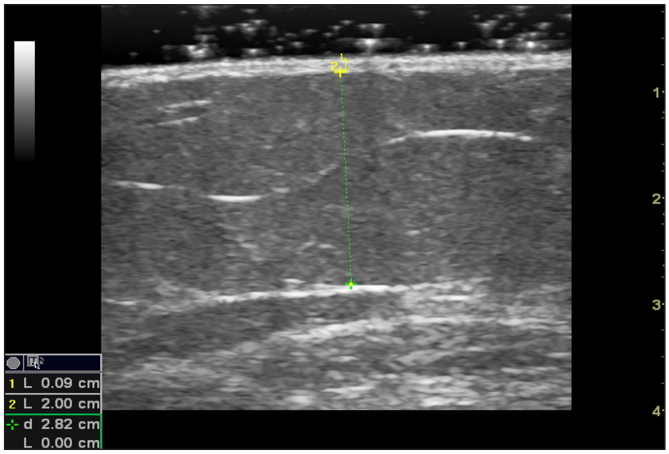

Figure 3. Ultrasonographic measurement of the dermal and subdermal thickness of the thigh

RESULTS

Comparison Between All Lipedema Patients and FMS Group

The mean age of the 53 females with lipedema was 52±11.8 years, and for the 32 females with FMS it was 51.9±10.1 years (p>0.05). There was statistically significant difference between the two groups with respect to body mass index (BMI) values (p<0.001). The extremity volumes and soft tissue thicknesses were higher in lipedema group than FMS group p<0.001). The FMS severity scores were higher in FMS group than Lipedema group (Table 1). The mean VAS score, general health, vitality, social functioning, role emotinal and mental health scores were better in lipedema patients than FMS patients (Table 2).

Comorbid Lipedema and FMS Group and FMS Group

In lipedema group, 21 (39.6%) patients have fulfilled the ACR 2016 FMS criteria. Comorbid Lipedema and FMS group FMS severity scores (SSS and WPI) were slightly lower than FMS patients. BMI and extremity volumes were not different between Lipedema without FMS and Comorbid lipedema and FMS group (Table 3).

Comparison between Lipedema without FMS Group, Bodily pain and VAS were more severe in Comorbid Lipedema and FMS group than the others. But all SF-36 components were better in lipedema without FMS group than Comorbid FMS and FMS group. Not surprisingly, mental health is better in lipedema without FMS group than the others (Table 4).

According to correlation analysis, there was no relationship between lipedema stage and FMS severity scores, VAS and SF-36 parameters (p>0.05).

Table 1. Demographic characteristics, extremity volumes and Fibromyalgia severity scores (SSS and WPI) of the all Lipedema and FMS patients

	Lipedema Group (n=53)	FMS Group (n=32)	p
Age (years) (mean±SD)	51.5±11.8	51.9±10.1	0.733*
BMI (kg/m²) (mean±SD)	39.4±5.2	29.3±3.1	<0.001*
Lipedema Stage n (%) Stage 1 Stage 2 Stage 3	 8 (15.9) 37 (69.8) 8 (15.9)		
SSS (median (interquartile))	6 (4-8)	9 (8-9)	<0.001[a]
WPI (median (interquartile))	10 (8-13)	15 (12-15)	0.002[a]
FSS (median (interquartile))	16 (9-21)	23 (21-24)	<0.001[a]
Extremity volume R (liter) (mean±SD)	12.9±2.1	7.9±2.6	<0.001*
Extremity volume L (liter) (mean±SD)	11.3±2.3	8.1±2.6	<0.001*
Fulfilled FMS Criteria (ACR 2016) n (%)	21 (39.6)	32 (100)	

SD: Standard deviation, BMI: Body mass index, SSS: Symptom severity score, WPI: Widespread pain index, FSS: Fibromyalgia severity scale, R: Right, L: Left, FMS: Fibromyalgia syndrome, ACR: American College of Rheumatology, *Student t test statistics, a Mann Whitney U Test statistics

Table 2. USG soft tissue thicknesses, VAS and SF-36 components of all lipedema and FMS patients

	Lipedema Group (n=53) (median (interquartile))	FMS Group (n=32) (median (interquartile))	p*
Thigh USG soft tissue thickness (mm)	38.5 (33.4-43.6)	14.39 (11.9-16.1)	<0.001
Pretibial USG soft tissue thickness (mm)	25 (18-30.9)	8.6 (7.6-9.8)	<0.001
VAS (0=best, 10=worst)	37 (12-53)	40 (25.5-45)	0.839
SF-36 Components (0=worst, 100=best)			
Physical components;			
Role physical	0 (0-75)	0 (0-37.5)	0.267
Physical functioning	40 (20-60)	30 (20-50)	0.244
Bodily pain	35 (10-57.5)	40 (20-38.7)	0.689
General health	35 (30-50)	30 (20-38.7)	0.014
Mental components;			
Vitality	50 (40-70)	30 (20-43.7))	<0.001
Social functioning	62.5 (50-75)	45.2 (25-63)	0.005
Role emotional	66.6 (0-100)	0 (0-33)	0.002
Mental health	64 (48-72)	40 (37-60)	<0.001

USG: Ultrasonography, VAS: Visuel analogue scale, SF-36: Short Form 36, *Mann Whitney U test statistics

Table 3. Demographic characteristics, extremity volumes and Fibromyalgia severity scores (SSS and WPI) of the comorbid Lipedema and FMS group, lipedema without FMS group and FMS patients

	Comorbid Lipedema and FMS Group 1 (n=21)	p (1-2)	Lipedema without FMS Group 2 (n=32)	p (2-3)	FMS Group 3 (n=32)	p (1-3)
Age (years) (mean±SD)	50.9±13.2	0.524*	51.9±10.9	0.655*	51.9±10.1	0.935*
BMI (kg/m²) (mean±SD)	38.7±4.7	0.476*	40±5.6	<0.001*	31.3±3.1	<0.001*
SSS (median (interquartile))	8 (6-9)	0.001[a]	4 (1-4)	<0.001[a]	9 (8-9)	0.037[a]
WPI (median (interquartile))	13 (10-15)	0.026[a]	9 (0-11)	<0.001[a]	15 (12-15)	0.304[a]
FSS (median (interquartile))	21 (17-24)	0.001[a]	10 (6-15)	<0.001[a]	23 (21-24)	0.199[a]
Extremity volume R (liter) (mean±SD)	11.8±2.8	0.696*	11.3±1.9	<0.001*	7.9±2.6	<0.001*
Extremity volume L (liter) (mean±SD)	11.8±2.8	0.561*	11.2±1.9	<0.001*	8.1±2.6	<0.001*
Fulfilled FMS Criteria (ACR 2016) n (%)	100 (100)		0 (0)		32 (100)	

SD: Standard deviation, BMI: Body mass index, SSS: Symptom severity score, WPI: Widespread pain index, FSS: Fibromyalgia severity scale, R: Right, L: Left, FMS: Fibromyalgia syndrome, ACR: American College of Rheumatology, *Student t test statistics, a Mann Whitney U Test statistics

Table 4. USG soft tissue thicknesses, VAS and SF-36 components of the comorbid lipedema and FMS group, lipedema without FMS group and FMS patients

	Comorbid Lipedema and FMS Group 1(n=21)	p* (1-2)	Lipedema without FMS Group 2 (n=32)	p* (2-3)	FMS Group 3 (n=32)	p* (1-3)
Thigh USG soft tissue thickness (mm)	39.9 (33.7-45)	0.174	36.1 (31-42.1)	<0.001	14.39 (11.9-16.1)	<0.001
Pretibial USG soft tissue thickness (mm)	28.1 (21.7-31.6)	0.124	22.9 (16.6-29.2)	<0.001	8.6 (7.6-9.8)	<0.001
VAS (0=best, 10=worst)	60 (50-71.25)	<0.001	27 (0-37)	0.001	40 (25.5-45)	<0.001
SF-36 Components (0=worst, 100=best)						
Physical components;						
Role physical	0 (0-75)	<0.001	75 (0-100)	<0.001	0 (0-37.5)	0.970
Physical functioning	25 (12.5-40)	0.125	67.5 (55-80)	<0.001	30 (20-50)	0.424
Bodily pain	22.5 (0-40)	<0.001	62.5 (54.3-78.1)	<0.001	40 (20-38.7)	0.001
General health	35 (22.5-40)	<0.001	55 (42.5-70)	<0.001	30 (20-38.7)	0.451
Mental components;						
Vitality	45 (30-65)	0.062	55 (50-70)	<0.001	30 (20-43.7)	0.01
Social functioning	62.5 (50-62.5)	0.002	75 (62.5-87.5)	<0.001	45.2 (25-63)	0.135
Role emotional	33 (0-100)	0.317	83.3 (0-100)	0.001	0 (0-33)	0.025
Mental health	60 (42-72)	0.133	70 (58-76)	<0.001	40 (37-60)	0.01

USG: Ultrasonography, VAS: Visuel analogue scale, SF-36: Short Form 36, *Mann Whitney U test statistics

DISCUSSION

In this study, we investigated the presence of FMS in lipedema patients and found that 39% of our lipedema patients met the ACR 2016 FMS diagnostic criteria. We found that the severity of FMS disease in comorbid lipedema and FMS patients was similar to FMS patients without lipedema. When we compared the quality of life of lipedema and FMS patients, we found that physical health of FMS patients was similar to lipedema patients, while their mental health was worse than lipedema patients. However, when we evaluated comorbid lipedema and FMS patients alone, we saw that the presence of lipedema and FMS in the same patient affects physical health more negatively than mental health. In the correlation analysis, we also did not find a significant relationship between the stage of lipedema and the parameters that determine the stage and severity of lipedema such as limb volumes and soft tissue thickness, and pain and quality of life. We also could not show a relationship between pain and disease severity in lipedema in this study.

What we saw in our clinical practice actually correlated with the results in our study. While there were no pain in some stage 3 patients, we also encountered very painful stage 1 patients. The latest lipoedema position document also agrees on this issue. According to the lipedema position document, the staging of lipedema is dependent on the subjective assessment of physicians and is based solely on morphological criteria. The actual symptoms of the patient are not taken into account. These stages do not reflect the clinical reality. Some patients have stage 3 lipoedema and have severe disproportionate adipose tissue in their limbs but have no or mild symptoms. Some patients have stage 1 lipoedema but complain of severe pain and restlessness in their legs.[3] However, Chakraborty et al.[11] reported that pain intensity and neuronal cell body distribution in the skin are stage dependent. They also identified neuropathic pain in lipoedema, evidence of neurogenic inflammation on skin biopsy, and increased cutaneous mechanical sensitivity. They also observed that neuronal density (Tuj-1+ dermal neuron) decreased in the abdomen across the lipedema stages; this suggests a systemic change associated with changes in lipedema tissue and neuronal density. Neurogenic features of lipoedema pain aside, neuropathic/nociplastic pain is also inherent in FMS disease. Serra et al.[12] reported that abnormal C nociceptor activity and increased mechanical sensitivity might contribute to the tenderness and pain suffered by FMS patients. In addition, small fiber neuropathy was detected in FMS patients.[13] These studies suggest that these two soft tissue pain syndromes can share common neuropathic/nociplastic features in the pathogenesis.

There were no pain in cardiogenic edema and lymphedema. If edema was the cause of pain, these patients should also have pain. In addition, contrary to its name, edema could not be detected in lipoedema. There is disproportionate accumulation of adipose tissue.[3] Some authors have suggested that the pain in lipedema is caused by tissue damage that is responsible for inflammatory and hypoxic processes. Adipose tissue increase causes local increase in proinflammatory hormones (adipokines).[3,14] Compared with normal subjects, the amount of sodium detected by magnetic resonance imaging was found to be increased in the skin and subcutaneous adipose tissues of people with lipedema. This is known as an indicator of inflammation. The authors stated that tissue sodium and adipose content might be an objective imaging-based biomarker that can be used in the differential diagnosis of lipoedema and obesity.[15] However, others speculated that the pain experienced by lipedema patients might be more related to the way the brain and nervous system interpret the stimulus, rather than tissue damage. The etiopathogenesis of FMS, as well as lipedema, depends on the biopsychosocial model of medicine and the complex mind-body relationship.[2,3]

For the last 20 years, researchers have defined FMS as nociplastic pain.[16] This type of pain is consistent with the definition of fibromyalgia as part of the group of central sensitivity syndromes.[17] Of course, the pathogenesis of FMS cannot be explained by a single etiological factor. It is known that genetic factors also play a role in the etiopathogenesis.[2] Peripheral mechanisms also play an important role in the pathogenesis of FMS. The high prevalence of FMS in patients with rheumatoid arthritis may be an evidence that joint pain, as a source of peripheral pain, can initiate the nociplastic process as a painful stimulus from the periphery.[18] Treatment of peripheral pain generators such as osteoarthritis leading to improvement in FMS symptoms suggest that the peripheral nervous system is involved in the pathogenesis. Peripheral nociceptive impulses are also thought to increase central sensitization. Centralized pain, also referred to as central sensitization or as nociplastic pain/FMS, is seen in patients with OA, inflammatory joint diseases as well as chronic low back and neck pain, complex regional pain syndrome, carpal tunnel syndrome, lateral epicondylitis, joint hypermobility syndrome. It also affects the patient's pain level, disease activity measures, and treatment selection and outcomes.[19] The comorbidity of lipoedema and FMS may activate the central sensitization of lipoedema as a peripheral pain generator, resulting in the onset or exacerbation of FMS symptoms. In addition, excessive load on the joints caused by obesity and excessive fat storage in lipedema patients may also contribute to the nociplastic process.

Physical and mental stresses are known as factors that worsen pain.[20] Psychological disorders are common in FMS patients and affect the patient's life and even disease severity.[21] Lifetime prevalence of anxiety disorders is 60% and depression is 14-36% in FMS patients.[22] Antidepressants especially duloxetine and milnacipram are FDA-approved medicines in FMS. These medicines are effective for pain rather than depressive symptoms.[23] Psychological problems have also been investigated in patients with lipedema. In a study conducted at the Földi Clinic[24], 50% of 150 lipedema patients had a mental health disorder that started 12 months before the development of lipedema-related pain. 80% of women with lipedema had psychological symptoms prior to the onset of lipedema-related pain. There is no evidence that lipoedema causes mental health problems. However, psychological problems may contribute to the development of lipedema. Moreover, depression and posttraumatic stress disorders were associated with patients' pain severity.[24] Studies have found an increase in inflammatory markers in people with depression, social stress, or posttraumatic stress disorder without any association with the underlying somatic disease.[25,26] Considering the psychological vulnerability of patients with lipoedema, chronic stress and psychological symptoms can create a vicious circle by activating inflammatory mediators, increasing pain intensity and worsening mental stress.[3] When we compared patients with lipedema and FMS in our study, we found that both diseases were equally badly affected in the physical health components of SF-36. However, in the mental health component, we observed that FMS patients were affected more badly than lipedema patients. However, we would expect the physical functions and mobility of lipedema patients to deteriorate further. Only VAS scores of comorbid lipedema and FMS patients were higher than FMS patients. In addition, while the BMI of lipedema patients is higher, their physical functions are similar to those of FMS patients, which indicates that FMS is a disease that can cause serious disability.

Angst et al.[4] evaluated the frequency of FMS in lipedema and found it to be 34%. It is a rate similar to our rate. In this study, it was observed that the comorbidity of these two chronic soft tissue pain syndromes negatively affected the patient's quality of life. In addition, in our study, lipedema was evaluated systematically in FMS patients and FMS patients without lipedema were included. In Angst et al 's study, FMS patients were not evaluated for lipedema. In our study, lipedema was ruled out by evaluating the extremity volumes and soft tissue thickness of FMS patients. This is one of the strengths of our work. However, despite the diagnostic criteria of both diseases, stage 1 lipoedema patients cannot be distinguished from FMS.

These two soft tissue pain syndromes can share common neuropathic/nociplastic features in the pathogenesis. The comorbidity of lipoedema and FMS may activate the central sensitization of lipoedema as a peripheral pain generator, resulting in the onset or exacerbation of FMS symptoms. In addition, excessive load on the joints caused by obesity and excessive fat storage in lipedema patients may also contribute to the nociplastic process. despite the diagnostic criteria of both diseases, stage 1 lipoedema patients cannot be distinguished from FMS. With our current knowledge, we cannot distinguish which disease is the cause and which is the effect, but we can see that these two diseases have a lot in common in terms of clinical and pathogenetic aspects.

One of the limitation of our study is that we did not use disease specific severity and quality of life scales for lipedema and FMS. Although there are specific scales for FMS, specific scales for lipedema are not widely used. Another limitation of our study is the small number of patients .

CONCLUSION

FMS and lipedema are two common chronic soft tissue conditions. They have many common features such as their localization, pain characteristics, gender distribution, clinical course, comorbidities and non-curative treatment options. The comorbidity of these two diseases in a patient also negatively affects physical and mental functions. Therefore, investigation and treatment of comorbid FMS in lipedema patients may contribute to their quality of life and pain.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara Training and Research Hospital Clinical Researches Ethics Committee (Date: 08.02.2023, Decision No: 1200/2023).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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The relationship between prognostic nutritional index and mortality in geriatric COVID-19 patients

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ABSTRACT

Aims: The aim of this study is to examine the relationship between prognostic nutritional index (PNI) and mortality in geriatric patients who admitted to hospital due to COVID-19.

Methods: In this retrospective cohort study, geriatric patients admitted to the emergency department of a tertiary hospital and hospitalized for COVID-19 were examined. Demographic data, laboratory results, in-hospital mortality status of the patients were recorded. The relationship between PNI values and in-hospital mortality was analyzed.

Results: The study was completed with 316 patients whose data were fully accessible. The mean age of the patients was 77.3±7.9 years and 167 (52.8%) were male. When the cut-off value of PNI level in identifying in-hospital mortality was≤42, the sensitivity was 92.3%, the specificity was 44.9%, and the positive predictive value was 57.5 and the negative predictive value was 87.8

Conclusion: This study demonstrates the prognostic importance of PNI in geriatric COVID-19 patients. Low PNI values were associated with higher in-hospital mortality rate. The use of PNI can be considered an important tool in evaluating the COVID-19 prognosis of elderly patients and developing more individualized treatment strategies.

Keywords: COVID-19, mortality, prognostic nutritional index

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has become a significant crisis affecting life worldwide and straining health systems.[1,2] COVID-19 can be more severe in elderly individuals and patients with comorbidities.[3] Therefore, there is an increasing need for determinants that assess and optimize management strategies for the prognosis of COVID-19 in geriatric patients. Nutritional status is an important factor in terms of disease prognosis and quality of life in elderly patients. Malnutrition has been associated with length of hospital stay, risk of infection, mortality, and morbidity. Current literature data report that malnutrition develops in approximately 50% of all hospitalized patients and in approximately 44% of surgical patients.[4] The likelihood of developing malnutrition has been found to be associated with the length of hospitalization, the severity of the disease, and surgical stress.[5] Furthermore, studies have shown that as the malnutrition process extends, the risk of morbidity and mortality increases.[6]

The prognostic nutritional index (PNI), calculated based on serum albumin levels and lymphocyte count, is an index that evaluates patients' nutritional status and immune functions.[7] Previous studies have revealed the importance of PNI in the prognosis and treatment processes of various diseases.[8] There are also studies on the prognostic significance of PNI in geriatric COVID-19 patients.[9,10] This study aims to assess the prognostic value of PNI in geriatric COVID-19 patients and its relationship with clinical outcomes. This information can contribute to developing more effective and individualized approaches in the treatment of elderly patients with COVID-19 infection.

METHODS

This retrospective cohort study includes geriatric COVID-19 patients who presented to the emergency department and were hospitalized at Şişli Hamidiye Etfal Training and Research Hospital between January 1, 2021, and January 1, 2022. This study has been approved by the Şişli Hamidiye Etfal Ethics Committee,

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and the confidentiality of all patients' data has been protected (Date: 04.04.2023, Decision No: 2289). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.[11]

The patients included in the study consisted of patients aged 65 and over who were diagnosed with COVID-19 and admitted to the hospital.Diagnosis was confirmed based on symptoms, physical examination findings, and real-time reverse transcription-polymerase chain reaction (RT-PCR) tests.[12] The criteria in the Ministry of Health guidelines were used for admission to the hospital. According to these criteria, patients with comorbidities with tachycardia (pulse >125/min), tachypnea (respiratory rate >22/min), hypotension (<90/60 mmHg), or hypoxemia (SpO_2 <93%) were hospitalized.[13] Patients under the age of 65, those with negative RT-PCR test results, and those with a history of malnutrition (cachectic patients, patients with stroke) were excluded from the study. Patients' demographic information, clinical findings, laboratory results, and treatment processes were obtained from hospital records. PNI values were calculated using serum albumin levels and lymphocyte counts recorded at the time of presentation. The PNI formula is as follows: 10 x serum albumin level (g/dL) + 0.005 × lymphocyte count (mm^3).[9] The primary outcome of the study has been determined as the in-hospital mortality rate.

Statistical Analysis

Descriptive criteria were presented as mean and standard deviation, and percentage distribution. The normality of the data distribution was checked with the Kolmogorov-Smirnov test. In the comparison of sociodemographic, clinical, and laboratory findings between deceased and surviving patients, Pearson Chi-Square analysis was used for comparing distributions, and the Student's t-test was used for comparing continuous variables. Upon finding PNI to be significant as a mortality indicator, receiver operating curve (ROC) analysis was performed to determine sensitivity, specificity, and cut-off points, and the area under the curve (AUC) was calculated. In all analyses, results with a p-value <0.05 were considered statistically significant. Variables with a significant relationship as a result of univariate analysis were then analyzed by logistic regression analysis. Statistical analyses were performed using SPSS (IBM Corp., Armonk, NY, USA).

RESULTS

The study was completed with 316 patients who had complete data available. The mean age of the patients was 77.3±7.9, with 167 (52.8%) being male. Patients were divided into two groups as survivor and non-survivor according to their in-hospital mortality status, and their demographic (age, gender), laboratory, and clinical characteristics were compared (**Table 1**). The mean age and the average number of males in the non-survivor group were higher than in the survivor group (p-values were 0.001 and 0.033, respectively). The mean albumin level in the non-survivor group was lower, while no difference was detected between the groups in terms of mean lymphocyte count (p-values were 0.006 and 0.06, respectively). The mean PNI values of the non-survivor group were found to be significantly lower than those of the survivor group (p:0.001).

As a result of the ROC analysis of PNI level in predicting in-hospital mortality among study population, the area under the curve was 0.816 (95% CI 0.769-0.857), the Youden index was 0.528 (p<0.001). When the cut-off value of PNI level in identifying in-hospital mortality is ≤42, the sensitivity is 92.3%, the specificity is 44.9%, and the positive predictive value is 57.5 and the negative predictive value is 87.8 (**Table 2**, **Figure**).

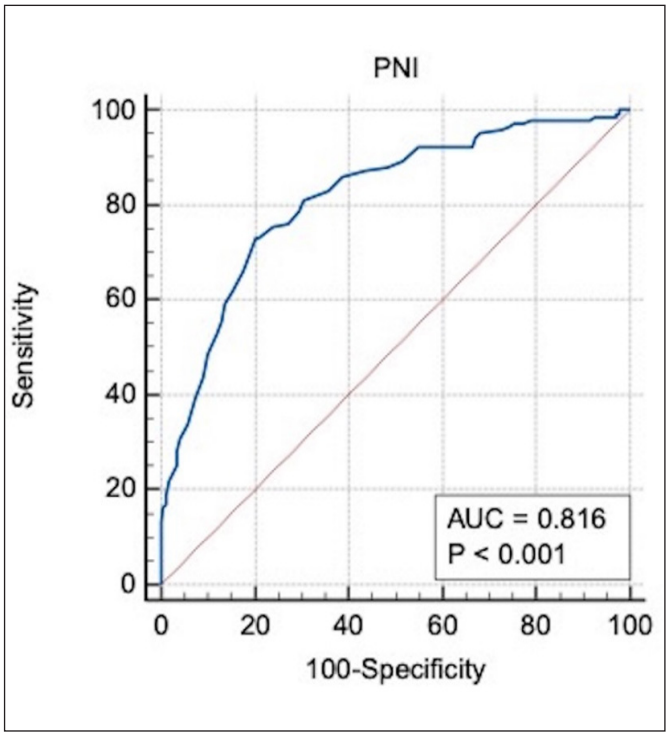

Figure.Receiver operating characteristic curve of the PNI score in predicting in-hospital mortality among patients with COVID-19

As a result of the logistic regression analysis, when adjusted for age, gender, clinical and laboratory characteristics, the probability of being a non-survivor was 16% higher in those with a low PNI score than those with a high score (p:0.001) (**Table 3**).

Table1. General characteristics of the patients included in the study

	Survivor	Non-survivor	Total	p value
	Mean±SD/n-%	Mean±SD/n-%	Mean±SD/n-%	
Gender				0.033
Woman	91 (52.6)	58 (40.6)	149 (47.2)	
Man	82 (47.4)	85 (59.4)	167 (52.8)	
Age, years	75.8±7.6	79±8	77.3±7.9	0.001
Systolic blood pressure (mmHg)	127.2±19.2	127.9±25.8	127.5±22.3	0.789
Diastolic blood pressure (mmHg)	73.9±115	71.6±14.8	72.9±13.1	0.129
Pulse rate (bpm)	83.3±13.7	95.3±20.6	88.3±17.9	0.001
spO_2 (%)	93.3±4.6	88±10	90.9±8	0.001
Temperature (°C)	36.7±0.7	37±0.8	36.8±0.8	0.005
White blood cells (10^3u/L)	7.1±3.7	10±5.3	8.4±4.7	0.001
Neutrophil (10^3/mm^3)	5.7±6.7	8.1±4.9	6.7±6.1	0.001
Lymphocyte (10^3/mm^3)	1.5±2.9	1.0±0.8	1.3±2.2	0.06
Haemoglobin (g/L)	12.4±2	11.9±2.3	12.2±2.1	0.083
Platelet (10^3u/L)	212.1±99.9	233.6±101.9	221.7±101.2	0.059
Urea (mg/dL)	50±28.7	84±63.2	65.1±50.1	0.001
Albumin (g/L)	36.1±4.4	29.4±4.6	33.1±5.6	0.006
AST (IU/L)	39.1±31.5	82.4±363.6	58.4±244.7	0.115
ALT (IU/L)	26.5±22.3	47±190.8	35.7±128.8	0.157
Creatinine (mg/dL)	1.3±3.1	1.7±1.7	1.5±2.6	0.109
Chronic obstructive pulmonary disease	16 (11)	17 (14.8)	33 (12.6)	0.356
Diabetes mellitus	64 (42.7)	38 (33)	102 (38.5)	0.111
Hypertension	84 (55.6)	54 (46.2)	138 (51.5)	0.124
Congestive heart failure	12 (8.3)	23 (20.2)	35 (13.5)	0.005
Coronary artery disease	29 (19.9)	18 (15.9)	47 (18.1)	0.415
Atrial fibrillation	6 (4.1)	3 (2.7)	9 (3.5)	0.537
Chronic renal failure	7 (4.8)	19 (17)	26 (10.1)	0.001
Admission unit				0.001
Inpatient service	159 (89.8)	60 (42)	219 (68.4)	
Intensive care unit	18 (10.2)	83 (58)	101 (31.6)	
Prognostic nutritional index (PNI)	43.6±15.2	34.6±6.7	39.6±12.9	0.001

Table 2. Diagnostic values and cut-off level of the PNI score to predict in-hospital mortality among patients with COVID-19

	AUC	Cut-Off	Sensitivity	Specificity	+LR	-LR	PPV	NPV	Youden Index
PNI	0.816(0.769-0.857)	≤42	92.3	44.9	1.7	0.2	57.5	87.8	0.528

Prognostic nutritional index (PNI), AUC: Area under the curve, LR: likelihood ratio, PPV: Positive predictive value, NPV: Negative predictive value

Table 3. Examination of the relationship between age, gender, clinical features, laboratory characteristics, and PNI with mortality by logistic regression analysis

	Odds Ratio	%95 Confidence interval	p value
Age	1.037	0.988-1.089	0.143
Gender Woman Man	1.230	0.559-2,.06	0.606
Pulse rate (bpm)	1.019	0.994-1.044	0.139
SpO_2 (%)	0.898	0.837-0.964	0.003
Temperature (°C)	1.534	0.948-2.481	0.081
White blood cell (10^3u/L)	1.631	1.167-2.279	0.004
Neutrophil (10^3/mm^3)	0.662	0.466-0.940	0.021
Urea(mg/dL)	1.006	0.996-1.015	0.243
Congestive heart failure	1.608	0.512-5.052	0.416
Chronic renal failure	2.630	0.719-9.621	0.144
PNI	0.841	0.774-0.914	0.001

Prognostic nutritional index (PNI)

DISCUSSION

In this study, the prognostic significance of PNI in geriatric COVID-19 patients was evaluated, and it was found that low PNI values were significantly associated withhigher in-hospital mortality rates. These results suggest that PNI may be an important determinant for COVID-19 prognosis in elderly patients.

As the number of individuals infected with COVID-19 increases, so does the potential burden on healthcare systems. For all these reasons, the development of markers that can predict the prognosis of the disease, as well as early diagnosis, is becoming increasingly important. Identifying laboratory tests that contribute to the diagnosis and follow-up of COVID-19 patients is essential not only for assisting in the diagnostic process but also for classifying patients in terms of disease severity and mortality risk.

In the early stages of the COVID-19 pandemic, healthcare systems around the world were pushed to the brink of collapse, and researchers examined various prognostic models for this purpose.[14] PNI is one of them. Previous studies in the literature have shown that PNI is an important factor affecting the prognosis of various diseases. In a study conducted in China with 122 patients, it was found that COVID-19 patients with severe forms had lower PNI values than those with nonsevere forms.[15] In a meta-analysis covering 13 studies with data from 4204 patients, it was emphasized that low PNI values could be a useful prognostic tool in COVID-19 patients.[16] In a study by Wang and colleagues, COVID-19 patients were divided into critical and non-critical groups and various characteristics were compared, with lower PNI values found in the critical group, and PNI was emphasized as an independent factor predicting critical patients.[17] In a study involving COVID-19 patients in Wuhan, the primary outcome was defined as in-hospital mortality, and although lower PNI, advanced age, and neutrophil-to-lymphocyte ratio were detected in the non-survivor group, logistic regression analysis concluded that PNI was the only useful parameter.[18] The two components of PNI, lymphocytes and albumin, have been shown to be associated with poor prognosis in COVID-19.[19,20] However, studies in the literature have shown that the PNI formulation provides more successful prognostic predictions.

This study's results support the existing knowledge on the prognostic importance of PNI in geriatric COVID-19 patients and provide a significant basis for adopting more individualized approaches in managing these patients.

One of the important results of this study was that the albumin levels of the non-survivor group were lower than those of the survivor group. Previous studies have shown that hypoalbuminemia can be seen in patients with COVID-19 infection. Although the pathophysiology of this event has not been clearly explained, it has been thought that it may develop secondary to increased capillary permeability, decreased protein synthesis, decreased half-life of serum albumin, decreased serum albumin total mass, increased volume of distribution, and increased expression of vascular endothelial growth factor.[21]

Another important result of this study is that the non-survivor group had statistically significant congestive heart failure and chronic kidney failure compared to the survivor group. When the literature is examined, it has been reported that comobirdity is associated with a poor prognosis in COVID-19 patients, and that the rate of having at least one comorbidity in patients with a poor prognosis may exceed 70%.[2]

Finally, the logistic regression analysis of the data obtained in the study shows that not only the PNI, but also the white blood cell, neutrophil count and sPO_2 values were statistically significant. As a matter of fact, while there are lower sPO_2 values in patients who lost their lives due to COVID-19 in the literature, they have higher white blood cell and neutrophil count values.[19] In the light of this information, our study was found to be compatible with the literature.

However, this study has some limitations. Firstly, due to its retrospective nature, there may be a lack of some crucial data and the possibility of observation bias. Secondly, because it is a single-center study, the generalizability of the results to geriatric COVID-19 patients in different geographies and healthcare systems is limited. In the future, multicenter and prospective studies can further strengthen our knowledge on this subject.

CONCLUSION

This study reveals the prognostic importance of PNI in geriatric COVID-19 patients. Low PNI values have been found to be associated with in-hospital mortality rates. The use of PNI can be considered an important tool for assessing the prognosis of elderly patients with COVID-19 and developing more individualized treatment strategies.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Şişli Hamidiye Etfal Ethics Committee (Date: 04.04.2023, Decision no: 2289).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Can myometrial thickness measurement predict the amount of postpartum hemorrhage and delivery type?

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ABSTRACT

Aims: This study aims to determine the effect of the myometrial thickness on the amount of postpartum bleeding and to investigate its role as an auxiliary method in predicting postpartum hemorrhage.

Methods: This prospective study includes 305 pregnant women in two groups, vaginal delivery, and cesarean section patients. The fundal, mid anterior, and lower uterine segment myometrium thicknesses were measured. In the postpartum period, the amount of bleeding and the type of delivery was recorded, and the relationship between myometrial thickness measurements was determined.

Results: The amount of bleeding in the patients who had a cesarean section was higher than in those who had a vaginal delivery ($p<0.01$). The myometrium of the patients who had a cesarean section was thicker than those who had a vaginal delivery ($p<0.05$). Measurements above the cut-off value of 6.1 mm determined for the mid-anterior myometrium thickness measured in the latent phase were associated with a cesarean section with a sensitivity of 63% and a specificity of 66% ($p=0.011$).

Conclusion: Fundal myometrium thickness measured in the active phase and lower uterine segment myometrium thickness measured in the 2nd stage predict postpartum bleeding in patients with a vaginal delivery. Mid-anterior myometrium thickness measured in the latent phase can predict the probability of cesarean delivery.

Keywords: Myometrial thickness, postpartum hemorrhage, cesarean section, birth

INTRODUCTION

Almost one million mothers worldwide die yearly due to pregnancy-related complications.[1] One of the most feared situations during childbirth can be expressed as postpartum hemorrhage(PPH). Although PPH has been defined in many ways in the literature, the most popular definition is bleeding of more than 500 ml after vaginal delivery, more than 1000 ml after cesarean section, or a decrease of more than 10% in hematocrit level.[2,3] Postpartum hemorrhage occurs in 4-6% of births. Worldwide, postpartum hemorrhage accounts for 8% of maternal deaths in developed regions and 20% in developing regions.[3]

Since postpartum hemorrhage is a life-threatening condition, risk factors, prevention strategies, and what to do when faced should be known by today's obstetricians. Although many risk factors that may cause PPH have been identified, there are no clear objective indicators to help us predict the amount of bleeding that may occur during delivery.

Physiological changes in the uterine muscle layer from the implantation process of the fetus to the time of birth have been the source of many studies.[4-6] In this study, myometrial measurements were evaluated to determine the risk of PPH, one of the leading causes of maternal mortality, before birth. In this context, this study aims to investigate the relationship between uterine myometrial thickness measurements and the amount of postpartum bleeding and delivery method using ultrasonography (USG), which was introduced into obstetric practice about 50 years ago.

METHODS

This study was conducted prospectively in Bursa Yüksek İhtisas Training and Research Hospital Department of Obstetrics and Gynecology. The study was carried out with the permission of Bursa Yüksek İhtisas Training and Research Hospital Clinical Researches Ethics Committee (Date: 05.02.2020, Decision No: 2011-KAEK-25 2020/02-12). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The patient group included in the study consisted of patients at term (38-41 weeks of gestation), 18-40 years of age, single, with a head presentation, and hospitalized in the delivery room in the latent phase. Patients with multiple pregnancies, malpresentation, and comorbidity were out of the study.

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Oxytocin and amniotomy were applied to the study group according to ACOG guidelines and in the same standards. Accordingly, oxytocin was administered at 500 c.c isotonic solutions, with a dose of 5 mU per minute, with an increase of 5 mU per minute until an adequate uterine contraction activity was established, a condition of increasing to a maximum dose of 30 mU/min.[7]

While oxytocin initiated in pregnant women who were not in the active phase was considered an induction application, oxytocin initiated in pregnant women who were in the active phase but did not have sufficient uterine contraction was considered an augmentation application. The definition accepted by the world as at least three painful uterine contractions (total 200-250 Montevideo units) within 10 minutes and 6 cm cervical dilation for active labor was accepted. Myometrial thickness measurement was added to the fetal biometric measurements. While measurements were made in the latent phase, active phase, and the second stage of labor in the patient group who delivered vaginally, only the latent phase measurements were made in the patient group who delivered by cesarean section.

The myometrium was defined as the echo-homogeneous layer between the serosa and decidua of the uterus. Myometrial thickness measurements were made from the fundal, mid-anterior, and lower uterine segments of the uterus. Lower uterine segment measurement was made 2 cm above the bladder echo, mid-anterior segment measurement was made 1 cm above the umbilicus level, and fundal measurement was made from the part of the uterus that corresponds to the uterine curve area below the xiphoid.[8] The measurement methods taken are shown in **Figure 1** below.

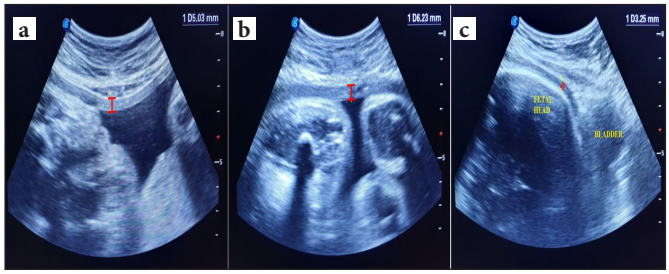

Figure 1. Myometrium thickness measurement method.

A: Fundus myometrial thickness; B: Midanterior myometrial thickness; C: Low uterine segment myometrial thickness

Each measurement was made by the same person. In patients who delivered vaginally, 9 measurements were taken from a patient in total, from 3 different regions in 3 different time periods, while measurements were taken from 3 regions only in the latent phase in patients who delivered by cesarean section. At the same time, age, gravida, parity, birth week, BMI, hospitalization time, cervical dilatation, amniotic fluid amount, delivery type, birth weight, 1st and 5th minute Apgar scores, prenatal and 6th hour postpartum hemogram, hematocrit and mean erythrocyte volume (MCV), 24-hour bleeding amounts learned with the help of pads were evaluated, recorded, and examined.

The amount of bleeding in the evaluated patient groups was estimated by the physician who gave birth during the intrapartum period, and during the service follow-up, the calculation was made based on the studies in the literature with the help of the patient diaper and sterile pad (100 cc) used in the clinic.[9] Sterile delivery bags could not be used due to technical limitations.

Statistical Analysis

Statistical analysis of the study was performed using the IBM SPSS 26.0 (Statistical Package for the Social Sciences, version 26.0) program. We analyzed the normality assumptions of the data by using descriptive methods with histogram graphics in which the normal distribution curve is drawn and the Kolmogorov-Smirnov test, which is used in cases where the sample is more than 30. The data were explained using descriptive statistics (arithmetic mean±standard deviation (SD), minimum (min.) ve maximum (max.)). The independent t-test was used to compare the two groups if the data showed normal distribution. The Mann-Whitney U test, one of the non-parametric tests, was used if the data did not show normal distribution. We preferred the Chi-square test for the comparison of categorical data.

Multiple linear regression analysis was performed to examine the independent effects of different predictors on the amount of postpartum bleeding and to develop a mathematical model. The backward LR method was used to determine the predictors.

In addition, the receiver operating characteristic curve (ROC curve) was created to evaluate the prediction of myometrial thickness measurements for cesarean section. Sensitivity and specificity were calculated with the areas under the curve (AUC). A cut-off point was determined in the cesarean section groups according to the vaginal delivery groups.

The results obtained from all analyzes were interpreted considering the 0.05 significance level.

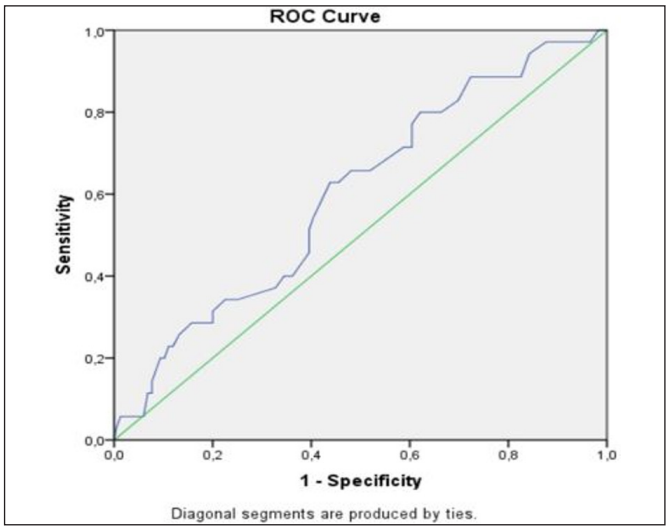

Figure 2. ROC analysis curve of latent phase mid anterior myometrial thickness according to delivery groups

RESULTS

This study includes 305-term pregnant women admitted to the delivery room in the latent phase planned for vaginal delivery. The patients were divided into two groups: the patient group with a vaginal delivery and the cesarean delivery group. There were 235 (77%) patients who had a vaginal delivery and 70 (23%) patients who delivered by cesarean section. Cesarean section indications were of three types. Of these, 32 (45.7%) were due to acute fetal distress, 30 (42.8%) were due to non-progressed labor, and 8 (11.5%) were due to cephalopelvic disproportion. The characteristic features of the patients are available in Table 1.

In the study, nine measurements were taken from 235 patients who had spontaneous vaginal delivery in 3 different periods (latent phase, active phase, 2nd stage) and from 3 different regions (fundus, mid anterior, lower uterine segment). Measurements were taken from 3 different regions only in the latent phase of the patients who gave birth by cesarean section. The comparison of the measurements made in the latent phase of the patients in the vaginal delivery and cesarean section group is shown in Table 1. The myometrium thickness of the patients in the cesarean section group was statistically significantly thicker than the myometrium of the patients who had a vaginal delivery ($p<0.05$).

Myometrial thicknesses of the patients who had spontaneous vaginal delivery were evaluated separately for nulliparous and multiparous patient groups. The measurement values related to this are shown in Table 2. Accordingly, myometrial thicknesses of nulliparous patients were thinner than those of multiparous patients. While no difference was there between the measurements taken from the lower segment in the active phase between these two groups ($p>0.05$), a statistically significant difference was found between the other eight measurements ($p<0.05$).

Table 1. The sociodemographic characteristics and findings of the study population

	Vaginal delivery (n=235)				Cesarean delivery (n=70)				p
	$\bar{x}$	SD	Min.	Max.	$\bar{x}$	SD	Min.	Max.	
Age (y)	24.35	5.34	18	37	24.06	5.05	18	39	0.81
Gestational age (wk)	39.	0.94	38	41	39.34	1.10	38	41	0.33
Gravidity	2.2018	1.33	1	8	1.91	1.16	1	5	0.086
Parity	0.99	1.08	0	4	0.71	1.01	0	3	0.038*
Nulliparous (n,%)	103 (43.8%)				42 (60%)				0.017*
Multiparous (n,%)	132 (56.2%)				28 (40%)				
Vaginal examination (cm)	3.20	2.20	1	5	3.32	2.09	1	5	0.52
BMI (kg/m²)	27.73	3.93	20.4	41.4	28.70	3.70	23	39.4	0.028*
AFI (SDP) cm	3.37	1.16	2	7.9	3.27	1.00	2.1	6.2	0.52
Hospitalization (d)	1.10	0.37	1	4	2.13	0.38	2	4	<0.01*
Birth weight (g)	3277	408	2470	4490	3246	387	2460	4260	0.55
APGAR-1.minute	8.87	0.71	3	9	8.59	1.20	3	9	<0.01*
APGAR-5.minute	9.90	0.55	5	10	9.71	0.71	7	10	<0.01*
Amount of bleeding (cc)	394.13	67.3	150	700	542.71	125	250	1000	<0.01*
Fundus Latent (mm)	5.42	1.06	3.1	8.2	5.79	1.30	3.1	8.7	0.03*
Midanterior Latent (mm)	6.12	1.63	3.2	11.0	6.71	1.70	3.4	11.0	0.01*
Low Segment Latent (mm)	3.15	0.55	2.1	4.8	3.34	0.60	2.4	4.9	0.02*

*p < 0.05, $\bar{x}$: Mean, SD: Standard Deviation, Min: Minimum, Max: Maximum, y: year, wk: week, kg: kilogram, m²: meter square, cm: centimeter, d: day, g: gram, Student-t test was performed

Table 2. Comparison of myometrium thicknesses of vaginal delivery patients by parity

	Spontaneous Vaginal Delivery (n=235)								p
	Nullipara (n=103)				Multipara (n=132)				
	$\bar{x}$	SD	Min.	Max.	$\bar{x}$	SD	Min.	Max.	
Fundus Latent (mm)	5.13	0.96	3.7	8.2	5.65	1.09	3.1	8.1	<0.01*
Midanterior Latent (mm)	5.71	1.59	3.2	9.8	6.43	1.60	3.4	11.0	<0.01*
Low Segment Latent (mm)	3.06	0.47	2.3	4.4	3.23	0.59	2.1	4.8	0.02*
Fundus Active (mm)	4.94	1.17	3.3	8.2	5.36	1.24	3.2	10.0	<0.01*
Midanterior Active (mm)	5.35	1.49	3.0	10.0	5.97	1.50	2.8	9.8	<0.01*
Low Segment Active (mm)	2.82	0.39	2.2	3.9	2.93	0.52	2.1	4.7	0.12
Fundus Stage 2 (mm)	6.88	1.37	4.9	11.4	7.40	1.24	5.4	10.8	<0.01*
Mid anterior Stage 2 (mm)	6.97	1.28	5.0	10.1	7.75	1.51	5.2	11.7	<0.01*
Low Segment Stage 2 (mm)	2.56	0.28	2.1	3.5	2.66	0.38	2.0	3.8	0.02*

*p < 0.05, $\bar{x}$: Mean, SD: Standard Deviation, Min: Minimum, Max: Maximum, mm:millimeter, Student-t test was performed

It was observed that the myometrium thicknesses of all three regions were thinned when the patients transitioned from the latent phase to the active phase during labor follow-up. When transitioning from the active phase to the 2nd phase, it was observed that the thickness of the lower segment continued to thin. In contrast, the thickness of the fundus and mid-anterior myometrium increased significantly and even exceeded the values measured in the latent phase.

Fundus, mid anterior, and lower segment myometrium thickness parameters in the patient group's first and second stages of labor followed by vaginal delivery were analyzed by multiple linear regression analysis. After the backward method, fundus thickness in the active phase and lower segment thickness in the 2nd stage was determined as the predictors that most affected the amount of postpartum hemorrhage. The findings are presented in Table 3. In this context, it can be stated that the fundal measurement taken in the active phase and the lower segment measurement taken in the 2nd phase significantly predict the amount of postpartum bleeding and explain 9% of it (R=.30, R2=.09, p<0.01). In addition, when the t-test results regarding the significance of the regression coefficients are examined, fundus measurement in the active phase (β=-0.20, p=0.02) and lower segment measurement taken in the 2nd stage (β=-0.20, p=0.02) significantly predict the amount of postpartum hemorrhage.

Table 3. Multiple linear regression analysis of vaginal postpartum bleeding amount and myometrial thickness parameters and Cesarean section midanterior myometrial thickness ROC analysis chart

Variables	B	Std. error	β	t	p	
Fundus active	-10.85	3.48	-.20	-3.12	.002*	
Low segment stage 2	-38.62	12.51	-.20	-3.09	.002*	
AUC (%95)	**Cut off (mm)**	**p**	**Sens. (%)**	**Spes. (%)**	**PPV (%)**	**NNPV (%)**
0,600 (0.526-0,673)	6,1 mm	0.011*	63	66	56.2	62.9

RF: Risk factor, AUC: Area under the curve, mm: milimeter, Sens.: sensitivity, Spes.: Specificity, PPV: Positive Predictive Value, NPV: Negative Predictive Value ve *p < .05 significiant value

As a result of the multiple linear regression analysis, the model that can predict the amount of bleeding after vaginal delivery was created as follows. Amount of bleeding= 551+(-11 × Active Fundus Measurement) + (-39 × 2nd Stage Low Segment Measurement)

Accordingly, it is thought that a decrease of 1 mm in these two measurements in patients who delivered vaginally will increase the amount of bleeding by 50 c.c..

ROC analysis was also performed regarding myometrial thickness parameters to predict cesarean delivery. A cut-off point was determined in the cesarean section groups according to the vaginal delivery groups. Accordingly, the area under the curve was most determined in mid anterior myometrial thickness (AUC=0.600). When Table 3 is examined, when the mid anterior myometrium thickness is measured as 6.1 mm and above in the latent phase, the probability of cesarean delivery with 63% sensitivity and 66% specificity was determined (p=0.011).

DISCUSSION

The patient group of the study consists of patients who were admitted to the delivery room in the latent phase and followed up for vaginal delivery. The evaluation was made by dividing them into two groups according to the type of birth. When the characteristics of the patients were examined, a significant difference was found between parity, length of hospital stay, body mass index, and Apgar scores of newborns at 1 and 5 minutes (p<0.05). The reason for the significant difference between newborn Apgar scores was thought to be that 46% of the indications of the patient group who had cesarean section were fetal distress. In the study by Eyowas et al.[10] in 2016 examining the neonatal effects of delivery type, 1st minute Apgar scores were found to be significantly higher in the vaginal delivery group than in the cesarean section group (p=0.001). However, no significant correlation was found between the 5th minute Apgar scores (p=0.055).

In the study of Buhimschi et al.[8] the myometrial thicknesses of patients in active and non-active labor were compared and recorded during labor. Accordingly, the myometrium thickness of the active labor group was calculated to be statistically significantly thin on the fundal and mid anterior lines (p<0.01), but no statistically significant difference was found between the lower uterine segment thicknesses (p>0.05). At the same time, while the myometrium thickens significantly in the fundus and mid-anterior line in the second stage of labor (p<0.05), the postpartum effect is reversed (fundal dominance). In the study of Durnwald et al.[11] in 2008, the myometrial thickness was evaluated according to the week of gestation, uterine region, and patients with a previous cesarean section, and the myometrial thickness of the nulliparous patient group was calculated to be statistically significantly thinner than the multiparous patient group (p<0.05). In this study, results have been obtained that support these two studies. The myometrial thickness of the nulliparous patient group was significantly thinner than the multiparous patient group (p<0.05). At the same time, it was observed that the thickness of the myometrium was thinned in the active phase. In the

second stage, while the lower segment continued to thin, it was observed that the fundus and the mid-anterior line significantly thickened.

The generally accepted definition for postpartum hemorrhage is 500 cc of bleeding in vaginal delivery, 1000 cc in cesarean section, or more than 10% decrease in hematocrit value.[12] In the bulletin published by ACOG in 2017, PPH was defined as bleeding more than 1000 cc at birth or developing hypovolemia symptoms.[6] Some studies have emphasized that the patient's vital signs and the development of hypovolemia symptoms are more important than laboratory values for PPH.[13]

In a Cochrane analysis prepared by Diaz et al.[14] different techniques were presented to help predict PPH. One is sterile delivery bags; the other is hemoglobin concentration in spectrophotometry and venous blood. However, although these techniques are thought to provide more precise results in measuring blood loss, their accessibility is difficult. One of the study's limitations is measuring the amount of bleeding with visual estimation during the intrapartum period and using sterile pads in the postpartum period.

In a study by Stafford et al.[15] estimated and measured blood loss in vaginal delivery and cesarean section were compared. A significant difference was found between the delivery groups regarding blood loss. In this study, the amount of bleeding in the patient group who had a cesarean section was higher than in the group who had a vaginal delivery ($p<0.01$).

In the study of Biguzzi et al.[16] with 6011 women, there are data showing that nulliparity is a risk factor for PPH. Our article showed that myometrial thickness was thinner in nulliparous patients than in multiparous patients, which was thought to be the inverse correlation. The significant parameters in the correlation table were examined with the multiple linear regression model. It was determined that the fundal measurement in the active phase and the lower segment measurement in the 2nd phase were the predictors that most affected the bleeding in the patients who had vaginal deliveries, regardless of parity ($p=0.02$). In this study, fundal measurements in the nulliparous patient group with vaginal delivery and lower segment measurements in the multipara patient group with vaginal delivery were found to have a moderate negative correlation with the amount of bleeding.

Regular uterine contractions that increase with the active phase in vaginal delivery may be more associated with the fundus. The descent of the fetus, which starts after the active phase, from the fundus to the lower segment also supports this situation. At the same time, lower segment myometrium thickness measured after a fully dilated cervix was determined as one of the parameters affecting the amount of postpartum hemorrhage. This makes it essential to evaluate the lower uterine segment, the thinnest and shortest uterine segment in the 2nd stage, in predicting postpartum hemorrhage. Invasive procedures are mainly applied to the lower segment, and adjacent structures in postpartum hemorrhage also support this situation.

Myometrium thicknesses in the latent phase of the patient groups who had cesarean section and vaginal delivery were also compared. It was found that the myometrium thicknesses measured from 3 regions were statistically different ($p<0.05$). ROC analysis of myometrial thicknesses was performed to evaluate the prediction of cesarean delivery. The area under the curve was the highest in the measurements made from the mid-anterior line (AUC=600). The cut-off value for the mid-anterior line was 6.1 mm. For the values measured above, the probability of cesarean delivery was predicted with a sensitivity of 63% and a specificity of 66% ($p=0.011$).

In the thick myometrium tissue, vascularization may occur more, and uterine contractions may be more frequent and stronger. Considering that the more hypoxic environment, which occurs due to more frequent and strong uterine contractions in pregnant women receiving oxytocin induction, increases the possibility of cesarean section, it can be thought that the increase in myometrium thickness may also be a marker for cesarean section prediction. The fact that fetal distress constituted the majority of cesarean section indications in the study supports this situation. Although myometrial thickness parameters are statistically significant in predicting cesarean section, more long-term prospective studies are needed to strengthen its diagnostic feature due to its low specificity.

The limitations of the study were that the study was conducted in a single center, the amount of bleeding could not be measured with more objective criteria, and the interobserver variability in estimating the amount of intrapartum bleeding.

CONCLUSION

As a result of the data obtained, fundal myometrium thickness measured in the active phase and myometrial thickness measured from the lower uterine segment in the 2nd stage were found to be associated with the amount of bleeding in patients who had a vaginal delivery. When the myometrium thickness measured from these two regions became thinner, an increase in the amount of bleeding was observed.

At the same time, myometrial thickness measured from the mid anterior line in the latent phase may also indicate a relationship with cesarean section. It has been observed that the increase in myometrium thickness measured from the mid anterior line also increases the cesarean section rates.

These findings and relationships revealed in the study suggest that examining myometrial changes that show physiological changes in labor with different studies may contribute more to the practice of obstetrics.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bursa Yüksek İhtisas Training and Research Hospital Clinical Researches Ethics Committee (Date: 05.02.2020, Decision No: 2011-KAEK-25 2020/02-12).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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