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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Analysis of Tibial Fractures and Treatment After Trauma in Pregnant Women

Gebelerde Travmaya Bağlı Tibia Kırıklarının Analizi

Ali Erkan Yenigul[1], Nefise Nazli Yenigul[2]

[1]Sanlıurfa Training and Research Hospital, Department of Orthopedics and Traumatology; [2]University of Health Sciences School of Medicine Sanlıurfa Mehmet Akif Inan Research and Training Hospital, Department of Obstetrics and Gynecology, Sanlıurfa, Turkey

ABSTRACT

Aim: *Our hospital has the most comprehensive obstetrics clinic in our province, and the treatment of pregnant women with trauma is performed intensively in our hospital. In this study, we aimed to evaluate pregnant women with tibial fractures, the treatment of these pregnant women, and their maternal and fetal health outcomes.*

Material and Method: *This study was conducted as a retrospective trial between January 2017 and October 2019. Pregnant women with tibia fractures who were operated on in our hospital were included. Their demographic features, data during surgery, and maternal-fetal outcomes were analyzed.*

Results: *Eleven patients who met the study criteria were identified. Two patients had a tibia fracture after a traffic accident, and the other nine patients had a tibia fracture after a fall. None of the eleven pregnant women who underwent surgical treatment for tibial fractures had pregnancy complications due to trauma or orthopedic surgery.*

Conclusion: *Posttraumatic non-obstetric surgery conditions in pregnant patients can be managed with a multidisciplinary approach and an experienced team by reducing the complication rate. Our study shows that tibial fracture operations in pregnant patients can be successfully treated with a professional team before maternal/fetal mortality and morbidity develops.*

Key words: *pregnancy; tibia fracture; surgery in pregnant women*

ÖZET

Amaç: *Bizim hastanemiz ilimizdeki en kapsamlı kadın hastalıkları ve doğum kliniğine sahiptir ve travmalı gebelerin tedavisi hastanemizde yoğun bir şekilde yapılmaktadır. Bu yüzden bu çalışmada özellikle tibia kırığı olan gebeleri, bu gebelerin tedavisini ve anne bebek sağlığı açısından sonuçlarını değerlendirmeyi amaçladık.*

Materyal ve Metot: *Bu çalışma Ocak 2017 ile Ekim 2019 arasında retrospektif olarak planlandı. Hastanemizde travma sonrası tibia kırığı olan ve ameliyat edilen gebe hastalar dahil edildi. Hastaların demografik özellikleri, ameliyat sırasındaki verileri ve maternal-fetal sonuçları analiz edildi.*

Bulgular: *Çalışma kriterlerine uyan onbir gebe tespit edildi. Hastalardan ikisinde araç içi trafik kazası sonrası tibia kırığı olurken diğer dokuz hastada düşme sonrası tibia kırığı olduğu saptandı. Tibia kırığı nedeniyle cerrahi tedavi uygulanan onbir gebenin hiçbirinde travma veya ortopedik ameliyat nedenli gebelik komplikasyonu tespit edilmedi.*

Sonuç: *Gebe hastalarda travma sonrası non-obstetrik nedenli ameliyat durumları multidisipliner bir yaklaşım ve deneyimli bir ekip ile komplikasyon oranı çok azaltılarak yönetilebilir. Çalışmamızda gösteriyor ki gebe hastalarda tibia kırığı nedenli ameliyatlar maternal/fetalmortalite ve morbidite gelişmeden deneyimli bir ekiple başarılı şekilde tedavi edilebilir.*

Anahtar kelimeler: *gebelik; tibia kırığı; gebelerde operasyon*

Introduction

Trauma affects 7 %of all pregnancies and eqıires admission in 4 of 1000[1]. It has been shown to complicate up to 8 %of all pregnancies[2]. It's mostly seen as falls, in-vehicle, or out-of-vehicle traffic accidents in pregnant women. Depending on the severity of the trauma, the maternal or fetal status may be negatively affected. Posttraumatic fractures are more difficult to treat in pregnant women due to anatomical and physiological changes. There are often case presentations in the literature on trauma in pregnant women, and there are no studies or analyses involving many patients. In addition, there is no case series showing the surgical treatment of pregnant women with isolated tibial fractures and how the mother and baby are affected after this surgery. Our hospital has the most comprehensive obstetrics clinic in our province, and the treatment of

İletişim/Contact: *Ali Erkan Yenigül, Sanlıurfa Training and Research Hospital, Department of Orthopedics and Traumatology, Sanlıurfa, Turkey* • ***Tel:*** *0505 825 46 19* • ***E-mail:*** *alierkanyenigul@hotmail.com* • ***Geliş/Received:*** *09.06.2022* • ***Kabul/Accepted:*** *23.02.2022*

ORCID: *Ali Erkan Yenigül, 0000-0002-2690-9488* • *Nefise Nazlı Yenigül, 0000-0003-3365-8899*

pregnant women with trauma is performed intensively in our hospital. Therefore, in this study, we aimed to evaluate pregnant women with tibial fractures, the treatment of these pregnant women, and their maternal and fetal health outcomes.

Material and Methods

This study was conducted as a retrospective trial in the Sanlıurfa Research and Training Hospital between January 2017 and October 2019. Pregnant women with tibia fractures who were operated on in our hospital were analyzed. The University ethics committee approved this study protocol (No: 19/07/08). It was made according to Helsinki Declaration. Informed consent was obtained from all participants.

Inclusion criteria were; pregnant women aged 18–40 years who were admitted to our orthopedics and traumatology clinic after trauma and operated on for tibial fractures due to trauma. Patients whose medical information and radiographs could not be reached, whose fracture location on tibia radiographs were not clear, tibial radiographs could not be taken correctly, patients who had begun treatment in another hospital after trauma, who had surgery or who applied to our hospital and refused the treatment we recommended were excluded from the study. The patients were evaluated firstly in the emergency department, then by an orthopedist and obstetrician. The participants diagnosed were admitted to the orthopedic clinic for operation. The obstetricians performed preoperative and postoperative obstetric recommendations.

The tibial fracture classification was performed by X-ray according to AO (Arbeitsgemeinschaftf¨urOste osynthesefragen) classification system. Although there are different classifications of tibial fractures, similar studies in the literature have used the AO classification. For these reasons, we preferred to use the AO classification. The extremity fractures after trauma were grouped as right and left. The operation was determined as plate screw or intramedullary nailing according to the selected implant. Spinal anesthesia was preferred for surgeries. The anesthetic application time was calculated on the anesthesia form in pregnant women. The operation time was kept as short as possible to reduce the side effects and complications related to anesthesia. Lead aprons were used in the operating room to protect the pregnant woman from radiation and tried to get as few X-rays as possible. The number of X-rays taken perioperatively was checked from the recording unit on the scope device. Antibiotic cephalosporin derivatives of pregnancy category B and paracetamol were used as analgesics.

Patient information system and radiology archive were used to examine patient clinical information and radiographic; maternal age, parity, type of trauma, tibial fracture classification, fracture side, type of surgery, type of anesthesia, duration of surgery, number of X-rays, gestational week of fracture, mode of delivery, obstetric complications if any, meconium at birth were recorded.

After the surgery, control x-rays were taken in the protected x-ray room, after protective measures were taken for the baby and the mother. Gestational age was calculated using the first day of the last menstrual period (LMP) and confirmed by the first trimester or early second-trimester ultrasonography.

Results

Of the 573 patients with tibial fractures who were referred to our hospital for post-traumatic surgery on the dates indicated, 19 were pregnant. Five patients were treated at another health center. Radiographs of the remaining two patients could not be reached. One of the pregnant women gave birth in an external center and could not be accessed. Eleven patients who met the study criteria were identified. The mean age of the pregnant women was 26 (20–37), the mean parity was 4 (1–7), and the mean gestational week was 24 (4–30) weeks. Table 1 shows the demographic and clinical outcomes of the patients included in the study.

Two patients had a tibia fracture after a traffic accident, and the other nine patients had a tibia fracture after a fall. Tibia fracture classification according to AO classification, the fracture types of patients were respectively 42. A1/4F. 2A, 42. B2/4F. 2B, 42. A2, 43. A1, 43. A1, 43. B3, 41. C2/4F. 2A, 42. A2,43. B3.1.43. A1.2.42. B2, 4F2B (Table 1). Four patients had right tibia fractures and seven left tibia fractures. Six of the eleven tibial fractures were accompanied by fibula fractures. Intramedullary nailing was performed in two of eleven pregnant women with tibial fractures, and osteosynthesis was performed with plate and screw in the other patients. In Figure 1, an example of treatments with intramedullary nailing and plate-screw are given in postoperative x-rays. The mean operation time was 70 minutes (62–81 minutes), and the mean number of X-rays was 9 (6–14).

Table 1. *Demographic and clinical characteristics of pregnant patient with a tibia fracture*

Case no	Age	Parity	GAD (weeks)	Trauma	Classification	Side	OP	Time of operation	X-ray (n)	Anesthesia	Mode of delivery	Pregnancy complications	MAS
1	26	5	28	Fall	42.A1, 4F.2A	Right	Plate	62	6	Spinal	VD	None	None
2	28	4	29	Fall	42.B2, 4F.2B	Left	Nail	70	10	Spinal	C/S	None	None
3	37	7	28	Fall	42.A2	Left	Plate	75	6	Spinal	VD	None	None
4	20	1	29	Accident	43.A1.2	Left	Plate	50	8	Spinal	C/S	None	None
5	24	3	26	Fall	43.A1.2	Right	Plate	78	7	Spinal	VD	None	None
6	20	3	30	Fall	43.B3.1	Right	Plate	80	11	Spinal	VD	None	None
7	32	6	4	Fall	41.C2, 4F.2A	Left	Plate	81	9	General	C/S	None	None
8	29	4	27	Accident	42.A2	Left	Plate	72	14	Spinal	VD	None	None
9	22	6	26	Fall	43.B3.1	Right	Plate	68	8	Spinal	C/S	None	None
10	31	2	24	Fall	43.A1.2	Left	Plate	65	12	Spinal	VD	None	None
11	22	4	20	Fall	42.B2, 4F.2B	Left	Nail	75	9	Spinal	C/S	None	None

GAD: Gestational age at delivery, OP: Operation type, MAS: Meconium-stained Amniotic fluid, VD: Vaginaldelivery, C/S: Sectio

Figure 1. *Intramedullary nailing and plate-screwin postoperative x-rays.*

Six pregnancies were usually delivered, and five pregnancies were delivered by cesarean section for non-traumatic reasons. The indication for cesarean section was obstetric in all five patients. None of the babies had meconium in the amniotic fluid at birth. None of the eleven pregnant women who underwent surgical treatment for tibial fractures had pregnancy complications due to trauma or orthopedic surgery.

Discussion

We found that the etiology of traumatic tibial fractures in pregnant women in our hospital was primarily due to falls. Although the fracture types were various, most were treated with osteosynthesis with plate and screw. In addition, the treatment processes of these fractures did not negatively affect maternal and fetal outcomes.

The aim of treating post-traumatic injuries during pregnancy is to reduce the morbidity and mortality of the mother and the baby. When this situation is encountered, it should be remembered that the most important thing is to treat the mother. The evaluation of trauma in pregnant women should be done with a multidisciplinary approach with many physicians in adult branches[3]. Most postoperative traumatic orthopedic

injuries are treated conservatively (splint, plaster, bandage, and medical treatments) without any operation. Conservative treatment is the primary treatment option for orthopedic traumas in pregnant women. Still, emergency surgery should be performed on open fractures, circulatory problems, and fractures that require open reduction. While elective operations can be postponed in pregnant women, there is no contraindication for performing emergency orthopedic operations[11].

The operation may be necessary for long bone fractures such as tibia, femur, and humerus. In these patients, maternal and fetal health should be evaluated simultaneously; surgical methods appropriate for a gestational week should be preferred and followed by an experienced physician team. Fracture of the tibia is the most common long bone fracture, and tibia fracture is generally associated with fibula fracture[4]. When we analyzed the classification in our study, we observed that fibula fracture was accompanied in six patients.

Just over half of trauma during pregnancy occurs in the third trimester. In our study, except for one patient, the others were in the second and third trimesters. The rate of adverse effects on fetus health after radiation exposure is related to gestational week[5]. 8–15 gestational weeks of the central nervous system are affected. Studies have not reported any teratogenicity in radiation exposure of less than ten rads[1]. Developmental retardation, microcephaly, and mental retardation can be seen in high-dose radiation exposure in the fetus. ACOG (The American College of Obstetricians and Gynecologists) did not report fetal death and birth deformity at 5 rad and below exposures[6]. In our study, the abdomen and pelvis of all operated on pregnant women were covered with lead vests. A small number of control radiographs were performed to reduce radiation exposure. The average number of scopies taken is nine, and the extremity x-ray (average 200 mini rad) rad value does not exceed 5 Rads in total. Due to this, the total radiations of the radiographs taken during surgery were below the risk values.

Anesthetic drugs affect cell signaling, mitosis, DNA synthesis, cellular differentiation, and organogenesis[7]. There is no optimal anesthetic technique for all general anesthetic drugs across the placenta. Therefore regional anesthesia should be preferred to minimize fetal exposure to anesthetic agents. Spinal anesthesia could not be performed on one of the pregnant women in our study because she had a lumbar vertebra fracture after trauma. The other ten patients underwent spinal anesthesia to minimize radiation exposure to the pregnant and fetus. In addition, the mother's vital values may be monitored during the operation period, and fetal monitoring may be necessary[8]. The patient can be positioned on a backboard with a 15 tilt to relieve vena cava compression. Preoperatively and postoperative obstetrics evaluated pregnant women, and enoxaparin sodium 0,4 ml was administered to all patients to prevent deep vein thrombosis and embolism. In our study, doppler or NST (Non-Stress Test) follow-up was not required during the operation since our operation time was not long.

In the study performed by El-Kady et al.[9], it was stated that traumas during pregnancy would have poor perinatal outcomes and would increase maternal mortality and morbidity. Ali Jameel et al.[10] reported that fetal mortality might increase to 65 %after trauma. In contrast to the literature in our study, it was found that the conditions that we identified as post-traumatic complications were not present in pregnant women. No disorders were leading to maternal or fetal death or preterm birth. This may be due to minor traumas in pregnant women, or there was a team of experienced obstetricians.

Moreover, we included only patients with tibia fractures who were regularly operated on and followed up. Other long bone fractures may be associated with obstetric complications. In this case, our inclusion criteria may have affected this outcome.

Among the strengths of the present study was that the tibial fractures caused by trauma in pregnant women were the first case series in the literature. Nevertheless, our study has some limitations. First, its design was retrospective. Therefore determination of perinatal clinical features is limited. Second, as we are the hospital with the highest number of births in the country, there may be limitations in obtaining some records and patients who cannot be included in the study.

Posttraumatic non-obstetric surgery conditions in pregnant patients can be managed with a multidisciplinary approach and an experienced team by reducing the complication rate. Our study shows that tibia fracture operations in pregnant women can be successfully treated with a professional team before maternal/fetal mortality and morbidity develops. More extensive studies are needed to investigate fractures in different bones to clarify other long bone fractures in pregnancies.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

The Effects of *Allium Czelghauricum* (Liliaceae), *Lathyrus Karsianus* (Fabaceae) and *Onosma Nigricaule* (Boraginaceae) Extracts on Oxidation Parameters in Malathion Treated Mice

Malatiyon Verilen Farelerde Oksidasyon Parametreleri Üzerine Allium Czelghauricum (Liliaceae), Lathyrus Karsianus (Fabaceae) ve Onosma Nigricaule (Boraginaceae)'den Elde Edilen Ekstraktların Etkileri

Dincer Erdag[1], Abdullah Dogan[2]

[1]Department of Medical Services and Techniques, Atatürk Vocational School of Health Services; [2]Department of Pharmacology and Toxicology, Faculty of Veterinary Medicine, Kafkas University, Kars, Turkey

ABSTRACT

Aim: *It was aimed to determine antioxidant properties of extracts obtained from Allium czelghauricum, Lathyrus karsianus and Onosma nigricaule species and antioxidant effects of plant extracts on malathion-induced oxidant parameters in mice.*

Material and Method: *Expermental animals were seperated into ten groups, each consisting of ten mice. First group was designed as a control group. Second group received 0.2 mL/kg of saline, and third group received the same dose of corn oil. Fourth (100 mg/kg malathion), fifth (100 mg/kg Allium czelghauricum), sixth (100 mg/kg Lathyrus karsianus), seventh (100 mg/kg Onosma nigricaule), eighth (100 mg/kg malathion+100 mg/kg Allium czelghauricum), ninth (100 mg/kg malathion+100 mg/kg Lathyrus karsianus) and the tenth group (100 mg/kg malathion+100 mg/kg Onosma nigricaule) were given daily intraperitoneally in the determined amounts. Applications were made for 21 days. After administration, total oxidant and total antioxidant capacities, body and liver weights, and histopathological changes in the liver were investigated in the serum and liver of mice.*

Results: *It is observed that plant extracts significantly inhibit the dose dependent concentrations of nitric oxide radical. A high amount of polyphenolic compounds were detected in plant extracts. While applied malathion mice weighed lighter, an increase in their liver was observed. Pathological changes were found in the liver of mice given malathion in histopalogical examinations. Total oxidant capacity (TOC) of serum and liver was significantly higher compared with control group; however, a decrease was observed in total antioxidant capacity (TAC). While the TOC in the serum and liver of mice given malathion and plant extract decreased compared to the malathion group, it was found that there was an increase in TAC.*

Conclusion: *In vitro study, it was revealed that methanol extracts of plants have antioxidant effects. In addition, it was determined that plant extracts exhibited antioxidant effects against the oxidant effect caused by malathion.*

Key words: *malathion; antioxidant; extract*

ÖZET

Amaç: *Allium czelghauricum, Lathyrus karsianus ve Onosma nigricaule türlerinden elde edilen ekstraktların antioksidan özellikleri ile farelerde malatiyon kaynaklı oksidan parametreler üzerine bitki ekstraktlarının antioksidan etkilerinin belirlenmesi amaçlanmıştır.*

Materyal ve Metot: *Deney hayvanları her grupta 10 adet fare olmak üzere toplam 10 gruba ayrıldı. Birinci grup kontrol grubu olarak tasarlandı. İkinci gruba 0,2 mL/kg dozda serum fizyolojik, üçüncü gruba ise yine aynı dozda mısır yağı verildi. Dördüncü (100 mg/kg malatiyon), beşinci (100 mg/kg Allium czelghauricum), altıncı (100 mg/kg Lathyrus karsianus), yedinci (100 mg/kg Onosma nigricaule), sekizinci (100 mg/kg malatiyon+100 mg/kg Allium czelghauricum), dokuzuncu (100 mg/kg malatiyon+100 mg/kg Lathyrus karsianus) ve onuncu gruptakilere (100 mg/kg malatiyon+100 mg/kg Onosma nigricaule) belirlenen miktarlardaki maddeler günlük olarak intraperitonal yolla verildi. Uygulamalar 21 gün süreyle yapıldı. Uygulamadan sonra farelerin serum ve karaciğerinde total oksidan (TOK) ve total antioksidan kapasite (TAK)'leri, vücut ve karaciğer ağırlıkları ile karaciğerde histopatolojik değişiklikler araştırıldı.*

Bulgular: *Bitki ekstraktlarının nitrik oksit radikalini doza bağlı olarak çalışılan konsantrasyonlarda istatistiksel yönden anlamlı şekilde inhibe ettiği görüldü. Bitki ekstraktlarının önemli miktarda polifenolik bileşikleri içerdiği tespit edildi. Malatiyon verilen farelerin vücut ağırlıklarında azalma meydana gelirken, karaciğer ağırlıklarında artış gözlendi. Histopalojik incelemelerde malatiyon verilen farelerin karaciğerinde patolojik değişimlere rastlandı. Malatiyon uygulanan farelerin serum ve karaciğerinde TOK düzeyi kontrol grubuna göre istatistiksel olarak önemli ölçüde artış gösterirken, TAK düzeyinde ise düşüş gözlenmiştir. Malatiyon ile birlikte bitki ekstraktı verilen farelerin serum ve karaciğerinde TOK düzeyi malatiyon grubuna göre düşüş gösterirken, TAK düzeyinin ise arttığı tespit edilmiştir.*

Sonuç: *İn vitro çalışmada bitkilerin metanol ekstraktlarının antioksidan özelliklerinin olduğu ortaya kondu. Ayrıca, malatiyonun neden olduğu oksidan etkiye karşı bitki ekstraktlarının antioksidan etki gösterdiği belirlendi.*

Anahtar kelimeler: *malation; antioksidan; özüt*

İletişim/Contact: *Dinçer Erdağ, Department of Medical Services and Techniques, Atatürk Vocational School of Health Services, Kafkas University, Kars, Turkey* • ***Tel:*** *0474 242 68 40* • ***E-mail:*** *dincererdag@hotmail.com* • ***Geliş/Received:*** *18.05.2021* • ***Kabul/Accepted:*** *19.12.2021*

ORCID: *Dinçer Erdağ, 0000-0001-7137-4403* • *Abdullah Doğan, 0000-0003-2008-6713*

Introduction

Malathion [O, O-dimethyl-S– (1.2-dicarbethoxyethyl) phosphorodithioate] is one of the organic phosphorous insecticides that have very prevalent usage against a variety of bugs for the protection of agricultural products and public health[1]. Nearly all chemical insecticides possess a neurotoxic effect, display toxic effects on the nervous system in target organisms[2]. Malathion is a kind of wide-spectrum insecticide, causes accumulation of acetylcholine on synapsis at nerve endings, inhibiting acetylcholinesterase, degrading acetylcholine that takes a role transmission of neural impulses in target organisms. Therefore, at target organisms that contact with the medication, firstly warnings emerge and later, paralysis follows these warnings[3].

Pesticides induce degradation of cellular activities, affecting cell structure and metabolism. One of the factors that lead to cellular damage is the formation of free radicals produced by pesticides[4]. These radicals occur continuously during metabolism in cells under aerobic conditions. The radicals formed under normal circumstances are removed from the environment by cell buffer systems. However, under certain conditions, excess free radicals arise and could not be disposed of by these buffer systems. If reactive oxygen types could not be eliminated with antioxidant defense systems, cellular damage emerges as a result of lipid peroxidation[5].

In many studies, it is illustrated that some plant varieties are good for diseases, other ones have features protecting from diseases. In the studies conducted on the plants with protective characteristics, it is determined that such plants carry substances that show a high-level antioxidant property. It is demonstrated in the studies carried out that such plants are rich in terms of chemical substances such as polyphenol, vitamins[6].

Plant varieties belonging to the Boraginaceae family may grow in Turkey. This family has 154 species and also a variety of around 2500[7]. Boraginaceae, a cosmopolite family show spreading mostly in tropical and mild regions, including Turkey[8].34 species and variety more than 300 belonging to this family grow in Turkey[9–11]. *Onosma nigricaule* about the Boraginaceae family is an endemic variety for Turkey. This plant variety finds an area of usage in the treatment of wounds and burns in the Eastern Anatolia Region[12]. The extracts obtained from some *Onosma* varieties, especially plant extract of *Onosma hispidum* is employed s antioxidant, antibacterial, antiviral, and anti-inflammatory agent in traditional medicine. In addition, *Onosma* varieties are also utilized in relieving pains and treatment the diseases like bronchitis, tonsillitis, hemorrhoid, etc. among the public. *Onosma hispida* is beneficial as a laxative and anthelmintic too. Furthermore, this plant is also administered against the ailments like inflammation, itch, wound, and kidney stone as well as the diseases such as eye diseases, blood disorders, and stomach aches[13].

Some plant species belonging to the Fabaceae family, which are also distributed in the flora of Turkey, have medical importance. It has been reported that it has traditionally been used in the treatment of various diseases[14]. Plant species belonging to this family are mainly consumed by humans and animals as foodstuffs, and some species are used in ornamental plants and pharmaceutical industries[15]. It has been reported that some species belonging to the family have antibacterial and antifungal activities[16], and some species also show strong antioxidant activity[17]. *Lathyrus* species are used worldwide as animal and human food. Pastor-Cavada et al.[18] researched the antioxidant activity of phenolic compounds found in the seeds of 15 wild *Lathyrus* species spreading in Southern Spain. It has been shown that the *Lathyrus* species studied have phenolic compounds with stronger antioxidant activity than the commonly consumed species such as soy, chickpea, and broad bean. *Lathyrus karsianus* is a plant species in the Fabaceae family and there are more than 200 species of the *Lathyrus* genus in the world[19].

Although the Liliaceae family is cosmopolitan, it is more common in tropical and temperate regions. In this family, there are important ornamental plants, aromatic plants, and vegetables as well as the plant species used in drug production[20]. The benefits of *Allium* species for human health are well known. For example; remarkably, *Allium sativum* (garlic) has prophylactic and therapeutic effects in some diseases (fungi). Evidence obtained from research has shown that the genus *Allium* plays an important role in the treatment and prevention of pathogenic infections, tumors, and cardiovascular diseases. Chemical compounds present in the *Allium* genus have been reported to potentially significantly reduce the level of lipid peroxidation in experimental animals[21]. One of the species of the genus *Allium*, *Allium czelghauricum* is in the Liliaceae family and is endemic to Turkey.

This study, it was aimed to determine the antioxidant effects of methanol extracts obtained from endemic plant species *Onosma nigricaule* (Boraginaceae),

Lathyrus karsianus (Fabaceae), and *Allium czelghauricum* (Liliaceae) against oxidation caused by malathion in mice (*Mus musculus*).

Material and Method

Plant material

Onosma nigricaule (Boraginaceae), *Lathyrus karsianus* (Fabaceae), and *Allium czelghauricum* (Liliaceae) plant species were collected from province Kars between May September 2011 and left for drying in the shade in a way not to expose to sun rays. After the drying procedure, only the foliage of the plants was received and ground through a grinder till becoming powder well, made ready for the procedure on taking the extract.

Animals

Approval was taken from Kafkas University Animal Experiments Local Ethics Committee for research (Decision no: 26.11.2010/48). A total of 100 mice (*Mus musculus*) of the same species who are not used in any study and not copulated before were used during the research. Male mice that have approximately 22–35 g weight, with weeks of 7–8, reached puberty period were taken the test. Mice were distributed in a manner to become 10 pieces in each group and placed in cages (Total 10 groups). Animals were accommodated in standard cages in an illuminated environment for 12 hours and in a dark environment for 12 hours, fed with normal mouse feed and tap water and as *ad libitum* in 22±2°C ambient temperature.

Preparation of plant extracts

Extract taken from plants was realized with the Soxhlet extraction system. A Jacketed heater was used for extract taking procedure. For extract taking process, methanol was used as a solvent. Samples of dried plant foliage were made powder via grinding. From this plant powder, 25 g was weighed and used for each test. It was placed in a roll made from filter paper. This roll was put in a soxhlet device. After that, a balloon incorporating 400 mL methanol was placed in a jacketed heater properly. The device was heated in a way methanol is boiled regularly (65 ^{0}C). This extract-taking procedure continued until the color of the solvent was clarified. After completion of the procedure, methanol was evaporated completely in an evaporator with water tromp under low pressure[22]. Extract substance was obtained in a tube. Later, extract substance found in the glass container was packaged in a manner to be protected from light with aluminum folia, stored in -35 ^{0}C. Total polyphenolic substance content of obtained extract, the radical-scavenging effect of nitric oxide (NO) was looked at. These effects were compared with standard substances known to have antioxidant capacity. These extracts were solubilized in physiological saline in the next stage later and injected into testing animals intraperitoneally.

Establishing experiment groups

The following test groups were formed in a manner that 10 male mice exist in each group. The chemical substance and extracts were solubilized with proper solutions in a way chemical substance and extracts are 100 mg/10 mL (Malathion was solubilized in corn oil, plant extracts in physiological saline). In conclusion, excluding the negative control group, solvent, physiological saline, or corn oil were injected with the calculation of 0.2 mL/20 g mouse to other groups. 1st Group: This group was designed as a negative group, no substance application was made to mice (C). 2nd Group: Physiological saline (0.9% NaCl), carrier substance of plants extract was applied to mice daily intraperitoneally (ip) during 21 days (0.2 mL/20 g) (S). 3rd Group: Corn oil, carrier substance of malathion was applied to mice daily ip (0.2 mL/20 g) (CO). 4th Group: Malathion was solubilized in corn oil for 21 days and applied to mice ip at daily 100 mg/kg dose (0.2 mL/20 g) (M). 5th Group: Plant extract *Allium czelghauricum* (Liliaceae) was solubilized in serum physiologic (0.9% NaCl) for 21 days and applied to mice ip at daily 100 mg/kg dose (0.2 mL/20 g) (A). 6th Group: Plant extract *Lathyrus karsianus* (Fabaceae) was solubilized in serum physiologic (0.9% NaCl) for 21 days and applied to mice ip at daily 100 mg/kg dose (0.2 mL/20 g) (L). 7th Group: Plant extract *Onosma nigricaule* (Boraginaceae) was solubilized in serum physiologic (0.9% NaCl) for 21 days and applied to mice ip at daily 100 mg/kg dose (0.2 mL/20 g) (O). 8th Group: Plant extract *Allium czelghauricum* (Liliaceae) at 100 mg/kg dose + malathion at 100 mg/kg dose was applied daily to mice ip for 21 days (0.2 mL/20 g) (MA). 9th Group: Plant extract *Lathyrus karsianus* (Fabaceae) at 100 mg/kg dose + malathion at 100 mg/kg dose was applied daily to mice ip for 21 days (0.2 mL/20 g) (ML). 10th Group: Plant extract *Onosma nigricaule* (Boraginaceae) at 100 mg/kg dose + malathion at 100 mg/kg dose was applied daily to mice ip for 21 days (0.2 mL/20 g) (MO).

Determination of total polyphenolic substance

Determination of total soluble phenolic substances of the extracts of plant *Onosma nigricaule, Lathyrus karsianus*, and *Allium czelghauricum* prepared in methanol was established by using Folin-Ciocalteu separator according to Slinkard and Singleton method[23].

Nitric oxide radical scavenging activity

Nitric oxide free radical scavenging activity of the methanol extracts obtained from plant *Onosma nigricaule, Lathyrus karsianus*, and *Allium czelghauricum* was measured with partial modification of Badami et al.[24] and Kumar et al.[25] methods. Sodium nitroprusside produces NO by itself in aqueous solutions and physiologic pH and this NO radical also generates nitrite (NO_2) ions, interacting with the oxygen in the environment. Nitrite anion formed was colored with Griess reaction at 548 nm, NO determination in the environment was made by reading at spectrophotometry[26].

Determination of total antioxidant and total oxidant capacities

Antioxidant and quantity of antioxidant in plasma and liver tissue was measured employing the use of total antioxidant capacity (TAC) assay kit and total oxidant capacity (TOC) assay kit (Rel Assay Diagnostics, Clinical Chemistry Solutions) [27]. Concerning antioxidant and oxidant capacities in plasma and liver tissue, the analysis method was used by modifying partially.

Measuring live weight

Just before administering medication, the weights of animals in all groups were measured (the first day that application is started). Animals were put in a container whose tare is determined in a way to obstruct their move and weighted in a digital scale. This procedure was repeated every week during the application period. After the application ended (21st day), animals were weighed again before euthanasia. Live weights of animals were compared, using statistical methods and the difference between groups was detected.

Measuring the weight of the liver

At the end of the study, the liver tissues which are received from testing animals killed with cervical dislocation under ether anesthesia were put in a sterile container and weighted in sensitive digital scales. Weights of liver tissues taken from animals were compared with the use of statistical methods and difference between groups was determined.

Histopathological examinations

At the end of the study, liver tissues of the experimental animals that were euthanized were taken and examined histopathologically. Liver samples taken from all experimental mice were detected in 10% formaldehydesolution. After the tissues were serially passed through graded alcohols, methylbenzoate, and benzol solutions, these tissues were blocked in paraffin. Sections of 5 μm thickness were taken from the tissues in the paraffin blocks and stained with Hematoxylin-Eosin (HE)[28] and evaluated under a light microscope (Olympus BX51; Olympus Optical Co., Osaka, Japan). Microscopic pictures were taken from the cases deemed necessary. In the evaluation of liver damage, the liver surface area observed in experimental and control groups; (i) extent of hepatocellular necrosis, (ii) cloudy bloating and hydropic degeneration, (iii) vacuolar degeneration, (iv) bile duct hyperplasia, (v) anisocytosis and anisocytosis, (vi) severity and prevalence of polymorph and mononuclear inflammatory cell infiltration were evaluated semi-quantitatively in six different categories.

Statistical calculations

One-Way ANOVA test was utilized for statistical calculations. Test groups were studied comparatively with control groups. Results were determined in average ± standard deviation (X ± SD) and showed a statistical difference of $p<0.05$. All calculations were utilized, using SPSS (16.0–2010) packaged software.

Results

Determination of total polyphenolic substance

Polyphenols are compounds that catch radicals (thanks to hydroxyl groups). They react with free radicals and turn them into ineffective, so harmless compounds. These effects may also be called free radical scavenging (cleaning) activity. Furthermore, these features gain antioxidant characteristics to polyphenolic compounds. Therefore, their levels in plants are very important. As they are efficient on antioxidant parameters, levels of phenolic compounds in studied plants were determined in the research. The amount of the phenolic substance found in plants was detected, using Folin-Ciocalteu solution. Total phenolic substance content of methanol extracts of *Onosma nigricaule, Lathyrus karsianus*, and *Allium czelghauricum* plants was. For this calculation, it was benefited from the standard pyrocatechol graphic presented below and

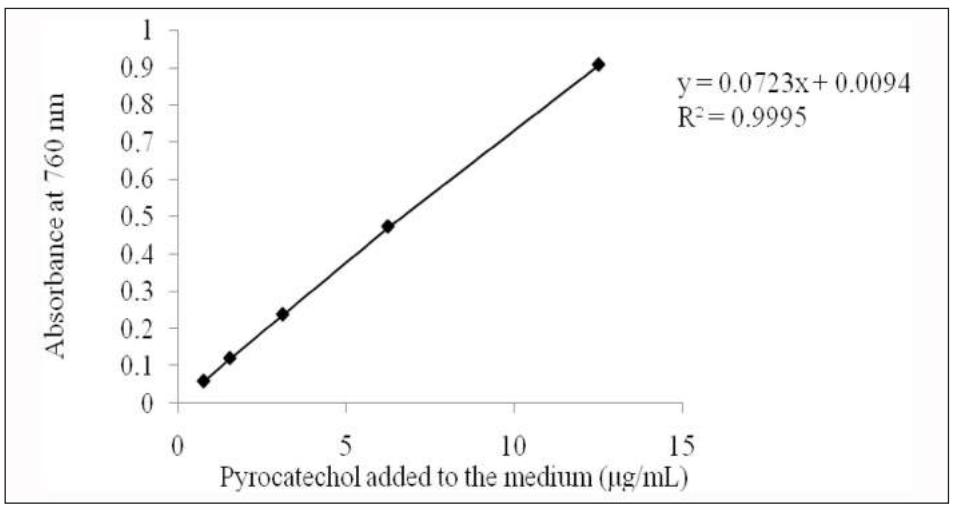
the following formula. Results were determined as phenolic substance equal to microgram pyrocatechol. From standards, it was calculated that the curve obtained is r^2=0.9995 (Graph 1).

Pyrocatechol(µg)=[Absorbance 0.0094]/0.0723(r^2=0.9995)

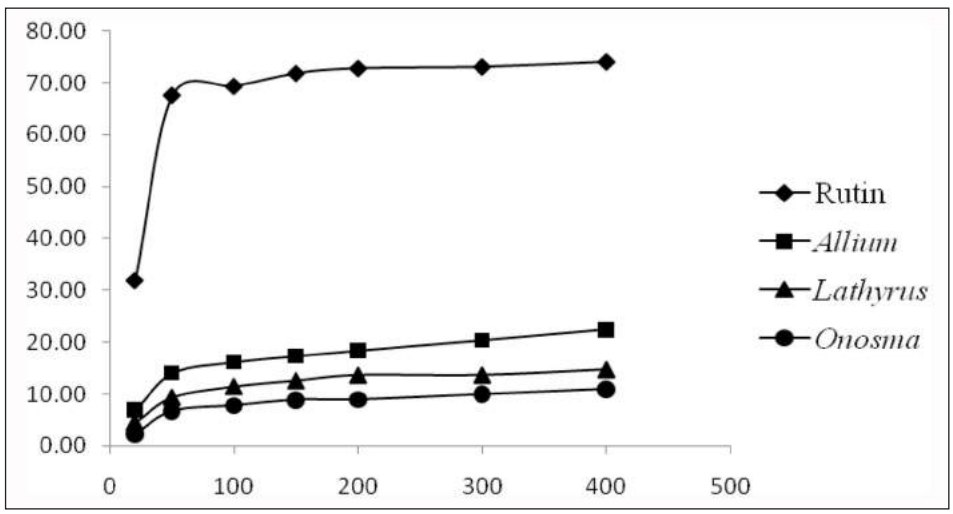
From here, it was detected that 1 mg of *Onosma nigricaule* contains 43.53 µg, 1 mg *of Lathyrus karsianus* 54.15 µg, and 1 mg of *Allium czelghauricum* contains 62.85 µg conjugate substance.

Nitric oxide radical scavenging activity

Nitric oxide radical scavenging % activities of *Onosma nigricaule, Lathyrus karsianus*, and *Allium czelghauricum* and routine standard substance are shown graphically, taking averages of data obtained after three testings (Graph 2). It was stated that nitric oxide scavenging effects of the plants show parallelism with the polyphenolic compound they contain. It was determined that the nitric oxide scavenging effect decreased following the order of *Allium czelghauricum, Lathyrus karsianus*, and *Onosma nigricaule* plant extract (routine 72% at 400 µg/mL dose, *Allium czelghauricum* extract 22.44%, *Lathyrus karsianus* extract 14.70% and *Onosma nigricaule* extract cleared 10.96% NO). The difference was found significant between routine and plant extracts (P<0.01). Considering the rate of a polyphenolic compound, it was detected that plant extracts had the scavenging effect at adegree close to that of a routine substance.



Graph 1. *Pyrocatekol standard graphic.*



Graph 2. *Comparison of the NO radical scavenging activities of Allium czelghauricum, Lathyrus karsianus, Onosma nigricaule, and rutin.*

TAC of plasma

Early death was observed in the groups and was not included in the calculation. The changes observed in the plasma TAC levels of the groups are shown in Table 1. When plasma TAC was compared as per groups, TAC groups of control, serum, and corn oil groups were found higher than other groups. TAC was detected low in the group that malathion was given. TAC degrees calculated in the groups that only plant extract was given illustrated similarity with control groups. However, according to the results obtained, it was observed that TAC value increased due to giving plant extract with malathion. The difference between plasma TAC levels attained from the plant extract groups that were given along with malathion and the malathion with a control group was found statistically significant. Concerning all groups, it was seen that TAC levels were low about control and the groups that serum and corn oil were given.

TOC of plasma

The changes determined in the plasma TOC of the groups are shown in Table 1. Plasma TOC was found low for control, serum, and corn oil. It was witnessed that the TOC level was at the highest level for the malathion group. It was detected that TOC levels for the groups that plant extract was administered are close to the controlling group. According to the results obtained, it was determined that plant extract decreases the oxidation malathion that emerges. However, the results taken from the group that malathion and plant extract were given together were detected higher than that of the control group. The difference is the highest between malathion and control group, was found statistically significant ($p<0.05$). TOC levels did not show a substantial difference statistically among the groups that malathion and vegetable extract were administered together.

TAC of liver

The changes determined in the liver TAC of the groups are shown in Table 2. It was observed that TAC in the liver lowered for the group that malathion was given. It was detected that plant extract increased TAC for the groups that malathion was administered. This difference was found significant than control groups.

TOC of liver

Variations in liver total oxidant capacities of groups are illustrated in Table 2. TOC of liver were found higher than the group malathion was given. As per the results, it was detected that compared to the control group, plant extract decreased the oxidation caused by malathion ($p<0.05$). Between the groups of control, serum, control oil, and the group only plant extract were administered, no apparent difference was observed from the point of liver antioxidants.

Measuring body weight

The changes in the body weights of the experimental groups on day 0th and day 21st are shown in Table 3. When the live weights of groups were compared in a slice of time specified, it was determined no substantial difference was available between groups on the 0th day ($P>0.05$). However, it was monitored that a decrease was present for body weights of 21st day for malathion group as compared to other groups. This was also found statistically significant ($P<0.05$).

Measuring liver weight

The changes determined in the liver weights of the experimental groups are shown in Table 4. When liver weights of testing groups were checked against daily test groups, it was seen that an increase occurred in the malathion group compared to other groups. This was also found statistically significant ($P<0.05$).

Histopathological findings

Damage to liver samples taken from mice in all groups was graded semi-quantitatively according to the criteria reported in the material and method. In the control group, diffuse, focal parenchymal, or centrilobular (periacinar, zone 3) liver necrosis, which is the most important criterion of liver intoxication, could not be detected (Fig. 1). Parenchymal, mild-moderate, coagulative necrosis was detected in the liver of mice in the malathion group. In addition, vacuolar degeneration in hepatocytes around the vena centralis and multinucleated hepatocytes regenerating in the liver parenchyma were observed (Fig. 2). A limited anisocytosis and anisocytosis were observed in the liver of mice in the group's given plant extract with malathion (Fig. 3).

Discussion

Today, many pesticide species used for agricultural pest control exist. These are obtained naturally and semi-synthetically. The synthetic compounds may be classified as compounds with organic chlorine, phosphorus, carbamate, pyrethroid, and nicotinamide. One of the

Table 1. *Observed changes in plasma total antioxidant capacity and total oxidant capacity*

Groups	TAC (mmolTroloxEquiv. /L)	TOC (μmol H_2O_2Equiv. /L)
C (n=7)	1.047±0.053[a]	0.157±0.636[a]
S (n=7)	1.069±0.043[a]	0.178±1.244[a]
CO (n=7)	1.091±0.072[a]	0.181±0.823[a]
M (n=10)	0.421±0.029[b]	1.078±2.166[b]
A (n=10)	0.956±0.092[ac]	0.241±1.026[ac]
L (n=10)	0.921±0.060[ac]	0.257±0.482[ac]
O (n=9)	0.879±0.097[ac]	0.262±0.546[ac]
MA (n=9)	0.732±0.030[d]	0.694±1.039[d]
ML (n=9)	0.745±0.078[d]	0.705±0.702[d]
MO (n=9)	0.670±0.034[d]	0.759±0.634[d]

[a,b,c,d]: The difference between the means with different letters in the same column is statistically significant (P<0.05). (TAC: Total antioxidant capacity, TOC: Total oxidant capacity, C: Control, S: Physiological saline, CO: Corn oil, M: Malathion, A: *Allium czelghauricum*, L: *Lathyrus karsianus*, O: *Onosma nigricaule*, MA: Malathion + *Allium czelghauricum*, ML: Malathion + *Lathyrus karsianus*, MO: Malathion + *Onosma nigricaule*).

Table 2. *Changes determined in liver total antioxidant capacity and total oxidant capacity*

Groups	TAC (mmolTroloxEquiv. /L)	TOC (μmol H_2O_2Equiv. /L)
C (n=7)	2.112±0.183[a]	19.854±0.669[a]
S (n=7)	2.178±0.185[a]	18.906±0.935[a]
CO (n=7)	2.158±0.186[a]	19.597±0.410[a]
M (n=10)	1.441±0.160[b]	28.092±0.631[b]
A (n=10)	1.956±0.163[ac]	20.203±0.661[a]
L (n=10)	1.945±0.167[ac]	21.254±0.632[a]
O (n=9)	1.928±0.140[ac]	20.883±0.569[a]
MA (n=9)	1.618±0.182[d]	23.678±1.284[c]
ML (n=9)	1.588±0.091[d]	23.924±1.101[c]
MO (n=9)	1.569±0.120[d]	24.505±0.854[c]

[a,b,c,d]: The difference between the means with different letters in the same column is statistically significant (P<0.05). (TAC: Total antioxidant capacity, TOC: Total oxidant capacity, C: Control, S: Physiological saline, CO: Corn oil, M: Malathion, A: *Allium czelghauricum*, L: *Lathyrus karsianus*, O: *Onosma nigricaule*, MA: Malathion + *Allium czelghauricum*, ML: Malathion + *Lathyrus karsianus*, MO: Malathion + *Onosma nigricaule*).

Table 3. *Body weight measurement (g)*

Groups	0. Day (X ± Sx)	21. Day (X ± Sx)
C (n=7)	27.86±2.77	31.86±3.01
S (n=7)	27.86±2.80	31.00±2.45
CO (n=7)	27.86±2.42	30.57±1.62
M (n=10)	27.27±2.31	26.72±1.33*
A (n=10)	27.90±2.63	32.20±1.23
L (n=10)	26.80±2.87	32.50±1.35
O (n=9)	27.56±2.08	32.22±1.15
MA (n=9)	27.22±1.58	30.78±1.41
ML (n=9)	27.78±1.58	30.56±1.17
MO (n=9)	28.00±3.43	30.67±2.52
General average	27.58±0.76	30.90±0.56

*: Statistically significant (P<0.05). (TAC: Total antioxidant capacity, TOC: Total oxidant capacity, C: Control, S: Physiological saline, CO: Corn oil, M: Malathion, A: *Allium czelghauricum*, L: *Lathyrus karsianus*, O: *Onosma nigricaule*, MA: Malathion + *Allium czelghauricum*, ML: Malathion + *Lathyrus karsianus*, MO: Malathion + *Onosma nigricaule*).

Table 4. *Liver weight measurement (g)*

Groups	X ± Sx
C (n=7)	1.92±0.15
S (n=7)	1.84±0.13
CO (n=7)	1.78±0.12
M (n=10)	2.48±0.10*
A (n=10)	1.65±0.13
L (n=10)	1.91±0.05
O (n=9)	1.90±0.06
MA (n=9)	1.99±0.09
ML (n=9)	1.96±0.09
MO (n=9)	1.98±0.06
General average	1.87±0.03

*: Statistically significant (P<0.05). (TAC: Total antioxidant capacity, TOC: Total oxidant capacity, C: Control, S: Physiological saline, CO: Corn oil, M: Malathion, A: *Allium czelghauricum*, L: *Lathyrus karsianus*, O: *Onosma nigricaule*, MA: Malathion + *Allium czelghauricum*, ML: Malathion + *Lathyrus karsianus*, MO: Malathion + *Onosma nigricaule*).

well-known groups among these is comprised of insecticides with organic phosphor. Within organic phosphorous insecticides, many compounds like malathion, parathion, dichlorvos, etc. are available. Malathion is among the most widely used organic phosphorus. They are absorbed easily from mucosas and transmitted into the blood. It exposes to bio-activation in the body. Their effect mechanism is associated with autonomous ganglions and the enzyme degrading acetylcholine, acting as transmitter substance at neuromuscular junctions of the parasympathetic nervous system, in other words, inhibiting acetylcholinesterase irrevocably. However, it is also established that malathion enhances free radical formation. Determination of the roles of free radicals in aging, the emergence of diseases like tumors reveals how important chronic malathion exposure is.

In this study, the effects of methanol extract obtained from plant species *Allium czelghauricum*, *Lathyrus karsianus* ve *Onosma nigricaule* on oxidative stress induced by malathion were investigated. The research was planned in vitro and *in vivo*. *In vitro* study, levels of polyphenolic compounds in plants were detected. Later, methanol extracts of the plant were applied on

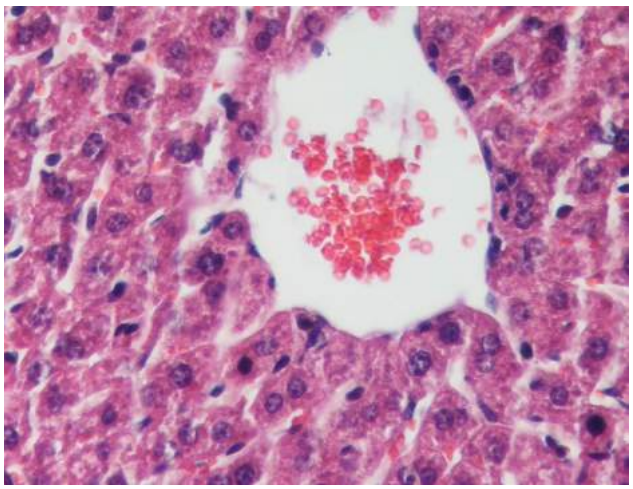


Figure 1. *Relatively normal hepatocytes around vena centralis. (HE x40).*

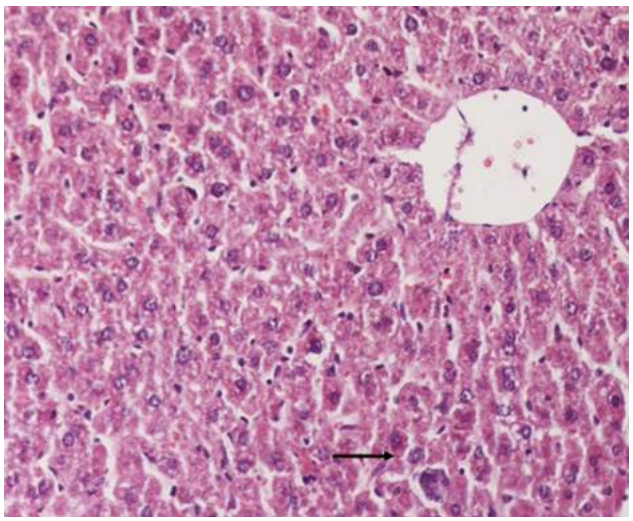


Figure 2. *Vacuolar degeneration of hepatocytes around vena centralis and multinucleated hepatocyte regenerated in liver parenchyma (arrow). (HE x20).*

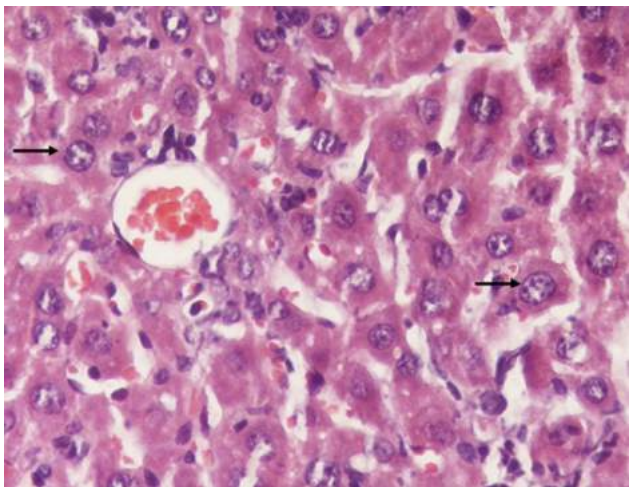


Figure 3. *Mild anisocytosis and anisokaryosis in hepatocytes (arrows). (HE x40).*

rats and its effects on oxidative parameters caused by malathion were determined. In general, it was observed that plant extracts used in the research scavenge NO radical formed experimentally. When these effects were matched against standard antioxidant substances, it was shown that plant extracts had quite high antioxidant activity. Furthermore, it was also detected that these antioxidant effects increased depending on higher concentrations of plant extracts. The plants studied are endemic, they grow in the region. Lack of any former study related to this kind of plant put forward the importance of the study. Additionally, in terms of understanding the importance of endemic plant species and protecting these plants, research results are evaluated with great importance and as attention-grabbing.

Carrying medication raw materials by plants and understanding their importance in treatment at the same time has caused making prevalent studies on them in recent years. At the same time, leading to serious disease of free radicals has induced concentration of studies on antioxidant impacts of plants. It is seen many studies are carried out to that end. The Liliaceae family includes a large and significant portion of flowering plants, and besides the plant species used in drug production in this family, there are important ornamental plants, aromatic plants, and vegetables[29]. The benefits of *Allium* species for human health are well known. It has been confirmed as a result of many studies that some precursor compounds and sulfur-containing compounds of *Allium* species have anti-oxidative activity. These chemical compounds have been reported to potentially significantly reduce the level of lipid peroxidation in experimental animals[30]. In this study, polyphenolic compounds among antioxidant substances were found higher in *Allium* species than in other plants (62.85 μg/mg). Tepe et al.[31] researched the antioxidant activities of methanol extract of a total of 5 *Allium* species, two of which are endemic, in the flora of Turkey. 1.1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activities of extracts obtained from plants were investigated, and also carotene/linoleic acid levels were analyzed. As a result, it has been reported that these *Allium* species, which are widely distributed in the flora of Turkey, have potent antioxidant properties. Ahmed et al.[32] have analyzed the impact of ginger (*Zingiber officinale* Rosc) on the oxidative stress formed by malathion for rats. They have evaluated lipid peroxidation, glutathione, and dependent enzymes and the enzymes scavenging free oxygen radicals to the

rats exposed to malathion sub-chronically. They have determined the existence of an increase in malondialdehyde (MDA) level in serums, superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) enzyme activities in erythrocytes, glutathione reductase (GR) and glutathione-S-transferase (GST) activities of the rats that malathion is administered at 20 ppm level for four weeks. Furthermore, a drop is observed in glutathione (GSH) levels in the blood. It is monitored that ginger (*Zingiber officinale* Rosc) given with feed to rats daily decrease lipid peroxidation and oxidative stress considerably. Finally, they have detected that free radical formation increases at organophosphate-induced poisoning, ginger has a protective effect against that. Therefore, it is indicated that ginger is a plant having medical importance and the products generated from this plant may be beneficial too.

Many studies have been conducted on herbal polyphenolic compounds, and it has been reported that these compounds have very strong antioxidant activity, neutralize free radicals in the body, prevent cardiovascular diseases, and even delay aging[33]. Some plant species belonging to the Fabaceae family have medical importance. It has been reported that it has traditionally been used in the treatment of various diseases[34]. It has been reported that some species belonging to the family have antibacterial and antifungal activities[35], and some species also show strong antioxidant activity[36]. Pastor-Cavada et al.[18] researched the antioxidant activity of phenolic compounds found in the seeds of 15 wild *Lathyrus* species spreading in Southern Spain. It has been shown that the *Lathyrus* species studied have phenolic compounds with stronger antioxidant activity than the commonly consumed species such as soy, chickpea, and broad bean.

Pesticides cause significant changes in antioxidative enzyme metabolism both in natural plant species and in cultivated ecological species. Acute or chronic toxic effects include mutagenicity and organ toxicity. Alp et al.[37] investigated the effects of caffeic acid phenyl ester and ellagic acid on oxidative stress caused by acute malathion toxicity in rats. They have shown that caffeic acid phenyl ester and ellagic acid have antioxidant effects on oxidative stress in acute malathion intoxication. Cadirci et al.[38] has searched the effect of the root extract obtained from plant *Onosma armeniacum* on the oxidative stress formed on ethanol in stomach tissue of rats. The same researchers have examined some oxidant and antioxidant parameters in stomach tissue. They have detected the vegetable extract at 25, 50, 100, and 200 mg/kg doses, used in the study decreases ethanol-based stomach ulcer substantially, additionally hinders the decrease in total glutathione level depending on the damage occurred in stomach tissue of the rats that ethanol is applied. The roots of *Onosma* species are used for the treatment of various diseases such as bronchitis, tonsillitis, hemorrhoid, and relieving pains. Tosun et al.[39] have investigated anti-inflammation and antinociceptive activities of the chloroform and ethanol extract acquired from *Onosma aucheranum*, *Onosma isauricum*, *Onosma sericeum*, *Onosma tauricum* Pallas ex Willd. var. *Brevifolium* and *Onosma tauricum* Pallas ex Willd. var. *Tauricum* species that show spreading in Turkey. In conclusion, *Onosma aucheranum*, *Onosma isauricum, and Onosma sericeum* species have displayed efficient anti-inflammation and antinociceptive activity.

Consequently, the data obtained with tests that are conducted with various free radical scavenging systems in *vitro* test environments about methanol extract taken from the foliage of the plant *Allium czelghauricum*, *Lathyrus karsianus,* and *Onosma nigricaule* have revealed these plants free radical scavenging and antioxidant activity meaningfully. This circumstance may result from the phenolic compounds present within the plant.

The effect of plant extracts that in vitro antioxidant impact is determined on antioxidant and oxidant parameters for the rats that malathion is administered in vivo test environment have been investigated. Malathion has given rise to an increase in total oxidant capacity of liver tissue and plasma for rats and accordingly it is detected that it also enhances oxidative stress. It is considered that this increase depends on the escalation in the amount of free radical. At the same time, malathion has caused a decrease in the body weights of test animals. Again, an increase is observed for liver weights of rats that malathion is administered. Organophosphate insecticides have been shown to cause a decrease in the body weight of experimental animals in studies[40,41,42]. In this study, a decrease in body weight and body weight gain of the experimental animals was observed. 3 weeks after the application, compared to the group treated with malathion and plant extracts, compared to the control groups. It is estimated that the reason for this decrease in body weight may arise due to nutrient intake and poisoning. Because it was observed that the food intake for 3 weeks decreased significantly in the experimental animals in

these groups compared to the control groups. However, necrosis and atrophic structures in tissues can also cause a decrease in body weight.

In addition, pesticides are known to cause histopathological and cytopathological changes in various tissues of mammals as well as other living species. The liver and kidneys are among the tissues most damaged by pesticides. Because pesticides are metabolized in the liver and are generally excreted by the kidneys[41,43–45]. In addition to the direct interaction of pesticides with cell structures, it is thought that toxic intermediates resulting from changes in metabolism also play a role in the emergence of these negative effects. Kalender et al.[46] examined the effect of vitamin C and E on malathion-induced hepatotoxicity in rats. The rats were given daily 27 mg/kg malathion and 200 mg/kg vitamin C + vitamin E by oral gavage for four weeks. The liver tissues of both the malathion-given group and the malathion + vitamin given group were examined histopathologically by light microscopy analysis, and some pathological disorders were found in the rats in the malathion group. As a result, it has been stated that vitamins C and E can reduce the hepatotoxicity caused by malathion, but their protective effects are limited. In our study, the liver tissues of both the malathion group and the groups that were given malathion and plant extract were examined histopathologically by light microscopy analysis. Some pathological disorders were observed in the mice in the group given malathion. Plant extracts, on the other hand, reduced these pathological disorders. This may arise from the oxidative stress caused by malathion. Plant extracts have also lowered this oxidative stress. It is monitored an increase in total antioxidant capacities of liver tissues and plasma of the testing animals plant extracts are along with together malathion. This case means that plant extracts show an anti-oxidative effect against the oxidative impact free radicals induce. Therefore, it is concluded that conducting a variety of studies in pharmacognosy, pharmacodynamic, pharmacokinetic, and pharmaceutical chemistry fields is required for a better understanding of the medical importance of tested plants.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Percutaneous Endoscopic Gastrostomy: A Retrospective Analysis in a Secondary Care Hospital

Perkütan Endoskopik Gastrostomi: İkinci Basamak Hastanede Retrospektif Analiz

Hasan Cantay[1], Ali Karatas[2]

[1]Department of General Surgery, Kafkas University Faculty of Medicine; [2]Gastroenterology Clinic, Kars Harakani State Hospital, Kars, Turkey

ABSTRACT

Aim: *It was aimed to reveal data on indications of percutaneous endoscopic gastrostomy (PEG) insertion in a secondary care hospital, postoperative complications, and follow-up.*

Material and Method: *The data of 34 patients with PEG insertion indication between 2018 and 2020 were evaluated retrospectively. The age, sex, primary diagnosis, comorbidity status, postoperative complications, whether tracheostomy was performed, and first gastrostomy or change status of the patients, who were given a PEG indication, considering they could not take food orally and would require to be fed enterally for a long time, were evaluated.*

Results: *74.2% of the cases were hospitalized in the intensive care unit, and the most common indications of PEG were neurological diseases with a rate of 67.7%, malignancy with a rate of 22.6%, and other causes such as trauma and electrical burns with a rate of 9.7%. There were no significant complications of the PEG procedure, and minor complications developed in two patients. No mortality was observed in the PEG procedure.*

Conclusion: *In cases where enteral feeding will take longer than 4–6 weeks, PEG is a preferred method for providing enteral nutritional support to prevent malnutrition. With low morbidity and mortality, the PEG method is a safe and practical feeding method and can be safely applied in a secondary care hospital.*

Key words: *gastrostomy; percutaneous endoscopic gastrostomy; enteral nutrition; feeding tube; endoscopy*

ÖZET

Amaç: *2. Basamak hastanedeki perkütan endoskopik gastrostomi (PEG) takılma endikasyonlarını, işlem sonrası komplikasyon ve takipleri ile ilgili verileri ortaya koymaktır.*

Materyal ve Metot: *2018–2020 tarihleri arasında PEG takılma endikasyonu konulan 34 hastanın verileri retrospektif olarak değerlendirildi. Uzun süre oral alamayan ve enteral beslenemeyeceği düşünülerek PEG endikasyonu konulan hastaların yaşları, cinsiyetleri, primer tanıları, komorbidite durumu, işlem sonrası komplikasyonları, trakeostomi açılıp açılmadığı, ilk gastrostomi ya da değişim durumları değerlendirildi.*

Bulgular: *Vakaların %74,2'si yoğun bakımda yatmakta olup, PEG endikasyonu olarak en sık %67,7 ile nörolojik hastalıklar, %22,6 ile malignite ve %9,7 ile travma ve elekrik yanığı gibi diğer nedenler şeklindeydi. PEG işlemine ait major komplikasyon olmayıp, iki hastada minor komplikasyon gelişti. PEG işlemine ait mortalite gözlenmedi.*

Sonuç: *Enteral beslemenin 4–6 haftadan uzun süreceği durumlarda, malnütrisyonun önlenmesi için enteral beslenme desteğinin sağlanmasında PEG tercih edilen bir yöntemdir. Düşük morbidite ve mortalitesiyle PEG yöntemi güvenli ve pratik bir beslenme yöntemi olup, 2. basamak hastanede güvenle uygulanabilir.*

Anahtar kelimeler: *gastrostomi; perkütan endoskopik gastrostomi; enteral beslenme; beslenme tüpü; endoskopi*

Introduction

Malnutrition is a condition that causes delays in recovery and increases morbidity and mortality by increasing susceptibility to infections, causing repeated hospitalizations and prolonged hospital stays. Enteral nutritional support is provided to prevent malnutrition in patients who cannot be fed naturally but do not have a functional disorder in the gastrointestinal tract[1,2]. In cases where enteral feeding will take longer than 4–6 weeks, percutaneous endoscopic gastrostomy (PEG) is a preferred method[3–5]. PEG is usually performed in patients with chronic underlying diseases. The most common indications of PEG are cerebrovascular diseases, various chronic neurological diseases such as Parkinson's disease, dementia, motor neuron diseases, head and neck traumas, and specific malignancies[6]. Although PEG has complications such as tube dislocation, PEG site infection, aspiration pneumonia, gastric perforation, and colocutaneous fistula, it is the most

İletişim/Contact: *Hasan Çantay, Department of General Surgery, Kafkas University Faculty of Medicine, Kars, Turkey* • ***Tel:*** *0533 623 55 76* • ***E-mail:*** *hasan_cantay@hotmail.com* • ***Geliş/Received:*** *01.08.2021* • ***Kabul/Accepted:*** *13.08.2021*

ORCID: *Hasan Çantay, 0000-0003-3309-8879* • *Ali Karataş, 0000-0002-2464-1975*

commonly used method to provide enteral nutrition in patients with swallowing difficulties[4,7].

The study aimed to reveal data on indications of percutaneous endoscopic gastrostomy insertion in a secondary care hospital, postoperative complications, and follow-up.

Material and Method

In our study, the data of 34 patients with PEG insertion indication between May 2018 and December 2020 in the endoscopy unit of the General Surgery and Gastroenterology clinic of Kars Harakani State Hospital were evaluated retrospectively. The age, sex, primary diagnosis, comorbidity status, postoperative complications, whether tracheostomy was performed, and first gastrostomy or change status of the patients, who were given a PEG indication, considering they could not take food orally and would need to be fed enterally for a long time, were evaluated. Nasogastric feeding was discontinued 12 hours before the procedure in patients who would undergo PEG, and prophylactic antibiotics were administered to all patients. In addition, the patients were evaluated before the procedure for pathologies that hinder the gastroscopy procedure, contraindications such as diffuse ascites in the abdomen, bleeding disorders, and gastrointestinal obstruction. The procedure was performed under sedation using an 18 or 20-fr gastrostomy tube. Immediately after the procedure, 20–30 cc of water was given through the tube to test for leakage, and 24 hours after the procedure, the amount was gradually increased, and the patients were fed through the gastrostomy tube.

Approval for the study was obtained from the Kafkas University Ethics Committee of the Faculty of Medicine (dated 24.12.2020, numbered 285).

Statistical Analysis

SPSS version 21 for Windows software package was used for statistical analysis. Frequencies and percentages as descriptive criteria were used.

Table 1. *Reasons for failure in PEG application*

Cause of failure	n
Laryngeal cancer that does not allow passage from the esophagus	2
Lung cancer invading the esophagus	1

Results

The result was unsuccessful in 3 of 34 patients with PEG insertion indication. Two of these patients had laryngeal cancer that did not allow the passage of the endoscope, and one patient had lung cancer that completely invaded the esophagus (Table 1). Two of these three patients underwent gastrostomy by laparotomy. The PEG procedure was successfully applied to the remaining 31 patients.

Seventeen (54.8%) of the cases were male, 14 (45.2%) were female, and the mean age was 62.7 (21–90). Twenty-three (74.2%) cases were hospitalized in the intensive care unit, and 8 (25.8%) were hospitalized in the palliative care unit. Tracheostomy was present in 3 (9.7%) of the patients.

PEG was inserted for the first time in 26 cases, and the gastrostomy tube was replaced with a new one in 5 cases.

PEG insertion indications are shown in Table 2. Neurological diseases were the most common indication in 21 (67.7%) patients, with cerebrovascular events taking the first place with 48.4%. Other neurological diseases were dementia, ALS (Amyotrophic Lateral Sclerosis), cerebral palsy, neuro-Behcet's disease, and Parkinson's disease. In addition, there were indications for malignancy in 7 (22.6%) patients and other causes such as trauma and electrical burns in 3 (9.7%) patients.

Table 2. *Distribution of cases by etiology*

Distribution of cases by etiology	n (%)
Malignancy	
Head and neck cancer	3 (9.7)
Lung cancer	2 (6.5)
Esophageal cancer	1 (3.2)
Glioma	1 (3.2)
Neurological diseases	
Cerebrovascular events	15 (48.4)
ALS	1 (3.2)
Cerebral palsy	1 (3.2)
Dementia	2 (6.5)
Neuro-Behçet's disease	1 (3.2)
Parkinson's disease	1 (3.2)
Other	
Trauma	2 (6.5)
Electrical burn	1 (3.2)

Although there were no significant complications, minor complications developed in two (6.4%) patients, including infection at the catheter site, they were treated with conservative follow-up and antibiotic therapy. No mortality related to the PEG procedure was observed in the patients.

Discussion

In our study, the success rate in patients with PEG was 91.2%. In patients with the unsuccessful result, the cause was tumors that obstruct the lumen. In two studies in the literature, success rates were reported as 99% and 97%, respectively[8,9]. In these studies, the cause of failure was also tumors obstructing the lumen, and it was emphasized in one study that dilatation may be successful in cases with tumors obstructing the lumen[10]. However, they reported a mortality rate of 0.9% after dilatation. In our study, the fact that the masses were at a very high level prevented the application of dilatation. In the study of Özgüç et al., gastrostomy was surgically inserted in cases where the PEG procedure was unsuccessful[9]. Our study performed gastrostomy surgically on two patients with an unsuccessful procedure.

In our study, the majority of the cases (74.2%) were patients hospitalized in the intensive care unit. In the studies in the literature, the procedures mainly were applied to the patients in the intensive care unit with a rate of 70% and 86.2%, respectively[9,11].

There are controversial results in the literature on the use of prophylactic antibiotics. However, contrary to many studies, a meta-analysis study also argues that antibiotic prophylaxis is not needed, reporting that single-dose prophylactic antibiotic use prevents wound infection[12–14]. In our study, each patient's prophylactic antibiotics were routinely administered before the procedure.

Although studies show that PEG feeding can be initiated 1 hour after the procedure or within the first 12 hours, in our study, PEG feeding was started 24 hours after the procedure[14–16].

One indication of PEG is dysphagia, and the most common cause of dysphagia is neurological diseases[17]. However, the indications have expanded nowadays, and the PEG procedure is also applied in conditions that may cause malnutrition, such as metabolic, cardiac, and trauma[18]. In addition, PEG indication is also present in cancer patients, predominantly head and neck cancers[19]. In our study, following the literature, neurological diseases were the most common PEG indication with a rate of 67.7%, and malignancies took second place with 22.6%.

The rate of minor complications after PEG insertion has been reported as 8–30% and the rate of significant complications as 1–4% [20]. There were no significant complications in our study, and our rate of minor complications was 6.4%.

In our study, no mortality related to the PEG procedure was observed, and mortality from the PEG procedure was close to zero in all studies in the literature. Furthermore, almost all of the reported causes of mortality are associated with a primary disease [21–23].

In conclusion, the PEG procedure has low morbidity and mortality, and our study's indications and complication rates are compatible with the literature. Furthermore, PEG is a simple, safe, and practical feeding method and can be safely applied in a secondary care hospital.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

How Did the COVID-19 Pandemic Affect the Sexual Behavior of the Female Nurses Working in the North-Eastern Black Sea Region of Turkey? A Descriptive Study

COVID-19 Pandemisi Türkiye'nin Doğu Karadeniz Bölgesi'nde Çalışan Kadın Hemşirelerin Cinsel Davranışlarını Nasıl Etkiledi? Tanımlayıcı Bir Çalışma

Neslihan Bezirganoglu Altuntas[1], Sema Baki Yildirim[2], Huri Guvey[3], Yesim Bayoglu Tekin[1]

[1]Department of Obstetrics and Gynecology, Trabzon Kanuni Educational and Research Hospital, Trabzon; [2]Department of Obstetrics and Gynecology, Faculty of Medicine, Giresun University Maternity and Children's Hospital, Giresun; [3]Department of Obstetrics and Gynecology, Private Parkhayat Hospital, Kütahya, Turkey

ABSTRACT

Aim: *Both coronavirus disease 2019 (COVID-19) and related precautions have led to social, economic, and psychological difficulties. We aimed to investigate the effects of COVID-19 on the sexual behavior of nurses working in the Blacksea region of Turkey.*

Material and Method: *This descriptive study included 120 female nurses older than 18 years, not menopausal, and married or in a regular sexual relationship. A questionnaire was administered to participants behind certain gynecologists between October 2020 and November 2020. According to the power analysis results, a sample size of 114 participants would allow us to reach a 5% deviation and a 95% confidence interval at an anticipated frequency of 50%. The Kolmogorov-Smirnov test, paired sample t-test, and McNemar test were applied. Demographic characteristics, frequency of sexual intercourse each month, use of contraception, desire to become pregnant, the existence of the menstrual disorder and vaginal infection, and female sexual function index (FSFI) scores of the participants were evaluated four weeks before onset and during the pandemic.*

Results: *While the frequency of sexual intercourse monthly significantly decreased during the pandemic (P=0.01), contraception use (P=0.50), desire to become pregnant (P=0.72), menstrual disorder (P=1), and frequency of vaginal infection (P=1) did not show a significant difference from before the pandemic. The total FSFI score of participants significantly decreased during the pandemic (P<0.001).*

Conclusion: *Sexual function of nurses deteriorated during the COVID-19 process, even though there was no change in their sexual health. Such studies can raise awareness and help apply early and adequate support policies to protect nurses from these adverse aspects of the pandemic and help them better handle its effects.*

Key words: *nurse; sexual function; menstrual disorder; female sexual function index; contraception; COVID-19*

ÖZET

Amaç: *Hem Koronavirus 2019 hastalığı (COVID-19) hem de ilişkili önlemler sosyal, ekonomik ve psikolojik zorlanmalara yol açmıştır. COVID-19'un Türkiye'nin kuzeydoğu Karadeniz Bölgesi'nde çalışan hemşirelerin cinsel davranışları üzerindeki etkisini incelmeyi amaçladık.*

Materyal ve Metot: *Bu tanımlayıcı çalışma, 18 yaşından büyük, menapozda olmayan, evli ve düzenli cinsel ilişkisi bulunan 120 kadın hemşireyi içermektedir. Ekim 2020-Kasım 2020 tarihleri arasında katılımcılara belirli jinekoloji uzmanları gözetiminde bir anket uygulanmıştır. Güç analizi sonuçlarına göre 114 katılımcılı bir örneklem büyüklüğü beklenen %50 sıklıkta, %5 sapma ve %95 güven aralığına ulaştırma imkanı sağlamaktadır. Kolmogorov-Smirnov testi, eşleştirilmiş gruplar t testi ve McNemar testleri uygulanmıştır. Katılımcıların demografik özellikleri, pandemi başlangıcından 4 ay önceki ve pandemi sürecindeki aylık cinsel birliktelik sıklığı, kontraseptif kullanımı, gebe kalma isteği, menstruel bozukluk ve vajinal infeksiyon varlığı ve kadın cinsel işlev indeks skoru değerlendirilmiştir.*

Bulgular: *Pandemi sürecindeki aylık cinsel birliktelik sıklığı pandemi öncesi döneme göre belirgin azalma gösterirken (P=0,01), kontraseptif kullanımı (P=0,50), gebe kalma isteği (P=0,72), menstruel bozukluk (P=1), ve vajinal infeksiyon sıklığı (P=1) pandemi öncesi döneme göre anlamlı değişiklik göstermemiştir. Ancak katılımcıların total kadın cinsel işlev indeksi skoru pandemi döneminde belirgin azalma göstermiştir (P<0,001).*

Sonuç: *COVID-19 sürecinde hemşirelerin cinsel sağlığında değişiklik olmamasına karşın cinsel işlevinde bozulma kaydedilmiştir. Bu sonuçlar sayesinde pandeminin etkilerinden korumak ve pandemi etkilerini daha rahat karşılamak amacıyla erken ve yeterli destek verilmesi gerektiği düşünülmektedir.*

Anahtar kelimeler: *hemşire; cinsel fonksiyon; menstruel bozukluk; kadın cinsel işlev ölçeği; kontrasepsiyon; COVID-19*

İletişim/Contact: *Huri Guvey, Department of Obstetrics and Gynecology, Private Parkhayat Hospital, 100. Yıl Quarter Dumlupınar Avenue, No: 26, Kütahya, Turkey* • ***Tel:*** *0533 565 53 58* • ***E-mail:*** *huriguvey@gmail.com* • ***Geliş/Received:*** *22.09.2021* • ***Kabul/Accepted:*** *29.12.2021*

ORCID: *Neslihan Bezirganoğlu Altuntaş, 0000-0002-6352-4085 • Sema Baki Yıldırım, 0000-0001-5321-0739 • Huri Güvey, 0000-0002-8603-6981 • Yeşim Bayoğlu Tekin, 0000-0003-0865-3201*

Introduction

The novel coronavirus that emerged in December 2019 in Wuhan City, China, has spread rapidly across the globe, escalating into a pandemic with major public health implications[1]. COVID-19 infection was first identified in Turkey on March 11, 2020, and the first death occurred on March 17, 2020. When this study was performed, the northeastern Black Sea area had one of the highest rates of COVID-19 infection in Turkey[2]. The increasing patient population raised the workload of healthcare professionals who were already struggling with the pandemic on the front line. Both the risk of infection and the increased workload have been shown to contribute to psychological distress and, in some cases, mental health disorders[3]. Given the established connection between stress and impaired sexuality, it is reasonable to conclude that the psychological consequences of the pandemic would also cause damage to the sexual lives of front-line health workers[4,5]. Recently, a study confirmed this opinion by revealing the negative effect of the COVID-19 pandemic on the sexual behavior of health care professionals[2].

Although outbreaks caused great pain to the entire medical staff, previous studies demonstrated that they affected nurses more than doctors[6]. This was most likely due to the nature of the nurse's job, which required her to participate in both treatment and primary care services face to face, resulting in spending extended time with patients. Additionally, a recent paper confirmed increased anxiety and stress among nurses during the COVID-19 pandemic due to their fear of contracting the virus or unknowingly infecting others[7]. Therefore, the potential sexual problems nurses face during the COVID-19 pandemic need further consideration.

Sexual health, as a part of the general health definition, is crucial for overall well-being[8]. Few research has been conducted to determine the effect of COVID-19 on healthcare providers' sexual health and behavior[9]. As a result, literature on the impact of COVID-19 on the sexual behavior of one of the most psychologically vulnerable groups, nurses, is still scarce. This study aimed to determine how COVID-19 affected the sexual behavior of female nurses working in Turkey's one of the most affected regions, the North-Eastern Black Sea area.

Materials and Methods

Study Population and Protocol

This observational study was conducted between October 2020 and December 2020 in 2 tertiary care centers in Turkey's North-Eastern Black Sea region. Female nurses working at these centers, older than 18 years old, not menopausal, married, or in a regular sexual relationship (lasting at least six months) were eligible for inclusion. Participants who had a gynecological operation, urinary incontinence, pelvic organ prolapse, malignancy, psychiatric or neurological disease, cardiac or renal disease, or a positive test for COVID-19, and those living with someone who tested positive for COVID-19 were excluded. A questionnaire form (supplementary document 1) was administered to participants behind the certain gynecologists in each center participants were examined regarding gynecological complaints. The questionnaire covered two-time frames: at least four weeks before the pandemic in Turkey (March 2020) and the period following the pandemic's beginning.

The Institutional Ethics Committee approved the study. Informed consent was obtained from all participants.

Measures

Baseline demographic characteristics including age, body mass index (calculated as weight in kilograms divided by square of height in meters), gravidity, parity, abortion count, alcohol consumption, and smoking were recorded. Frequency of sexual intercourse monthly, use of contraception, desire to become pregnant, history of the menstrual disorder and vaginal infection, and female sexual function index (FSFI) scores of the participants in each period were evaluated and compared. The FSFI developed by Rosen (female sexual function index in English-supplementary document 2) consists of 19 questions and assesses sexual functioning in women across six distinct domains: desire, arousal, lubrication, orgasm, satisfaction, and pain[10]. Answers to four of the questions were assigned 1–5 points, and answers to the remaining 15 questions were assigned 0–5 points. The total FSFI score ranges from 2–to 36, with higher scores indicating better female sexual function. As confirmed by Aydin and Aslan (female sexual function index in Turkish-supplementary document 3), the FSFI was found to be a reliable and valid method for assessing the sexual function of Turkish women[11].

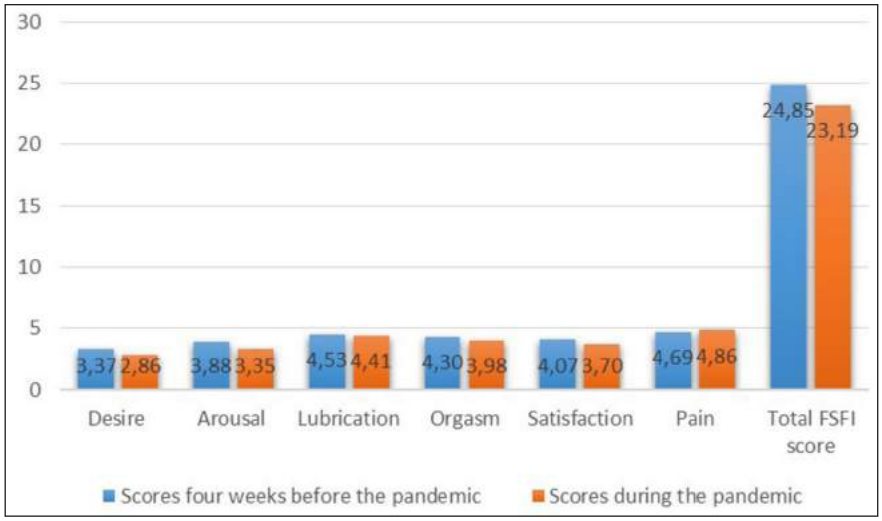

Figure 1. *Study flowchart.*

Table 1. *Demographic characteristics of the female nurses*

Variables	n=120
Age (year) (SD)	39.90±6.70
BMI (kg/m^2) (SD)	26.0±5.10
Gravidity (SD)	2.20±1.00
Parity (SD)	1.84±0.60
Abortion (SD)	0.40±0.10
Alcohol consumption n,%	
Yes	12 (10%)
No	118 (90%)
Smoking n,%	
Yes	33 (27.50%)
No	87 (72.50%)

Plus-minus values are mean ± standard deviation, SD: standard deviation, BMI: Body mass index.

Statistical Analysis

SPSS version 25 (SPSS Statistics for Windows, Version 25. Armonk, NY, IBM Corp.) was used for statistical analysis. The Kolmogorov-Smirnov test was used to evaluate the distribution of normality. Numerical variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. The Wilcoxon and McNemar tests compared average sexual desire, arousal, lubrication, orgasm, satisfaction, pain domain scores, total FSFI scores, and frequency of monthly sexual intercourse with the participants at two defined periods. McNemar test was used to compare percentages of contraception use, desire to become pregnant, the existence of menstrual disorder, and vaginal infection. P<0.05 was considered statistically significant.

Results

After excluding 18 nurses for not meeting inclusion criteria, 30 for declining to participate, and 10 for not completing the questionnaire, from187 participants, 120 nurses were enrolled in the study (Fig. 1). The demographic characteristics of the final sample (n=120) are presented in Table 1. The mean age and body mass indexes were 39.90±6.70 years and 26.00±5.10, respectively. The mean gravidity, parity, and abortion count were 2.20±1.00, 1.84±0.60, and 0.40±0.10, respectively. Alcohol consumption percent of participants was 10% (n=12) and smoking ratio was 27.70% (n=33).

While the frequency of sexual intercourse each month significantly decreased during the pandemic (p<0.05), contraception use (p=0.52), desire to become pregnant (p=0.72), menstrual disorder (p=1), and frequency of vaginal infection (p=1) did not show a significant difference as depicted in Table 2.

The total FSFI score of participants significantly decreased during the pandemic compared to pre-pandemic (p<0.001), as did sexual desire (p<0.001), arousal (p<0.001), lubrication (p<0.001), orgasm (p<0.001)

Table 2. *Comparison of participants' sexual behavior and health parameters before the pandemic and during the pandemic*

	Before the pandemic	During the pandemic	p value
Frequency of sexual intercourse each month	7.20±4.86	6.63±4.90	**0.010**
Contraception use	106 (88.30%)	108 (90%)	0.500
Desire to become pregnant	11 (9.10%)	13 (10.80%)	0.720
Menstrual disorder	1 (0.80%)	2 (1.60%)	1
Vaginal infection	4 (3.30%)	4 (3.30%)	1

Plus-minus values are mean ± standard deviation SD: standard deviation.

Table 3. *Comparison of participants' FSFI scores before the pandemic and during the COVID-19 pandemic*

Domains of FSFI	Before the pandemic	During the pandemic	p value
Desire	3.37±1.02	2.86±1.02	<0.001
Arousal	3.88±1.14	3.35±1.11	<0.001
Lubrication	4.53±1.15	4.41±1.06	<0.001
Orgasm	4.30±1.20	3.98±1.15	<0.001
Satisfaction	4.07±0.88	3.70±0.98	<0.001
Pain	4.69±1.36	4.86±1.26	0.010
Total FSFI score	24.85±5.19	23.19±4.96	<0.001

Plus-minus values are mean ± standard deviation SD: standard deviation, FSFI: Female Sexual Function Index.

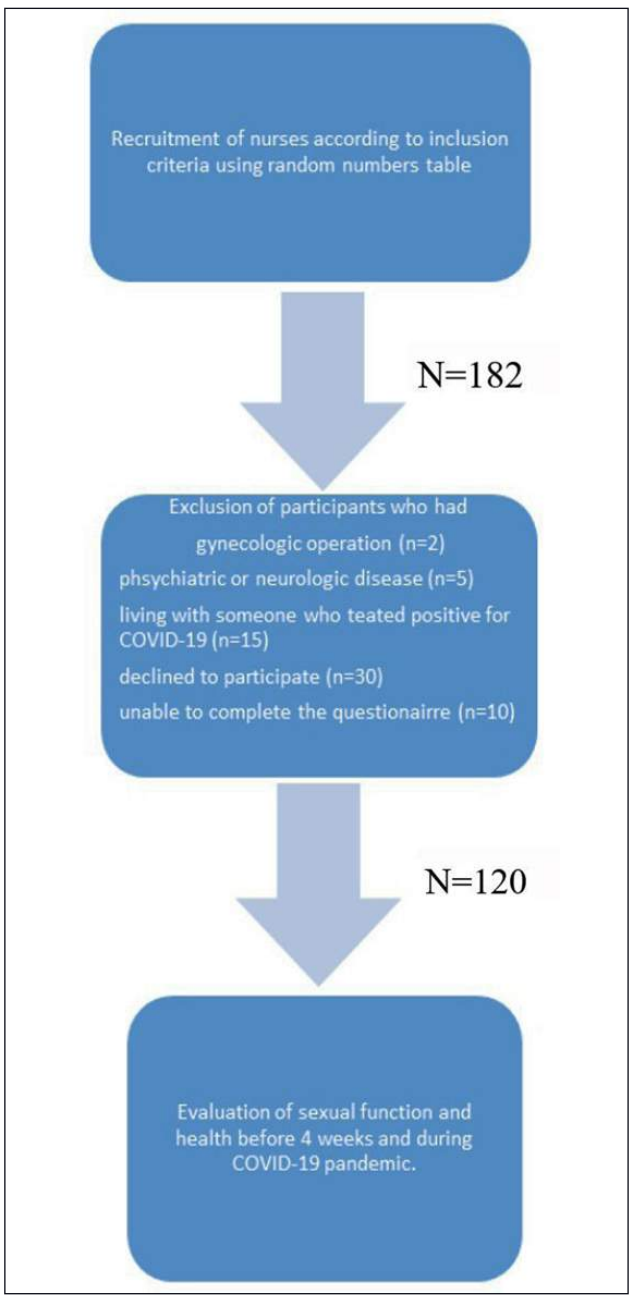

Figure 2. *Changes in FSFI domains and total FSFI scores of participants.*

and satisfaction (p<0.001). The pain score was significantly higher during the pandemic (p=0.01), as described in Table 3 and Fig. 2.

Discussion

The COVID-19 outbreak affected the lives of many individuals, especially healthcare workers, in many ways, including their sexual life. According to our study results, contraception use and desire to become pregnant among nurses did not differ between periods; pre-pandemic and during the pandemic. However, the frequency of sexual intercourse monthly and all domains of FSFI score, including; sexual desire, arousal, lubrication, orgasm, and satisfaction, significantly decreased during the pandemic (p<0.05).

According to a survey of non-healthcare workers, both pregnancy desire and contraceptive use declined dramatically during the pandemic[12]. It was suggested that difficulties accessing the health system for pregnancy care affected women's pregnancy intention, and the unavailability of contraceptive methods decreased their use during the pandemic. Similarly, an Italian study reported 37.3% of participants who desired pregnancy before the pandemic abandoned that intention due to concerns about economic difficulties and pregnancy outcomes[13]. Another survey from Shangai revealed that approximately one-third of participants canceled their pregnancy plans due to fears of healthcare services[14]. In this study, we did not see the effect of pandemics on pregnancy desire. This may be because healthcare professionals have greater access to contraception and prenatal care than the general public. Additionally, the percentage of nurses who already desired pregnancy before the pandemic was low in our sample.

Although it is believed that the stress on women caused by the pandemic may affect menstrual disorders[15], similar to our result, a questionnaire-based cross-sectional study of 200 women found no difference in the incidence of menstrual disorders compared to before the pandemic[12]. Dysmenorrhea has been reported to improve with increasing age and parity; therefore, the median age of our study population may affect the findings[16]. Furthermore, the analysis relied on data obtained via the questionnaire only; menstrual history and a medical examination were not performed.

Considering the inevitable increase in stress and anxiety of front-line nurses, an association between anticipated depression and diminished sexual appetite is not surprising. While a study by Mathew et al. on depressed people revealed perplexing findings such as 23% of men reporting an increase in sexual interest during the depression period, it also said that women appeared to exhibit decreased sexual interest more during the depression period, with just 9% reporting an increase in sexual interest compared to 35% reporting a substantial decrease in sexual interest[17]. Furthermore, some studies supported these mixed findings. Yuksel et al. found that although the total FSFI score was significantly lower, the frequency of sexual intercourse, sexual desire, and lubrication increased during the pandemic.[12] Nevertheless, our results are in line with most previous studies conducted to investigate the sexual health of females during the pandemic[18,19]. Cocci et al. reported that 53.3% of the participants expressed less satisfaction in sexual relations than in the pre-pandemic period[20]. Similarly, Li et al., whose study included a large sample, reported that 22% of participants had reduced sexual desire, and 41% experienced a decline in the frequency of sexual intercourse[21]. As revealed, nurses who suffered more severe depression and anxiety symptoms during the pandemic also experienced sleep disturbances due to heavy work hours[22]. Because of the increased time spent working at hospitals during the pandemic, nurses have limited time with their partners. In addition to lack of time, the desire to prevent contaminating their partner with COVID-19 might affect their hesitation to engage in intimacy. When these factors are added to the stress and sleep disturbances, nurses' overall FSFI scores and scores in five domains (all but pain) decreased during the pandemic.

One of the limitations of our study is that remembering the period before the pandemic might have been difficult for participants. Although the sample size was sufficient according to our analysis, larger, multicountry studies would shed more light on the issue and be more generalizable. However, we believe that conducting the research at two separate tertiary centers increased the power of our study. To our knowledge, the study was one of the first studies to investigate the effects of COVID-19 on the sexual behavior of nurses.

In conclusion, the frequency of sexual intercourse monthly, sexual desire, arousal, lubrication, orgasm, satisfaction, and total FSFI score of nurses significantly decreased during the pandemic compared to the pre-pandemic period, whereas only the pain score increased. Thus, we concluded that the sexual function scores of nurses have deteriorated during the COVID-19 process. Prospective studies should further examine the biological, psychological, and sexual behavioral effects of the COVID-19 outbreak on nurses struggling on the front line. Such studies can raise awareness and help apply early and adequate support policies to protect nurses from these adverse aspects of the pandemic and help them better handle its effects.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Ureteral Balloon Complications in Ureteroscopy

Üreteroskopide Üreteral Balon Komplikasyonları

Kursat Cecen

Department of Urology, Ağrı İbrahim Çeçen University, Ağrı, Turkey

ABSTRACT

Aim: *Complications of ureteral balloon used in the endoscopic treatment of ureteral stones were investigated.*

Material and Method: *This retrospective study evaluated patients who underwent ureteral balloon dilatation by a single surgeon between 2015 and 2018 and followed up for at least one year. Intraoperative complications were determined according to the modified Satava complication classification, while postoperative complications were determined according to the Clavien classification. In the postoperative follow-up, patients with a residual stone size of less than 4 mm were considered successful treatment.*

Results: *A total of 54 patients were included in this investigation. Stones were detected in the kidney in 16 (29.6%) patients and the ureter in 38 (70.4%) patients. The ureteroscope diameters used in those operations were 8.5–11.5 fr., and the ureteral access sheath diameters were 10–12 fr. Balloon dilatation was performed in 20 (37.1%) patients because the ureteral access sheath could not be passed and in 34 (62.9%) patients because the ureteroscopy could not be passed. Successful treatment was achieved in 47 (87.03%) patients. Due to balloon dilatation, intraoperative complications developed in 5 (9.2%) patients. Perforation was observed in 1 (1.85%) patient, lost access and subsequent ureteral stricture in 1 (1.85%) patient, and mucosal injury in 3 (5.55%) cases. General complications (fever, hematuria, calculus, and late ureteral stricture) were reported in 6 (11.1%) patients.*

Conclusion: *The surgeon's experience does not reduce ureteral balloon complications. There is a need for more studies by experienced surgeons who are well standardized on this subject.*

Key words: *urolithiasis; dilatation; ureteroscopy; complication*

ÖZET

Amaç: *Endoskopik üreter taşı tedavisinde kullanılan üreteral balon komplikasyonları araştırıldı.*

Materyal ve Metot: *2015–2018 yılları arasında bu konuda deneyimli tek cerrah tarafından üreteral balon dilatasyonu yapılan ve operasyon sonrası en az 1 yıl takibi olan hastalar retrospektif olarak çalışmaya dahil edildi. Operasyon anında gelişen komplikasyonlar modifiye Satava komplikasyon sınıflamasına göre, sonrasında olanlar Clavien sınıflamasına göre belirlendi. Postoparatif takiplerde rezidü taş boyutu <4 mm olan hastalar başarılı tedavi olarak değerlendirildi.*

Bulgular: *Çalışmaya 54 hasta dahil edildi. Taşlar 16 (%29,6) hastada böbrek içinde 38 (%70,4) hastada üreterde saptandı. Çalışmada kullanılan üreteroskop çapları 8,5–11,5 fr., üreteral access sheath çapları 10–12 fr. olarak belirlendi. 34 (%62,9) hastada üreteroskop, 20 (%37,1) hastada üreteral access sheath geçmediği için balon dilatasyon yapıldı. Çalışmada 47 (%87,03) hastada başarılı tedavi sağlandı. Balon dilatasyona bağlı 5 (%9,2) hastada intraoperatif komplikasyon gelişti. 1 (%1,85) hastada perforasyon, 1 (%1,85) hastada lost access ve sonrasında üreteral darlık ve 3 (%5,55) hastada mukozal yaralanma görüldü. Postoperatif 6 (%11,1) hastada genel komplikasyonlar (ateş, hematüri, taşyolu ve geç dönem üreteral darlık) görüldü.*

Sonuç: *Üreteral balon komplikasyonlarını cerrahın deneyimi azaltmamaktadır. Bu konuda iyi standardize edilmiş deneyimli cerrahların daha çok çalışmalarına ihtiyaç vardır.*

Anahtar kelimeler: *üriner taşlar; dilatasyon; üreteroscopy; komplikasyon*

Introduction

Ureteroscopic laser lithotripsy (ULL) is a widely used surgical method to treat urinary stones[1]. In retrograde procedures, an unforeseen obstacle in many patients is the calibration of the ureteral orifice or the ureter[2]. Dilatation of the ureter with a balloon is a method that allows the passage of instruments to reach the stones. Yet, complications related to the balloon affect many urologists' preference for this technique[2,3]. There are multicenter researches evaluating the efficacy and safety of balloon dilatation of the ureter. The present study evaluates the effectiveness and reliability of the results of a single surgeon who had experience in this field.

Material and Method

This study adhered to the tenets of the Helsinki Declaration of the World Medical Association and received full approval from the Scientific Research Ethics

İletişim/Contact: *Kürşat Çeçen, Department of Urology, Ağrı İbrahim Çeçen University, Ağrı, Turkey* • ***Tel:*** *0533 774 42 92* • ***E-mail:*** *kursatcecen36@gmail.com* • ***Geliş/Received:*** *28.10.2021* • ***Kabul/Accepted:*** *23.02.2022*

ORCID: *Kürşat Çeçen, 0000-0003-3662-9399*

Committee of Agri Ibrahim Cecen University (2021-305). The 2015–2018 period records of a single surgeon (KC), who had previous experience of 40 cases, were reviewed. Patients who underwent ureteral balloon dilatation and had at least 1-year of postoperative follow-up were included in the study retrospectively. Patients with ureteral stricture, upper urinary tract malignancy, or previous abdominal or pelvic radiation were excluded.

Demographic and clinical data were recorded by determining the age, gender, stone number, location and size, previous procedures, use of JJ stent, use of a balloon, duration of surgery, and hospitalization. The endoscopic intervention was started using 1 or 2 guidewires in all procedures. In cases where the instruments failed to reach the stones, urethrography was performed to determine the location and size of the narrow segment. Then, UroMax 18fr. /6 cm (Boston Scientific®) balloon dilator was used in 18 cm H_2O pressure under fluoroscopy; the ureteroscope was withdrawn with the help of imaging; ureteral damage was checked, and the operation continued. Intraoperative complications were determined according to the modified Satava classification, and postoperative complications were determined according to the Clavien classification. The postoperative ureteral stricture was diagnosed by endoscopy and urethrography, performed upon hydronephrosis development. In the postoperative follow-up, patients with a residual stone size of less than 4 mm were considered successful treatment.

Results are given as mean ± standard deviation (SD). Data were analyzed using IBM SPSS-Statistics 24.0.

Results

Within the study criteria, 54 patients were enrolled. The mean follow-up time was 13 months. 16 (29.6%) of the stones were inside the kidney, 38 (70.4%) were in the ureter, and a JJ stent was used in 54 cases (100%). Demographic and stone characteristics of the patients are given in Table 1. The ureteroscope diameters used in the study were 8.5–11.5 fr., and the ureteral access sheath diameters were 10–12 fr. Balloon dilatation was performed in 20 (37.1%) patients because the ureteral access sheath could not be passed and in 34 (62.9%) patients because the ureteroscope could not be passed. Ureteral balloon usage indications are given in Table 2. In the present study, stone-free status was achieved in 47 (87.03%) patients.

Due to balloon dilatation, intraoperative complications developed in 5 (9.2%) patients. In 1 (1.85%) of these patients, perforation was seen, and open surgical repair was performed. Lost access was seen in 1 (1.85%) patient, the procedure was repeated, but then ureteral stricture developed with minimal hydronephrosis. No progression was detected in the follow-ups, and no additional procedures were required. In 3 (5.55%) patients with mucosal injury, stricture did not develop during follow-up.

In 6 (11.1%) patients and 1 (1.85%) of them had late ureteral stricture due to intraoperative lost access. According to the intraoperative modified Satava classification and postoperative Clavien classification, Complications are given in Tables 3 and 4.

Discussion

Success and complications in endoscopic treatment of ureteral stones depend on many factors. Using stone retrieval devices that prevent stone migration, such as baskets, stone cones, and entrapment increases success[4]. Diameter of ureteroscope and use of ureteral balloon dilatator in narrow calibrated and difficult ureters affect success and complications[5]. The presence of patients with previous ureteral stricture or radiotherapy is also a determinant factor. The ureteroscope diameters used in our study were variable; whether stone retrieval catheters were used or not could not be determined. These are the limitations of the present study. On the other hand, conveying the experience and complications of ureteral balloon use by a single experienced surgeon (KC) in this field is a strong aspect of the study.

The use of stone cone, basket, and entrapment also enhances success in ULL[4,6]. Studies in the literature have reported that the success rates increased from 75–80% to over 90–95% using these instruments[2–4]. Although the use of stone retravel catheters was not detected in our study, the success rate was 87.3%, in line with the literature.

The incidence of the difficult ureter in ULL has been reported as 8–11% [5,7,8]. Huffman and Bagley's study on the use of ureteral balloon in 122 patients said that ureteral perforation developed in 1 patient, but stricture did not develop afterward[9]. The study by Nicholas J. Kuntz et al. determined intraoperative complications as 5% and postoperative as 11%[7]. Among 155 patients included in their research,

Table 1. *The characteristics of the patients and stones (n/%)*

Number of patients (n)	54
Age (mean, years ± SD)	39.26±14.02
Male:female ratio	22:32
Stone size (mm^2)	77.17±21.10
Stone location (n / %)	
Proximal ureter	4/7.4
Middle ureter	11/24.2
Distal ureter	23/42.5
Intrarenal	16/29.6
Operation time (munite)	27.75±6.58
Duration of hospitalization (day)	1.32±0.67

Table 2. *Indications for ureteral balloon dilation (n / %)*

Failure to place access sheath	20/37.1
Failure to pass ureteroscope	34/62.9
Tight ureteral orifice	44/81.4
Tortuous ureter	4/7.45
Not specified	6/11.1

Table 3. *Intraoperative complications by modified Satava classification (n/%)*

Satava 1	
Mucosal splitting/tear	3/5.55
Satava 2	
Perforation	1/1.85
Lost access	1/1.85

Table 4. *Postoperative complications by Clavien grade (n/%)*

Clavien 2	
Fever	3/5.55
Clavien 3b	
Excessive hematuria	1/1.85
Steinstrasse	1/1.85
Ureteral stricture	1/1.85

ureteral perforation was observed in 3 (1.9%) patients and lost access in 1 (0.64%) patient. Nonetheless, this was a multicenter study. The data of the single experienced surgeon in our examination revealed a perforation in 1 patient (1.85%), and there was no stricture development after open repair. In 1 (1.85%) of the patients, stricture developed due to lost access, but hydronephrosis did not increase in the follow-ups. Most of the general complications were fever, hematuria, etc., related to ULL, and the ratios were similar. In a study on 9600 patients, the use of a ureteral balloon was 20–40%, and intraoperative complications were reported as 3.8–7% and postoperative complications as 2.5–4.6%[10]. However, in many studies, the rates are different because the complications cannot be fully standardized. For instance, complications such as mucosal injuries and calculus were not included, and classification was not used. In our analysis, the use and standardization of the Satava and Clavien classifications revealed the complication rate as 11.1%. Not but what, in our study, all cases were difficult ureters requiring a ureteral balloon.

In difficult ureters, a double j stent, which is an alternative to ureteral balloons, can be placed and waited for 2–3 weeks[2,3,5]. In particular, in difficult ureters, some studies have reported 5% stricture in ULL operations without a ureteral balloon[5,11]. Results in multicenter, multi-surgeon studies may be misleading as the instruments used cannot be standardized, and the learning curves of the surgeons are not known. Complications, especially perforation and strictures, are somewhat more expected in difficult ureters. In our case, ureteral strictures developed in 1 (1.85%) patient, which did not affect kidney functions. Even in the hands of experienced surgeons, using a ureteral balloon in difficult ureters does not seem to reduce complications.

The ureteroscope diameters used in our study were variable; whether stone retravel catheters were used or not could not be determined. On the other hand, conveying the experience and complications of ureteral balloon use by a single experienced surgeon (KC) in this field is a strong aspect of the study. The surgeon in our study had a balloon dilator learning curve of 40 cases. This learning curve may be insufficient. Nevertheless, having a certain experience did not significantly reduce complications. The fact that there were 54 patients in the study is another limitation, and there is a need for standardized studies on this subject with a higher number of patients.

Conclusion

The surgeon's experience (previous experience of 40 cases) does not reduce ureteral balloon complications compared to current literature. There is a need for more studies by experienced surgeons who are well standardized on this subject.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

The Role of Prognostic Nutritional Index and Systemic Immune-Inflammation Index in Determining Ulcerative Colitis Severity

Prognostik Nutrisyonel İndeksin ve Sistemik İmmün-İnflamasyon İndeksin Ülseratif Kolit Hastalık Şiddetinin Belirlenmesindeki Rolü

Ibrahim Ethem Guven[1], Batuhan Baspinar[1], Rasim Eren Cankurtaran[2], Ertugrul Kayacetin[2]

[1]Department of Gastroenterology, Ankara City Hospital; [2]Department of Internal Medicine, Department of Gastroenterology, Ankara Yildirim Beyazit University School of Medicine, Ankara, Turkey

ABSTRACT

Aim: *Ulcerative colitis (UC) is a chronic, idiopathic, relapsing inflammatory disease of the gastrointestinal tract. In recent years, biochemical parameters have been widely used to determine the disease activity of UC. The present study aimed to determine the relationship between the prognostic nutritional index (PNI), systemic immune-inflammation index (SII), and disease activity.*

Material and Method: *All adult patients followed in the IBD unit of the Ankara City Hospital Gastroenterology Department between March 1st, 2019, and March 31st, 2021, were included in this retrospective study. We analyzed the relationship between the SII, PNI, and the endoscopic severity of UC. In addition, PNI and SII were compared between the active and remission group. Disease activity was described by the Rachmilewitz endoscopic activity index (EAI).*

Results: *The study group consisted of 402 patients. One hundred sixty-five of these patients were in the endoscopic remission group, and 237 were in the endoscopically active group. SII, NLR, and PLR values were significantly higher in the active UC group, and PNI values exhibited a lower mean than inactive UC patients (p<0.05 for all parameters). In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with the endoscopic activity index (respectively, R=0.29, R=0.24, R=0.38, R=-0.32; and for all parameters, p<0.001).*

Conclusion: *PNI and SII were significantly associated with UC activity. PNI and SII may be useful tools for assessing disease activity in UC.*

Key words: *ulcerative colitis; disease activity; nutrition*

ÖZET

Amaç: *Ülseratif kolit (ÜK) gastrointestinal sistemin kronik, idiyopatik, tekrarlayan inflamatuar bir hastalığıdır. Son yıllarda ÜK'in hastalık aktivitesini belirlemek için biyokimyasal parametreler yaygın olarak kullanılmaktadır. Bu çalışmada, prognostik nutrisyonel indeksi (PNİ) ve sistemik immün-inflamasyon indeksi (SII) ile hastalık aktivitesi arasındaki ilişkinin belirlenmesi amaçlanmıştır.*

Materyal ve Metot: *Bu retrospektif çalışmaya Ankara Şehir Hastanesi Gastroenteroloji Bölümü İBH ünitesinde 1 Mart 2019 ile 31 Mart 2021 tarihleri arasında takip edilen tüm erişkin hastalar dahil edildi. PNİ ve SII ile ÜK'in endoskopik aktivite şiddeti arasındaki ilişki analiz edildi. Ek olarak PNİ ve SII aktif ve remisyondaki hasta grupları arasında karşılaştırıldı. Hastalık aktivitesinin belirlenmesinde Rachmilewitz endoskopik aktivite indeksi (EAİ) kullanıldı.*

Bulgular: *Çalışma grubu 402 hastadan oluşuyordu. Bu hastaların 165'i endoskopik olarak remisyon grubunda, 237'si endoskopik olarak aktif gruptaydı. Aktif ÜK grubunda, SII, NLR ve PLR değerleri, inaktif ÜK hastalarına kıyasla anlamlı olarak daha yüksekti ve PNI değerleri daha düşük saptandı (p<0,05 tüm parametreler için). Ek olarak, NLR, PLR, SII pozitif olarak ve PNİ negatif olarak endoskopik aktivite indeksi ile korele saptandı (sırasıyla, R=0,29, R=0,24, R=0,38, R=-0,32; ve tüm parametreler için p<0,001).*

Sonuç: *PNİ ve SII, ÜK aktivitesi ile önemli ölçüde ilişkiliydi. PNİ ve SII, ÜK'de hastalık aktivitesinin değerlendirilmesi için faydalı bir araç olabilir.*

Anahtar kelimeler: *ülseratif kolit; hastalık aktivitesi; nutrisyon*

İletişim/Contact: *İbrahim Ethem Güven, Department of Gastroenterology, Ankara City Hospital, Ankara, Turkey* • ***Tel:*** *0505 759 66 63* • ***E-mail:*** *drethemgvn@gmail.com* • ***Geliş/Received:*** *04.11.2021* • ***Kabul/Accepted:*** *20.03.2022*

ORCID: *İbrahim Ethem Güven, 0000-0002-7436-6414* • *Batuhan Başpınar, 0000-0003-3143-2642* • *Rasim Eren Cankurtaran, 0000-0002-3687-3845* • *Ertuğrul Kayaçetin, 0000-0002-8822-3991*

Introduction

Ulcerative colitis (UC) is an immune-mediated bowel disorder characterized by chronic and recurrent inflammation of colonic mucosa[1]. There is often rectal involvement, and the inflammation spreads from the rectum to the proximal colon[2]. The natural course of the disease is characterized by relapse and remission periods[3]. During exacerbations, the main symptoms are bleeding, fever, and abdominal pain[4]. Early detection of the disease activity is important for both treatment success and prevention of complications that can affect the quality of life[5].

Colonoscopy is the most sensitive and specific diagnostic step for diagnosing and determining the disease activity and severity. However, the assessment of disease activity by colonoscopy is an invasive procedure and not easily accessible[6]. Therefore, noninvasive inflammatory biomarkers are needed for early detection of the disease activity.

White blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) are frequently evaluated to assess inflammation severity in UC. However, an optimal test has not yet been developed, and the currently used biomarkers are nonspecific[7]. In recent years, the prognostic nutritional index (PNI), the systemic immune-inflammation index (SII), the platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) have been adapted as an indicator of inflammation and have been widely studied to define the severity of inflammation in rheumatic diseases, diabetes mellitus, arterial hypertension, several cardiovascular diseases, and malignancies[8–11].

Herein, we aimed to evaluate the relationship between SII, PNI, and endoscopic activity in patients with UC.

Material and Methods

Patients

All adult patients followed in the Inflammatory Bowel Disease Unit of the Ankara City Hospital Gastroenterology Department between March 1st, 2019, and March 31st, 2021, was employed in this retrospective study. The UC diagnosis was made based on clinical, radiological, laboratory, endoscopic, and histological findings. The patient's demographic characteristics, disease duration, medication history, endoscopic activity score, disease localization, and laboratory test results were obtained from hospital records. Exclusion criteria were hematological disease and malignancy, acute bacterial or viral infection or chronic infectious diseases, autoimmune diseases, steroid usage within the previous week, neoplastic disorders, chronic liver disease, or chronic renal failure. This study was approved by Ankara City Hospital Scientific Research Assessment and Ethics Committee (Approval No: E1/1753/2021).

Laboratory Values

NLR, PLR, SII, and PNI were calculated by the formulas mentioned below:

- NLR: neutrophil count/lymphocyte count
- PLR: platelet count/lymphocyte count
- SII: platelet count × NLR
- PNI: 10 × albumin (g/dL) +0.005 × lymphocyte count

Disease Activity

The endoscopic disease activity and severity in patients with UC were determined by the Rachmilewitz endoscopic activity index (EAI) based on colonoscopy findings. The EAI score is <4 points for the remission group. Based on the severity of inflammation, the EAI score is regarded as 4–9 points for the mild/moderate active group and 10–12 points for the severe active group.

Statistical Analysis

Statistical analysis was performed with SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA). The normality of distribution was tested using the Kolmogorov-Smirnov test for continuous variables. The results were presented as mean ± standard deviation (SD) for variables with normal distribution and median (interquartile range, IQR 25%–75%) for variables with the abnormal distribution. Statistical comparisons of continuous variables were performed using the independent samples t-test or Mann-Whitney U test regarding the distribution pattern. Comparisons of categorical variables were performed using the chi-square test. Spearman's or Pearson's test was used for the correlation analysis. A two-tailed $p<0.05$ was considered statistically significant.

Results

A total of 402 UC patients were enrolled in the presented study. One hundred sixty-five of these patients

were in the endoscopic remission group, and 237 were in the endoscopically active group. No significant difference was found in group comparisons regarding age, gender, and lymphocyte counts. The median disease duration of UC patients after diagnosis was 84.0 (48.0–141.0) months. The medication history and disease location of all patients are presented in Table 1.

Platelet, WBC, neutrophil, CRP, and sedimentation values were higher in the active disease group. The mean hemoglobin and albumin values were lower than the remission group ($p<0.05$ for all parameters). SII, NLR, and PLR values were significantly increased in the active UC group, and PNI values exhibited a lower mean than the remission group ($p<0.05$ for all parameters).

According to the severity of the disease, the active patient group was also separated into two groups mild/moderate and severe. While no significant difference was observed in age, gender, and disease duration between the two groups, there was a significant difference between hemoglobin, platelet, WBC, neutrophil, albumin, CRP, and sedimentation values ($p<0.05$ for all parameters). SII, NLR, and PLR values were significantly higher, and PNI values were significantly lower in patients in the severe UC group versus the mild to moderate UC group ($p<0.05$ for all parameters) (Table 2).

In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with EAI (respectively, R=0.29, R=0.24, R=0.38, R=-0.32; and for all parameters $p<0.001$) (Table 3).

Discussion

This retrospective study revealed significantly higher SII, NLR, PLR values, and lower PNI values in the

Table 1. *Baseline clinical and laboratory parameters of study population*

	Total (n=402)	Active (n=237)	Remission (n=165)	P value
Age, (years)	47.4±13.7	47.6±13.7	47.2±13.7	0.75
Gender male, n (%)	238 (59)	148 (62)	90 (55)	0.12
Disease duration, month	84.0 (48.0–141.0)	84.0 (36.0–142.0)	84.0 (48.0–132.0)	0.80
Endoscopic activity index	5.5±3.8	8.3±2.3	1.6±1.4	**<0.001**
Hemoglobin, g/dl	13.4±1.7	13.2±1.8	13.8±1.6	**0.01**
Platelet, $x10^3/mm^3$	300.5±96.4	320.1±109.3	272.4±64.7	**<0.001**
WBC, $x10^3/mm^3$	7.4±1.9	7.9±2.0	6.7±1.5	**<0.001**
Neutrophil, $x10^3/mm^3$	4.6±1.6	5.0±1.8	4.0±1.1	**<0.001**
Lymphocyte, $x10^3/mm^3$	1.9±0.7	2.0±0.7	1.9±0.6	0.67
Albumin, gr/dL	4.4±0.4	4.3±0.4	4.6±0.2	**<0.001**
CRP, mg/dL	2.0 (0.6–10.0)	7.0 (2.1–16.0)	0.6 (0.3–0.9)	<0.001
Sedimentation, mm/hour	11.0 (6.0–20.0)	15.0 (7.0–23.0)	8.0 (5.0–12.0)	**<0.001**
NLR	2.6±1.5	2.9±1.8	2.2±0.8	**<0.001**
PLR	152.6 (117.9–187.7)	159.4 (122.5–205.8)	148.0 (114.8–173.0)	**<0.001**
SII x 10^3	672.2 (468.0–910.6)	768.3 (525.5–1045.2)	596.8 (419.0–726.5)	**<0.001**
PNI	54.8±5.5	53.8±6.2	56.2±4.0	**<0.001**
Medication history, n (%)				
5-ASA	291 (72)	156 (66)	135 (82)	**0.001**
5-ASA + AZA	48 (12)	38 (16)	10 (6)	**0.002**
5-ASA + anti-TNF	51 (13)	37 (16)	14 (9)	**0.03**
5-ASA + AZA + anti-TNF	11 (3)	5 (2)	6 (4)	0.36
Localization, n (%)				
Proctitis	76 (19)	28 (12)	48 (29)	**<0.001**
Left-sided colitis	231 (58)	141 (60)	90 (55)	0.30
Pan-colitis	94 (23)	67 (28)	27 (16)	**0.005**

Results are expressed as: mean ± SD or median (IQR) or frequency (%), WBC: white blood cell, CRP: C-reactive protein, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index, 5-ASA: 5-aminosalicylic acid, AZA: azathioprine, TNF: tumor necrosis factor

Table 2. *Baseline clinical and laboratory parameters according to the severity of the disease*

	Mild/Moderate (n=137)	Severe (n=100)	P value
Age, (years)	47.0±13.7	48.5±13.6	0.39
Gender male, n (%)	84 (61)	64 (64)	0.68
Disease duration, month	84.0 (48.0–145.0)	72.0 (24.0–120.0)	0.16
Endoscopic activity index	6.6±1.5	10.5±0.9	**<0.001**
Hemoglobin, g/dl	13.7±1.6	12.6±1.89	**<0.001**
Platelet, x10^3/mm^3	308.6±110.6	335.9±105.9	**0.027**
WBC, x10^3/mm^3	7.5±1.7	8.3±2.3	**0.006**
Neutrophil, x10^3/mm^3	4.7±1.5	5.5±2.0	**0.001**
Lymphocyte, x10^3/mm^3	2.0±0.6	1.9±0.8	0.38
Albumin, gr/dL	4.5±0.3	4.2±0.5	**<0.001**
CRP, mg/dL	3.1 (0.9–8.3)	15.5 (7.5–32.0)	**<0.001**
Sedimentation, mm/hour	11.0 (6.0–18.0)	20.0 (10.2–29.7)	**<0.001**
NLR	2.6±1.7	3.2±1.7	**0.006**
PLR	154.4 (115.6–191.5)	170.4 (133.5–244.2)	**0.007**
SII x 10^3	704.2 (480.1–954.3)	863.4 (650.8–1386.5)	**<0.001**
PNI	55.2±4.8	51.7±7.2	**<0.001**
Medication history, n (%)			
5-ASA	97 (71)	59 (59)	**0.048**
5-ASA + AZA	18 (13)	20 (20)	0.16
5-ASA + anti-TNF	19 (14)	18 (18)	0.40
5-ASA + AZA + anti-TNF	2 (2)	3 (3)	0.65
Localization, n (%)			
Proctitis	21 (15)	7 (7)	**0.048**
Left-sided colitis	79 (58)	62 (62)	0.55
Pan-colitis	36 (26)	31 (31)	0.45

Results are expressed as: mean ± SD or median (IQR) or frequency (%), WBC: white blood cell, CRP: C-reactive protein, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index, 5-ASA: 5-aminosalicylic acid, AZA: azathioprine, TNF: tumor necrosis factor

Table 3. *Correlation between Endoscopic activity index and different inflammatory variables in study population*

	Rho	p
NLR	0.294	<0.001
PLR	0.245	<0.001
SII	0.385	<0.001
PNI	-0.328	<0.001

NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SII: systemic immune-inflammation index, PNI: prognostic nutritional index.

active UC group compared to the inactive UC group. Also, NLR, PLR, and SII were significantly higher, and PNI was significantly lower in patients in the severe UC group versus the mild to moderate UC group. In addition, the NLR, PLR, and SII were positively, and PNI was negatively correlated with the endoscopic activity index.

UC is a chronic inflammatory disease of the colonic mucosa, and the clinical course of the disease is characterized by remission and relapse[12]. Early activation diagnosis is important as it reduces the need for surgery and enables early treatment modification[13]. Clinical evaluation of disease activation is determined by evaluating the radiological, endoscopic, and pathological findings[14]. Colonoscopy is the standard gold method for assessing the disease activity, allowing direct visibility of the mucosa and biopsy. However, there are some limitations, such as the increased risk of complications and lack of accessibility of the process[15]. Therefore, non-invasive methods to evaluate disease activation have attracted more attention in recent years[16]. In this concept, calprotectine is frequently used as a non-invasive inflammatory marker. However, lack of availability in all clinics and high cost limits the routine use of calprotectine[17].

In routine clinical practice, WBC count, CRP, and ESR have been widely used in the follow-up of UC[18]. However, due to their low sensitivity and specificity, they don't accurately reflect the activity of the disease[19]. In recent years, NLR and PLR values have been widely used to determine the disease activity of UC, and it has been shown that there is a significant relationship between the disease activity index and high NLR and PLR values[20]. Moreover, the SII index has been proposed by Hu et al. as a valuable marker of inflammation and contains information about three cell types[21]. The significance of SII has been demonstrated in many disease groups such as cancer and coronary artery disease[22,23]. By the literature, we have also shown higher NLR, PLR, and SII values in the active UC patient group, and they are correlated with the endoscopic activity index.

Albumin synthesis is negatively affected by the systemic inflammation process[24]. The catabolic state activated by inflammatory cytokines has suppressed the negative acute-phase reactants synthesis. Additionally, active gastrointestinal involvement in UC patients can lead to hypoalbuminemia by causing malabsorption and protein loss[25]. Moreover, functional inflammatory changes can decrease lymphocyte production due to dysregulation of apoptosis of the lymphocytes[26]. In the light of the above, the PNI index, which is calculated by albumin and lymphocyte values, has been more sensitive since it combines two components. In this concept, the PNI index was widely used to assess disease activity in rheumatic diseases such as Behçet's disease and systemic lupus erythematosus[27,28]. Our study revealed that UC activity was negatively correlated with PNI value.

In conclusion, this study demonstrates that SII, PNI, NLR, and PLR values were strongly associated with disease activity and endoscopic severity in UC, which can help determine the disease's endoscopic severity.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

The Effect of the Practical Treatments for Acute Heart Failure on Mortality: A Real-World Study

Akut Kalp Yetmezliğinde Uygulanan Tedavilerin Mortalite Üzerine Etkisi: Bir Gerçek Dünya Çalışması

Fatih Koksal[1], Mustafa Aldemir[1], Fatih Levent[1], Sadik Volkan Emren[2], Cem Nazli[2]

[1]Bursa Yuksek Ihtisas Education and Research Hospital, Bursa; [2]Izmir Katip Çelebi University Ataturk Education and Research Hospital, İzmir, Turkey

ABSTRACT

Aim: *The mortality of chronic systolic heart failure has been decreased thanks to state-of-the-art therapy. However, the mortality rate is still high in acute heart failure (AHF). Our study was planned to investigate the mortality rates and predictors of mortality in AHF.*

Material and Method: *A single-center retrospective study was conducted on 805 patients hospitalized due to AHF between March 2009 and June 2013. The patients were separated into two main groups: the decompensated heart failure group (DHF), which comprised the patients with signs of right heart failure with or without pulmonary edema (722 patients – 89.7%), and the acute pulmonary edema group (PE) presenting only with pulmonary edema (83 patients – 10.3%). The two groups were compared for the patient-related variables. The survival analysis of the groups based on the etiology was performed. Finally, the independent predictors for 2-year mortality in AHF were investigated.*

Results: *The 2-year mortality rate was higher in DHF than in PE (51.4% vs. 31.6% p<0.001). The mortality rates of ischemic cardiomyopathy, nonischemic cardiomyopathy, and heart failure with preserved ejection fraction (HFpEF) were 52.8%, 39.6%, and 47.3%, respectively (p=0.389). Advanced age, previous cerebrovascular diseases, anemia, hyponatremia, hypoalbuminemia, lower left ventricular ejection fraction (LVEF), and lower systolic blood pressure predicted increased 2-year mortality independently. In contrast, usage of beta-blockers during hospitalization predicted reduced 2year mortality independently.*

Conclusion: *Mortality rate was similar between different heart failure types. Various laboratory and clinical parameters predict mortality, whereas beta-blockers and ACE inhibitors reduce mortality.*

Key words: *mortality; acute heart failure; ACE inhibitors; beta blockers*

ÖZET

Amaç: *Güncel tedavi uygulamalarıyla kronik sistolik kalp yetmezliği mortalitesinde azalma sağlanmıştır. Ancak akut kalp yetmezliğinde (AKY) mortalite hala yüksektir. Bizim çalışmamızda AKY hastalarında mortalite oranları ve mortalitenin ön gördürücülerinin neler olduğu araştırılmıştır.*

Materyal ve Metot: *Çalışmamız Mart 2009 ve Haziran 2013 tarihleri arasında AKY tansıyla yatırılan 805 hastayı içeren tek merkezli retrospektif bir çalışmadır. Çalışmadaki hastalar iki ana gruba ayrıldı: pulmoner ödemin eşlik ettiği ya da etmediği sağ kalp yetmezliği kliniği ile başvuran hastaları içeren (722 hasta – %89,7) dekompanze kalp yermezliği (DKY) grubu, sadece pumoner ödem klinği ile başvuran hastaları içeren (83 hasta – %10,3) pulmoner ödem grubu (PÖ). İki grup arasında hastalara ait değişkenler istatiksel olarak karşılaştırıldı. Etiyolojiye göre ayrılmış hasta gruplarının sağ kalım analizi yapıldı. En sonda da AKY de 2 yıllık mortaliteyi öngören bağımsız faktörler araştırıldı.*

Bulgular: *İki yıllık mortalite DKY grubunda PÖ grubundan daha fazlaydı (%51,4 ve %31,6 p<0,001). İskemik kardiyomiyopati, non iskemik kardiyomiyopati, korunmuş ejeksiyonlu kalp yetmezliği (kEFKY) hastalarında mortalite oranları sırasıyla %52,8, %39,6 ve %47,3 idi. (p: 0,389). İleri yaş, serebrovasküler olay öyküsü, anemi, hiponatremi, hipoalbuminemi, düşük sol ventrikül ejeksiyon fraksiyonu (SVEF), düşük sistolik kan basıncı 2 yıllık artmış mortaliteyi öngören bağımsız faktörler olarak bulunurken hastane yatışında beta bloker kullanımı mortaliteyi azaltan bağımsız faktör olarak bulundu.*

Sonuç: *Mortalite oranları farklı kalp yetmezliği gruplarında benzer saptandı. Çeşitli klinik ve laboratuvar parametreleri AKY de mortaliteyi artıran öngördürücüler olurken beta bloker ve anjiyotensin dönüştürücü enzim (ADE) inhibitör kullanımı mortaliteyi azaltan öngördürücüler oldu.*

Anahtar kelimeler: *mortalite; akut kalp yetmezliği; ACE inhibitörü; beta bloker*

İletişim/Contact: *Fatih Koksal, Department of Cardiology Bursa Yuksek Ihtisas Education and Research Hospital, Bursa, Turkey* • ***Tel:*** *0507 796 48 62* • ***E-mail:*** *dr.fatihkoksal@hotmail.com* • ***Geliş/Received:*** *19.11.2021* • ***Kabul/Accepted:*** *23.12.2021*

ORCID: *Fatih Köksal, 0000-0002-4197-4683* • *Mustafa Aldemir, 0000-0003-0165-0809* • *Fatih Levent, 0000-0002-7160-4050* • *Sadık Volkan Emren, 0000-0002-7652-1123* • *Cem Nazlı, 0000-0003-2231-3780*

Introduction

Heart failure (HF) is a phenomenon that occurs as a result of deterioration in cardiac filling or pumping. The practical guidelines state HF as a clinical syndrome including cardinal symptoms and signs (e.g., breath shortness, ankle edema fatigue, elevated jugular venous pressure, pulmonary crackles, S3 heart sound) due to structural or functional heart disease[1-3].

The current guidelines prefer a classification for HF based on left ventricle ejection fraction (LVEF): heart failure with preserved ejection fraction (HFpEF), defined by an LVEF ≥50%, heart failure with reduced ejection fraction (HFrEF) if the LVEF is <40%, and heart failure with mid-range ejection fraction (HFmrEF) if the LVEF is 40–49%[2].

HF is one of the main reasons for mortality in the world. Increased lifetime due to the administration of advanced treatments in cardiovascular disease has increased the prevalence of HF and healthcare costs [2,4].

The mortality benefit of medical therapy in HFrEF has been shown in numerous studies. In contrast, no treatment has been found to ameliorate the mortality in HFpEF[5].

Acute heart failure (AHF) is the sudden occurrence or worsening of HF's signs and symptoms.AHF can be diagnosed for the first time (de novo) or manifest as chronic heart failure decompensation. It can be fatal if not treated immediately[2].

Determining the etiology and predisposing factors of acute heart failure rapidly-it has been mentioned in the 2016 ESC heart failure guideline widely- is essential for the proper treatment[2]. Medication for acute heart failure can also be challenging because there are no sufficient data for the effects of the medications which are proven beneficial for systolic heart failure (angiotensin-converting enzyme inhibitors, beta-blockers, angiotensin receptor blockers, ivabradine mineralocorticoid receptor antagonists, etc.)[6-10].

This study aimed to determine the mortality rates of patients hospitalized due to AHF and the variables that affect mortality in AHF.

Materials and Method

The study was a retrospective study conducted in a single center (Izmir Katip Celebi University Ataturk Training and Research Hospital). One thousand one hundred fifty-two patients hospitalized with a diagnosis of AHF between March 2010 and June 2013 were recorded. AHF was defined as the sudden occurrence or aggravating of HF's signs and symptoms. The patients' clinical and laboratory characteristics were obtained from the "hospital information management system." The exclusion criteria were hospitalization due to a non-cardiovascular disease (diabetic coma, acute renal failure, etc.), 'dry patients'(with no congestion/ pulmonary edema), insufficient hospital information management system data, and discharge on the same day. After considering these criteria, 805 patients were eligible for this study. The patients were separated into two main groups based on clinical presentation: the decompensated heart failure group(DHF), which comprised the patients with signs of right heart failure with or without pulmonary edema (722 patients -89.7%), and the acute pulmonary edema group(PE) presenting only with pulmonary edema (83 patients -% 10.3). İzmir Katip Çelebi University Ethics Committee approved the study. Non-invasive Clinical Tria for this study with the decision number 212, dated 11.11.2013.

Statistical Analysis

SPSS 21 (IBM) statistics program was used for the statistical analysis. Since the variables were shown to distribute normally by the Shapiro-Wilk test, the categorical and continuous variables of the patients were compared across the dichotomous dependent variables (DHF and PE groups) using chi-square, Fischer exact, one-way ANOVA as appropriate. To identify the independent predictors for two year mortality in AHF, a multivariate Cox proportional-hazards regression model analysis was conducted among the variables of which the p-value was shown <0.05 using univariate cox regression analysis. The variables with a p-value of below 0.05 in that model were accepted as independent predictors.

Results

20.2% of the 805 patients (51.4% men with a mean age of 72 + 12 years) had no previous history of HF (de novo AHF). Clinical and demographic findings of the patients are shown in Table 1.

Hypertension, hyperlipidemia, and chronic renal failure were more prevalent in PE (p:<0.05), whereas history of atrial fibrillation was more prevalent in DHF (p<0.05). On admission, the mean heart rate and systolic/diastolic blood pressure were higher in PE

Table 1. *Clinical and Demographic findings on admission*

Variables	Decompensated heart failure (n: 722)	Acute pulmonary edema (n: 83)	p
Age Mean ± SD	71.53±12.28	72.00±12.17	0.739
Male n (%)	378 (52.4%)	36 (43.4%)	0.121
LVEF% Mean ± SD	38.67±15.23	45.90±12.40	**<0.001**
De novo Heart Failure n (%)	141 (19.5%)	21 (26.5%)	0.134
Coronary artery disease n (%)	341 (47.2%)	42 (50.6%)	0.560
Thyroid disease n (%)	109 (15.1%)	6 (7.2%)	0.052
Hypertension n (%)	393 (54.4%)	58 (69.9%)	**0.007**
Diabetes Mellitus n (%)	307 (42.5%)	44 (53.0%)	0.068
Hyperlipidemia n (%)	133 (18.4%)	27 (32.5%)	**0.002**
Severe valvular heart disease n (%)	84 (11.6%)	5 (6.0%)	0.123
Cerebrovascular disease n (%)	54 (7.5%)	7 (8.4%)	0.756
ICD n (%)	101 (14.0%)	9 (11.3%)	0.429
CRT n (%)	5 (0.7%)	0 (0.0%)	0.447
Atrial fibrillation n (%)	251 (34.8%)	16 (19.3%)	**0.005**
COPD n (%)	213 (29.5%)	22 (26.5%)	0.570
Chronic renal failure* n (%)	286 (39.6%)	44 (53.0%)	**0.019**
Smoking n (%)	187 (25.9%)	23 (27.7%)	0.722
Class 3 Obesity** n (%)	35 (4.7%)	5 (7.2%)	0.317
Valvular heart surgery n (%)	37 (5.1%)	3 (3.6%)	0.789
ACE inhibitors/ARB n (%) (n: 678)	253 (41.1%)	27 (43.5%)	0.706
Beta blockers n (%) (n: 678)	278 (45.1%)	32 (51.6%)	0.329
MRAs n (%) (n: 678)	193 (31.3%)	9 (14.5%)	**0.006**
Furosemid n (%) (n: 678)	345 (56.0%)	20 (32.3%)	**<0.001**

ACE: Angiotensin-converting enzyme, ARB: Angiotensin II receptor blocker, COPD: chronic obstructive pulmonary disease, CRT: Cardiac resynchronization therapy, ICD: Implantable cardioverter defibrillator, LVEF: left ventricular ejection fraction, MRA: Mineralocorticoid receptor antagonist
* glomerular filtration rate less than 60 ml/min/1.73 m^2 for at least three months
** body mass index more than 40

(p:<0.05). The mean left ventricular ejection fraction (LVEF) was significantly lower in DHF (38.67% vs. 45.90% p<0.001). The rate of hyponatremia (sodium <135 meq/l) was higher among DHF (p<0.05). The clinical variables and biomarkers are shown in Table 2.

The patients were also separated into the groups based on the mechanism of HF: ischemic cardiomyopathy(ICM -32.5%), non-ischemic dilated cardiomyopathy (NICM-4.4%), valvular heart failure (15.6%), high output heart failure (2.9%) and heart failure with preserved ejection fraction-HFpEF(28.1%). The etiology for 16.6% of the patients could not be identified.

The acute comorbidities on admission were as follows: infection (20.2%), stage 3 hypertension (16.7%), acute coronary syndrome (12.2%), and arrhythmia (38.2%).132 (%16,3) of the patients underwent coronary angiography due to suspicion of coronary ischemia. 23 of those patients (2.8%) underwent percutaneous transluminal coronary angioplasty (PTCA) following angiogram. Two patients died during PTCA. The most common arrhythmia observed in the study was atrial fibrillation (AF) (33.2%). Seventy-eight of the patients with AF (9.6%) were newly diagnosed. Only five patients (0.6%) were diagnosed with ventricular tachycardia.

The medication history could be recorded for 678 patients (616 for DHF and 62 for PE). Mineralocorticoid receptor antagonist (MRA) and furosemide usage were observed more commonly in DHF (p<0.05). Angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARB) and digoxin were ordered more commonly in DHF at hospitalization (p<0.05). Prescription rates of ace inh/arb,

Table 2. *Examination and laboratory findings on admission*

Variables	Decompensated heart failure (n: 722)	Acute pulmonary edema (n: 83)	p
Systolic blood pressure (mmhg mean ± SD)	129.2±33.3	184.4±56.8	**<0.001**
Diastolic blood pressure (mmhg mean ± SD)	74.6±18.4	104.2±25.6	**<0.001**
Heart rate bpm, mean ± SD)	92±33.6	103±42.4	**0.001**
Saturation (mean% ± SD)	86.83±14.78	80.12±16.91	**0.008**
Sodium<135 mEq/l n (%)	483 (66.9%)	45 (54.2%)	**0.021**
Potasium >5.5 mmol/l n (%)	70 (9.7%)	4 (4.9%)	0.145
Albumine<3.5 gr/dl n (%)	183 (25.3%)	14 (16.9%)	0.089
FBG >200 mg/dl n (%)	117 (16.2%)	17 (20.5%)	0.322
Hemoglobine<12 g/dl n (%)	246 (34.1%)	28 (33.7%)	0.951
ACE inhibitors/ARB n (%)	431 (59.7%)	63 (75.9%)	**0.004**
Beta blockers n	413 (57.2%)	52 (62.7%)	0.341
MRAs n (%)	203 (28.1%)	26 (31.3%)	0.539
Digoxin n (%)	198 (27.4%)	11 (13.3%)	**0.005**

ACE: Angiotensin-converting enzyme, ARB: Angiotensin II receptor blocker, FBG: Fasting blood glucose, MRA: Mineralocorticoid receptor antagonist.

Table 3. *Mortality rates for subgroups of acute heart failure*

	In hospital mortality	1-month mortality	6-month mortality	12-month mortality	24-month mortality
Ischemic cardiomyopathy	20 (5.5%)	51 (14.9%)	103 (30.0%)	143 (41.7%)	181 (52.8%)
Nonischemic cardiomyopathy	1 (2.0%)	3 (6.3%)	8 (16.7%)	13 (27.1%)	19 (39.6%)
SevereValvular heart disease	5 (4.1%)	19 (16.1%)	43 (36.7%)	49 (41.5%)	57 (48.3%)
High-output heart failure	0 (0.0%)	2 (8.7%)	4 (17.4%)	8 (34.8%)	10 (43.5%)
HFpEF	5 (2.0%)	25 (10.4%)	61 (25.3%)	75 (31.1%)	114 (47.3%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (100%)

HFpEF: Heart failure with a preserved ejection fraction.

beta-blocker, and MRA at discharge were 49.1%, 49.9%, and 33.6%, respectively. There were no statistically significant differences between the medications prescribed at discharge rates except that MRA was prescribed more commonly in DHF (34.8% vs. 10.8%, p<0,01).

The in-hospital mortality, 1- year mortality, and 2-year mortality data of the groups separated by the etiology were shown in Table 3. The 2-year mortality was 52.8% among the ICM patients, whereas it was 39.6% among the NICM group. There were no statistically significant differences in the 2 -year mortality between the groups (p=0,389). The survival rates of groups are shown in Fig. 1. According to the clinical status, the 2-year mortality rate was higher in DHF than in PE (51.4% vs. 31.6% p<0,001). Moreover, the two-year mortality rate was lower in de novo AHF than in acutely decompensated chronic HF (41.9% vs. 51.2% p:0,039).

The Cox proportional-hazards model revealed that advanced age, previous cerebrovascular diseases, anemia, hyponatremia, hypoalbuminemia, lower LVEF, and lower systolic blood pressure were independent predictors for increased risk of 2-year mortality. In contrast, usage of beta-blockers at hospitalization and ACE inhibitors at discharge were predictors for improved two-year mortality (Table 4).

Discussion

Our study showed that the in-hospital, one-year, and two-year mortality rates in AHF patients were 3.8%, 35.7%, and approximately 50%, respectively. The in-hospital and 1-year mortality rates were comparable to those found in the previous large studies[11-13]. In the Cox proportional-hazards model, advanced age, lower LVEF, cerebrovascular event, low systolic blood pressure, hypoalbuminemia, and hyponatremia were

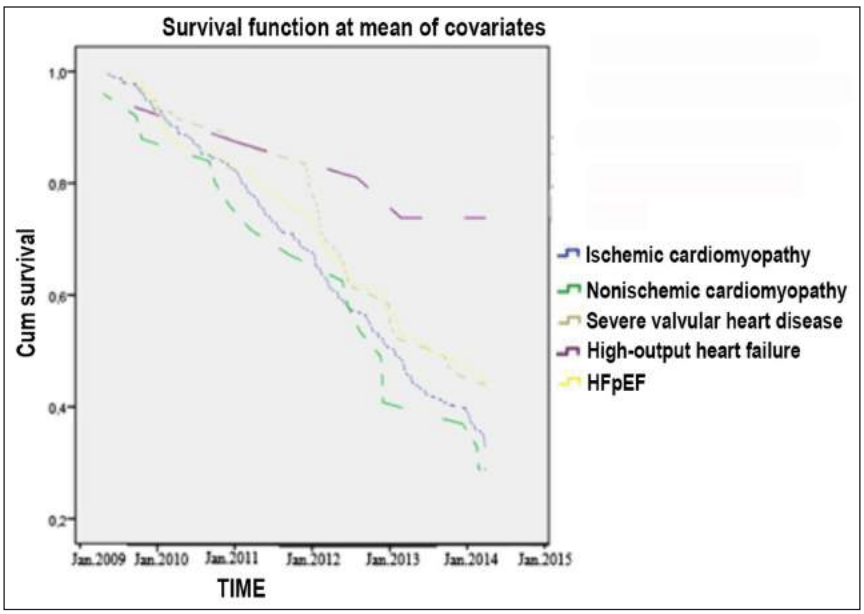

Figure 1. *Survival analysis of acute heart failure patients.*

Table 4. *Independent predictors of 2-year mortality in acute heart failure*

Univariate analysis				Multivariate analysis			
Variables	HR	95% CI	P value	Variables	HR	95% CI	P value
Male	0.866	0.653–1.149	0.319	Age	1.037	1.021–1.053	<0.001
Age	1.036	1.023–1.049	<0.001	LVEF	0.981	0.968–0.993	0.003
LVEF	0.965	0.937–0.977	0.005	De novo HF	1.105	0.708–1.724	0.661
De novo HF	0.978	0.959–0.997	0.006	CVD	2.130	1.101–4.121	0.025
CAD	0.909	0.685–1.205	0.507	Systolic BP	0.988	0.980–0.996	0.003
CVD	2.236	1.285–3.893	0.004	Diastolic BP	0.999	0.983–1.014	0.869
Diabetes	1.167	0.878–1.552	0.287	Hyperlipidemia	0.780	0.512–1.189	0.249
Systolic BP	0.988	0.983–0.993	<0.001	CRF	1.033	0.988–1.104	0.352
Diastolic BP	0.979	0.970–0.988	<0.001	Sodium<135 mEq/l	1.351	1.124–1.629	<0.001
Hyperlipidemia	0.629	0.442–0.897	0.010	Albumine<3.5 gr/dl	1.629	1.062–2.500	0.025
Thyroid disease	0.911	0.609–1.362	0.649	Hemoglobine<12 g/dl	1.102	0.951–1.257	0.574
Atrial fibrillation	0.951	0.706–1280	0.739	Beta blocker in hospital	0.532	0.334–0.848	0.008
COPD	0.770	0.564–1.050	0.099	ACE inh/ARB in hospital	0.971	0.632–1.490	0.892
CRF	1.259	1.045–1.353	<0.001	ACEinh/ARBatdischarge	0.774	0.510–0.984	0.015
Beta blockers usage	1.097	0.757–1.589	0.624	Beta blocker at discharge	0.950	0.604–1.495	0.826
ACEinh/ARB usage	1.269	0.879–1.831	0.203	ICD	0.640	0.202–2.024	0.447
HR on admission	0.997	0.991–1.004	0.402	DHF	0.888	0.448–1.761	0.733
Sodium<135 mEq/l	1.762	1.303–2.384	<0.001				
Albumine<3.5 gr/dl	2.577	1.821–3.647	<0.001				
Hemoglobine<12 g/dl	2.168	1.596–2.946	<0.001				
Beta blocker in hospital	0.610	0.457–0.814	0.001				
ACE inh/ARB in hospital	0.526	0.471–0.657	0.002				
MRA in hospital	0.812	0.593–1.113	0.195				
ACE inh/ARBatdischarge	0.576	0.433–0.766	<0.001				
Beta blocker at discharge	0.475	0.357–0.633	<0.001				
MRA at discharge	1.089	0.808–1.468	0.575				
ICD	0.640	0.423–0.969	0.035				
DHF	2.281	1.388–3.750	0.001				

ACE: Angiotensin-converting enzyme, ARB: Angiotensin receptor blocker, BP: Blood pressure, CAD: Coronary artery disease, CHF: Chronic renal failure, glomerular filtration rate less than 60 ml/min/1.73 m2 for at least three months, COPD: Chronic obstructive pulmonary disease CVD: Cerebrovascular disease, DHF: Decompensated heart failure, HR: Heart rate, HF: Heart failure, ICD: Implantable cardioverter-defibrillator, LVEF: left ventricular ejection fraction, MRA: mineralocorticoid receptor antagonist.

independent predictors that increased two year mortality. In contrast, the usage of beta-blockers during hospitalization and ACE inhibitors at discharge were determined as predictors that decreased two year mortality.

AHEAD Main, a study conducted to determine long-term survival rates in AHF, showed that one-year and three-year survival rates of patients were 79.7% and 64.5%, respectively[11]. In the EFICA study, 1-year mortality among AHF was 46.5%[12]. In ADHERE trial, the in-hospital mortality of the 65.180 patients with AHF was 4.1%, whereas the one-year mortality was 36%[13]. ALARM HF revealed that the overall hospital death rate was 12% among AHF[14]. In both OPTİMIZE trial and the ESC-HF Pilot trial, in-hospital mortality was reported in 3.8% of AHF patients[15,16]. Our study's hospital mortality rate was similar to ADHERE, OPTİMIZE, and ESC-HF Pilot but lower than ALARM HF. The higher in-hospital mortality rate in ALARM HF was attributed to the severity of ALARM patients. (the incidence of cardiogenic shock was 11.7%)[14]. One year mortality rate of our study was comparable to ADHERE, higher than AHEAD Main, and lower than the EFICA study. Those differences in the rates were considered to be driven by many factors, including the patients' heterogeneity and difference in the design of the studies.

There was no statistically significant difference between the 2-year mortality rates of ICM and NICM. The clinical studies investigating the difference in prognosis between ICM and NICM have produced conflicting results[17-19].

Harjola et al.showed that age, low plasma sodium, previous myocardial infarction, and creatinine level were independent predictors for one-year mortality in AHF patients[20]. Similarly, hyponatremia and older age were independent predictors in our study. Previous large studies also revealed that hypoalbuminemia, hyponatremia, lower systolic blood pressure, and lower LVEF were independently associated with mortality in heart failure[21-25]. Similar to our study, the meta-analysis of Prins et al. revealed that non-withdrawal of beta-blockers in AHF was an independent predictor for increased survival time[26]. The neutral effect of MRA on mortality was primarily attributed to the etiologic heterogeneity in AHF.

The study was designed as a retrospective study and conducted in a single center. Due to the study's design, patient compliance with medical treatment after discharge was unknown. The medications other than ACE inhibitors /ARB, beta-blockers, and MRA were not assessed for effects on mortality.

Conclusion

In our study, mortality rates in AHF were similar to those in the large-scale studies. While hypoalbuminemia, hyponatremia, lower systolic blood pressure, and lower LVEF on admission increased 2-years mortality, beta-blocker use during hospitalization and ACE inhibitors administration at discharge decreased two years of mortality.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Results of Conservative Treatment in Osseous Mallet Finger: A Retrospective Case Series

Osseöz Mallet Parmak Tedavisinde Konservatif Tedavinin Sonuçları: Retrospektif Olgu Serisi

Murat Altan[1], Mehmet Demirel[2], Omer Ayik[3]

[1]Sarıkamış State Hospital, Orthopaedics and Traumatology Department, Kars; [2]Istanbul University, Istanbul Faculty of Medicine, Orthopaedics and Traumatology Department, Istanbul; [3]Ataturk University Faculty of Medicine, Orthopaedics and Traumatology Department, Erzurum, Turkey

ABSTRACT

Aim: *This study investigated conservative treatment's clinical and radiological results in osseous mallet fingers.*

Material and Method: *26 patients (17 males, 9 females; mean age=32.4 age range=18–48) diagnosed with osseous mallet finger injury were retrospectively reviewed and included in this retrospective study. Mallet finger injuries were categorized according to the Wehbe-Schneider classification. Distal interphalangeal joint (DIJ) angulation, radiographic union, osteoarthritis, and dorsal fragment occurrence were examined on anteroposterior and lateral X-rays. Crawford's criteria were used to evaluate the functional outcomes.*

Results: *According to Wehbe-Schneider classification, 13 patients were type IA, 11 were type IB, and 2 were type IC. The mean time of the admission to our clinic after trauma was 1.09 days (range, 0–9). The mean follow-up was 7.38 months (range=6–10 months). The mean postoperative visual analog scale score for pain was 0.01 (range=0–2) at the last visits. The mean DIP extension deficits were 4.03° (range=0–10°). A dorsal hump was detected in 7 patients at the last follow-up. According to Crawford's criteria, functional outcomes were perfect in 9 patients, as good in 12, moderate in 4, and poor in 1.*

Conclusion: *Evidence from this study has revealed that conservative treatment is an effective treatment modality in the management of osseous mallet fingers with satisfactory radiological and clinical outcomes.*

Key words: *osseous mallet; conservative treatment; percutaneous; K wire*

ÖZET

Amaç: *Bu çalışmanın amacı, osseöz mallet parmaklarda konservatif tedavinin klinik ve radyolojik sonuçlarını araştırmaktır.*

Materyal ve Metot: *Osseöz mallet parmak yaralanması tanısı alan 26 hasta (17 erkek, 9 kadın; ortalama yaş=32,4 yaş aralığı=18–48) retrospektif olarak incelendi. Mallet parmak yaralanmaları Wehbe-Schneider sınıflamasına göre sınıflandırıldı. Anteroposterior ve lateral grafilerde distal interfalangeal eklem (DIE) açılanması, radyografik kaynama, osteoartrit ve dorsal fragman varlığı incelendi. Fonksiyonel sonuçları değerlendirmek için Crawford kriterleri kullanıldı.*

Bulgular: *Wehbe-Schneider sınıflamasına göre 13 hasta tip IA, 11 hasta tip IB ve 2 hasta tip IC idi. Travma sonrası kliniğimize ortalama başvuru süresi 1,09 gün (aralık, 0–9) idi. Ortalama takip süresi 7,38 aydı (aralık=6–10 ay). Son kontrollerde ağrı için ortalama postoperatif vizüel analog skala skoru 0,01 (aralık=0–2) idi. Ortalama DIP ekstansiyon defisiti 4,03° (aralık=0–10°) olarak kaydedildi. Son kontrolde 7 hastada dorsal hörgüç saptandı. Crawford kriterlerine göre fonksiyonel sonuçlar 9 hastada mükemmel, 12 hastada iyi, 4 hastada orta ve 1 hastada kötü olarak belirlendi.*

Sonuç: *Bu çalışma, osseöz mallet parmakların tedavisinde konservatif tedavinin, tatmin edici radyolojik ve klinik sonuçlarla birlikte etkili bir tedavi yöntemi olduğunu ortaya koymuştur.*

Anahtar kelimeler: *osseöz mallet; konservatif tedavi; perkütan; K teli*

Introduction

An osseous mallet finger is a deformity caused by an avulsion fracture of the distal phalanx at the terminal extensor tendon bony insertion. Mallet finger is a common injury in young to middle-aged males and older females. The disorder usually occurs in the work environment or during participation in sports.

If untreated, the distal phalanx may progressively assume a fixed position, and the proximal phalangeal joints may gradually be hyperextended. Although several treatments are available for managing osseous mallet fingers, the literature's optimal treatment choice is controversial. Conservative treatment of mallet finger fracture has been extensively reported, including continuous rigid aluminum splinting, prefabricated

İletişim/Contact: *Murat Altan, Sarıkamış State Hospital, Orthopaedics and Traumatology Department, Kars, Turkey* • ***Tel:*** *0506 686 96 66* • ***E-mail:*** *altanmurat88@gmail.com* • ***Geliş/Received:*** *25.11.2021* • ***Kabul/Accepted:*** *02.04.2022*

ORCID: *Murat Altan, 0000-0001-5602-1458* • *Mehmet Demirel, 0000-0003-1131-7719* • *Ömer Ayık, 0000-0002-3437-6394*

splints, plaster casting, and custom-made orthosis[1]. Numerous surgical techniques have been described, including open reduction and K-wire fixation, pin fixation alone, tension band wire, and pull-out steel wires[2]. Each of the surgical procedures used to treat mallet fractures has a risk of complications. Consequently, there is no traditional surgical treatment[3].

This study aimed to present clinical and radiological results of conservative treatment in managing osseous mallet fingers.

Material and Methods

In this retrospective study, 32 patients with an osseous mallet finger injury (20 males, 12 females) treated conservatively in a single tertiary care center between 2018 and 2020 were included. Informed consent was obtained from each study participant, and approval of the institutional review board was obtained.

Inclusion criteria were: 1) type I-A, B, or C osseous mallet finger injury according to Wehbe-Schneider classification; 2) complete medical records and radiographic images; and 3) being willing to participate in the study. Patients with Wehbe-Schneider type II fractures were excluded as such fractures frequently require surgical treatment on account of the volar subluxation. Moreover, tendinous mallet fingers, comminuted fractures, injuries older than two weeks, patients with other injuries to the same finger, open fractures, and patients <18 years old were excluded from our study.

One of the patients was operated on due to the development of volar subluxation in the 1 st-week controls and was excluded from the study. In addition, 3 of the patients were excluded from the study as they did not come for their sixth-month follow-up, and 2 of the patients were excluded from the study owing to their non-compliance with conservative treatment (removing the splint early). Thus, 26 patients who met the inclusion criteria were included.

Reviewing the injuries, five patients had sports injuries, two were involved in an assault, 13 had fallen from a height, and six had work-related injuries. The affected fingers were index finger (n=2), middle finger (n=3), ring finger (n=10) and little finger (n=11).

Distal interphalangeal joint (DIJ) angulation, radiographic union, osteoarthritis, and dorsal fragment occurrence were evaluated on lateral X-rays. DIJ angulation was examined on the lateral X-rays with a line drawn in the middle point of both the middle and distal phalanx in its transverse axis to measure the angulation, and exact angulation could be determined with the digital X-ray software.

Crawford's criteria[4] were used to evaluate the functional outcomes that provide excellent for full DIJ extension, full flexion, no pain; good for 0–10° of extension deficit, full flexion, no pain; fair for 10–25° of extension deficit, any flexion loss, no pain; and poor for >25° of extension deficit or persistent pain. The extensor lag in the injured finger's DIPJ was additionally measured with a standard steel finger goniometer using a dorsal approach.

Conservative Technique

All patients were administered volar aluminum orthotic splint without restricting the proximal interphalangeal joint in the neutral position and were emphasized the significance of maintaining the exact position of the injured finger. Patients were revealed to apply the volar splint full time for six weeks without motion, followed by a night orthotic splint for two weeks with passive flexion. Patients were strictly followed in the first week, second, and third week for the appropriate usage control of the splint.

Physical Therapy

All patients were applied the volar splint full time throughout the first six weeks without motion. At the end of the 6th week, passive flexion exercises were commenced without extensor lag. Night orthosis was afterward practiced for two further weeks for all patients. Splint duration was extended for five patients whose union time exceeded six weeks. Patients were evaluated by goniometric measurements of the range of motion of DIJ and extensor lag in the DIJ.

Clinical Evaluation

All patients were routinely observed in the sixth month following the beginning of physical therapy. At each visit, the patients were assessed with distal interphalangeal joint flexion, extension lag, final angulation, visual analog scale score, and radiographic union. All data, such as pain scores, fingernail and skin inflammation, and volar subluxation in the X-ray, were recorded.

Results

Clinical Results

Seventeen male and nine female patients were treated conservatively, and their average age was 32.4 years (range=18–48 years). Mallet finger injuries were

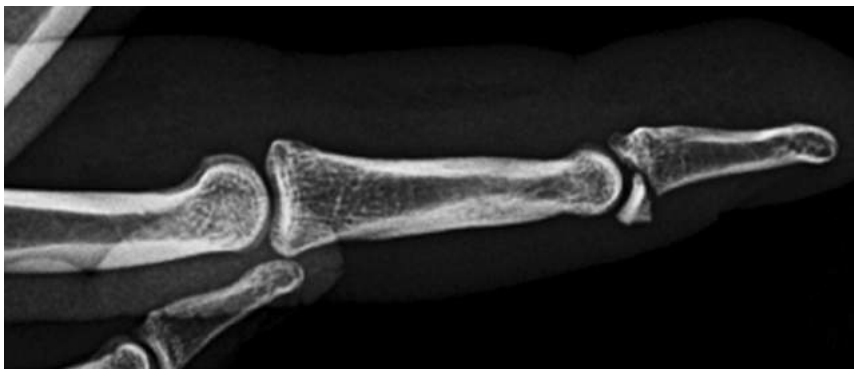

Figure 1. *Type 1B Mallet Finger Injury Lateral X-Ray.*

Figure 2. *Mallet injury with complete union Lateral X-Ray.*

Figure 3. *Clinical dorsal hump.*

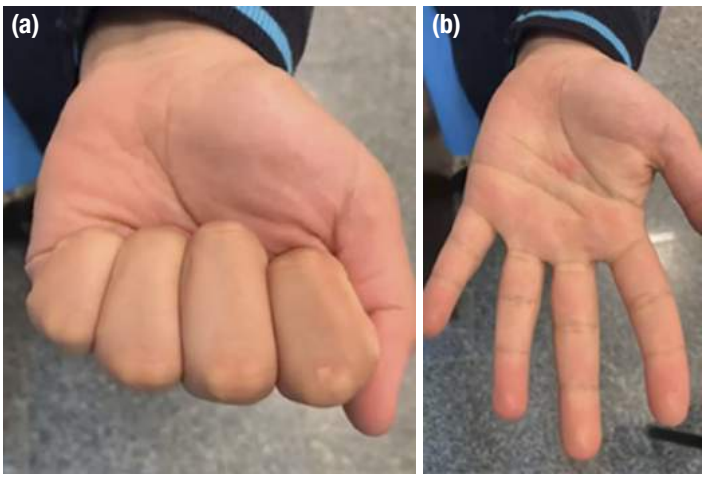

Figure 4. a, b. *Full flexion range of motion after complete union* ***(a)****. Full extension range of motion after complete union* ***(b)****.*

evaluated in all patients according to Wehbe-Schneider type IA-B and C. 13 patients were type IA, 11 were type IB, and 2 were type IC (Fig. 1).

The mean time of the admission to our clinic after trauma was 1.09 days (range, 0–9). Treatment was started promptly after patients applied. There was an injury of the little finger in 11 patients, a ring finger in 10 patients, three patients in the middle, and two patients with the index finger injuries. Dominant and non-dominant hands were affected in 15 and 11 patients consecutively.

Six patients were admitted with work accidents, 13 patients with falls, five patients with sports-related injuries, and two patients with assault-related injuries.

The mean follow-up was 7.38 months (6–10 months). The mean postoperative visual analog scale score for pain was 0.01 (range, 0–2) at the last visit.

The mean DIP flexion degrees at the final controls were 71.3° after conservative treatment (40–80°). The mean DIP extension deficits were 4.03° (0–10°) (Fig. 2). Dorsal hump was detected in 7 patients at the last follow-up, but it was absent in 19 patients (Fig. 3).

According to Crawford's criteria, nine patients had perfect, 12 had good, 4 had moderate, and one patient had poor results in the conservative treatment (Fig. 4). In 4 patients, volar subluxation was observed in the follow-up for one week, and they were operated on and excluded from the study. Superficial skin necrosis, osteomyelitis, nail bed problems, and skin infection were not detected.

Radiographic Results

The mean time to union was determined as 6.07 weeks (5–8 weeks) on lateral radiographs. Final DIJ angulation was 4.88° on lateral radiographs (0–12°). In 1 patient, the development of osteoarthritis was observed on lateral radiographs during the follow-up.

Discussion

Treatment options for osseous mallet finger injury are still controversial. While numerous publications in the literature recommend surgical treatment and describe various surgical techniques, conservative treatment alternatives are also plentiful in the literature.

When the current literature is reviewed in detail, it has been discerned that the complication rates of surgical treatment methods are reported to be high. Examples of reported complications include; pin tract infection, nail deformities, spur formation, loss of fracture reduction, subsequent removal by open surgical technique in hook plate technique, and an avulsed bone fragment.

Surgeons have proposed surgical treatment in cases with a displaced fracture where more than one-third of the articular surface is affected or when volar subluxation is present[5]. In the light of this knowledge, volar subluxation was recognized on the lateral X-ray in one of the patients treated conservatively in the first week of the follow-up, and a surgical decision was performed. This condition constitutes a significant clue concerning the necessity of close follow-up and reasonable evaluation of lateral radiographs.

Complication rates in 21 to 31% have been reported using lengthening block fixation, comparable to the complication rate in several studies[6–9].

Some studies also report pin site infection and iatrogenic communication of small fracture fragments during insertion of intra-fragmentary K-wire complications[10].

Open surgical techniques for mallet fractures may apply to late cases, including direct internal fixation of the fragment. In all circumstances, this can be technically challenging due to the fragment's small size, and placement of implants into the small proximal fragment may result in further fragmentation of bone. Some authors' practice of treating mallet fracture informed that strong fixation of the fracture and protection of the blood supply of the dorsal fragment is not manageable[1].

In addition, superficial skin necrosis, osteomyelitis, nail bed problems, and skin infections can be seen in patients undergoing open surgery[11].

Ishiguro's method is also among the surgical options. Still, its disadvantages include exposed wires that delayed their return to physical activity and affected their work during the early postoperative period[12].

The dorsal hump can be encountered due to the fragment's dorsal displacement in patients treated conservatively; however, a similar condition can be found in patients who underwent open surgery or patients who underwent percutaneous K wire.

Some authors recommend the hook plate technique as an alternative for manipulating small, avulsed fragments[13]. Nevertheless, the disadvantages of this method include the fact that the plate is palpable just under the skin and then the requirement of removing the plate by open surgical technique.

Furthermore, trans-fixation K-wires were used to fix the DIP joint may cause iatrogenic nail bed injury, bone fragment rotation, chondral damage, or osteoarthritis[14].

Additionally, some authors have reported some disadvantages of repeated attempts during insertion in surgical procedures. Examples are articular cartilage damage leading to secondary osteoarthritis, particularly if more than one attempt during pin insertion is needed, and iatrogenic nail bed injury[15].

A review of the literature reveals that the overall complication rate of open treatment is 53%. Major complications include infection (20%), permanent nail deformities (18%), joint incongruity (18%), fixation failure (13%), and bony prominence (11%)[16].

A volar aluminum splint is preferred for patients in this study, treated conservatively. Although the dorsal splint application was practical, the higher rate of skin complications due to the less soft tissue in the dorsal region was the fundamental reason for our volar splint application.

Although some authors limited splints to <5 weeks in the early union, the use of splints in patients in our study was completed to 6 weeks.

Stack splint application has been studied with hypotheses that patient compliance will be better and functional results superior to other regimens. Nevertheless, it has been determined that patient compliance is low and only half of the patients have satisfying outcomes, although severe skin complications have not been encountered. Therefore, the authors reported that they no longer prefer to use it[17].

Many studies did not reveal a significant difference between surgical and conservative treatments. For this reason, most authors prefer conservative methods in mallet finger treatment[18–20].

Studies supporting conservative treatment include Stern et al.[21] found lower complication rates in conservative treatment.

Likewise, Smit et al.[22] compared surgical and conservative treatment methods and recommended that the best treatment choice for uncomplicated mallet finger injuries is provided with orthotic methods.

In their meta-analysis covering studies published between 1966-and 1998, Geyman et al.[23] recommended that conservative methods are appropriate for most mallet injuries, even for fractures of more than 1/3 of the articular surface.

In this study, the efficacy of conservative treatment and the positive effects of conservative treatment on the functional status of patients to avoid the potential complications of surgical treatment is aimed to confirm.

Various publications regarding surgical methods have been reviewed in the literature, and the results were found to be similar in comprehensive series.

The lack of a control group can be declared as the weakness of this study.

Conclusion

This study reveals that conservative treatment is cost-effective, efficiently applicable, and found at high rates in the literature. While various complications of surgical treatments are avoided, it has been determined that appropriate functional results can be achieved in patients with conservative treatment.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Assessing Medication Adherence of Emergency Medicine Specialists Using the MMAS-8

Acil Tıp Uzmanlarının İlaç Uyumunun MMAS-8 Kullanılarak Değerlendirilmesi

Damla Anbarli Metin[1], Arda Kocatas[2]

[1]Department of Emergency Medicine, Karabuk University Faculty of Medicine, Karabuk; [2]Department of Emergency Medicine, Bakirçay University Cigli Training and Research Hospital, Izmir, Turkey

ABSTRACT

Aim: *Although doctors in the emergency medicine department report high career and life satisfaction rates, burnout and stress may occur after working many years, resulting in several incompatibilities and risks. The Morisky Medication Adherence Scale (MMAS-8) is a simple, reliable, verified self-report measure to assess medication adherence. In our study, we planned to evaluate the treatment compliance of emergency medicine specialists with the MMAS-8 scale.*

Material and Method: *This study employed a cross-sectional descriptive design. The emergency medical experts were contacted online to self-report their medication-taking behaviors using the MMAS-8. The MMAS-8 was evaluated using factor analysis. The treatment combinations of emergency medicine specialists were assessed in terms of chronic disease, the number of night shifts, and the number of medications used.*

Results: *The MMAS-8 was assessed by KMO and Barlett analyses for structural validity and adequate sampling group evaluation. The average score obtained from the MMAS-8 was found to be 3.99±2.52. When chronic disease and medication adherence were considered, the MMAS-8 scores revealed low adherence in cases of chronic diseases (p=0.025).*

Conclusion: *The treatment of patients with chronic diseases is very difficult. As found in this study, although the patients were doctors, medication adherence was low. It is known that emergency medical professionals have a high incidence of chronic diseases and mortality. Furthermore, low medication adherence with chronic or acute treatment increases risks.*

Key words: *emergency medicine specialist; MMAS-8; medication adherence*

ÖZET

Amaç: *Acil tıp uzmanlığı; yüksek kariyer ve yaşam doyum oranları bildirilmesine rağmen uzun süreli devam edenlerde tükenmişlik ve stres sorunu söz konusudur. Bu stres ve tükenmişlik bir çok uyumsuzluk ve riski de yanında getirmektedir. Tedavi uyumunun değerlendirilmesi için basit, güvenilir ve doğrulanmış bir öz bildirim aracı olarak MMAS-8 ölçeği kullanılmaktadır.*

Materyal ve Metot: *Çalışmamız, kesitsel tanımlayıcıdır. Online olarak ulaşılan acil tıp uzmanları kendilerini MMAS-8 ile değerlendirdiler. MMAS-8 ölçeği faktör analizi ile değerlendirildi ve acil tıp uzmanların tedavi uyumları kronik hastalık varlığı, gece vardiya sayısı ve kullanılan medikasyon sayısı açısından değerlendirildi.*

Bulgular: *MMAS-8 ölçeğinin yapı geçerliliği ve yeterli örneklem grubunun değerlendirilmesi için KMO ve Barlett analizleri ile uyumlu olarak değerlendirilmiştir. MMAS-8 skorlaması ortalama değeri 3,99±2,52 olarak değerlendirilmiştir. Kronik hastalık varlığı ve tedavi uyumu değerlendirildiğinde; kronik hastalığı olan vakalarda MMAS-8 skoru düşük uyum olarak değerlendirilmiştir (p=0,025).*

Sonuç: *Kronik hastalığı mevcut olan hastaların tedavi uyumları oldukça zordur. Çalışmamızda gösterdiği gibi hastanın kendisi doktor olsa da tedavi uyumundaki sorun değişmemektedir. Acil tıp uzmanlarının kronik hastalık eğilimlerinin ve mortalitesinin yüksek olduğunu bilinmektedir. Bu durumun üstüne kronik ya da akut tedavilerine uyumlarının düşük olması var olan risklerini daha da artırmaktadır.*

Anahtar kelimeler: *acil tıp uzmanı; MMAS-8; tedavi uyum*

Introduction

It is a difficult decision to choose a field of medical expertise. Such decisions determine an individual's career and future lifestyle[1]. Patient and case diversity were important motivations for specializing in emergency medicine[2–4]. Excessive clinical workload, an unhealthy lifestyle, long shifts, and night shifts were related to burnout and stress[5–7]. Moreover, excessive workload, an unhealthy lifestyle, and night shifts are defined as factors associated with the release of stress in the lives of emergency medicine specialists and the development of burnout[8,9]. Stress and burnout cause several incompatibilities and risks.

İletişim/Contact: *Damla Anbarlı Metin, Department of Emergency Medicine, Karabuk University Faculty of Medicine, Karabuk, Turkey* • ***Tel:*** *0554 314 95 92* • ***E-mail:*** *damla_2012@hotmail.com* • ***Geliş/Received:*** *21.12.2021* • ***Kabul/Accepted:*** *11.02.2022*

ORCID: *Damla Anbarlı Metin, 0000-0001-9873-4587* • *Arda Kocataş, 0000-0003-4196-8993*

A simple, reliable, and verified self-report tool can better understand medication adherence and identify new treatment modalities[10]. For this purpose, an eight-item Morisky Medication Adherence Scale (MMAS-8) was developed[11]. The MMAS-8 is simple, and it is the most commonly used self-report method for determining the level of medication adherence[12–13].

Hypertension, diabetes, hyperlipidemia, and psychiatric disorders have been examined in inpatient groups, such as chronic obstructive pulmonary disease patients. This study set out to assess whether a group of emergency medicine specialists whose lifestyles were unstable and working under severe stress was adhering to the prescribed medications.

Materials and Methods

This study used a cross-sectional descriptive design. After obtaining IRB approval from Katip Çelebi University, emergency medical specialists were contacted for data collection in the following year. The emergency medicine specialists who were reached online responded to the MMAS-8 items. In addition to this data set, demographic data and chronic diseases were also recorded.

The MMAS-8 is a scale consisting of 8 items. The first seven questions are close-ended with yes/no answers. Question 8 includes four choices: never/rarely, occasionally, sometimes, and usually/always. Scores <6, 6–7, and 8 are classified as low, medium, and high medication adherence. The evaluation of the MMAS-8 takes about 5–6 minutes[11]. The scale has been translated and adapted into Turkish[14].

Demographic data of emergency medical specialists and average medication adherence scores were analyzed using descriptive statistics. Because the data were not normally distributed, Mann-Whitney U tests were used to analyze the data related to medication adherence.

Factor analysis was conducted to evaluate the data set. The Cronbach Alpha value and the total correlation of the items were assessed to determine whether the psychometric tests could be used. Before starting the factor analysis, Kaiser Meyer Olkinn (KMO) and Barlett tests were performed to determine the suitability of the factor analysis. The Cronbach Alpha coefficient was used to evaluate the internal reliability. SPSS 22 package program was used for data analysis.

Table 1. *Demographic data of emergency medicine specialists*

Demographic data		n	%
Gender	Woman	31	43.1
	Man	41	56.9
Chronic disease	Yes	42	58.3
	No	30	41.7
		mean ± SD	
Age		36.5±6.3	
Number of night shifts		7.26±2.3	
Number of drugs used continuously		1.38±1.8	

Results

The average age of emergency medicine specialists who participated in this study was 36.5±6.3, and 58% of the participants were male. While 5% of them were not working night shifts, 52% had 7 or 8-night shifts per month. As shown in Table 1, the average number of night shifts per month was 7.26±2.3.52.5% of the participants had a chronic disease. Thyroid problems (31.8%) were found to be the most common disorder, followed by psychiatric disorders (20.5%) and diabetes (18.2%) (Fig. 1).

KMO and Bartlett tests were performed to assess the structural validity of the MMAS-8 and the adequacy of the sample group. The KMO value was 0.758 and considered appropriate for analyzing the fundamental variables. Similarly, Bartlett tests showed that test results and scale items were correlated, and factor analysis could be performed (x^2 211.480, $p<0.05$). The items, factor loads, and reported variants are shown in Table 2. The factor load of the scale items was above 0.40, and the Cronbach Alpha coefficient of the items was 0.793.

The average score obtained from the MMAS-8 was found to be 3.99±2.52. The MMAS-8 scores revealed medication adherence below a score of 6. When the presence of chronic disease and medication adherence were considered, the MMAS-8 scores of 32 cases with chronic diseases (44.4% of the total number of cases) were found as low adherence (p=0.025) (Table 3).

Discussion

This study investigated the medication adherence of emergency medicine specialists using the MMAS-8. The validity and reliability studies of the Turkish

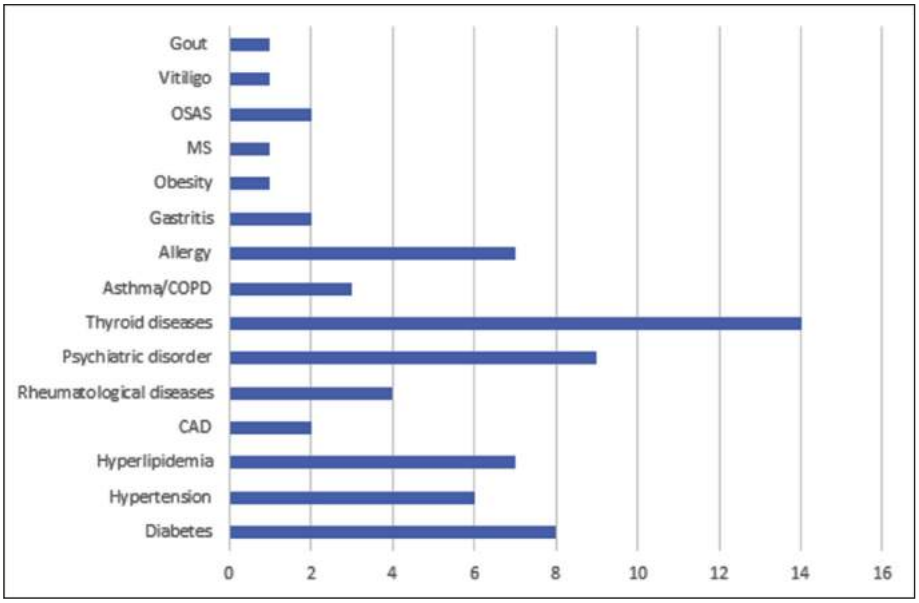

Figure 1. *Chronic disease distribution of emergency medicine specialists (OSAS: Obstructive sleep apnea syndrome; MS: Multiple sclerosis; COPD: Chronic obstructive pulmonary disease; CAD: coronary artery disease).*

Table 2. *Factor distributions of MMAS-8 score*

1. Do you sometimes forget to take your medicine?	0.762
2. People sometimes skip taking their medication for reasons other than forgetting. Thinking about the past two weeks, were there any day (s) when you didn't take your medicine?	0.860
3. Have you ever interrupted or stopped taking your medicine without telling your doctor because you felt bad when you took it?	0.450
4. Do you sometimes forget to carry your medicine with you when you travel or leave home?	0.494
5. Did you take all your medicines yesterday?	0.528
6. Do you sometimes stop taking your medication when you feel like your symptoms are under control?	0.592
7. Taking medication every day is a real hassle for some people. Do you ever have trouble sticking to a treatment plan?	0.677
8. How often do you have difficulty remembering to take all your medications?	0.574

Explained variance: 61.8

Table 3. *Medical adherce distribution of emergency medicine specialists*

	Chronic Disease			
MMAS-8	Yes	%	No	%
Low adherence	32	44.4	17	23.6
Moderate adherence	8	11.1	6	8.3
High adherence	2	2.7	7	9.7

MMAS-8 score Mean ± SD: 3.99±2.52 (range 0–8)

translation of the MMAS-8 were conducted with emergency medical specialists[14]. The KMO value was 0.58 and was considered suitable for analyzing fundamental variables. Similarly, Bartlett tests showed that the test results and scale items were correlated and could be evaluated by factor analysis (x^2 211.480, $p<0.05$). The factor load of the items was above 0.40, and the Cronbach Alpha coefficient was 0.793. These values show that the MMAS-8 can be used and evaluated with the study group.

The MMAS-8 is a widely used scale for medication adherence. It is especially used to assess adherence to the treatment of hypertensive patients. Hacihasanoğlu Aşilar et al. found that in the study which validated the Turkish translation of the MMAS-8 that medication adherence was low in hypertensive patients[15]. The treatment of patients with chronic diseases is very difficult.

Studies have been conducted on assessing medication adherence and the MMAS-8 in cases of hypertension. In the compilation and meta-analysis, in which 28 studies from 15 countries were evaluated, the number of comorbidities and the number of prescribed drugs were correlated[16]. In our study, the medication adherence of the group with a chronic disease was lower. When looking at the number of chronic diseases in people with chronic diseases, those with a low number of chronic diseases were found to have worse treatment combinations. This can be because patients are

often not familiar with treatment methods, or those with poor medication adherence may lack a complete diagnosis.

The use of oral anticoagulants in patients with atrial fibrillation was evaluated. It was found that the presence of the patient's emotional reactions (such as anger, grief, and depression) was associated with poor medication adherence[17]. Working in emergency medicine causes tiring and stressful lifestyles, leading to burnout and emotional reactions, increasing medication adherence.

Hypertension, heart failure, atrial fibrillation, type 2 diabetes, ulcerative colitis, and several other similar disease groups were examined for medication adherence[18–20]. In general, a chronic disease reduces medication adherence; however, when we examined the sub-group without a chronic disease in our study, medication adherence was not high.

Although many studies have been conducted with disease groups, there is a lack of research on medication adherence of a physician group or health worker group. Emergency medical specialists are different from other branches of medical specialization. They continue to live a life that disrupts the circadian rhythm, which affects all spheres of life. For this reason, just as the likelihood of having a chronic disease has increased, so may the lifestyle and treatment combinations. Since the routine of doctors specializing in emergency medicine regularly includes night shifts, and the participants in this study reported a similar number of night shifts per month, no assessment could be made between the number of night shifts and the treatment combinations. In our study, emergency medical specialists received an average score of 3.99±2.52 from the MMAS-8. Values below 6 points reveal a low medication adherence. This study did not investigate the impact of gender, several night shifts, and age on medication adherence. We found that the treatment of patients with chronic diseases was more problematic. However, the number of chronic diseases or the number of medications used does not change the low level of medication adherence.

Emergency medical specialization is a department that works in shifts during the assistant period. It is known that this form of professional training is the cause of chronic sleep problems, chronic hypertension, and increased cardiovascular mortality[21]. However, after the years spent as an assistant, which increases the risk of disease, emergency experts continue to work an average of 7–8 night shifts per month. These shifts contribute to ongoing risks. In addition, as in our study, the medication adherence of emergency medical specialists with chronic diseases is low. Therefore, there is an increased risk of chronic disease. The mortality and morbidity of emergency medical specialists with low medication adherence and chronic disease will increase. The night/day routine may contribute to delays in or irregular medication use, including missing scheduled medication hours.

As shown in this study, even if the patient is a doctor, the problem with medication adherence does not change. Although they gave rational answers to questions 3 and 6 because of their profession, it did not affect the overall results obtained from the MMAS-8 scores of emergency medical specialists. The results show that the medication adherence of emergency medical specialists is low.

We know that emergency medical specialists' chronic disease and mortality rates are higher than those of other specialization branches. The findings from this study suggest that low medication adherence with chronic or acute treatment increases risks.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Effect of Covid-19 on Social Support Perception and Stress in Healthcare Workers at a Tertiary Hospital

Bir Üniversite Hastanesindeki Sağlık Çalışanlarında Covid-19'un Sosyal Destek Algısına ve Strese Etkisi

Atakan Yilmaz[1], Gulay Tasdemir Yigitoglu[2], Halis Yilmaz[3]

[1]Department of Emergency Medicine; [2]Department of Psychiatric Nursing, Pamukkale University, Faculty of Health Science; [3]Pamukkale University, Health Science Institute, Denizli, Turkey

ABSTRACT

Aim: *Healthcare workers may be at higher risk of Covid-19 transmission due to sharing the same setting with infected people for a long time, increasing their susceptibility to stress. This study set out to identify the effect of Covid-19 on social support perception and stress levels in healthcare workers based at a tertiary hospital.*

Material and Method: *This is a descriptive and cross-sectional study. The healthcare workers practicing at a tertiary hospital constituted the study population. Those giving their informed consent to enroll in the study between April 18 and May 18, 2020, were included in the study. Data were collected through an introductory information form, the Acute Stress Symptom Scale (ASSS), and the Multidimensional Scale of Perceived Social Support (MSPSS). The statistical analyses were performed with the Statistical Package for the Social Sciences v.24.0. The data set was evaluated through mean scores, standard deviation, number and percentage, Mann Whitney U test, Kruskal Wallis Variance Analysis, and Spearman Correlation Analysis.*

Results: *The mean ASSS score of healthcare workers was 1.40±0.83, while the total MSPSS score was 70.9±14.56. The mean scores of sub-dimensions in the perceived social support scale were identified as family 25.07±4.78, friends 22.57±6.01, and significant other 23.27±6.94. A weak, negative correlation was revealed between healthcare workers' ASSS scores and the sub-dimensions of family, friends, significant other, and the total scale score ($p<0.05$).*

Conclusion: *It can be concluded that healthcare workers' acute stress symptom level was mild, while their multidimensional social support perception was relatively high. Most notably, in risky times such as pandemics, it may be important to intensify social support by mobilizing social support resources to minimize their stress level and organizing regular training programs explaining the importance of this effort for healthcare workers.*

Key words: *Covid-19; healthcare worker; social support perception; stress*

ÖZET

Amaç: *Sağlık çalışanları, enfekte kişiler ile aynı ortamda uzun süreli olmalarından dolayı daha fazla covıd-19 bulaş riski ile karşı karşıya kalabilmekte, bundan kaynaklı olarak da daha fazla stres altında olabilmektedirler. Bu çalışma bir üniversite hastanesindeki sağlık çalışanlarında covid-19'un sosyal destek algısına ve strese etkisini belirlemek amacıyla planlanmıştır.*

Materyal ve Metot: *Araştırma tanımlayıcı ve kesitsel nitelikte bir araştırmadır. Araştırmanın evrenini bir üniversite hastanesinde çalışan sağlık çalışanları oluşturmuştur. Araştırmaya 18 Nisan-18 Mayıs 2020 tarihleri arasında çalışmaya katılmayı kabul edenler alınmıştır. Tanıtıcı bilgi formu, Akut Stres Belirti Şiddeti Ölçeği (ASBÖ) ve Çok Boyutlu Algılanan Sosyal Destek Ölçeği (ÇBASDÖ) ile veriler toplanmıştır. Bu veriler "Statistical Package for the Social Sciences 24.0" kullanılarak analiz edilmiştir. Verilerin değerlendirilmesinde ortalama, standart sapma, sayı ve yüzde, Mann Whitney U testi, Kruskal Wallis Varyans Analizi ve Spearman Korelasyon Analizi kullanılmıştır.*

Bulgular: *Sağlık çalışanlarının ASBÖ puan ortalaması 1,40±0,83, ÇBASDÖ toplam puanı 70,9±14,56'dır. Katılımcıların sosyal destek ölçeği alt boyut ölçek puan ortalamaları Aile 25,07±4,78, Arkadaş 22,57±6,01 ve Özel Bir İnsan 23,27±6,94 olarak bulunmuştur. Sağlık çalışanlarının ASBÖ ile Aile, Arkadaş, Özel Bir İnsan alt boyutları ve ölçek genel toplam arasında zayıf düzeyde, negatif bir ilişki olduğu saptanmıştır ($p<0,05$).*

Sonuç: *Sağlık çalışanlarının akut stres belirti düzeyinin hafif olduğu, çok boyutlu sosyal destek algılarının ise oldukça yüksek olduğu sonucuna varılmıştır. Özellikle pandemi gibi riskli dönemlerde, sağlık çalışanlarının stres düzeylerini düşük seviyede tutmak için sosyal destek kaynaklarını harekete geçirerek sosyal desteğin artırılması ve bunun sağlık çalışanları için önemini anlatan düzenli eğitim programlarının hazırlanması önemli olabilir.*

Anahtar kelimeler: *Covid-19; sağlık çalışanı; sosyal destek algısı; stres*

İletişim/Contact: *Atakan Yılmaz, Pamukkale Üniversitesi Hastanesi Acil Tıp Ana Bilim Dalı, 20070 Kınıklı, Denizli, Türkiye* • ***Tel:*** *0258 296 4874* • ***E-mail:*** *dr_atakanyilmaz@yahoo.com* • ***Geliş/Received:*** *26.12.2021* • ***Kabul/Accepted:*** *11.02.2022*

ORCID: *Atakan Yılmaz, 0000-0002-9773-5681* • *Gülay Taşdemir Yiğitoğlu, 0000-0002-8075-7155* • *Halis Yılmaz, 0000-0002-7454-2780*

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Introduction

The World Health Organization announced a new pandemic on March 11, 2020[1]. Due to the pandemic conditions in Turkey, extraordinary measures have been taken to contain the viral infection from 2020 until now. Our lives have inevitably undergone radical shifts in such a critical situation because of mobility restrictions and social relationships. The psychosocial impact of infectious diseases on an individual, social and international scale is well-established[2]. With the announcement of the pandemic and the adopted measures, assessments such as the disrupted routine of daily life, feelings of uncertainty, fears of infection, and thoughts of inhabiting an anti-hygienic area unveil the psychological effects of the pandemic as well as its physiological impact. From the past to the present, pandemics have been responsible for many casualties, physical strains, and mental problems. Healthcare workers, whom many different infectious diseases have afflicted, are among the groups with the highest potential to be affected by future epidemics[3]. These professionals may be at higher risk of Covid-19 transmission than other members of the society due to sharing the same setting with infected people for a long time, increasing their susceptibility to stress[4]. Previous research has suggested that their stress during past epidemics (SARS and MERS) was at severe levels[5,6]. In addition, healthcare workers reportedly experience a feeling of uncertainty and stigmatization due to caring for these people, going to work reluctantly, or planning to resign from their posts. Thus this long-term tension heightens their level of stress[4,7]. The ever-increasing number of positive and suspicious cases, heavy workload, lack of personal protective equipment, and absence of specific drugs add to their emotional burden. The research on healthcare workers reveals that they developed several psychological reactions during the 2003 SARS outbreak[8,9]. Further studies on the SARS outbreak also report that healthcare professionals in contact with infected patients were afraid of transmitting the disease to their families, friends, and co-workers[8,10].

Working with Covid-19 patients has been turned into a means of stigmatization by society. Healthcare workers may be stigmatized as community members who need to be avoided in social terms because of their contact with suspected or infected cases, causing them not to benefit from social support affordances sufficiently. In addition, healthcare workers in risky areas socially isolate themselves not to contaminate the disease, especially those at home with underlying diseases who stay away from their families and homes. Long shifts, an ever-increasing number of patients, working with protective equipment, the physical strain caused by protective equipment, being constantly alert due to the risk of infection, loss of spontaneity and autonomy, and the need to follow up-to-date information about the outbreak further multiply the stress produced by Covid-19[2,4].

Stress can be described as the organism's reaction to any change that puts pressure on the body[11]. Lazarus and Folkman take stress as the interpretation of the dangerous situation arising from interaction with the environment by the individual[12]. For Cüceloğlu, when internal and external conditions and efforts to adapt to the environment make things difficult for the individual to handle, they create a burden beyond their physical and psychological limits, defined as stress[13]. Stress can be divided into two acute stress and chronic stress. It has been suggested that short-term stress can alert the organism to danger and may be protective, while chronic stress might contribute to many diseases[14]. Prolonged stress plays a role in suppressing the immune system by disrupting the cytokine balance and reducing the function of immune protective cells[15]. Stress is an inevitable part of human life in modern societies, frequently mentioned in daily life conversations. Individuals may often be under intense stress, even if they are unaware of it[16]. Stress adversely affects individuals' physiological and psychological well-being, and they behave differently when confronted with danger. When they think they cannot cope with risk, they move away from it and exhibit avoidance behavior; conversely, when they feel they can handle danger, they try to adapt to the existing situation by fighting the dangerous situation[17]. In that regard, social support is a prominent factor in minimizing and managing stress[18]. It is well-documented in the literature that social support proves effective in reducing stress[18–20].

Social support refers to the availability of individuals around us who can provide emotional information and financial support[12]. This support can be a protective element in psychological well-being against the detrimental effects of trauma and stress in society arising from disasters and unexpected events[21]. In their study on healthcare workers, Bozdağ and Ergün found that the perceived social support provided by family members was high[22]. In addition, Wang et al. reported that 53.8% of the participants experienced moderate

to severe psychological problems while 8.1% suffered high-stress levels during the Covid-19 outbreak in China[23]. Working actively during outbreaks is a challenge in itself. Previous reports have revealed that being a healthcare worker commissioned in an outbreak brings about a high biopsychosocial stress[24].

The significance of this study lies in gaining an insight into stressful experiences associated with Covid-19 in healthcare workers and shedding light on what might be specific psychological and behavioral interventions in the future. Furthermore, the data to be obtained from the study can improve the current working conditions of the healthcare personnel, notably frontline workers. This study at an early stage of the Covid-19 outbreak in Turkey is one of the earliest studies performed in the relevant field. It is expected to make insightful contributions to the pertinent literature.

This study set out to identify the effect of Covid-19 on social support perception and stress levels in healthcare workers based at a tertiary hospital.

Materials and Methods

Study Design

When this descriptive and cross-sectional study was performed, 1729 healthcare workers were employed in the Health Research and Application Center of Pamukkale University. The participants were not selected through a particular sample selection method. Of the initial cohort of 1729 healthcare workers employed in the hospital, 448 individuals who agreed to participate for one month following the ethics committee approval were recruited for this study. The healthcare workers who were on leave, took sick leave and refused to participate were excluded from the scope of the study. The study was carried out between April 18 and May 18, 2020, in the health above facility that functioned as a pandemic hospital at the same time. About the working plan of the hospital, the regular clinics maintained their daily routine, while a pandemic clinic where healthcare personnel worked in the rotation was built.

Data Collection

The researchers utilized an introductory information form, Acute Stress Symptom Scale, and Multidimensional Scale of Perceived Social Support to collect the research data.

Introductory Information Form

Devised by the researchers themselves, the Introductory Information Form consists of items aimed at identifying the descriptive characteristics of healthcare workers (age, gender, marital status, status of parenthood, profession, educational background, current department, working experience, health status, and status of examining or care-giving to Covid-19 patients).

Acute Stress Symptom Scale (ASSS)

The "Severity of Acute Stress Symptoms-Adult (National Stressful Events Survey Acute Stress Disorder Short Scale," one of the scales recommended by the American Psychiatric Association to be utilized before the initial interview with patients and to evaluate the treatment process, has been devised to evaluate the severity of acute stress symptoms in the DSM-5 scale. The validity and reliability of the scale in the Turkish context were investigated by Aşçibaşi et al., and the Cronbach alpha coefficient was calculated as 0.95, indicating a good internal consistency[25]. On the other hand, the Cronbach alpha value turned out to be 0.851 in this study. The scale comprises seven items that evaluate the severity of acute stress disorder symptoms developing due to a post-traumatic experience in individuals aged 18 and older. Each item asks the respondent to rate the severity of the acute stress disorder lasting over the past seven days. Each item in the scale is evaluated with a five-point rating (0=Not at all; 1=A little bit; 2=Moderately; 3=Quite a bit. and 4=Extremely). The resulting score ranges between 0 and 28. High scores imply the presence of severe acute stress disorder symptoms. The total mean score is calculated by dividing the total raw score by the number of items on the scale[25].

Multidimensional Scale of Perceived Social Support (MSPSS)

The multidimensional Scale of Perceived Social Support (MSPSS) was developed by Zimet et al. in the USA[26], and Eker, Arkar, and Yaldiz[27] assessed the validity and reliability of its Turkish version. The scale consists of 12 items in total and 3 sub-dimensions, specifically family (items 3, 4, 8, 11), friends (items 6, 7, 9, 12), and significant other (items 1, 2, 5, 10). Each item is graded along a 1–7 interval scale, ranging from "very strongly disagree=1" to "very strongly agree=7". The score for each sub-dimension is obtained by adding the scores of the four items in that sub-dimension, while the total score of the scale is calculated by adding

all sub-dimension scores. The higher the obtained score is, the higher the perceived social support is. About the scale's reliability, Cronbach's Alpha coefficients for each sub-dimension are reported as family=0.85, friends=0.88, and significant other=0.92, whereas the coefficient of the scale as a whole is 0.89[27]. In this study, likewise, the Cronbach's Alpha value for each sub-dimension was calculated as family=0.886, friends=0.878, and significant other=0.910, while the coefficient of the scale as a whole was found as 0.909.

Data Analysis

The statistical analyses were performed with the Statistical Package for the Social Sciences v.24. The dataset was evaluated through mean scores, standard deviation, number and percentage, Mann Whitney U test, Kruskal Wallis Variance Analysis, and Spearman Correlation Analysis. A p-value of <0.05 was set as the limit for statistical significance.

Ethical Considerations

The current study was performed in compliance with the principles of the Declaration of Helsinki. Ethics approval was granted by the Non-interventional Studies Ethics Board of the university (date: 16.04.2020; number: 60116787-020/34300). The required institutional and scale permissions were sought and received. The healthcare workers enrolled in the study provided their informed verbal consent.

Results

Table 1 presents an overview of the descriptive characteristics of the enrolled healthcare workers. Their mean age was 36.70±7.65. As to gender, slightly more than half were male (55.8%). Around two-thirds of the study population reported to be married (67.0%) and have children (65.6%).

Table 2 illustrates the mean scores of both scales. The mean score of the respondents completing ASSS was calculated as 1.40±0.83, whereas the total mean score of MSPSS corresponded to 70.90±14.56. Concerning the sub-dimensions of MSPSS, the mean scores were found as 25.07±4.78 for family, 22.57±6.01 for friends, and 23.27±6.94 for significant others.

Significant within-group differences were observed in ASSS scores in relation to gender, profession, health status, background for psychological problems, and job satisfaction (p<0.05). However, no significant

Table 1. *Descriptive characteristics of healthcare workers (n=448)*

Descriptive characteristics		n (%)
Mean age		36.70±7.65
Age intervals	21–32 years old	146 (32.6)
	33–44 years old	223 (49.8)
	45–56 years old	79 (17.6)
Gender	Male	250 (55.8)
	Female	198 (44.2)
Marital status	Married	300 (67.0)
	Single	148 (33.0)
Parenthood	Yes	294 (65.6)
	No	154 (34.4)
Profession	Staff – Cleaning staff	229 (51.1)
	Nurse	75 (16.7)
	Doctor	56 (12.5)
	Office staff	34 (7.6)
	Emergency medical technician (EMT)	27 (6.0)
	Medical secretary	21 (4.7)
	Health technician	6 (1.3)
Educational background	Primary school	83 (18.5)
	Secondary school	46 (10.3)
	High school	122 (27.2)
	University	130 (29)
	Post-graduate	67 (15)
Current department	Ward	145 (32.4)
	Pandemic outpatient policlinic	143 (32.0)
	Pandemic ward	52 (11.6)
	Outpatient clinic	44 (9.8)
	Intensive care unit	38 (8.5)
	Pandemic intensive care unit	20 (4.5)
	Emergency department	5 (1.1)
Pre-Covid-19 department	Ward	170 (38.0)
	Emergency department	104 (23.3)
	Others (administrative units, technical services, operating room)	73 (16.3)
	Outpatient clinic	54 (12.1)
	Intensive care unit	46 (10.3)
Examining or care-giving to Covid-19 patients	No	246 (54.9)
	Yes	202 (45.1)
Having Covid-19 PCR test	No	374 (83.5)
	Yes	74 (16.5)
Work experience	1–5 years	122 (27.2)
	6–11 years	179 (40.0)
	12–17 years	91 (20.3)
	18–23 + years	56 (12.5)
Experience in current department	1–5 years	318 (71.0)
	6–11 years	83 (18.5)
	12–17 years	34 (7.6)
	18–23 + years	13 (2.9)
Health status	I have no health problem	368 (82.1)
	I have a medical diagnosis and condition for which I am receiving treatment	80 (17.9)
Background for psychological problems	I have had no psychological problems	341 (76.1)
	I have had psychological problems but received no support	48 (10.7)
	I had pharmaceutical treatment	46 (10.3)
	I had pharmaceutical treatment along with psychotherapy	9 (2.0)
	I was admitted to a clinic for psychiatric treatment	4 (0.9)
Job satisfaction	Satisfied	253 (56.5)
	Partly satisfied	168 (37.5)
	Dissatisfied	27 (6.0)

Table 2. *ASSS and MSPSS mean scores of healthcare workers (n=448)*

Scales	Med (min-max)
ASSS mean score	1.40±0.83 1.43 (0–4)
MSPSS total mean score	70.90±14.56 75 (12–84)
Family	25.07±4.78 28 (4–28)
Friends	22.57±6.01 24 (4–28)
Significant other	23.27±6.94 27 (4–28)

ASSS: Acute Stress Symptoms Scale, MSPSS: Multidimensional Scale of Perceived Social Support.

difference was noted in other sub-groups, such as age, marital status, parenthood, educational background, current department, pre-Covid-19 department, examining or care-giving to Covid-19 patients, and work experience, and experience in the present department ($p>0.05$) (Table 3).

Table 4 provides a breakdown of MSPSS scores by some descriptive characteristics of the enrolled healthcare workers. A significant difference was revealed in the family sub-dimension by marital and parenthood status, educational background, having a Covid-19 PCR test, background for psychological problems, and job satisfaction ($p<0.05$). Besides, a significant difference was evident in the sub-dimension of significant other by marital and parenthood status, work experience, and job satisfaction ($p<0.05$). According to the marital and work-life satisfaction of the participants, it was found that there was a significant difference in the MSPSS scale total ($p<0.05$). On the other hand, no statistical significance was observed in the sub-dimension of friends by some descriptive characteristics of the respondents ($p>0.05$).

The relationship between the healthcare workers' ASSS and MSPSS scores is tabulated in Table 5. A weak, negative correlation was noted between ASSS and the total mean score of MSPSS and its sub-dimensions, including family, friends, and significant other ($p<0.05$).

Discussion

Carried out at the early stage of the Covid-19 outbreak in Turkey, this study was intended to identify the impact of Covid-19 on stress and social support perception among healthcare workers at a tertiary hospital. Several striking results were obtained in the study. The first is the observation that the acute stress symptom of healthcare workers was at a mild level, while the other was high levels of multidimensional social support perception.

Stress has developed into an inevitable part of human life, frequently mentioned in daily conversations. Individuals may often be under intense stress, whether they are aware of it or not; individuals may often be under intense stress[16]. It can be classified into two acute stress and chronic stress. The former can alert the organism to danger and may have a protective effect. At the same time, the latter might lead to multiple diseases and exert an adverse impact on the physiological and psychological well-being[14]. In cases where healthcare workers cannot control their work and are assigned to care for infected patients against their own will, their stress levels may increase, and their psychological well-being might be impaired. A feeling of insecurity constitutes one of the risk factors for their psychological well-being. As confidence in equipment and infection control procedures is boosted, stress and emotional exhaustion may be decreased. The frontline medical staff engaging with patients with Covid-19 is reported to be at higher risk relation to psychological problems, including psychological distress, insomnia, alcohol, and drug abuse, acute stress disorder, post-traumatic stress disorder, depression, anxiety, burnout, anger, high perception of stress, and resort to non-adaptive coping strategies more often[28–30]. In this study, the acute stress symptom levels of the enrolled healthcare workers were assessed as mild, which is also confirmed by some previous reports[2,31,32]. Nevertheless, some lines of counter-evidence to our findings also exist in the literature. For instance, reports reveal that frontline healthcare workers have been exposed to severe work-induced stress during the Covid-19 outbreak[33].18.9% of them have developed symptoms of high levels of job-related stress in this pandemic process[34]. In addition, healthcare workers were under increased stress during the SARS outbreak in Taiwan, designating this process as a traumatic experience[35]. The research on the SARS epidemic signals the concerns about health risk, social isolation, and work-induced anxiety as the main drivers of stress among healthcare staff[36]. A systematic review study argues that high levels of acute stress disorder, anxiety, burnout, depression, and post-traumatic stress disorder develop in healthcare workers both during and after outbreaks[37]. One should bear in mind that our respondents' lower stress levels may have something to do with the hospital's standard operating procedure where the study was carried out.

Moreover, these relatively lower stress levels could be explained by adequate provision of personal protective equipment, regulation of working periods,

Table 3. *ASSS mean scores of healthcare workers by some descriptive characteristics (n=448)*

Descriptive characteristics		ASSS ($\bar{X}$ ± S.D.)	Statistical test
Age intervals	21–32 years old	1.39±0.78	KW=2.011 0.366
	33–44 years old	1.43±0.84	
	45–56 years old	1.30±0.89	
Gender	Male	1.22±0.80	Z=-3.971 **0.0001***
	Female	1.54±0.83	
Marital status	Married	1.42±0.87	Z=-0.307 0.759
	Single	1.38±0.81	
Parenthood	Yes	1.34±0.77	Z=-0.663 0.507
	No	1.43±0.86	
Profession	Staff – Cleaning staff	1.29±0.78	KW=18.859 **0.002***
	Nurse	1.67±0.77	
	Doctor	1.61±0.66	
	Office staff	1.61±0.94	
	Emergency medical technician (EMT)	1.30±0.86	
	Medical secretary	1.24±0.75	
	Health technician		
Current department	Ward	1.38±0.75	KW=6.086 0.298
	Pandemic outpatient policlinic	1.51±0.94	
	Pandemic ward	1.34±0.97	
	Outpatient clinic	1.29±0.80	
	Intensive care unit	1.49±0.97	
	Pandemic intensive care unit	1.61±0.79	
	Emergency department		
Examining or care-giving to Covid-19 patients	No	1.36±0.85	Z=-0.986 0.324
	Yes	1.44±0.81	
Having Covid-19 PCR test	No	1.38±0.82	Z=-0.537 0.591
	Yes	1.46±0.89	
Work experience	1–5 years	1.33±0.77	KW=2.99 0.393
	6–11 years	1.42±0.83	
	12–17 years	1.33±0.87	
	18–23 + years	1.55±0.91	
Experience in current department	1–5 years	1.46±0.85	KW=7.647 0.054
	6–11 years	1.21±0.74	
	12–17 years	1.24±0.8	
	18–23 + years	1.30±0.86	
Health status	I have no health problem	1.36±0.84	Z=-2.033 **0.042***
	I have a medical diagnosis and condition for which I am receiving treatment	1.58±0.79	
Background for psychological problems	I have had no psychological problems	1.27±0.77	KW=29.174 **0.0001***
	I have had psychological problems but received no support	1.76±0.84	
	I had pharmaceutical treatment	1.81±0.96	
	I had pharmaceutical treatment along with psychotherapy	1.84±1.01	
Job satisfaction	Satisfied	1.24±0.76	KW=21.524 **0.0001***
	Partly satisfied	1.55±0.88	
	Dissatisfied	1.87±0.83	

ASSS: Acute Stress Symptoms Scale, KW: Kruskal Wallis Variance Analysis, Z: Mann Whitney U test.
*p<0.05

arrangement of in-clinic work shifts, the age interval of nearly half of the healthcare workers (49.8%) ranging between 33 and 44, and working experience of the majority to be six years or more. Individuals are estimated to develop more effective coping strategies in managing stress and crises as their working experience increases. Furthermore, half of the respondents reported job satisfaction, good health status, and low rates of examining or caring for Covid-19 patients (45.1%) could account for their low-stress level. The

Table 4. *MSPSS mean scores of healthcare workers by some descriptive characteristics (n=448)*

Descriptive characteristics		MSPSS total score $\bar{X}$ ± S.D.	Family $\bar{X}$ ± S.D.	Friends $\bar{X}$ ± S.D.	Significant other $\bar{X}$ ± S.D.
Marital status	Married	68.00±15.06	24.40±5.04	22.19±5.94	21.41±8.22
	Single	72.33±14.12	25.40±4.61	22.75±6.05	24.18±6.02
		Z=-3.373 **0.001***	Z=-2.434 **0.015***	Z=-1.333 0.183	Z=-3.629 **0.0001***
Parenthood	Yes	69.32±15.21	24.43±5.23	22.63±6.04	22.26±7.74
	No	71.73±14.17	25.40±4.49	22.53±6.01	23.79±6.43
		Z=-1.897 0.058	Z=-2.511 **0.012***	Z=-0.138 0.89	Z=-2.168 **0.03***
Educational background	Primary school	67.27±19.09	23.93±6.51	21.72±6.84	21.61±8.25
	Secondary school	71.87±14.30	25.85±4.22	22.43±6.16	23.59±7.33
	High school	72.04±13.01	25.17±4.57	23.14±5.75	23.73±6.70
	University	72.37±13.33	25.68±3.92	22.90±5.85	23.78±6.40
	Post-graduate	69.82±12.70	24.57±4.28	22.01±5.59	23.24±6.20
		KW=4.618 0.329	KW=10.397 **0.034***	KW=3.785 0.436	KW=5.069 0.280
Having Covid-19 PCR test	No	71.30±14.56	25.28±4.63	22.66±5.97	23.36±7.02
	Yes	68.89±14.49	24.00±5.36	22.12±6.27	22.77±6.52
		Z=-1.801 0.072	Z=-2.042 **0.041***	Z=-0.835 0.404	Z=-1.668 0.095
Work experience	1–5 years	70.86±13.83	24.68±5.04	22.62±5.58	23.56±6.41
	6–11 years	69.23±15.53	24.96±5.09	21.99±6.68	22.28±7.47
	12–17 years	72.44±14.98	25.48±4.35	23.00±5.93	23.96±6.86
	18–23 + years	73.82±11.56	25.59±3.70	23.59±4.56	24.64±6.10
		KW=5.008 0.171	KW=2.186 0.535	KW=1.522 0.677	KW=10.128 **0.018***
Background for psychological problems	I have had no psychological problems	71.98±13.24	25.52±4.17	22.79±5.88	23.67±6.63
	I have had psychological problems but received no support	68.88±15.57	23.17±5.42	22.63±5.29	23.08±6.51
	I had pharmaceutical treatment	66.50±19.65	23.78±6.98	21.22±7.41	21.50±8.13
	I had pharmaceutical treatment along with psychotherapy	65.69±19.60	24.77±5.69	21.31±6.52	19.62±10.06
		KW=5.062 0.167	KW=17.30 **0.001***	KW=2.285 0.515	KW=5.84 0.12
Job satisfaction	Satisfied	71.30±16.68	24.37±5.43	22.96±6.48	23.96±7.26
	Partly satisfied	68.20±15.72	24.04±5.03	21.74±6.49	22.42±6.97
	Dissatisfied	72.65±13.26	25.83±4.40	23.07±5.58	23.75±6.86
		KW=9.238 **0.01***	KW=23.25 **0.0001***	KW=4.413 0.11	KW=10.513 **0.005***

MSPSS: Multidimensional Scale of Perceived Social Support, KW: Kruskal Wallis Variance Analysis, Z: Mann Whitney U test.
*p<0.05

Table 5. *Correlation between ASSS and MSPSS scores of healthcare workers (n=448)*

	MSPSS Sum	Family	Friends	Significant other
ASSS				
r	-0.236*	-0.234*	-0.250*	-0.155*
p	0.000	0.000	0.000	0.001

ASSS: Acute Stress Symptoms Scale, MSPSS: Multidimensional Scale of Perceived Social Support.
*p<0.05

applauding of healthcare workers by the public at home at a specific time in the evenings, organization of support campaigns on social media, the broadcasting of programs aimed at healthcare workers, and the prayers said for them in mosques every day during the period when the study was performed may also have contributed to the lower levels of stress in healthcare workers.

Social support refers to the social network lending psychological and physical support to maximize an individual's resilience to combat stress[19]. In addition, the multidimensional scale of perceived social support covers three sub-dimensions, including "family," "friend," and "significant other"[26]. Within this framework, we can define social support as enjoying the presence of folks that a person counts on and is assisted by their family, friends, or acquaintances and gaining indirect access to those people's resources up to a certain degree. In the pandemic, the support given to healthcare workers through a psychosocial organization and family and social environment can be a protective factor when at sufficient levels. Conversely, insufficient psychosocial support may be a major underlying risk factor for individuals' psychological well-being.

Similarly, social rejection and isolation pose a significant challenge to the mental health of healthcare

workers[30]. There is scientific evidence that the social support perception of healthcare professionals proves to be high in the Turkish context[38]. Another line of research has established that the delivery of social support is most likely to minimize anxiety and stress levels[18]. Consistent with previous scientific works, healthcare workers' total social support perception and the sub-dimensions of family, friends, and significant others proved significantly high. Positive public support to healthcare workers and adequate personal protective equipment and medical supplies in the hospital might have heightened our respondents' perceived social support. Besides, this finding also indicates that healthcare workers' high social support perception may be key to alleviating their stress.

Our findings reveal more increased acute stress symptoms in our male respondents than their female counterparts. Other research on the psychological state of healthcare workers also reports corresponding results to those of our study[28]. On the contrary, some lines of counter-evidence in the pertinent literature document higher stress levels among women[23,33,39–41]. As for the underlying reasons why male medical staff reported higher stress levels in our study, we believe that their avoidance of verbally expressing the stress they experienced during the outbreak and their inability to share their feelings with their acquaintances may have played a role.

We established a significant relationship between acute stress symptom levels and the profession of the respondents, and consistent with the previous findings[2,29,42], these levels turned out to be higher in nurses than in other healthcare workers. A study conducted during the SARS outbreak likewise revealed that nurses were more susceptible to stress[43]. This may result from nurses coming into more close contact with infected patients and providing prolonged care-giving.

Generally speaking, a negative mood is likely to heighten individuals' stress levels[17,44]. Stress may exert an adverse effect on our mental and physical well-being. Besides, suffering from a physical or psychological disorder may also double stress levels[45]. Our findings broadly support the work of previous studies in this area linking acute stress symptoms of healthcare workers with their physical and psychological disorders. Accordingly, healthcare workers reporting having physical and psychological disorders ended up with higher stress levels.

Another notable finding from our analysis is a significant increase in acute stress symptom levels of healthcare workers reporting dissatisfaction. As identified by previous research, healthcare workers' sense of fulfillment in their work mediates their stress levels and job satisfaction[46,47].

Social support theory argues that the support given by the family can potentially reduce stress and protects individuals' physical and psychological well-being[48,49]. Our results signal a significant relationship between our respondents' total social support perception and their marital status and job satisfaction. In addition, the family sub-dimension was significantly correlated with marital status, parenthood status, educational background, having a Covid-19 PCR test, background for psychological problems, and job satisfaction. Social support, which can be conceptualized as the resources provided by family members, relatives, and other close social circles, can mediate people's physical health and well-being[50]. Moreover, social support can mediate the emergence, course, and duration of numerous physical or mental disorders[51]. In this study, high scores for the family sub-dimension are thus an expected outcome in the individuals who are married, have children, have a strong education background, and do not have a Covid-19 PCR test because such descriptive characteristics as marriage and parenthood are included in the family sub-dimension. As the education level of individuals increases, their skills of self-expression, effective exploitation of social support channels, social sharing, and socialization may be improved correspondingly. Furthermore, the other sub-dimension of significant other was significantly associated with marital status, parenthood, working experience, and job satisfaction. However, the sub-dimension of friends indicated no significant relationship with some sociodemographic characteristics. The underlying reason for the lack of a significant relationship in this sub-dimension might be the imposition of social restrictions and the lockdown process.

Individuals' awareness that they are loved and valued by their social circle and that people to help them are around in case of need can inspire confidence and happiness in them[52]. High social acceptance contributes positively to social support and facilitates coping with stress. Confident that they will be accepted and supported by their social circle, individuals are less affected by unfavorable situations than those who think otherwise. In this way, when they encounter

an unfavorable situation, they can take a step to cope with the challenges without stress[53]. During the pandemic process, mobilizing social support resources, such as support from family, friends, and significant others, can serve as a protective factor for lowering stress levels and maintaining mental health when at sufficient levels. Healthcare workers whose daily lives are affected by the pandemic, such as getting in less contact with family members, become more vulnerable to stress and experience major mental health problems[30,37]. The research conducted in the Chinese context during the Covid-19 outbreak reveals that social support to healthcare workers exerts a favorable effect on mental health[54], proves to be the strongest protective factor for coping with stress and maintaining mental health[55], and helps to minimize anxiety and stress levels as well as to improve their self-efficacy[18]. As substantiated by previous reports in this field, a weak negative correlation was noted between acute stress symptom severity of healthcare workers and their multidimensional perceived social support and its sub-dimensions in this study. In other words, it has been suggested that as their stress symptom severity decreases, their social support perceptions tend to increase.

The generalizability of our results is subject to some limitations. One source of weakness which could have affected our results is that the information obtained from healthcare workers belongs to the specified dates. Another limitation is that the present study is cross-sectional, and its sample size is small. Thus these findings might not be representative of other contexts. Finally, the surveys and scales utilized in our study are based on self-report, so the reported results may have reflected a subjective assessment.

Our results suggest that healthcare workers' acute stress symptom levels are mild, while their multidimensional social support perceptions are quite high. Given some descriptive characteristics of our respondents, a statistical significance was evident in their levels of acute stress symptoms and perceived social support. Our analyses also revealed a weak, negative correlation between acute stress symptom levels and the total mean score of multidimensional perceived social support and its sub-dimensions of family, friends, and significant other. Based on these findings, we suggest several courses of action to minimize the stress levels of healthcare workers during the pandemic process, such as supplying a sufficient amount of personal protective material, increasing the number of staff, the use of protective materials, meeting basic needs (food and liquid intake), providing required information about the care-giving of Covid-19 patients, and creating resting areas. Psychological programs can also be organized to maximize coping strategies for healthcare workers. In addition, it would be of great value to develop multidisciplinary mental health teams (psychiatrists, psychiatric nurses, clinical psychologists) in health facilities to alleviate their burden. Most notably, in risky times such as pandemics, it may be important to intensify social support by mobilizing social support resources to minimize their stress level and organizing regular training programs explaining the importance of this effort for healthcare workers.

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Conflict of Interest Statement

The authors declare that they have no conflicts of interest.

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Predictors of Paroxysmal Atrial Fibrillation: Heart Rate Variability and Heart Rate Turbulence

Paroksismal Atriyal Fibrilasyonun Öngördürücüleri: Kalp Hızı Değişkenliği ve Kalp Hızı Türbülansı

Mustafa Candemir, Burak Sezenoz, Huseyin Murat Ozdemir

Department of Cardiology, Gazi University Faculty of Medicine, Ankara, Turkey

ABSTRACT

Aim: *Autonomic dysfunction is one of the major contributors to atrial fibrillation (AF) development and recurrence. Predicting AF using autonomic dysfunction parameters such as heart rate variability (HRV) and heart rate turbulence (HRT) in patients with risk factors may influence our daily practice. Thus we compare HRV and HRT measurements derived from 24 hours Holter ECG between paroxysmal AF (PAF) patients and healthy subjects.*

Material and Method: *A total number of 116 patients were included in this case-control study. All patients underwent a 24-h Holter ECG monitoring. HRV (VLF, LF, HF, SDNN, SDANN, ASDNN, rMSSD, pNN50) and HRT parameters [turbulence onset (TO) and turbulence slope (TS)] were analyzed and compared between groups. According to their HRT parameters, all participants were divided into three groups (HRT-0: normal TO, TS; HRT-1; abnormal TO or TS; HRT-2: abnormal TO and TS). A p-value <0.05 was considered significant.*

Results: *All HRV parameters were impaired in patients with PAF (p<0.05 for all parameters). There was a statistically significant difference between groups in TO (PAF 1.23±2.56; control -1.02±1.35; p= <0.001) and TS (PAF 2.59±2.39; control 3.75±1.49; p=0.002) values. In addition, 62% of the PAF patients were in HRT-2 group, on contrary; healthy subjects were predominantly in HRT-0 group (79%).*

Conclusion: *Abnormal HRV and HRT values may reflect an increased risk of PAF. Patients should be closely monitored when both TS and TO are impaired. AF's potential complications may be prevented by early detection and proper treatment using non-invasive, reproducible, easily accessible 24-h ECG Holter monitoring.*

Key words: *autonomic dysfunction; heart rate variability; heart rate turbulence; paroxysmal atrial fibrillation*

ÖZET

Amaç: *Otonomik disfonksiyon, atriyal fibrilasyon (AF) gelişmesine ve tekrarlamasına en büyük sebep olan faktörlerden biridir. Risk faktörleri olan hastalarda kalp hızı değişkenliği (KHD) ve kalp hızı türbülansı (KHT) gibi otonomik disfonksiyon parametrelerini kullanarak AF'yi tahmin etmek günlük pratiğimizi etkileyebilir. Bu çalışmada, paroksismal AF (PAF) hastaları ve sağlıklı denekler arasında 24 saatlik Holter EKG'den elde edilen KHD ve KHT ölçümlerini karşılaştırmayı amaçladık.*

Materyal ve Metot: *Bu vaka-kontrol çalışmasına toplam 116 hasta dahil edildi. Tüm hastalara 24 saatlik Holter EKG monitörizasyonu yapıldı. KHD (VLF, LF, HF, SDNN, SDANN, ASDNN, rMSSD, pNN50) ve KHT parametreleri [türbülans başlangıcı (TO) ve türbülans eğimi (TS)] analiz edildi ve gruplar arasında karşılaştırıldı. Tüm katılımcılar KHT parametrelerine göre üç gruba ayrıldı (KHT-0: normal TO, TS; KHT-1; anormal TO veya TS; KHT-2: anormal TO ve TS).*

Bulgular: *PAF'lı hastalarda tüm KHD parametrelerinin bozulduğu bulundu (tüm parametreler için p<0,05). TO (PAF: 1,23±2,56; kontrol: -1,02±1,35; p= <0,001) ve TS (PAF: 2,59±2,39; kontrol: 3,75±1,49; p=0,002) değerlerinde gruplar arasında istatistiksel olarak anlamlı fark vardı. Ayrıca PAF hastalarının %62'si HRT-2 grubunda iken sağlıklı denekler ağırlıklı olarak HRT-0 grubundaydı (%79).*

Sonuç: *Anormal KHD ve KHT değerleri, artan PAF riskini yansıtabilir. Hem TS hem de TO bozuk olan hastalar yakından izlenmelidir. AF'nin olası komplikasyonları, invaziv olmayan, tekrarlanabilir, kolay erişilebilir 24 saatlik EKG Holter monitörizasyonu kullanılarak erken teşhis ve uygun tedavi ile önlenebilir.*

Anahtar kelimeler: *otonomik disfonksiyon; kalp hızı değişkenliği; kalp hızı türbülansı; paroksismal atriyal fibrilasyon*

İletişim/Contact: *Mustafa Candemir, Gazi University, Faculty of Medicine, Department of Cardiology, 06560, Ankara, Turkey* • ***Tel:*** *0544 804 47 44* • ***E-mail:*** *mstfcndmr@hotmail.com* • ***Geliş/Received:*** *11.01.2022* • ***Kabul/Accepted:*** *22.03.2022*

ORCID: *Mustafa Candemir, 0000-0002-3645-3912* • *Burak Sezenöz, 0000-0002-6386-7045* • *Hüseyin Murat Özdemir, 0000-0001-5218-0742*

Introduction

Atrial fibrillation (AF), the most common sustained arrhythmia, is associated with an increased risk of heart failure, stroke, and all-cause mortality. Although there are variously responsible for the initiation and maintenance of AF[1], autonomic dysfunction is an important contributor in this setting. Although paroxysmal atrial fibrillation (PAF) is a common clinical form of AF, clinical course and absence of symptoms frequently can delay the time of diagnosis. The onset of PAF episodes may show circadian variation. It is more prevalent in the morning, suggesting autonomic involvement[2].

Heart rate turbulence (HRT) and heart rate variability (HRV) are easily detectable and reliable measurements derived from 24-h electrocardiogram (ECG) monitoring. These parameters can provide information about the sympathetic system (SS) and parasympathetic system (PSS) influence on the cardiovascular system. Decreasing the dominance of the PSS and increasing the dominance of the SS in the heart causes impairment in HRV and HRT parameters. Impaired values are associated with poor prognosis in patients with acute myocardial infarction, heart failure, and diseases[3–5]. It has been shown that some HRV and HRT parameters are impaired in chronic AF[6,7].

Previously the importance of different HRV parameters was evaluated in AF patients[8]. However, the role of HRV and HRT parameters was never addressed in PAF patients without structural heart disease. This study investigated the relationship between all HRV and HRT parameters and the development and recurrence of AF in patients with PAF.

Materials and Methods

Study Population

This is a case-control study conducted between March 2017 and February 2019. A total of 116 patients were included in this study. The study population was divided into two groups. Group 1 consists of the patients with newly or previously diagnosed PAF with 12-lead ECG. Group 2 consisted of age and sex-matched patients admitted to our outpatient clinic with palpitation providing an adequate number of ventricular premature beats (VPBs) for HRT measurement. Patients with structural heart disease, moderate-severe valve disease, known significant coronary artery disease, stroke, inflammatory disease, malignancies, chronic kidney disease (GFR <60 ml/min), endocrine disorders (hyper/hypothyroidism), left ventricular systolic dysfunction (EF <50%), sustained arrhythmias and sleep apnea; were excluded from the study. Informed consent form signed by all participants. The study was approved by the local ethical committee (approval no: 28.09.2015/12).

HRV and HRT Analysis

All subjects underwent 24-h Holter ECG monitoring (GE medical systems technologies, version 8.0.3, Milwaukee, USA). All recordings were analyzed by the Holter software and then reviewed manually. All VPBs were scanned and those detected as artifacts were deleted. In at least 70% of Holter recordings, the patients were in sinus rhythm, and ectopic beats were <10%. At least five VPBs were taken into account to avoid any misinterpretation. The software Holter program measured HRV and HRT parameters.

Two measurements (time domain and frequency domain) for HRV signals were analyzed to appraise the ANS function. The measurements and abbreviations are given in Table 1.

Two phases of HRT were quantified numerically as turbulence onset (TO) and turbulence slope (TS)[9]. Definitions and properties of TO and TS are given in Table 1. The patients were divided into three groups as follows;

i) patients with normal HRT (HRT-0),

ii) patients with abnormal TO or TS (HRT-1),

iii) patients with abnormal TO and TS (HRT-2).

Statistical Analysis

SPSS (version 23.0) statistical program was used for data analysis. Kolmogorov-Smirnov test was used for the distribution pattern of numerical data. Standard deviation was used for normal distribution data, and the interquartile range was used for non-normal distribution. Categorical data were presented as percentages. The student t-test was used for comparisons between groups regarding the means of the numerical variables, and the Mann–Whitney U test was used to compare medians. Categorical data were compared using the Pearson Chi-square test. P-values <0.05 were considered statistically significant.

Table 1. *Abbreviations, definitions and features of HRV and HRT parameters*

HRV parameters	
Time domain	
SDNN	The standard deviation of normal-to-normal (NN) intervals
SDANN	The standard deviation of the average NN interval, calculated over 5-min periods
ASDNN	Average standard deviation of the averages of all normal-to-normal R-R intervals in all 5-min segments of the entire recording
rMSSD	Root mean square successive differences that reflect short-term oscillations
pNN50	The percentage of normal-to-normal intervals more than 50 ms
Frequency domain	
VLF	Very low frequency (0.003–0.04 Hz)
LF	Low frequency (0.04–0.15 Hz)
HF	High frequency (0.15–0.4 Hz)
LF/HF ratio	Low frequency/high frequency ratio
HRT parameters	
TO	Turbulence onset. Percentage change RR intervals after VPBs compare to pre-VPB period. TO represents the initial acceleration of heart rate following VPB.
TS	Turbulence slope. Maximum positive regression slope obtained over any 5 consecutive sinus RR intervals within the first 15 sinus RR intervals following the VPB. TS represents the late deceleration of heart rate after VPB. TO ≤% 0 (negative TO) and TS >2.5 ms/RR (positive TS) were accepted as normal values.

VPB: ventricular premature beats.

Results

The baseline demographic features were similar, as shown in Table 2. The mean age was 59.5±10.8 (52.9±7.3 vs. 51.0±9.8 in groups 1 and 2, respectively). 44% of the total study population were male (51 male, 65 female). The median time to diagnosis in the PAF group was 66.6 (33.3–84.0) months. 8 patients in the control group and 28 patients in the PAF group received b-blockers. There were no patients in the control group using anticoagulant (either vitamin K antagonist or direct oral anticoagulant (DOAC)); on the contrary, 24 patients were under anticoagulant therapy (10 patients vs. 14 patients, warfarin and DOAC, respectively) in PAF group (Table 2). The baseline ECGs of all patients were in sinus rhythm.

There were no significant differences in the groups' minimum, median, and maximum heart rates. HRV parameters (HF, LF, VLF, ASDNN, rMSSD, SDANN, SDNN, pNN50) were all lower ($p<0.05$ for all parameters), and LF/HF ratio was increased in PAF patients compared with controls ($p=0.003$). VPBs counts were also similar (26.50 (11.75–65.00) in group 1; 32.50 (14.00–74.00) in group 2, $p=0.86$). There was a statistically significant difference between groups in TO (PAF 1.23±2.56; control -1.02±1.35;

Table 2. *Baseline clinical and laboratory parameters*

	PAF (N=58)	Control (N=58)	P
Age, (years)	59.8±10.8	59.2±10.9	0.73
Gender male, n (%)	25 (43)	26 (45)	0.85
BMI, (kg/m2)	25.9±3.6	25.9±3.9	0.97
Hypertension, n (%)	24 (43)	28 (48)	0.58
Diabetes, n (%)	18 (31)	21 (36)	0.55
Smoking, n (%)	21 (36)	24 (41)	0.57
EF%	60.8±3.6	61.3±4.0	0.55
Left atrial diameter (cm)	32.8±3.8	31.9±3.4	0.21
Creatine, mg/dL	0.81±0.18	0.79±0.16	0.62
Sodium, mmol/L	138.5±3.2	137.8±3.5	0.30
Potassium, mmol/L	4.19±0.45	4.26±0.32	0.34
WBC ($x10^3$/ml)	7.53±2.18	7.80±2.4	0.55
Hemoglobin, g/dL	12.1±2.3	11.8±1.7	0.54
AF duration (months)	66.6 (33.3–84.0)	N/A	N/A
Medications, n (%)			
Beta-blocker	28 (48)	8 (14)	<0.001
Diltiazem	9 (16)	0 (0)	0.003
ACEI or ARB	16 (28)	21 (36)	0.32
Warfarin	10 (17)	0 (0)	0.001
DOAC	14 (24)	0 (0)	<0.001
OAD/Insulin	15 (26)	21 (36)	0.23

Results are expressed as: mean ± SD or median (IQR) or frequency (%). PAF: paroxysmal atrial fibrillation, EF: Ejection fraction, ACEI: angiotensin-converting enzyme inhibitor, ARB: angiotensin receptor blocker, DOAC: direct oral anticoagulants, OAD: oral anti-diabetic drug.

p<0.001) and TS (PAF 2.59±2.39; control 3.75±1.49; p=0.002) values (Table 3). 79% of the control group and 10% of the PAF group were in HRT-0; on the contrary, 2% of the control group and 62% of the PAF group were in HRT-2, which were both statistically significant (p<0.001) (Table 4). The remaining 28% of PAF patients and 19% of control patients were in the HRT-1 group.

Discussion

In this study, we evaluated the characteristics of HRV and HRT parameters that are affected by the SS and PSS of the heart in patients with PAF. All HRV parameters were decreased, and the LF/HF ratio was increased in PAF patients. In addition, patients with PAF were predominantly in the HRT-2 group, whereas AF-free patients were predominantly in the HRT-0 group.

Several electrophysiological mechanisms were defined in the development of AF. The initiation of AF is related to atrial premature beats (APBs) originating from pulmonary veins[10]. Autonomic dysfunction such as SS predominance may increase the likelihood of APB occurrence and shortening of APB coupling interval resulting in more frequent AF episodes[11]. Several studies demonstrate the relationship between autonomic nervous system (ANS) dysfunction and AF onset. ANS precipitates AF through enhanced automaticity, triggered activity, and facilitating reentrant substrate[12].

Paroxysmal AF has a better prognosis with lesser thromboembolic events, but; identifying patients with a high risk of AF development in the follow-up is important because paroxysmal AF may degenerate into permanent AF[13–15]. Conventional risk factors such as heart failure, diabetes mellitus, left atrial dilatation, age, and risk scores (CHA_2DS_2-VASc) are the most common predictors of AF in our daily practice; the most reliable risk factor for AF is AF itself[16]. It is also known that the exact incidence of atrial fibrillation is underestimated because most of the episodes are asymptomatic[17,18]. Therefore novel clinical indicators of the development and progression of AF are essential. Predicting these patients and modifying their therapy according to recent guidelines may improve long-term outcomes in these patients.

HRV parameters provide reliable information about the cardiac PSS/SS balance. VLF is related to SS, and reduced VLF is associated with various arrhythmias[19]. LF reflects both SS/PSS tonus, whereas HF reflects the predominant vagal tonus. Increased LF/HF ratio indicates it pronounced cardiac SS activity[20]. SDNN was shown to be an indicator of proper cardiac PSS function. Besides, some previous studies demonstrated that SDNN is the best HRV parameter to assess cardiovascular autonomic innervation[19]. RMSSD and pNN50 are also related to PSS predominance and are associated with sudden cardiac death when impaired[21]. Increased PSS and decreased SS influence on the heart are responsible for AF development. In the light of these data, studies investigating the relationship between AF and HRV have been conducted. Low HRV recordings from 2 minutes of ECG recording were related to an

Table 3. *24-h Holter ECG findings of study population*

	PAF (N=58)	Control (N=58)	P
Minimum HR (beat/min)	52.9±7.3	51.0±9.8	0.23
Average HR (beat/min)	77.9±7.7	76.1±7.7	0.21
Maximum HR (beat/min)	144.1±15.6	140.3±17.9	0.24
Total QRS	106784.6±15319.6	103735.9±14174.9	0.27
VLF	26.7±8.7	33.9±10.4	<0.001
LF	23.5±10.4	30.2±20.5	0.03
HF	13.1±5.7	18.9±8.4	<0.001
LF/HF ratio	1.8±0.5	1.5±0.5	0.003
SDNN	133.9±37.0	152.3±53.7	0.034
SDANN	117.6±27.7	134.4±46.3	0.013
ASDNN	55.0±15.8	66.5±32.8	0.017
rMSSD	33.7±10.2	39.5±12.5	0.008
pNN50	13.6±10.6	17.8±9.2	0.023
Tonset	1.23±2.56	-1.02±1.35	<0.001
Tslope	2.59±2.39	3.75±1.49	0.002
PVBs	26.50 (11.75–65.00)	32.50 (14.00–74.00)	0.86

Results are expressed as: mean ± SD or median (IQR) or frequency (%). PAF: paroxysmal atrial fibrillation; VPBs: premature ventricular beats, HR: heart rate, To: turbulence onset, Ts: turbulence slope.

Table 4. *HRT status of PAF and controls*

	PAF (N=58)	Control (N=58)	P
HRT-0, n (%)	6 (10)	46 (79)	<0.001
HRT-1, n (%)	16 (28)	11 (19)	0.27
HRT-2, n (%)	36 (62)	1 (2)	<0.001

Results are expressed as: frequency (%). PAF: paroxysmal atrial fibrilation, HRT: Heart rate turbulence.

increased risk of sudden cardiac death and incidence of AF in population-based studies[22,23]. The interaction between abnormal HRV values and prognostic implications also demonstrated an increased risk of AF incidence among patients with relevant risk factors[24]. Relevant studies showed a significant association between HRV and AF recurrence after index episode[25,26].

HRT is associated with HRV parameters, which are also derived from 24 hours Holter recordings. Moreover, HRT, which is thought to represent the PSS predominance better, was a stronger predictor of cardiovascular prognosis than HRV. Previously published studies have described the role of HRT in predicting sudden cardiac death, ventricular arrhythmia after myocardial infarction, and heart failure[5,27]. HRT defines the fluctuations of normal sinus rhythm after and VPBs due to baroreceptor reflex mechanism and represents noninvasive cardiac autonomic functions (28). Combining different screening modalities in high-risk patients (such as HRV and HRT analysis) may improve our understanding of the precise contribution of ANS to AF pathophysiology. In the future, these parameters may be used as a therapeutic target.

Our study showed that PAF patients have abnormal HRV and HRT compared to control subjects which reflects the possible role of ANS on PAF development. Normal values of HRV parameters and HRT-0 may be used as an exclusion parameters. In addition, HRT-2 may serve as a strong predictor of PAF development. HRT-1 did not differ between groups, and the utility of one abnormal HRT parameter is questionable compared to HRT-0 and HRT-2. Close monitoring of subgroups of patients with abnormal HRT, especially HRT-2, may be feasible. This study evaluated all HRV and HRT parameters in patients with PAF, which were not included in previous similar studies. The major limitation of our study is the limited number of patients. Although atrial HRT measurements are not routinely used in clinical trials, especially considering that APCs play an important role in AF development, measuring atrial HRT may contribute to our study. Several factors that affect the HRV and HRT, such as medical therapy (b-blockers, RAAS blockers, anti-arrhythmic drugs), may intervene with our results. PAF group was more likely under AV nodal blocking agents, which may influence our results. Additionally, we can not rule out the presence of PAF, which may influence our results.

In conclusion, our study showed that PAF patients have abnormal HRV and HRT compared to control subjects which reflects the possible role of ANS on PAF development. Patients at risk of AF may be distinguished by using this technique. Close monitoring of subgroups of patients with abnormal HRT, especially HRT-2, may be feasible. Besides, proper precautions may reduce the rate of cardiovascular complications. Future prospective studies are needed to confirm our results and their impact on long-term prognosis.

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Conception and design of the study or analysis and interpretation of data, or both (MC, BS, HMO);

Manuscript drafting or critical revision for important intellectual content (MC, BS, HMO);

Final approval of the manuscript submitted (MC, HMO).

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

What Do Medical Students Know About Space Medicine?

Tıp Öğrencileri Uzay Tıbbı Hakkında Ne Biliyor?

Seref Emre Atis

Karabuk University, Faculty of Medicine, Department of Emergency Medicine, Karabuk, Turkey

ABSTRACT

Aim: *In medical practice, education is mainly carried out in inpatient care. There is limited attention to specific training focusing on the medical branches like space medicine. Educating medical students can assist them in becoming potential candidates or educators in space medicine, and this education could become a necessity for future generations. In the present study, we aimed to assess the medical school students in Turkey for their level of awareness in this field.*

Material and Method: *Our study is designed as a cross-sectional study comprising students studying medicine. Participants in different grades who agreed to fill the awareness questionnaire focusing on space medicine were included. Participants were asked to fill out a questionnaire consisting of 16 questions. The questions included in the questionnaire were asked in different forms, such as multiple-choice, open-ended questions, and questions scaled from 1 to 10.*

Results: *A total of 318 participants were included in the study. The mean age of the participants was 21.3±2.1 years. It was found that 42.1% of the students did not know space medicine. Similarly, 56.3% of the participating students were unaware that this specialty was among the medical fields. 60.7% of participants incorrectly answered the questions about their knowledge of the potentially encountered problems in space. It was found that 43.1% of the participants were unaware of the presence of any space agency; of those who were informed about their presence, only as few as 9.9% responded with the Turkish Space Agency. 6.6% of the participants believed that the Scientific and Technological Research Council of Turkey (TUBITAK) was Turkey's official space agency.*

Conclusion: *Medical faculty students have limited knowledge of space medicine, and half of them were not aware of the presence of the aerospace medicine field.*

Key words: *student; education; awareness; aerospace medicine; celestial*

ÖZET

Amaç: *Tıbbi pratikte, eğitim çoğunlukla hasta bakımıyla ilgili alanlara odaklanmıştır. Uzay tıbbı alanı gibi özellikli eğitim gerektiren alanlara gösterilen ilgi oldukça sınırlıdır. Bu konuda tıp öğrencilerine verilecek eğitim onları uzay tıbbı alanında potansiyel bir aday ve eğitici haline getirebilir ve gelecek nesiller için bu eğitim gereklilik haline gelecektir. Bu çalışmada amacımız Türkiye'deki tıp fakültesi öğrencilerinin uzay tıbbı ile ilgili farkındalıklarını araştırmaktır.*

Materyal ve Metot: *Çalışmamız kesitsel nitelikte olup, tıp fakültesi öğrencileri kapsamaktadır. Uzay tıbbı ile ilgili anketimize katılmayı kabul eden farklı dönemlerdeki tıp fakültesi öğrencileri çalışmaya dahil edildi. Çalışmada katılımcılara 16 sorudan oluşan bir anket düzenlendi. Anketteki sorular, çoktan seçmeli, açık uçlu ve 1'den 10'a kadar değişen puanlamaları olan farklı soru tiplerinden oluşmaktadır.*

Bulgular: *Toplamda 318 katılımcı çalışmaya dahil edildi. Katılımcıların yaş ortalaması 21,3±2,1 yıldı. Öğrencilerin %42,1'inin uzay tıbbı ile ilgili bir fikri olmadığı saptandı. Benzer şekilde, öğrencilerin %56,3'ü bu branşın tıp bölümleri arasında yer olduğunu bilmiyordu. Uzayda meydana gelebilecek potansiyel tehlikelerle ilgili sorulara katılımcıların %60,7'si yanlış cevap verdi. Çalışmada katılımcıların %43,1'inin herhangi bir uzay ajansını bilmedikleri, uzay ajansları ile ilgili bilgisi olanların ise sadece %9,9'nun bildiği uzay ajansı için Türkiye Uzay Ajansı cevabını verdiği saptandı. Katılımcıların %6,6'sının ise Türkiye'nin resmi uzay ajansını Türkiye Bilimsel ve Teknolojik Araştırma Kurumu (TÜBİTAK)'nu sandığı ortaya çıktı.*

Sonuç: Tıp fakültesi öğrencilerinin uzay tıbbı ile ilgili bilgileri oldukça sınırlıdır ve bu öğrencilerin yarısı uzay tıbbı bölümünün varlığından haberdar değildir.

Sonuç: *Tıp fakültesi öğrencilerinin uzay tıbbı ile ilgili bilgileri oldukça sınırlıdır ve bu öğrencilerin yarısı uzay tıbbı bölümünün varlığından haberdar değildir.*

Anahtar kelimeler: *öğrenci; eğitim; farkındalık; uzay tıbbı; göksel*

Introduction

In medical practice, education is mainly carried out in inpatient care, and medically well-equipped settings are focused on this care. There is limited attention to specific training focusing on the medical branches that entail various challenging conditions[1]. One of these medical branches is space medicine. In the 1950 s, space medicine emerged as a branch of medicine to assist humanity's exploration of space[2]. Today, there are even cardiopulmonary resuscitation guidelines regulated explicitly for the field of space medicine[3]. Soon,

İletişim/Contact: *Şeref Emre Atiş, Karabuk University, Faculty of Medicine, Department of Emergency Medicine, Karabuk, Turkey* • ***Tel:*** *0506 928 81 86* • ***E-mail:*** *dremreatis@gmail.com* • ***Geliş/Received:*** *20.01.2022* • ***Kabul/Accepted:*** *07.02.2022*

ORCID: *Şeref Emre Atiş, 0000-0002-5094-6000*

it will be mandatory to include medical doctors during space travels. It is, therefore, necessary to train the medical staff for this specific purpose and ensure that they are skilled in a wide range of fields, from preventive medicine to surgical intervention[4]. Educating medical students, both through training and raising awareness of this field, can assist them in becoming potential candidates or educators in space medicine. This education could become a necessity for future generations[5].

In the present study, we aimed to assess the medical school students in Turkey for their level of awareness in this field.

Material and Method

Study Design

Our study is designed as a cross-sectional study comprising students studying medicine at Karabuk University, Faculty of Medicine. After the local ethics committee's approval (Approval no: 2021/707).

Selection of the Participants

The study population consisted of students of varying grades studying at Karabuk University, Faculty of Medicine, 2021–2022. Participants who agreed to fill the awareness questionnaire focusing on space medicine were included. Participants who did not agree to participate in the study and did not answer all the survey questions were excluded from the study.

Data Collection

Participants were asked to fill out a questionnaire consisting of 16 questions, which took approximately 3 min to complete (Appendix 1). The questions included in the questionnaire were asked in different forms, such as multiple-choice, open-ended questions, and questions scaled from 1 to 10. With this questionnaire, after asking questions about the demographic data of the students (age, gender), which class they are in, whether they have knowledge about space medicine and whether there will be a need for a physician in any way in space travel in the future, there is a question about whether they are interested in this subject or not.

Statical Analysis

The descriptive statistics used to summarize the research data were expressed as median, minimum, and maximum values in the case of continuous (numerical) variables depending on whether they conform to the normal distribution, and as numbers and percentage values in the case of categorical variables. Conformity of numerical variables to normal distribution was checked with the Shapiro-Wilk, Kolmogorov-Smirnov, and Anderson-Darling tests. The Kruskal-Wallis H test compared more than two independent groups in cases where the numerical variables did not conform to normal distribution.

In comparing the differences between the categorical variables by the groups, Pearson's chi-squared test was used for RxC tables with five or more expected cells, and the Fisher-Freeman-Halton Exact test was used for RxC tables with less than 5expected cells.

Statistical analyses were conducted with "Jamovi project (2021), Jamovi (version 2.2.2.0) [Computer Software] (retrieved from https://www.jamovi.org) and JASP (version 0.16) (retrieved from https://jasp-stats.org) software. Probability (p) values of ≤0.05 were deemed to indicate statistical significance.

Results

A total of 318 participants were included in the study. The mean age of the medical faculty students was 21.3±2.1 years. Of these participants, 133 were male, and 185 were female. Ninety-five (29.9%) of the participants were in the second-grade level, 69 (21.7%) were in the third-grade level, 48 (15.1%) were in the sixth-grade level, 43 (13.5%) were in the fifth-grade level, 39 (12.3%) were in the fourth-grade level, and 24 (7.5%) were in the first-grade level (Table 1).

As shown in Table 2, the distribution of the responses given by the study participants to the question of "Is space medicine a specialization in our country?" revealed statistically significant differences between

Table 1. *Participants' demographic data and grades*

	Participants (n=318)
Mean age (years)	21.3±2.1
Gender	
Male	133 (41.8)
Female	185 (58.2)
Grade Levels (3rd question)	
1 st-grade	24 (7.5)
2nd-grade	95 (29.9)
3rd-grade	69 (21.7)
4th-grade	39 (12.3)
5th-grade	43 (13.5)
6th-grade	48 (15.1)

Descriptive statistics were expressed as mean and standard deviation values in the case of numerical variables depending on whether they conform to the normal distribution and as numbers and percentage (%) values in the case of categorical variables.

the grade levels (p=0.005). There was no significant difference between the groups created based on the grade levels in other variables (p>0.05 for each variable). Participants mostly agreed with the question, "I think more medical problems would emerge in longer-term and touristic space travels." Similarly, they mostly agreed with the question, "Would you be interested in these topics were they to be included in the curriculum of the Faculty of Medicine?" (median 8.0, interquartile range 25–75 [7.0, 10.0], median 8.0, interquartile range 25–75 [5.2, 10.0], respectively).

When asked about the topics of interest in space medicine, 265 (83.3%) students mentioned protecting the health of the crew members of the spaceship, 240 (75.5%) students mentioned finding solutions to possible health problems, 235 (73.9%) students mentioned of recording physiological changes, 197 (61.9%) students mentioned of identifying potential problems, 177 (55.7%) students mentioned of telemedicine (remote assistance) options, and 101 (31.8%) students mentioned of non-human biological studies (Table 3). As shown in Table 4, when given four different factors that possibly affect the human physiology during space travel, 307 (96.5%) students stated that they think "loss of gravity" is one of the factors that would affect human physiology during space travel, 243 (76.4%) students said that they think "radiation" is one of the factors that would affect human physiology during space travel, 193 (% 60.7) students stated that they think "photons" is one of the factors that would affect human physiology

Table 2. *Questions about space medicine-part-1*

	Total (n=318)	1st grade (n=24)	2nd grade (n=95)	3rd grade (n=69)	4th grade (n=39)	5th grade (n=43)	6th grade (n=48)	p
Have you ever heard of space medicine? (4th question)								
No	134 (42.1)	13 (54.2)	40 (42.1)	35 (50.7)	12 (30.8)	20 (46.5)	14 (29.2)	0.100*
Yes ∇	184 (57.9)	11 (45.8)	55 (57.9)	34 (49.3)	27 (69.2)	23 (53.5)	34 (70.8)	
through social media or the internet	136 (73.9)	9 (81.8)	39 (70.9)	27 (79.4)	15 (55.6)	18 (78.3)	28 (82.4)	0.429*
through academia/university	33 (17.9)	2 (18.2)	10 (18.2)	5 (14.7)	10 (37.0)	3 (13.0)	3 (8.8)	
through books	15 (8.2)	0 (0.0)	6 (10.9)	2 (5.9)	2 (7.4)	2 (8.7)	3 (8.8)	
Is space medicine a medical specialty in our country? (5th question)								
Yes	65 (20.4)	1 (4.2)	18 (18.9)	7 (10.1)	10 (25.6)	10 (23.3)	19 (39.6)	**0.005***
No	74 (23.3)	6 (25.0)	23 (24.2)	20 (29.0)	12 (30.8)	8 (18.6)	5 (10.4)	
I have no idea	179 (56.3)	17 (70.8)	54 (56.8)	42 (60.9)	17 (43.6)	25 (58.1)	24 (50.0)	
At what altitude does space start? (6th question)								
50 km	19 (6)	0 (0.0)	6 (6.3)	6 (8.7)	1 (2.6)	1 (2.3)	5 (10.4)	0.071*
100 km (correct answer)	120 (37.7)	8 (33.3)	42 (44.2)	23 (33.3)	13 (33.3)	16 (37.2)	18 (37.5)	
150 km	51 (16)	2 (8.3)	19 (20.0)	15 (21.7)	6 (15.4)	3 (7.0)	6 (12.5)	
200 km	67 (21.1)	3 (12.5)	18 (18.9)	13 (18.8)	9 (23.1)	15 (34.9)	9 (18.8)	
250 km	61 (19.2)	11 (45.8)	10 (10.5)	12 (17.4)	10 (25.6)	8 (18.6)	10 (20.8)	
Do you think there will be a need for a doctor during space travels in the future? (10th question)								
Yes	279 (87.7)	21 (87.5)	84 (88.4)	64 (92.8)	32 (82.1)	36 (83.7)	42 (87.5)	0.438*
No	8 (2.5)	0 (0.0)	3 (3.2)	1 (1.4)	0 (0.0)	1 (2.3)	3 (6.2)	
Doctors will soon be replaced by artificial intelligence.	31 (9.7)	3 (12.5)	8 (8.4)	4 (5.8)	7 (17.9)	6 (14.0)	3 (6.2)	
Do you think there will be changes in the mechanism and duration of action or efficacy of medications during their use in space? (11th question)								
Yes	257 (80.8)	22 (91.7)	81 (85.3)	55 (79.7)	31 (79.5)	33 (76.7)	35 (72.9)	0.450*
No	14 (4.4)	0 (0.0)	3 (3.2)	2 (2.9)	3 (7.7)	1 (2.3)	5 (10.4)	
I have no idea	47 (14.8)	2 (8.3)	11 (11.6)	12 (17.4)	5 (12.8)	9 (20.9)	8 (16.7)	
Is it possible to get a bacterial, viral, or fungal infection in space? (12th question)								
Yes	191 (60.1)	17 (70.8)	54 (56.8)	38 (55.1)	28 (71.8)	24 (55.8)	30 (62.5)	0.760*
No	43 (13.5)	4 (16.7)	13 (13.7)	11 (15.9)	3 (7.7)	6 (14.0)	6 (12.5)	
I have no idea	84 (26.4)	3 (12.5)	28 (29.5)	20 (29.0)	8 (20.5)	13 (30.2)	12 (25.0)	
I think more medical problems would emerge in longer-term and touristic space travels (13th question)	8.0 [7.0, 10.0]	8.0 [7.0, 9.2]	8.0 [7.0, 9.5]	8.0 [7.0, 10.0]	8.0 [7.0, 9.0]	9.0 [7.0, 10.0]	9.0 [7.0, 10.0]	0.423**
Would you be interested in these topics were they to be included in the curriculum of the Faculty of Medicine? (15th question)	8.0 [5.2, 10.0]	7.5 [5.8, 10.0]	9.0 [6.0, 10.0]	8.0 [6.0, 10.0]	8.0 [5.0, 9.0]	8.0 [5.5, 10.0]	8.0 [5.0, 10.0]	0.331**

Descriptive statistics were expressed as mean and standard deviation values in the case of numerical variables depending on whether they conform to the normal distribution and as numbers and percentage (%) values in the case of categorical variables.

* Pearson'chi-squared test or Fisher-Freeman-Halton test was used.

** Kruskall-Wallis H test was used.

during space travel, and 193 (% 60.7) students said that they think "strong nuclear force" is one of the factors that would affect human physiology during space travel.

Question about the health problems that develop in those returning from space, 240 (75.5%), 272 (85.5%), 221 (69.5%), 177 (55.7%), and 97 (30.5%) students responded that they think low blood pressure, muscle wasting, reduction in body mass, radiation-induced diarrhea, and sunstroke, respectively, are the health problems that develop in those returning from space (Table 5). Regarding the medical specialties related to space medicine, 83.6%, 63.2%, 62.6%, and 58.5% of the students responded that they think physiology, emergency medicine, internal medicine, and pathology are related to space medicine (Table 6).

As shown in Table 7, when asked whether they knew of any space research institute, 181 (56.9%) students gave a positive answer. In this context, 151 (83.4%), 18 (9.9%), and 12 (6.6%) stated that they are aware of NASA (National Aeronautics and Space Administration), Turkish Space Agency (TUA), and TUBITAK (Scientific and Technological Research Council of Turkey), respectively.

Discussion

There is no existing curriculum published explicitly in space medicine for the students of medical faculties[6]. However, according to Wilderness Medicine Societies, pre-specialty training in less-known medical areas might be useful[5]. To the best of our knowledge, our study is the first in Turkey to assess the medical faculty students for their level of awareness of space medicine. It was found that 42.1% of the students who participated in our study did not know space medicine. Similarly, 56.3% of the participating students said they were not aware that this specialty was among the medical fields in Turkey.

There is only a single study in the literature reporting that training in space medicine would be helpful. In a study by Babu et al., the researchers included 1 st– and 2nd-grade medical faculty students trained based on a 3-month curriculum covering space medicine. After completing the curriculum, the participating students were asked whether the respective training was useful. According to the study results, 100% of the participants stated that they had more information about these lesser-known fields, whereas 95% indicated that they were able to form ideas regarding these lesser-known fields based on the scientific studies shown as a part of the curriculum[1]. In our study, only 37.7% of the participants correctly answered the question about the altitude at which outer space starts.

Table 3. *Questions about space medicine-part-2*

7th question	Participants (n=318)
What are the topics of interest to space medicine? (All answers are correct)	
Protection of the health of the crew members of the spaceship (yes)	265 (83.3)
Finding solutions to possible health problems (yes)	240 (75.5)
Recording physiological changes (yes)	235 (73.9)
Identification of possible problems (yes)	197 (61.9)
Telemedicine (remote assistance) options (yes)	177 (55.7)
Non-human biological studies (yes)	101 (31.8)

Descriptive statistics were expressed as numbers and percentage (%) values for categorical variables.

Table 4. *Questions about space medicine-part-3*

8th question	Yes	No
What are the factors that affect human physiology during space travel?		
Loss of gravity (true)	307 (96.5)	11 (3.5)
Radiation (true)	243 (76.4)	75 (23.6)
Photons (false)	193 (60.7)	125 (39.3)
Strong nuclear force (false)	193 (60.7)	125 (39.3)

Descriptive statistics were expressed as numbers and percentage (%) values for categorical variables.

Table 5. *Questions about space medicine-part-4*

9th question	Yes	No
What are the health problems that develop in those returning from space?		
Low blood pressure (true)	240 (75.5)	78 (24.5)
Radiation-induced diarrhea (false)	177 (55.7)	141 (44.3)
Muscle loss (true)	272 (85.5)	46 (14.5)
Sunstroke (false)	97 (30.5)	221 (69.5)
Reduction in body mass (true)	221 (69.5)	97 (30.5)

Descriptive statistics were expressed as numbers and percentage (%) values for categorical variables.

Table 6. *Questions about space medicine-part-5*

14th question	Participants (n=318)
Which medical specialties are related to space medicine?	
Physiology (yes)	266 (83.6)
Emergency Medicine (yes)	201 (63.2)
Internal Medicine (yes)	199 (62.6)
Pathology (yes)	186 (58.5)
Anesthesia & Reanimation (yes)	139 (43.7)
General Surgery (yes)	122 (38.4)
Brain Surgery (yes)	105 (33.0)

Descriptive statistics were expressed as numbers and percentage (%) values for categorical variables.

Table 7. *Questions about space medicine-part-6*

16th question	Participants (n=318)
Do you know of any Space Research Institute?	
No	137 (43.1)
Yes ▽	181 (56.9)
NASA	
Yes	151 (83.4)
No	30 (16.6)
Turkish Space Agency	
Yes	18 (9.9)
No	163 (90.1)
TUBITAK	
Yes	12 (6.6)
No	169 (93.4)
Other space research institutes	
Yes	74 (40.9)
No	107 (59.1)

Descriptive statistics were expressed as numbers and percentage (%) values for categorical variables.

Similarly, a high rate of participants (60.7%) incorrectly answered the questions about their knowledge of potentially encountered space problems. The Aerospace Medicine training programs have been conducted in Turkey since 1986, where military hospitals initially conducted them, and today, they are being conducted by the University of Health Sciences[7]. Most participants agreed that the curriculums should cover a more significant part of the content specialized in space medicine, which indicates that the majority is still not well-informed about this field. Although space medicine is a specialty in the United States and the United Kingdom, it is still not considered in many countries. Moreover, it is seen that people, who are interested in the field, must-visit other countries to attend this specialized courses[8]. We believe that incorporating the courses aimed at raising awareness of space medicine in the medical school curriculum and organizing courses and congresses focusing on space medicine will enhance the knowledge of this field in the students at medical faculties.

Various problems are predicted to arise in the communication among Earth-based mission control centers during space travels, such as the Mars mission in the 2030 s. Therefore, it has been planned to assign a medical doctor, skilled in a wide range of medical subjects, as a member of the flight crew[9,10]. Of the students who participated in our study, 87.7% (n=279) stated that more doctors might be needed in the future and that there may be more medical problems encountered during space travel in the future. Finally, the Turkish Space Agency was established in 2018 to develop and manage space technologies in Turkey and is still being operated within the national space program[11]. However, our study found that 43.1% (137) of the participants were unaware of the presence of any space agency. Of those informed about their presence, most of the responses pointed at NASA, whereas only as few as 9.9% (n=18) responded to the Turkish Space Agency. According to another result of the present study, 6.6% of the participants believed that the Scientific and Technological Research Council of Turkey (TUBITAK) was Turkey's official space agency. This rate indicates that the awareness regarding the presence of the Turkish Space Agency is deficient even among the medical students in Turkey. To tackle this low rate indicating a lack of awareness of the Turkish Space Agency, we believe that more efforts should be put in to promote the agency, both through the internet and television channels.

Similarly, the Turkish Space Agency and the Board of Specialty in Medicine in Turkey can collaborate to incorporate rare disease-related topics into the curriculum and raise awareness of space medicine. The major limitation of the present study is that it is a single-centered study. More and better results can be obtained with further studies conducted across various medical faculties.

In conclusion, it has been found that the students of the medical faculties have limited knowledge of space medicine and half of them were not aware of the presence of the aerospace medicine field in Turkey. We think it would be beneficial to implement this department, whose importance is increasing daily, to the curriculum to raise awareness among medical students.

Acknowledgment

None.

Conflicts of Interest

The author reports that there is no conflict of interest.

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Appendix 1

Space Medicine Awareness Survey

Today, interest in space tourism and interstellar travel has increased. Soon, the need for people who have knowledge about space will increase in the field of medicine as in every field. The aim of this study is to measure the awareness of the students of the Faculty of Medicine about Space Medicine. Some of the questions are short answers, some multiple-choice, and some are designed as checkboxes. Two questions were designed as scoring. During the survey, no questions regarding your personal data will be asked, and the information you provide is not made up of questions that will reveal who you are in any way. The data obtained here will be used for scientific study purposes and will not be shared with any third-party institution or organization. We thank you for your valuable contribution.

Do you accept to participate in the survey? (Yes or no)

1st Question: How old are you?

2nd Question: Please state your gender (Male or Female)

3rd Question: Which grade are you in medical school? (1st to 6th grade)

4th Question: Have you ever heard of space medicine? (Please choose only one answer)

- ☐ No

If yes

- ☐ through social media or the internet
- ☐ through academia/university
- ☐ through books

5th Question: Is space medicine a medical specialty in our country? (Please choose only one answer)

- ☐ Yes
- ☐ No
- ☐ I have no idea

6th Question: At what altitude does space start? (Please choose only one answer)

- ☐ 50 km
- ☐ 100 km
- ☐ 150 km
- ☐ 200 km
- ☐ 250 km

7th Question: What are the topics of interest to space medicine? (You can tick more than one option)

- o Protection of the health of the crew members of the spaceship
- o Finding solutions to possible health problems
- o Recording physiological changes
- o Identification of possible problems
- o Telemedicine (remote assistance) options
- o Non-human biological studies

8th Question: What are the factors that affect human physiology during space travel? (You can tick more than one option)

- o Loss of gravity
- o Radiation
- o Photons
- o Strong nuclear force

9th Question: What are the health problems that develop in those returning from space? (You can tick more than one option)

- o Low blood pressure
- o Radiation-induced diarrhea
- o Muscle loss
- o Sunstroke
- o Reduction in body mass

10th Question: Do you think there will be a need for a doctor during space travels in the future? (Please choose only one answer)

- ☐ Yes
- ☐ No
- ☐ Doctors will soon be replaced by artificial intelligence

11th Question: Do you think there will be changes in the mechanism and duration of action or efficacy of medications during their use in space? (Please choose only one answer)

- ☐ Yes
- ☐ No
- ☐ I have no idea

12th Question: Is it possible to get a bacterial, viral, or fungal infection in space? (Please choose only one answer)

- ☐ Yes
- ☐ No
- ☐ I have no idea

13th Question: I think more medical problems would emerge in longer-term and touristic space travels? Please choose one number (**1** strongly disagrees - **10** is I totally agree)

1 2 3 4 5 6 7 8 9 10

14th Question: Which medical specialties are related to space medicine? (You can tick more than one option)

- o Physiology
- o Emergency Medicine
- o Internal Medicine
- o Pathology
- o Anesthesia & Reanimation
- o General Surgery
- o Brain Surgery

15th Question: Would you be interested in these topics were they to be included in the curriculum of the Faculty of Medicine? (**1** strongly disagrees - **10** is I totally agree)

1 2 3 4 5 6 7 8 9 10

16th Question: Do you know of any Space Research Institute?

- ☐ No
- ☐ If yes, please write the institution name below

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ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Effect of Education Given to Nursing Students on Their Palliative Care Knowledge and Attitudes

Hemşirelik Öğrencilerine Verilen Eğitimin Palyatif Bakım Bilgi ve Tutumlarına Etkisi

Aysegul Ozturk Birge, Tulin Beduk

Ankara University Faculty of Nursing, Department of Nursing, Ankara, Turkey

ABSTRACT

Aim: *This study aimed to evaluate the effect of education given to nursing students on their palliative care opinion, knowledge, and attitudes.*

Material and Method: *The study used a single group pre-test/post-test method. The study was carried out between 11–26 December 2017 with the participation of second-grade nursing students enrolled at a university. The study sample consisted of 105 students before the training and 98 students after the training. The study data were collected using a palliative care knowledge, opinion form, and the Frommelt Attitudes Toward Care of the Dying Scale (FATCOD). In the analysis of the data, McNemar chi-square for dependent groups, t-test, and Pearson's correlation test were used.*

Results: *The mean age of the students was 19.71±1.01 years. The percentage of the students who had clinical practice experience in the palliative care unit during their education was 11.4%, while 32.4% were determined to have already been given palliative care. Before and after the training, the students stated that the place of effective/quality palliative care service was mostly palliative care units. The students reported that the most challenging symptoms in palliative care management would be delirium, pain, dyspnea, and fatigue. The proportion of the students who wanted to work in palliative care after graduation decreased after the training (p>0.05). The students' mean pre-training palliative care knowledge score was 9.95±2.00, and it was found to increase to 12.29±2.42 significantly after the training (t/p=-7.881/0.000). The mean FATCOD score of the students who wanted to work in palliative care after graduation (114.66±8.76) was determined to be higher compared to the students who did not want to (108.24±8.88) (t=3.468, p=0.001). In addition, there was a positive but weak correlation between students' mean post-training palliative care knowledge score and their mean FATCOD score (r=0.285, p=0.004).*

Conclusion: *The education given to the students about palliative care was found to create positive differences in their knowledge and attitudes. However, it was determined that education reduced the willingness of postgraduate students to work as palliative care nurses.*

Key words: *attitude; knowledge; nursing; palliative care; education*

ÖZET

Amaç: *Bu çalışmada hemşirelik öğrencilerine verilen eğitimin palyatif bakım görüş, bilgi ve tutumlarına etkisinin değerlendirilmesi amaçlandı.*

Materyal ve Metot: *Çalışmada tek gruplu bir ön test / son test yöntemi kullanıldı. Araştırma, 11-26 Aralık 2017 tarihleri arasında bir üniversiteye kayıtlı 2. sınıf hemşirelik öğrencilerinin katılımıyla gerçekleştirildi. Araştırmanın örneklemini eğitim öncesi 105 öğrenci, eğitim sonrası 98 öğrenci oluşturdu. Araştırmanın verileri, palyatif bakım bilgisi, görüş formu ve Ölmekte olan Hastanın Bakımına İlişkin Tutum Ölçeği (FATCOD) kullanılarak toplandı. Verilerin analizinde, bağımlı gruplar için McNemar ki-kare, t-testi ve Pearson's korelasyon testi kullanıldı.*

Bulgular: *Öğrencilerin yaş ortalaması 19.71 ± 1.01 idi. Eğitimleri süresince palyatif bakım ünitesinde klinik uygulama deneyimi yaşayan öğrencilerin oranı %11.4 olarak bulunurken, %32.4'ünün palyatif bakım verdiği belirlendi. Eğitim öncesi ve sonrasında öğrenciler etkili/kaliteli palyatif bakım hizmetinin yerinin daha çok palyatif bakım üniteleri olduğunu belirtti. Öğrenciler palyatif bakım yönetiminde en zorlayıcı semptomların deliryum, ağrı, nefes darlığı ve yorgunluk olacağını bildirdi. Eğitim sonrasında mezuniyet sonrası palyatif bakımda çalışmak isteyen öğrencilerin oranı azaldı (p>0.05). Öğrencilerin eğitim öncesi palyatif bakım bilgi puanı ortalaması 9.95 ± 2.00 olup, eğitim sonrasında 12.29 ± 2.42'ye anlamlı olarak arttığı belirlendi (t/p=-7.881/0.000). Mezuniyet sonrası palyatif bakımda çalışmak isteyen öğrencilerin FATCOD puan ortalamasının (114.66 ± 8.76), istemeyenlere göre daha yüksek olduğu belirlendi (108.24± 8.88) (t = 3.468, p = 0.001). Ayrıca, öğrencilerin eğitim sonrası palyatif bakım bilgi puanı ortalaması ile FATCOD puan ortalaması arasında pozitif ancak zayıf bir korelasyon olduğu bulundu (r = 0.285, p = 0.004).*

Sonuç: *Öğrencilere palyatif bakım konusunda verilen eğitimin bilgi ve tutumlarında olumlu farklılıklar yarattığı görüldü. Ancak eğitimin, mezuniyet sonrası öğrencilerin palyatif bakım hemşiresi olarak çalışma isteklerini azalttığı belirlendi.*

Anahtar kelimeler: *bilgi; eğitim; hemşirelik; palyatif bakım; tutum*

İletişim/Contact: *Ayşegül Öztürk Birge, Ankara University Faculty of Nursing, Department of Nursing, Ankara, Turkey* • ***Tel:*** *0319 14 50 / 2848* • ***E-mail:*** *birge@ankara.edu.tr* • ***Geliş/Received:*** *03.11.2021* • ***Kabul/Accepted:*** *02.04.2022*

ORCID: *Ayşegül Öztürk Birge, 0000-0003-2918-1274* • *Tülin Bedük, 0000-0002-4514-9381*

Introduction

According to the population characteristics of Turkey, life expectancy is known to be 78 years on average, and the first three causes of death are known to be chronic diseases such as circulatory system, cancer, and respiratory system diseases[1]. In addition, with the current 8.2% elderly population, the country's population is aging every other day[1]. Besides, patients who need palliative care receive care mainly in intensive care units and emergency departments for symptom management[2]. All these data show that the need for palliative care in Turkey is increasing gradually.

The international association for hospice and palliative care has focused on developing four main topics for hospice and palliative care. These are training strategies for cost-efficient palliative care, access to drugs, health policies, and implementation of palliative care services[3]. A quality palliative care service can be provided with a holistic approach that involves a team of well-trained experts, a collaboration between hospitals, necessary legal arrangements, and well-coordinated home care services.

Palliative care is recognized as a separate area of expertise in countries like the US, Britain, Canada, and Australia. Australia has established the "Palliative Care Curriculum for Nursing Education" to train specialist nurses[4]. In a study examining palliative medicine education in universities in the European region, 13 out of 43 countries were determined to have palliative medicine education. The countries where palliative care in medical education is best provided were Israel, Norway, England, Belgium, France, Austria, Germany, and Ireland[5]. There is no subspecialty program in palliative care in faculties of medical sciences and master's degree programs in palliative care nursing in nursing schools in Turkey. Palliative care covers a limited place in medical and nursing undergraduate education. Nurses who will give this service are educated through in-service training programs after graduation, and the larger part of the education is given theoretically[4].

Palliative care aims to improve patients' quality of life by reducing physical, psychological, and spiritual suffering[6]. In many studies in the literature, positive changes have been observed in students' palliative care knowledge and attitudes through educational interventions[7–9]. The European Association for Palliative Care (EACP) 2004 document on palliative care nursing education is widely known and used in many countries to support nursing education[10]. The American Association of Colleges of Nursing (AACN) established the End of Life Nursing Education Consortium (ELNEC) in 2010 to promote the development of palliative care. The association provides training worldwide[11]. In one study, after the ELNEC education, students' correct responses to questions about palliative care philosophy, symptom management, communication, and mourning process increased significantly[8]. The education of healthcare professionals who provide palliative care is expected to improve the quality of life and cost savings of patients and their relatives[6]. Positive results have been obtained in studies investigating the effects of palliative care[10]. It is stated that palliative care reduces the symptom burden and hospitalizations of the patients and enables them to stay at home safely[12].

In palliative care, end-of-life patients are served, and the quality of care can be provided by nurses who can comfortably reflect on their feelings and thoughts about death and end-of-life care[13]. Nursing students' attitudes towards death and the dying patient are important factors affecting the quality of care[14]. This is also necessary for emotional support and compassionate care in service delivery[13]. Current research confirms that healthcare providers feel inadequate to address patients' spiritual concerns and need continuing education on these issues[15]. It is necessary to talk about death and ensure the continuity of education so that students can gain insight into their individual effects and feelings in the face of death and ultimately realize a good/honorable death process[14].

The importance of education of qualified health professionals supported in terms of knowledge and skills is evident in the effective delivery of palliative care[10,16]. The nurse has an important place in the multidisciplinary team providing palliative care. This study aimed to evaluate the effect of education given to nursing students on their palliative care opinion, knowledge, and attitudes.

Material and Methods

Design and Setting

The study used a single group pre-test/post-test method. Ankara University, Faculty of Health Sciences, Nursing Department, where the study was carried out, is an institution giving four-year education. The internal Medicine Nursing course is given in the fall semester of the second grade. Before taking this

course, students take basic medical sciences and "Basic Principles and Practices in Nursing" courses. The study consisted of students taking the Internal Medicine Nursing course at Ankara University Faculty of Health Sciences. During the 2017–2018 academic year, 197 students took this course.

Participants

The study sample consisted of 105 students before the training and 98 students after the training. The participants included in the study were taking the Internal Medicine Nursing Course at Ankara University Faculty of Health Sciences. Also, they volunteered to participate in the study. *The inclusion criteria*: Taking the Internal Medicine Nursing Course for the first time and attending the palliative care course. *The exclusion criterion*: Refusing to volunteer to participate in the study.

Data Collection

To test the comprehensibility of the questionnaire forms to be administered in the study, 10 nursing students who were not in the universe of the study were asked to fill out the forms. Necessary corrections were made accordingly, and the forms were finalized. The pilot study was carried out on 11 December 2017.

The students agreeing to participate in the study were administered the data collection forms as a pretest before 12 December 2017. The study data were collected using a student information form, the palliative care knowledge and opinion form, and the Frommelt Attitudes Toward Care of the Dying Scale (FATCOD). The Palliative Care Training session was held on 26 December 2017 in the last hour of the Internal Medicine Nursing course in the 2017–2018 Academic Year. The training content was prepared based on the literature (Table 1).[8,17,18]. The training was provided by the researcher, who has palliative care experience. Students performed clinical practice within the scope of the internal medicine nursing course for 14 weeks, two days a week. Educational content was discussed using the students' own clinical experiences. The training took 5 hours. Immediately after the training, the posttest was administered. The training was held in a conference hall with 220 people using a computer-aided power-point presentation, and a board was used to carry out the discussion and write down important points.

Description of Data Collection Tools

The Student Information Form: This form was designed by the researchers based on the literature[8,19,20]. The form involved 12 questions aiming to determine socio-demographic characteristics of the nursing students (age, gender, high school education, clinical practice experience), death experience, and their working status in the palliative care unit (experiencing death in

Table 1. *Palliative care education content*

The content of the education	Teaching technique
What is palliative care?	Narration, Question-answer, Discussion, Demonstration, Case presentation
What is the purpose of palliative care?	
History of Palliative Care	
Principles of Palliative Care	
Duties of the Palliative Care Team and the Nurse	
Palliative Care Services Offered in Turkey	
Criteria for Acceptance to Palliative Care Unit and Home Care	
Palliative Care in Health Education	
Barriers to Providing Palliative Care	
Ethical Principles and Dilemmas in Palliative Care	
Symptom Management in Palliative Care (Pain, dyspnea, fatigue, anorexia and cachexia, mucositis, nausea and vomiting, constipation, dehydration, delirium)	
Communication Problems and Management in Palliative Care	
Death and Mourning Process	

first degree relatives, time elapsing after loss, the status of giving care to dying patients in the clinic, the feelings experienced while providing care to these patients, the status of receiving education on death, working experience in palliative care unit).

The Palliative Care Opinion Form: The researchers prepared the Palliative Care Opinion Form based on the literature [5,8,18]. This form consisted of a total of 8 questions about the definition of palliative care, who the recipients are, where these services can be managed more effectively, the most common symptoms of palliative care patients, which of these symptoms the students would have difficulty managing, the desire for working in the palliative care unit after graduation, and the barriers that limit palliative care.

The Palliative Care Knowledge Form: No valid and reliable measurement tool measures the palliative care knowledge of nursing students in Turkey. To determine the palliative care knowledge of the students, a 17-item form was prepared to evaluate their knowledge and attitudes toward palliative care[18,21,22]. The form consisted of statements evaluating the knowledge of palliative care philosophy, pain, nutrition, dyspnea, fatigue and delirium management, skills for coping with stress, and team collaboration. For content validity, the form was submitted to the opinions of two experts in internal medicine nursing and a faculty member in the field of public health nursing. These experts, whose opinions are taken, have the knowledge and experience for palliative care. Accordingly, the content validity index of the form was determined to be one (1) in the analysis performed according to the Davis technique[23]. The students were asked to mark each item in the form of "True," "False," or "I do not know." There were 9 true and 8 false items (item 1, 3, 5, 8, 9, 13, 16, 17) in the form. The total score in the form is calculated by scoring each correct answer as 1 and each incorrect or "I don't know" response as 0. The highest score that could be obtained from the form was 17, and increased scores indicated an increase in the level of knowledge.

FATCOD, Form B: This is a 30-item scale developed by Katherine H Murray Frommelt in 2003. The scale contains an equal number of expressions, including positive and negative attitudes[24]. A Likert-type scale is scored between "1- Strongly disagree" and "5- Strongly agree". The total score is calculated by inversing the items for negative attitudes (3, 5, 6, 7, 8, 9, 11, 13, 14, 15, 17, 19, 26, 28, 29) and summing them with positive items. The total score obtained from the scale varies between 30 and 150, and high scores indicate a more positive attitude. The validity and reliability study of the Turkish version was carried out by Çevik & Kav in 2013 [25]. Cronbach's Alpha value of the Turkish version of the scale was 0.69.

Statistical Analysis

SPSS (Statistical Package for Social Sciences) version 15 was used to analyze the study data and create the tables. Frequency, percentage, mean, and standard deviation values were used to present the data regarding nursing students' sociodemographic characteristics, palliative knowledge, and opinions. According to the Kolmogorov Smirnov test, the mean scores obtained from the FATCOD scale showed a normal distribution. The relationship between independent variables (gender, the status of experiencing the loss of a person, status of receiving education on death, clinical experience of palliative care and desire to work in palliative care units, the experience of caregiving to dying patients) and post-training mean FATCOD scores were analyzed with independent samples t-test. McNemar Chi-Square (x^2) test and t-test for dependent groups were employed to compare nursing students' pre-and post-training knowledge and opinions on palliative care. Pearson's correlation was used to determine the relationship between students' mean post-training palliative care knowledge score and their mean score from the FATCOD scale. In all statistical analyses, $p<0.05$ was accepted as the significance level.

Ethical Consideration

The Ethics Committee approved the study of Ankara University with decision number 01/12 on 06 December 2017. It complies with the principles of the Declaration of Helsinki. Institutional permission and written informed consent were obtained from all students.

Results

Participants

The mean age of the students participating in the study was 19.71±1.01 (18–24) years, and 90.5% of the participants were female. The mean duration of students' clinical practice experience was 2.87±1.6 (1–8) months. Of the participants, 71.4% were found to do clinical practice in internal clinics, while 25.7% were determined to practice in intensive care units. When students' experiences regarding the loss of a person

and giving palliative care were examined, 33.3% of the students were found to experience the loss of a friend or relative. The time elapsed after the loss was determined to be 25 months over in 62.9% of them. Of the students, 57.1% reported that they had already given care to a dying patient, and the frequently felt emotion while providing the care was helplessness in 47.6% and grief and despair in 37.1%. Also, 21% of the students were found to have received training on death, 11.4% had done clinical practice in the palliative care unit, and 32.4% had given care to a palliative care patient.

Pre and Post-training Opinions about Palliative Care

The proportion of students who correctly defined palliative care before the training was 69.5%, and it increased to 93.9% after the training. Before the training, 73.3% of the students stated that palliative care should be given to patients with end-stage heart failure, while 66.7% said it should be given to cancer patients. After the training, the rate of students who could identify palliative care patient groups increased. Before and after the training, the majority of the students stated that the place for effective/quality palliative care service was palliative care units. When the place where dying patients want to receive care was questioned before the training, 42.9% of the students responded to the question as home, and 47.6% responded as a palliative care unit. After the training, there was a decrease in the rate of "home care" responses (37.8%) and an increase in the rate of "palliative care" responses (55.1%). Before the training, students said the most common symptoms of the patients who receive palliative care were pain (85.7%), fatigue (63.8%), and dyspnea (44.8%). After the training, the students reported the same symptoms with different percentages, such as 90.8% (pain), 65.3% (dyspnea), and 41.8% (fatigue). The students thought the symptoms that would be the most challenging in the management of palliative care were delirium, pain, fatigue, and dyspnea (Table 2).

When the students were asked about what hindered the provision of palliative care, 38.1% defined it as the lack of trained health professionals before the training. After the training, 33.7% described the barriers to the provision of palliative care as both the lack of trained health professionals and the inadequacy of palliative care centers in terms of number and bed capacity. The rate of those who wanted to work in palliative care units after graduation was 41.9% before the training, and it was found to decrease to 36.7% after the training (p=0.382). Before the training, 74.3% of the students were found to agree on the item "Is it inevitable that health professionals working in palliative care units will experience burnout?" this proportion increased to 87.8% after the training (p=0.037) (Table 2).

Palliative Care Knowledge and Attitudes

When palliative care knowledge of the students before and after the training was compared, the rate of correct responses to nine of the 17 items was found to significantly increase after the training (item 3, 6–8, 13–17) (Table 3). Although it is not shown in the table, the mean pre-training palliative care knowledge score of the students was 9.95±2.00 (3–15), and it was found to increase to 12.29±2.42 (7–16) significantly after the training (t/p=-7.881/0.000).

The students' pre and post-training mean FATCOD scores were 106.93±8.48 (83–126) and 110.60±9.32 (87–135), respectively. The scores were found to increase significantly (t/p=-2.802/0.006). Independent sample t-test was used to analyze the difference between independent factors (gender, experiencing the loss of a person, the status of receiving training on death, clinical palliative care experience and willingness to work in palliative care units, the experience of giving care to a dying patient) which may affect the burden of giving care to a dying patient on the student after the training and the mean FATCOD score. Accordingly, the mean FATCOD scores of the students who wanted to work in palliative care units after graduation (114.66±8.76) were higher than those of the students who did not want to (108.24±8.88), and the difference between the scores was found significant (t=3.468, p=0.001). In addition, there was a positive but weak correlation between the mean post-training palliative care knowledge score and the mean FATCOD score (r=0.285, p=0.004). According to the analysis results, no other variables significantly differed in the FATCOD mean score. When the difference between pre and post-training mean item scores of the FATCOD scale of the students was examined, a statistically significant increase was found in the responses given to most items after the training (Table 4).

Discussion

Palliative care is a human right. It is an approach to improving the life quality of patients and their relatives. In palliative care, life and death are seen as normal processes. Death is neither delayed nor accelerated[6].

Table 2. *Students' opinions on palliative care*

	Pre-training (n: 105)		Post-training (n: 98)	
Opinions on palliative care. What is palliative care?	n	%	n	%
It is the care given only to cancer patients in the end-stage of life.	1	1	1	1
It provides the management of symptoms related to life-threatening diseases.	73	69.5	92	93.9
It is the care provided only in palliative care units.	4	3.8	2	2
Palliative care covers only applications involving pain control.	7	6.7	3	3.1
It aims to extend the life of the patient.	20	19	-	-
Who are the recipients of palliative care?				
Cancer patients	70	66.7	88	89.8
Terminal-stage patients with heart failure	77	73.3	90	91.8
Terminal-stage patients with a renal disease	67	63.8	73	74.5
Patients with advanced stage respiratory failure	62	59	75	76.5
AIDS patients	33	31.4	61	62.2
Patients with advanced stage dementia	29	27.6	52	53.1
Patients with advanced motor neuron disease	40	38.1	57	58.2
Where should effective/quality palliative care be given?				
Home care services	19	18.1	18	18.4
Palliative care units	76	72.4	64	65.3
General hospital services	2	1.9	-	-
General hospital intensive care units	8	7.6	-	-
Home care services and palliative care units	-	-	12	12.2
All	-	-	4	4.1
Where should your dying patient receive care?				
At home	45	42.9	37	37.8
Palliative care units	50	47.6	54	55.1
General hospital services	2	1.9	-	-
General hospital intensive care units	8	7.6	-	-
Home care services and palliative care units	-	-	7	7.1
Indicate the three most common symptoms experienced by patients receiving palliative care.				
Pain	90	85.7	89	90.8
Dyspnea	47	44.8	64	65.3
Fatigue, weakness	67	63.8	41	41.8
What symptom do you think will challenge you most in palliative care management?				
Pain	31	29.5	37	37.8
Dyspnea	8	7.6	15	15.3
Fatigue	10	9.5	1	1
Delirium	41	39	41	41.8
What is the most important obstacle limiting the provision of palliative care?				
Lack of trained health professionals	40	38.1	33	33.7
Inadequate number and bed capacity of palliative care centers	21	20	33	33.7
Unawareness of patients who need palliative care about palliative care services	25	23.8	14	14.3
All	5	4.8	10	10.2
No idea	14	13.3	8	8.2
Would you like to work in the palliative care unit after graduation?				
Yes	44	41.9	36	36.7
No	61	58.1	62	63.3
Is it inevitable that health professionals working in palliative care units will experience burnout?				
Yes	78	74.3	86	87.8
No	27	25.7	12	12.2

Table 3. *Comparison of students' correct response rates for palliative care before and after training*

	Pre-training (n: 105)		Post-training (n: 98)		
Statements on palliative care knowledge	n	%	n	%	p
1. Palliative care should only be given to patients who cannot find treatment with medication. (F)	86	81.9	84	85.7	0.700
2. Long-term use of opioids often leads to addiction. (T)	76	72.4	71	72.4	1.000
3. There is no choice other than the central venous line in cases where the peripheral intravenous line cannot be employed. (F)	32	30.5	45	45.9	0.020*
4. Stage of the disease determines the method of pain treatment. (T)	91	86.7	87	88.8	0.839
5. Nonpharmacological approaches have no effect on pain management. (F)	80	76.2	77	78.6	1.000
6. Drowsiness related to electrolyte imbalance may reduce the need for sedation in the last days of life. (T)	29	27.6	52	53.1	0.000*
7. It is appropriate to use respiratory depressants for the treatment of severe dyspnea in the late stages of a disease. (T)	22	21	51	52	0.000*
8. Placebo is suitable for the treatment of some types of pain. (F)	12	11.4	55	56.1	0.000*
9. Men often deal with grief more easily than women. (F)	46	43.8	40	40.8	0.532
10. Chronic pain symptoms are different from acute pain symptoms. (T)	78	74.3	85	86.7	0.072
11. The pain threshold decreases more often in cases of anxiety and fatigue. (T)	86	81.9	81	82.7	1.000
12. Prevention and effective treatment of oral mucositis are important in maintaining nutrition. (T)	98	93.3	93	94.9	0.774
13. Patients who experience fatigue and exhaustion must be taken to bed rest. (F)	37	35.2	57	58.2	0.003*
14. Delirium is an acute and fluctuating deterioration in attention, consciousness, and perception. (T)	85	81	90	91.8	0.023*
15. Preventing delirium is more effective than treating it. (T)	69	65.7	88	89.8	0.001*
16. Diagnosis of a patient with a fatal disease should be concealed from the patient to enhance the capacity of the patient to cope with the disease (F)	69	65.7	80	81.6	0.025*
17. Palliative care can also be carried out without a multidisciplinary team. (F)	49	46.7	69	70.4	0.001*

McNemar x^2 test was applied in dependent groups, *p<0.05. T: Right, F: False

Table 4. *Comparison of students' mean FATCOD scores before and after training*

Items	Pre-training $\bar{X} \pm$ S. D.	Post-training $\bar{X} \pm$ S. D.	p
1. Giving care to the dying person is a worthwhile experience.	4.60±0.60	4.66±0.62	0.482
2. Death is not the worst thing that can happen to a person.	3.43±1.01	3.41±1.17	0.896
3. I would be uncomfortable talking about impending death with the dying person.	2.23±1.18	2.66±0.98	0.007*
4. Caring for the patient's family should continue throughout the period of grief and bereavement.	3.73±1.10	4.32±0.85	0.000*
5. I would not want to car efor a dying person.	3.51±1.07	3.42±0.96	0.594
6. The nonfamily caregivers should not to be the one to talk about death with the dying person.	3.14±1.13	3.13±1.01	0.952
7. The lenght of time required giving care to a dying person would frustrate me.	3.48±1.09	3.62±1.02	0.413
8. I would be upset when the dying person I was caring for gave up hope of getting better.	1.73±0.80	1.78±0.73	0.652
9. It is difficult to form a close relationship with the dying person.	2.34±0.92	2.48±1.09	0.307
10. There are times when the dying person welcomes death.	3.68±0.74	3.87±0.83	1.102
11. When a patient asks, "Am I dying" I think it is best to change the subject to something cheerful.	3.44±1.02	3.77±1.09	0.044*
12. The family should be involved in the physical care of the dying person.	4.24±0.73	3.02±1.08	0.000*
13. I would hope the person I'm caring for dies when I am not present.	3.51±1.14	3.52±1.15	0.953
14. I am afraid to become friends with a dying person.	3.38±1.13	3.35±1.14	0.850
15. I would feel like running away when the person actually died.	3.23±1.05	3.02±1.08	0.177
16. Families need emotional support to accept the behavior changes of the dying person.	4.37±0.65	4.46±0.54	0.266
17. As a patient nears death, the nonfamily caregiver should withdraw from his/her involvement with the patient.	3.81±0.82	3.79±0.93	0.863
18. Families should be concerned about helping their dying member maket he best of his/her remaining life.	4.48±0.59	4.50±0.64	0.913
19. The dying person should not be allowed to make decisions about his/her physical care.	3.76±1.02	4.10±0.96	0.026*
20. Families should maintain as normal an environment as possible for their dying member.	4.34±0.61	4.16±0.68	0.046*
21. It is beneficial for the dying person to verbalize his/her feelings.	4.52±0.54	4.51±0.57	0.885
22. Care should extend to the family of the dying person.	4.33±0.74	4.52±0.66	0.060
23. Caregivers should permit dying persons to have flexible visiting schedules.	3.97±0.98	4.26±0.83	0.013*
24. The dying person and his/her family should be the in-charge decision-makers.	3.65±1.08	4.01±0.90	0.006*
25. Addiction to pain relieving medication should not be a concern when dealing with a dying person.	3.57±0.94	4.17±0.89	0.000*
26. I would be un comfortable if I entered the room of a terminally ill person and found him/her crying.	2.62±1.17	2.44±1.06	0.313
27. Dying persons should be given honest answers about their condition.	3.85±0.78	4.13±0.78	0.016*
28. Educating families about death and dying is not a nonfamily caregiver responsibility.	3.83±0.99	3.66±1.11	0.235
29. Family members who stay close to a dying person often interfere with the professional's job with the patient.	2.17±0.64	2.24±0.70	0.445
30. It is possible for nonfamily caregivers to help patients prepare for death.	3.78±0.74	4.09±0.73	0.003*

In dependent groups t-test was applied, * p<0.05.

When students' responses regarding palliative care were examined according to this philosophy before the training, 19% of the students were found to define palliative care as a process of extending patients' life. In contrast, no students agreed with this view after the training. Most of the students thought that the place for effective/quality palliative care service was palliative care units.

Symptom management, patient advocacy, and communication are highly important factors in maintaining palliative care[26]. According to the students who participated in the study, the three most common symptoms experienced by patients receiving palliative care were pain, fatigue-weakness, and dyspnea, respectively. After the training, delirium, pain, dyspnea, and fatigue were determined to be the symptoms that the students would have difficulty in managing. In a study, the training needs of nurses and physicians regarding palliative care were found as end-of-life communication (66.7%), ethical issues (66.7%), delirium management (60%), pain assessment and management (51.7%), intervention in dyspnea (45%), spiritual care (40%), intervention in insomnia (36.7%), loss of appetite (33.3%), nausea and vomiting (30%), and intervention in intestinal problems (20%) [27]. When these results are examined, given the low number of students attending the clinic in the palliative care unit and providing care to the patient in need of palliative care, the students can be said to have a good awareness of identifying the common symptoms of palliative care.

In the study, the students were asked about what hindered the provision of palliative care most. Before the training, the students responded to this question by marking the options such as the lack of educated health professionals (38.1%), the lack of information about palliative care services (23.8%), and inadequate number and bed capacity of palliative care centers (20%). In a study investigating the knowledge of the families of patients receiving palliative care in Turkey, 68% of the families reported not knowing about palliative care. Besides, 45.8% of the families obtained information from people receiving palliative care and 25% from their close friends[17]. People can not request or evaluate a service they have no idea of[12]. One of the most important ways of raising the awareness of patients and their relatives is to increase the professionals' awareness who will provide the service through education.

Care for dying patients requires coping with many stressors. Otherwise, health professionals who constantly witness losses will inevitably suffer burnout after a while[28]. Sometimes, burnout can occur due to intensive working conditions. Besides, burnout can also be experienced due to reasons such as the impossible demands of people in agony, the vulnerability of the patients, and the perfectionist personality characteristics[28]. The number of students who stated that they would like to work in the palliative care unit after graduation decreased after the training. Also, most students regard the burnout of healthcare workers working in palliative care units as inevitable. In another study, a group of students who had received ELNEC training was asked whether they would be interested in palliative and end-of-life care certification to improve their nursing practices. 60.4% of these students responded negatively to this question[8]. The nurses who decide to work in palliative care after graduation should be selected among volunteers aware of the definition of the task. In this way, it will be possible to increase the quality of care and reduce the risk of burnout. A systematic review evaluating the prevalence of burnout in healthcare professionals working in palliative care determined that nurses mostly experienced emotional exhaustion (19.5%) and depersonalization (8.2%)[29].

The rate of correct responses of the students to the statements in the palliative care knowledge form after the training was relatively high. The rate of correct answers to the statement "the use of respiratory depressant drugs for the treatment of severe dyspnea in the end stages of a disease is appropriate" increased from 21% to 52%, and the rate of correct responses to the statement "the use of placebo is appropriate for the treatment of certain types of pain" increased from 11.4% to 56.1%. Also, there was a significant increase in the rate of correct responses to the statements such as "Preventing delirium is more effective than treating it," "Diagnosis of a patient with a fatal disease should be concealed from the patient to enhance the power of the patient to cope with the disease," and "Palliative care services can be carried out without a multidisciplinary team." In a study evaluating the palliative care knowledge of 220 nursing students from five different nursing schools in Jordan, the palliative care knowledge of the students was found to be inadequate. 44% of the students who participated in the study stated that "Drugs that can cause respiratory depression during terminal stages of a disease are suitable for the treatment of severe dyspnea," and 31% in the same study stated that "Accumulation of

losses makes burnout unavoidable for people working in palliative care"[21]. In another study conducted with Saudi nursing students, students' knowledge of palliative care philosophy and pain management was inadequate[30]. In the study, the percentage of correct answers to some questions about pain, dyspnea, and fatigue management was low before the training. However, the rates of correct responses to these items increased through training.

Student nurses are often caught unprepared for patient care due to inadequate training in patient care during the death process, which causes them to experience feelings of anxiety, sadness, and inadequacy in the care process[7,14]. Witnessing the death of a person you give care and caring to a person approaching death is highly stressful and causes intense emotions[31,32]. For this reason, for the caregiver and the recipient to end up with harmony in this process, they should receive training regarding their knowledge and attitudes. In a systematic review study, the palliative care education given to nursing students positively affected students' attitudes towards dying patient care positively[7]. In the study, the mean FATCOD scores of the students who wanted to work in the palliative care units after graduation was determined to be significantly higher. As the palliative care knowledge score increased, the FATCOD score was found to increase, too. The positive attitudes of students who want to work in these units towards death willingly is an expected and desired state. In a study conducted in China, 23.8% of nursing students were reluctant to work in palliative care. The factors affecting this situation were fear of facing death and death anxiety in 56.2% and a distressing and depressive working environment in 78%[32].

As a result, it is seen that the educational interventions given before and after graduation affect the knowledge and attitude towards palliative care positively[9,16,33,34].

Limitations

This study has a few limitations. First of all, palliative care training was provided in a single five-hour meeting. Students did their clinical practice mostly in internal clinics. A limited number of students could go into clinical practice in only two palliative care wards. Second, no valid and reliable measurement tool measures student-specific palliative care knowledge.

For this reason, a form based on the literature was prepared by the researchers, and only the content validity was evaluated. However, after the implementation of the study was completed, a test adaptation study was found that measured the clinical nurses' knowledge of palliative care[35]. Third, the palliative care information form covers only the structure and process of palliative care, symptom management, and grief.

Conclusion

In this study, the palliative care training given to nursing students created significant differences in the students' opinions, knowledge, and attitudes. Also, as the palliative care knowledge score increased, the mean FATCOD score was found to increase, too, and a weak but significant correlation was between them. Volunteering to work in palliative care units was determined to affect the mean FATCOD score. After the training, there was a decrease in nursing students' desire to work in palliative care units after graduation. Students had an average of 3 months of clinical experience, so they likely thought they would have difficulty in critical patient and family care. We think that palliative care education showed the truth in these results, but inadequacy in failing to cope with death and mourning was also influential.

The content of palliative care education to be given to nursing students should be arranged according to the needs of the students. More emphasis should be placed on issues where students feel inadequate or challenged. Also, it is important to provide clinical practice opportunities where students can perform or observe palliative care practices in the clinic to meet the educational goals.

Prolonging the life expectancy through medical and technological developments has resulted in a change in the population pyramid, bringing about a gradually growing elderly population. This necessitates the provision of palliative care at the undergraduate level of the nursing curriculum. Therefore, palliative care should be placed in undergraduate education programs and not postponed until graduation.

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OLGU SUNUMU / *CASE REPORT*

A Rare Cause of Left Lower Quadrant Pain: Acute Appendicitis in a Patient with Intestinal Malrotation

Sol Alt Kadran Ağrısının Nadir Bir Nedeni: İntestinal Malrotasyonlu Bir Hastada Akut Apandisit

Mesud Fakirullahoglu[1], Nurhak Aksungur[2]

[1]Department of General Surgery, Erzurum Regional Education and Research Hospital; [2]Department of General Surgery, Atatürk University Faculty of Medicine, Erzurum, Turkey

ABSTRACT

Acute appendicitis is the most common surgical cause of acute abdominal pain. Normally, abdominal pain secondary to acute appendicitis is localized in the right lower quadrant, whereas in case of intestinal malrotation or situs inversus totalis, the abdominal pain is localized in the left lower quadrant. These conditions may lead to delay in diagnosis and treatment. In this case report, it is aimed to present the diagnosis and treatment process of an atypically localized acute appendicitis case due to intestinal malrotation in the light of the literature.

Key words: *abdominal pain; appendicitis; intestinal malrotation*

ÖZET

Akut apandisit, akut karın ağrısının en sık cerrahi nedenidir. Normalde akut apandisite sekonder karın ağrısı sağ alt kadranda lokalize olurken, intestinal malrotasyon veya situs inversus totalis durumunda karın ağrısı sol alt kadranda lokalizedir. Bu durumlar tanı ve tedavide gecikmeye neden olabilmektedir. Bu olgu sunumunda intestinal malrotasyona bağlı atipik lokalize akut apandisit olgusunun tanı ve tedavi sürecinin literatür eşliğinde sunulması amaçlanmıştır.

Anahtar kelimeler: karın ağrısı; apandisit; intestinal malrotasyon

Introduction

Acute appendicitis is the most common emergency surgical abdominal pathology[1,2]. The appendix vermiformis is typically located in the lower right quadrant of the abdomen. On the other hand, the localization of appendix vermiformis may change due to various reasons. For example, malrotation problems such as situs inversus totalis (SIT) and intestinal malrotation (IM) cause the appendix vermiformis to be detected in different quadrants. In these diseases, the appendix vermiformis can be detected in the left lower quadrant[3,4]. Therefore, when acute appendicitis occurs in these patients, the pain is in the left lower quadrant.

This case report it is aimed to present the diagnosis and treatment process of an atypically localized acute appendicitis case due to intestinal malrotation in the light of the literature.

Case Report

A 36-year-old male patient was admitted to the Emergency Department of Erzurum Regional Education and Research Hospital, Erzurum, Turkey, with complaints of nausea, vomiting, anorexia, and abdominal pain, which had started 24 hours ago. Abdominal pain first started around the umbilicus and soon settled in the left lower quadrant. The patient had no previous history of surgery and no other disease.

The vital findings of the patients were as follows: blood pressure 125/72 mmHg, pulse rate 114 beats/min (bpm), respiratory rate 16 times/min, body temperature 38.1°C, oxygen saturation on room air 94% -96%. The patient's physical examination showed localized tenderness, defense, and rebound in the left lower quadrant. Other systemic physical examinations of the patient, including rectal examination, were unremarkable.

In laboratory, the leukocyte count (16.500/mm3) and C-reactive protein (CRP) level (80 mg/dL) were higher. The other blood parameters and urinalysis were normal. On plain radiography, gas shadows were

İletişim/Contact: *Mesud Fakirullahoğlu, Atatürk Mahallesi Çat Yolu Caddesi No:36, 25240, Yakutiye, Erzurum* • ***Tel:*** *0507 449 27 79* • ***E-mail:*** *fakirullah_mesud@hotmail.com* • ***Geliş/Received:*** *17.11.2021* • ***Kabul/Accepted:*** *11.12.2021*

ORCID: *Mesud Fakirullahoğlu, 0000-0002-5871-5688* • *Nurhak Aksungur, 0000-0003-4477-5775*

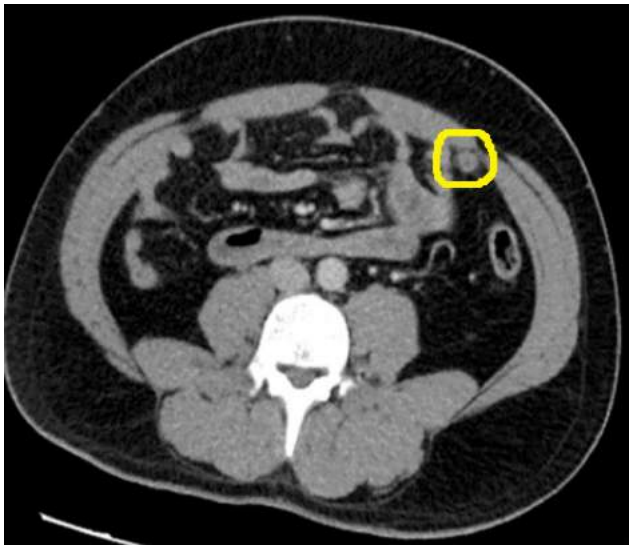

Figure 1. *Computed tomography revealed an appendix vermiformis with a diameter of 9.7 mm in the left lower quadrant.*

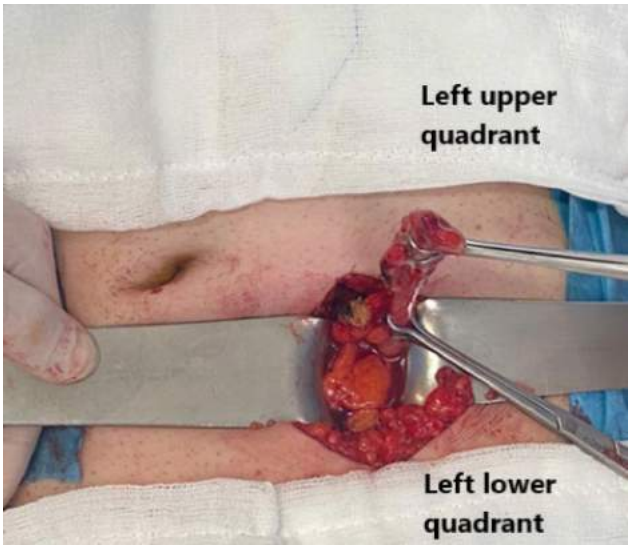

Figure 2. *Intraoperative view of the appendix vermiformis.*

observed in the left lower quadrant of the abdomen. Since no pathology was detected in ultrasonography, intravenous contrast-enhanced computed tomography (CT) was planned to establish the correct diagnosis. Computed tomography revealed acute appendicitis in the left lower quadrant accompanied by intestinal malrotation (Fig. 1).

Emergency surgery with a left paramedian incision was planned. On exploration, acute suppurative appendicitis was seen (Fig. 2). The patient who underwent appendectomy was followed-up in the service during the postoperative period. He was discharged on the second postoperative day without complications.

Discussion

Acute appendicitis is the most common surgical cause of acute abdominal pain. Acute appendicitis manifests itself with symptoms such as pain starting in the peri-umbilical region, loss of appetite, nausea, vomiting, and fever[1,4]. The most important feature of the pain is its displacement, and as the inflammation increases, the pain is localized to the right lower quadrant[2]. The presentation of acute appendicitis imitates various gastrointestinal and genitourinary diseases like gastritis, cholecystitis, pyelonephritis, and diverticulitis. Unfortunately, the atypical presentation of acute appendicitis with left lower quadrant pain can be misleading. Therefore, the diagnosis and treatment process is delayed.

The differential diagnosis of left lower-quadrant pain includes gastrointestinal, gynecologic, and renal/ureteric pathologies. Gastrointestinal pathologies are left colon diverticulitis, epiploic appendicitis, constipation, incarcerated hernia, infectious colitis, inflammatory bowel disease, and omental infarctus[5–7]. In addition, in cases with different localization than expected, as in intestinal malrotation (IM) and situs inversus totalis (SIT), the diagnosis of acute appendicitis may be delayed[4,8]. IM occurs when there is either non-rotation or incomplete rotation of the primitive intestinal loop around the superior mesentery artery axis during the first ten weeks of fetal life[9]. In SIT, all intra-abdominal and intra-thoracic organs are positioned as mirror images. The appendix vermiformis is located in the left lower quadrant in both pathologies.

There is no specific difference in laboratory findings in acute appendicitis cases, whether right-sided localized or left-sided localized. As in our case, leukocytosis and elevated CRP levels are expected changes. Urinalysis can help differentiate renal colic. Although plain radiography and ultrasonography provide information about the diagnosis of acute appendicitis located in the left lower quadrant, computed tomography has an accuracy rate of up to 90% for both differential diagnosis and correct diagnosis[10]. In the present case, we initially suspected left colon diverticulitis. However, the underlying intestinal malrotation delayed the correct diagnosis of acute appendicitis. Malrotation was detected in the patient after a CT scan.

In cases diagnosed with left-sided acute appendicitis, treatment can be performed with open surgery or laparoscopy, depending on the surgeon's experience and technical possibilities[11]. Although there is no difference in technical procedure, the possibility of encountering Ladd bands in malrotation cases should be considered.

Conclusion

Acute appendicitis with atypical localization due to malrotation should be considered in patients with left lower quadrant pain, and the correct diagnosis should be made quickly using appropriate imaging tools.

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OLGU SUNUMU / *CASE REPORT*

A Rare Cause of Acute Abdomen: Pneumatosis Cystoides Intestinalis

Nadir Bir Akut Karın Nedeni: Pnömatozis Sistoides İntestinalis

Tolga Kalayci, Murat Kartal

General Surgery Clinic, Erzurum Regional Education and Research Hospital, Erzurum, Turkey

ABSTRACT

Pneumatosis cystoides intestinalis (PCI) is a rare disease defined as the presence of gas in the small intestine or colon wall. A 55-year-old female patient was admitted to the emergency service with a complaint of abdominal pain lasting for two days. PCI and intraperitoneal free air were seen on the abdominopelvic computed tomography scan. The patient underwent an emergency laparotomy. There was no perforation and ischemic bowel segment on exploration. Air bubbles were seen only in the wall of the small bowel loops. No surgical procedure was considered for the patient. The patient was discharged on the seventh day without complication.

Key words: *acute abdomen; pneumatosis cystoides intestinalis; laparotomy*

ÖZET

Pnömatozis sistoides intestinalis (PSİ), ince bağırsakta veya kolon duvarında gaz varlığı olarak tanımlanan nadir bir hastalıktır. 55 yaşında bir kadın hasta iki gündür süren karın ağrısı şikâyeti ile acil servise başvurdu. Abdominopelvik bilgisayarlı tomografi taramasında, PSİ ve periton içi serbest hava görüldü. Hastaya acil laparotomi yapıldı. Eksplorasyonda perforasyon ve iskemik barsak segmenti yoktu. Sadece ince bağırsak kıvrımlarının duvarında hava kabarcıkları görüldü. Hastaya herhangi bir cerrahi işlem düşünülmedi. Hasta yedinci günde komplikasyonsuz olarak taburcu edildi.

Anahtar kelimeler: akut abdomen; pnömatozis sistoides intestinalis; laparotomi

Introduction

Pneumatosis cystoides intestinalis (PCI) is a rare disease defined as the presence of gas in the small intestine or colon wall. PCI may also develop spontaneously, although the incidence increases due to pulmonary diseases, systemic diseases, and intestinal diseases. In studies, the prevalence of incidentally detected PCI cases in patients who underwent computed tomography (CT) was reported as 0.37% [1]. It was first described by the pathologist DuVernoi in 1730[2]. The etiology of PCI has not been fully elucidated. The disease, classified in two forms as idiopathic (15%) and secondary (85%), may present different clinical findings. In the idiopathic or primary form, air cysts are located in the mucosa and submucosa. In addition, no obvious etiological factor was found in the idiopathic form. Air cysts are mostly located in the intestinal wall in the secondary form. In the etiology of secondary form, pulmonary diseases, systemic diseases, intestinal diseases, drugs, and iatrogenic causes can play a role.

The asymptomatic disease can be seen during diagnosis, while life-threatening severe clinical pictures may also occur. If PCI is detected early, it can be treated with a conservative approach. In advanced cases, surgical intervention may be required.

This case report presents a case of PCI who underwent diagnostic laparotomy with intra-abdominal free air on computed tomography.

Case Report

A 55-year-old female patient applied to the emergency department of an external center with abdominal pain and nausea with vomiting for two days. Upon the presence of right subdiaphragmatic free air in the standing direct abdominal radiograph, the patient was referred to our hospital for further examination. The patient had no history of previous surgery and no comorbid disease. There had never been a similar episode of abdominal pain before.

İletişim/Contact: *Murat Kartal, Erzurum Regional Education and Research Hospital, General Surgery Clinic, Erzurum, Turkey* • ***Tel:*** *0507 191 96 09* • ***E-mail:*** *m.kartal2587@gmail.com* • ***Geliş/Received:*** *08.02.2022* • ***Kabul/Accepted:*** *24.03.2022*

ORCID: *Tolga Kalaycı, 0000-0002-6977-1757* • *Murat Kartal, 0000-0003-1396-5365*

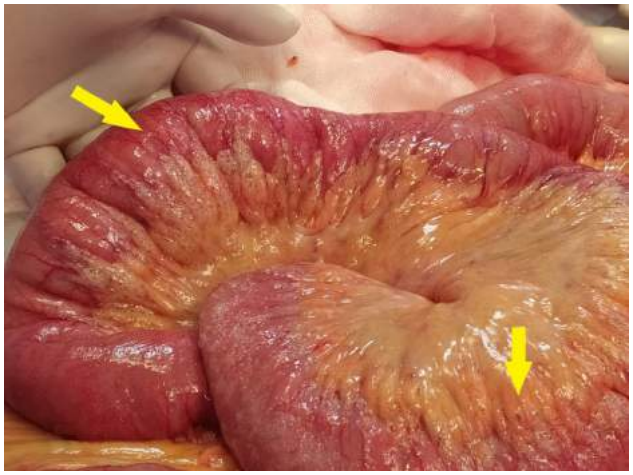

Figure 1. *Intraoperative image of pneumatosis cystoides intestinalis.*

Figure 2. *Air bubbles in the wall of the small intestine.*

At the time of admission to the hospital, the patient's arterial blood pressure was 132/86 mmHg, oxygen saturation on room air was 90%, pulse rate was 98 beats/min, and body temperature was 37.6°C. In the abdominal examination of the patient, there was widespread tenderness and defense in all abdominal quadrants, but there was no rebound. Other system examinations were normal. There was normal stool contamination on rectal touch. Laboratory examination revealed leukocytosis (white blood cell count=13200 µl/ml), elevated C-reactive protein (51 mg/L), aspartate aminotransferase elevation (78 IU/L), and alanine aminotransferase elevation (63 IU/L). Other parameters were unremarkable.

In the standing direct abdominal X-ray, free air was observed in the right subdiaphragmatic area. Intra-abdominal organ perforation clinic was considered in the patient, and abdominal computed tomography (CT) with contrast was performed to evaluate the perforation localization. There was intra-abdominal free air and PCI on a CT scan at the small intestine segments. The patient underwent a diagnostic laparotomy. At laparotomy, diffuse air bubbles were observed in the small intestine wall from the jejunum to the distal ileum (Fig. 1 and 2). No gastrointestinal organ perforation was observed. No ischemic bowel loop was observed. No additional intra-abdominal pathology was detected during the exploration, and the surgery was terminated by placing a drainage catheter in the pouch of Douglas.

The patient was started on ciprofloxacin 400 mg/200 ml (intravenously every 12 hours) and metronidazole 500 mg/100 ml (intravenously every 8 hours) in line with the postoperative period the recommendation of the infection clinic. Oral feeding of the patient, whose complaints regressed in the postoperative period, was opened on the 2nd postoperative day. The drain of the patient who tolerated oral feeding was removed on the 5th postoperative day, the patient's current antibiotherapy was completed for seven days, and the patient was discharged on the 7th postoperative day.

Discussion

More than 90% of pneumoperitoneum occurs as a result of gastrointestinal perforations. Although gastric or duodenal perforation due to peptic ulcer is considered the most common cause of pneumoperitoneum[3], pneumatosis cystoides intestinalis (PCI) is also a rare cause of pneumoperitoneum.

PCI is defined as the presence of air in the small intestine or colon wall. The diagnosis of PCI can be made preoperatively through radiological imaging methods or intraoperatively. In the etiology of PCI, pulmonary diseases (such as pulmonary fibrosis, asthma), systemic diseases (such as systemic lupus erythematosus, scleroderma), intestinal diseases (such as diverticulitis, intestinal obstruction, enteritis), drugs (such as lactulose, corticosteroids, sorbitol, chemotherapeutic agents), and iatrogenic causes (postoperative anastomosis, barium trauma, endoscopy, jejunostomy tube) can play a role. On the other hand, PCI can rarely be seen spontaneously in rare cases[4]. In the present case, spontaneous PCI was considered because the patient had no known systemic disease, drug use, or history of surgery.

Although there may be symptoms such as vomiting, nausea, abdominal pain, diarrhea, and abdominal bloating before hospital admission, most cases are asymptomatic. Sometimes, life-threatening conditions such as toxic megacolon, intestinal ischemia, or intestinal obstruction may occur[5]. The presented patient had nausea with vomiting and severe abdominal pain that lasted for about two days without relief.

In the radiological diagnosis of PCI, an appearance suggestive of intraperitoneal free air is common. PCI diagnosis is made in the abdominal CT taken for further evaluation after free air is seen on plain X-ray, an easily accessible imaging method in emergency services. This appearance is caused by the perforation of air-filled cysts in the intestinal wall. CT imaging is important in arranging the conservative or surgical treatment of the disease. Intestinal ischemia, total obstruction, or air in the portal vein indicate that the treatment should be planned surgically[6]. While evaluating the etiology of abdominal pain in our case, an abdominal CT was performed, and PCI was diagnosed due to free air under the right diaphragm in the direct X-ray. In our case, diagnostic laparotomy was planned for our patient because the examination findings were positive, and GIS perforation could not be excluded.

PCI management includes emergency diagnostic laparotomy or conventional treatment. Emergency diagnostic laparotomy should be considered in patients with signs of peritonitis, metabolic acidosis, or portal vein gas[7]. Recognition of pneumoperitoneum that does not require surgery is important in preventing unnecessary surgical interventions that cause infections, complications, or prolonged recovery periods in patients[8]. In our case, emergency laparotomy was decided because of peritonitis findings, high inflammatory markers, and radiological intraperitoneal free air. However, no perforation was detected during exploration.

Regardless of the underlying cause of PCI and the presence of symptoms, all patients should be treated medically. Ciprofloxacin and metronidazole therapy should be administered for their activity against aerobic and anaerobic bacteria to control possible overgrowth of hydrogen-producing bacteria that alter the gut microbiota[9]. Ciprofloxacin and metronidazole were started in the treatment of our case, and the treatment was continued for one week.

In conclusion, PCI may present with an asymptomatic or life-threatening clinic. This situation highlights the importance of carefully evaluating clinical and radiographic findings in PCI's diagnosis and treatment approach in the emergency department. Although PCI clinic may occur due to accompanying comorbid diseases or after drug use, it can also happen spontaneously.

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