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Research article

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The relationship between the communication skills of intern physicians and their exposure to violence

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Abstract

Background/Aim: Violence against healthcare workers has become a major problem worldwide. This study aimed to examine the relationship between the communication skills of interns and their exposure to violence.

Methods: This cross-sectional study comprised 287 students working as intern physicians at the Ondokuz Mayis University Faculty of Medicine within the academic year of 2018-2019. It was conducted with 234 volunteering individuals. The data were collected through a questionnaire, consisting of 33 questions in total, applied with a face-to-face interview. The Communication Skills Scale was used, as well as questions about sociodemographic characteristics and violence. The level of statistical significance was set at $P<0.05$.

Results: Eighty-six (36.8%) intern physicians stated that they had been subjected to violence in the last year. Eighty-four (97.7%) of these participants stated that they were subjected to verbal violence and 5 (5.8%) to physical violence. While there was no significant difference between the participants in terms of being exposed to at least one type of violence or verbal violence, the mean scale score was significantly lower in those who were exposed to physical violence ($P=0.032$).

Conclusion: The inadequacy of interns in communication was not included among the main reasons for verbal violence. Although the communication skills of interns who were exposed to physical violence were lower, it is necessary to work on larger groups to make a community-wide assessment.

Keywords: Communication, Intern Medical staff, Violence

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Introduction

Violence in the field of health is defined as "any event perpetrated by the patient, patient relatives or other individuals which poses a risk for the healthcare worker including threatening behavior, verbal threat, economic abuse, physical and sexual assault" [1].

Healthcare workers around the world are at elevated risk for violence. According to the World Health Organization (WHO) data, 8% to 38% of healthcare workers are subjected to physical violence at some time in their professional life, and verbal violence at much higher rates. They can even be targets of collective or political violence in disasters or under other extraordinary conditions. The perpetrators of violence are mostly patients or visitors, and those most at risk are nurses, other staff directly involved in patient care, and the emergency room staff [2, 3].

Violence in health is becoming more common in our country, and according to a report published by the Turkish Medical Association, a total of 15,841 cases of violence were experienced in 2018, including 661 physical, 12,179 verbal, and 3,001 both physical and verbal violence. However, only 11,204 events were brought to justice [4, 5]. A practice was initiated by the Ministry of Health to report violent incidents and provide legal aid to healthcare workers who were subjected to violence, and a "113 White Code Call Center" was established to provide 24/7 service [6]. The calls to the center are mostly being made by physicians [4, 7]. Unfortunately, intern physicians are among the groups subjected to violence, which affects both their education processes and their future professional practices negatively [8, 9]. Exposure to violence not only causes physical and mental problems, but also negatively affects interpersonal relationships, decreases motivation, and causes absenteeism and changes in career choice.

A significant part of the violence in health is due to communication problems in the relationship between the physician and patient. A study revealed that approximately 40% of the patients' complaints were caused by communication problems [4]. The development of interpersonal communication skills is important in all areas that require human relations, and individuals can influence the feelings, thoughts, and behaviors of the people around them with this skill. Therefore, communication skills are of great importance in establishing correct and effective communication and in eliminating or reducing communication conflicts [10].

This study aimed to determine the relationship between the communication skills of intern physicians who work at Ondokuz Mayis University Faculty of Medicine and their exposure to violence in the workplace in the last year.

Materials and methods

This cross-sectional study includes 287 students who worked as intern physicians at the Ondokuz Mayis University Faculty of Medicine within the academic year of 2018-2019. When the frequency of violence against healthcare workers was considered 62% [11], with 80% power and 5% type-1 error, and a deviation value of 10%, the minimum sample size was 180. When the 20% reserve list was added, it was aimed to reach at least 225 interns. The study was conducted with 234 interns who agreed to participate. A prequestionnaire was administered to 15 students of similar ages to detect comprehension problems and to assess whether the questions were in agreement with the research aims. After the prequestionnaire, a few questions were modified, and the implementation phase began. The data were collected through a questionnaire form applied face-to-face. Students were allowed to answer questions in an environment where they were alone, without specifying their identity. The study was based on the declaration of persons. Approval was obtained from Ondokuz Mayis University Clinical Research Ethics Committee (OMU-KAEK 2018/11) for this study. In the questionnaire form of 33 questions, the Communication Skills Scale (CSS) was used, as well as questions about sociodemographic characteristics and violence. CSS scale, developed by Korkut [12], consists of 25 questions that individuals can answer by considering their relationships. Ranging from 0 to 4 (0 = never, 4 = always) for each question, the lowest and highest scores that can be obtained from the 5-point Likert-type scale are 0 and 100, respectively. The higher the score obtained from this scale, which has a test-retest scale reliability of 0.76 and a Cronbach alpha coefficient of 0.80 (P<0.001 for both), the more successful the individuals consider themselves in terms of communication skills [12].

Statistical analysis

SPSS 22.0 program was used for statistical analysis of the data. Among the continuous variables, data conforming to the normal distribution were expressed as mean (standard deviation), non-normally distributed data, as median (range), and categorical variables, as frequency (%). Compliance of data to normal distribution was assessed with the Kolmogorov-Smirnov test. In the comparison of two groups of data conforming and not conforming to a normal distribution, the independent samples t-test, and Mann-Whitney U test, respectively, were used. P<0.05 was considered significant.

Results

One hundred nineteen (50.9%) of the 234 intern physicians who voluntarily participated in the study were female and the mean age was 25.9 (7.9) years. The median time that the participants had spent as interns was 6 (1-16) months. Eighty-six (36.8%) interns stated that they were exposed to violence during their duty within the last year. The number of female and male interns exposed to violence was 54 (45.4%), and 32 (27.8%), respectively. There was a statistically significant difference between the genders in terms of exposure to violence (P=0.005). The characteristics of the violence that interns were subjected to are presented in Table 1. Accordingly, verbal violence was the most common type (97.7%). Violence mostly occurred between 08:00 and 16:00 (66.3%), and those who resorted to violence most were the patient relatives (58.1%). Among all, 64.0% of the interns did not report this violence to any department.

Among the opinions of the interns about the reasons for the violence, the most common answers were "low education levels of patients and their relatives and not obeying the rules" (65.4%) and "misunderstanding and communication problems" (60.7%) (Table 2).

While the mean overall CSS score was 73.5 (9.6), it was 75.1 (7.9) among females and 71.9 (10.9) among males

(P=0.012). While there was no significant difference between the interns in terms of exposure to at least one type of violence or verbal violence (P>0.05), the scale score was significantly lower in those who were exposed to physical violence (P=0.032) (Table 3).

Table 1: Distribution of exposed violence according to various characteristics

Characteristics related to violence	n	%
Violence in last year (n:234)		
Exposed	86	36.8
Not exposed	148	63.2
Type of violence* (n:86)		
Verbal	84	97.7
Physical	5	5.8
Time of violence (hours) * (n:86)		
08:00-16:00	57	66.3
16:00-24:00	50	58.1
24:00-08:00	37	43.0
Time of violence (shift)* (n:86)		
Working hours	57	66.3
Out of hours	64	74.4
Perpetrator*(n:86)		
Relatives of the patient	50	58.1
Healthcare worker	41	47.7
Patient	38	44.2
Post-violence applied unit *(n:86)		
Nowhere	55	64.0
Unit manager	9	10.5
White code	3	3.5
Medical chamber	2	2.3
Police or private security	2	2.3
Institution manager	1	1.2

* There was more than one answer.

Table 2: Participants' opinions on the reasons for violence (n:234)

Causes of violence	n	%*
Low education level of patients and their relatives and not following the rules	153	65.4
Misunderstanding and communication problems	142	60.7
Excessive workload	135	57.7
Disease psychology	122	52.1
Health policies implemented	119	50.9
Excessive requests of patients and their relatives	106	45.3
Long waiting period of the patients	101	43.2
Other	29	12.4

* There was more than one answer.

Table 3: Distribution of CSS scores by type of violence exposed

Type of violence	CSS Score Mean (SD)	P-value
At least one type of violence		
Exposed	73.7 (9.3)	0.849
Not exposed	73.4 (9.9)	
Verbal		
Exposed	74.2 (9.0)	0.433
Not exposed	73.2 (10.0)	
Physical		
Exposed	64.0 (9.1)	0.032
Not exposed	73.7 (9.5)	

CSS: Communication Skills Scale, SD: Standard deviation

Discussion

This study found that the prevalence of exposure to violence in interns was 36.8% in the last year, and in studies involving interns across the country, this rate was ranged between 16.6-65.5% [9, 13, 14]. In a meta-analysis conducted in Iran [15], 59% of medical faculty students and 61.9% of healthcare workers were exposed to violence at work in the last year [11]. Varying rates of exposure to violence are likely because the period of exposure to violence is stated differently in the studies, or violence is perceived as physical violence by the respondents.

Verbal violence is the most common form of violence against healthcare professionals both in our country and abroad [8, 13, 16, 17]. The interns in the study were also exposed to verbal violence the most. Considering that anger is initially expressed verbally, this is an expected finding.

The fact that violence mostly occurs between 08:00 and 16:00 is similar to the distribution of the White Code applications in a hospital in Istanbul [4]. In an international study, it was reported that the majority of incidents took place after working hours [16]. However, it would be more accurate to take into account the number of patient visits between the relevant hours to talk about a definite relationship between certain hours of the day and the frequency of violent incidents.

Although the ranking of the people who perpetrate violence against healthcare professionals differs in studies, it is seen that most violence is perpetrated by patients and their relatives [17-19]. However, the striking point is that although the people who used violence most were identified as relatives of the patients in this study, health care workers took second place as the perpetrators of violence. In a study conducted at a medical school in Ankara, when the interns were asked about the last person who committed violence against them, the answer was mostly the senior staff [13]. In a study conducted in Iran, 44.6% of the violence to medical school students in the last year was committed by nurses and other employees [15]. Considering that violence against healthcare professionals causes burnout and decreased job satisfaction, the reasons for the attitudes and behaviors of other healthcare professionals towards the interns and medical students should be examined [17].

After the violent incidents occurring in various health institutions, most healthcare workers generally prefer not to report this incident through any official channel [13, 18, 20]. Not wanting to deal with the legal procedure due to workload, lack of information about which unit to apply and how, or not believing that the applications will have deterrent consequences for the perpetrators of violence can be shown among the reasons for a similar result in the present study. In a study involving medical students, most participants stated that they thought they would not receive adequate support after a possible incident of violence, and it was seen that very few had an idea about the White Code procedure [20]. The code systems used to report emergencies in hospitals are also used in various countries of the world. For example, in the United States, the Hospital Association of Southern California proposed the gray code for unarmed attackers and silver for armed attackers to eliminate the confusion created by the code classification that varies according to the hospital [21]. In studies conducted abroad, healthcare workers often do not report the violence they are exposed to. In a study involving healthcare professionals in the United States, 96% of the employees who were subjected to violence knew that they had to report it electronically, but only 12% reported it officially [22]. The reasons are fear of the aggressor or family, shame about being the subject of aggression, and considering violence as a routine part of the work [23]. In a study conducted in India, physicians who were subjected to violence and did not report it stated that they saw it as a useless and time-wasting process [24].

The intern physicians participating in the study cited the reasons for violence as the low level of education of the patients and their relatives and not obeying the rules. There are different findings in the literature regarding the reasons for violence from the healthcare professionals' perspective. In studies involving interns, responses such as "not behaving as expected" and "patients waiting for a long time for an examination " were the most common reasons for violence [13, 25]. In a study conducted in India, medical faculty students pointed out illiteracy as the

most common cause of violence of the patients and lack of information for the violence committed by the doctors [26]. These differences may be related to the internal dynamics such as the management of the health institutions in question, or the patients and their relatives, which varies according to the institution where the studied individuals work. Additionally, it may be related to factors such as personal characteristics, communication methods, or the skills of the colleagues.

While the CSS scores of the interns who were exposed to any type of violence or verbal violence were similar, the scale scores of the individuals exposed to physical violence were significantly lower. In a similar study, there was no significant difference in terms of scale scores between healthcare workers who were exposed to violence and those who were not [27]. However, in a review study, the communication skills of healthcare trainees increase with the employees' self-confidence in managing patients' aggressive attitudes [28]. We believe that this data is generalizable due to the scarcity of studies in this area and the difference in research methods used. Due to the nature of the communication between people, each violent event has its reasons. In addition to reasons such as poor moral judgments, low empathy and reasoning ability, male gender, young age, past violence, substance use, psychotic illnesses, personality disorders, rapid social changes in the society, economic inequalities, social norms that encourage violence, non-enforcement of laws, a weak legal system and the easy supply of lethal devices such as firearms increase the risk in terms of interpersonal violence [29, 30]. Considering the "low education level of patients and their relatives and them not following the rules" and "misunderstanding and communication problems" among the main reasons stated in our study, increasing health literacy and providing education to all segments of the society to improve communication skills should not be passed on. Preventing unnecessary applications to health institutions will be beneficial to reduce the workload of healthcare workers, as well as the waiting time of patients and their relatives in health institutions. We think that all regulations regarding these practices will contribute to the prevention of violence against healthcare workers. More scientific studies and evidence are needed to develop new policies and alter health managers' approaches in this regard.

Limitations

This study has some limitations. Communication skills are measured by self-reports; hence, our data is subjective. The study sample represents the intern physicians working at Ondokuz Mayis University. Since there were individuals who were at the beginning of their internship among the participants, they may not have been in risky environments in terms of exposure to violence.

C**onclusion**

In the light of existing data, it would not be the right approach to highlight the inadequacy of healthcare professionals in communication, especially among the main factors that cause verbal violence. The low CSS score of interns who were subjected to physical violence compared to those who did not put their communication skills in the foreground, especially in physical violence. However, the small number of people in this group should be considered in terms of the validity of the statistical evaluation, and larger groups should be studied to make a community-wide assessment.

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Long term outcome in obstetric brachial plexus injury at a tertiary care center

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The study approval was obtained from the ethics committee of Izmir Bakircay University, faculty of medicine, with the number 343/323.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Obstetric brachial plexus injury (OBPI) is caused by traction to the brachial plexus during labor. Traction injury may vary from neurapraxia or axonotmesis to neurotmesis and can cause edema, avulsion, or rupture of the nerve. Improvement in the first two weeks after birth is a good indicator of outcome. The disability varies according to the location and severity of the effect in the plexus. However, most injuries are transient, with a total return of function in many cases. This study aimed to obtain clues for the prevention and follow-up of obstetric brachial plexus injuries by revealing the outcome and clinical features.

Methods: In this retrospective cohort study, hospital records of patients with brachial plexus injury due to delivery were reviewed between January 2017 and September 2021. Injury levels, birth weights, other injuries at birth, maternal age, gravidity, gestation time, and treatment response were recorded. Brachial plexus injuries of the patients were classified per the NARAKAS classification. The Spearman correlation and Pearson correlation tests were used for correlation analyses. The variables were evaluated with the Chi-Square and Student's t-tests. The normality of the distribution was assessed with the Kolmogorov-Smirnov test. A value of $P<0.05$ was considered statistically significant.

Results: Thirty-nine cases were included in the study (21 males, 18 females). The mean and median birth weights were 3857 (392) grams, and 3880 (3100-4600) grams, respectively. The median gestational week of birth was 39 weeks. Most mothers were primigravida. All patients were born by vaginal delivery. Per the NARAKAS classification, 29 patients (74.4%) were in group 1, 5 patients (12.8%) were in group 2, 4 patients (10.3%), in group 3, and 1 patient (2.5%) was in group 4. The mean follow-up period was 23.2 (14.1) months. Twenty-four patients recovered spontaneously; six had sequelae without functional impairment, five had sequelae with functional impairment, and two had contractures. The relationship between the NARAKAS groups and birth weight was insignificant ($P=0.09$). There was a significant correlation between the NARAKAS group and recovery ($P<0.001$). A correlation was found between sequelae and functional loss ($P=0.01$) and the NARAKAS group. Functional loss was not related to maternal age, week of birth, birth weight, baby gender ($P=0.15$, $P=0.30$, $P=0.20$, $P=0.15$ respectively).

Conclusion: Permanent functional loss in brachial plexus injury is associated with the NARAKAS classification, and patients in groups 3 and 4 should undergo imaging as soon as possible. Electromyography (EMG), a complex invasive procedure for the newborn, should be preferred if there is no satisfactory recovery. We recommend performing brachial plexus magnetic resonance imaging before EMG to give the patient a chance for early surgery.

Keywords: Brachial plexus injury, NARAKAS, Outcome, Children, Birth weight

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Introduction

Obstetric brachial plexus injury (OBPI) was at similar rates in numerous studies and is estimated to be between 1.5 and 4 per 1000 births [1–3].

Brachial plexus injury mostly involves the C5 and C6 spinal nerves. The patients' rate of spontaneous recovery is the highest at this level. Less involvement is observed in C5-C7 and C7-T1 localizations, with high rates of loss of function [4]. Generally, these infants are diagnosed with brachial plexus injury at the first examination. The difficulty is to determine the level of damage. Early identification of the affected spinal nerves and their severity is essential to determine the prognosis, for which clinical examination, electromyography (EMG), and plexus magnetic resonance (MR) are used [5, 6]. We aimed to determine the risk factors for obstetric brachial plexus injury, measure the prognostic differences between patients with and without functional sequelae, and find out which diagnostic test should be used in these patients.

Materials and methods

This retrospective cohort study was conducted in a tertiary care hospital between January 2017 and September 2021. Thirty-nine patients with obstetric brachial plexus injury were followed for about two years. Patients' birth weight, number of births, maternal age, gestational week, delivery type, health personnel accompanying the birth, predisposing factors, location and severity of the injury, treatment methods, the long-term outcomes, and NARAKAS groups were recorded [7] (Table 1).

Table 1: NARAKAS Classification

Group	Level	Clinic Presentation
Group 1	C5-C6	Shoulder abduction, shoulder external rotation, elbow flexion, and wrist extension
Group 2	C5-C6-C7	Wrist flexors, finger flexors, intrinsic muscles of the hand
Group 3	C5-T1 without Horner syndrome	Upper extremity flaccid paralysis
Group 4	C5-T1 with Horner syndrome	Upper extremity flaccid paralysis and miosis, ptosis, and enophthalmos

The patients were examined for the first time in the neonatal unit, then at two weeks of age. After the 2nd week, they were followed monthly for the first six months and every 2-3 months thereafter.

Selection bias was avoided by recruiting every patient diagnosed with brachial plexus injury in the outpatient clinic between the specified dates.

Statistical analysis

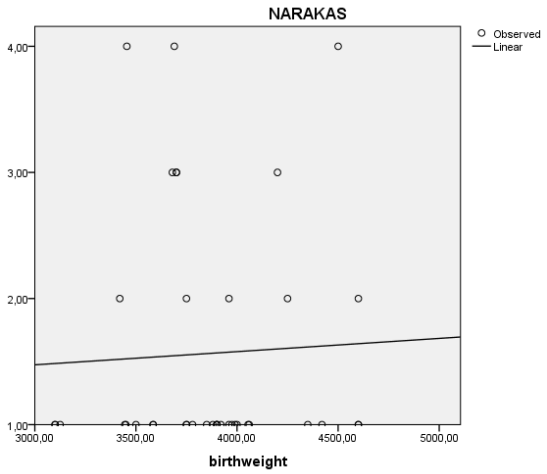
The Spearman and Pearson correlation tests were used to analyze ordinal and continuous variables, respectively. Calculations of the mean, median, frequency, and standard deviation (SD) were made using the Statistical Package for Social Sciences (SPSS) software for Windows, version 23.0, and the results were given as mean (SD). The variables were evaluated with the Chi-Square and Student's t-tests. The student's t-test was used to compare the means between the two groups. The normality of the distribution was evaluated with the Kolmogorov-Smirnov test. A value of $P<0.05$ was considered statistically significant.

The study approval was obtained from the ethics committee of Izmir Bakircay University, Faculty of Medicine, with the number 343/323. Informed consent forms were obtained from all parents.

Results

Twenty-one patients were male, and 18 were female. The mean and median birth weights were 3857 (392), and 3880 (3100-4600) grams, respectively. The median gestational week of birth was 39 weeks. The mean maternal age was 28.05 (4.99) (21-39) years. Most mothers were primigravida. All patients were born by vaginal delivery. The doctors managed 26 deliveries, and nurses managed the rest. There was no relationship between the groups of NARAKAS and the health personnel who assisted the birth. The brachial plexus injury rate was 4.5 per 1000. The accompanying findings were Horner syndrome in 4 patients, clavicle fractures in 11 patients, and hypoxic-ischemic encephalopathy in 2 patients. Per the NARAKAS classification, 29 patients (74.4%) were in group 1, 5 patients (12.8%), in group 2, 4 patients (10.3%), in group 3, and 1 patient (2.5%) was in group 4. The mean follow-up period was 23.2 (14.1) months. Twenty-six patients recovered spontaneously, 6 had sequelae without functional impairment, 5 had sequelae with functional impairment, and 2 had contractures. The relationship between the NARAKAS groups and birth weight was insignificant ($P=0.09$) (Figure 1).

Figure 1: NARAKAS classification and birth weight distribution



Plexus MRI was performed in 14 patients, and EMG was performed in 11 patients. EMG was performed when there was no improvement in the second or third visits of the patients. Although surgery was recommended to four patients, only one underwent surgery in the 5th month.

Patients received physical therapy, surgical treatment, or just observation. The treatments applied and their results are shown in Table 2. NARAKAS groups and recovery were correlated ($P=0.003$). Physical therapy is still administered to patients with sequelae.

Table 2: Treatment and outcome of the patients

	Surveillance	Physiotherapy	Surgery
Complete recovery	19	7	-
The residual deficit without loss of function	-	6	-
The residual deficit with loss of function	-	5	-
Contracture	-	1	1

No correlation was found between NARAKAS groups and birth weight ($P=0.089$). NARAKAS groups and sequelae with functional loss were significantly correlated ($P=0.01$). Twenty mothers were primiparous.

Rhere was no relationship between functional loss and maternal age, week of birth, birth weight, and baby gender (P=0.15, P=0.30, P=0.20, P=0.15 respectively).

Discussion

Between the years of our study, the rate of brachial plexus injury in our hospital was 4.5 per 1000 live births, higher than in the literature. This may be attributed to the very low number of cesarean sections in our hospital, the high number of immigrant patients admitted for emergency delivery without follow-up, and the insufficient number of midwives.

Macrosomia, breech presentation, maternal diabetes mellitus, use of assistive devices during delivery, and having a child with brachial plexus palsy in previous births are risk factors for brachial plexus palsy [4]. However, no consensus or meta-analysis studies recommend cesarean section in patients with these risk factors. In addition, macrosomia is defined as a newborn weight of over 4000 g, whereas in our patients, the average birth weight was 3880 g. Even if there was an indication for a cesarean section in macrosomia, our patients would still be born by vaginal delivery. However, studies drew attention to cases over 3800 g [8]. The fact that the gestational week of the patients was above 39 weeks seems to be a risk factor in our study. Similar results are available in the literature [9]. There are studies in which spontaneous recovery is quite high in obstetric brachial plexus injury compared to our study [10]. The rate of recovery without sequelae is 82% in our patients.

Group 1 and group 4 patients often do not experience management difficulties. Almost all NARAKAS group 1 patients recover within two weeks to 2 months. The cases with C5-T1 involvement and Horner syndrome should undergo surgery as soon as possible.

All NARAKAS group 1 patients recovered without sequelae. Contracture was observed in the patient in group 4. Although early surgery was recommended, he underwent surgery in the fifth month. However, it is often difficult to decide when to perform surgery in patients in groups 2 and 3. In a study of 66 infants, normal upper extremity use was achieved in cases whose biceps function improved before 3 months of age [11]. However, long-term functional outcomes were worse in infants whose biceps function improved at 4, 5, and 6 months. Another study observed that if there was no movement against gravity in the proximal muscle groups when the babies were six months old, severe muscle weakness continued in the future [12].

When the infant was one month old, examination and EMG findings were superior in detecting brachial injury than the examinations performed in the first week. Although the false-positive and false-negative rates are lower in the tests performed at three months of age, it seems appropriate to examine them at one month since it may cause a delay in patients requiring surgery. In addition to the time of examination, early detection of localization is also crucial in determining the prognosis. Elbow extension, elbow flexion, and motor unit potentials in biceps muscle evaluations revealed the detection rate of mild and severe cases as 93.6% [10]. It implies that children should be referred to centers where physiotherapy and surgery can be performed if active elbow extension is insufficient when the infant is one month old. Needle EMG should be performed on the patient who cannot achieve elbow flexion. The absence of MUPs in the biceps muscle in EMG is an indication for referral to surgery centers [13]. If there is any disability in the 1st-month evaluations of the patients under follow-up, we initiate physical therapy. If there is limited forearm flexion in the 1st month of evaluation, we recommend plexus MRI and/or EMG in addition to physical therapy and plexus MRI in a patient with NARAKAS group 4 in the first evaluation.

Although electromyography and nerve conduction studies are considered "overly optimistic" in infants, early examinations can save costs later, but invasive procedures such as sedating the baby during the examination may be required [14]. EMG is performed in the first week after birth for medico-legal reasons to distinguish intrauterine or delivery damage. It is performed in patients with brachial plexus injury who have not recovered after the 1st month, those who will undergo tendon transfer, to identify candidates for surgical exploration, and to determine the appropriate surgical procedure [13].

In severe cases, plexus MRI is superior to an invasive technique such as EMG, which may lead to misdiagnosis in the first month, in not missing the chance of early surgery. Plexus magnetic resonance imaging is important in determining the location of the damage (pre-ganglionic or post-ganglionic) and distinguishing between complete ruptures and avulsions [15].

New protocols are implemented instead of MRI protocols that require sedation and long-term imaging. Rapid non-sedated volumetric Cube Proton Density MRI protocol detected the location and severity of the injury quickly and accurately without sedation [16, 17].

The accompanying findings were Horner syndrome in 4 patients, clavicle fracture in 11 patients, and hypoxic-ischemic encephalopathy in 2 patients in our study. About 26% of patients with a clavicular fracture also sustained a brachial plexus injury. This incidence is consistent with the other data from Turkey [9].

Limitations

The main limitation of this study is its retrospective nature and the lack of a control group.

Conclusion

Among many factors such as maternal age, primiparity, birth weight, and gestational age, only the NARAKAS group was a predisposing factor that could indicate permanent damage in infants with brachial plexus injury. All patients with NARAKAS group 3-4 should be assessed for early imaging and early surgery. Plexus MRI seems a suitable method for these patients. EMG can be preferred in patients with Horner's syndrome or in patients whose wrist flexion has not improved after one month of age.

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Determination of bone age and evaluating the applicability of Greulich-Pyle standards among the Turkish children

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Ethics Committee Approval
The study protocol was approved by the Ethical Committee of Afyonkarahisar Health Sciences University (2020/561).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Bone age (BA) is important in the diagnosis and follow-up of pediatric growth disorders. Skeletal maturation can vary according to the geographical region and climate. The goal of this study is to investigate whether Greulich-Pyle (GP) method is suitable for detecting BA for Turkish children for all age groups and both genders.
Methods: In our retrospective cohort study, the roentgenograms of all pediatric patients who visited the pediatrics or pediatric endocrinology outpatient clinics and underwent left hand and wrist radiographs for suspicious trauma or BA determination were examined with reference to the GP atlas. Patients without evidence of chronic disease or growth disorders with body size and weight values between the 25th-75th percentile were included. Poor quality roentgenograms were excluded.
Results: Radiographs of 665 patients were analyzed and 310 (161 boys and 149 girls, age range 13-203 months) patients were included. The rate of concordant BA with CA was significantly higher in the children above 120 months of age and low BA was significantly higher among the children aged 120 months or below (P<0.001). The rate of concordant BA with CA was significantly higher among girls and low BA was significantly higher among boys (P=0.014). Among patients aged 120 months or below, low BA was significantly higher in the boys (P<0.001). There were no significant differences between the boys and girls aged 120 months and above (P=1.000)
Conclusion: Although widely used in the determination BA, local studies on the accuracy and reliability of the GP method are insufficient in less developed countries. The accuracy of this method in Turkish children, especially boys under the age of 10 years, is controversial, and correct standards should be developed.

Keywords: Bone age, Greulich-Pyle, Chronogical age, Wrist and hand, Skeletal maturation

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Introduction

Bone age (BA) determination is used in various areas, including medical, sporting, and forensic fields [1, 2]. Medical reasons often include endocrine, genetic, orthopedic, and renal disorders. It plays an important role in the diagnosis and treatment of pediatric growth disorders for pediatric endocrinologists. Adult height and growth potential can be estimated from BA radiographs in a child with a growth abnormality. The starting time and duration of the treatment in children who need hormonal therapy depends on the correct evaluation of BA [3, 4].

The most common methods used to determine BA are Greulich-Pyle (GP) and Tanner-Whitehouse2 (TW2) techniques. Studies have shown that there is no significant difference between these two methods in determining the BA [1, 3, 5-8]. The GP method is more preferred because it is less time consuming and practical [1-3]. GP, which is still the most widely used worldwide method in detecting BA, was published by Greulich and Pyle in 1959 under the title "Radiographic atlas of skeletal development of the hand and wrist".

The GP atlas contains reference radiographic images of the left wrist and hand created according to the male and female standards from birth to the age of 19 for males and 18 for females. However, the reference images in this atlas are based on 'Caucasian' children residing in the United States whose economic and educational statuses are above average, and uses the measurements compiled in the 1930s [1, 9]. Thus, the radiographic standards used in this method are based on a narrow population that is homogeneous both genetically and socio-economically. It is unclear whether these skeletal maturation standards, which use data from the first half of the twentieth century, are applicable in the existing populations that differ geographically, genetically, and socio-economically from the GP reference population. In fact, studies conducted in many countries attempted to evaluate the accuracy of the GP atlas in various populations [1-21]. Some studies found that GP atlas can be used for bone age determination in the population they have studied [2-4, 10, 15, 17, 20]. However, studies in developing countries have raised doubts about the accuracy of the GP atlas [1, 11, 12, 14, 21].

Although it is widely used in the determination of BA, local studies on the accuracy and reliability of the GP method are insufficient. To date, only a few studies were performed in Turkey regarding detecting BA with only the GP method [3, 10, 11]. Only one of these studies was conducted in all age groups and both genders and consisted of 228 patients [3]. In most of these studies, children over the age of 7 or 10 years were included. Büken et al. [10] examined girls and boys only over 11 years of age, and Koç et al. [11] examined only male patients over 7 years of age. Our study is the first one evaluating the accuracy and reliability of the use of the GP method only in the determination of BA in all age groups (13-203 months) with the highest number of patients (310 patients) in the Turkish population for both genders.

This study aimed to investigate whether the GP atlas is suitable for detecting BA for Turkish children for all age groups and both genders.

Materials and methods

The roentgenograms of all pediatric patients who visited the pediatrics or pediatric endocrinology outpatient clinics and underwent left hand and wrist radiographs for suspicious trauma or BA determination between 01.01.2020-01.12.2020 were examined retrospectively.

The patients meeting all the following criteria were included in the study: 1) No chronic disease or long-term drug use. 2) No clinical evidence of growth disorders, with values of body size and weight between the 25th and 75th percentiles for a normal age-related population. 3) Normal findings on the radiograph (without bone (including fractures) or soft tissue abnormalities).

Poor quality roentgenograms (poor sharpness or positioning and incomplete radiographs or images with artifacts) were excluded. Images with fractures, patients with known congenital anomalies, arthritis or any obvious disease of the hand and wrist that could affect skeletal maturation or interfere with BA determination were excluded. Patients whose body size and weight values were not measured were also excluded.

Digital wrist and hand images were taken from the Picture Archiving and Communication System. Posteroanterior (PA) or anteroposterior (AP) views including the distal ulna, radius, metacarpals, carpals, and phalanges were used. The BA within 2 SD of the normative data in the GP atlas were accepted as normal. The BA above or below 2 SD were considered abnormal.

The images were examined by three radiologists with 25 years, 15 years and 10 years of experience and BA was evaluated according to the GP atlas (9). The radiologists were blinded to the chronological age (CA) of each patient. Three radiologists made joint decisions for BA.

The radiographs of 665 patients were analyzed and a total of 310 patients who met the criteria were included in the study.

The study protocol was approved by the Ethics Committee of Afyonkarahisar Health Sciences University (2020/561).

Statistical analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). Histogram and Q-Q plots were used to determine whether the variables are normally distributed. Data were given as mean (standard deviation) (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t test. Categorical variables were analyzed with the Chi-square test. Bonferroni correction method was used for pairwise comparisons. $P<0.05$ was considered statistically significant.

Results

We included 310 children (161 boys and 149 girls) in our study, with a mean age of 107.80 (49.48) months (range 13-203). The mean ages of the males and females were 111.41 (52.98) months (range 13-203) and 103.91 (45.26) months (range 14-196), respectively ($P=0.180$). The ages of 188 (60.65%) children were ≤120 months and that of 122 (39.35%) children were >120 months.

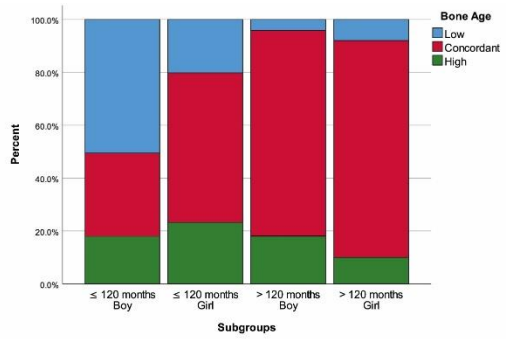
We divided the children into four subgroups according to age and gender. We had 89 (28.71%) boys and 99 (31.94%) girls aged ≤120 months, 72 (23.23%) boys and 50 (16.13%) girls aged >120 months. The mean BA was 106.80 (53.93) months (range 12- 210). BAs were lower than CA in 72 (23.23%) children, concordant with CA in 181 (58.39%) children and higher than CA in 57 (18.39%) children (Table 1, Figure 1).

Table 1: Summary of variables

	Value n(%)
Gender	
Boy	161 (51.94%)
Girl	149 (48.06%)
Age (months)	107.80 (49.48) (13 - 203)
≤ 120	188 (60.65%)
> 120	122 (39.35%)
Subgroups	
≤ 120 months Boy	89 (28.71%)
≤ 120 months Girl	99 (31.94%)
> 120 months Boy	72 (23.23%)
> 120 months Girl	50 (16.13%)
Bone age (months)	106.80 (53.93) (12 - 210)
Low	72 (23.23%)
Concordant	181 (58.39%)
High	57 (18.39%)

Data are given as mean (standard deviation) (minimum - maximum) for continuous variables and as frequency (percentage) for categorical variables

Figure 1: Bone age estimates with regards to the subgroups



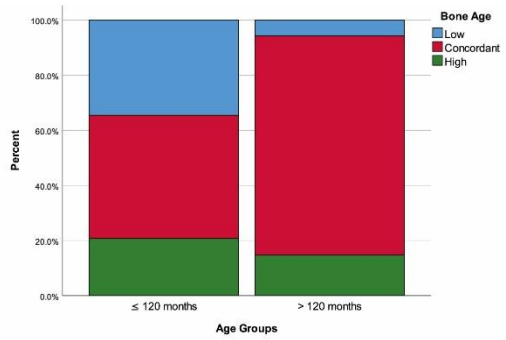
The concordant BA percentage was significantly higher among the children aged 120 months (79.51%) than among those aged ≤120 months (44.68%). Low BA percentage was significantly higher among children aged ≤120 months (34.57%) than in the children aged >120 months (5.74%) (P<0.001). High BA percentages were similar (Table 2, Figure 2).

Table 2: Bone age estimates with regards to the age groups

	Age groups		
	≤ 120 months (n=188)	> 120 months (n=122)	*P*-value
Bone age			
Low	65 (34.57%)	7 (5.74%)	<0.001
Concordant	84 (44.68%)	97 (79.51%)	
High	39 (20.74%)	18 (14.75%)	

Data are given as frequency (percentage)

Figure 2: Bone age estimates with regards to the age groups



The rate of concordant BA with CA was significantly higher among girls (65.10%) than among boys (52.17%). Low BA percentages were significantly higher among the boys (29.81%) than among the girls (16.11%) (P=0.014). High BA percentages were similar (Table 3, Figure 3-6).

Table 3: Bone age estimates with regards to gender

	Gender		
	Boy (n=161)	Girl (n=149)	*P*-value
Bone age			
Low	48 (29.81%)	24 (16.11%)	0.014
Concordant	84 (52.17%)	97 (65.10%)	
High	29 (18.01%)	28 (18.79%)	

Data are given as frequency (percentage)

Figure 3. Bone age estimates with regards to gender

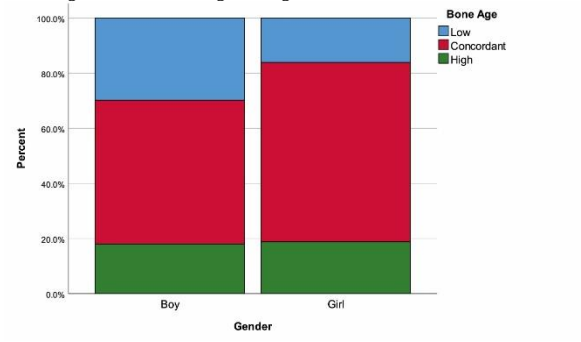


Figure 4. Boxplot of the age with regard to gender

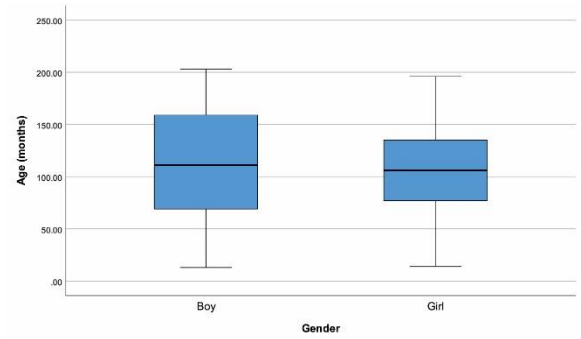


Figure 5: Left wrist and hand radiographs of a 147-month-old and female patient. With reference to the Greulich-Pyle atlas, the bone age is consistent with chronological age.

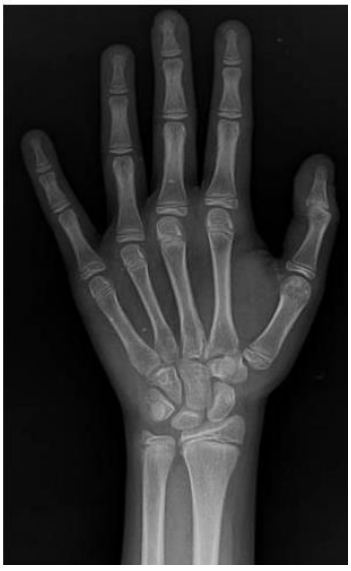
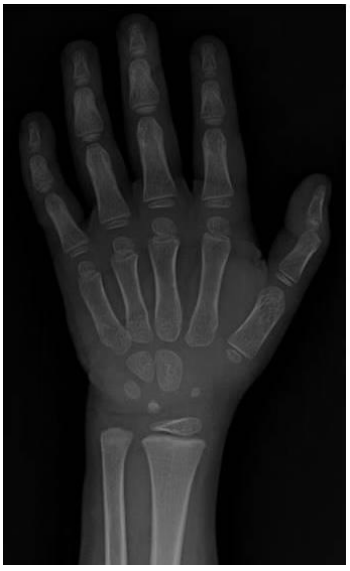


Figure 6: Radiograph of left wrist and hand is given. Based on Greulich-Pyle atlas, the bone age is lower than the chronological age in the 77-month-old male patient.



Among patients aged ≤120 months, we found significant differences between the subgroups with regards to BA estimates (P<0.001). Concordant BA percentage was significantly higher in girls (56.57%) than in boys (31.46%). Low BA percentage was significantly higher in boys (50.56%) than in girls (20.20%) (P<0.001). High BA percentages were similar between the boys and girls. There were no significant differences between boys and girls aged >120 months with regards to BA estimates (P=1.000) (Table 4).

Among the boys, concordant BA percentage was significantly higher in those aged >120 months (77.78%) than those aged ≤120 months (31.46%). Low BA percentages were significantly higher among those aged ≤120 months (50.56%)

than in those aged >120 months (4.17%) (P<0.001). High BA percentages were similar between boys aged ≤120 months and those aged >120 months (Table 4).

Among the girls, concordant BA percentages were significantly higher in those aged >120 months (82.00%) than in those aged ≤120 months (56.57%) (P=0.036). Low and high BA percentages were similar between girls aged ≤120 months and those aged >120 months (Table 4).

Table 4: Bone age estimates with regards to subgroups

	Subgroups				
	≤ 120 months Boy (n=89)	≤ 120 months Girl (n=99)	> 120 months Boy (n=72)	> 120 months Girl (n=50)	*P*-value
Bone age					
Low	45 (50.56%) [a]	20 (20.20%) [b]	3 (4.17%) [c]	4 (8.00%) [bc]	<0.001
Concordant	28 (31.46%) [a]	56 (56.57%) [b]	56 (77.78%) [c]	41 (82.00%) [c]	
High	16 (17.98%) [a]	23 (23.23%) [a]	13 (18.06%) [a]	5 (10.00%) [a]	

Data are given as frequency (percentage). Same letters denote the lack of statistically significant difference between subgroups.

Discussion

Identifying the BA and comparing it with the CA is very important, especially for pediatric endocrinologists, to understand whether patients are growing properly, to make treatment decisions if necessary and to monitor treatment outcomes. Today, BA is often determined from the left wrist and hand radiographs with reference to the GP atlas. However, skeletal maturation may vary depending on the geographical region, and socioeconomic and ethnic group differences [2]. Our study was conducted to determine whether the GP atlas is adequate for Turkish children born after the 2000s.

The GP atlas is based on research conducted by T. Wingate Todd on radiographs of the left wrist and hand. The method involves direct comparison with standard same-sex radiographs by analyzing features such as ossification centers, bone numbers and contours, and examination of growth plates. Standards are classified by sex and give median skeletal maturity for CA [3, 9].

In TW2, which is the other method used much more rarely in the determination of BA, a bone-specific approach is taken, and a separate grading is assigned for each bone of the hand and wrist with the average or median grading used as BA [3]. GP atlas is more preferred in the determination of the BA because it can be applied more easily in daily practice and does not cause time loss.

There are some studies conducted in various countries that determine BA according to the GP atlas. Mora et al. [4] analyzed BA according to the GP atlas for African American and European American children, found significant differences of BA and concluded that the GP standards are unclear for European and African American children. Groell et al. [2] evaluated BA for 47 European children and concluded that the GP atlas could be safely used for European children. Van Rijn et al. [15] examined the Dutch children's BA and found the GP method usable for BA determination. Al Shamrani et al. [17] evaluated the radiographs of 392 patients taken due to trauma in United Kingdom. They observed that there was no significant difference between BA and CA when the GP atlas was used. De Donno et al. [18] examined 300 healthy Italian children and stated that GP atlas yielded results compatible with CA. Dantas et al. [19] investigated the applicability of the GP atlas for the Brazilian population on 150 cases between the ages of 5 and 18 years. They stated that BA is often greater than CA in the female age group, nevertheless, this method is reliable in determining the BA. In a study in South Africa, Govender et al. [1] evaluated the radiographs of 102 patients aged between 0 and 21 years retrospectively. They reported that BA was significantly low in the GP method for both genders and that a novel method should be developed for their country.

There are also studies in the literature questioning the accuracy of the GP method in the Turkish population. Büken et al. [10] evaluated the left-hand wrist radiographs of 251 patients, including boys and girls older than 11 years. They stated that the method could be used by clinicians. Cantekin et al. [20] examined the BAs of 757 boys and girls over the age of 7 years according to the GP atlas. They conducted a BA examination on eastern Turkish children and stated that the average differences between BA and CA were practically insignificant. In our study, we found that BA and CAs were concordant in girls and boys over 10 years of age, and there was incompatibility in boys younger than 10 years of age.

Güngör et al. [21] examined the left-hand wrist radiographs of 535 male and female patients over 10 years of age in the Mediterranean region of Turkey. The difference between CA and BA was significant. BA was smaller in males between the ages of 10 and 15 years and greater in females between the ages of 10 and 18 years. They stated it is appropriate to use GP method in Southern Turkish children, although a revision was needed to get better results and minimize errors [21]. Unlike this study, we found BA and CA to be compatible in patients over 10 years of age in both genders in our study.

In the study of Koç et al. [11], in which 225 male patients over 7 years of age were examined, it was stated that Turkish boys may have a different skeletal maturation process than American children. Therefore, it was concluded that the GP Atlas is not fully applicable to Turkish boys to determine BA but that it can be used with some modifications. In our study, we obtained similar results and found that BA was significantly lower in boys in all age groups.

In a study designed by Aydin et al. [3] on 228 patients, including all age groups and genders in Turkish children, it was stated that the GP atlas could be used for the determination of BA in Turkish children safely. Among the studies evaluating the reliability of GP atlas in determining BA in Turkish children in the literature, Aydin et al.'s [3] study includes all age groups and both genders. Our study also includes all age groups and both genders with more patients. Although similar age groups and both genders were included, the results of Aydın et al.'s study differ from ours. While they [3] stated that the GP atlas is applicable for Turkish children, we found that BA was significantly lower in boys, especially those under 10 years of age.

This study was designed to avoid the impact of growth retardation and obesity on skeletal maturation by including children with known height and weight values between the 25th and 75th percentiles. In our study, when we compared both genders in all age groups, BA was significantly lower in males and significantly concordant in females. Among patients aged ≤120 months, BA was significantly lower in males, while it was

concordant with CA in females. Over 120 months, significantly concordant BAs and CAs were found in both genders.

Limitations

Our study has two limitations: First, due to its retrospective design, the nutritional status or medical history of the patients was known to the extent stated in the anamnesis. It is possible for some patients to have nutritional deficiency or systemic diseases not specifically mentioned in the anamnesis. However, on the other hand, it actually reflects the examined population in this respect. Second, the children participating in this study were all from the same geographic region; therefore, the differences between our results and the GP method may be partly due to the geographic location or climate differences.

Conclusion

Recent studies have shown that skeletal maturation can vary according to the geographical region and climate. The GP atlas, which is frequently used, was created based on regional and old data. The accuracy of the GP atlas in determining BA in Turkish children, especially males under the age of 10 years, is controversial and correct standards should be developed with data based on the Turkish population.

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The risk of developing colorectal cancer in individuals aged 50-70 years and behavioral changes in high-risk individuals regarding a fecal occult blood test

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Ethics Committee Approval
The study protocol was approved by the Ethics Committee of Ege University Faculty of Nursing (Number: 14.12.2015-147).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The prognosis of colorectal cancer (CRC) is highly associated with its stage; therefore, it is important to determine the risk factors. Risk determination tools such as CRC-PRO are patient-friendly since they are non-invasive, and highly successful in predicting the cancer risk. This study aimed to determine the risks of getting CRC in individuals aged 50-70 years and the early diagnosis behaviors of individuals, who were deemed at high risk based on a Fecal Occult Blood Test (FOBT).
Methods: This single-group quasi-experimental follow-up study was conducted in a family health center in Turkey between December 2016-December 2017. The data were collected using the "CRC Predicted Risk Online (CRC-PRO)" and "stages of change form." The patients were educated at the risk determination stage. Along with telephone counseling conducted with individuals in the first and sixth months, the changes in FOBT were noted.
Results: The CRC-PRO mean risk scores of the males and females were 1.37 (0.74), and 0.79 (0.40), respectively. Among them, 33.5% of males and 25.8% of females had a risk of CRC. After they were educated for FOBT, their behaviors positively and significantly changed from the risk determination stage until the 6th-month follow-up.
Conclusion: With the use of risk determination tools, individuals' lifestyle characteristics can be determined, and health education can be provided to change them.

Keywords: Colorectal cancer, Fecal occult blood test, Stage of change

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Introduction

According to Global Cancer Statistics (GLOBOCAN) [1], cancer is the second leading cause of death globally, and colorectal cancer (CRC) is the fourth most common cancer in both males and females worldwide. CRC is also the second most common cause of death due to cancer. According to the data of Turkey Statistical Institute (TSI) [2], it constitutes 8.1% of female cancers and 8.9% of male cancers. In Turkey, CRC is the third and fourth most common cause of death due to cancer in females and males, respectively [2].

The prognosis of CRC is highly associated with its stage. It is possible to detect and treat premalignant adenomatous polyps and early-stage localized cancers with early diagnosis programs [3]. CRC is preventable and treatable when diagnosed early. Informing the society, risk determination and the implementation of screening programs are significant for detection of cancer in the asymptomatic period. Studies showed that risk determination and screening reduced CRC mortality [3, 4].

CRC screenings include a fecal occult blood test (FOBT) every two years, a sigmoidoscopy every 5 years, and a colonoscopy every 10 years between the ages of 50-70 years in Turkey [5]. Although colonoscopy is known to reduce cancer mortality, it has certain disadvantages such as cost, anxiety, and rarely, intestinal perforation [6]. Moreover, screening programs such as colonoscopy in countries with limited resources are not considered cost-effective. These screening programs are generally implemented on individuals who are indicated to be at risk [7]. The determination of risk factors and conducting screenings for early diagnosis in high-risk individuals, instead of screening programs, are considered more effective [8]. The rate of CRC varies according to the type of risk factors and lifestyle characteristics [4]. Being at high risk for CRC is considered as having a family history of colon cancer and being above the age of 50 years. Although the highest increase in risk for CRC is genetically based, more than 50% of CRCs develop due to lifestyle. Therefore, it is important to determine the risks of cancer development by taking into account other risk factors, as well [4, 6].

Risk assessment can be performed using the “Harvard Risk Index” [5], “United States National Cancer Association Index” [5] and the “Colorectal Cancer Predicted Risk Online (CRC-PRO)” [6], which was developed using the Cox proportional hazards model in the recent years. Risk determination tools are highly successful in predicting cancer risk [7-9]. While the total risk score for CRC can be calculated with these tools, the awareness of individuals regarding their lifestyle also increases. Primary prevention is important, for which healthy lifestyle behaviors, such as healthy nutrition, physical activity, non-smoking, and non-consumption of alcohol should be adopted [10]. Risk assessment tools such as CRC-PRO assess the healthy lifestyle behaviors of the individuals. Moreover, risk determination tools are patient-friendly since they are non-interventional [6]. These types of risk determination tools are also suitable for the use of health care professionals during consultations [9]. Health care professionals play a key role in alerting the community to the early detection of CRC since they usually have the closest contact with the community [11].

The conceptual framework of our study is based on the Transtheoretical Model (TTM), created by Prochaska and DiClemente. The TTM is used in the design of various health behavior change interventions [12], such as smoking cessation, exercising, protection from sun exposure, and sexually transmitted diseases, and then for identifying behavioral changes for early diagnosis tests such as mammography, Breast Self-Examination, PAP test, FOBT, and colonoscopy. Especially in recent years, researchers use the TTM in behavioral changes for the early screening of CRC [13-17]. The TTM is a dynamic, 4-6 stage process that evaluates the individuals' behavioral changes from precontemplation to relapse [13]. Some changes in stages were necessary for determining the behavioral changes in the early diagnosis of cancer, because smoking cessation or mammography do not require continuity. However, the FOBT must be repeated at certain periods [13, 14, 17, 18]. For CRC, the FOBT includes screenings that need to be repeated at certain periods. Therefore, the stages of change defined in the TTM are appropriate for use in explaining behavioral changes.

The purpose of this study was to determine the risks of developing CRC in individuals aged 50-70 years and the behavioral changes of individuals at risk regarding a FOBT.

Research questions

1. What is the risk of developing CRC in the next 10 years among females?
2. What is the risk of developing CRC in the next 10 years among males?
3. What are the behavior changes in individuals with high CRC risk after FOBT?

Materials and methods

This single-group quasi-experimental follow-up study was conducted between December 2016 and December 2017. A total of 4500 individuals aged between 50-70 years who were registered to a Family Health Center (FHC) in İzmir-Turkey constituted the study population. FHCs in the district were classified according to age, income status and the state of having a chronic disease, which were defined as CRC risk factors in the literature, and one was selected by the purposeful sampling method. The reason for carrying out the study in an FHC was to determine the risk of CRC in healthy individuals and to perform a fecal occult blood test freely on the groups at risk.

The selected FHC was in a middle socio-economic class district that allows immigrants from different regions, where the median age was 37.01 years [19]. In the calculation made with the sampling from a finite population formula, the required sample size was 445 individuals aged between 50-70 years. The inclusion criteria were as follows:

- Being 50-70 years old
- Having no medical conditions that prohibited the FOBT test
- Having health insurance
- Volunteering

The Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) checklist was used in the study design and manuscript drafting [20]. The research data

were collected using the CRC-PRO for Men and Women, and the stages of change form was used for FOBT.

"CRC-PRO for Men" and "CRC-PRO for Women" are risk prediction tools created by Wells et al. [6] considering the risks of individuals diagnosed with CRC (n=2765) and using the Cox proportional hazards analysis. These tools calculate the risk of CRC in the individual online (Colorectal Cancer-10 year Predicted Risk Online) as a percentage within a 10-year period [21]. It consists of twelve questions for females and thirteen questions for males. The common questions are about weight, height, age, ethnicity, years of smoking, amount of daily alcohol use, educational level, family history of cancer, diagnosis of diabetes mellitus, and the use of multivitamins. In the form developed for men, the time spent actively by doing sports, the frequency and amount of red meat consumption, and the use of anticoagulants are asked additionally. In females, the use of estrogen and whether they take anti-inflammatory drugs are also questioned. The risk of CRC is between 0.2-15% for men and 0.1-20% for women. The median values were 1.0% and 1.6% for females and males, respectively. For males, low CRC risk indicates <1.6% while the high CRC risk indicates >1.6% risk. For females, the respective values are <1.0% and 1.0% [6, 21]. This tool needs to be tested for validity in different populations because it is an index questioning universally known risk factors and does not include the expressions that may vary individually, such as opinion and attitude. The accuracy of this tool in determining CRC risk was good, 0.681 in males and 0.679 in females [6, 21].

Stages of change form: Behavioral changes of individuals regarding FOBT were created according to the Stages of Change Form developed by Prochaska and Diclemente (1982) [12]. In the literature, the stages of behavioral change regarding FOBT within the framework of the TTM were evaluated differently: The TTM stages of Bui et al. [13] and Kwak et al. [15] were used in this study. The stages were classified as follows:

1. Precontemplation: The individual has not taken this test and does not consider taking it in the future.
2. Contemplation: The individual has not taken the FOBT but is thinking of taking it.
3. Action/Maintenance: The individual took the FOBT at least once within 2 years and is thinking of taking it again within the next 2 years.
4. Relapse risk: The individual has previously taken the FOBT on time but does not think of repeating it in the future.
5. Relapse: The individual took the FOBT more than 2 years ago but does not think of taking it within the next 2 years.

The CRC-PRO for Men and CRC-PRO for Women was applied by face-to-face interviews conducted with individuals in the FHC where the study was conducted. The individuals were given individualized information for 20 minutes with a standard education brochure on the same day. The Education Brochure is a two-page education tool prepared by the researchers with reference to the training prepared by the National Health Directorate [22]. This brochure includes information about the definition, causes and symptoms of CRC, the measures to be taken in high-risk individuals, and the early diagnosis of the disease. It was used to provide standard education to all individuals interviewed in the risk determination stage. This standard education was conducted in a meeting room in the FHC.

After the implementation of the CRC-PRO for Men and CRC-PRO for Women, the behavioral changes of high-risk individuals in terms of FOBT were followed with the questions in the stages of change in the FOBT behaviors form, which was prepared based on the TTM, by face-to-face interviewing at Time 0 and tailored telephone counseling conducted one month later (Time 1) and after 6 months (Time 2) [13, 15] (Figure 1).

While the behavior of taking the FOBT is the outcome variable of the study, the score for men and women obtained from the CRC-PRO for Men and CRC-PRO for Women is the main independent variable.

Permission was obtained from Dr. Michael Kattan, who developed the tool, to use the CRC-PRO for Men and CRC-PRO for Women. Written permissions were obtained from Ege University, Faculty of Nursing Ethics Committee (Number: 14.12.2015-147), the Provincial Directorate of Health, and the individuals participating in the study.

Statistical analysis

Data were analyzed using the SPSS 17.0 statistical software. Number, percentage distribution and mean were used in the analysis of data. For repeated measures, the Friedman test was used to examine and compare the time periods and the Bonferroni correction test. A level of P <0.05 was considered statistically significant.

Results

Among all, 47.3% of the participants were males (n=193), and 52.7% were females (n=252), and all were Caucasian. The mean age and the mean years of education of the males were 59.80 (7.36) years (50-70 years) and 8.88 (3.75) years (0-15), respectively. Their mean body mass index (BMI) was 27.86 (3.57) kg/m^2 (21- 38 kg/m^2). Among them, 54.9% smoked, and 13.5% consumed alcohol. 9.3% of males were using multivitamins while the study was conducted, and 22.3% had Diabetes Mellitus (DM). 23.8% of the family members of the males had received the diagnosis of cancer at any stage of their life. 37.3% of the males were exercising, 24.9% used aspirin, 53.6% regularly consumed red meat, and 45.0% consumed red meat once a week (Table 1).

The mean age and the mean years of education of the females were 56.82 (6.73) years (50-70 years) and 6.25 (3.23) years (0-15), respectively. Their mean body mass index (BMI) was 29.88 (5.30) kg/m^2 (17-44 kg/m^2). Among them, 21.8% smoked, and none consumed alcohol. 20.3% of females were using multivitamins while the study was conducted, and 38.5% had Diabetes Mellitus (DM). 30.2% of the family members of the females had received the diagnosis of cancer at any stage of their life, 83.4% did not use nonsteroidal anti-inflammatory drugs (NSAIDs), and 92.9% had never received estrogen supplements (Table 2).

Table 1: Men' risk factors for colorectal cancer development according to CRC-PRO (n=193)

Risk factors	n	%
Age (Mean)(SD)	193	59.80 (7.36)
Education years (Mean)(SD)	193	8.88 (3.75)
Body mass index (Mean)(SD)	193	27.86 (3.57)
Smoking		
Yes	106	54.9
No	87	45.1
Alcohol intake		
Yes	26	13.5
No	167	86.5
Regular use of multivitamins		
Yes	18	9.3
No	175	90.7
History of diabetes		
Yes	43	22.3
No	150	77.7
Family history of cancer		
Yes	46	23.8
No	147	76.2
Physical activity per day		
Yes	72	37.3
No	121	62.7
Regular use of aspirin		
Yes	49	24.9
No	144	75.1
Red meat intake		
Regular	111	53.6
No	82	46.4
CRC-PRO risk score (Mean)(SD)	193	1.37 (0.74)

SD: Standard deviation

Table 2: Women' risk factors for colorectal cancer development according to CRC-PRO tool (n=252)

Risk factors	n	%
Age (Mean)(SD)	252	56.82 (6.73)
Education years (Mean)(SD)	252	6.25 (3.23)
Body mass index (Mean)(SD)	252	29.88 (5.30)
Smoking		
Yes	55	21.8
No	197	78.2
Alcohol intake		
Yes	0	0.0
No	252	100.0
Regular use of multivitamins		
Yes	51	20.3
No	201	79.7
History of diabetes		
Yes	97	38.5
No	155	61.5
Family history of cancer		
Yes	76	30.2
No	176	69.8
Regular use of NSAIDs		
No	210	83.4
Yes, but not currently	23	9.1
Yes, currently	19	7.5
Use of estrogen		
Yes, currently	12	5.0
Yes, previously	5	2.1
No	235	92.9
CRC-PRO risk score (Mean)(SD)	252	0.79 (0.40)

According to the CRC-PRO for men and CRC-PRO for women, the mean risk score of CRC development within the next 10 years were 1.37 (0.74) (0.3-4.5) and 0.79 (0.40) (0.2- 2.1), respectively (Tables 1 and 2). Therefore, 33.5% of men and 25.8% of women in the study group were at high risk for CRC.

The behavioral changes of high-risk individuals in terms of FOBT were followed with the questions in the stages of change in the FOBT behaviors form. In the first test (Time 0) (n=131), it was determined that 35.9% of the high-risk individuals had previously heard about the FOBT but did not take it and were not thinking of taking it in the future (precontemplation), 34.3% had not taken the FOBT but were thinking of taking it (contemplation), 19.9% had previously taken the FOBT in time and were thinking of taking it in the future (action/maintenance), 5.3% had previously taken the FOBT (relapse risk), and 4.6% had previously taken the FOBT, but did not want to repeat it (relapse) (Table 3).

During the 1st-month follow-up (Time 1) (n=98), 29.6% of those who needed to take the FOBT were in the precontemplation stage, 14.3% were in the contemplation stage, 45.9% were in the action/maintenance stage, 8.2% were in the relapse risk stage and 2.0% were in the relapse stage (Table 3).

During the 6th month follow-up (Time 2) (n=45), 2.2% of the individuals who needed to take the FOBT were in the precontemplation stage, 2.2% were in the contemplation stage, 77.8% were in the action/maintenance stage, and 17.8% were in the relapse risk stage. The stages the individuals were in changed significantly from baseline until the 6th-month follow-up (x^2=113.968, P<0.001). The effect size was 1.534 in terms of FOBT behavior between the follow-ups (Table 3).

Table 3: The stages of change for FOBT according to the follow-ups of individuals who are at high risk for CRC

Stages of change	Time 0		Time 1 (1st month)		Time 2 (6th month)		Significance test[a]		Effect size (d) (Time 0-Time 2)
	n	%	n	%	n	%	x^2	*P*-value	
Precontemplation	47	35.9	29	29.6	1	2.2			
Contemplation	45	34.3	14	14.3	1	2.2	113.968	<0.001	1.534
Action/Maintenance	26	19.9	45	45.9	35	77.8			
Relapse risk	7	5.3	8	8.2	8	17.8			
Relapse	6	4.6	2	2.0	0	0.0			
Total	131	100.0	98[b]	100.0	45[b]	100.0			

[a] : Friedman analyses with Bonferroni correction, Cronbach Alpha: 0.025 (α/2 = 0.025) [b] : Individuals who did not take the FOBT test previously (follow-up).

Discussion

In our study, according to the CRC-PRO for Men and Women tool, one out of every three people in the whole sample group had CRC risk within the next 10 years and men had a higher risk than women, per the total risk score (33.5% vs. 25.8%). This result is consistent with the GLOBOCAN [23] data, according to which, men get colorectal cancer 1.5 times more than women. In study by Ries et al. [24], men had a higher CRC risk than women. The modifiable risk factors examined in CRC-PRO are obesity, smoking and alcohol use, exercise, red meat consumption, nonsteroidal anti-inflammatory drugs and estrogen use, and the presence of DM. The mean BMIs of men and women in our study were in the overweight range and 38.5% of women and 22.3% of men had DM. The prevalence of obesity and DM in our country is almost twice the world average [25, 26]. Among our patients, alcohol consumption was low in men (13.5%), and women did not drink alcohol. Nearly half of men and one-fifth of women were smokers. Retrospective studies in which the risk factors for CRC were assessed reported that obesity was responsible for 3.9% of CRC development, having DM increased the risk by 1.20-1.22 times, and alcohol use increased the risk between 1.17-1.44 times [27, 28]. De Rosa et al. [29] determined that the presence of CRC in the first-degree relatives of individuals increased the risk by 2-4 times. While the incidence of CRC in family members is between 9-11% in the world, it is between 10.3-25.2% in Turkey [29]. In our study, the incidence of CRC in family members was high, found in 17.2% of men and 32.4% of women. It can be said that the incidence of CRC is higher in family members in our country. In our study, NSAID and aspirin use were higher, and the use of estrogen was lower compared to those reported in the literature [7, 27]. More than one-third of the individuals in our study were physically active every day. Various studies reported that the use of NSAIDs or aspirin decreased CRC development by 16-38% and that the use of estrogen and doing physical activity decreased the risk by 0.4-0.8 times and 1.06 times, respectively [27, 28]. In our

study, about one-tenth of men consumed red meat every day. A meta-analysis concluded that red meat consumption increased CRC development by 1.12 times [30]. In our study, the rate of red meat consumption was low.

The early diagnosis of CRC with a FOBT is effective in decreasing morbidity and mortality [7, 8]. Screening programs with a FOBT are conducted in many countries, as well as in Turkey [5, 22]. The success of these screening programs surely depends on participants' continuity for taking the FOBT. In our study, the ratio of individuals who took the FOBT at least once at Time 0 was 29.8%. In a study conducted in 14 Asia-Pacific countries including 7915 individuals, 30.4% of the individuals had previously taken the FOBT [31]. Bronner et al. [32] determined that the rate of taking any early diagnosis test for CRC was 18-34% among the individuals in Israel. Our results and the data from the literature show that approximately one-third of individuals take the FOBT for the early diagnosis of CRC, without any health professional informing them about it. The early diagnosis behaviors of the individuals are associated with the welfare level of the countries. The cost of FOBT is a serious obstacle to showing early diagnosis behavior [13, 31]. However, the FOBT has been offered free of charge to individuals aged 50 years and older since 2014 in our country [22]. The behavioral change to take the FOBT can be achieved by education. Individuals show 5-15% increased early diagnosis behaviors in education-intervention studies [17].

While the rate of individuals who had taken the FOBT and were in the stage of taking it was 45.9% at Time 1 after education was provided, this rate increased to 77.8% at Time 2. In the Action and Maintenance stage, there was a 57.9% difference in the desired direction. The effect size in the stages of change in terms of taking the FOBT between Times 0-2 was high. In the study by Ilgaz and Gözüm [9] conducted on the agricultural workers in Turkey, the ratio of taking the FOBT was 7% before being informed and increased to 89% after information was given. Temucin and Nahcivan [33] determined that the navigator nurse program in Turkey was effective in CRC early diagnosis screenings. In the same study, the rates of taking the FOBT in the experimental group in the 3rd and 6th-month follow-ups were 82% and 84%, respectively. Hendren et al. [34] examined the effect of telephone counseling on CRC cancer screening and determined that individuals exhibited significant early diagnosis behaviors within 1 year compared to the control group (16.6% vs. 37.7%). Christie et al. [18] reported that the behavioral change for early diagnosis of CRC was not affected by any sociodemographic variables of individuals and that only providing information about the subject had a positive effect on changing the early diagnosis behavior of individuals. They concluded that there is a need for increased follow-up and informing the individuals to take the FOBT [9, 17, 18, 33, 34].

Limitations

Only the individuals who came to the FHC and volunteered to participate in the study were included. On the other hand, the FHC, where the research was conducted, had a relatively high population and socio-cultural diversity. The individuals with high risk who did not come to the FHC during the study may have been excluded. However, reaching a sufficient sample size increased the generalizability of our results. Self-reporting is a major limitation in our study. The follow-ups were performed within the framework of TTM.

Conclusions

In this study, according to the CRC-PRO for Men and Women tool, almost one in three men and one in four women were at risk of developing CRC in the next 10 years. After informing about the FOBT performed based on the TTM, a significant and positive change occurred from the risk determination stage (Time 0) until the 6th-month follow-up (Time 2) in taking the FOBT. The difference in the stages of change for taking the FOBT had a high effect size. These results revealed that health care professionals could promote desirable behaviors through education in the early diagnosis behaviors of individuals.

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Occupational fatigue and sleep quality among the physicians employed in the emergency service of a COVID-19 pandemic hospital

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Ethics Committee Approval
The study was approved by Noninvasive Clinic Ethical Committee of the Medical Faculty of Harran University (Decision No:18, Dated: 29th June 2020).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Outbreaks of infectious diseases, including the current COVID-19, are associated with major psychological distress and significant symptoms of mental illness. Healthcare workers may experience sleep problems, anxiety, depression, and stress when facing a major public health threat. This study aimed to assess the levels of occupational fatigue and sleep quality among the physicians working in the emergency service of a COVID-19 pandemic hospital.
Methods: This descriptive study was conducted in July 2020 in Şanlıurfa Province Mehmet Akif Inan Training and Research Hospital. The sample group included 194 physicians. The Introductory Information Form prepared by the researchers, the Occupational Fatigue Exhaustion/Recovery (OFER) Scale and the Pittsburgh Sleep Quality Index (PSQI) were used for data collection.
Results: The mean chronic fatigue subscale, mean acute fatigue subscale, mean recovery subscale, and mean Pittsburgh Sleep Quality Index scores were 65.30 (22.87), 69.03 (20.23), 43.93 (19.09), and 8.76 (3.20), respectively. Good and poor sleep quality levels were detected in 11.9% and 88.1% of the physicians, respectively. Sleep quality, gender, marital status, age, and anxiety status due to COVID-19 pandemic affected the occupational fatigue levels of the physicians (P<0.05).
Conclusion: Assessing and minimizing the levels of occupational fatigue and implementing interventions for increasing the quality of sleep among the physicians employed in the emergency department, which has a critical place in healthcare services, are necessary.

Keywords: Occupational fatigue, Pandemic, Physicians, Sleep quality

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Introduction

In the recent years, several infectious disease outbreaks such as the H1N1 influenza, the Ebola, particularly in West Africa and the Zika virus, seriously threatened the survival and improvement of humanity. Since December 2019, pneumonia emerged due to a novel coronavirus infection in Wuhan, Hubei Province, China, and became effective globally as a contagious infectious disease. On 31st January 2020, the World Health Organization (WHO) officially recognized the epidemic as a Public Health Emergency of International Concern (PHEIC) and suggested to name it "COVID-19" [1]. On 11 March, the WHO declared that the COVID-19 outbreak could be considered a "pandemic" since the virus increasingly spread worldwide [2]. Psychological factors play a vital role during any pandemic [3].

With its progression, the workload and pressure on the clinical staff to struggle against the pandemic also increased in parallel with the continuously amplified number of confirmed and suspected patients. The frontline healthcare professionals carry a high risk for infection while facing heavy workload. Because of the special and high-risk profession of the clinical frontline medical staff, they suffer an enormous psychological pressure that may affect sleep quality, as well as physical and mental health [4].

According to the previous studies that addressed the SARS and Ebola epidemics, the onset of a sudden and emergency life-threatening disease may induce extraordinary work pressure on the healthcare workers (HCWs) [5]. Doubtlessly, healthcare professionals were significantly burdened with the responsibility of combating against COVID-19. Certain healthcare professionals employed in the emergency, respiratory and critical care departments may experience sleep disorders, anxiety and depression [6].

Sleep quality is a key component of health. The clinical staff needs to achieve a good quality of sleep not only for performing well in treatment of the patients, but also for keeping their immune system strong to prevent infections [7]. The physical and psychological health of the medical staff are under risk during occupational performance under infectious circumstances, while anxiety and stress may also affect their sleep process adversely [8]. The impact of anxiety, stress and lessened perceived self-efficacy on sleep quality was shown in previous studies [9]. Numerous studies reported the adverse psychological reactions detected among the healthcare professionals during the SARS outbreak [11-13].

Studies report that the healthcare professionals had concerns about their families, friends and colleagues, a sensation of uncertainty and stigmatization regarding contagious infectious diseases while they reported reluctance for working or contemplating to resign. They also experienced high-level stress, anxiety, insomnia, and depression symptoms that may cause long-term psychological consequences [10-12]. Similar concerns about mental health, psychological adjustment and recovery of the healthcare professionals employed in treatment and critical care of the patients with COVID-19 are arising nowadays.

Humans are complicated physiological machines predisposed to error. The incidence of that error may increase due to fatigue, sleep deprivation and stress. Fatigue is the inability or unwillingness to continue performing effectively and may be caused by excessive workload, stress, sleep loss and circadian disruption. Fatigue and sleep deprivation are distinct entities. Fatigue is more responsible for the changes in performance than circadian rhythm disruptions and the grade of fatigue may vary depending on environmental conditions. Cognitive function may be deteriorated more compared with physical performance, and fatigued individuals manifest impaired learning and cognitive processes, memory defaults, and interpersonal dysfunction [13].

Extensive studies were conducted on the role of long working hours and the duration of shifts on work-related fatigue. Sleep deprivation, physical exhaustion and disruption of circadian rhythm are considered major contributors to work-related fatigue [14]. It is also supposed to be associated with numerous subjective factors such as age, anxiety, caffeine intake, sleep patterns, and a recent life event [15].

The healthcare professionals that are directly employed in the treatment and critical care of the patients with COVID-19 carry risk for psychological distress and various symptoms of mental health complications. The progressively increasing number of the confirmed and suspected cases, abundant workload, widespread media coverage, deficiency of specific drugs and lack of adequate support may all contribute to the mental burden [16].

This study aimed to assess sleep quality and occupational fatigue status in the frontline medical staff struggling against the COVID-19 pandemic.

Materials and methods

The data of this descriptive study were collected between 1-15 July 2020 corresponding to 110th-125th days of the pandemic, considering the date 11 March 2020 on which the first case of COVID-19 was reported in Turkey. A progressive period of the pandemic was selected to evaluate the level of occupational fatigue and sleep quality more accurately. The study universe included 220 physicians that were currently employed in the emergency service because of the pandemic in the Şanlıurfa Mehmet Akif Inan Training and Research Hospital. No sampling method was implemented in the study. One hundred and ninety-four (88%) physicians who accepted to participate were surveyed.

The data were collected through an online questionnaire created on Google forms. After the doctors were informed about the questionnaire by the researchers, the questionnaire link was shared on the doctors' social media groups. The responses were kept confidential. The Introductory Information Form prepared by the researchers, Occupational Fatigue Exhaustion/Recovery (OFER) Scale that measures occupational fatigue level and Pittsburgh Sleep Quality Index (PSQI) that assesses the sleep quality of the physicians during COVID-19 pandemic period were used for data collection. Filling the data collection forms took 15 minutes. The Introductory Information Form consisted of 23 questions addressing age, gender, marital status, number of children, working duration, weekly working duration, exposure to COVID-19, status of using a protective equipment, being faced with a COVID-19 patient, experience of being suspected for COVID-19, experience of COVID-19

positivity in the family or co-working staff in the work-place, health problems, cigarette smoking and exercise status.

The Occupational Fatigue Exhaustion/Recovery Scale (OFER)

OFER was developed by Winwood et al. to measure occupational fatigue in 2005. The acceptable Cronbach's alpha coefficient values of the scale were 0.93, 0.82 and 0.75 for chronic fatigue, acute fatigue and recovery, respectively. The scale consisted of 15 items and three subscales, as follows: (1) Chronic fatigue including 1-5 questions, (2) acute fatigue including 6-10 questions, (3) and recovery including 11-15 questions. The questiones were on experience about fatigue at work and home within the last few months. The questions including negative statements were coded reversely and scoring was performed on this base. A seven-point Likert scale (ranging between 0-strongly disagree to 6-strongly agree) was used for scoring. No total score was obtained in the scale, the scores were calculated independently for each subscale (item scores /30x100). High scores obtained from the subscales of chronic and acute fatigue indicated increased occupational fatigue while high scores obtained from the subscale of recovery exhibited achievement recovery between the shifts. Scores of 0-25, 25-50, 50-75 and 75-100 revealed low, moderate/low, moderate/high fatigue and high grades of fatigue, respectively [17]. In our study, the Cronbach's alpha coefficient values of the scale were 0.85, 0.84 and 0.75 for the subscales of chronic fatigue, acute fatigue and recovery, respectively.

Pittsburgh Sleep Quality Index (PSQI)

PSQI is a sleep questionnaire designed to assess sleep quality and length and the presence and severity of sleep disturbance within the last month. The scale consists of 19 items and measures seven subscales of sleep quality including subjective sleep quality (C1), sleep latency (C2), sleep duration (C3), habitual sleep efficiency (C4), sleep disturbances (C5), use of sleep medications (C6), and daytime dysfunction (C7). Total PSQI score was obtained by summing the seven subscores and ranges between 0-21. PSQI total score definitively distinguishes well sleepers (PSQI total score≤5) from poor sleepers (PSQI >5) [18]. In the present study, the Cronbach's alpha coefficient of the scale was 0.80.

Statistical analysis

SPSS 22.0 software package program was used for statistical analysis. The descriptive statistics (number, percent, average) were used for normally distributed variables, and the t-test and variance analysis were performed among the independent groups. A correlation analysis was carried out; $P<0.05$ indicated significance.

Ethics

The study was approved by the Noninvasive Clinic Ethics Committee of the Medical Faculty of Harran University (Decision No:18, Dated: 29 June 2020). The institutional approval of the study was obtained from Mehmet Akif Inan Training and Research Hospital while informed consent was taken from each participant.

Results

The sociodemographic characteristics of the participants are presented in Table 1. The study included 31.4% female and 68.6% male participants, with an overall mean age of 32.1 (5.79) years. Of the physicians, 43.8% had an occupational experience of 0-5 years, 29.9% smoked and 66.5% did not exercise. The flexible shift scheduling was supported by 84% of the physicians and the mean weekly working duration was 46.94 (12.18) hours.

Table 1: The sociodemographic characteristics of the emergency physicians (n=194)

Descriptive features		Number	Percentage (%)
Your Gender	Male	133	68.6
	Female	61	31.4
Marital Status	Married	118	60.8
	Single	76	39.2
Age	24-32	102	52.6
	33-54	92	47.4
Having a child	Yes	87	44.8
	No	107	55.2
Occupational experience	0-5 years	85	43.8
	6-10 years	63	32.5
	11-31 years	46	23.7
Do you support flexible shift scheduling?	Yes	163	84.0
	No	31	16.0
Your weekly work duration	0-40 hours	77	39.7
	40 -80 hours	117	60.3
Have you any health problems?	Yes	28	14.4
	No	166	85.6
Do you smoke cigarettes?	Yes	58	29.9
	No	136	70.1
Do you exercise?	Yes	65	33.5
	No	129	66.5

The experience of the study participants related with COVID-19 was presented in Table 2. Among the participants, 88.1% reported meeting with a COVID-19 patient while 61.9% were suspected for COVID-19, and 94.3% feared carrying the COVID-19 virus home.

Table 2: The experience of emergency physicians regarding COVID-19

Occupational Characteristic		Number	Percentage
Have you ever met with a COVID-19 positive patient?	Yes	171	88.1
	No	23	11.9
What is your contact status?	Low	46	23.7
	Moderate	86	44.3
	High	62	32.0
Did you experience suspicion of having COVID-19?	Yes	120	61.9
	No	74	38.1
Did the presence of COVID-19 positive healthcare staff make you feel anxious or fearful?	Yes	119	61.3
	No	75	38.7
Did you fear carrying the virus home?	Yes	183	94.3
	No	11	5.7

The mean scores obtained from the Occupational Fatigue/Exhaustion/Recovery and Pittsburgh Sleep Quality Index Scales by the emergency physicians are presented in Table 3. Mean chronic fatigue subscale, acute fatigue subscale, recovery subscale and Pittsburgh Sleep Quality Index scores were 65.30 (22.87), 69.03 (20.23), 43.93 (19.09) and 8.76 (3.20), respectively. Poor and good sleep quality levels were detected in 88.1% and 11.9% of the physicians, respectively.

Table 3: The mean scores of the physicians according to the occupational fatigue exhaustion/recovery scale and Pittsburgh sleep quality index scales

	Obtainable Min-Max	Received Min-Max	$\bar{X}$(Ss)
Chronic Fatigue	0-100	6-100	65.30 (22.87)
Acute Fatigue	0-100	16-100	69.03 (20.23)
Recovery	0-100	6-83	43.93 (19.09)
PSQI	0-21	2-18	8.76 (3.20)

The comparison between some variables of the emergency physicians based on Occupational Fatigue Exhaustion/Recovery and Pittsburgh Sleep Quality Index Scales is presented in Table 4. Females, those in the 24–32-year age group and single participants had significantly higher and lower scores in the subscales of chronic fatigue and recovery, respectively ($P<0.05$). Those experiencing fear and concerns due to the presence of COVID-19 positive hospital staff at their workplace had significantly higher and lower scores in the subscales of acute fatigue and recovery, respectively ($P<0.05$). Those with a poor sleep quality obtained significantly higher

scores from the subscales of chronic and acute fatigue and significantly lower scores in the recovery subscale (P<0.05).

Table 4: Comparison of between occupational fatigue exhaustion/recovery and variables

		Chronic Fatigue	Acute Fatigue	Recovery
Gender	Female	70.76 (22.15)	70.60 (18.21)	40.81(19.69)
	Male	62.80 (22.83)	68.32 (21.12)	45.36 (18.71)
	P-value	0.024 *	0.468	0.124
Age	24-32	68.52 (22.59)	69.90 (18.73)	44.34 (19.22)
	33-54	61.73 (22.76)	68.07 (21.83)	43.47(19.00)
	P-value	0.039 *	0.532	0.753
Marital status	Married	62.14 (21.95)	68.24 (21.07)	46.18 (18.71)
	Single	70.21(23.52)	70.26 (19.01)	40.43 (19.27)
	P-value	0.016 *	0.500	0.040 *
Did the presence of Covid positive healthcare staff make you anxious or fearful?	Yes	67.39 (22.71)	72.57 (18.21)	41.14 (17.49)
	No	62.00 (22.86)	63.42 (22.04)	48.35 (20.74)
	P-value	0.110	0.002 *	0.010 *
PSQI	Good sleep quality	47.68 (20.55)	52.75 (22.14)	56.37(18.98)
	Poor sleep quality	67.68 (22.16)	71.22 (18.98)	42.26 (18.69)
	P-value	0.001 *	0.001 *	0.001 *

* Significant with P<0.05, the t-test

Discussion

The physicians that participated in our study obtained moderate-high, moderate-high and moderate-low scores in chronic fatigue, acute fatigue and recovery subscales, respectively, in the OFER Scale. High and very high levels of occupational fatigue were detected in 78.8% and 42.2% of the physicians, respectively, in a study in China, and physicians working in the tertiary-care hospitals had high levels of fatigue [19]. In Taiwan, the level of fatigue among the physicians and nurses were higher than those of the administrative medical staff, with a fatigue prevalence rate of 30.9% [20]. The medical sector has a stressful working environment by nature. Particularly, the physicians who have critical importance since they work in the emergency department, and healthcare personnel who make the first contact with the patients feel this stress more intensely. Thus, an elevated level of occupational fatigue is an estimated consequence during the pandemic.

In the present study, the participants with poor sleep quality obtained higher scores from the chronic and acute fatigue subscales, and lower scores from the subscale of recovery. Similarly, studies conducted on occupational fatigue report that those with poor sleep quality have higher fatigue [21-23]. In our study, good and poor sleep quality levels were found in 11.9% and 88.1% of the physicians, respectively. Another study conducted on the physicians in Turkey determined that 24.3% and 75.7% had good and poor quality of sleep, respectively [24]. The mean sleep duration was 6.01 hours in our study. However, an adult should sleep at least 7 hours to achieve adequate sleep. Therefore, elevated fatigue is an inevitable consequence among the emergency physicians who sleep poorly and less than what is considered healthy.

In this study, females obtained higher scores from the subscale of chronic fatigue. Studies show that gender has no impact on the occupational fatigue [25, 26]. Many healthcare professionals feel a severe emotional and physical pressure in presenting healthcare services under pandemic circumstances. Besides, they have to consider the education of their children who cannot attend their schools properly, cook meals and do more intense house chores, as well as meet the increasing needs of hygiene. The level of occupational fatigue among the female healthcare professionals increases because of these mentioned circumstances during the pandemic.

Physicians between the ages of 24 and 32 years had higher scores in the chronic fatigue subscale. The level of occupational fatigue was higher among the young healthcare professionals in numerous other studies [20, 27]. This may result from the lower tolerance level and different perception of life among the young subjects, called the “Z Generation” who prefer to socialize via the internet.

We found that single individuals obtained higher and lower scores from the subscales of chronic fatigue and recovery, respectively. Some studies report that marital status is effective on occupational fatigue [27, 28] whereas some other studies disagree [19, 29]. Particularly during the pandemic, the deficiency of familial and spousal support induces a stress factor on the single physicians and thus, being a single physician may contribute to an increase in occupational fatigue.

The physicians who experienced fear and anxiety due to the COVID-19 positive healthcare staff in their hospital obtained higher and lower scores from the subscales of acute fatigue and recovery, respectively. Similarly, high levels of anxiety were encountered in the healthcare staff who provide healthcare service to COVID-19 patients in other studies carried out in a pandemic hospital [30, 31]. Another study conducted in Turkey reported that healthcare professionals experienced anxiety of being infected with COVID-19 and feared transmitting the disease to their families [32]. The increased anxiety among the front-line emergency department staff is an expected consequence because of their concerns for being infected through direct contact with suspected or confirmed COVID-19 patients. A high level of occupational fatigue among the healthcare professionals is acceptable due to the brilliant struggle against the complications of a first-encountered disease.

Conclusion

COVID-19 is very contagious, and it spreads rapidly. Frontline physicians have critical importance in this process and exert intense efforts. They present a brilliant healthcare service with a full effort to protect themselves and their families, and their workload progressively increases. Under these circumstances, their occupational fatigue inevitably rises. The female, single and young physicians, as well as the those with a poor quality of sleep and concerns due to the presence of COVID-19 positive co-workers in their hospitals had higher levels of occupational fatigue.

Assessing and minimizing the levels of occupational fatigue and implementing interventions for increasing the quality of sleep among the physicians employed in the emergency department, which has a critical place in healthcare services, are necessary.

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Assessment of myeloperoxidase (Mpo) gene polymorphism in cervical cancer

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Ethics Committee Approval
The ethical approval is obtained from Dokuz Eylül University Non-Interventional Research Ethics Committee on 10.03.2011 with approval number 2011/07-14.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Cervical cancer (CC) is the most common gynecological malignancy in women. In spite of a variety of treatment protocols, it is necessary to carefully investigate all factors that play a role in the pathogenesis of these tumors which may have mortal progression. In this context, in our study we aimed to assess the myeloperoxidase (MPO) gene polymorphism, an important inflammatory enzyme, among cervix cancer cases.

Methods: In this cross-sectional study, 79 cases diagnosed as cervical carcinoma between 1992-2012 is included. The cases without archival paraffin blocks and clinical follow-ups are excluded. All slides with tumor involvement are reviewed and the ones which demonstrate tumor's characteristics are determined. After block determination 3 sections with 10-micron thickness obtained from paraffin blocks and MPO gene polymorphism was shown using acil restriction endonuclease enzyme with the restriction fragment length polymorphism (RFLP) method after polymerase chain reaction (PCR). The histopathological parameters including tumor stage and type, lymph node metastasis, ovary and endometrium involvement, recurrence and late metastasis are compared with genotype using chi-square and Fisher's exact test.

Results: The mean age of cases was 51.3 (10.9) years. Of 79 cases, 29 (36.7%) had AG (adenine-guanine) and 50 (633%) had GG (guanine-guanine) genotypes. Only endometrium involvement was identified to have a statistically difference with MPO gene polymorphism among the assessed histopathologic parameters (P=0.015). When clinical parameters are assessed, there was no difference identified between genotype and mortality (P=0.622).

Conclusion: Cervical cancer is thought to have progressive and regressive characteristics of tumor development due to the inflammatory response of the host. Within this framework, in our study assessing gene polymorphism of one of the inflammatory response foundation stones of MPO, we identified more endometrial involvement for cases with AG genotype. We believe this significance will be encountered for more parameters in broad case series.

Keywords: Cervical cancer, Myeloperoxidase, MPO, Gene polymorphism

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Introduction

Cervical cancer (CC) is the fourth common cancer in women according to 2018 cervical carcinoma incidences [3] and is accepted as the most common gynecological malignancy with more than 500,000 cases identified in 2012 [2]. The most common histologic type of this tumor, with death rates ranking 311,000 worldwide [1], is squamous cell carcinoma (SCC) comprising two thirds of cases [3]. The second most-common histologic type is adenocarcinoma. Both types of tumor have similar etiology. Like other epithelial tumors the tumor size, tumor invasion depth, lymphovascular invasion and lymph node and/or distant metastasis effects prognosis [4]. In cervical cancer, human papilloma virus (HPV) has an important role in both intraepithelial and invasive neoplasia [5]. For carcinogenesis associated with HPV, factors related to HPV in addition to the inflammatory response of the host to the virus play roles. It is considered that this inflammatory response may be responsible for both regression and progression of the lesion [6].

The human genome comprises approximately $3x10^9$ base pairs and nearly 50,000 genes carrying genetic information are contained within 46 chromosomes. Almost 99.9% of human DNA is identical between two people and the genetic variation (variability) among humans is sourced in small differences in the DNA chains. The differences in some DNA sequences do not affect human phenotypes but some directly leads to diseases. Between these two endpoints, there are genetic differences involving anatomy, physiology, treatment response, side effects of medication, tendency towards infection, and predisposition towards cancer [7].

DNA nucleotide changes in the form of more than one allele at a locus is called polymorphism. Alleles in more than 1% of chromosomes of the general population comprise "genetic polymorphism". If the incidence of alleles is less than 1%, than they are named as "rare variants". Polymorphic alleles found in the regulatory regions of genes affect transcriptional regulation of genes and may cause phenotypic changes [8].

Myeloperoxidase (MPO) is an enzyme that contains iron. It is found in the lysosome of monocytes, and granules of neutrophils. MPO uses hydrogen peroxide (H_2O_2) produced by neutrophils and produces hypochloric acid (HOCl) and other oxidants [9, 10]. HOCl may oxidize 10-20 times the amount of proteins that H_2O_2 does, and strong oxidant products produced by MPO may result in DNA injury. The only enzyme that is known to form HOCl is MPO. It inhibits tissue matrix metalloproteinase inhibitor 1 (TIMP-1) increasing matrix metalloproteinase activity and destroying proteins in the matrix. The MPO system is an important bactericidal. MPO expression is coded on a single gene with 14 kb length on the long arm of the 17th chromosome bounded by myeloid cells [11]. There is a polymorphic region in the MPO gene (-463G/A). On the MPO gene, -463 type G polymorphism is correlated with increased MPO expression and as a result increased risk of a variety of cancer types like lung, esophagus, bladder and ovarian tumors [12-15]. However, there are contradictory publications are also exist [16].

In cervical cancer cases, MPO activity has not been observed, or been observed to be low in peripheral blood neutrophils. It is considered that this reduced anti-tumor activity may play a role in development of cervical cancer [17]. As a result, in our study we aimed to research the correlation between MPO genetic polymorphism cases with prognostic histopathologic factors reported in the literature and survival.

Materials and methods

The ethical approval is obtained from Dokuz Eylül University Non-Interventional Research Ethics Committee on 10.03.2011 with approval number 2011/07-14. After ethical approval, the study is conducted with 79 cases whom had "cervical carcinoma" diagnosis in Dokuz Eylul University Faculty of Medicine (DEUFM), Medical Pathology Department between 1992-2012. The cases without pathology archival material and clinical follow-ups are excluded from study. The non-pathological data are obtained from hospital information management system. Also the cases with no DNA extraction is not included in study.

The hematoxylin & eosin (H&E) stained slides with tumor involvement were reviewed and the slides which demonstrate tumor's characteristics is determined. The paraffin blocks that belongs to the selected slides are obtained from archive. 3 sections with 10-micron thickness are taken from these blocks and placed in 3 sterile and DNA-RNA free Eppendorf tubes. Between each case, the microtome device was cleaned with alcohol. Later DNA isolated from paraffinized sections had myeloperoxidase gene polymorphism determined with the PCR-RFLP method.

Genomic DNA paraffin commercial kits (Macherey-Nagel GmbH & Co. KG, Germany) were used. In the MPO gene (-463) polymorphic region, after polymerase chain reaction (PCR) (Biolabs Taq polymerase, M0320S, USA) restricted fragment length polymorphism (RFLP) was shown with Acil (Fermentas AciI, ER1791, Lithuania) restriction endonuclease enzyme.

PCR conditions to determine promotor region polymorphism of the MPO gene (-463):

1 cycle	94 °C for 5 min -preliminary denaturation
35 cycles	94 °C for 1 min – denaturation
	57 °C for 1 min – primer binding
	68 °C for 1 min - lengthening
1 cycle	68 °C for 10 min – final lengthening

Primer series;

MPO(F) 5′ - ACAGGTGAATCGCTGACATGCTGCCT - 3′
MPO(R) 5′- GAGACTCCCTGGAGGAAGAAGTTGAG - 3′

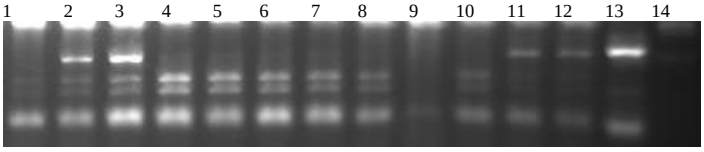
PCR product and fragment sizes;

PCR product;	350 base pair length
Fragment products;	AA genotype ; 289 + 61 base pair length
	AG genotype; 289 + 168 + 121 + 61 base pair length
	GG genotype; 168 + 121 + 61 base pair length

The obtained PCR products and products after enzyme fragmentation were separated in 2.5% agarose gel and stained with ethidium bromide to show in UV light. Figure 1 demonstrates a sample of DNA fragment analysis.

The PCR results are compared statistically with pathological parameters including tumor extensity, tumor type, lymph node involvement; parametrium, ovary, endometrium and abdominal fluid involvement.

Figure 1: Sample picture of DNA fragment analysis (Acil enzyme fragment) for MPO -463 promotor polymorphism stained with ethidium bromide (14: DNA length scale, 13: PCR product without fragmentation, 4-8,10: GG homozygote normal, 1-3,11,12: AG heterozygote mutant, 9: patient sample that could not be analyzed)



Statistical analysis

Statistical Package for the Social Sciences (SPSS) 15.0 program (SPSS Inc. Released 2006. SPSS for Windows, Version 15.0. Chicago, SPSS Inc.) is used for the analysis of the data. The Kolmogorov Smirnov test was applied to determine normal distribution of data for statistical analysis and then the chi-square test, Fisher's exact test, Kaplan Meier and regression analysis were used. Multivariate analysis could not be applied to create a model due to the lack of significance. And this cross sectional study results are reported according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

Results

The study included 79 cases with ages varying from 27 to 72 years at time of diagnosis and mean age was 51.3 (10.9) years (median 52). Cases with DNA not obtained during PCR and with missing data were excluded from the study. Of the 79 cases analyzed, SCC was the most commonly observed tumor type (86.1%). The number of non-SCC tumors were low, therefore they were grouped for statistical analyses. The other histologic types apart from squamous cell carcinoma were adenocarcinoma (5.1%) and adenosquamous carcinoma (8.9%).

Of the 79 cases, 29 (36.7%) had AG (adenine-guanine) and 50 (63.3%) had GG (guanine-guanine) genotypes. Analysis with pathological parameters revealed 18 cases with tumor limited to the cervix had AG (32.7%) genotype while 37 had GG (67.3%) genotype. In cases which tumors were not limited to the cervix, these numbers were as 10 AG (47.6%) and 11 GG (52.4%). There was no statistically significant difference between tumor stage and genotype with the chi-square test (P=0.229). Cases with squamous cell carcinoma diagnosis showed 23 AG (33.8%) genotype and 45 GG (66.2%) genotype. Non-SCC tumors had 6 AG (54.6%) and 5 GG (45.5%) genotype. Similar to tumor extencity, statistical assessment with Fisher's exact test did not identify statistical significance between tumor type and genotype (P=0.199). Of the 65 cases (82.3%) without lymph node (LN) involvement, 23 had AG (35.4%) and 42 had GG (64.6%) genotype. For the 14 cases (17.7%) with lymph node involvement, 6 had AG (42.9%) and 8 had GG (57.1%) genotype. No statistical significance was detected in Fisher's exact test between LN involvement and genotype (P=0.761).

62 cases (78.5%) with parametrium (PM) involvement revealed 22 AG (35.5%) and 40 GG (64.5%) genotype. In the 17 cases (21.5%) without parametrium involvement, 7 showed AG (41.2%) genotype and 10 GG (58.8%) genotype. In Fisher's exact test no significant difference was detected between PM involvement and genotype (P=0.778). 75 cases (95.0%) without ovarian involvement were found to have 26 AG (34.7%) genotype and 49 GG (65.3%) genotype, while for 4 cases (17.7%) with ovarian involvement, 3 had AG (75%) and 1 had GG (25%) genotype. No statistical significant difference is observed in Fisher's exact test for ovarian involvement and genotype (P=0.137). Similar to these results, there was no statistical significance observed with Fisher's exact test for AG and GG genotypes with abdominal fluid involvement (P=0.059) and vaginal involvement (P=0.738). For the 68 cases (86.1%) without EM involvement, the number of cases with AG genotype was 21 (30.9%) and the number of cases with GG genotype was 47 (69.1%). For the 11 cases with endometrium (EM) involvement, 8 had AG (72.8%) and 3 had GG (23.2%) genotype. Fisher's exact test revealed a statistically significant difference between EM involvement and AG and GG genotypes (P=0.015).

75 cases (95.0%) were found to have at least 1 year disease free survival on follow-up, and among these cases 27 had AG (36.0%) and 48 had GG (64.0%) genotype. For 4 cases who were deceased, AG and GG genotypes were equal with 2 cases each (50%). No statistically significant difference is detected between genotype and death (P=0.622). Analysis of 77 cases with local recurrence & metastasis and genotype did not show statistically significant difference in Fisher's exact test (P=0.619, P=1.000, respectively).

Discussion

Cervical carcinoma was reported as the most common cancer in low resource countries in last decade [1]. In 2018, annually estimated new cases were 569,847 worldwide [18]. HPV is one of the most important factors for cervical carcinogenesis and this made the tumor preventable through vaccines. The increase in screening of cervix including non-invasive/ minimal invasive methods lead to detection of precancerous lesions and even tumor formation in early stage. Moreover the death rates are also decreased [1].

MPO is released by degradation of cytoplasmic granules in neutrophils and monocytes and is a strong oxidant material due to products of reactions with H_2O_2. These products have important roles in the defense of the host against harmful targets like bacteria, fungi, viruses, malignant or non-malignant cells [19, 20]. However, this oxidant activity may stimulate procarcinogens and result in DNA injury mediated by H_2O_2 [21, 22].

With the advances in molecular techniques in recent years, gene polymorphism and neoplastic processes have attracted attention as another research area. Gene polymorphism of the MPO enzyme, with an important place in inflammatory processes, is one of these entities [23, 24].

There is a polymorphic region on the MPO gene (-463 G/A). MPO gene -463 type G polymorphism causes increased MPO expression. This increased expression has different effects on a variety of tumor types in the literature. A study of pulmonary cancer histological types from 2002 identified the MPO -463 A allele was a marker of reduced risk of small cell carcinoma in the smoking population [25]. Similarly, a study including 91 esophagus tumor and 241 non-tumor cases, associated the MPO -463 A allele with reduced esophagus cancer risk [14]. Additionally, the MPO G-463A homozygote variant was reported to be associated with reduced bladder cancer [15].

Considering gynecological malignancies, a study including 125 ovarian tumor cases and 193 controls, did not identify a statistically significance between MPO and ovarian cancer risk [16]. In our study, data related to SC development were not present, but the difference between clinical data related to SC prognosis and MPO gene polymorphism was searched. There was no statistically significant difference between AG-GG genotypes and tumor stage, tumor type, LN status, metastasis presence, PM and ovarian involvement. However, analyses with Fisher's exact test identified a statistically significant difference between EM involvement and AG and GG genotypes. According to this data, it is shown that those with AG genotype had more EM involvement.

When studies assessing gene polymorphism in cervical carcinoma are considered, it is noted that p53 codon 72, CD40, CD83, IL10 and IL18 have been investigated [26-30]. In studies about MPO and cervix, it is reported that MPO gene polymorphism is not associated with cervical intraepithelial neoplasia (CIN) formation [31]. On a meta-analysis study consisted of 5 eligible studies mentioned that presence of polymorphism, −463 G > A might be protective for cervical cancer and they concluded that larger sample sized studies are needed in this area [32]. In our study we just had two genotypes which makes not possible to discuss the data. And it is worth noting that more studies needs be done to reveal the effect of MPO gene polymorphism on cervical carcinoma formation and prognosis.

Limitations

The number of cases included in the study is limited. Therefore the genotype homogenization is poorly achieved. We suggest that the statistical significance we identified for EM involvement will be encountered for more parameters in broad case series with more homogenized genotype distribution.

Conclusion

Our study though MPO gene polymorphism just detected relationship with EM involvement and AG genotype and we could not reveal association with the majority of histopathologic prognostic factors.

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Investigating the psychological impact of COVID-19 on healthcare workers in the intensive care unit

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Ethics Committee Approval
Final confirmed ethical approval was obtained from the Social and Humanities Research Ethical Committee of Istinye University (Decision date: 16.04.2020, decision number: 2020/04.02). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: The disease caused by the SARS-CoV-2 virus, COVID-19, has become the first viral disease outbreak defined as a pandemic in the 21st century. Experience with previous endemics shows that critical care workers disproportionately suffer from depression and anxiety after facing such outbreaks; however, data are limited regarding the early phase of spread. Our aim was to investigate depression and anxiety in healthcare workers employed in ICUs during the initial phase of COVID-19 spread in Istanbul, Turkey, and possible relationships with various characteristics of healthcare workers.

Methods: This cross-sectional study evaluated descriptive and demographic characteristics, professions, COVID-19-related perceptions, depression and anxiety in healthcare workers from the 12 ICUs of six hospitals located in Istanbul, Turkey. The Beck Depression (Beck-D) and Anxiety (Beck-A) Inventories and the State-Trait Anxiety Inventory (STAI) TX-I and TX-II were used to assess depression and anxiety. Employees that worked in ICUs were included, regardless of profession, ICU type (neonatal/pediatric or adult), age, education and working status. We compared recorded data among employees with regard groups based on ICU type, sex, education status, profession, marital status, children, cohabiting status, and whether they were residing at their home. Additionally, multivariable regression analyses were performed to identify factors that were independently associated with scores obtained from the depression and anxiety scales.

Results: A third of the studied population were found to have moderate-to-severe levels of depression and anxiety according to the Beck-D and Beck-A scales. The STAI TX-I scores were similar in all comparison groups except for significantly higher scores in participants living with their family/friends (P=0.027). STAI TX-II scores were higher in pediatric/neonatal ICU workers (P=0.001), nurses (P=0.002), employees without children (P=0.046), and those residing in their home (P=0.031). Beck-D scores were higher in nurses (P=0.001), those with lower education (P=0.025), subjects without children (P=0.008) and individuals living with their family/friends (P=0.002). Beck-A scores were higher in participants with lower education (P=0.001), nurses (P<0.001), those without children (P=0.049), subjects living with their family/friends (P=0.001), and those not residing in their home (P=0.003). There were only weak correlations between COVID-19-related perceptions and scale scores. Multivariable regression showed that being a physician and living alone were independently associated with lower Beck-D and Beck-A scores.

Conclusion: The psychological impact of COVID-19 seems to be unassociated with disease-related perceptions during the early spread of disease, but about a third of ICU employees were found to have clinically-relevant levels of depression and anxiety. Our results show that nurses should receive continuous mental assessment and support, and that ICU employees may benefit from being provided with accommodation when caring for patients with diseases such as COVID-19.

Keywords: COVID-19, Healthcare workers, Anxiety, Depression, Altruism, Social support

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Introduction

Viral disease outbreaks have emerged as a frequent threat to the world, with recent examples such as SARS-CoV-1, MERS-CoV, H1N1, Zika and Ebola in the last 15 years [1]. Although the most recent outbreak (SARS-CoV-2 causing COVID-19) seems to have lower mortality/morbidity rates compared to most other examples, it has become the first to be defined as a pandemic in the 21st century [2]. As a result of its rapid transmission and fast rate of disease progression in severe cases, this disease exceeded the number of mortalities caused by all recent outbreaks combined, even before it was defined as a pandemic [3]. COVID-19 has caused or resurfaced healthcare deficiencies, major economic problems, international adversities and limitations in social support [4-7]. However, healthcare workers, who are often described to be on the frontlines of this 'war', are maybe the worst affected due to the possibility of disease contraction, increased workload, stigmatism, and the social/psychological impact of constant daily exposure to the worst cases of the disease [8-11].

In the response to COVID-19, lack of equipment, protective gear and limited access to supplies (both healthcare-related and personal) are among the problems that must be addressed immediately [12]; however, the psychological implications of these and other emerging problems, such as the possibility of carrying the disease to loved ones, being isolated from social surroundings, lack of mental support and the anxiety and depression caused by all aspects of facing this disease head-on [13], are also critical for an adequate response to this pandemic. Furthermore, our experience with previous epidemics has shown that, after intensive care unit (ICU) personnel return to routine workloads, the psychological impact of these events may lead to significant problems in the short and long term [14, 15].

It is evident that many factors are involved in healthcare workers' perception and response to such ordeals. Fear, stress, anxiety, depressive feelings, self-perception, social support, sufficient knowledge/training and altruism are among the most important personal attributes that determine an individual's role as a healthcare worker [16, 17]. These attributes are even more important for those in emergency or critical care, as it has been shown that these employees have a greater risk for psychiatric problems, including anxiety and depression [18]. These findings have recently been supported by results from studies investigating the mental well-being of healthcare workers who responded to COVID-19 in China [19, 20].

Our aim in this study performed during the early phase of the COVID-19 pandemic was to determine the depression- and anxiety-related problems (measured via self-report questionnaires) of healthcare workers employed in the ICUs of six hospitals in Istanbul, Turkey, and to identify whether these findings were associated with demographic or profession-related characteristics. In order to determine the influence of caring for patients with COVID-19, we included individuals from adult ICUs (who were actively responding to COVID-19) and pediatric ICUs (who were not receiving any patients with COVID-19 at the time of the study).

Materials and methods

In this cross-sectional study, the impact of the COVID-19 pandemic on Turkish healthcare workers employed in six adult and six pediatric ICUs (including one neonatal ICU) were analyzed via an online questionnaire form prepared on SurveyMonkey (tr.surveymonkey.com). Preparation of the form was performed after the first confirmed COVID-19 case was reported in Turkey (March 10, 2020). We planned to include all persons who were primarily employed in an ICU, regardless of profession, ICU type (pediatric or adult), age, education and working status (day, night or shifts). The inclusion of pediatric ICU staff and workers was done to be able to compare the characteristics of individuals with or without (or very limited) exposure to COVID-19 patients. Employees were asked two questions to determine their exposure to patients with COVID-19: (i) whether their ICU had admitted any patients with COVID-19, and (ii) whether they had directly cared for (or carried out their duties in a room with) patients diagnosed with COVID-19 as part of their employment.

Two weeks after the first case and on the day at which the confirmed number of cases surpassed 2000 (March 25), a total of 650 individuals from the following six institutions in Istanbul received the questionnaire: Acibadem University Hospital, Memorial Yeniyuzyil University Hospital, Istinye University Liv Hospital, Okmeydani Research and Training Hospital, Bakirkoy Dr. Sadi Konuk Research and Training Hospital and Goztepe Research and Training Hospital. For a response to be included in the analysis, we defined a threshold of at least 90% completion of the form. According to this definition, a total of 576 responses (88.6% of total) were accepted and received by March 30 –the day on which data gathering was completed.

Questionnaire

All participants filled a self-report questionnaire that included demographic/descriptive questions, work-related questions, and the State-Trait Anxiety Inventory (STAI) TX-I and TX-II scales in addition to Beck depression inventory (Beck-D) and Beck anxiety inventory (Beck-A) scales. We must note that, although the STAI-TX-I and the Beck-A scales investigate similar characteristics, we utilized both to be able to (i) ascertain whether the two STAI measures demonstrated any alterations (considering state/trait differences), and (ii) to be able to directly compare the results obtained from the Beck anxiety and STAI-TX-I scale if necessary. The questionnaire included queries about individuals' choices and actions based on the COVID-19-related problems among healthcare workers (disease-related perceptions). These included the assessment of self-perceptions regarding knowledge level, psychological effects, patient care and social isolation. Additionally, subjects were asked whether they were uncomfortable about going home after work, and whether they were temporarily living somewhere other than their home. Apart from these two, the remaining questions were assessed on a scale from 0 to 10. Scoring was as follows: 0 was defined as least perception or lack of bearing on the individual, while 10 indicated the highest degree of self-perception or influence on the individual. The questionnaire was prepared with respect to prior studies' findings and was given its final form after preliminary application of the questionnaire to a group of

residents and nurses employed in an ICU (n=19) who reported that the questionnaire was understandable.

Questions Specific to COVID-19 Perceptions

The following questions, prepared by the researchers and translated to English with the best possible explanatory context, were presented to all individuals. Each of these items were assessed on a scale from 0 to 10:

- How much knowledge do you feel that you have concerning COVID-19? (0: none, 10: complete)
- As an ICU worker, what is the level of psychological burden you feel due to COVID-19? (0: none, 10: heaviest burden ever felt in the ICU)
- How willing are you to care for patients with COVID-19? (0: not willing at all, 10: would volunteer if necessary)
- What is the degree of social isolation you feel due to COVID-19? (0: none, 10: worst social isolation ever felt)
- How uncomfortable do you feel about going home from the ICU during this period? (0: no change compared to usual, 10: extremely high discomfort / cannot go home)
- How worried are you about contracting COVID-19? (0: not worried at all, 10: constantly worrying during work)
- How much do you fear carrying home the virus causing COVID-19? (0: no fear at all, 10: worst fear ever felt)

We evaluated the answers to these questions as "disease-related perceptions" and investigated their correlations and/or relationships with other variables.

State-Trait Anxiety Inventory

This inventory has two subsections: the STAI TX-I is used to assess the 'state' anxiety levels of individuals, while the STAI TX-II is used to investigate 'trait' anxiety levels. The inventory was developed by Spielberger [21] and the Turkish validity and reliability study of the scale was performed by Oner and Le Compte [22]. Each subsection consists of 20 items. Total score ranges between 20-80 points in both sub-scales of the scale, and the level of anxiety is proportional to the score.

Beck depression and anxiety inventories

The depression and anxiety of individuals were assessed with the Beck-D and the Beck-A. The Beck-D consists of 21 items that are used to report the intensity of symptoms or attitudes related to depressive characteristics, each scored on a scale of 0 to 3 [23]. The Beck-A also consists of 21 items (for anxiety-related questions) that are scored in the same way as the Beck-D (from 0 to 3) [24].

Ethics

This study was conducted according to the Helsinki Declaration. Necessary permissions for the questionnaire and its application were obtained from the Deanery of the primary center of the study after a small-committee review of our study plan (due to precautions associated with the pandemic). Final confirmed ethical approval was obtained from the Social and Humanities Research Ethical Committee of Istinye University (Decision date: April 16, 2020; decision number: 2020/04.02).

Statistical analysis

All analyses were performed on SPSS v21 (SPSS Inc., Chicago, IL, USA). Q-Q and histogram plots were used to determine whether variables were normally distributed. Data are given as mean (standard deviation) or median (1st quartile - 3rd quartile) for continuous variables with regard to normality of distribution and frequency (percentage) for categorical variables. Normally distributed variables were analyzed with the independent samples t-test or one-way analysis of variances (ANOVA) depending on group count. Pairwise comparisons after initial ≥3-group analyses were performed with the Tukey test. Non-normally distributed variables were analyzed with the Mann-Whitney U or the Kruskal-Wallis tests depending on group count, and pairwise comparisons of these variables were performed with the Bonferroni correction method. Spearman correlation coefficients were calculated for the assessment of relationship between continuous variables. Multiple linear regression analysis (stepwise selection method) was performed to determine factors independently associated with total scale scores. Two-tailed p values of less than 0.05 were considered statistically significant.

Results

Among the 576 respondents, 285 were employed in pediatric ICUs and 291 were employed in adult ICUs. Mean age was 31.5 (8.1) years overall, 58% were females and 42% were males. 86.3% were continuing to stay in their own home. In terms of education status, 442 of the participants (76.7%) were university graduates or had received higher education; concurrently, 86.8% of the respondents were either physicians or nurses. With respect to exposure to patients with COVID-19, we found that 95.9% of adult ICU workers were aware that their ICU had admitted patients with COVID-19, while this value was 0% for pediatric ICUs. On the other hand, 93.5% of adult ICU workers and 8.1% of pediatric ICU workers reported that they had had direct exposure to a patient with COVID-19 or had carried out their duties in a room with a patient with COVID-19. Marriage status was evenly distributed, 48.1% were married and 51.9% were single; however, only 69 individuals (12%) lived alone in their household. The majority did not have children (63.5%) (Table 1).

When overall scores were evaluated, we found mean STAI-TX-I and TX-II scores to be 53.41 (10.55) and 44.20 (7.61) points, respectively. The Beck-D score showed normal results in 36.7% of participants, while the Beck-A score was normal in 38.2% of participants. Median Beck-D total score was 12 (7–20) and median Beck-A total score was 13 (7–21) points; however, the percentage of individuals with moderate or severe symptom intensity was 32.5% in Beck-D and 35.6% in Beck-A (Table 1).

When total scores obtained from each scale were compared with regard to groups, we found that only the STAI TX-II score demonstrated a significant difference with regard to being employed in a pediatric or adult ICU (P=0.001). Gender, marital status and number of people in the household were not associated with any of the scores; however, interestingly, those with children had lower total scores for STAI TX-II and Beck-D and Beck-A (P=0.046, P=0.008 and P=0.049, respectively) (Table 2).

Table 1: Summary of participants' characteristics and total scale scores

Parameter	Value
Intensive care unit type (n=576)	
Pediatric	285 (49.48%)
Adult	291 (50.52%)
Gender (n=576)	
Female	334 (57.99%)
Male	242 (42.01%)
Age, years (n=575)	30 (25 - 38)
Education status (n=576)	
Primary	8 (1.39%)
High	126 (21.88%)
University	289 (50.17%)
Masters	58 (10.07%)
Doctorate	95 (16.49%)
Profession (n=576)	
Doctor	164 (28.47%)
Nurse	336 (58.33%)
Medical Secretary	34 (5.90%)
Cleaning Staff	12 (2.08%)
Others (medical technician, administrative staff, etc.)	30 (5.21%)
Working years (n=573)	7 (3 - 14)
Has your ICU admitted any patients with COVID-19? (n=576)	
Adult ICU employees (‘Yes’)	279 (95.9%)
Pediatric ICU employees (‘Yes’)	0 (0%)
Have you had direct exposure to patients with COVID-19? (n=576)	
Adult ICU employees (‘Yes’)	272 (93.5%)
Pediatric ICU employees (‘Yes’)	23 (8.1%)
Marital Status (n=576)	
Married	277 (48.09%)
Single	299 (51.91%)
Children (n=576)	
None	366 (63.54%)
Present, age <16	177 (30.73%)
Present, age >16	33 (5.73%)
Number of people in household (n=576)	
≥ 6	42 (7.29%)
3 - 5	333 (57.81%)
2	132 (22.92%)
1	69 (11.98%)
Knowledge level (n=576)	8 (6 - 8)
Degree of psychological burden (n=576)	8 (7 - 10)
Willingness to care for patients with COVID-19 (n=574)	6 (4 - 8)
Degree of social isolation felt (n=576)	8 (5 - 10)
Degree of discomfort about going home (n=576)	10 (9 - 10)
Residing at home (n=576)	497 (86.28%)
Degree of worry concerning disease contraction (n=576)	8 (6 - 10)
Fear level of carrying the disease home (n=576)	10 (10 - 10)
STAI TX-I Total Score (n=571)	53.41 (10.55)
STAI TX-II Total Score (n=569)	44.20 (7.61)
Beck-D Total Score (n=569)	12 (7 - 20)
Normal	209 (36.73%)
Mild (10–16 points)	175 (30.76%)
Moderate (17–29 points)	140 (24.60%)
Severe (30–63 points)	45 (7.91%)
Beck-A Total Score (n=571)	13 (7 - 21)
Normal	218 (38.18%)
Mild (10–16 points)	150 (26.27%)
Moderate (17–29 points)	133 (23.29%)
Severe (30–63 points)	70 (12.26%)

Data are given as mean (standard deviation) or median (1st quartile - 3rd quartile) for continuous variables with regard to normality of distribution, and as frequency (percentage) for categorical variables

On the other hand, education level and profession were found to be significantly influential on both the depression and anxiety total scores of the Beck scales. The Beck-D and Beck-A scores were both found to be significantly higher in nurses compared to physicians (P=0.001 and P<0.001, respectively). Subjects with lower levels of education were found to have higher Beck-A scores compared to individuals that had received higher education (P=0.001). Finally, we also found that subjects who were not residing at their own home had significantly higher Beck-A scores than those that were residing at their homes (P=0.003); however, Beck-D scores were similar between these two groups. Additionally, there was a statistically significant but marginal decrease in STAI TX-II scores among individuals who were not residing at home (P=0.031) (Table 2).

Table 2: Comparison of total scale scores between groups

	STAI TX-I Total Score	STAI TX-II Total Score	Beck-D Total Score	Beck-A Total Score
Intensive care unit type				
Pediatric	54.08 (10.36)	45.28 (7.44)	13 (7 - 20)	12 (7 - 21)
Adult	52.76 (10.70)	43.15 (7.64)	12 (7 - 20)	13 (7 - 21)
P-value	0.134	0.001	0.662	0.445
Gender				
Female	53.44 (10.00)	44.06 (6.88)	12 (7 - 19)	13 (7 - 21)
Male	53.37 (11.29)	44.39 (8.51)	12 (7 - 21)	11 (6 - 22)
P-value	0.934	0.623	0.667	0.228
Education Status				
Primary & High	53.35 (10.50)	44.93 (6.93)	14 (8 - 20) [a]	15 (10 - 24)
University	53.82 (10.99)	44.27 (7.24)	12 (7 - 21) [ab]	12 (7 - 22) [a]
Master & Doctorate	52.69 (9.73)	43.44 (8.74)	11 (6 - 17) [b]	11 (6 - 16) [a]
P-value	0.558	0.251	0.025	0.001
Profession				
Physician	51.98 (10.05)	42.45 (8.00) [a]	11 (6 - 16) [a]	9.5 (6 - 15.5) [a]
Nurse	54.16 (10.37)	45.00 (7.11) [b]	14 (8 - 21) [b]	14 (8 - 23.5) [b]
Others	53.18 (12.08)	44.48 (8.30) [ab]	11 (7 - 22) [ab]	13 (4 - 21) [ab]
P-value	0.080	0.002	0.001	<0.001
Marital Status				
Married	54.30 (10.35)	44.06 (7.98)	12 (7 - 18)	12 (7 - 23)
Single	52.59 (10.68)	44.33 (7.25)	13 (8 - 21)	13 (7 - 21)
P-value	0.052	0.677	0.254	0.581
Children				
Absent	53.99 (10.30)	44.68 (7.57)	13 (8 - 21)	13 (7 - 21)
Present	52.40 (10.93)	43.37 (7.62)	10.5 (6.5 - 17)	11 (6 - 21)
P-value	0.081	0.046	0.008	0.049
Lives				
With Family/Friend	53.77 (10.45)	44.31 (7.48)	13 (7 - 20)	13 (7 - 22)
Alone	50.78 (10.95)	43.38 (8.50)	8 (5 - 16)	10 (4 - 13)
P-value	0.027	0.338	0.002	0.001
Residing at home				
Yes	53.35 (10.63)	44.47 (7.65)	12 (7 - 20)	12 (7 - 21)
No	53.81 (10.08)	42.47 (7.15)	13.5 (8 - 18)	15.5 (11 - 22)
P-value	0.718	0.031	0.471	0.003

Data are given as mean (standard deviation) or median (1st quartile - 3rd quartile) for continuous variables with regard to normality of distribution. Same letters denote the lack of statistically significant difference between groups in pairwise comparison.

Analysis of correlations between parameters yielded only a few notable findings. There were weak relationships between STAI TX-I total scores and two parameters: psychological effect of the disease (r = 0.426, P<0.001) and being afraid of contracting the disease (r = 0.403, P<0.001). Other correlations were too weak to be noted; nevertheless, a majority of analyses showed statistical significance (Table 3).

Table 3: Relationship between age, working year, answers to questions and total scale scores

		STAI TX-I Total Score	STAI TX-II Total Score	Beck-D Total Score	Beck-A Total Score
Age	r	-0.035	-0.131	-0.174	-0.139
	P	0.408	0.002	<0.001	0.001
Working year	r	-0.004	-0.112	-0.135	-0.107
	P	0.932	0.008	0.001	0.011
Knowledge level	r	-0.028	-0.159	-0.053	-0.066
	P	0.501	<0.001	0.204	0.116
Degree of psychological burden	r	0.426	0.154	0.310	0.245
	P	<0.001	<0.001	<0.001	<0.001
Willingness to care for patients with COVID-19	r	-0.179	-0.215	-0.146	-0.069
	P	<0.001	<0.001	<0.001	0.102
Degree of social isolation	r	0.367	0.296	0.287	0.140
	P	<0.001	<0.001	<0.001	0.001
Degree of discomfort about going home	r	0.384	0.141	0.260	0.201
	P	<0.001	0.001	<0.001	<0.001
Degree of worry concerning disease contraction	r	0.403	0.279	0.289	0.226
	P	<0.001	<0.001	<0.001	<0.001
Fear level of carrying the disease home	r	0.363	0.117	0.237	0.242
	P	<0.001	0.005	<0.001	<0.001

r: Spearman correlation coefficient

Multiple linear regression analyses for the Beck-D and Beck-A scales were performed to determine factors that demonstrated significant relationships with total score from each scale. The following variables were included in the models: ICU type, gender, education status, profession, marital status, children (present/absent), co-inhabiting (alone/shared) and residence status (home/other). Results were similar for both scales, being a physician and living alone were the only two variables found to be independently associated with lower Beck-D (P=0.007 and P=0.009, respectively) and lower Beck-A scores (P<0.001 and P=0.002, respectively) (Tables 4 and 5).

Table 4: Significant related factors with the Beck-D Scale total scores, multiple linear regression analysis

	β1	SE	β2	t	*P*-value	95% CI for β	
(Constant)	18.558	1.443		12.862	<0.001	15.724	21.392
Profession (Physician)	-2.398	0.884	-0.113	-2.711	0.007	-4.134	-0.661
Living Alone	-3.223	1.222	-0.109	-2.637	0.009	-5.624	-0.822

β1: Unstandardized β, β2: Standardized β, SE: Standard Error, Dependent Variable: Beck-D Total Score; R2=0.025; F=7.358; *P*=0.001

Table 5: Significant related factors with the Beck-A Scale total scores, multiple linear regression analysis

	β1	SE	β2	t	*P*-value	95% CI for β	
(Constant)	20.733	1.609		12.885	<0.001	17.573	23.894
Profession (Physician)	-3.927	0.982	-0.164	-3.999	<0.001	-5.856	-1.998
Living Alone	-4.146	1.363	-0.125	-3.042	0.002	-6.824	-1.469

β1: Unstandardized β, β2: Standardized β, SE: Standard Error, Dependent Variable: Beck-A Total Score; R2=0.044; F=12.946; *P*<0.001

Discussion

Healthcare workers throughout the world have been severely affected by the COVID-19 outbreak. Although some attention has been given to the physical and daily needs of healthcare workers, their psychological well-being has not received sufficient interest due to the immediate risks imposed by the disease. However, it is well established that healthcare workers employed in emergency and intensive care have significantly increased risks for adverse psychological outcomes [18].

Our investigation of ICU employees' depressive feelings and anxiety showed that education level, type of profession, having children, and cohabiting status (alone vs. not alone) were significantly influential on both depression and anxiety. However, interestingly, working in an ICU with or without COVID-19 patients (adult vs. pediatric ICU) had no bearing on the levels of depression or anxiety. This was in conflict with a very recent study from China that reported worse mental health outcomes in healthcare workers that were in the front lines during COVID-19 [12]. There are many factors that may influence an individual's response to threats of this magnitude. Among these, altruism, personal fear, family-related fear, stigmatism and social support seem to play an important role [25-27]. When these factors are assessed with regard to their face value, it is rather compelling to suggest that our findings (lower anxiety scores in those with children, higher scores in single people and lower scores in those that live alone) are conflicting. However, it is possible to associate these seemingly conflicting results with altruism and social support. The self-sacrificing attitude shown by healthcare workers in this crisis may have helped them to overcome fear and anxiety. For instance, considering the high education levels of this group, it is possible that knowing their children are relatively safe from COVID-19 could have reduced anxiety and depressive feelings, in addition to the mental support provided by their children. Also, those living alone could be feeling content for the fact that they have little possibility of transmitting the disease to a loved one. Finally, although it is a given that married people have the risk of carrying the disease home which would negatively affect their mental well-being, the fact that married couples have been shown to have higher levels of social support that improve health-related outcomes [28-30] may be an important factor that reduces their levels of anxiety and depressive feelings; thus causing a lack of statistical significance in pairwise comparison of marital status. We also believe that we should note the significantly higher Beck-A scores among individuals who were not residing in their homes (86.3% of the study group), indicating increased anxiety, most probably due to being afraid of the risk of carrying the disease to their loved ones at home. Another crucial finding to note was the fact that around one-third of all ICU employees were found to have either moderate or severe symptom intensity in both the Beck-D and the Beck-A scales.

With regard to questions specific to COVID-19 outbreak, we found that the majority of persons were highly concerned about this disease. However, it was interesting to observe that there were only weak correlations between disease-specific questions assessing the impact of these factors on individuals (from 0 to 10) and scores that were obtained from the depression or anxiety scales. We believe that these results can be explained by the fact that healthcare workers were coping well with the possibilities lying ahead, even though they were well aware of the dangers of this pandemic. Our belief is that the current study indicates the need for continuous social and mental support during the spread of COVID-19.

We also found that physicians had significantly lower scores compared to other healthcare workers; whereas nurses had higher scores than any other profession. A recent study by Zhu et al. also showed that nurses and medical technicians had higher levels of stress compared to physicians [31]. A previous study in Emergency Department workers responding to SARS also had similar findings and showed that nurses had a higher risk for stress when compared to other healthcare workers in emergency departments [32]. In a study similar to ours, Lai and colleagues also found that being a nurse (among other variables) was associated with worse mental health symptoms [12]. Our results with the Beck-D and Beck-A scores showed that nurses had worse results compared to other professions. The present findings support the majority of previous studies that indicate nurses may be especially vulnerable to the adverse psychological effects of disease outbreaks such as COVID-19 [12, 33, 34]. It is also noteworthy that physicians seem to consistently have lower degrees of severity in psychological evaluations and/or outcomes throughout these studies. A somewhat conflicting result was reported in healthcare workers caring for COVID-19 patients in Singapore. Particularly interesting was the fact that front-line nurses included in the study had significantly lower traumatization scores when compared with nurses that were not in the front-line of COVID-19 care [35]. The authors attributed this difference to the high preparedness level of their country (due to experience with SARS) and the possibility that front-line nurses had better overall experience and training. While this conclusion may indeed be true, it is also important to note that their study was performed in a period of almost 3 weeks in which the number of COVID-19 patients rose from 84 to 200, without any deaths [35]. Thus, it is arguable that healthcare workers in their sample were not representative of a group that had experienced the impact of COVID-19 to its full extent.

Zhu and colleagues reported that, increased risk for stress, depression and anxiety during COVID-19 were independently associated with the following risk factors: being female, having a history of mental disorder or chronic disease, having relatives with COVID-19, and being an employee for over 10 years (possibly due to age) [31]. In the current study,

multivariate regression analyses with Beck-D and Beck-A as dependent variables demonstrated that both of these scales were independently associated with the same two parameters: being a physician and living alone. Each of these parameters significantly reduced Beck-D and Beck-A scores. Therefore, contrary to the previous study, gender and working years were not found to be associated with any of the scores in our study group; however, our study was performed in the early period of the spread of COVID-19 in Turkey, which may be the cause of indifference in scores, especially with regard to the age parameter as the number of mortalities were relatively low in this period.

We believe our findings indicate the heightened senses of self-sacrifice and altruism among ICU workers in the face of this pandemic. However, we also conclude that social support mechanisms may be crucial in the long term. Particularly considering the possibility of increased workloads and exhaustion in the following weeks, we believe any and all precautions should be taken to protect the psychological well-being of healthcare employees, especially those employed in ICUs, in this trying period. Our conclusions regarding these results are supported by previous smaller-scale studies exploring this topic [36-38] and also a recent systematic review [39], as well as studies from Turkey which showed increased COVID-19-related anxiety among females [40] and worse mental-wellbeing among patients [41].

Limitations

These results in our group of healthcare workers should be cautiously evaluated, as this study was performed 2 weeks after the first case of COVID-19 was confirmed in Turkey (begun on the day with 2000 confirmed cases and ended on the day with over 10000 confirmed cases); additionally, we did not perform longitudinal follow-up. However, considering the speed of the spread and the fact that Istanbul had a disproportionally high number of COVID-19 patients (relative to population) at the time of the study, we believe our results represent the targeted sample very well. Another limitation is the fact that the spread of disease and the increase in mortalities after the study period could have influenced healthcare workers' perceptions and attitudes. It is also important to note that the baseline variations between employees of pediatric and adult ICUs could have affected the results. Additionally, since this is a cross-sectional study applying an online questionnaire, it may have been susceptible to recall bias and non-response bias. However, neither of these problems are likely to have affected outcomes; recall bias would have been minimal with regard to the fact that the questions consisted of personal or work-related parameters, and we ensured that non-response bias was virtually non-existent (88.6% response rate) by following up with potential participants and reminding them about the study and the questionnaire form sent to them. Sampling bias may also come to mind, but the response rate and the fact that all individuals working in the ICU were included in the study (regardless of any factors) is an important strength of the present study. Finally, we chose to apply both the STAI and Beck anxiety scales, because the STAI scale would have been more valuable to assess COVID-19-related variations in state and trait anxiety; whereas, the Beck scales would have been more reliable to assess possible contrasts in depressive and anxiety-related findings. Further studies must be carried out to investigate the psychological burden of COVID-19 on healthcare workers in the following weeks and months.

Conclusion

It seems that the psychological impact of COVID-19 on healthcare workers is largely unassociated with COVID-19-related perceptions, but a third of the participants had moderate or severe levels of depression and anxiety –which may have been clinically relevant and must be evaluated in future studies. Furthermore, univariate analyses suggest that nurses are a group which may need continuous support to ensure mental well-being, indicating the need for targeted interventions aimed at increasing coping during the pandemic. Multivariable regression showed that being a physician and living alone were independently associated with lower Beck-D and Beck-A scores. Therefore, providing accommodation for ICU employees who choose to stay away from their home during COVID-19 could reduce short and long-term problems related to depression and anxiety.

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Evaluation of radiographic measurements of the wrist in the Turkish population

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Ethics Committee Approval
The study was approved by Gaziosmanpasa Education and Research Hospital Ethical Committee (No: 130 / Date: 05.08.2020). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Wrist parameters measured on direct radiography are essential in diagnosing distal radius fractures and many specific wrist disorders and determining prognosis after treatment. Previous studies have shown the intercommunity variability of these parameters in the literature. To our knowledge, no study in the literature reflects the normal values in the Turkish population. This study aimed to determine the distribution and normal limits of parameters measured in posteroanterior (PA) and direct lateral radiographs of the wrist in our population between age and gender groups.

Methods: In this retrospective cohort study, patients who presented to 2 centers in our clinic between 2014-2020 and had PA and lateral wrist radiographs were retrospectively reviewed. Images from patients who had no significant osseous pathology and had not undergone wrist surgery were randomly selected, and 320 (201 female, 119 male) digital images were retrospectively analyzed. The mean age was 40.45 (13.71). The sample was divided into three groups (18-30, 31-50, over 51) according to age and into two groups according to gender. Radial inclination (RI), lunate fossa inclination (LFA), cord of radiocarpal arch (cord RC), radial shift (Radsh), radial height (RadH), ulnar variance (UV), third metacarpal height (3^{rd} MH), carpal height (CH), capitate height (CapH), lunate transverse length (LL), lunate uncovering length (LUL), scapholunate joint distance (SLD), distal radioulnar joint distance (RUD), volar tilt on lateral radiographs (VT), scapholunate angle (SLA) were measured. The lunate uncovering ratio (LUR) was measured in proportion to the lunate uncovering length (LUL) / lunate transverse length (LL); carpal height ratio (CHR) by proportioning carpal height (CH) / third metacarpal height (3^{rd} MH); revised carpal height ratio (rCHR) was calculated by proportioning the carpal height (CH) / capitate height (CapH).

Results: Although the RI and SL values of angular parameters were similar between the gender groups, the LFI and VT values were significantly higher in the female group (P=0.014 and P=0.004, respectively). All metric parameters were significantly superior in the male group (P<0.001). CHR and rCHR values were similar for proportional parameters, while LUR -values were significantly higher in the male group (P<0.001).

All angular measurement parameters, Cord RC, RadH, RadS, LL, LUL, SLD of metric parameters, and CHR and rCHR values of proportional parameters were similar between age groups (P>0.05). While UV values of metric parameters increased in parallel with age, RUD values decreased significantly (P<0.001). The values of the metric parameters CH 3^{rd} MH, CapH, and proportional parameters LUR values also differed between the groups without being correlated with age (P=0.011, P=0.003, P=0.009, P=0.019, respectively).

Conclusion: In our study, we have given the measurement parameters that can be used as a reference for the Turkish population, the relationships between gender and age groups, and the variability. These parameters can be helpful in the diagnosis and treatment of wrist pathologies, the design and development of implants for the treatment of wrist pathologies for our population.

Keywords: Database, Carpal indices, Turkish population, Wrist measurements, Distal radius angle

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Introduction

Even though the diagnosis of wrist disorders has become easier with the development of imaging techniques, direct radiography is the most common and the first imaging technique we use to evaluate the bony structures of the wrist compared to other radiological examinations [1].

Many parameters are associated with normal wrist structure and carpal pathology clinic on posteroanterior and lateral radiographs [2, 3]. These parameters are commonly used in orthopedic practice to diagnose and treat wrist and carpal pathologies.

For example, parameters such as volar tilt, radial inclination, radial shift, radial height, and ulnar variance are essential for understanding distal radius anatomy, anticipating instability, assessing reduction quality, and making surgical decisions after fractures and in the wrist with malunion [3, 4].

In addition, the carpal height index and the revised carpal height index are used to diagnose carpal collapse due to scapholunate injuries, Kienbock's disease, or rheumatologic diseases [2, 5].

The relationship of parameters such as ulnar variance, radial inclination, lunate fossa inclination, and lunate uncovering index with the pathogenesis of Kienbock's disease has also been studied in the literature [6]. Measurement of scapholunate angle and scapholunate distance; helps assess conditions such as scapholunate disintegration or DISI (dorsal intercalary segment instability) [2, 7]. Studies conducted in the literature show the variability of normal values of these parameters between different populations [2, 5, 8-12].

To our knowledge, no study in the literature reflects the normal values in the Turkish population. This study aimed to determine the distribution and normal limits of the parameters measured in posteroanterior (PA) and direct lateral radiographs of the wrist in our population between age and gender groups.

Materials and methods

The study was approved by Gaziosmanpasa Education and Research Hospital Ethical Committee (No: 130 / Date: 05.08.2020). This study was conducted according to the Helsinki Declaration principles.

In this retrospective cohort study, patients who presented to 2 centers in our hospital between 2014-2020 and had radiographs of the wrist PA and lateral wrist were retrospectively evaluated.

Radiographs of patients who presented with mild trauma to the hand and wrist, contralateral wrist radiographs of patients who presented with severe trauma for control, carpal tunnel, tenosynovitis, simple benign masses (such as ganglion, hemangioma, lipoma), and radiographs of patients who presented for any other reason were included in the study. Radiographs of patients whose skeletal maturity was not complete were excluded from the study. Radiographs of patients whose wrist radiographs showed evidence of osseous pathology, who had a history of previous fracture or orthopedic surgery, and whose radiographs showed malunion were excluded from the study. Consequently, the digital PA and lateral wrist radiographs of 320 patients (201 females, 119 males) were retrospectively analyzed.

The mean age was 40.45 (13.71), and the median was 41 (range 18-81). The sample was divided into three groups according to age. A total of 87 radiographs (27.2%) aged 18-30 years in group a, 150 radiographs (46.9%) aged 31-50 years in group b, and 83 (25.9%) radiographs (over 51 years) in group c. The radiographs of 201 females (62.8%) and 119 males were analyzed for gender characteristics. The descriptive data are summarized in Table 1.

Table 1: Descriptive statistical data for the measured parameters

	Mean ± SD	Median (Min-Max)
Age(years)	40.45 ± 13.71	41 (18 - 81)
Radial Inclination – RI (degrees)	24.14 ± 5.4	24.5 (9 - 39)
Lunate Fossa Inclination – LFI (degrees)	10.85 ± 5.0	11 (-4 - 27)
Volar Tilt – VT (degrees)	13.61 ± 10.96	13 (0 - 32)
Scafolunate Angle – SLA (degrees)	56.16 ± 12.22	58 (10 - 90)
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	29.64 ± 2.69	29.25 (24.2 - 38.8)
Radial Height – RadH (mm)	12.34 ± 2.06	12.2 (6 - 17.1)
Radial Shift – Radsh (mm)	13.41 ± 2.09	13.2 (8 - 20)
Ulnar Variance – UV (mm)	-0.08 ± 3.84	0 (-4 - 4)
Carpal Height – CH (mm)	32.69 ± 3.37	32.2 (23 - 42)
Length Of Third Metacarpal – 3rd MH (mm)	65.09 ± 34.7	63 (31 - 677)
Length Of Capitate – CapH (mm)	21.95 ± 2.28	21.9 (17 - 28.1)
Lunate Length – LL (mm)	14.96 ± 5.42	14.55 (10.6 - 106)
Lunate Uncovering Length – LUL (mm)	5.56 ± 1.71	5.4 (0 - 20.4)
Scafolunat Joint Space – SLD (mm)	1.97 ± 0.99	1.9 (0.7 - 17)
Distal Radioulnar Joint Space – RUD (mm)	1.69 ± 0.54	1.6 (0.8 - 3.6)
Carpal Height Ratio – CHR	0.52 ± 0.06	0.52 (0.05 - 1.13)
Revised Carpal Height Ratio – rCHR	1.49 ± 0.1	1.49 (1.23 - 1.81)
Lunate Uncovering Ratio – LUR	0.38 ± 0.1	0.38 (0 - 0.87)

Radiographic technique

Standard PA radiographs of the wrist; wrist in flexion-extension and ulnar-neutral position relative to radial deviation, forearm in pronation-neutral position relative to supination, elbow in 90 degrees-flexion, shoulder in 90 degrees -abduction. Radiographs of the ulnar styloid seen laterally from the ulnar head were accepted [10].

Standard lateral radiographs: Wrist and forearm in a neutral position, elbow in 90 degrees -flexion, shoulder in 0 degrees -abduction. In the lateral radiographs, the radius, capitate, and the third metacarpals were approximately in line with the sagittal plane. The pisiformis was between the volar edge of the scaphoid tuberosity and the capitate. Patients whose standardization of radiographs was inadequate and could not be taken in the appropriate position were excluded from the study.

Radiographs were performed using the automatic collimator Drgem Diamond 6 A (2013 South Corea) and the digital radiography system Drgem 82 SD (2012 South Corea); the technical values were kV: 60-70, mA: 200, mAs: 8.

By plotting reference lines on PA graphs, radial inclination (RI), lunate fossa inclination (LFA) angles, the cord of the radiocarpal arch (cord RC), radial shift (Radsh), radial height (RadH), ulnar variance (UV), third metacarpal height (3. MH), carpal height (CH), capitate height (CapH), lunate transverse length (LL), lunate uncovering length (LUL), scapholunate joint distance (SLD), distal radioulnar joint distance (RUD). Volar tilt (VT) and scapholunate angles (SLA) were measured on lateral radiographs.

The lunate uncovering ratio (LUR) was measured in proportion to the lunate uncovering length (LUL) / lunate transverse length (LL); carpal height ratio (CHR) by proportioning carpal height (CH) / 3 metacarpal height (3. MH); revised carpal height ratio (rCHR) was calculated by proportioning the carpal height (CH) / capitate height (CapH) (Figure 1). Two board-certified orthopedic surgeons performed measurements twice a month using PACS (Picture archiving and communication systems) Infinitt Pacs 7.0 software (INFINITT

Healthcare Co. Ltd., Seoul, South Corea) to reduce intraobserver and interobserver errors. To calculate the correlation between any two numerical variables Spearman Correlation Analysis was used. Statistical significance was determined as P=0.05 for all cases. Statistical analysis was conducted using IBM SPSS (Statistics Package for Social Sciences for Windows, version 21.0, Armonk, NY, IBM Corp.) package program.

The intraclass correlation coefficient (ICC) with 95% confidence interval (CI) was used to evaluate intraobserver and interobserver reliability. We defined values below 0.4 as indicating poor reliability, values between 0.4 and 0.59 as moderate reliability, values between 0.6 and 0.75 as good reliability, and above 0.75 as excellent reliability (Table 2).

Results

Although the RI and SL values of angular parameters were similar between the gender groups, the LFI and VT values were significantly higher in the female group (P=0.014 and P=0.004, respectively). All metric parameters were significantly superior in the male group (P<0.001). CHR and rCHR values were similar for proportional parameters, while LUR -values were significantly higher in the male group (P<0.001) (Table 3).

All angular measurement parameters, Cord RC, RadH, RadS, LL, LUL, SLD of metric parameters, and CHR and rCHR values of proportional parameters were similar between age groups (P>0.05). While UV values of metric parameters increased in parallel with age, RUD values decreased significantly (P<0.001). The values of the metric parameters CH 3rd MH, CapH, and proportional parameters LUR values also differed between the groups without being correlated with age (P=0.011, P=0.003, P=0.009, P=0.019, respectively) (Table 4).

Table 2: Inter and Intra Observer Reliability Estimates

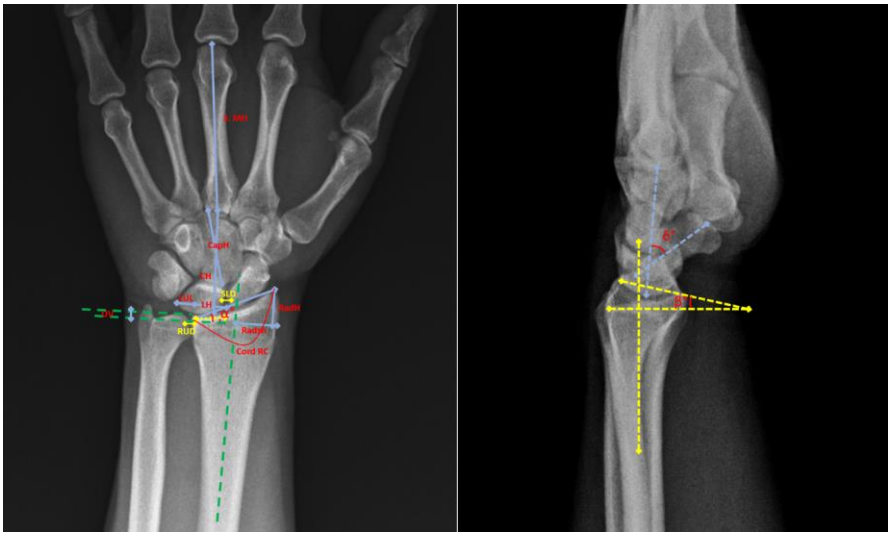
Parameter	Inter ICC	%95 CI	Intra ICC	%95 CI
Radial Inclination – RI (degrees)	0.907	0.907 (0.89-0.922)	0.924	0.924 (0.909-0.936)
Lunate Fossa Inclination – LFI (degrees)	0.912	0.912 (0.895-0.926)	0.929	0.929 (0.916-0.941)
Volar Tilt – VT (degrees)	0.906	0.906 (0.888-0.921)	0.928	0.928 (0.914-0.939)
Scafolunate Angle – SLA (degrees)	0.906	0.906 (0.887-0.921)	0.929	0.929 (0.916-0.941)
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	0.897	0.897 (0.878-0.914)	0.92	0.92 (0.905-0.933)
Radial Height – RadH (mm)	0.902	0.902 (0.883-0.918)	0.925	0.925 (0.911-0.938)
Radial Shift – Radsh (mm)	0.905	0.905 (0.887-0.92)	0.926	0.926 (0.911-0.938)
Ulnar Variance – UV (mm)	0.902	0.902 (0.883-0.918)	0.924	0.924 (0.91-0.937)
Carpal Height – CH (mm)	0.908	0.908 (0.89-0.923)	0.925	0.925 (0.911-0.938)
Length Of Third Metacarpal – 3rd MH (mm)	0.91	0.91 (0.893-0.925)	0.929	0.929 (0.915-0.941)
Length Of Capitate – CapH (mm)	0.898	0.898 (0.879-0.915)	0.92	0.92 (0.905-0.933)
Lunate Length – LL (mm)	0.908	0.908 (0.891-0.923)	0.924	0.924 (0.909-0.936)
Lunate Uncovering Length – LUL (mm)	0.89	0.89 (0.869-0.908)	0.913	0.913 (0.896-0.927)
Scafolunat Joint Space – SLD (mm)	0.867	0.867 (0.842-0.888)	0.896	0.896 (0.876-0.913)
Distal Radioulnar Joint Space – RUD (mm)	0.789	0.789 (0.752-0.821)	0.802	0.802 (0.767-0.833)

Table 3: Comparison of parameters according to gender groups

Gender	Female (201)	Male (119)	P-value
Radial Inclination – RI (degrees)	24.32 ± 4.89	23.45 ± 4.13	0.073(m)
Lunate Fossa Inclination – LFI (degrees)	25 (9 - 39)	24 (11 - 32)	
Volar Tilt – VT (degrees)	11.34 ± 5.38	10.01 ± 4.18	0.014(a)
Scafolunate Angle – SLA (degrees)	11 (-4 - 27)	10 (1 - 23)	
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	13.79 ± 5.51	12.03 ± 4.97	0.004(m)
Radial Height – RadH (mm)	14 (0 - 32)	12 (0 - 30)	
Radial Shift – Radsh (mm)	56.82 ± 12.62	55.04 ± 11.5	0.158(m)
Ulnar Variance – UV (mm)	58 (10 - 90)	56 (20 - 90)	
Carpal Height – CH (mm)	28.27 ± 1.67	31.96 ± 2.49	<0.001(a)
Length Of Third Metacarpal – 3rd MH (mm)	28.3 (24.2 - 32.6)	32.1 (25.4 - 38.8)	
Length Of Capitate – CapH (mm)	11.87 ± 2.02	13.13 ± 1.9	<0.001(a)
Lunate Length – LL (mm)	12 (6 - 17.1)	13 (6.3 - 17)	
Lunate Uncovering Length – LUL (mm)	12.88 ± 1.84	14.3 ± 2.18	<0.001(m)
Scafolunat Joint Space – SLD (mm)	13 (8 - 17.2)	14.5 (10 - 20)	
Distal Radioulnar Joint Space – RUD (mm)	0.25 ± 1.42	-0.15 ± 1.29	0.012(m)
Carpal Height Ratio – CHR	0 (-4 - 4)	0 (-4 - 3.2)	
Revised Carpal Height Ratio – rCHR	31.26 ± 2.65	35.1 ± 3.08	<0.001(a)
	31 (23 - 39)	35 (26 - 42)	
Radial Inclination – RI (degrees)	61.55 ± 4.0	66.21 ± 5.14	<0.001(m)
Lunate Fossa Inclination – LFI (degrees)	62 (49 - 73.7)	67 (49 - 79)	
Volar Tilt – VT (degrees)	20.93 ± 1.77	23.67 ± 2.0	<0.001(a)
Scafolunate Angle – SLA (degrees)	20.7 (17.1 - 25.9)	23.6 (17 - 28.1)	
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	14.16 ± 1.74	15.61 ± 1.75	<0.001(m)
Radial Height – RadH (mm)	14 (10.8 - 23.5)	15.5 (10.6 - 20.2)	
Radial Shift – Radsh (mm)	5.08 ± 1.34	6.29 ± 1.47	<0.001(a)
Ulnar Variance – UV (mm)	5 (0 - 9.7)	6.6 (2.4 - 9.7)	
Carpal Height – CH (mm)	1.82 ± 0.51	2.12 ± 0.52	<0.001(m)
Length Of Third Metacarpal – 3rd MH (mm)	1.8 (0.7 - 3.3)	2 (1.1 - 4.3)	
Length Of Capitate – CapH (mm)	1.62 ± 0.54	1.81 ± 0.53	<0.001(m)
Lunate Length – LL (mm)	1.5 (0.8 - 3.5)	1.6 (0.9 - 3.6)	
Lunate Uncovering Length – LUL (mm)	0.51 ± 0.04	0.52 ± 0.05	0.171(a)
Scafolunat Joint Space – SLD (mm)	0.51 (0.41 - 0.61)	0.52 (0.41 - 0.69)	
Distal Radioulnar Joint Space – RUD (mm)	1.5 ± 0.11	1.49 ± 0.1	0.324(a)
Carpal Height Ratio – CHR	1.5 (1.23 - 1.81)	1.49 (1.26 - 1.72)	
Revised Carpal Height Ratio – rCHR	0.36 ± 0.1	0.4 ± 0.08	<0.001(m)
	0.36 (0.11 - 0.87)	0.4 (0.19 - 0.66)	

(a) Anova T-test - (m) Mann Whitney U Test, Mean ± SD/Median (Min–Max)

Figure 1: Measurements made on PA and lateral radiographs



- Radial inclination (RI): is the angle formed by the line drawn from the tip of the radial styloid to the medial edge of the radial articular surface with the line drawn perpendicular to the long axis of the ulna [7].
- Lunate fossa inclination (LFI): it is the angle between the sclerotic line of the lunate fossa and the line drawn perpendicular to the long axis of the ulna [7].
- Volar tilt (VT): it is the angle between the line drawn perpendicular to the long axis of the radius and the line drawn between the most volar and dorsal points of the radial articular surface [7].
- Scaphulonate angle (SLA): it is the angle between the lunate axis and the scaphoid axis [7].
- Cord of the radiocarpal articular arc (cord RC): it is the direct measurement distance between the tip of the radial styloid and the medial edge of the radial articular surface [9].
- Radial height (RadH): the distance between the tip of the radial styloid and the lines drawn tangential to the distal cortical margin of the ulna and perpendicular to the long axis of the radius [13].
- Radial shift (Radsh): the distance between the long axis of the radius and the line tangential to the end of the radial styloid and drawn parallel to it through the most lateral point of the radial metaphysis [13].
- Ulnar variance (UV): it is the distance between the line intersecting the distal cortical margin of the ulna and drawn perpendicular to the long axis of the radius and the line passing through the medial part of the radial articular surface [7].
- 3rd metacarpal height (3rd MH): the length of the third metacarpal was measured along its long axis from the distal articular surface to the proximal articular surface [14].
- Carpal height (CH): the carpal height was measured along the proximal extension of the long axis of the third metacarpal bone from the articular surface of the base of the third metacarpal bone to the distal articular surface of the radius [14].
- Capitate height (CapH): the capitate length is the longest distance from the subchondral edge of the distal pole at the joint of the third metacarpal to the subchondral edge of the proximal pole at the joint between the carpals [14].
- Carpal height ratio (CHR) and revised carpal height ratio (rCHR): the carpal height ratio is determined by the ratio of the carpal height to the height of the third metacarpal. The revised carpal height ratio is also determined by the ratio of the carpal height to the capitate height [14].
- Lunate length (LL): distance between the ulnar and radial poles of the lunate [7].
- Lunate uncovering length (LUL): It is the perpendicular distance between the ulnar pole of the lunate bone and the line drawn parallel to the radial axis from the ulnar edge of the radius [7].
- Lunate uncovering ratio (LUR): is determined by the ratio of the LUL to the LL [7].
- Scapholunate joint distance (SLD): the scapholunate joint distance was measured from the most radial edge of the lunate to the most radial edge of the proximal scaphoid [15].
- Distal radioulnar joint distance (RUD): the width of the gap at the center of the distal radioulnar joint [16].

Table 4: Comparison of parameters according to age groups

Age group	(a) 18-30 (87)	(b) 31-50 (150)	(c) >=51 (83)	*P*-value
Radial Inclination – RI (degrees)	24.49 ± 4.32	24.19 ± 4.91	23.12 ± 4.36	0.153(k)
Lunate Fossa Inclination – LFI (degrees)	25 (15 - 35)	25 (11 - 39)	24 (9 - 32)	
Volar Tilt – VT (degrees)	11.69 ± 4.89	10.61 ± 4.84	10.39 ± 5.36	0.174(a)
Scafolunate Angle – SLA (degrees)	11 (1 - 27)	11 (-3 - 24)	10 (-4 - 25)	
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	12.94 ± 5.43	12.89 ± 5.19	13.77 ± 5.65	0.598(k)
Radial Height – RadH (mm)	12 (0 - 32)	13 (0 - 30)	13 (2 - 32)	
Radial Shift – Radsh (mm)	55.7 ± 11.74	55.87 ± 11.67	57.16 ± 13.7	0.486(k)
Ulnar Variance – UV (mm)	57 (10 - 90)	56 (20 - 90)	59 (20 - 89)	
Carpal Height – CH (mm)	29.03 ± 2.58	30.0 ± 2.88	29.62 ± 2.36	0.062(k)
Length Of Third Metacarpal – 3rd MH (mm)	28.8 (24.2 - 33.9)	29.5 (25 - 38.8)	29.4 (25.7 - 37.1)	
Length Of Capitate – CapH (mm)	12.21 ± 2.01	12.62 ± 1.98	11.97 ± 2.22	0.058(a)
Lunate Length – LL (mm)	12 (6.3 - 17)	12.35 (8 - 17.1)	12 (6 - 17)	
Lunate Uncovering Length – LUL (mm)	13.29 ± 1.99	13.62 ± 2.14	13.17 ± 2.08	0.227(a)
Scafolunat Joint Space – SLD (mm)	13.3 (8 - 17.9)	13.7 (8 - 20)	13 (9 - 18.5)	
Distal Radioulnar Joint Space – RUD (mm)	-0.41 ± 1.21	0.33 ± 1.39	0.24 ± 1.42	<0.001(k)
Carpal Height Ratio – CHR	0 (-3.6 - 2)	0 (-4 - 4)	0 (-4 - 3)	
Revised Carpal Height Ratio – rCHR	32.56 ± 3.59 33 (23 - 41.2)	33.22 ± 3.22 33 (26 - 42)	31.85 ± 3.27 31.7 (25 - 40.6)	0.011(a)
Radial Inclination – RI (degrees)	63.66 ± 5.4	63.93 ± 4.81	61.71 ± 4.55	0.003(a)
Lunate Fossa Inclination – LFI (degrees)	64 (49 - 76)	64 (51 - 79)	62.1 (49 - 73.7)	
Volar Tilt – VT (degrees)	22.07 ± 2.21	22.21 ± 2.27	21.35 ± 2.29	0.009(k)
Scafolunate Angle – SLA (degrees)	22.3 (17 - 26.7)	22.1 (17.2 - 28.1)	20.9 (17.1 - 28)	
Cord Of Radiocarpal Joint Arc – Cord RC (mm)	14.52 ± 1.61	14.9 ± 2.0	14.53 ± 1.9	0.283(k)
Radial Height – RadH (mm)	14.4 (11.5 - 18.3)	14.7 (10.6 - 23.5)	14.5 (11.2 - 23.5)	
Radial Shift – Radsh (mm)	5.82 ± 1.54	5.49 ± 1.46	5.31 ± 1.53	0.083(a)
Ulnar Variance – UV (mm)	5.8 (2.4 - 9.7)	5.4 (1.6 - 9.7)	5.1 (0 - 8.6)	
Carpal Height – CH (mm)	1.9 ± 0.52	1.98 ± 0.55	1.87 ± 0.51	0.372(k)
Length Of Third Metacarpal – 3rd MH (mm)	1.9 (0.7 - 3.4)	2 (1 - 4.3)	1.9 (0.9 - 2.9)	
Length Of Capitate – CapH (mm)	1.93 ± 0.54	1.67 ± 0.53	1.47 ± 0.46	<0.001(k)
Lunate Length – LL (mm)	1.8 (1.2 - 3.6)	1.5 (0.9 - 3.5)	1.4 (0.8 - 3.5)	
Lunate Uncovering Length – LUL (mm)	0.51 ± 0.05	0.52 ± 0.04	0.52 ± 0.05	0.244(k)
Scafolunat Joint Space – SLD (mm)	0.52 (0.41 - 0.69)	0.52 (0.41 - 0.63)	0.52 (0.41 - 0.69)	
Distal Radioulnar Joint Space – RUD (mm)	1.48 ± 0.11	1.5 ± 0.1	1.5 ± 0.1	0.262(a)
Carpal Height Ratio – CHR	1.48 (1.26 - 1.72)	1.49 (1.25 - 1.81)	1.51 (1.23 - 1.73)	
Revised Carpal Height Ratio – rCHR	0.4 ± 0.09 0.4 (0.19 - 0.65)	0.37 ± 0.09 0.37 (0.11 - 0.87)	0.37 ± 0.1 0.36 (0.11 - 0.63)	0.019(k)

(a) Anova T-test - (k) Kruskal Wallis Test --Mean ± SD/Median (Min–Max)

Discussion

The wrist is a region in the human body where many bones articulate. The anatomy of the bones and connective tissue is very complex. The radiographic anatomy of the wrist and hand have been discussed extensively in the literature. The angles, distances, and indexes that result from the relationship of these distances to each other on radiographs have been associated with many clinical situations [3, 4, 6, 7, 13-16].

Many articles in the literature examine the association of these measurement parameters with age and gender. We examined our radiographic studies in three subtitles: angular, metric, and proportional parameters.

Angular parameters are the angles measured between lines drawn between specific points on radiographic examinations.

Volar tilt (VT) and radial inclination (RI) angles are used to understand the anatomy and evaluate reduction quality after distal radius fractures [17]. Lower than normal VT and RI angles after distal radius fractures have been associated with poor clinical scores [3].

Normal values of the RI angle are reported in the literature to average 22 degrees (12-35) [18]. Schuind et al. [8] reported in their 1992 study that the average values of 23.8 ± 2.6 in 120 healthy individuals were 24.1 ± 2.5 degrees in men and 23.6 ± 2.7 degrees in women. Feipel et al. [2] in 1998 reported mean values of 25 ± 3 degrees in 80 healthy subjects. In the article published by Thienpont et al. [6] in 2004, values of 25.42 ± 4.8 degrees were reported on radiographs in 126 healthy subjects. Valencia et al. [11] reported mean values of 36.5 ± 4 degrees in their measurements of 112 healthy Mexican individuals in 2006. In a study performed on 300 healthy Egyptian individuals in 2009. 28.1 ± 8.1 degrees in males and 24.5 ± 5.9 degrees in females, and 25.5 ± 7.1 degrees in individuals aged 20-40 years and 27.1 ± 6.8 degrees in 40-60 years [9]. Katayama et al. [10] in a study conducted on 134 healthy Japanese individuals, values of 25.5 ± 2 degrees were found in men and 25.7 ± 1.9 1 in women.

In the graphs we examined, the mean RI angle was 24.14 ± 5.4 graphs (9-39). 24.32 ± 4.89 degrees (3-39) in the radiographs of the female group, 23.45 ± 4.13 degrees (11-32) in the radiographs of the male group, 24.49 ± 4.32 in the age group of 18-30 years, 24.19 ± 4.91 degrees in the age group of 31-50 years, and 23.12 ± 4.36 degrees in the group of over 50 years. No statistically significant difference was found between age and gender groups for RI values.

The normal values of the VT angle have been reported as an average of 11 degrees (3-20) in the literature [18]. Thienpont et al. [7], in their 2003 article, reported an average angle of 10.75 ± 2.8 ° on radiographs of 126 healthy individuals. A study from the Mexican population showed a mean VT angle of 17.98 ± 2.25 degrees in 112 healthy individuals [11]. Katayama et al. [10] measured radiographs of 134 healthy Japanese subjects and reported a VT angle of 11.8 ± 2.9 2, in men and 12.3 ± 3.3 degrees in women.

Our study obtained a mean VT angle of 13.61 ± 10.96 0- (0-32). We found a statistically significant difference between the mean values we found 13.79 ± 5.51 degrees in the female group and 12.03 ± 4.97 degrees in the male group. When evaluated between age groups, no statistically significant difference was found between the VT angles, which we found as 12.94 ± 5.43 degrees in the 18-30 years age group, 12.89 ± 5.19 degrees in the 31-50 years age group, and 13.77 ± 5.65 degrees in the over 50 years age group.

The effect of the lunate fossa inclination angle (LFI) on the development of clinical conditions such as Kienbock's disease, scapholunate dissociation (SLD) and concomitant carpal collapse, dorsal intercalated segment instability (DISI), and scapholunate advanced collapse (SLAC) have been investigated in previous studies [6]. Thienpont et al. [7] in their study published in 2003 on 41 SLD patients and 126 healthy individuals t found a mean LFI angle of 10.59 ± 3.1 degrees in the SLD group, while they measured mean values of 13.61 ± 4.4 degrees in the healthy individuals and found this difference to be statistically significant.

In 2004, Thienpont et al. [6] found a mean LFI angle of 13.81 ± 4.1 degrees in the Kienbock group and 13.61 ± 4.4 degrees in the control group in a comparative radiological study between 54 Kienbock patients and 126 healthy individuals. They classified this difference as not statistically significant. Measurements in the Egyptian population in 2009 showed a mean LFI angle of 13.61 ± 4.4 degrees for males, 12.1 ± 3.6 degrees for females, 12.86 ± 0.6 degrees for 20-40-year-olds, and 12.85 ± 0.71 degrees for 40-60-year-olds [9].

In our study, the mean LFI values were 10.85 ± 5.0 degrees (-4-27). We found the mean value 11.34 ± 5.38 degrees in females and 10.01 ± 4.18 degrees in males. We found 11.69 ± 4.89 degrees in the age group 18-30, 10.61 ± 4.84 degrees in the age group 31-50, and 10.39 ± 5.36 degrees in the age group 50+. There was a statistically significant difference in LFI values between gender groups but no significant difference between age groups.

SL angle is the angle measured between the scaphoid and the lunate on the lateral radiograph. It has been associated with the scapholunate gap with scaphoid ligament injuries and pathologies such as carpal collapse and DISI. Measurements defined normal values of 46 degrees (30-60), values above 60 degrees were associated with scapholunate dissociation, values

above 70 degrees with DISI, and values below 30 degrees with VISI [19,20].

Nakamura et al. [21], in their study of 84 healthy wrist radiographs in 1989, found an average SL angle value of 56 ± 7 degrees (42-70). Thienpont et al. [7] found an average angle of 53 ± 3.5 ° in 126 healthy radiographs and an angle of 53.80 ± 4.1 ° SL in their measurement of 41 patients with a scapholunate ligament injury in 2003. They found that this was not statistically significant. No other radiological study was found in the literature that examined the distribution of SL angles by age and gender.

In our study, the mean SLA values found were 56.16 ± 12.22 degrees (10 - 90). We found values of 56.82 ± 12.62 degrees in females, 55.04 ± 11.5 degrees in males, 55.7 ± 11.74 degrees in the age group 18-30, 55.87 ± 11.67 degrees in the age group 31-50, and 57.16 ± 13.7 degrees in the age group 50+. We did not found statistically significant difference between gender and age groups.

Metric parameters are the distance values measured on radiographs of the wrist, expressed in mm. Proportional parameters are other parameters obtained by proportioning the metric parameters to each other.

Cord RC indicates the topographic distance of the surface where the distal radius articulates with the carpal bones. In the database study of Schuind et al. [8] with 120 radiographs of the wrist, the mean values were 30.9 ± 1.7 mm in men, 27.0 ± 1.5 mm in women, 28.8 ± 2.7 mm in the 25-40 age group, and 29.3 ± 2.3 mm in the 41-60 age group. In a 2009 study, mean values of 30.8 ± 1.8 mm, 27 ± 1.5 mm in males, 28.9 ± 2.7 mm in the 20-40 age group, and 29.3 ± 2.3 mm in the 40-60 age group were reported [9]. In the study published by Nakamichi et al. [22] in 1995, it was reported that carpal height, third metacarpal height, and hand height, as well as small distances between radiocarpal joint arches, were associated with idiopathic carpal tunnel syndrome.

In our study group, the mean value of Cord RC was 29.64 ± 2.69 mm, in females 28.27 ± 1.67 mm, in males 31.96 ± 2.49 mm, in the age group 18-30 years 29.03 ± 2.58 mm, in the age group 31-50 years 30.0 ± 2.88 mm and the group above 51 years 29.62 ± 2.36 mm. While there was a significant difference in the measurements between the gender groups, there was no significant difference between the age groups.

RadH, Radsh, and UV values, along with RI and VT, are the parameters we most often use to make a surgical decision when evaluating reduction after distal radius fractures [4].

In the article published by Freiberg et al. [23] in 1976, RadH values of 13.6 mm in men, 11.6 mm in women, and 12.6 mm in the total group were reported. Mann et al. [24], in their 1993 article, reported a RadH value of 14 mm in men and 13 mm in women, a range of 10-18 mm in their radiological measurements.

Radsh is the expression in mm for the offset of the distal radius in the coronal plane concerning the radial axis. Normal values of 13.5 ± 3.8 mm have been reported [3].

Although UV is used to assess fractures of the distal radius, Kienbock's disease and its association with SL disintegration is also the subject of studies in the literature [3,4].

It has been reported in the literature that UV loss on the first radiograph is crucial for the expectation of instability and loss of reduction after fractures of the distal radius [4]. In addition, many articles are investigating the association between ulna-plus-wrist fractures with ulnocarpal abutment syndrome, in which the radius is shorter than the ulna, and Kienbock disease in ulna-minus patients with the short ulna. The level of evidence regarding these conditions was not shown to be high [25].

Schuind et al. [8] found an average UV of 0.9 mm in measurements they made on 120 healthy individuals in 1992 and reported a distribution between -5.0 and + 2.9 mm. They reported mean values of -0.9 ± 1.5 mm in males, -0.9 ± 1.4 mm in females, -0.9 ± 1.4 mm in those aged 25-40 years, and -0.8 ± 1.5 mm in those aged 41-60 years, with no significant differences between these values. Feipel et al. [2] reported UV values of -0.3 ± 2.3 mm in 80 asymptomatic subjects in their study published in 1995.

In the study of Japanese subjects by Nakamura et al. [26]published in 1991, lower and negative UV values were reported in males, and their tendency to decrease with age. This study also examined the association of UV with Kienbock disease and found no significant difference.

In 2004, Thienpont et al. [6] performed UV measurements on radiographs of 54 patients with Kienbock's disease and 126 healthy subjects. They reported the values of -0.89 ± 0.9 mm in the Kienbock group and -0.42 ± 1.4 mm in the control group and could not find any statistically significant difference between these values.

Also, in 2003, Thienpont et al. [7] performed measurements on 41 SLD and 126 healthy individuals. They measured UV values of -0.55 ± 1.48 mm in the SLD group and -0.42 ± 1.51 mm in the control group and reported that this was not statistically significant.

An article published in 2016 compared the radiographs of 166 Kienbock patients and 166 healthy subjects and reported that the values they found in the Kienbock group -0.12 ± 0.087 control group -0.07 ± 0.059 mm were statistically significant between the groups [27].

The mean RadH values among individuals in our study group were found to be 12.34 ± 2.06 (6 - 17.1) mm. It was 11.87 ± 2.02 mm in females, 13.13 ± 1.9 mm in males, 12.21 ± 2.01 mm in the age group 18-30 years, 12.62 ± 1.98 mm in the age group 31-50 years, and 11.97 ± 2.22 mm in the age group above 51 years.

The mean Radsh values were 13.41 ± 2.09 (8-20) mm for the whole group. It was 12.88 ± 1.84 mm in females, 14.3 ± 2.18 mm in males, 13.29 ± 1.99 mm in the age group 18-30 years, 13.62 ± 2.14 mm in age group 31-50 years, and 13.17 ± 2.08 mm in the age group above 51 years.

A statistically significant difference was found between gender groups for RadH and radsh values, while the difference between age groups was not considered significant.

The mean UV was -0.08 ± 3.84 (-4 - 4) mm. It was 0.25 ± 1.42 mm in females, -0.15 ± 1.29 mm in males, -0.41 ± 1.21 mm in the age group 18-30 years, 0.33 ± 1.39 mm in the age group 31-50 years, and 0.24 ± 1.42 mm in the age group above 51 years. Statistical analysis revealed significant differences between age and gender groups. Moreover, when UV values

were correlated with age, it was found that there was a significant decrease in UV values with increasing age.

CHR is used to assess the severity of conditions that cause carpal collapse, such as rheumatoid arthritis, Kienboeck's disease, scaphoid fracture, and wrist ligament injuries [5]. CHR was described in 1978 Youm et al. [28] as the ratio between the height of the third metacarpal bone and the height of the carpus to standardize measurements of carpal height depending on the individual. rCHR was determined in 1994 by Nattrass et al. [14] by comparing the height of the capitate and the carpal height, which allows calculation of the ratio of carpal height on radiographs of the wrist that did not include the third metacarpal bone in the imaging. In their study, Schiund et al. [8] reported CHR values of 54.3 ± 3.9% in males, 52.6 ± 13.4% in females, 52.6 ± 3.8% in ages 25-40, 54.2 ± 13.5% in ages 40-60, and a mean of 52.4 ± 9.9%. Feipel et al. [2] reported the mean CHR rate as 0.52 ± 0.07 and the rCHR rate as 1.48 ± 0.14 in their study published in 1995.

In their 2010 study of 135 male and 126 female wrist radiographs from the Taiwanese population, Wang et al. [5] determined a mean CHR of 0.52 ± 00.3 (0.43-0.59) in males and 0.50 ± 0.03 (0.043-0.057) in females.

Jehan et al. [12], in their 2019 study, determined a mean CHR value of 0.52 ± 0.05 and an rCHR value of 1.50 ± 0.06 from measurements on the radiographs of 120 healthy subjects and found that these values showed no statistically significant difference between age and gender groups.

In our study, the mean CHR value was 0.51 ± 0.06 for the whole group, 0.51 ± 0.04 in the female group, 0.52 ± 0.05 in the male group, 0.51 ± 0.05 in the age group of 18-30 years, 0.52 ± 0.04 in the age group of 31-50 years and 0.52 ± 0.05 in the age group of above 51 years. The rCHR value was 1.49 ± 0.1 for the total group, 1.5 ± 0.11 in the female group, 1.49 ± 0.1 in the male group, 1.48 ± 0.11 in the age group of 18-30 years, 1.5 ± 0.1 in the age group of 31-50 years and 1.5 ± 0.1 in the age group of above 51 years. No statistically significant difference was found between age and gender groups for both the values.

LUR; It is determined by proportioning LL and LUL values and is used to assess ulnar translation of the wrist, which develops after wrist ligament injuries and rheumatoid arthritis [29]. Schuind et al. [8] reported 32.3 ± 11.8% in males, 32.9 ± 10.3% in females, 32 ± 9.8% in the 25-40 age group, and 33.2 ± 12.1% in the 40-60 age group in their database study published in 1992. Wu et al. [29] reported mean LUR values of 35 ± 8% in males and 34 ± 9% in females for measurements performed on 176 male and 123 female radiographs. Thienpont et al. also reported 40.55 ± 10.2% in the SLD group and 39.33 ± 9.3% in the healthy group for the measurements they performed on the SLD group and healthy wrists. In addition, when they performed measurements between the Kienbock group and the healthy group, values of 33.65 ± 10.5% in the Kienbock group and 39.32 ± 9.3% in the healthy group were reported. No statistically significant difference was found in these values between the patient and control groups in either study [6, 7].

In our study, the mean LUR was 0.38 ± 0.1 for the whole group, 0.36 ± 0.1 for the female group, 0.4 ± 0.08 for the male group, 0.4 ± 0.09 for the age group 18-30 years, 0.37 ± 0.09 for the age group 31-50 years and 0.37 ± 0.1 for the group above 51 years. Statistical analysis revealed a significant difference between the age and gender groups.

SLD has been associated with SLA and scapholunate ligament injuries and related pathologies such as carpal collapse and DISI [15]. Although measurements greater than 5 mm are considered pathological, the 1991 article by Cautilli et al. [30] examined radiographs of 100 asymptomatic individuals. Mean values of 3.7 ± 0.6 mm were obtained, with females having 3.6 ± 0.5 mm and males having 4 ± 0.5 mm.

In the 2012 article by Picha et al. [15], radiographs of subjects with and without pain in the wrist were compared. It was measured that an SL interval of more than 5 mm was present in 52% of subjects who were also asymptomatic. Katayama et al. [10] data published in 2015 from 134 healthy subjects reported mean values of 1.24 ± 0.15 mm in men and 1.2 ± 0.17 mm in women.

In our study, the mean SLD was 1.97 ± 0.99mm, 1.82 ± 0.51mm in the female group and 2.12 ± 0.52mm in the male group. The mean value of SLD was 1.9 ± 0.52mm in the age group of 18-30 years, 1.98 ± 0.55mm in the age group of 31-50 years, and 1.87 ± 0.51mm in the age group of above 51 years. Although there was a statistically significant difference in the score between the gender groups, no significant difference was found between the age groups.

Clinical examination and investigations such as MRI, CT, arthrography, lateral views in direct radiography, or PA radiographs in the clenched fist position are usually used to assess the stability of the distal radioulnar joint [21].

Iida et al. [16] Measured the distances of the distal radioulnar joint from the injured side and contralateral wrist, standard PA graphy and PA graphy in clenched fist position of 30 subjects with distal radioulnar joint injuries. The average distance of 1.0 ± 0.5 mm (0-2.1) in the intact wrist on standard radiographs and 1.4 ± 1.0 mm (0-2.7) was measured on the injured side, and there was no statistically significant difference between these values. With the wrists in the clenched fist position, an average distance of 3.0 ± 1.5 mm (0.4-6.5) was measured on the healthy side, while a distance of 3.6 ± 2.1 mm (0.6-10) was measured on the injured side, and this difference was found to be statistically significant.

The distance of the distal radioulnar joint on the PA radiograph was measured to be 1.5 ± 0.5 mm in males, 1.2 ± 0.21 mm in females, 1.65 ± 0.5 mm in individuals aged 20-40 years, and 1.35 ± 0.5 mm in individuals aged 40-60 years in Mohammad's measurements [9]. The study conducted by Katayama et al. [10], was reported to be 1.19 ± 0.17 mm in males and 1.13 ± 0.09 mm in females. While no statistically significant difference was found in both studies comparing genders, a significant decrease in the distal radioulnar joint distance was observed with age [9, 10].

In our study, the distance of the distal radioulnar joint (RUD) was measured on PA radiographs taken in the open position, and it was found that the mean value was 1.69 ± 0.54 mm. It was 1.62 ± 0.54 mm in the female group, 1.81 ± 0.53 mm in the male group, 1.93 ± 0.54 mm in the age group of 18-30 years, 1.67 ± 0.53 mm in the age group of 31-50 years, and 1.47 ± 0.46 mm in the group of above 51years. The values we

measured produced a statistically significant difference between the age and gender groups.

Limitations

The number of individuals in the group we measured can be considered large compared to similar studies, but it is still insufficient to reflect all community data. Our study group is not homogeneous enough in terms of age and gender distribution. Also, it is an advantage that we use data from two hospitals addressing two different populations and the use of two different X-ray machines for imaging, and the fact that different technicians performed the X-rays. Because the study was retrospective, most of the patients who were x-rayed were people with hand and wrist conditions who are treated in clinics for certain reasons. Still, it is not very easy to get an x-ray of the wrist for completely healthy subjects, considering the potential risks of radiation. No positioning device was used before the X-ray limited the study. Two authors made all measurements electronically using the PACS system twice, and interobserver and intraobserver reliability was checked. Although interobserver reliability was determined to be perfect for many parameters, a human factor in the measurements introduces a margin of error in obtaining these data. With new developments in software, making such measurements using artificial intelligence will reduce the margin of error and provide an important resource and time-saving in such measurements.

Conclusion

Measurement parameters in radiographs of the wrist have been associated with prediction, diagnosis, and treatment decisions of many pathologies affecting the wrist and the assessment of treatment outcome. Database studies have been performed in many populations reporting that measurements of these parameters differ between different populations. In addition, variability has been found between gender and age groups for some parameters.

To the best of our knowledge, this is the first study in the Turkish population that can be considered a database considering the measurement parameters in normal wrist radiographs with age and gender characteristics.

In our study, we have given the normal roentgenographic measurement parameters that can be used as a reference for the Turkish population and the relationships and variability according to age and sex between the bones of the Turkish population that serve as a reference point. These parameters can be helpful in our population in clinical research and the diagnosis and treatment of wrist pathologies such as osteonecrosis, instabilities, osteoarthritis, and distal radius fractures. Also, these parameters can be helpful in the design and development of implants for the treatment of wrist pathologies.

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Diagnostic performance of breast imaging with ultrasonography, magnetic resonance and mammography in the assessment of residual tumor after neoadjuvant chemotherapy in breast cancer patients

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Ethics Committee Approval
Approval for this study was granted from Gaziosmanpasa Training and Research Hospital Ethics Committee for Clinical Studies in July 2020 (reg:215)
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
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Abstract

Background/Aim: Following the administration of neoadjuvant chemotherapy (NAC), a complete pathological response (pCR) is seen at rates of up to 50-70% in breast cancer patients, especially in triple-negative (TNBC) and HER-2 enriched subgroups and related to increased pCR rates, studies to predict the pathological response with preoperative evaluation are ongoing. The aim of this study was to investigate the correlation of preoperative imaging in breast cancer patients receiving NAC with the pathological response.

Methods: The study, organized as a retrospective cohort study, included 129 breast patients who underwent surgery after NAC between April 2014 and February 2020. The demographic data of the patients, the clinical and radiological findings before and after NAC, operation findings, and the histopathological evaluation results were collected retrospectively from the patient files. The radiological images of the patients were examined by separating into groups of patients with ultrasonography (US), magnetic resonance imaging (MRI), US+MRI, and mammography (MG)+US. The NAC response on preoperative breast US and MG was evaluated according to the RECIST-1.1 system, and the NAC response on MRI with the Goorts et al grading system. In the histopathological examination of operation material, the Miller Payne grading system for breast tissue was used in the determination of NAC response.

Results: The mean age of the patients in the study was 49.17 (11.00) years. The vast majority of the patients (87.6%) were diagnosed with invasive ductal cancer, with 27.13% in luminal A, 35.65% in luminal B, 31.0% in HER-2 enriched, and 6.2% in TNBC subgroups. A statistically significant correlation was determined between the pathological response and the US+MRI, MRI, and US+MG groups, with agreement at a moderate level (Kappa: 0.653, $P<0.001$; Kappa: 0.443, $P<0.001$; Kappa: 0.481, $P=0.005$, respectively). Within all the groups, the group with the highest sensitivity and accuracy were seen to be the patients evaluated with US+MRI (66.67%, 90.91%, respectively).

Conclusion: The results of this study demonstrated that there is a correlation between the pathological response and US+MRI, MRI, and US+MG evaluation after NAC. The US+MRI group was found to have the highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. When possible, the use of these two imaging methods together in the preoperative evaluation of patients is a successful method in the prediction of pathological response.

Keywords: Breast cancer, Neoadjuvant chemotherapy, Complete pathological response, Complete radiologic response

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Introduction

Neoadjuvant chemotherapy (NAC) in locally advanced-stage breast cancer enable initially inoperable patients to become suitable for surgery by shrinking the tumor and increasing the applicability of breast-sparing surgery. By starting treatment with NAC, depending on the molecular subtype in early-stage tumors, the chemosensitivity of the tumor and the in vivo response can be evaluated. In studies comparing NAC with adjuvant chemotherapy, no difference has been determined regarding mean survival and disease-free survival. However, the prognosis is better in patients with a complete pathological response after NAC [1, 2].

Although the NAC response varies according to molecular subtype, the response is better in human epidermal growth factor receptor-2 (Her-2) enriched and triple-negative breast cancer (TNBC) subgroups, which constitute 20-25% of all breast cancers [3-5]. However, progression in the tumor during NAC or non-response may be seen. Early identification of these patients can help reorganize chemotherapy, reduce complications associated with treatment, and admit for early surgical treatment. The most preferred imaging methods are breast ultrasound (US), mammography (MG) and magnetic resonance imaging (MRI). The size of the tumor, distance to the skin, nipple, and pectoral muscle, border characteristics, additional focus, and continuing microcalcifications are of guidance to the surgeon for the operating technique to be selected. In the evaluation of breast masses, sensitivity in the determination of malignant lesions has been reported to be 75.0%-93.9% for the US, 56.2%-77.3% for MG, and 81%-89% for MRI [6-8].

Just as preoperative evaluation of the tumor after NAC helps the surgeon to select the operating technique, it can also save time in patients showing progression. In addition to shrinking the size, the tumor response is evaluated radiologically from the presence of fibrosis or necrosis, but differentiation of necrosis and fibrous hyperplasia from residual cancer cannot be made well with traditional US [9].

In evaluations made with MRI after NAC, the residual tumor is determined in the evaluation of operation material in 30%-50% of patients showing complete radiological response (rCR), and complete pathological response (pCR) is seen in 20% of patients with residual clinical disease [10, 11].

Therefore, the histopathological evaluation of operation material continues to be the gold standard in evaluating pathological response.

This study aimed to evaluate to what extent the NAC response can be predicted with preoperative imaging in patients applied with NAC after a breast cancer diagnosis in our hospital and investigate which tumor characteristics were more determinative of the prediction.

Materials and methods

Data collection

In this retrospective cohort study, ethics committee approval, (approval number: 215 and date: 30/12/2020), was obtained from the Gaziosmanpasa Training and Research Hospital Ethics Committee, to which our hospital is affiliated. Patient informed consent was not required due to the retrospective use of anonymous administrative data. All the female patients who underwent surgery after NAC because of breast cancer in our hospital between April 2014 and February 2020 were included in the study. After excluding patients determined with distant metastasis before treatment (n:3), patients who did not complete chemotherapy (n:2), and patients who refused surgical treatment after chemotherapy, the study was completed with 129 patients. The medical records were reviewed retrospectively regarding age, physical examination findings, medical history, drugs used in NAC, the breast US, MG, and MRI findings before and after NAC, and the tru-cut biopsy and pathology results.

Histopathological assessment

The pathological examination of the tru-cut biopsy and operation material was evaluated regarding histopathological diagnosis, histological-nuclear grade, Ki-67 level, hormone receptor, and Her-2 neu status. The Bloom-Richardson grading system was used in histological grading [12].

In the hormone receptor evaluation, a nuclear reaction >1% for estrogen receptor (ER) and progesterone receptor (PR) was accepted as positive. In the Her-2 evaluation, score 0 (<10% incomplete reaction) and score 1 (<10% incomplete reaction) were accepted as unfavorable, and score 3 (>10% strong reaction) was accepted as positive. Materials with a score of 2 (>10% moderately severe reaction ≤ 10% strong reaction) were re-evaluated with fluorescent in situ hybridization (FISH) analysis.

Clinicopathological definitions of breast cancer subtypes were made as follows [13].

Luminal A like: ER-positive, PR positive (>20%), Ki-67 low, Her-2 negative

Luminal B like: ER-positive, PR low (<20%), or ER-positive, Her-2 neu positive, any PR. Ki-67 value or low PR may be used to distinguish between Luminal A like, and Luminal B like.

Her-2 enriched (non-luminal): ER and PR negative, Her-2 neu positive

TNBC: ER, PR and Her-2 neu negative

US technique and image interpretation

The two experienced radiologists (NU and YK) conducted the US examinations using Toshiba Aplio 500 software version 6.0 (Toshiba Corporation, Tokyo, Japan) ultrasound scanner with a 5–14 MHz linear-array transducer.

MG technique and image interpretation

Mammographic images from two planes (mediolateral oblique and craniocaudal) were obtained using a digital mammography unit (Giotto Image MC, IMS, Italy). The images were evaluated according to the ACR 2013 lexicon, and the final BIRADS assessment category was determined.

MRI technique and image interpretation

MR imaging studies were performed using a 1.5 Tesla unit (GE Signa HDx, GE Medical Systems, USA) using 8-channel phased-array breast surface coil. All MR images were reviewed by two radiologists with 10 years of experience in interpreting breast MR imaging (NU and YK), on a PACS imaging workstation (Infinitt PACS; Infinitt Healthcare, Seoul, Korea).

Chemoradiotherapy and surgery

All the patients included in the study were applied with anthracycline-based therapy with 4AC+T (doxorubicin plus cyclophosphamide followed by paclitaxel) as the NAC regimen. In addition, Transtuzumab was added to the treatment of patients in the Her-2-positive group. Surgical treatment was applied as breast-conserving surgery, subcutaneous mastectomy, or mastectomy. Sentinel lymph node biopsy was performed with excision of at least three lymph nodes in patients with clinically negative axilla, and axillary lymph node dissection was performed in patients with sentinel lymph node biopsy positivity and those with N2-3 before NAC.

Assessing the chemotherapy response according to the radiographic results

The lesions were evaluated radiologically twice, at the time of diagnosis and after NAC with US, MRI, and MG. The Response Evolution Criteria in Solid Tumors (RECIST1.1) criteria were used to measure the NAC response of lesions on US and MG. The largest single diameter, or in multifocal, multicentric lesions, the total of the long axes of all the target lesions were used in the measurements [14].

According to these criteria, radiological determination has been defined as follows;

Complete response (rCR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in short axis to <10 mm.

Partial response (rPR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Progressive Disease (rPD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on the study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).

Stable disease (rSD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest total diameters in the examination [15].

The response to NAC on MRI was evaluated according to the Goorts et al. Classification;

Type 0: complete radiologic response (rCR);

Type 1: concentric shrinkage > 3 mm without surrounding lesions;

Type 2: crumbling: shrinkage with residual multinodular lesions;

Type 3 diffuse contrast enhancement in whole quadrants;

Type 4: stable disease (rSD), i.e. no response, shrinkage <3 mm or increase <3 mm

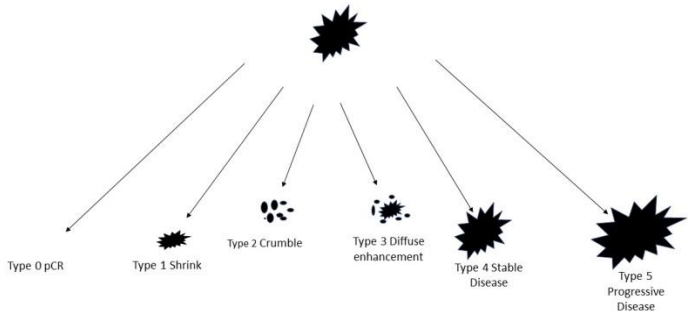
Type 5: progressive disease (rPD), i.e. increase in tumor size >3 mm or new lesions.

Types 1, 2, and 3 on MRI were accepted as a partial radiological response (rPR), and Types 4 and 5 as radiological no response (rNR) [16, 17]. The responses on MRI after NAC in breast cancer are shown in Figure 1.

Assessing the chemotherapy response according to the histopathological evaluation

The NAC response in breast tissue was evaluated using the Miller Payne grading system [18]. According to this pathological system, evaluation has been defined as following: Grade 1, no reduction in overall cellularity (pathological no response, pNR); Grade 2, a minor loss of tumor cells (up to 30% loss); Grade 3, an estimated reduction between 30% and 90% in tumor cells; Grade 4, marked the disappearance of tumor cells (more than 90% loss); and Grade 5 is defined as no identifiable malignant cells, although ductal carcinoma in situ may be present (complete pathological response, pCR). The statistical evaluations made comparisons of Miller Payne Grade 5 pCR, Grades 2, 3, 4 (partial pathological response -pPR) and Grade 1 (pathological no response -pNR).

Figure 1: MRI-based response patterns of breast carcinomas [17]. (Permission to present this figure is granted by Copyright Clearance Center)



Statistical analysis

Data obtained in the study were analyzed statistically using IBM SPSS Statistics 21.0 and medCalc version 20.015 software. In the comparison of continuous variables between groups, One-Way ANOVA was used. The Chi-square test was applied to categorical variables. In the evaluation of the agreement between pathological response and radiological response, Kappa coefficients were calculated. A value of $P<0.05$ was accepted as statistically significant. According to the pathological response status, the predictive values of radiological response were evaluated with diagnostic tests (sensitivity, specificity, positive predicted value, negative predicted value, accuracy). The terminology was defined as follows:

Sensitivity = True positive/(True positive + False negative)
Specificity = True negative/(True negative + False positive)
PPV = True positive/(False positive + True positive)
NPV = True negative/(False negative + True negative)
Accuracy = True positive + True negative/Total number of cases [19].

Results

Patients' demographics

The evaluation was made of 129 female patients who underwent surgery following NAC because of breast cancer. The mean age of the patients was 49.17 (11.00) years.

The mean tumor size was 35.09 (17.93) mm before treatment and 15.92 (19.22) mm after treatment (Tumor diameter was measured by US in the US and US+MG groups, while the measurement was made with MRI in the MR and MRI+US groups). The mean time from the last chemotherapy session to surgery was 22.41 (14.67) days. The diagnosis was of invasive ductal cancer in 112 (87.6%) patients, invasive lobular cancer in 13 (10.07%), and other tumor types in 3 (2.33%) (1 medullar, two metaplastic). The subgroups were determined as 35 (27.13%) luminal A, 46 (35.56%) luminal B, 40 (31.0%) Her-2 enriched, and 8 (6.2%) TBNC. Pre and post-treatment radiological evaluation was made with US in 42 patients, US+MRI in 22, MRI in 46, and US+MG in 19. The clinicopathological data of the patients are shown in Table 1.

Table 1: Clinicopathologic data of the patients in four groups

Characteristic	US(n:42) Mean(SD)		MRI(n:46) mean(SD)		US+MRI(n:22) mean(SD)		US+MG(n:19) mean(SD)		Total(n:129) mean(SD)		*P*-value[1]
Age (year)	50.49(11.43)		47.72(11.24)		48.41(9.67)		50.74(11.21)		49.17(11.00)		0.602
Before treatment tumor size (mm)	34.68(17.2)		34.11(18.42)		41.32(19.84)		31.33(16.11)		35.09(17.93)		0.364
Post-surgery tumor size (mm)	16.52(18.62)		15.77(20.24)		17.59(21.84)		12.83(15.52)		15.92(19.22)		0.882
Last imaging-operation period (day)	22.15(14.65)		22.9(15.78)		20.55(12.95)		23.79(14.76)		22.41(14.67)		0.910
Last imaging-chemotherapy period (day)	30(10.97)		29.83(9.6)		28.81(8.65)		32.4(13.37)		30.11(10.43)		0.806
	n	%	n	%	n	%	n	%	n	%	P-value[2]
Pathology											
Invasive ductal cancer	37	88.09	40	86.96	17	77.27	19	100.0	113	87.6	0.556
Invasive lobular cancer	4	9.53	5	10.87	4	18.18	0	0.0	13	10.07	
Other tumor types	1	2.28	1	2.17	1	4.45	0	0.0	3	2.33	
Tumor subtype											
Luminal A	12	28.57	14	30.43	6	27.27	3	15.78	35	27.13	0.984
Luminal B	16	38.09	15	32.6	7	31.81	8	42.1	46	35.65	
Her-2 enriched	12	28.57	14	30.43	7	31.81	7	36.84	40	31.0	
TNBC	2	4.76	3	6.52	2	9.09	1	5.26	8	6.2	
ER											
Present	5	11.9	6	13.04	3	13.63	5	26.31	19	14.72	0.489
Absent	37	88.1	40	89.96	19	86.37	14	73.69	110	85.28	
PR											
Present	9	21.42	11	23.91	5	22.72	8	42.1	33	25.58	0.352
Absent	33	78.58	35	76.09	17	77.28	11	57.9	96	74.42	
Her-2											
Present	27	64.28	30	65.21	13	59.1	12	63.16	82	63.56	0.968
Absent	15	35.72	16	34.79	9	40.9	7	36.84	47	36.44	
Grade											
1	0	0.0	1	2.17	0	0.0	0	0.0	1	0.78	0.513
2	29	69.06	23	50.0	14	63.63	10	52.63	76	58.91	
3	13	30.94	22	47.83	8	36.37	9	47.37	52	40.31	
Miller Payne											
1 (pNR)	3	7.14	4	8.69	1	4.54	2	10.52	10	7.75	0.943
2 (pPR)	7	16.66	4	8.69	3	13.63	4	21.05	18	13.95	
3 (pPR)	15	35.71	17	37.0	9	40.9	3	15.78	44	34.1	
4 (pPR)	6	14.28	6	13.0	3	13.63	3	15.78	18	13.95	
5 (pCR)*	11	26.19	15	32.6	6	27.27	7	36.84	39	30.23	

[1]: One-Way ANOVA, [2]: Chi-Square test, US: ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography TNBC: Triple negative breast cancer, ER: Estrogen receptor, PR: Progesterone receptor, Her-2: Human epidermal growth factor receptor-2, pCR: Complete pathological response, pPR: Pathological partial response, pNR: Pathological no response

Table 2: The correlations between radiological imaging methods and pathological response

Radiological response category	Pathological response category						Total		*P*-value
	pCR		pPR		pNR				
	n	%	n	%	n	%	n	%	
US									
rCR	4	36.36	3	10.71	0	0	7	16.66	Kappa=0.141
rPR	7	63.63	22	78.57	3	100	32	76.19	*P*=0.246
rNR (rSD)	0	0	3	10.71	0	0	3	7.14	pX^2=0.2
Total	11	100	28	100	3	100	42	100	
US+MRI									
rCR	4	66.66	0	0	0	0	4	18.18	Kappa=0.653
rPR	2	33.33	15	100	1	100	18	81.82	*P*<0.001
Total	6	100	15	100	1	100	22	100	pX^2=*0.001*
MRI									
rCR	8	53.33	1	3.7	0	0	9	19.56	Kappa=0.443
rPR	6	40	24	88.88	3	75	33	71.73	*P*<0.001 pX^2=0.019
Concentric shrinkage	5	33.33	16	59.33	3	75	24	52.17	
Crumbling	1	6.67	7	25.87	0	0	8	17.36	
Diffuse enhancement	0	0	1	3.68	0	0	1	2.2	
rNR	1	6.66	2	7.4	1	25	4	8.69	
rSD	0	0	1	3.7	0	0	1	2.17	
rPD	1	6.66	1	3.7	1	25	3	6.52	
Total	15	100	27	100	4	100	46	100	
US+MG									
rCR	4	57.14	0	0	0	0	4	21.05	Kappa=0.481
rPR	3	42.86	10	100	2	100	15	78.95	*P*=0.005
Total	7	100	10	100	2	100	19	100	pX^2=*0.013*

US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography, pCR: Complete pathological response, pPR: Pathological partial response, pNR: Pathological no response, rCR: Radiological complete response, rPR Radiological partial response, rNR: Radiological no response, rSD: Radiological stable disease rPD: Radiological progressive disease

Table 3: The sensitivity, specificity, PPV, NPV and accuracy of imaging modalities according to pathological response

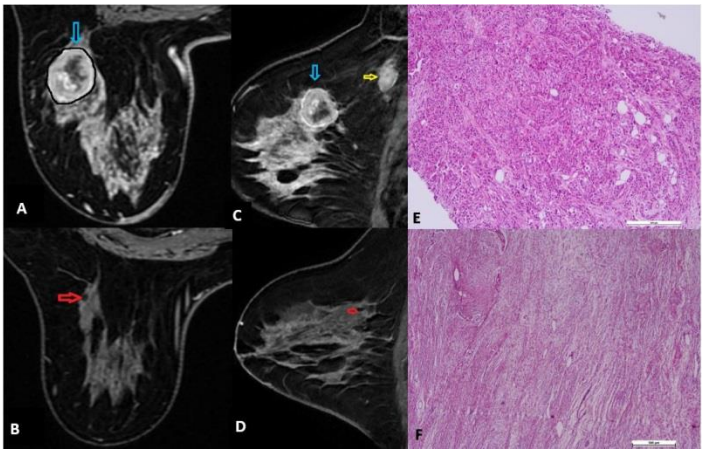
Radiological Response	Complete Pathological Response				
Radiological Complete Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	36.36 (10.93-69.21)	90.32(74.25-97.96)	57.14(26.08-83.44)	80(71.61-86.39)	76.19(60.55-87.95)
MRI	53.33(26.59-78.73)	96.77(83.30-99.92)	88.89(52.35-98.31)	81.08(71.31-88.08)	82.61(68.58-92.18)
US+MRI	66.67(22.28-95.67)	100(79.41-100)	100	88.89(72.07-96.13)	90.91(70.84-98.89)
US+MG	57.17(18.41-90.10)	100(73.54-100)	100	80(62.97-90.39)	84.21(60.42-96.62)
	Pathological Partial Response				
Radiological Partial Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	78.57(59.05-91.70)	28.57(8.39-58.10)	68.75(59.98-76.35)	40(18.30-66.49)	61.91(45.64-76.43)
MRI	88.89(70.84-97.65)	52.63(22.86-75.55)	72.73(61.97-81.36)	76.92(51.37-91.32)	73.91(58.87-85.73)
US+MRI	100(78.20-100)	57.14(18.41-90.10)	83.33(68.01-92.16)	100	86.36(65.09-97.09)
US+MG	100(69.15-100)	44.44(13.70-78.80)	66.67(52.72-78.20)	100	73.68(48.80-90.85)
	Pathological No Response				
Radiological No Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	0(0-70.76)	92.31(79.13-98.39)	0	92.31(91.64-92.93)	85.71(71.46-94.57)
MRI	25(0.63-80.59)	92.86(80.52-98.50)	25(4.25-71.48)	92.86(88.01-95.84)	86.96(73.74-95.06)
US+MRI	0(0-97.5)	100(83.89-100)	-	95.46(95.46-95.46)	95.46(77.16-99.89)
US+MG	0(0-84.19)	100(80.49-100)	-	89.47(89.47-89.47)	89.47(66.86-98.70)

US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography, PPV: Positive predictive value, NPV: Negative predictive value

Evaluation of radiological and pathological response

Of the 24 patients with complete radiological response, pCR was seen in 20, and pPR in 4. In the evaluation made with US, rCR was determined in 7 (16.66%) patients, rPR in 32 (76.19%), and the disease had remained stable in 3 (7.14%). In the evaluation made with US+MRI, rCR was determined in 4 (18.18%) patients and rPR in 18 (81.82%). A 51-year-old woman with HER2-positive cancer who demonstrated pathological and radiological complete response shown in Figure 2. In the evaluation of 46 patients with MRI only, rCR was observed in 9 (19.56%), rPR in 33 (71.73%) (24 concentric shrinkage, eight crumbling, 1 diffuse enhancement), and rNR in 4 (8.69%). Of the 19 patients evaluated with MG+US, rCR was determined in 4 (21.05%) and rPR in 15 (78.95%).

Figure 2: 51-year-old woman with HER2-positive cancer who demonstrated pathological and radiological complete response. A-C) On axial and sagittal contrast MRI images show a malignant mass in the left breast before chemotherapy (blue arrow). There is lymphadenopathy in the left axilla (yellow arrow), B-D) No contrast enhancement is observed in the mass after chemotherapy. Axillary lymphadenopathy has regressed. The clip is viewed in post-chemotherapy images (red arrow), E) Before chemotherapy nuclear grade III invasive ductal carcinoma in tru-cut biopsy (H+E stain, x4), F) After chemotherapy pathological complete response in mastectomy (H+E stain, x10)



A statistically significant correlation was determined between the pathological response and US+MRI, MRI, and US+MG evaluations, with agreement at a moderate level (Kappa: 0.653, $P<0.001$; Kappa: 0.443, $P<0.001$; Kappa: 0.481, $P=0.005$, respectively). No significant relationship was seen between US alone and the pathological response ($P=0.246$). Of the patients determined with rCR on US, the residual tumor was present in 42.85% in the examination of operation material. This rate was 12.5% with MRI, and pCR was present in all the patients with rCR in the MRI+US evaluation. In contrast to these findings, the rate of pCR seen in the patients not showing complete response radiologically (rPR and rNR) was 20% with US, 18.91% with MRI, and 11.11% with US+MRI.

There was no statistically significant relationship between tumor subtypes and the radiology-pathology relationship in any group ($P>0.05$). The correlations between the radiological imaging methods and the pathological response are shown in Table 2.

When the imaging methods' sensitivity, specificity, PPV, NPV, and accuracy rates were examined in respect of pCR prediction, the highest sensitivity (66.67%) was determined with US+MRI. The specificity and PPV were found to be 100% for both US+MRI and US+MG. The US+MRI group had NPV of 88.89% and the highest accuracy rate of 90.91%. For pPR, US+MRI and US+MG had 100% sensitivity and NPV, and the highest specificity value of 57.14% was in the US+MRI group. The PPV in the US+MRI group was 83.33% and accuracy was determined to be 86.36%. The findings are shown in Table 3.

Discussion

Since the 1970s, NAC has been an inseparable part of breast cancer treatment, and the treatment of approximately 18% of patients diagnosed with breast cancer starts with NAC [20, 21].

This treatment provides shrinkage in tumor size, regression in axillary nodal disease, and increases the applicability of breast-conserving surgery, which can be evaluated as the efficacy of chemotherapy eradicating potential micrometastatic disease and rendering previously inoperable patients suitable for surgery. In addition, the development of pCR has a positive effect on prognosis. Therefore, histopathological grading systems are the gold standard in the evaluation of response following NAC [22, 23].

In this study, evaluation of chemotherapy response before surgery was applied with breast US, MRI, and/or MG during and after NAC in patients planned to undergo surgery, and the predictive values of these methods were investigated.

In a study by Kenue et al. [24], the predictive value of US and MG for pCR were investigated in patients receiving NAC for breast cancer, and it was concluded that US could more accurately predict residual tumor size following NAC. The sensitivity, specificity, and PPV were found to be 45.8%, 93.8%, and 68.8%, respectively for US, and 54.2%, 86.3%, and 54.2% for MG. There was reported to be no statistically significant difference between the two methods. In the same study, the two methods combined were found to have a sensitivity of 45.8% and specificity of 93.8%.

In a study by Peitinger et al. [25], the use of US and MG together was found to increase accuracy. In predicting pCR with the combined use of the two methods, sensitivity was reported to be 78.6%, specificity 92.5%, and accuracy 88.9%.

Another study evaluated the response to treatment after NAC with US, MG, and tomosynthesis, and reported that the diagnostic power in predicting pCR after NAC was similar between the three imaging modalities [26].

In the current study, the prediction of pCR with US and US+MG after NAC, sensitivity was found to be 36.36% and 57.17%, respectively, specificity 90.32% and 100%, PPV 57.14% and 100%, NPV 80% and 80%, and accuracy 76.19% and 84.21%. Mammography alone was not used in any patient of this study, and the evaluation was made together with US. Of the patients thought to have rCR with US evaluation, the residual tumor was determined in 42.85% on examination of the operation material.

Zhang et al. [27], evaluated US, MG, and MRI in respect of the prediction of pCR after NAC and reported sensitivity, specificity, accuracy, PPV, and NPV to be 36.2%, 90.2%, 71.0%, 67.3%, and 71.9% respectively for US, and 44.4%, 92.9%, 75.6%, 77.7%, and 75.0% for MRI. It was also seen that the accuracy of US was lower for IDC than for other types, and the sensitivity was higher. When the molecular subtypes were examined, sensitivity was highest in the hormone receptor positive and Her-2 positive groups and accuracy was higher in those with hormone receptor positivity. Sensitivity and

PPV were found to be higher in small tumors. When MRI and US were used together, the prediction of pCR was not affected by tumor size, subtype, or histological type.

A study evaluated the MRI prediction of pCR, and reported sensitivity of 97.2%, specificity 44.44%, and accuracy of 84.14%, with the highest sensitivity values obtained in the Her-2 enriched group [28].

In another study by Morrow et al. [29], the efficacy of MRI in the prediction of the response following NAC was examined. They found that MRI doesn't predict pCR with sufficient accuracy with 63.4%PPV and 84.1% NPV.

In a study by Hayashi et al. [30], a patient group was examined in which 26.1% developed pCR after NAC. pCR was determined in 196 of 247 patients with a complete response on MRI and in 154 of 182 patients with a complete response on MRI+US. Sensitivity, specificity, and accuracy were calculated as 84.8%, 95.1%, and 79.4%, respectively for MRI, and 66.6%, 97.3%, and 86.8% for MRI and US together.

In the current study, MRI was found to have a sensitivity of 53.33%, specificity 96.77%, PPV 88.89%, NPV 81.08%, and accuracy 82.61%. If USG added to MRI, we found sensitivity 66.67%, specificity 100%, PPV 100%, NPV 88.89%, and accuracy 90.91%. Thus, the highest accuracy was obtained when these two imaging methods were used together in the MRI+US group. In the histopathological examination of the postoperative specimen, the residual tumor was determined in 12.5% of patients thought to have a complete response on MRI. Histopathologically, the subtypes did not show any effect on sensitivity and specificity.

The limitation of this study was that it was conducted in a single-center, and thus the number of patients was limited. All imaging modalities were performed based on our hospital protocol. Therefore, the results may not be generalizable. In addition, further studies are required to produce similar results to predict the correlation between the radiological response and the pathological response, including more parameters that could affect this correlation.

Conclusions

To sum up, the studies conducted to predict the response following NAC in the preoperative period raise the question of whether a complete response can be known before surgical excision, and can the patient be followed up without surgery. As none of the imaging methods could predict pCR at 100%, the policy of wait and see without surgery does not seem to be an option under current conditions. In most studies evaluating imaging methods, MRI has been advocated as superior to US and MG. However, evaluation with US is a lower-cost and more easily accessible method with fewer contraindications. The current study results demonstrated that MRI+US was the imaging method with the highest sensitivity and accuracy in imaging after NAC. The use of these two methods together provides a better preoperative evaluation.

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Use of uterine artery Doppler velocimetry values to predict pregnancy in intrauterine insemination cycles in couples with unexplained infertility

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Ethics Committee Approval
The Local Ethic Committee of Umraniye Training and Research Hospital, Istanbul, Turkey has approved this study (Ethics Committee Approval No: B.10.1.TKH.4.34.H.GP.0.01/178).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: It is known that pregnancy success in IUI cycles performed in couples with unexplained infertility is below 20% even under the best conditions. Predicting the success in IUI cycles and directing patients to appropriate assisted reproductive treatment is essential for the time and budget. In this context, we aimed to investigate the use of uterine artery Doppler velocimetry values to predict pregnancy in intrauterine insemination (IUI) cycles in couples with unexplained infertility.

Methods: In this prospective cohort study, couples with unexplained infertility were randomly assigned to two groups: clomiphene citrate (CC) and gonadotropin. The CC group used 50-150 mg CC daily between the 5th and 9th days of the menstrual period, while the gonadotropin group used 37.5-75 IU of recFSH daily from the 3rd day of the menstrual period until the dominant follicle developed. Ovulation was triggered by recHcg when at least one dominant follicle of 17 mm or larger was detected. Intrauterine insemination was performed 36 hours after the trigger. Uterine artery flow pulsatility index (PI), resistance index (RI) and the systolic-diastolic ratio (S/D) were measured in all patients by Doppler ultrasound on the 3rd day of menstruation and trigger day. Uterine artery Doppler values of the group that achieved pregnancy and those who could not conceive were compared as the main outcome of the study.

Results: The study was designed over 143 IUI cycles, 89 cycles in the gonadotropin group and 54 cycles in the CC group. In 143 IUI cycles, 24 (16%) pregnancies were obtained, seven (12%) in the CC group and 17 (12%) in the gonadotropin group. In both CC and gonadotropin cycles, mean age, BMI, duration of infertility, hormone levels on the third day of menstruation, endometrial thickness on 3rd day of menstruation and on the trigger day, dominant follicle number and mean follicle diameter were similar in the pregnant and non-pregnant groups ($P<0.05$). There was no statistical difference in uterine artery Doppler values (RI, PI and S/D) measured neither on the 3rd day of the cycle nor on the trigger day between pregnant and non-pregnant groups in patients receiving CC or gonadotropin ($P<0.05$).

Conclusion: Considering the hormonal changes in stimulated cycles or other factors that may have an impact on endometrial blood flow and endometrial receptivity, we think that only uterine artery Doppler velocity measurement values are not effective in predicting pregnancy success in CC or gonadotropin-induced IUI cycles.

Keywords: Infertility, Uterine artery, Insemination, Pregnancy

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Introduction

Unexplained infertility, which covers 25 % of infertile couples, is a diagnosis generally used for couples in which all standard tests such as ovulation tests, hormone levels, tubal patency and semen analysis are normal [1]. Impaired endocrinological balance or reproductive physiology, immunologic and genetic disturbances are thought to be the potential causes of unexplained infertility [2]. In this context, blood flows in the uterine or spiral arteries were investigated in patients with unexplained infertility, especially in the last decade. Studies have suggested that endometrial perfusion is impaired in women with unexplained infertility, especially during the peri-implantation period [3, 4]. In the light of this information, we aimed to evaluate the effectiveness of uterine artery Doppler velocimetry values as a predictor of a successful pregnancy in intrauterine insemination cycles in couples with unexplained infertility.

Materials and methods

The study was conducted in Obstetrics and Gynecology Department of Istanbul Umraniye Training and Research Hospital between 01/06/2020 and 31/11/2021. Couples with unexplained infertility were informed about CC and gonadotropin treatments, and the choice of drug to be used by the patient was made according to the couples' own decision. Accordingly, the couples were divided into two groups as clomiphene citrate (CC) and gonadotropin. While the CC group used 50-150 mg CC (Koçak Farma İlaç ve Kimya Sanayi A.Ş.) daily between the 5th and 9th days of menstruation, the gonadotropin group used recombinant follicle stimulating hormone (rec FSH) (Gonal-f Merck İlaç Ecza ve Kimya Tic. A.Ş.) from the 3rd day of menstruation with a daily starting dose of 37.5 or 75 IU/day. The dose was increased by 37.5 IU/day in tandem with follicle development until at least one dominant follicle developed. Ovulation was triggered with 250 mcg recombinant human chorionic gonadotropin (rec hCG) (Gonal-f Merck İlaç Ecza ve Kimya Tic. A.Ş) when at least one dominant follicle of 17 mm or larger was detected, and intrauterine insemination (IUI) was performed by a soft cannula 36 hours after the trigger. The gonadotropin group was given 20 mg of oral dydrogesterone (Abbott Laboraturarları İthalat İhracat ve Ticaret Limited Şirketi) daily for post-insemination luteal support, whereas luteal support was not given to the CC group. Serum beta-hCG tests were performed 14 days after the IUI. Clinical pregnancy was then confirmed via transvaginal ultrasound scanning of intrauterine gestational sac with fetal cardiac activity. Luteal support of the patients who achieved pregnancy in the gonadotropin group was continued until the 10th gestational week.On the 3rd day of menstruation and on the trigger day, the endometrial thickness was measured by transvaginal ultrasound, and the uterine artery flow Pulsatility Index (PI), Resistance Index (RI), and the systolic-diastolic ratio (S/D) were measured by Doppler ultrasound. FSH, LH, estradiol, TSH, prolactin, and progesterone levels of the patients on the 3rd day of menstruation were analyzed with the Abbott Architect i200 SR device in accordance with the manufacturer's recommendations. Transvaginal ultrasound evaluations of the patients were performed by the same specialist and with the same ultrasound device (Hitachi Aloka Prosound F37).Patients under the age of 40, those with a BMI of 29.9 kg/m2 or less, non-smokers, least one tube shown to be open according to the results of hysterosalpingography and whose partner's spermiogram result was normospermic according to WHO 2010 criteria were included in the study. Patients with polycystic ovary syndrome, any systemic or autoimmune disease, congenital uterine anomaly, myoma causing deformation in the uterine cavity, diagnosis of endometrioma or endometriosis, or previous uterine or ovarian surgery were not included in the study.Body mass index (BMI) had been measured as; BMI (kg/m2)

The Local Ethic Committee of Umraniye Training and Research Hospital, Istanbul, Turkey has approved this study (Ethics Committee Approval No: B.10.1.TKH.4.34.H.GP.0.01/178).

Statistical analysis

Statistics were performed with the SPSS 25.0 package program. The distribution of the data was found to be normal with the Kolmogorov Smirnov test. In addition to descriptive statistical methods (mean, standard deviation, frequency, etc.), t-test and chi-square tests were also used alongside parametric data while evaluating the findings of this study. Significance has been determined at $P<0.05$ levels for all values.

Results

Between June 2020 and November 2021, 173 ovulation induction (OI) cycles, 97 with gonadotropin and 76 with CC were performed on 173 infertile couples who met the study criteria. Eight cycles were canceled in the gonadotropin group because 2 cycles of follicles did not develop, 4 cycles were from spontaneous ovulation, and 2 cycles were from hyperstimulation. In the CC group, 22 cycles were canceled because 6 cycles of follicles did not develop, 3 cycles were due to spontaneous ovulation, 6 cycles of cystic development, 1 cycle male partner could not give sperm sample on the day of IUI, and six patients did not come for follicle follow-ups. The study was designed with 89 cycles in the gonadotropin group that underwent IUI after OI and 54 cycles in the CC group. In this study, no adverse side effects or undesirable results occurred in any patient due to drugs used for OI or during blood collection for hormone tests or during transvaginal ultrasound examinations.

In this study, 24 pregnancies (16%) were obtained in 143 IUI cycles, 7 pregnancies (12%) in IUI cycles with CC and 17 (19%) in IUI cycles with gonadotropins. Those who became pregnant and those who could not conceive were compared among themselves in terms of age, BMI, duration of infertility, hormone levels on the third day of menstruation, endometrial thickness on the third day of menstruation and on the trigger day, number of dominant follicles, average follicle size, and uterine artery Doppler values on the 3rd day of menstruation and the trigger day.

In the CC-induced cycles, mean age, BMI, infertility duration, hormone levels on the third day of menstruation, endometrial thickness in the basal period and on the trigger day, dominant follicle number, and mean follicle size were similar in pregnant and the non-pregnant groups (Table 1). There was no significant difference in the mean uterine artery Doppler values

(PI, RI and S/D) measured on the 3rd day of menstruation and on the trigger day between the pregnant and the non-pregnant groups (Table 2).

Table 1: Comparison of demographic and clinical characteristics between pregnant and non-pregnant groups in CC group

	Pregnant Group n=7	Non-pregnant Group n=47	*P*-value
Age (Years)	29.29 (5.62)	29.17 (5.64)	0.960
BMI (kg/m2)	26.11 (5.64)	25.46 (4.29)	0.717
Duration of infertility (Years)	2.5 (1.3)	3 (2.3)	0.561
Basal FSH (mIU/mL)	6.80 (2.76)	7.06 (2.24)	0.783
Basal LH (mIU/ml)	4.67 (1.64)	5.75 (2.73)	0.317
Basal Estradiol (pg/ml)	40.71 (16.87)	43.66 (20.36)	0.718
Basal Progesterone (ng/mL)	0.29 (0.25)	0.21 (0.13)	0.238
Prolactin (ng/mL)	16.11 (5.87)	16.79 (6.57)	0.797
TSH (mU/mL)	1.86 (1.16)	2.20 (1.38)	0.532
Basal endometrial thickness (mm)	3.2 (1.0)	3.6 (1.0)	0.352
Trigger day endometrial thickness (mm)	7.9 (1.7)	9.2 (2.6)	0.221
Number of dominant follicles	1.2 (0.4)	1.4 (0.5)	0.492
Mean dominant follicle diameter (mm)	19.7 (1.5)	19.5 (2.0)	0.845

Independent t test

Table 2: Doppler velocimetry of uterine arteries among the pregnant and non-pregnant groups in the CC group

	Pregnant Group n=7	Non-pregnant Group n=47	*P*-value
Right uterine artery PI on the 3rd day of menstruation	1.73 (0.55)	1.83 (0.57)	0.663
Right uterine artery RI on the 3rd day of menstruation	0.76 (0.08)	0.77 (0.08)	0.879
Right uterine artery S/D on the 3rd day of menstruation	4.70 (1.88)	4.90 (1.86)	0.797
Left uterine artery PI on the 3rd day of menstruation	1.75 (0.63)	1.81 (0.62)	0.813
Left uterine artery RI on the 3rd day of menstruation	0.75 (0.11)	0.77 (0.09)	0.509
Left uterine artery S/D on the 3rd day of menstruation	4.64 (2.09)	4.89 (1.87)	0.741
Trigger day right uterine artery PI	2.06 (0.64)	2.08 (0.88)	0.970
Trigger day right uterine artery RI	0.83 (0.07)	0.81 (0.06)	0.661
Trigger day right uterine artery S/D	6.29 (1.80)	5.48 (1.82)	0.275
Trigger day left uterine artery PI	1.99 (0.78)	2.18 (0.64)	0.477
Trigger day left uterine artery RI	0.82 (0.07)	0.82 (0.07)	0.940
Trigger day left uterine artery S/D	5.96 (2.06)	5.41 (1.88)	0.475

Independent t test

In gonadotropin-induced cycles, mean age, BMI, infertility duration, hormone levels on the third day of menstruation, endometrial thickness in the basal period and on the trigger day, dominant follicle number, and mean follicle size were similar in pregnant and the non-pregnant groups (Table 3). There was no statistical difference in the mean uterine artery Doppler values (PI, RI and S/D) measured on the 3rd day of menstruation and on the trigger day between the pregnant and the non-pregnant groups (Table 4).

Table 3: Comparison of demographic and clinical characteristics between pregnant and non-pregnant groups in the gonadotropin group

	Pregnant Group n=17	Non-pregnant Group n=72	*P*-value
Age (Years)	28.9 (4.6)	29.56 (5.07)	0.649
BMI (kg/m2)	25.7 (4.0)	24.70 (4.01)	0.717
Duration of infertility (Years)	2.3 (1.0)	2.6 (1.2)	0.516
Basal FSH (mIU/mL)	6.48 (1.65)	6.99 (2.13)	0.362
Basal LH (mIU/ml)	5.89 (2.54)	6.76 (2.92)	0.261
Basal Estradiol (pg/ml)	42.53 (20.89)	39.71 (21.12)	0.621
Basal Progesterone (ng/mL)	0.19 (0.9)	0.22 (0.13)	0.388
Prolactin (ng/mL)	17.51 (5.39)	17.74 (6.12)	0.889
TSH (mU/mL)	2.09 (1.02)	1.98 (0.82)	0.652
Basal endometrial thickness (mm)	3.8 (1.3)	3.9 (1.2)	0.795
Trigger day endometrial thickness (mm)	10.1 (2.3)	10.1 (2.0)	0.965
Number of dominant follicles	1,4 (.5)	1.2 (0.4)	0.111
Mean dominant follicle diameter (mm)	18.4 (1.7)	18.4 (1.5)	0.952

Independent t test

Table 4: Doppler velocimetry of uterine arteries among the pregnant and non-pregnant groups in the gonadotropin group

	Pregnant Group n=17	Non-pregnant Group n=72	*P*-value
Right uterine artery PI on the 3rd day of menstruation	1.81 (0.62)	1.77 (0.45)	0.782
Right uterine artery RI on the 3rd day of menstruation	0.77 (0.10)	0.78 (0.07)	0.405
Right uterine artery S/D on the 3rd day of menstruation	5.08 (2.20)	4.72 (1.42)	0.405
Left uterine artery PI on the 3rd day of menstruation	1.94 (0.76)	1.85 (0.54)	0.575
Left uterine artery RI on the 3rd day of menstruation	0.77 (0.10)	0.78 (0.08)	0.782
Left uterine artery S/D on the 3rd day of menstruation	5.03 (2.01)	4.93 (1.71)	0.831
Trigger day right uterine artery PI	1.80 (0.44)	1,90 (0.50)	0.485
Trigger day right uterine artery RI	0.76 (0.07)	0.79 (0.11)	0.382
Trigger day right uterine artery S/D	4.63 (1.67)	5.33 (1.61)	0.114
Trigger day left uterine artery PI	1.85 (047)	1.88 (0.52)	0.848
Trigger day left uterine artery RI	0.77 (0.07)	0.78 (0.07)	0.598
Trigger day left uterine artery S/D	5.03 (1.47)	5.18 (1.70)	0.728

Independent t test

Discussion

In this study, we investigated the effect of uterine artery Doppler values in predicting pregnancy in patients with unexplained infertility who underwent IUI after OI. We did not find a significant difference in uterine artery Doppler values measured neither on the 3rd day of the stimulated cycle, nor on the trigger day between the pregnant and non-pregnant groups in patients receiving CC or gonadotropin.

In the literature, there are many studies investigating Doppler values of uterine, endometrial or ovarian arteries in spontaneous or stimulated menstrual cycles. In these studies, different results were reported according to the characteristics of the patients included in the study, the agents used in assisted reproductive treatments, and the different days in which Doppler values were evaluated during the cycle.

Kupesic and Kurjak [5] investigated blood flow in the uterine and spiral arteries in both spontaneous and stimulated cycles. They stated that the uterine artery blood flow pulsatility index decreased in spontaneous menstrual cycles one day before ovulation, but this change did not occur in stimulated cycles. In 2000, Hsieh et al. [6] compared the PI and RI at different sampling sites of the uterine and spiral arteries in the early and mid-menstrual phases during IUI cycles after OI. They stated that there was no significant difference in the PI and RI values of the uterine and spiral arteries at different sampling sites and phases of the stimulated cycles.

Wakeman et al. [7] evaluated uterine and ovarian blood flow during the follicular phase of the menstrual cycle, in women who could and could not conceive. They found that in the late follicular phase of natural conception cycles, there is an increased uterine artery peak systolic rate compared to non-conception cycles, which is not seen in CC-induced cycles where conception occurs. Akihito et al. [8] examined the blood flow of the endometrium in both CC-stimulated cycles and spontaneous menstrual cycles; they revealed that CC-stimulated cycles have lower endometrial perfusion in the periovulatory period than spontaneous cycles.

In a study published by Güzel et al. [9] in 2015, no significant difference was found in uterine artery or ovarian artery Doppler values between pregnant and non-pregnant

groups in CC-induced cycles. Kim et al. [10] compared uterine artery Doppler values, endometrial and subendometrial blood flow parameters in the pregnant and non-pregnant groups in CC-stimulated IUI cycles. While they found that the uterine artery Doppler values were similar in the pregnant and non-pregnant group, they found that the endometrial vascularization index (VI), flow index (FI) and vascularization flow index (VFI) scores were higher in the pregnant group. Similar to the results of the two studies above, we did not detect any difference in uterine artery Doppler values in the pregnant and non-pregnant groups in CC-stimulated IUI cycles in this study.

Ivanovski et al. [11] investigated uterine and arcuate artery Doppler values on the trigger day for predicting the success in vitro fertilization cycles. They found that the mean uterine artery PI and RI were significantly lower in the pregnant group compared to the non-pregnant group. Similarly, in a study published in 2015, the effect of uterine and arcuate artery Doppler values measured on the trigger day in predicting pregnancy in patients receiving in IVF treatment was investigated. In this study, the mean PI and RI of both uterine and arcuate arteries were found to be significantly lower in pregnant women than in non-pregnant women [12]. Apart from the IVF treatment cycles mentioned above, Yaltı et al. [13] investigated the pulsatility index of the uterine, and ovarian arteries on the trigger day in patients who conceived and did not become pregnant among patients who underwent IUI after OI with gonadotropin. In this study, which included 57 patients, right, left and mean uterine artery PI and right, left and mean ovarian stromal artery PI were found to be significantly lower in the pregnant group than in the non-pregnant group. Unlike these studies, we did not find any difference in uterine artery Doppler values in gonadotropin-induced IUI cycles in pregnant and non-pregnant women in our study.

In 2004, Ng et al. [14] compared endometrial and subendometrial blood flows in natural and stimulated cycles in the same patients undergoing IVF treatment. This study revealed that endometrial and subendometrial Doppler flow indices were significantly lower in stimulated cycles than in natural cycles and were reduced in approximately 60% of patients after ovarian stimulation. Again, the same authors evaluated uterine artery Doppler values, endometrial and subendometrial blood flows in infertile patients undergoing IVF treatment in both natural and gonadotropin-induced cycles in 2006. It has been reported that the increased serum E2 concentration in stimulated cycles, it causes vasodilation in the myometrium and a decrease in blood flow towards the endometrial and subendometrial regions. Therefore, uterine blood flow measurement may not reflect endometrial and subendometrial blood flow, especially in stimulated cycles [15].

Limitations

The limited number of participants and the lack of evaluation of endometrial and subendometrial blood flows are limiting factors for this study.

Conclusion

We could not find a significant difference in uterine artery Doppler values measured neither on the 3rd day of the menstrual cycle nor on the trigger day between pregnant and non-pregnant groups in patients receiving CC or gonadotropin. Considering the hormonal changes in stimulated cycles or other factors that may have an impact on endometrial blood flow and endometrial receptivity, we believe that only uterine artery Doppler values are not effective in predicting pregnancy success in CC or gonadotropin-induced IUI cycles.

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Endovascular treatment of nonfunctional vascular access through retrograde arterial access: A single-center experience with midterm follow-up

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Ethics Committee Approval
The study was approved by the Institutional Review Board (IRB) of Okan University Hospital (Number: 56665618-204.01.07).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Nonfunctional vascular access is treated through venous or brachial artery access traditionally. However, each route has its drawbacks. This study aimed to evaluate the feasibility, safety, and effectiveness of retrograde arterial access (RAA) in the treatment of nonfunctional vascular access with mid-term results.

Methods: Patients with nonfunctional vascular access who were treated through RAA between January 2019 and December 2020 were included in this cohort study. Patient demographics, lesion characteristics, procedural details, technical and clinical outcomes were noted.

Results: Thirty-six interventions were performed on 30 patients. Twenty-nine occlusions and seven long segment stenoses were treated. The radial artery was accessed in 34 cases, the interosseous and ulnar arteries were accessed in one case each. The technical and clinical success rates were 100% and 97.2%, respectively (35/36). Venous rupture was encountered in three patients. No puncture-site complication was observed. The mean follow-up time was 14.3 (range: 6-24) months. None of the patients showed signs of hand ischemia and the accessed arteries were patent at Color Doppler Ultrasound examinations. Post-intervention primary patency rates were 100%, 73.3%, 47.5% at 1, 6 and 12 months, respectively. Post-intervention secondary patency rates were 100%, 93.3%, 84.8% at 1, 6 and 12 months, respectively.

Conclusion: RAA is effective and safe in the treatment of nonfunctional vascular access with comparable outcomes to traditional routes. The low access-site complication rates make this access site an attractive salvage route when traditional approaches are not feasible.

Keywords: Retrograde arterial access, Vascular access, Transradial access, Interventional radiology, Arteriovenous fistula

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Introduction

Permanent vascular access is needed to maintain adequate hemodialysis for patients with end-stage kidney disease (ESKD). National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-KDOQI) 2019 guidelines suggest an autogenous arteriovenous fistula (AVF) placement as the first-line option of vascular access, followed by prosthetic arteriovenous grafts (AVG) in preference to central venous catheters due to lower infection rates, if it is consistent with the patient's ESKD Life Plan [1, 2].

Percutaneous transluminal angioplasty was widely used as the first-line treatment of nonfunctional hemodialysis access [1, 3]. The traditionally used technique is percutaneous direct antegrade/retrograde venous access [4]. Brachial artery access was proposed for when the venous route is not feasible [3]. However, each route has its advantages and drawbacks [5]. Retrograde arterial access (RAA) through the radial artery is widely accepted as the primary access for coronary interventions due to its minimally invasive nature, and low access site complication rates [6, 7]. Also, transulnar access (TUA) was found to be safe when transradial access (TRA) cannot be used [8]. Experience in the non-coronary intervention era is still growing [9-11]. However, there is still limited data on the use of RAA in vascular access interventions.

The objective of this study was to report the feasibility, safety, effectiveness, and mid-term follow-up results of the endovascular treatment of nonfunctional vascular access through RAA.

Materials and methods

Study design and patient population

This cohort study was designed as a retrospective file review and the protocol was approved by the institutional ethics committee of Okan University Hospital (No:56665618-204.01.07). The medical records of 212 patients with ESKD who underwent endovascular treatment of nonfunctional AVG and AVF between January 2019-December 2020 were reviewed. Patients fulfilling the following criteria who were treated with retrograde arterial access were included: (1) Long segment stenotic/occluded downstream vein of AVF/AVG that precluded venous access (2) Multi-level lesions (3) A negative Allen's test. The exclusion criteria were as follows: (1) Severely calcified arteries (2) Infected AVFs/AVGs (3) End-to-end radial-cephalic anastomosis (4) History of severe contrast media allergy. All patients gave written consent before the initial treatment; however, informed consent was waived.

The radial artery was preferred when (1) the radial-cephalic fistula anastomosis was located >2 cm proximal to the styloid process, (2) the radial artery diameter was >2 mm, (3) the Allen test was negative. TRA was contraindicated when (1) the radial artery had a high origin that is proximal to the brachial-cephalic/basilic fistula location, (2) a severe, circumferential calcification, (3) occluded radial artery. When TRA was not technically feasible, the interosseous artery or the ulnar artery was used as an alternative access site per the operators' discretion.

Endovascular treatment

Vascular access was obtained with a micropuncture set (Mini Access Kits, Merit MAK™, Merit Medical South Jordan, Utah, USA). The artery was punctured under sonographic guidance with a 21G needle. 0.018" guidewire was inserted and a 4F introducer sheath was advanced. The system was upsized to a 6F sheath (Glidesheath Slender, Terumo, Tokyo, Japan) over a 0.035" guidewire. The sheath was flushed with a combination of nitroglycerin (100 mcg) and verapamil hydrochloride (2.5 mg) every 15-20 minutes to avoid vasospasm. A bolus dose of 5000 IU, followed by an infusion of 1000 IU/h unfractionated heparin were administered to maintain the activated coagulation time (ACT) between 250–300 s.

Stenotic/occluded segments were passed with a combination of 0.018" guidewire (Boston Scientific, Marlborough, MA, USA), or a 0.035" hydrophilic guidewire (Radiofocus®, Terumo Medical Corporation, Tokyo, Japan), and 4-5F vertebral catheters (Cordis, Hialeah, Florida, USA). Balloon angioplasty was performed with 6-10 mm-diameter balloon catheters (Sterling, Boston Scientific, Marlborough, MA, USA). Self-expandable stents (Innova™, Boston Scientific Corp, Natick, MA, USA) were used under the following circumstances: (1) A residual stenosis of more than 30% (2) Persistent leaks after balloon angioplasty.

In patients with acutely thrombosed AVFs/AVGs, first, the intravenous cannulas were inserted in the thrombosed segments, and a total dose of 2-4mg tissue plasminogen activator (tPA) alteplase (Actilyse®, Boehringer-Ingelheim, Ingelheim am Rhein, Germany) diluted in 20cc saline was administered at a rate of 1-2 mg/h. Subsequently, aspiration thrombectomy was performed with 6F catheters and the balloon was inflated at a low pressure to macerate the thrombi. Once blood flow was reestablished, a diagnostic angiogram was obtained to elicit the culprit lesion. The stenotic segments were treated with balloon angioplasty (Figure 1).

Hemostasis was achieved with manual compression or a radial compression device (TR band, Terumo Medical Corporation, Tokyo, Japan).

Outcomes

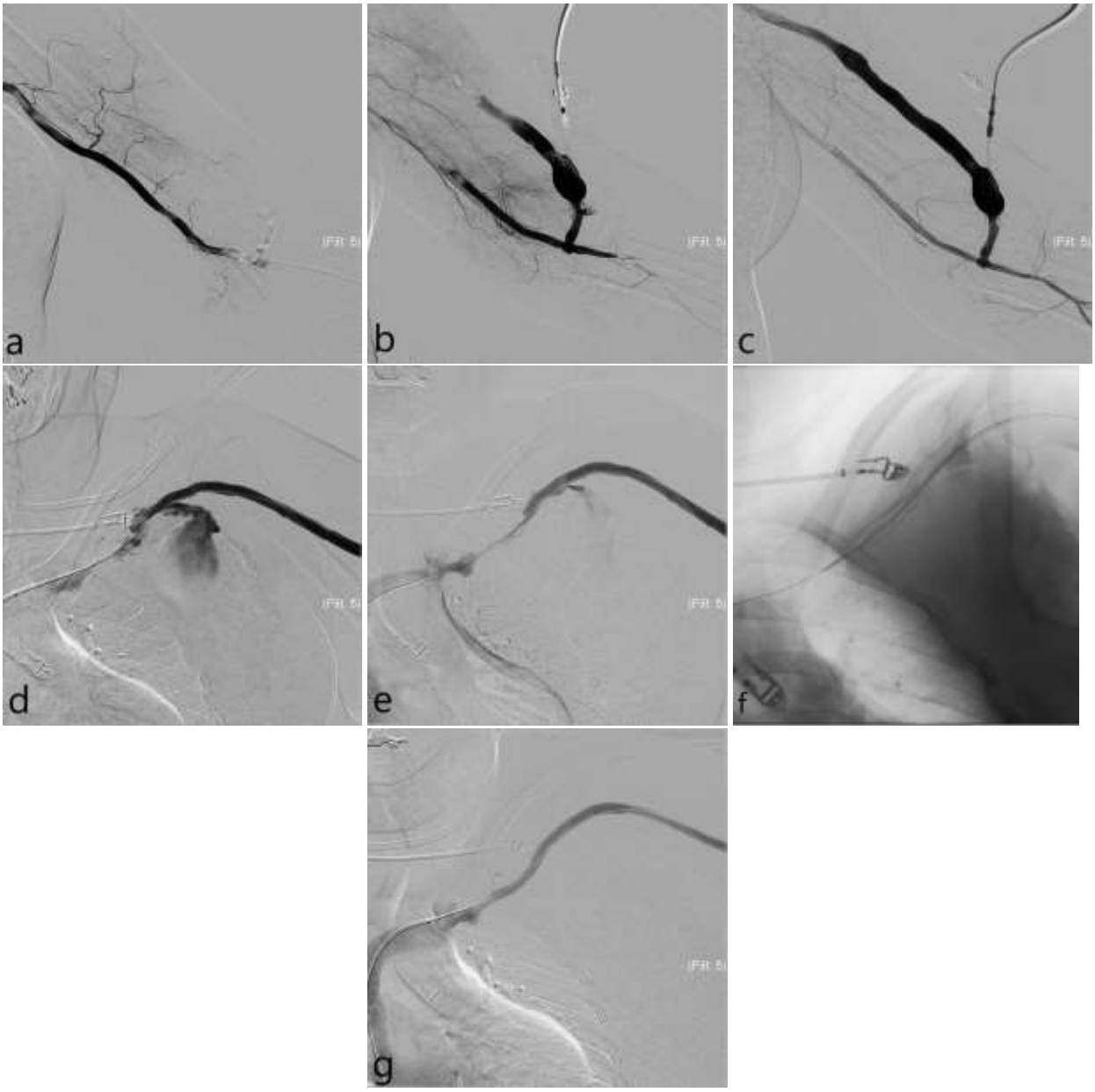
Complications and outcomes were classified according to the guidelines of the Society of Interventional Radiology [12] and recommended standards defined by Sidawy et al [13]. Technical success was defined as less than 30% residual stenosis at the endpoint of the intervention. Clinical success was defined as at least one successful dialysis session following endovascular treatment.

Post-intervention primary patency was defined as the interval after endovascular treatment until thrombosis or the need for reintervention due to unsuccessful hemodialysis. Post-intervention secondary patency was defined as the interval after endovascular intervention until access abandonment or thrombosis.

Follow-up

All interventions were outpatient procedures. After the first successful dialysis session, an initial follow-up examination was scheduled at the first week, 1, 3, 6, 12 months, and annually thereafter. AV access and the radial artery were evaluated with clinical examination and color Doppler ultrasound (CDUS). All

Figure 1: A 49-year-old female presented with a sudden loss of thrill. (a) Diagnostic angiogram demonstrates complete occlusion of the brachial-cephalic fistula. (b) Control fistulogram following 2 mg tPA infusion shows partial recanalization. (c, d) Subsequent balloon angioplasty, fistulography demonstrates complete restoration of flow. Residual stenosis, venous rupture, and contrast extravasation at cephalic arc are observed. (e, f) Leak persisted after stent placement and a telescoping construct was formed with second stent deployment. (g) Completion angiography shows restoration of the flow and complete cessation of the leak.



patients were followed at their respective hemodialysis unit or via telephone interviews. The patients were referred for further evaluation when signs of vascular access dysfunction were detected.

Statistical analysis

A power analysis was performed with G*Power version 3.1.9.2 to determine the sample size. A minimum number of 26 samples was calculated to reach a power level of 0.8.

The frequency distribution of qualitative variables and the mean and standard deviation of continuous variables were reported as descriptive statistics. The number of endovascular interventions per patient was found. Kaplan–Meier analyses were used to estimate cumulative patency rates. All analyses were performed using IBM SPSS Statistics version 23 software (SPSS Statistics v23, IBM Corporation, Somers, New York).

Results

Thirty-six RAA procedures were performed on 30 patients. Eight were male and the mean age was 62.5 (range: 26-79) years. Patient demographics, and vascular access characteristics are presented in Table 1. Among all, 26.7% (8/30) of the patients were diabetic, and 33.3% (10/30) had a history of coronary artery disease. None of the patients were current smokers. All patients had mature AVF/AVG before nonfunction. Twenty-six patients had autogenous vascular access, while four patients had non-autogenous vascular access with a prosthetic graft.

Lesion characteristics, procedural details, and the outcomes are presented in Table 2. The treatment indication was long-segment stenosis in seven cases and long segment occlusion of AV access in 29 cases. In the occlusion group, the culprit lesion was perianastomotic stenosis in 16 cases, cephalic arch stenosis in 4 cases, brachiocephalic vein stenosis in 5 cases, intent stenosis in 2, and hypertrophic valve in one case. In one case, the etiology of the thrombosis could not be elicited. One

patient had multilevel lesions, long segment occlusion of the AVG and downstream vein, and concomitant short segment stenosis of the central veins. Treatment was attempted within 48 hours of acute occlusion in all cases.

Table 1: Patient demographics and vascular access characteristics

Variable	Number or mean	% or range
Age	62.5	26-79
Sex		
Male	8	36.4
Female	22	63.6
Treated limb		
Right	12	40
Left	18	60
Comorbidities		
Diabetes mellitus	8	26.7
Cardiovascular event	10	33.3
Hypertension	14	46.7
Type of vascular access		
Autogenous	26	86.7
Prosthetic	4	13.3
Vascular access location		
Brachial-cephalic	14	46.8
Brachial-basilic	12	39.9
Radial-cephalic	4	13.3
Previous endovascular intervention	4	13.3

Table 2: Lesion characteristics, procedure details, outcomes

Variables	Number or mean	% or range
Lesion type		
Stenosis	7	19.4
Occlusion	29	80.6
Lesion length (cm)	30.3	7-46
Access site		
Radial	34	94.4
Ulnar	1	2.8
Interosseous	1	2.8
Complications		
Major	0	0
Minor	3	8.3
Technical success	36	100
Clinical success	35	97.2

The radial artery was accessed in thirty-four procedures. One patient with a history of coronary intervention presented with a completely occluded autogenous brachial-cephalic forearm fistula. The radial artery was occluded at CDUS examination. In this case, endovascular treatment was performed via interosseous artery access. One patient presented with rethrombosis of the AVG. CDUS showed an irregular and thickened wall of the radial artery owing to the previous intervention, but no significant stenosis was detected. The ulnar artery was used as the access site.

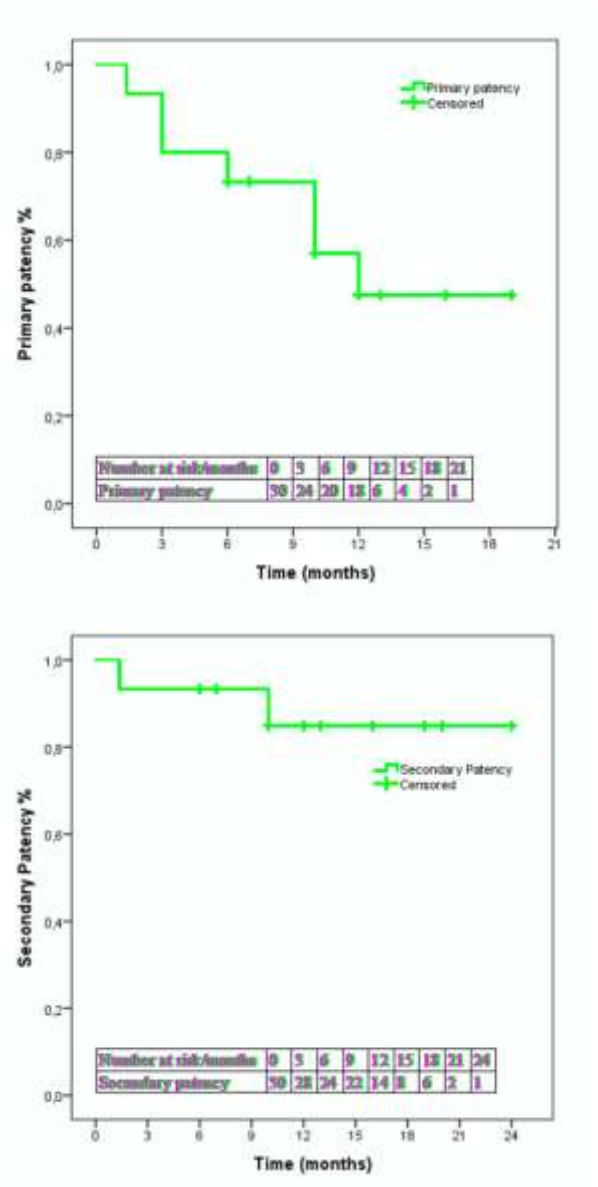
Retrograde arterial catheterization was performed successfully in all procedures. After angiography, residual stenosis was <30% in all lesions, corresponding to a technical success rate of 100%. In 35/36 cases (97.2%), patients underwent at least one successful dialysis session after the treatment. One patient developed rethrombosis two days after the treatment. Physical examination revealed extensive arm edema and RDUS showed acute thrombosis in the outflow vein. After consulting with the nephrologist and vascular surgeon, dialysis access was abandoned, and a tunneled central venous catheter was placed through the right internal jugular vein. Eventually, new vascular access was created by placing a prosthetic brachial-basilic straight graft.

No major complication was observed during the hospital stay. Venous rupture occurred in three patients (3/36 [8.3%]) after balloon dilation. The rupture site was the perianastomotic vein in two patients, which was treated with prolonged balloon inflation with low pressure and manual compression. Venous rupture at the cephalic arch site with subsequent expansive chest wall hematoma was encountered in the other case. Extravasation persisted even after three prolonged balloon inflations for three minutes. A combination of bare stent placement and prolonged balloon inflation was used but failed to halt bleeding. Eventually, a second bare stent was placed within the first stent to form telescoping stenting. Extravasation ceased immediately. The patient recovered well and underwent successful dialysis sessions.

Distal embolism into the arterial circulation was not encountered in any of the patients. All three distal access arteries were patent in all patients after the procedure and at follow-up on CDUS examination. None of the patients developed significant (>70%) stenosis or signs of hand ischemia.

The mean follow-up was 14.3 (range 6-24) months. The post-intervention primary patency rates were 100%, 73.3%, 47.5% at 1, 6 and 12 months, respectively. A mean of 1.6 interventions was performed per patient to maintain adequate dialysis during the follow-up period. The post-intervention secondary patency rates were 100%, 93.3%, 84.8% at 1, 6 and 12 months, respectively (Figure 2).

Figure 2: (a, b) Kaplan-Meier curves showing estimated primary and secondary functional patency rates



Discussion

Our retrospective patient series showed excellent technical success rates (100%) with high clinical success (35/36 [97.2%]) in the treatment of nonfunctional AV access through retrograde arterial access in patients in whom traditional routes were not feasible. A relatively high complication rate (3/36 [8.3%]) was encountered, which was managed by endovascular means, and no access site complication was observed.

Traditionally, vascular access lesions are treated through direct venous access with a retrograde or antegrade fashion. Though most lesions are treated successfully, this route has some distinct disadvantages. A second sheath is needed when multilevel lesions are detected. When AV access is occluded, retrograde injection of the contrast media through the venous access might not reveal the anastomosis site and afferent artery structure. Retrograde injection of contrast media might result in the dislodging of the thrombi into the arterial branches. The brachial artery has been used as an alternate route to overcome this issue, but puncture site complication rates are reported as up to 12% [3, 7]. Achieving hemostasis after brachial sheath removal can be troublesome, especially in obese patients, and inadvertent manual compression of the access site may lead up to rethrombosis of the AV access.

RAA offers several advantages to overcome these drawbacks. It is possible to visualize the entire conduit clearly, while contrast media is injected close to the anastomosis site with an antegrade fashion. The venous route has potential kinks and steep angulations, and the brachial route has a U-turn at the anastomosis site. In contrast, RAA has a straighter course that gives increased torque ability to the wire tip and increases support in advancing devices. One sheath is enough to treat multi-level lesions of the outflow vein and central veins [14]. Achieving hemostasis is relatively safer, and access site-related complications (prolonged bleeding time, hemorrhage, vasospasm) do not cause compromised blood flow in vascular access, which reduces the risk of early rethrombosis [5, 15]. In complex cases, in which the proximal radial artery is anastomosed to the perforator of the median antecubital vein (Gracz fistulae), catheterizing the anastomosis site through the retrograde venous route might be quite challenging [16]. RAA will facilitate the guidewire to directly pass through the anastomosis that will shorten the procedure time and forestall unsuccessful guidewire manipulations.

There are also drawbacks to RAA. First, although, most lesions can be treated with ≤6F sheaths safely, larger sheaths are needed when central venous lesions coexist, which will increase the risk of post-intervention access artery occlusion [17]. However, if a satisfactory collateral flow in the hand is confirmed with both the Allen test and a CDUS examination, the repercussion of this result is negligible [18]. Second, a high origin of the radial artery from either the brachial or axillary artery has a prevalence of up to 7% [19]. When the brachial artery is used as an inflow artery of the conduit, careful CDUS examination is crucial to exclude this variation to avoid unnecessary punctures. When a high origin of the radial artery variation is encountered, brachial or interosseous/ulnar artery might be the preferred access site. Third, if the conduit is created with a prosthetic brachial-antecubital forearm loop graft, catheterization of the anastomosis site and advancing balloon catheters over the guide wires might be problematic owing to the steep angulation. Fourth, the prevalence and severity of vascular calcification are higher in dialysis patients than in the other groups, which makes radial and other hand arteries more challenging [20]. In these cases, the crisscross technique or antegrade brachial artery access could be a better option.

A few studies are investigating the feasibility, safety, and effectiveness of RAA in the treatment of nonfunctional AV access [5, 14, 21-26]. Most studies include autogenous radial-cephalic direct wrist access. Wang et al. treated 69 lesions (65 stenoses, 4 total occlusions) in 49 patients with radial-cephalic fistulae. Forty-two (60.9%) patients had perianastomotic outflow vein stenosis. They reported a technical success of 91.3% (63 of 69 lesions) and clinical success of 96% (48 of 50 lesions) [21]. Le et al. performed 50 therapeutic procedures through TRA. They achieved a technical success rate of 88% and a clinical success rate of 84%. They also reported the functional patency rates of 88.5%, 84.2%, and 83.0% at 1, 6, and 12 months, respectively [22].

In the current study, we achieved a technical success rate of 100%, and a clinical success rate of 97.2%, which is corroborated with previous reports using either traditional routes or TRA [3, 4]. Our primary and secondary patency results were also comparable with early studies and NKF-KDOQI recommendations [4, 27, 28]. The complication rate (3/36 [8.3%]) was higher than previous reports [29]. Venous rupture was encountered in three patients with totally occluded AV access. The use of tPA in addition to high dose heparin might explain the high rate of bleeding complication.

Post-intervention radial artery occlusion was reported within a wide range, between 0.8-38% [30]. Chen et al. treated 131 patients with dysfunctional Brescia-Cimino fistula. A 6F sheath was placed through TRA. Sixteen patients had multiple radial artery punctures for reintervention during follow-up. They reported weak radial artery pulse in two patients, but no occlusion was observed [15]. Lin et al. [25] performed 165 interventions in 101 patients (69 AVG, 32 AVF). They reported distal embolism in three patients, which were treated by surgical interventions. Severe vasospasm was encountered in two patients, in whom additional access was required to perform endovascular treatment. Using higher doses of heparin and shorter compression times reduces the risk of radial artery occlusion after intervention [31, 32].

In our study, accessed arteries were patent at CDUS examinations performed before discharge and follow-up visits. No major complication was observed at the puncture site. One patient presented with rethrombosis of the AV access six months after the initial intervention. The radial artery wall was thickened and irregular. The lumen was patent, and flow dynamics were within normal limits. Treatment was performed through TUA without any access site complications.

Limitations

The limitations of our study include the sparse number of patients, and its retrospective nature, which made randomizing impossible. In addition, the number of patients in whom the ulnar artery and interosseous artery were used for access was limited, and they were utilized only when transradial access was not

eligible. RAA was preferred over antegrade brachial artery access at the operators' discretion, which may cause selection bias. RAA was the only route used for treatment; therefore, comparing it with venous and/or brachial artery routes was not possible. Long-term results are needed.

Conclusion

Our study demonstrated that RAA is feasible, safe, and effective in the treatment of nonfunctional AV access with high technical and clinical success rates. Low access site complication rates make this access site an attractive salvage route when traditional routes are not feasible.

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The benefit of hearing aids in adults with hearing loss during the Covid–19 pandemic

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Ethics Committee Approval
This research was approved by the Ethics Committee of the Ankara Yildirim Beyazit University and implemented according to the Helsinki Declaration (approval no: 16739). All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Hearing aids, cochlear implants, and guidance are highly effective in improving communication skills and the quality of life of individuals with hearing loss. During the Covid-19 pandemic, patients with hearing loss, especially those living far from city centers, faced insufficient device use due to their inability to go to the hospitals and device centers. This study aimed to evaluate the effects of remote monitorization of sound amplification in adults using cochlear implants and/or hearing aids during the lockdown period.

Methods: In this cross-sectional study, we recruited 98 individuals with post-lingual cochlear implants (n=38) and hearing aids (n=60). Patients on hearing aids followed before the Covid-19 pandemic were guided with a remote computer connection during the pandemic. All participants filled out the Spatial Hearing Questionnaire (SHQ), the short version of Speech Spatial Quality of Questionnaire (SSQ12), Short Form-36 quality of life questionnaires (SF-36), Satisfaction with Amplification in Daily Life Questionnaire (SADL), and the Coronavirus 19 Phobia Scale (C19P-S) via google questionnaire.

Results: During the lockdown period, there were significant increases in the spatial perception scores (SSQ12) of cochlear implant and hearing aid users ($P<0.05$). A moderate correlation was found between SSQ12 and SHQ scores in cochlear implant (r=0.482, $P=0.021$) and hearing aid users (r=0.512, $P=0.011$). During the lockdown period, the SADL overall scores were significantly higher among cochlear implant users ($P<0.05$). When the subscales of SF-36 for both cochlear implant and hearing aid users were compared with the normative values of these subtests (energy/vitality, role limitations due to physical dysfunctions and emotional problems, mental health, and pain), it was observed that there was a significant improvement in the scores of individuals using hearing aids and cochlear implants ($P<0.05$).

Conclusion: During the lockdown period, hearing performance, quality of life, and hearing aid satisfaction of patients using cochlear implants and hearing aids increased after tele-audiology guidance.

Keywords: Cochlear Implantation, Tele-Audiology guide, Covid-19 pandemic, Speech Spatial Quality of Questionnaire (SSQ)

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Introduction

There are approximately 360 million people with hearing loss worldwide. Hearing loss was associated with social life, professional status, and economic detriment [1]. In developing countries with a high prevalence of hearing loss, access to auditory health services may be limited, especially in extreme situations such as a pandemic [2].

The 2019 coronavirus disease (SARS-CoV-2), a novel coronavirus type (2019-nCoV) that causes severe acute respiratory disease, first presented with cases of pneumonia of unclear origin in the Chinese city of Wuhan on December 31, 2019, and rapidly affected the world [3-5]. The world health organization (WHO) declared the new coronavirus outbreak as an international global health emergency on January 30, 2020 [6]. The first case in Turkey was reported on March 11, 2020 [7]. New coronavirus 2019 (Covid 19) was seen in 179.241.734 people, and the number of people who died was 3.889.723 by June 24, 2021. The number of positive cases continues to increase day to day [7]. In our country, people tried to continue their everyday lives under prohibitions and restrictions, such as decreasing social relations, and staying home as much as possible, while being continuously exposed to an information flow about the disease [8].

Auditory rehabilitation, cochlear implants, and/or hearing aids, are electronic devices that are effective in improving communication and the quality of life of patients with hearing loss [9, 10]. These patients had difficulties in reaching the hospitals during the pandemic. Since the Covid-19 pandemic began, many patients using hearing aids could not be followed up in hospitals. For this reason, the audiology guidance of patients using cochlear implants or hearing aids was performed remotely.

Telemedicine is useful for providing health-related services and information to poorly serviced areas through telecommunications technology [11]. It enables audiologists to connect safely, efficiently, and effectively to hearing-impaired patients in remote areas with geographical and economic barriers, while allowing clinicians to perform diagnostic tests, or hearing aid/cochlear implant placement/fitting and training safely [12, 13].

Our current study investigates the effects of sound amplification on the quality of life of the patients who began using hearing aids or cochlear implants before the pandemic. It was also determined how much the patients' satisfaction was affected after the pandemic.

Materials and methods

In this study, the effects of sound amplification were investigated remotely during the pandemic among patients who received hearing aids or cochlear implants before the pandemic. This research was approved by the Ethics Committee of the Ankara Yildirim Beyazit University and implemented according to the Helsinki Declaration (approval no: 16739). Informed consent forms were signed by all participants.

Participants

Sixty individuals (27 M+33 F) with a mean age of 52.12 (10.7) (range: 18-75) years using hearing aid(s) with moderate (n=30) or moderate to severe (n=30) sensorineural hearing loss in both ears and 38 adult patients (20 M+18 F) with a mean age of 33.30 (15.41) (range: 22-51) years who were using a cochlear implant with severe or severe sensorineural hearing loss in both ears, according to the classification of Clark et al. (Clark 1981), were included in this study. The pure-tone average was assessed at 500, 1000, and 2000 Hz. All participants had a history of post-lingual hearing loss and were regularly followed up for cochlear implants or hearing aids for at least one year. The demographic characteristics of the participants are summarized in Table 1. The short version of Speech Spatial Quality of Questionnaire (SSQ12), Speech Hearing Questionnaire (SHQ), 36-Item Short Form Survey (SF-36), Satisfaction with Amplification in Daily Life (SADL) questionnaire, and Coronavirus Anxiety Scale were administered to all individuals participating in the study. There had been SSQ12 and SADL data of participants from 2017 to July 2020 to assess participants' cochlear implant and hearing aid(s) satisfaction before the pandemic. We called all participants within an average of 1 month after guidance and asked them to fill out the questionnaires online. Two participants with cochlear implants were using both hearing aids and cochlear implants. During the pandemic, the patients were contacted via zoom to provide guidance.

Table 1: Demographic data of the participants

Features	Cochlear Implant (n=38)	Hearing Aid (n=60)
Age, median (years)	22-51 (33.30)	18-75 (52.12)
Female (%)	18 (47.3)	33 (55)
Male (%)	20 (52.6)	27 (45)
Pure-tone average, median dB)	65.7 (61.5 - 80.4)	58.1 (48.2 - 68.7)
Device usage time (month) (SD)	17.4 (9.07)	12.8 (17.4)

Pure-tone average at 0.5, 1, and 2 kHz in the better-hearing ear, SD: Standard Deviation

Tele-Audiology guide procedure

A video conference system (Zoom) was used to guide the patients (Tele-Audiology Guide). Nvidia antivirus application was used on our computer and the computers communicating. After comfortable communication was established with the patients by checking the internet connections of both sides, guidance was initiated. According to Penteado and others, antivirus and firewall protection were temporarily turned off to improve connection performance. For this purpose, access to sites other than these applications was blocked to protect against viruses. In each session, basic strategies, training, and recommendations were given to the patient. Using visual and sensory data, we aimed to improve speech intelligibility with voiced and consonant monosyllabic words. Each patient was interviewed separately by the same audiologist once a week for 8 weeks, and 45-minute guidance was provided about device use and difficulties encountered during communication.

A short form of Speech, Spatial and Qualities of Hearing Questionnaire (SSQ12)

SSQ yields an audiological measurement of the individual's hearing loss by assessing the direction, distance, and movement components and how this loss affects the individual's life (i.e., disabilities or participation restrictions). The original full version of SSQ has three different subscales and 49 items evaluating speech perception and hearing quality (voice clarity and listening effort), as well as spatial hearing [14]. There are many short versions of SSQ available. However, the SSQ12 short version was preferred because it contains the same number of questions as the hearing-impaired questionnaire in clinical settings [15]. It has nine pragmatic subscales: Speech in Quiet,

Speech in Noise, Speech in Speech Contexts, Multiple Speech Flow Listening, Localization, Distance and Movement, Decomposition, Identification of Sound, Quality and Naturalness, and Listening Effort. Each question is scored between 0-10 ("0" indicates that the specified status is not possible, "10" indicates that the specified status is excellent) [15].

Satisfaction with Amplification in Daily Living (SADL)

The SADL questionnaire is a highly reliable questionnaire for evaluating the benefit of hearing aids [16]. The 15-question questionnaire includes the subscales of positive impact, service and cost, negative impact, and personal image (7-point Likert-type). The most critical aspect of the SADL questionnaire is that the patient satisfaction from amplification can be scored manually. We used the Turkish version of the SADL questionnaire [17].

SF 36 Quality of Life Scale

SF 36 quality of life scale, one of the most common scales used to evaluate life quality, was developed in 1992 by Ware et al [18]. We used the Turkish version of this scale, developed by Demiral et al [19]. The SF36 scale consists of 36 items and the following 8 subscales: Physical function (10 items), social function (2 items), role limitations due to physical functions (4 items), role limitations due to emotional problems (3 items), mental health (5 items), energy/vitality (4 items), pain (2 items) and general health perception (5 items). While only the second question in the scale includes the perception of change in health in the last 12 months, other questions are evaluated considering the last four weeks. The fourth and fifth questions of the scale are answered with yes/no. The other questions (3, 5, and 6) are evaluated with Likert-type scores. The subscales evaluate health between 0 and 100, and 0 indicates unhealthiness, while 100 indicates being healthy [18].

Coronavirus 19 Phobia Scale (C19P-S)

Coronavirus 19 Phobia Scale (C19P-S) is developed to measure the fear reactions experienced by individuals during the Covid-19 pandemic. The five-point Likert type scale consists of seven items (1: Strongly disagree – 5: Strongly agree). The C19P-S consists of four sub-scales: Psychological, Somatic, Social, and Economic status. The total C19P-S score is obtained by the sum of the sub-dimension scores and ranges from 20 to 100 points. The higher the score, the higher the level of anxiety related to the Covid-19 pandemic [20].

Statistical analysis

Statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS 23.0 for Windows; SPSS Inc., Chicago, IL, USA SPSS). The impact of the guidance on hearing and amplification in cochlear implant and hearing aid users was assessed by comparing the scores before and after the pandemic. The cochlear implant and hearing aid groups (before and after) were compared with the paired sample t-test with Bonferroni correction. The relationship between SSQ12 and SHQ was assessed with the Pearson correlation coefficients. The sample size required for each hearing aid group (cochlear implant and hearing aid) to achieve a clinically relevant sample in the original efficacy trial using the main outcome measure with a two-sided significance level of 0.05, an effect size of 0.5, and a power of 90% (G*Power Version 3.1) was 24 participants.

Results

The time spent giving guidance and information, and the overall consultation time for each individual was measured.

The SSQ12 scores of the cochlear implant users (P=0.001) and hearing aid(s) users (P=0.024) significantly increased after the pandemic compared to the SSQ12 scores obtained pre-pandemic (Table 2).

Table 2: Average scores and standard deviations of Spatial Hearing Questionnaire (SHQ), short form of Speech, Spatial and Qualities of Hearing Scale (SSQ12) over time and Satisfaction with Amplification in Daily Life (SADL) questionnaire scores.

	CI (n=38)		MHL (n=30)		MSHL (n=30)	
	M	SD	M	SD	M	SD
SSQ12 overall scores In the process of covid 19	4.57	0.31	5.37	0.76	4.12	1.53
SSQ12 overall scores	6.14	0.88	7.01	0.87	6.92	1.75
SHQ overall scores	59.4	8.07	62.54	13.10	60.52	12.28
SADL positive effect	38.8	4.20	41.1	3.72	40.53	4.74
SADL personal image	14.2	1.41	12.7	2.93	12.7	2.14
SADL adverse features	5.23	1.24	6.02	0.89	5.42	1.12
SADL service and cost	2.88	0.47	4.71	0.28	4.56	0.54

CI: Cochlear Implant, MHL: Moderate Hearing Loss, MSHL: Moderate- Severe Hearing Loss, M: Mean, SD: Standard Deviation, SSQ12: Short Form of Speech, Spatial and Qualities of Hearing Scale, SHQ: Spatial Hearing Questionnaire, SADL: Satisfaction with Amplification in Daily Life

The data of the participants using hearing aid(s) and/or cochlear implants, the SSQ12, SHQ, SADL scores, and their comparisons are shown in Table 2. The mean SHQ and SSQ12 scores of patients using cochlear implants during the pandemic were 59.46 (SD: 8.07, min: 43, max: 80.28), and 6.14 (SD: 0.88, min: 4.3, max: 8.07), respectively. The mean SHQ and SSQ12 scores of all individuals using hearing aid(s) were 61.3 (SD: 12.63, min: 49.2, max: 79.2), and 6.96 (SD: 1.30, min:1.3, max:8.47), respectively.

A moderate correlation was found between SSQ12 and SHQ scores of cochlear implant (r=0.482, P=0.021) and hearing aid (r=0.512, P=0.011) users.

The SADL overall score and positive impact scores of cochlear implant users before the pandemic were significantly lower than the SADL scores during the pandemic (P<0.05). However, no significant difference was observed among the patients using hearing aids (P>0.05). The overall SADL scores were similar with regards to remote and face-to-face guidance (P>0.05) and among patients using hearing aids (P>0.05).

SF36 results of both hearing aid and cochlear implant users were compared according to the normalization results performed by Jenkinson et al. in healthy individuals. The subscale mean scores of the SF-36 and the normative data of healthy individuals by Jenkinson are shown in Table 3 [21].

Table 3: Average scores of SF-36 in individuals using cochlear implants and hearing aid (s) and healthy individuals (normative data)

Eight variables of SF36	Patient scores (CI)		Patient scores (HA)		Normative data	
	M	SD	M	SD	M	SD
PF	88.1	13.6	71.4	10.1	89.4	16.1
RLPH	95.3	17.2	83.6	17.1	84	32
RLEP	84.2	21.5	84.1	14.2	80.3	33.6
EF	60.2	11.5	57.5	22.7	58.2	19.9
EP	66.2	10.1	78.7	10.7	80.3	33.6
SF	87.7	12.1	92.4	12.7	86.7	20.5
P	95.7	9.2	87.2	8.73	79.4	22
GH	72.5	9.3	78.5	14.5	74.1	20.3

PF: Physical Functioning, RLPH: Role Limitations due to Physical Health, RLEP: Role Limitations due to Emotional Problems, EF: Energy/Fatigue, EP: Emotional Problems, SF: social functioning, P: pain, GH: general health, CI; Cochlear implantation, HA: Hearing

There was no significant difference between the physical function (P=0.655), social function (P=0.06), and general health perception subscales (P=0.225) and the normative values of SF-36 among the cochlear implant users.

Among our study population, significant differences were found between the role limitations due to physical functions (P=0.001), role limitations due to emotional problems (P=0.039), mental health (P=0.018), energy/vitality (P=0.045), and pain subscales (P=0.001) and the normative values of the SF-36.

The physical function (P=0.027), role limitations due to emotional problems (P=0.019), social function (P=0.001), pain subscale (P=0.012), and general health perception (P=0.001) of hearing aid users significantly differed from the normal values of SF-36.

The SF-36 scores of both hearing aid and cochlear implant users did not differ with age or gender (P>0.05).

C19P-S scores of individuals using hearing aids (41.6 (14.3)) and cochlear implants (47.6 (15.17)) were above the normal limit (20-100). The mean psychological, somatic, social, and economic subscale scores of hearing aid users were 12.1 (4.9), 9.55 (2.3), 11.7 (4.3), and 8.2 (3.5), respectively. Among cochlear implant users, the mean scores of the subscales in the same order were 13.1 (4.9), 12.42 (2.3), 11.8 (4.3), and 10.3 (3.5), respectively.

Discussion

It should be ensured that patients' follow-ups continue routinely and reliably despite the clinical difficulties associated with social distancing during the pandemic. Therefore, specialists of various fields began exploring new methods to continue providing the required health services. Telehealth aims to provide health services to those who have no or inadequate access to these services across the world using information technology, and functions in the same way as face-to-face healthcare services [22, 23]. Tele-Audiology Guide can be used for cochlear implants or traditional hearing aid users, especially in areas far from practitioners during the pandemic.

In our study, the SSQ12 scores of cochlear implant and hearing aid users were lower before Covid-19 compared to scores obtained during the Covid-19 pandemic. According to the study of Zhang et al. [24], the SSQ49 and SHQ scores improved from the first 6 months until the first year of the implant and plateaued thereafter. The increase in SSQ12 scores in our study after the guidance was given showed that patients continued to benefit from cochlear implants. This finding was supported by the study of Zhang et al. [24], which showed that SHQ12 scores increased between the 12^{th}-24^{th} months of receiving implants [24].

In our study, a moderately significant relationship was observed between overall SSQ12 and SHQ scores, while in the study of Zhang et al. [24], the two were strongly correlated. This may be related to individual differences.

During Covid 19, the SF-36 questionnaire was used to assess the general health of patients using cochlear implants and hearing aid(s). Although the SF-36 does not have a scale to measure hearing and communication impairment [25], it is important because it provides detailed information about the overall health assessment of patients. Cochlear implants and/or hearing aid(s) can be affected by many factors while helping to regain quantitative improvements in auditory perceptions of individuals with hearing impairment. One of these factors is the psychological state of cochlear implant and hearing aid users. In many studies, cochlear implants are reported to have a positive effect on the patients' quality of life [26, 27]. Additionally, significant differences were observed in SF-36 general health scores after receiving hearing aids with regards to the amount of hearing loss, attention, and gender [28].

According to the study of Olze et al. conducted in 2011, the psychological conditions of individuals with unilateral hearing loss and using cochlear implants significantly affect their quality of life [26]. Demiral et al. reported that the pre-implantation SF-36 physical score (52.07) was higher than post-implantation scores (45.21) and the SF-36 psychological score (42.91) increased after cochlear implant use (48.33) (19). In our study, although there was a significant increase in the patients' role limitations due to physical functions, role limitations due to emotional problems, and pain average scores, cognitive abilities also increased, and fatigue decreased. This showed the success of getting guidance, while also revealing some deficiencies. This may be because cochlear implant users place more emphasis on hearing health than hearing aid users. This finding was compatible with that of the study by Ou et al. [29].

The relatives of only two patients (71 and 64 years old) who had problems with internet connection and communication with the device during the interviews helped.

In our study, the patients' C19P-S sub-scales scores (fear of getting the disease) were moderate. However, after guidance by the audiologist, an increase was observed in the general quality of life and hearing health in most patients.

Limitations

The hearing function of the patients could not be assessed both objectively and subjectively, because tele-audiology or telemedicine was not fully widespread in Turkey. Another limitation is the inability to make age-specific evaluations due to the lack of age differences in the patient population participating in our study. Future studies should research telerehabilitation with a more developed network structure and standardized methods.

Conclusion

Tele-medicine and tele-audiology are used in many countries for hearing aids, cochlear implants, and directive guidance for device use among patients with hearing loss and have been used primarily to reach patients in rural areas, far from hospitals. The observation of a positive increase in the overall scores of the SSQ12, SHQ, SADL questionnaires, and the SF-36 general quality of life scale showed the benefit of guidance, even in adverse situations. These findings are important in terms of preparing the ground for developing useful tele-audiology guides or telerehabilitation practices, such as an Internet-Based Tele-audiometry system in Turkey.

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Factors related to necrosis at the T junction in reduction mammoplasty

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Ethics Committee Approval
The study was approved by the Ethics Committee of Balıkesir University with the decision number 2021/246.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Reduction mammoplasty is an effective and patient-satisfying operation in terms of relieving physical complaints such as back pain, shoulder collapse, and intertrigo due to macromastia. The most used incision is the wise pattern, which allows for easy intervention to the excess vertical and horizontal skin. However, long incisions may cause wound healing problems. The necessity of wide dissection may cause perfusion problems in the lateral and medial flaps at the T junction, where the tips of the flaps meet with the inframamarial sulcus. In the literature, T junction dehiscence is discussed under delayed healing complications. This study aimed to reveal the specific effects of the factors that were shown to cause delayed healing in general on the T junction area.

Methods: In this retrospective cohort study, the effects of age, smoking habits, comorbidities, resection volume, and body mass index on T junction dehiscence were investigated among 56 patients who underwent reduction mammoplasty with wise pattern technique. The combined effects of all possible factors effective on dehiscence were investigated by multivariate logistic regression analysis.

Results: The median age of the patients was 44.3 (12.5) years. Their mean body mass index was 26.0 (24.0-27.0) kg/m^2, and 13% of the patients had comorbidities. The rate of dehiscence at the T junction was 28.6%. The most effective factors on the development of dehiscence were smoking and increased body mass index. Logistic regression analysis revealed that smoking increased the risk of T junction dehiscence by 8.543 times (95% Confidence Interval: 1.454-50.213) (P=0.018). No relationship was found between age, resection volume, comorbidities, and T junction dehiscence.

Conclusion: The risk of dehiscence in the T junction increased in the patients who smoked and who had a high body mass index. The effect of smoking was much greater on T junction healing than its effect on general wound healing complications. T junction dehiscence should not be considered a delayed wound healing complication solely, but as a flap perfusion problem and preoperative measures should be taken accordingly.

Keywords: Wise pattern, T junction, Perfusion, Smoking, Wound healing

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Introduction

Reduction mammoplasty is performed for aesthetic and functional reasons or symmetry after breast reconstructions [1, 2]. Although many techniques were defined, the Wise pattern is the most frequently used [3]. The Wise pattern technique effectively reduces excess vertical and horizontal skin, but long incisions cause wound healing problems [4].

Wound healing problems can occur on the horizontal or vertical legs of the incision, or around the areola. However, the most common site is the T junction. Problems related to the T junction are covered under delayed wound healing complications in most studies. Smoking, high body mass index [5-9], advanced age [8] and resection volume [10] may be related to wound healing problems.

At the T junction, randomly fed medial and lateral flaps join the inframammary sulcus and perfusion is poor. Usually, dehiscence occurs because of perfusion problems rather than those related to wound healing. Chan et al. [11] noted that the principles of flap surgery are valid in wise pattern breast reductions and Galliano et al. [12] emphasized that the tension created by the lateral flap may cause skin necrosis in the lateral or medial flap at the T junction. For this reason, we considered the dehiscence of the T junction separate from the wound healing problems occurring in other areas of the incision and aimed to investigate the effects of the factors of delayed healing on the T junction area. We believe that predicting the patient group that is expected to have problems at the T junction will be beneficial in terms of prevention.

Materials and methods

The study was conducted on 56 patients with available medical records who consented to participate, among 67 patients who underwent wise pattern breast reduction between January 2020 and August 2021. Written and verbal consent was obtained from all patients and the study was approved by the Ethics Committee of Balıkesir University with the decision number 2021/246. The effects of age, concomitant diseases, smoking, body mass index, and resection amount on the dehiscence at the T junction were investigated.

Superficial epidermal necrosis and full-thickness necrosis occurring in the lateral or medial flaps were considered T junction dehiscence, regardless of size (Figure 1, 2), while dehiscence without skin necrosis or open wounds with suture exposure was not. The smoking status of the patients was questioned, and habitual smokers and occasional smokers who had smoked within 6 weeks before the operation were considered smokers.

Statistical analysis

Whether discrete numerical variables were normally distributed was investigated with the Shapiro-Wilk test. Discrete numerical variables were expressed as mean (standard deviation) or median (25^{th}-75^{th} percentiles), while categorical variables were presented as the number of cases and percentage (%). The intergroup difference in terms of mean age was evaluated with the student's t-test, and those of body mass index and the resected volume were assessed with the Mann Whitney U test. Categorical variables were evaluated using Continuity corrected $\chi 2$, Fisher Freeman Halton, or Fisher's exact probability tests. The combined effects of all possibly effective factors on wound dehiscence were investigated by multivariate logistic regression analysis. Based on univariate statistical analysis, all variables with $P<0.25$ were included in the regression model as candidate factors. In addition, the odds ratio and 95% confidence intervals were calculated for each variable. Data analysis was performed by IBM SPSS Statistics 25.0 (IBM Corporation, Armonk, NY, USA) package program. The results were considered significant when $P<0.05$.

Results

The median age of the patients was 44.3 (12.5) (range: 19-64) years. Their mean body mass index was 26.0 (24.0-27.0) kg/m^2. Thirteen percent had comorbidities, the most common being diabetes mellitus (DM). Among all, 55.4% smoked. The total resected amount was approximately 1200 g (950-1400). Breast reduction was performed leaving the superior medial pedicle in 60.4%, the inferior pedicle in 25%, with the Thorek technique in 5%, and leaving the superior pedicle in 3%. The rate of dehiscence at the T junction was 28.6% (Table 1).

Table 1: Demographic and clinical characteristics of the patients

	n=56
Age (years)*	44.3(12.5)
Age range (years)	19-64
Body mass index (kg/m2) **	26.0 (24.0-27.0)
Concomitant disease	13 (23.2%)
DM	9 (16.1%)
HT	6 (10.7%)
Other	2 (3.6%)
Smoking history	31 (55.4%)
Resection amount **	1200 (950-1400)
Pedicle	
Superomedial	34 (60.7%)
Inferior	14 (25.0%)
Thorek method	5 (8.9%)
Superior	3 (5.4%)
Dehiscence	16 (28.6%)

*Data are presented as mean (standard deviation). ** Descriptive statistics are expressed in median (25^{th}–75^{th} percentile). DM: Diabetes Mellitus, HT: hypertension

The patients with and without T junction dehiscence were similar in terms of mean age, comorbidities (except hypertension), the amount resected, and pedicles used ($P>0.05$). On the other hand, among patients with dehiscence, the mean body mass index, and the incidences of hypertension and smoking were significantly higher ($P=0.011$, $P=0.049$, and $P=0.006$, respectively) (Table 2).

Table 2: Demographic and clinical characteristics of the patients with and without dehiscence

	With Dehiscence (n=40)	Without dehiscence (n=16)	*P*-value
Age (years) *	42.5(12.9)	48.5(10.5)	0.107†
Body Mass Index (kg/m2) **	26.0 (23.0-26.7)	27.0 (25.2-30.7)	0.011‡
Concomitant disease	8 (20.0%)	5 (31.3%)	0.486¶
DM	5 (12.5%)	4 (25.0%)	0.259¶
HT	2 (5.0%)	4 (25.0%)	0.049¶
Other	2 (5.0%)	0 (0.0%)	>0.999¶
Smoking habitus	17 (42.5%)	14 (87.5%)	0.006¥
Resection amount **	1200 (900-1475)	1200 (1125-1337.5)	0.362‡
Pedicle			0.953§
Superomedial	25 (62.5%)	9 (56.3%)	
Inferior	10 (25.0%)	4 (25.0%)	
Thorek method	3 (7.5%)	2 (12.5%)	
Superior	2 (5.0%)	1 (6.2%)	

* Data are presented as mean (standard deviation). Descriptive statistics are expressed in the median (25^{th}–75^{th} percentile). †Student's t-test. ‡ Mann Whitney U test. ¶ Fisher's exact probability test. ¥ Continuity corrected $\chi 2$ test. § Fisher Freeman Halton test. DM: Diabetes Mellitus. HT: Hypertension

The significant predictors of dehiscence were evaluated by multiple logistic regression analysis. Any variable with a p-value of <0.25 in the univariable test was considered a candidate for the multivariable model, along with all variables of known clinical importance. Hypertension was excluded from the model

because when evaluated overall, it did not have a significant or potential effect on dehiscence.

Smoking and increased body mass index were the significant predictors of T junction dehiscence. The history of smoking, for which correction was made, increased the dehiscence risk by 8.543 times (95% Confidence Interval: 1.454-50.213) (P=0.018). The probability of dehiscence also increased with body mass index (odds ratio = 1.419; 95% CI: 1.052-1.913 and P=0.022) (Table 3).

Table 3: The examination of the combined effects of all possible factors on dehiscence using multivariate logistic regression analysis

	Odds ratio	95% confidence interval		*P*-value
		Lower limit	Upper limit	
Age	1.052	0.985	1.123	0.134
Body mass index	1.419	1.052	1.913	0.022
Smoking history	8.543	1.454	50.213	0.018

Discussion

Reduction mammoplasty, an operation with high patient satisfaction, was shown to improve the quality of life by relieving the symptoms of macromastia, such as back pain, headache, and rash [13]. It can be performed by a vertical incision or the wise pattern technique. Although vertical mammoplasty has gained popularity with advantages such as less scarring and longer preservation of projection, the wise pattern method is still the most used [3, 4]. A shorter learning curve, and better control of horizontal and vertical skin excesses, especially in patients with poor skin elasticity, are the advantages of the wise pattern technique [3].

Since breast reduction operations are performed in a relatively young and healthy patient group, complications are usually mild [9]. The most common complication is wound healing disorders [5-9], which are considered minor complications in many studies [3-12]. However, the patient's need for postoperative dressing and prolonged care, as well as the increase in the number of postoperative visits reduce the cost-effectiveness of the operation [14]. Studies report wound healing complication rates of up to 100%, and associate it with smoking, high body mass index [14], and increased resected volume [8].

Wound healing complications occur mostly at the T junction area in wise pattern breast reductions. This is where the medial and lateral flaps meet with the inframammarian sulcus. Its dehiscence was mostly discussed under delayed wound healing complications and not evaluated separately [5-9]. However, in wise pattern reductions, the main problem is superficial or full-thickness skin necrosis due to ischemia in the medial or lateral flaps.

Perfusion problems at the T junction may be related to the operation technique, such as excessive undermining, damage to the subdermal plexus due to excessive traction of the flaps during the operation, and tight closure. However, other factors that may cause dehiscence at the T junction were not specifically investigated.

The patients in this study were middle-aged, relatively healthy, and normal or slightly overweight. The smoking rate was 55.4%. The rate of smoking among women in Turkey is 31.2% [15]. The reason for the high rate of smoking in our study may be due to our evaluation of occasional smokers within the smoker group. Studies show that the adverse effects of one cigarette on skin vascularity and wound healing are minimized after 6 weeks [16, 17]. Therefore, we considered occasional smokers who had smoked within 6 weeks preoperatively as smokers.

According to our study, the factor that has the greatest effect on the dehiscence at the T junction is smoking. In their study examining the effect of smoking on breast reduction operations, Chan et al. [11] reported that problems related to wound healing are increased by 3.5 times in smokers. In similar studies examining the effect of smoking on breast reduction operations, complications related to wound healing were increased most frequently in smokers at similar rates [18, 19]. We found that smoking increases the risk of dehiscence at the T-junction area by 8.5 times. This significant difference observed between the literature and our study may be because we examined the wound healing problems at the T junction area specifically. In this area, the perfusion of the medial and lateral random flaps is the weakest. Nicotine induces endothelial wall damage, inhibits capillary blood flow, and releases catecholamines [19]. The T junction may be where the adverse effects of smoking on vascularity are most pronounced. We showed that wound healing complications caused by smoking are much more common at the T junction, compared to the general wound healing problems. This result confirms that wound healing complications are not delayed healing problems but rather are related to poor perfusion.

In our study, increased body mass index also increased dehiscence risk at the T junction. Studies examining the effects of obesity on complications in breast reduction operations presented different results [20]. A study of 3558 cases by Fishcer et al. [6] found that obesity increases wound healing complications, because of the adverse effects of obesity on myofibroblast activity and collagen maturation. Nizzo et al. [21] emphasized that obesity did not increase the complications related to wound healing in the adolescent population and attributed this to the fact that the young population was not exposed to the chronic effects of obesity compared to the adult population. The breast predominantly comprising fatty tissue with poor vascularity instead of glandular structure with rich vascularity in patients with high body mass index may further weaken the flap perfusion in the T junction area. Different results presented in studies regarding the effect of obesity on wound healing complications can be eliminated by specific studies on T junction dehiscence.

Among our patients, age, resection volume, and comorbidity did not affect T junction dehiscence. Although meta-analyses present different results regarding age, it is a common opinion that increased resection amount and comorbidity increase wound healing complications [6,7,9]. The fact that our study was conducted with a relatively small number of patients (for example, there were 6 patients with hypertension, which is also shown to affect dehiscence), may be the reason for this discrepancy.

T junction dehiscence is more common among smokers and obese patients. This makes it necessary to take additional precautions for T junction dehiscence in planned breast reduction operations among these patients. Some authors require smoking cessation 6 weeks before the operation [18]. Likewise, obese patients may be encouraged to lose weight. However, the

applicability of these recommendations is controversial. Studies on obese patients showed that the quality of life increased after the operation despite minor complications, and breast reduction operations were cost-effective in the obese patient group as well [20]. The use of incisional vacuum therapy reduced delayed wound healing complications that may occur after breast reduction operations [12, 14]. However, few studies are available and their effects on flap perfusion, which is the main cause of T junction problems, are not clear. In our opinion, dermal flap modifications made to reduce tension in the T junction area are quite reasonable [4, 22]. Although there is a need for controlled studies, it is a fact that decreased tension at the T junction will positively affect the perfusion of the lateral and medial flaps. Future studies may focus on the use of local vasodilator agents in flap surgery in this risky patient group to increase flap fusion at the T junction.

Conclusion

Smoking and high body mass index increase the risk of dehiscence at the T junction. High-risk patients must be informed of this complication preoperatively. Additional measures should be planned to increase flap perfusion at the T junction.

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MRI histogram analysis of optic nerves in children with type 1 neurofibromatosis

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Ethics Committee Approval
The study was approved by the Ethics Committee of Fırat University (Issue: E-97132852-050.01.04-49705; Date: 03.06.2021).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Type 1 neurofibromatosis (NF1) is the most common neurocutaneous disease affecting numerous systems. Optic pathway glioma (OPG) is a common tumor in children with NF1 and often has variable clinical presentations. In this study, histogram analysis parameters of optic nerves were measured in the magnetic resonance images (MRI) of children with NF1 and compared with a control group.
Methods: This case-control study consisted of three groups: Ten patients with NF1 without optic pathway glioma (bilateral optic nerve, n: 20), four patients with NF1 with bilateral optic pathway glioma (n: 8), and nineteen healthy controls (n: 38). ROIs were placed on bilateral pre-chiasmatic optic nerves in the images. With histogram analysis, average gray level intensity (mean), the standard deviation, minimum, median, and maximum intensity, uniformity, entropy, kurtosis, variance, skewness, size% M, size% U, size% L, and percentiles were measured.
Results: Mean, median, 3%, 5%, 10%, 25%, and 75% values were higher in NF1 patients with optic pathway glioma (NF1-OPG) than in NF1 patients without optic pathway glioma (NF1-woOPG), and the control group (P<0.001). The same values were significantly higher in the NF1-woOPG group compared to the control group (P<0.001). The minimum, maximum, 1%, 90%, 95%, 97%, and 99% values were significantly higher in the NF1-OPG and NF1-woOPG groups than the control group (P<0.001). The entropy value was significantly higher in the NF1-OPG group than the NF1-woOPG and control groups (5.73, 4.93, and 5.25, respectively, P=0.016).
Conclusion: MRI histogram analysis revealed significant differences between NF1-OPG, NF1-woOPG, and healthy individuals in terms of optic nerves. Thus, we think that it can be used to monitor the optic nerves of children with NF1.

Keywords: Type 1 Neurofibromatosis, Image processing, Magnetic resonance imaging, Optic nerve

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Introduction

Type 1 neurofibromatosis (NF1) is the most common neurocutaneous disease affecting numerous organs. Its prevalence is approximately 1/2500-3000 [1]. Patients with NF1 are predisposed to tumor development, especially in the central nervous system. Pilocytic astrocytoma with low mitotic activity is the most common tumor. These tumors most occur in the optic pathway [2]. Although optic pathway gliomas tend to grow slowly and are mostly benign, their clinical progression varies greatly. The prevalence of OPG in children with NF1 is approximately 15-20%. Almost 30-50% of them become symptomatic and progressive vision loss occurs [3]. Patients are evaluated with intermittent ophthalmic examinations. There may be difficulties in evaluating the visual acuity of young children. Treatments such as chemotherapy, radiotherapy, and surgery are used in patients with reduced visual acuity. Therefore, markers are needed to predict the likely changes in the optic nerves. Imaging findings are not sufficient to evaluate the microscopic and macroscopic structure of the optical pathways or to predict the clinical course [4]. The determination of the microstructural changes of the optic nerves in NF1 may contribute to the estimation of the clinical course in these children and determine follow-up and treatment.

Histogram analysis, one of the texture analysis methods, is widely used for tumor characterization, determination of normal and abnormal tissues, guiding radiotherapy, diagnosing interstitial lung disease, and deciding various prognostic factors [5-9]. The digital medical images consist of units called pixels. Each pixel contains a quantitative value of the gray level density that forms the basis of the image. Histogram analysis enables the calculation of the grayscale levels of all pixels in the region of interest (ROI). Thus, it provides a more detailed evaluation of the structure of tissues compared to the human eye [10].

In this study, we compared the histogram analysis parameters of the optic nerves in the MRIs of children with NF1 with a control group.

Materials and methods

Study population

Approval for this case-control study was obtained from the non-interventional research ethics committee of our university (Date: 27.05.2021, Decision number: 2021/07-22). All pediatric patients diagnosed with NF1 according to the diagnostic criteria whose brain MRIs were performed in our hospital between January 2015 and February 2021 were analyzed [11]. Patients whose brain MRI was performed with a different device and with a different protocol were excluded from the study. Finally, fourteen children (4 patients with bilateral optic glioma) with NF1 were included. Nineteen age- and gender-matching healthy controls with normal visual acuity and neurological examination, and no pathological findings in the brain MRI comprised the control group. The study consisted of three groups: NF1-woOPG, NF1-OPG, and control.

Image acquisition

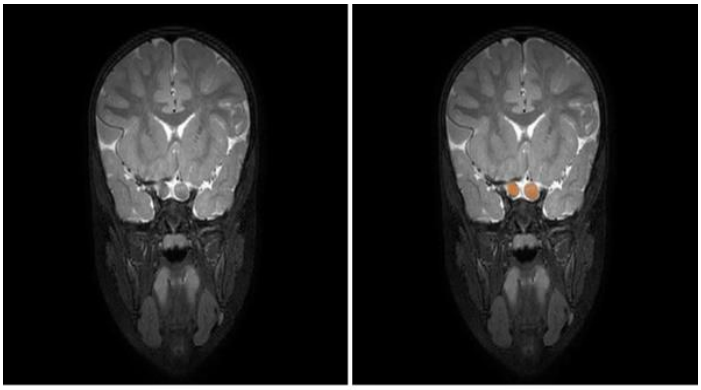
A 3 Tesla (T) scanner was used to obtain the MRI scans of the patients (Philips, Ingenia, Netherlands, 3T). T2-weighted images were obtained in the coronal plane (Repetition time: 2500 ms, time echo: 260 ms, slice thickness: 1 mm, spacing between slices: 0.5 mm).

Image analysis

The histogram yields information about pixels, which are small units of the image [10]. This information contains the mean gray level intensity (mean), median, standard deviation of the histogram, minimum and maximum intensity values, uniformity, kurtosis, entropy, skewness, variance, size %mean, size %upper, size %lower (size% M, size% U, size% L) and percentiles [12-14]. Entropy shows the inhomogeneity of gray level density within the ROI [15]. Uniformity shows the uniform distribution of gray tones in the measured area [16]. Skewness expresses the asymmetry in the distribution of gray tones [16]. Kurtosis is the peak value of the distribution [16].

Images were transmitted to an iMac computer (Apple Inc., 27-inch, Cupertino, CA, USA). Horos Open-Source Medical Image Viewer V.3.3.6 imaging software (Nimble Co LLC d/b/a Purview in Annapolis, MD, USA, and Horosproject.org) was used for histogram analysis in the ROI. An ROI was placed in the bilateral pre-chiasmatic optic nerves in coronal T2-weighted images without exceeding the boundaries (Figure 1).

Figure 1: Coronal T2-weighted MR image (a, b) showed ROI placement on the bilateral optic nerves of a patient with NF1-OPG



The mean gray level intensity, standard deviation, variance, uniformity, entropy, kurtosis, skewness, size% M, size% U, size% L, and percentiles were calculated in the ROI. A program written in MATLAB was used to analyze the images (version R2017a, Natick, MA, MathWorks, USA).

Statistical analysis

The data were expressed in mean (standard deviation). Statistical analysis was performed with the IBM SPSS 25 program. The Kolmogorov-Smirnov test was used to assess the normality of distribution. The Chi-Square test was used to compare the groups in terms of gender. ANOVA and Kruskal-Wallis tests were performed to compare other parameters. $P<0.05$ indicated statistical significance. Receiver-operating characteristic (ROC) analysis was performed to differentiate the significant values of the NF1-OPG group from the control and NF1-woOPG groups.

Results

There were 5 males and 5 females in the NF1-woOPG group, 4 males in the NF1-OPG group, and 12 males and 7 females in the control group. The mean ages of the control, NF1-woOPG, and NF1-OPG groups were 9.37 (4.04) years, 9.30 (3.76) years, and 8.00 (4.96) years, respectively (P=0.683).

The mean, median, 3%, 5%, 10%, 25%, and 75% values were significantly higher in the NF1-OPG group compared to the NF1-woOPG and the control groups, and in the NF1-woOPG group compared to the control group. The minimum, maximum, 1%, 90%, 95%, 97%, and 99% values were significantly higher in the NF1-OPG and NF1-woOPG groups compared to the control group, and similar between the NF1-OPG and the NF1-woOPG groups.

The entropy value was significantly higher in the NF1-OPG group compared to the NF1-woOPG group and the control group, and similar between the NF1-woOPG and the control groups. The other parameters were comparable (Table 1 and 2) (Figure 2).

Table 1: Histogram analysis of optic nerves according to the groups

	Control (38) Mean (SD)	NF1-woOPG (20) Mean (SD)	NF1-OPG (8) Mean (SD)	*P*-value
Age	9.37 (4.04)	9.30 (3.76)	8.00 (4.96)	0.683†
Mean	154.80 (33.20)	215.41 (54.26)	268.70 (87.22)	<0.001†
SD	43.90 (11.72)	54.50 (17.08)	48.14 (13.92)	0.125†
Minimum	81.05 (32.82)	129.40 (57.55)	166.25 (73.07)	<0.001†
Maximum	268.16 (67.95)	363.75 (87.54)	389.38 (63.32)	<0.001*
Median	149.28 (32.52)	210.58 (56.59)	267.13 (93.14)	<0.001†
Variance	2060.54 (1085.45)	3247.14 (2005.36)	2486.64 (1553.81)	0.125†
Entropy	5.25 (0.23)	4.93 (0.51)	5.73 (1.14)	0.016†
Size %L	14.36 (4.68)	14.31 (6.44)	16.16 (3.88)	0.651*
Size %U	15.42 (3.79)	15.66 (4.21)	15.79 (3.45)	0.958*
Size %M	70.22 (6.11)	70.02 (9.63)	68.05 (6.86)	0.752*
Kurtosis	3.32 (1.18)	4.05 (3.06)	3.25 (1.41)	0.588†
Skewness	0.57 (0.62)	0.78 (0.72)	0.18 (0.67)	0.101*
Uniformity	0.23 (0.07)	0.21 (0.09)	0.28 (0.13)	0.325†
1st percentile	81.19 (32.78)	129.45 (57.51)	178.40 (84.05)	<0.001†
3rd percentile	87.97 (31.39)	135.37 (54.88)	186.60 (87.39)	<0.001†
5th percentile	92.96 (30.98)	143.55 (51.42)	194.93 (83.77)	<0.001†
10th percentile	103.71 (31.37)	155.02 (47.76)	207.75 (86.11)	<0.001†
25th percentile	124.83 (31.54)	174.94 (47.63)	234.44 (93.30)	<0.001†
75th percentile	178.24 (35.99)	243.81 (58.03)	303.53 (86.76)	<0.001†
90th percentile	215.44 (44.12)	291.53 (69.05)	331.10 (84.11)	<0.001†
95th percentile	241.33 (57.35)	320.56 (80.21)	348.85 (79.61)	<0.001†
97th percentile	253.00 (63.35)	337.21 (87.62)	362.51 (76.62)	<0.001*
99th percentile	267.40 (67.07)	363.20 (87.63)	376.18 (69.92)	<0.001*

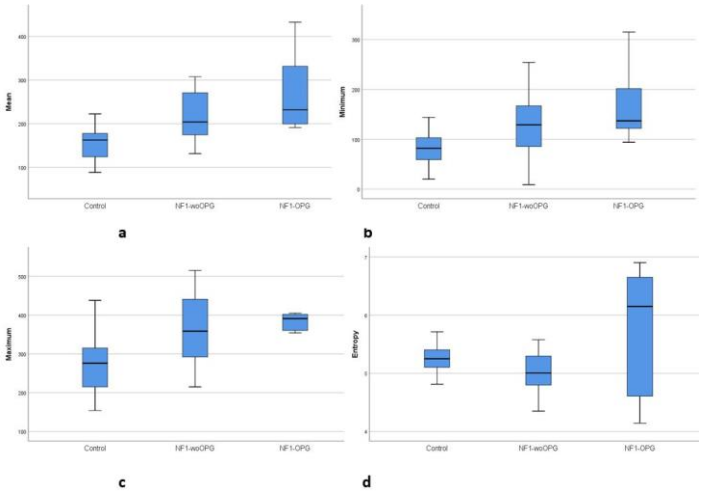
SD: Standard Deviation, * ANOVA Test, † Kruskal-Wallis Test

Table 2: Significantly differing parameters between the groups

	P-value*		
	Control versus NF1-woOPG	Control versus NF1-OPG	NF1-woOPG versus NF1-OPG
Mean	<0.001	<0.001	0.030
Minimum	0.001	<0.001	0.157
Maximum	<0.001	<0.001	0.687
Median	<0.001	<0.001	0.025
Entropy	0.064	0.044	0.001
1st percentile value	0.002	<0.001	0.052
3rd percentile value	0.002	<0.001	0.036
5th percentile value	0.001	<0.001	0.027
10th percentile value	<0.001	<0.001	0.021
25th percentile value	0.001	<0.001	0.010
75th percentile value	<0.001	<0.001	0.019
90th percentile value	<0.001	<0.001	0.241
95th percentile value	<0.001	<0.001	0.580
97th percentile value	<0.001	0.001	0.697
99th percentile value	<0.001	0.001	0.908

* Post Hoc Tukey HSD Test

Figure 2: (a) mean, (b) minimum, (c) maximum and (d) entropy value distributions of groups



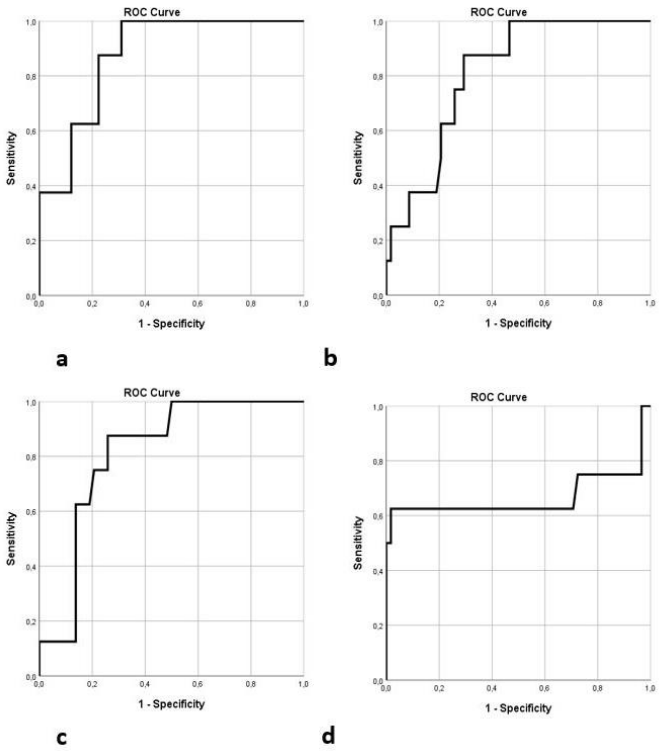
In the ROC analysis for mean value (Figure 3a), when AUC = 0.875 and the threshold=197.27, the NF1-OPG group could be distinguished from the NF1-woOPG and the control groups with 87.5% sensitivity and 77.6% specificity.

In the ROC analysis for minimum value (Figure 3b), when AUC = 0.809 and threshold=114.5, the NF1-OPG group could be distinguished from the NF1-woOPG and the control group with 87.5% sensitivity and 70.7% specificity.

In the ROC analysis for maximum value (Figure 3c), when AUC = 0.813 and threshold=363.5, the NF1-OPG group could be distinguished from the control and the NF1-woOPG groups with 75.0% sensitivity and 79.3% specificity.

In the ROC analysis for entropy value (Figure 3d), when AUC = 0.667 and threshold=5.77, the NF1-OPG group could be distinguished from the NF1-woOPG and the control groups with 62.5% sensitivity and 98.3% specificity.

Figure 3: (a) mean, (b) minimum, (c) maximum and (d) entropy value Receiver-Operating Characteristic (ROC) graphs for distinguishing the NF1-OPG group from the control and NF1-woOPG groups



Discussion

Type 1 Neurofibromatosis is a neurocutaneous disease with high morbidity, affecting many organs and systems [17]. OPG is a common central nervous system tumor in children with NF1 [1]. The clinical course is variable. While some children may experience rapid tumor progression and vision loss, some present with regression despite similar neuroimaging findings. The imaging method primarily used in the diagnosis and follow-up of these tumors is MRI [18]. Neuroimaging findings are not sufficient to evaluate these tumors in terms of microstructural aspects [19, 20]. Prognostic factors are needed to predict the development of OPG and the possible clinical course in these children. A study conducted to evaluate the clinical course of children with OPG reported that the increased mean permeability values in dynamic contrast MRI may suggest aggressive OPG [4]. Another study performed with diffusion-weighted MRI in children with OPG stated that high apparent diffusion coefficient values may be related to the rapid progression of the tumor [21].

Histogram analysis is an increasingly popular method of texture analysis. It provides numerical acquisition of pixel-level differences in areas that the human eye cannot distinguish on images [22]. In the literature, histogram analysis has been used in the detection and classification of brain tumors in numerous diseases such as multiple sclerosis, acute ischemia, Alzheimer's, and tinnitus [23-27]. In a study on multiple sclerosis patients, histogram analysis showed a difference in the structure of the optic nerve compared to the controls [28]. In another study, a difference was found in histogram analysis parameters between the normal optic nerves and the enhanced and non-enhanced optic nerves in patients with optic neuritis [29]. We found significant differences between the optic nerves of the healthy controls and the NF1-woOPG and NF1-OPG children using MRI histogram analysis. In addition, the MRI histogram parameters in the optic nerves that were considered normal in conventional MRI in children with NF1 were found to differ from those of healthy individuals. This may contribute to the evaluation of normal optic nerves with MRI, especially in young children whose visual acuity cannot be measured clearly on ophthalmological examination.

Limitations

This is a retrospective study involving a small patient population. The number of patients with NF1-OPG was sparse. Also, there were not enough patients who underwent imaging with a more easily accessible MR device with a lower Tesla, so patients who underwent MRI with a 3T MR device were included for a more homogeneous analysis. To the best of our knowledge, no previous studies are evaluating the optic nerves of children with NF1 by MRI histogram analysis. We think that our study will be a guide for future studies with larger and homogeneous patient series.

Conclusion

There is a need for markers that will provide insight into the development and progression of OPG in children with NF1. Using MRI histogram analysis, we found significant differences between the optic chiasms of children with NF1-woOPG, NF1-OPG, and healthy children. We think that it is promising that the optic nerves of patients with NF1-woOPG, which appear normal in MRI studies, differ from the optic nerves of healthy individuals in histogram analysis. According to our study, MRI histogram analysis may be a viable option in evaluating optic nerve changes in NF1.

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Journal of Surgery and Medicine

Bilateral talus neck fracture in an 11-year-old patient resulting from a fall from height: A case report

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Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
No conflict of interest was declared by the authors.

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Abstract

We here present an 11-year-old patient with bilateral Hawkins type 3 talus neck fractures resulting from a fall from height. When the patient was brought to the Emergency Department, the ankles were edematous and there were bilateral talus neck fractures with subtalar dislocation. The taluses on both sides were entered with anteromedial and anterolateral incisions, and after an open reduction, the fractures were fixed with one cannulated screw from the anterior and one from the posterior side. No additional edema developed. The patient was followed up for 2 days in the ward, then discharged with outpatient follow up recommendations. Pediatric bilateral talus neck fractures are rare and must be treated immediately.

Keywords: Bilateral talus neck fracture, Pediatric fractures, Trauma

Introduction

Pediatric talus neck fractures are not common, and bilateral fractures are exceedingly rare. These fractures occur because of high energy trauma, and may be accompanied by soft tissue lesions, other bone fractures, and other life-threatening injuries [1].

The talus plays a key role in a considerable proportion of foot and ankle movements. However, intraosseous blood circulation in the talus is insufficient and it is fed extraosseously by vessels originating from the tibialis posterior, peroneal, and dorsalis pedis arteries [2, 3]. The ratio of displacement of the fracture and whether the subtalar-navicular joint is dislocated have significant effects on the blood supply of this bone [4, 5].

Diagnosis is usually made by anteroposterior and lateral x-rays. Computed tomography (CT) can be used to better understand the fracture morphology and the presence of other accompanying bone pathologies.

Talus neck fractures are orthopedic emergencies. While plaster casting may be sufficient for non-displaced type 1 fractures, the treatment for types 2, 3, and 4 fractures is open reduction followed by fixation with compression screws.

Bilateral talus neck fractures are rare in children and require more thorough care than in adult patients.

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Case presentation

Following a fall from height, an 11-year-old boy was brought to the Emergency Department. Both ankles were sensitive, painful, and edematous. Radiographs revealed bilateral Hawkins type 3 talus neck fractures (Figure 1, 2). Following emergency closed reduction of both ankle fractures, placement of splints and elevation, the patient was admitted for emergency surgery.

Open reduction and internal fixation were planned for both ankles. Both lower extremities were prepared, and the operation began on the right side. The talus was reached with anteromedial and anterolateral incisions. Open reduction of the fracture was performed both medially and laterally. For fixation, a screw was advanced from the anteromedial aspect posteriorly, and one screw was advanced percutaneously postero-anteriorly. The left-side ankle was then treated. The fracture line was reached with anteromedial and anterolateral incisions and open reduction was performed; then, the fracture was fixed with two screws. The reductions and fixations were confirmed with fluoroscopy (Figure 3 – 6). The patient was followed up in the ward for two days and no additional edema developed. Informed consent was obtained from the patient's family for scientific presentation.

Figure 1: Preoperative right-side view of the Hawkins type 3 talus fracture (arrow)

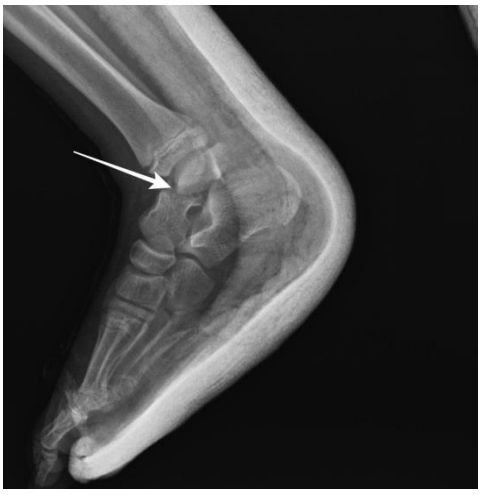


Figure 2: Preoperative left side view of the Hawkins type 3 talus fracture (arrow)

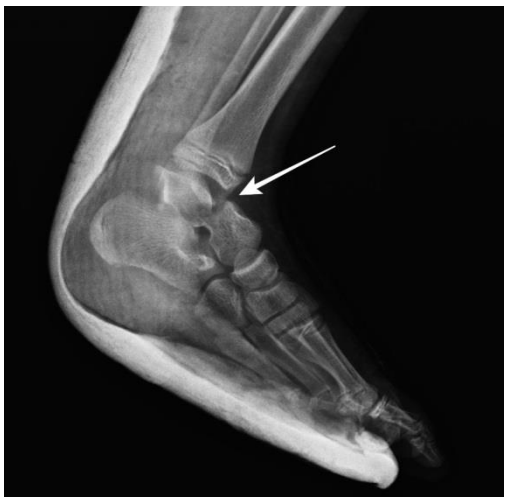


Figure 3: Postoperative right side anteroposterior view

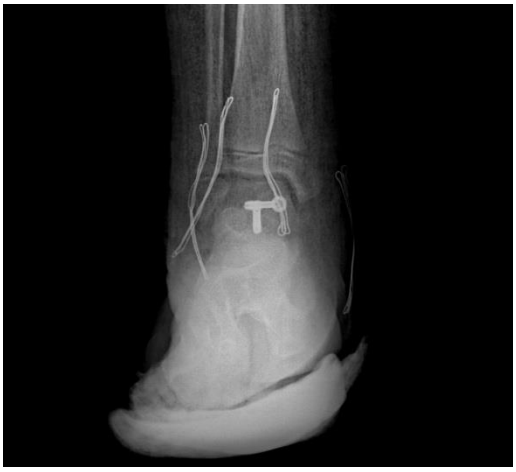


Figure 4: Postoperative right side lateral view

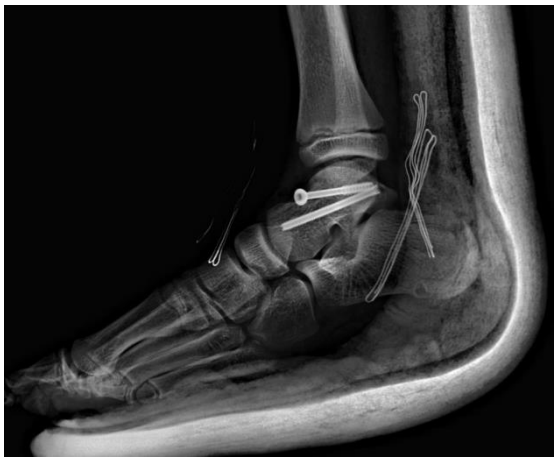


Figure 5: Postoperative left side anteroposterior view

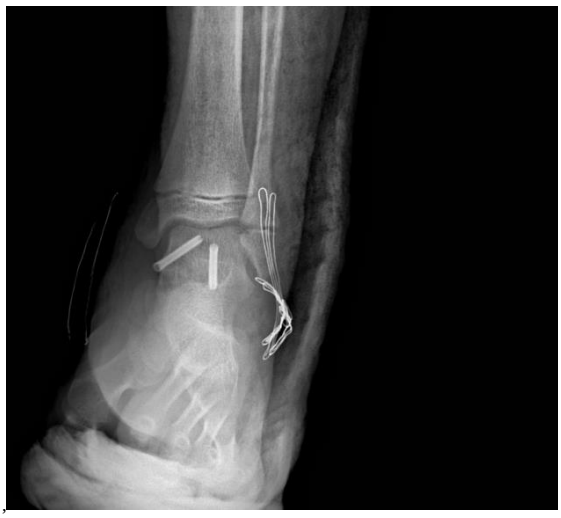
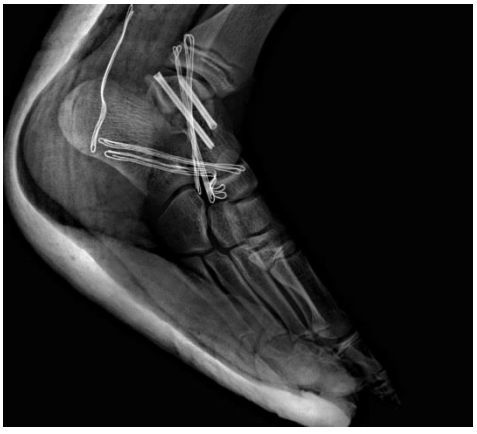


Figure 6: Postoperative left side lateral view



Discussion

Talus neck fractures generally result from axial load bearing while the foot is in dorsiflexion [6, 7]. This mechanism was classified by Hawkins according to the degree of displacement of the fracture.

In 1970, Hawkins [8] published the surgical results of 57 talus fractures of 55 patients. In non-displaced fractures (type 1), there was no avascular necrosis (AVN) and union was obtained in all fractures without problems. In type 2 fractures, which included subtalar joint dislocation, no non-union was observed and AVN was observed at the rate of 42%. In type 3 fractures accompanied by both subtalar and tibiotalar joint dislocation, the rates of non-union and AVN were 11% and 91%, respectively. Due to the high rates of non-union and AVN, talus neck fractures must be treated immediately, and fixation should be performed as anatomically as possible.

Canale and Kelly [9] evaluated the clinical and radiological outcomes of 71 talus neck fractures of 70 patients with a mean 12.7-year follow-up period. There were some type 1 fractures which developed AVN; however, the clinical outcomes of those cases were very good. In type 3 fractures, the clinical results were closely related to subtalar dislocation and the reduction of fracture fragments. The main aims of treatment should be a thorough evaluation of all talus neck fractures, not leaving the joint subluxated after the operation, and obtaining anatomic alignment of all the fracture fragments as much as possible. It should be kept in mind that following fracture union, the clinical results can be good, independent of AVN.

Talus fractures are uncommon in childhood, and bilateral fractures are very rare. To the best of our knowledge, no pediatric bilateral talus fractures were reported in the literature.

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Journal of Surgery and Medicine

Moyamoya disease in a pediatric case: A case report

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Abstract

Moyamoya disease is extremely rare. In children, it is one of the rare causes of ischemic stroke. We present a 4-year-old female patient diagnosed with Magnetic Resonance Imaging (MRI) and Magnetic Resonance Angiography (MRA). In the case with chronic lacunar infarct in the white matter on magnetic resonance imaging, a cigarette smoke image characterized by diffuse collateral vascular networks was observed in MRA imaging. Since it is rare, we think that MRI and MRA imaging is safe and contributes to the diagnosis of the disease in children with mental and motor development retardation.

Keywords: Moyamoya, Magnetic resonance imaging, Lacunar infarct

Introduction

Moyamoya disease can occlude the Willis Polygon and the internal carotid artery. It is a rare cause of ischemic stroke in children [1, 2]. Collateral circulation networks are formed to provide vascularization of the brain due to occlusion. Collaterals, especially at the level of the basal ganglia, are considered to have a cigarette smoke pattern because they have a typical appearance in Magnetic Resonance Angiography (MRA) images. The disease shows a bimodal course in the age of onset, and there are two peaks: At the age of 5 years in children and at the age of 40 years in adults [3]. Moyamoya disease may be associated with other diseases such as neurofibromatosis, Down syndrome and sickle cell anemia. Radiological examinations are very useful in diagnosing this disease. Here, we present a case of a 4-year-old who was diagnosed incidentally by magnetic resonance imaging and magnetic resonance angiography.

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Informed Consent
The authors stated that the written consent was obtained from the parents of the patient presented with images in the study.

Conflict of Interest
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Case presentation

A 4-year-old girl was brought to the emergency room by her family with seizures. She had had seizures before and did not use her left hand much. Physical examination revealed somewhat retarded mental and motor development compared to her peers. No diffusion restriction in favor of acute ischemic infarct was detected in the diffusion Magnetic Resonance Imaging (MRI). In the brain MRI examination, there were sequalae of lacunar infarct in the deep white matter and adjacent to the caudate nucleus body on the right (Figure 1A). Laboratory tests, such as a complete blood count, Protein C-S, fibrinogen, homocysteine, were requested from the patient to reveal coagulation disorders that may cause thrombosis. The results were normal. In the Magnetic Resonance Angiography examination, the cavernous segment of the internal carotid artery was occluded on the right (Figure 1B). Widespread collaterals were also seen at this level and at the basal ganglia levels. On the 3D images, a typical appearance in the form of cigarette smoke, secondary to the collaterals, was observed (Figure 2 A-B). In the light of these findings, we diagnosed the patient with Moyamoya disease. Permission was obtained from the patient's father to publish this case and the MR images.

Figure 1: Cranial MRI imaging A) Sequelae of lacunar infarct area in Flair sequence, adjacent to the caudate nucleus body on the right (red arrow) B) Occlusion in the cavernous segment of the right internal carotid artery in MR Angiography examination (red arrow).

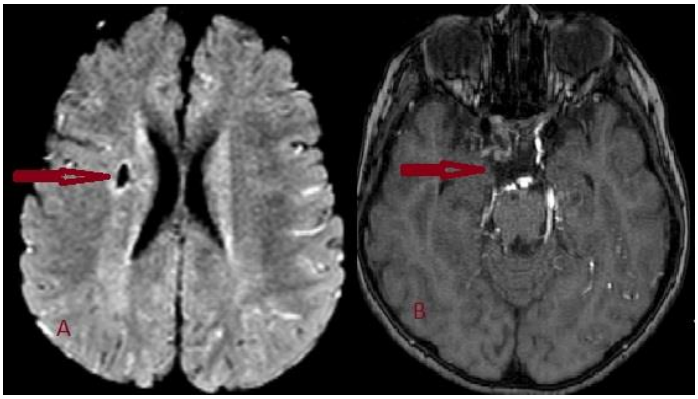
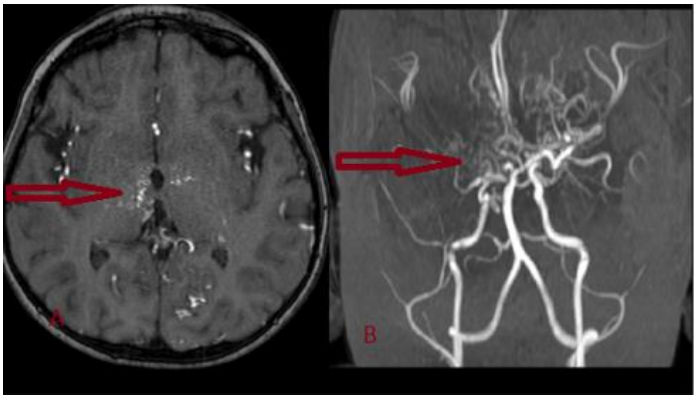


Figure 2: Cranial MR Angiography A) Axial MR Angiography image shows the collateral vascular network at the level of the basal ganglia, more prominent on the right (red arrow) B) 3D MR Angiography image shows typical cigarette smoke appearance characterized by collateral networks (red arrow).



Discussion

The etiopathogenesis of Moyamoya disease is not fully known. However, a genetic predisposition is presumed. The disease is especially common in Japan, and its incidence is higher in families with relatives with the same disease [5]. HLA B 40 antigen is considered suspicious for the disease, especially in those under 10 years of age. In addition, in some studies, fibroblast growth factor was high in the cerebrospinal fluid of these patients [6], which may lead to intimal thickening, smooth muscle proliferation and elastin deposition, causing suprasellar internal carotid artery stenosis. In addition, thinning of the tunica media layer and tortuous changes in the internal elastic lamina are observed [7]. However, since these are pathological findings, there is no data on this in our case. We observed multiple anastomoses in the Willis polygon region on magnetic resonance angiography images. Treatment unfortunately targets the symptoms in the acute phase. Antiepileptic drugs can be used to reduce seizures. In our case, symptomatic treatment was administered, and antiepileptic drugs were not needed. The prognosis of the disease changes with age and course, and the prognosis of the form with epileptic attacks is better than that with infarcts [8]. In our case, the prognosis was poor because of her young age and progression with infarct. MR Angiography examination plays an important role in the early diagnosis and follow-up of the disease and provides an advantage to detect even the smallest stenoses beforehand. In our case, the disease was diagnosed incidentally by Magnetic Resonance Angiography [9].

Conclusion

Moyamoya disease is very rare. Moreover, it does not have typical clinical findings. Therefore, it is usually at the end of the differential diagnosis list of clinicians. However, it has a specific appearance in radiological MR Angiography, which is of great use in diagnosing the disease. In this case, we wanted to draw attention to the importance of radiological imaging by presenting a case that was diagnosed incidentally.

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Journal of Surgery and Medicine

A rare case: A giant right coronary artery aneurysm mimicking a paracardiac mass

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Abstract

Giant coronary artery aneurysms are extremely rare pathologies that can be confused with paracardiac and mediastinal masses, which are usually diagnosed incidentally. In this case report, an 83-year-old patient with a 70x35 mm thrombosed right coronary artery aneurysm misdiagnosed as a paracardiac mass will be discussed in light of the literature.

Keywords: Coronary, Giant, Paracardiac

Introduction

Giant coronary artery aneurysms are extremely rare pathologies. An increase in diameter of at least 1.5 times from the adjacent arterial segment indicates an aneurysm. Coronary artery aneurysms are more common in male patients and in the right coronary artery [1]. Herein, we report an 83-year-old male presenting with a right paracardiac mass, suspected to be a malignant tumor in the emergency department, who was finally diagnosed with a right giant coronary artery aneurysm.

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The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
No conflict of interest was declared by the authors.

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Figure 1: Chest X-Ray revealed a suspicious mass image in the right paracardiac area

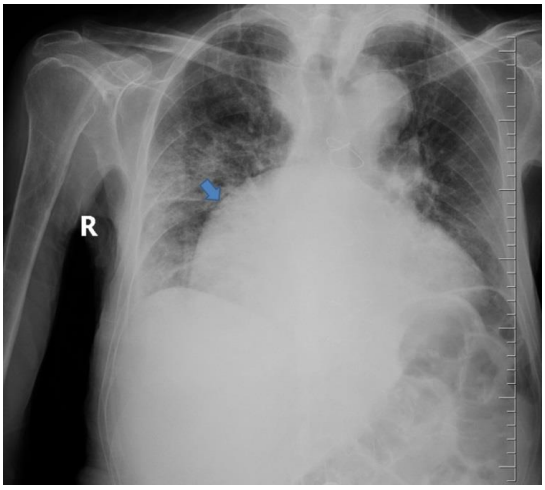


Figure 2: In coronal view, Contrast-enhanced CT angiography revealed a giant coronary artery aneurysm (70x35mm) compressing the right atrium and the right ventricle

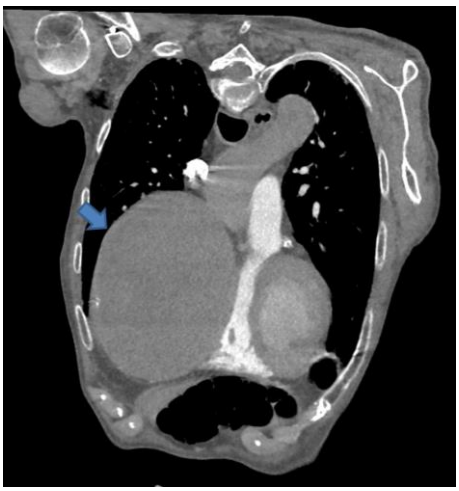


Figure 3: A: Unenhanced Thorax CT revealed a giant coronary artery aneurysm in the axial image -arrow, B: Contrast-enhanced CT angiography revealed a giant coronary artery aneurysm in the right coronary artery in the axial image, and consolidation areas in both images-dashed arrow

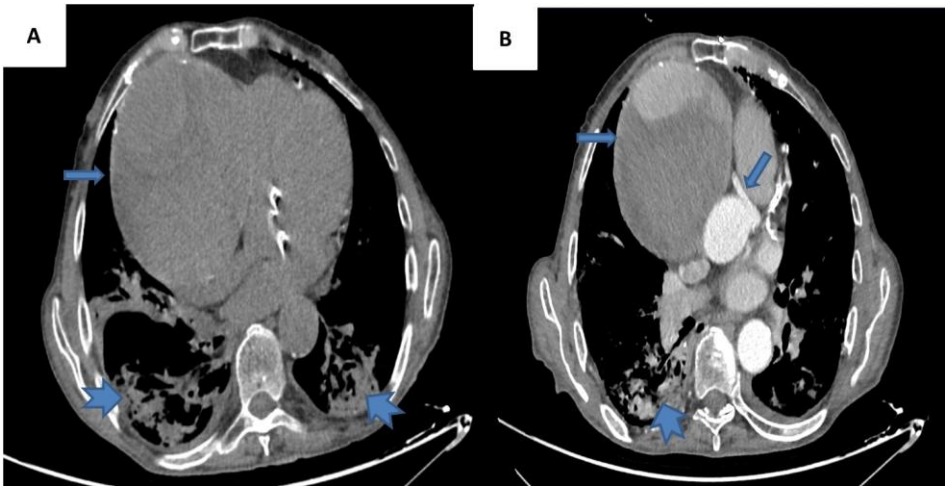
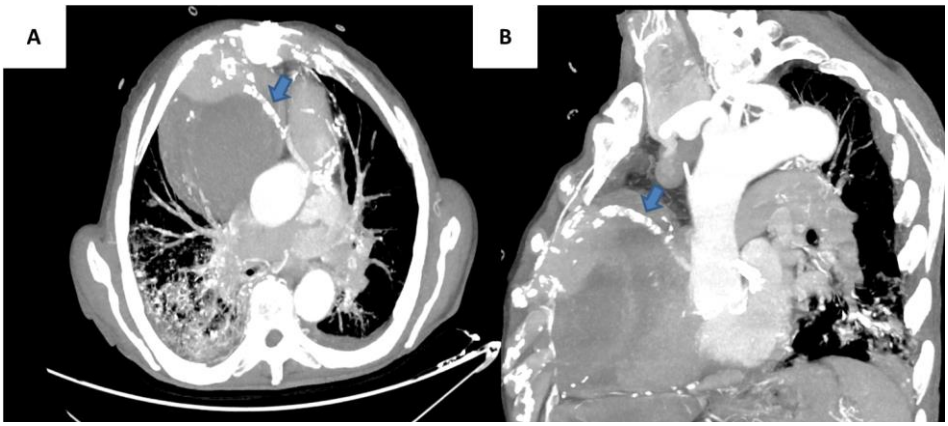


Figure 4: Giant coronary artery aneurysm and right coronary artery in axial MIP image (A) and sagittal MIP image (B) on contrast-enhanced CT angiography



Case presentation

An 83-year-old male patient with hypertension, coronary artery disease, and a previous CABG operation (17 years ago) was admitted to the emergency department of our hospital with complaints of shortness of breath and cough. On physical examination, fine crackles were heard in the basal segments of both lungs, and a lesion with a suspicious mass appearance in the right paracardiac region was observed in the posteroanterior chest radiograph (Figure 1). In the non-contrast thorax computed tomography (CT) obtained with the preliminary diagnosis of pneumonia, a large soft tissue was seen to extend from the right paracardiac area to the right hemithorax, and a CT angiography was performed with the differential diagnosis of a mass or an aneurysm. The lesion, a 70x35 mm giant right coronary artery aneurysm, showed contrast filling in the arterial phase, but was mostly thrombosed (Figures 2, 3, 4). Echocardiography revealed an aneurysmatic dilatation compressing the right atrium more than the ventricle, and there was no gradient increase or flow alternans. No hypotension was observed during patient follow-up. Due to the patient's age and comorbidities, additional surgical intervention was not considered, and he was followed up with recommendations.

Discussion

Coronary artery aneurysm was first described by Charles Bougon in 1812 [2]. Today, coronary artery aneurysms (CAA) refer to a dilated vascular structure that increases at least 1.5 times in size compared to the adjacent arterial segment [3]. The giant CAA incidence ranges between 0.02-2% [4]. The diameter limit for giant aneurysms is controversial in the literature, and the most commonly accepted limit for adults is ≥2 cm [5].

The common feature of CAAs is congenital or acquired weakening of the vascular wall structure and secondary dilatation [6]. In pathological examinations, thinning in the media layer of the vascular wall is typical [7]. It is examined in three main categories according to the pathogenesis of CAA, as follows: Atherosclerosis, and inflammatory and non-inflammatory processes. While the most common cause in adulthood is atherosclerosis, the most common cause in children is Kawasaki disease [9].

Our patient had no underlying vasculitis, collagen tissue disease, or infectious processes and no family history. He underwent CABG 17 years ago due to occlusion in four vessels, and no aneurysm was detected in his routine follow-up. Damage to the vascular wall secondary to the previous operation and chronic atherosclerosis process may be the underlying factors.

Atherosclerosis is the most common predisposing factor for CAA, it is more common in males, generally seen in the 7th decade and at an older age compared to other factors [10]. Atherosclerotic aneurysm patients are generally asymptomatic. Whether the presence of CAA is an independent risk factor for death in these patients is still controversial [10, 11]. Although most patients are asymptomatic and diagnosed incidentally, serious complications such as angina pectoris, sudden death, fistulae, pericardial tamponade, compression of the surrounding vascular structures, or congestive heart failure can be observed in the patients with CAA [12].

ECG-triggered CT angiography, MR/MR angiography, transthoracic echocardiography and cardiac angiographic catheterization are used for diagnosis. The structure and shape of the aneurysm, its morphological features, aneurysm diameter, wall calcification, luminal stenosis, and the presence of significant stenosis in other coronary arteries should be assessed. Differential diagnoses include sinus Valsalva aneurysms, venous grafts, and pathologies originating from the heart, pericardium, and mediastinum [13].

A surgical approach is frequently recommended for giant CAAs. Its treatment includes aneurysm ligation and distal bypass grafting, isolated coronary artery bypass grafting, aneurysm plication and patching with the saphenous vein. Invasive procedures cannot be performed on certain patients due to comorbidities. Antiplatelet and antithrombotic therapy were recommended to prevent the formation of an intact thrombus and distal embolization in patients who cannot undergo surgery [14].

Nowadays, less invasive percutaneous treatments have come to the fore on selected patients. Especially Polytetrafluoroethylene (PTFE) coated stents were used for this purpose and have proven successful in some patient groups. However, more comprehensive studies are required regarding the long-term results [15].

Conclusion

Giant coronary artery aneurysms are extremely rare pathologies that can be confused with mediastinal and cardiac masses. The correct diagnosis is very important to avoid severe complications of a biopsy, such as catastrophic bleeding. For this reason, CT and CT angiography play a key role in its diagnosis.

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Journal of Surgery and Medicine

Hydronephrosis due to bladder carcinoma

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Abstract

Giant hydronephrosis is a rare entity that most often develops due to obstruction at the ureteropelvic junction. The other etiologic factors include bladder and ureter tumors. Giant hydronephrosis can cause long-term complications such as hypertension, renal failure, rupture of the kidney, and malignant change if left undiagnosed or diagnosed late. A 73-year-old male patient was admitted to the hospital with complaints of difficulty in urination and brown colored urine. The patient's hemoglobin and hematocrit levels were low. Radiologically, there was widespread cystic development in the right kidney, a giant hydronephrosis, and a mass in the bladder. In the surgical material sent after the diagnosis of urothelial carcinoma by bladder biopsy, there was urothelial carcinoma in the bladder and right ureter. Since hydronephrosis may develop due to bladder and ureter tumors, which may result in nephrectomy, the early diagnosis of these tumors will reduce such serious complications. The early diagnosis and treatment of a giant hydronephrosis will increase the patient's quality of life by minimizing complications such as hypertension, kidney failure, and kidney rupture.

Keywords: Bladder, Kidney, Carcinoma, Hydronephrosis

Introduction

Hydronephrosis is defined as the enlargement of the pelvicalyceal system due to obstruction and stasis of urinary flow [1]. Congenital ureteropelvic junction obstruction is the most common cause of giant hydronephrosis in children and adults [2, 3]. A rare cause of hydronephrosis is bladder and ureter cancer [4, 5]. Giant hydronephrosis is defined as a kidney containing more than 1000 ml of urine in the renal collection system [6]. It has been also defined as a kidney that holds more than 1.6% of the body fluid in the renal collecting system [7]. In our patient, the hydronephrotic kidney was 21x10 cm in size. We aimed to contribute to the literature with this rare case.

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Informed Consent
The authors stated that the written consent was obtained from the patient presented with images in the study.

Conflict of Interest
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Case presentation

Written informed consent was obtained from the patient. A 73-year-old male patient was admitted to the hospital with complaints of difficulty in urination and brown-colored urine. The patient's hemoglobin and hematocrit levels were low. Radiologically, there was widespread cystic development in the right kidney, a mass in the bladder, and a mass in the lower part of the right ureter.

In the macroscopic examination of the nephroureterosistoprostatectomy material sent to the pathology laboratory, the right kidney was cystic, 21x14x9 cm in size. The distal ureter was 3.5 cm in diameter and there was a mass in the bladder (Figure 1). Approximately 1500 cc of brown-colored fluid was drained. The parenchyma of the kidney had almost completely disappeared. The wall of the cyst was 0.1 cm in the thinnest part and 0.5 cm in the calyceal area where it was the thickest. There was chronic pyelonephritis in the cyst wall (Figure 2). There was a mass containing papillary structures that almost filled the bladder. There was also a papillary tumoral mass narrowing the lumen in the distal ureter. Paraffin blocks were prepared from tissue samples taken from tumoral masses in the bladder and ureter. Four-micron sections taken from tissue samples were stained with hematoxylin and eosin. Histopathological examination revealed a papillary high-grade invasive urothelial carcinoma in both the bladder and the ureter. Hydronephrosis of the right kidney was considered secondary to a malignant tumor in the bladder and right ureter.

Figure 1: Giant hydronephrosis in the right kidney (left), a mass in the ureter, and a mass in the bladder

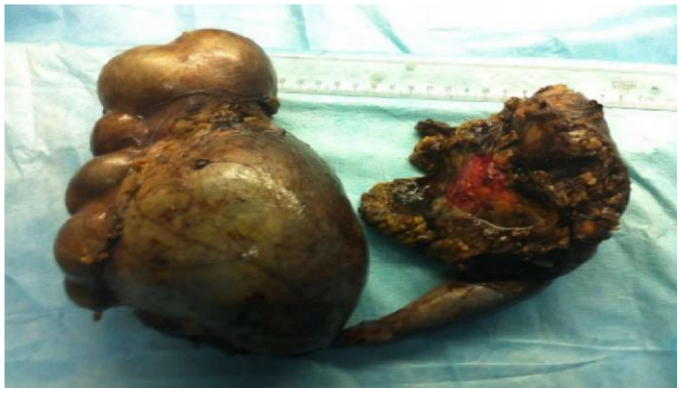
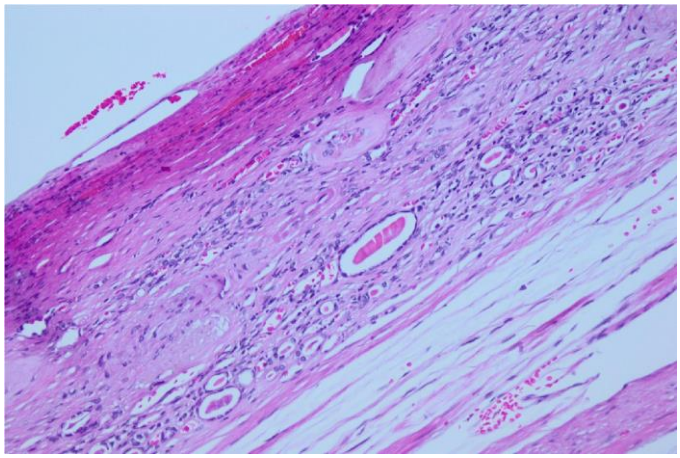


Figure 2: Chronic pyelonephritis findings in the cyst wall of the hydronephrotic kidney



Discussion

Hydronephrosis is the enlargement of the pelvicalyceal system due to blockage and stasis of urine flow [1]. While giant hydronephrosis is frequently encountered in developing countries, it is rare in developed countries [8]. So far, only around 500 cases of giant hydronephrosis were reported in the literature [2]. The incidence of hydronephrosis due to bladder carcinoma ranges between 7.2-54.1% in the literature [9]. The number of tumor cases causing hydronephrosis was 9 in a study of 100 patients performed by Ilgi et al. [5]. Of these 9 cases, 7 were in the ureter and 2 were in the bladder.

The patient usually remains asymptomatic until late due to the slow progression of the disease [10]. The most common symptom of giant hydronephrosis is an abdominal mass. Less common symptoms are flank pain, hematuria, fever, acute abdominal pain, and recurrent urinary tract infections [10-12]. Rare symptoms are intestinal obstruction, respiratory distress, hypertension, pedal edema, obstructive jaundice, and contralateral ureteropelvic junction obstruction [13].

Giant hydronephrosis can cause long-term complications such as hypertension, renal failure, rupture of the kidney, and malignant transformation if left undiagnosed or diagnosed late. Difficulties in treatment will also increase over time due to the delay in diagnosis [8].

Conclusion

Since hydronephrosis may develop due to bladder and ureter tumors, which may result in a nephrectomy, the early diagnosis of these tumors will reduce such serious complications. The early diagnosis and treatment of a giant hydronephrosis will increase the patient's quality of life by minimizing complications such as hypertension, kidney failure, and kidney rupture.

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Journal of Surgery and Medicine

Re: A case of acute renal failure requiring emergency hemodialysis due to hypothermia-associated rhabdomyolysis

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Abstract

We have read the article titled “A case of acute renal failure requiring emergency hemodialysis due to hypothermia-associated rhabdomyolysis” published by Vural et al. with great interest. Acute renal failure is an uncommon diagnosis in patients presenting to the emergency department, and rhabdomyolysis is a relatively rare cause. The etiologic factors for rhabdomyolysis may be classified as hereditary and acquired (traumatic, and non-traumatic) causes. We thank the authors for this informative and successful case presentation. In this letter we also would like to mention a few important points and present an interesting phenomenon that we encountered.

Keywords: Emergency, Hemodialysis, Hypothermia, Rhabdomyolysis, Renal failure

Dear Editor,

We have read the article titled “A case of acute renal failure requiring emergency hemodialysis due to hypothermia-associated rhabdomyolysis” published by Vural et al. with great interest [1]. Acute renal failure is an uncommon diagnosis in patients presenting to the emergency department, and rhabdomyolysis is a relatively rare cause. The etiologic factors for rhabdomyolysis may be classified as hereditary and acquired (traumatic, and non-traumatic) causes [2]. We thank the authors for this informative and successful case presentation. We also would like to mention a few important points and present an interesting phenomenon that we encountered.

Muszkat et al. [3] investigated mortality-related factors in sixty-seven geriatric hypothermia patients who were similar to Vural et al.’s [1] case. They grouped the patients with and without creatine kinase values greater than 300 U/L. While high creatine kinase value was associated with mortality in the univariant analysis, this relationship could not be demonstrated in the multivariate analysis, which revealed that only coma and high potassium level at admission were associated with mortality. They reported that 26.8% of the patients had a creatine kinase value above 300 U/L, all of which were exposed to trauma. However, Muszkat et al. [3] did not share the patients' mean or median creatine kinase values.

On the other hand, the 2021 Resuscitation Guidelines, published by the European Resuscitation Council, recommend targeted temperature management for adults with return of spontaneous circulation in coma (with any initial rhythm) after out-of-hospital or in-hospital cardiac arrest. They suggest that a constant target temperature of 32°C to 36°C is maintained for at least 24 hours [4]. However, Ciapetti et al. [5] presented a case of therapeutic hypothermia-associated rhabdomyolysis.

We believe that hypothermia-related rhabdomyolysis cases, which Varol et al. [1] defined, will increase even more with the widespread use of therapeutic hypothermia. Emergency medicine specialists and anesthesiologists should be alert for hypothermia-associated rhabdomyolysis, especially in patients who received therapeutic hypothermia.

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Ethics Committee Approval
The letter is not a study with human participants. There are no experiments on animals. This letter does not contain any studies on human participants or animals performed by the author. There is no identifying information of participants.

Conflict of Interest
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