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About the Health Sci. Q.

Health Sciences Quarterly (Health Sci. Q.) journal as known by the name of "Journal of Scientific Perspectives" until April 2021 which has been published since 2017 is an international peer-reviewed journal of HOLISTENCE ACADEMY. It is published quarterly in January, April, July, and October. All manuscripts submitted for publication are evaluated by the editor-in-chief, section editor, editorial board, and referees. In addition, the journal provides a medium for highlighting selected articles reporting highly significant original findings, as Editor's Choice Manuscripts.

Aims and Scope

Health Sciences Quarterly (Health Sci. Q.) is an open-access journal that publishes original research papers, case reports, and reviews, clinical studies covering a wide range of subjects in life sciences and medicine as well as clinical and experimental investigations only in English.

Researchers in health sciences will find much of great use and interest in the Health Sci. Q.

HSQ aims to supply scientists of health with resources in order to provide the scientific knowledge through the publication of peer-reviewed, high quality, scientific papers and other material on all topics related to Medicine, Pharmacy and pharmaceutical sciences, Dentistry, Nursing, Bioethics, History of medicine, Health economics, Pharmacoeconomics, Medical education, Public health, and Epidemiology.

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ORIGINAL ARTICLE

The effect of different doses of retinyl palmitate (vitamin A) on placental volume in rats

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Abstract

Vitamin A and its derivatives are essential for embryonic development, but an overdose of vitamin A is toxic to the offspring. The placenta is an interface that nourishes and protects the embryo. Although there are numerous publications on the effect of vitamin A on the placenta, there is insufficient information on the changes in the morphology of this organ caused by different doses. The aim of our study was to demonstrate the effect of retinyl palmitate administered at different doses on the volume of the placenta and its component, the decidua. Pregnant rats were divided into 6 groups between gestation day 10 and 12. The first group received 10.000 IU/kg, the second group 20.000 IU/kg, the third group 50.000 IU/kg, the fourth group 100.000 IU/kg and the fifth group 200.000 IU/kg oral vitamin A. The control group received 1 ml of corn oil on the same days. On day 19 of gestation, placentas were collected and 5 μm sections were stained with *Massons's trichrome*. The volumes of total placenta and decidua were estimated using the *Cavalieri* volume estimation method. All placental volumes of the experimental groups were larger than those of the control groups. The decidual volume increased abruptly at a dose of 50.000 IU/kg and remained higher than the control volume at higher doses. The ratio between the decidual and placental volumes increased at 50.000 IU/kg and was smaller than the control at 200.000 IU/kg. A large placental volume is thought to be an indicator of placental insufficiency. Although our results suggest that an increase in placental volume above 10.000 IU/kg may have a negative effect on placental function, we conclude that the imbalance between decidual and placental volume above 50.000 IU/kg strengthens the suggestion that placental insufficiency may have increased after this dose.

Keywords: Vitamin A, placenta, volume

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Introduction

Vitamin A and its derivatives (retinoic acid (RA), retinoids) are essential for the regulation of important biological functions such as cell division, differentiation, growth, development and immunity. Vitamin A is essential for the maintenance of healthy growth [1,2]. Multivitamin supplements are routinely given to pregnant women to prevent congenital malformations [3]. Retinoids are very important for maternal health; they are absolutely necessary for the development of the placenta and the developing embryo. RA the retinoid synthesized in embryonic tissues essentially controls the expression of numerous important target genes for development. Alterations in the levels of RA result in abnormal embryonic development. Studies in animal models have shown that severe deficiency of maternal vitamin A leads to early embryonic death [4]. Fetal developmental abnormalities are observed when vitamin A deficiency occurs at lower levels [5]. On the other hand, vitamin A overdose is teratogenic in the embryo and has membranolytic and hepatotoxic effects in adults [6]. Studies conducted in recent years have shown that vitamin A doses that do not cause macroscopic morphological abnormalities can lead to behavioral disorders and mental insufficiency [7]. Since the embryo cannot synthesize vitamin A on its own, the developing mammalian embryo receives vitamin A through a maternal-fetal barrier, the placenta [8]. The presence of measurable fetal liver vitamin A at birth demonstrates the effectiveness of the placenta in transporting retinol during pregnancy [9,10]. It is evident that retinol crosses the placenta, but the mechanism of transfer to the fetus and how it is transferred is not fully understood [11].

The ability of retinoids to cross the placental barrier in humans, mice, rats, and monkeys has been investigated in previous studies [10,12-14]. These studies show that the transfer of each vitamin A derivative to the embryo is supported in a particular way. It has also been found that the placenta is capable of metabolizing some retinoids and producing retinoids from maternal precursors [15]. It has been suggested that the placenta serves as a vitamin A depot until the

embryonic liver becomes functional. In addition, it has been suggested that the placenta acts as a retinoid buffer by releasing retinoids when maternal retinoid uptake is insufficient and stores retinoids to protect the embryo from the potential toxic effects caused by excess maternal retinoids [16].

The placenta is known to harbor nuclear retinoid receptors. In addition, RA inducible genes (stimulated by retinoic acid or Stra) are expressed in placental regions involved in maternal-embryonic exchange [4]. Therefore, it is important to study the effects of retinoids on the placenta.

Understanding the differentiation and morphology of the placenta in various experimental animals is undoubtedly necessary to understand human development. The rat placenta consists of three main parts: the basal zone, the decidual zone, and the labyrinth zone. The basal zone is located near the decidual layer and contains various cell types. These cells are trophoblast stem cells, trophoblast giant cells, and glycogen cells. The labyrinthine zone contains the maternal cavities and blood vessels. Although the uteroplacental compartment in rats has similarities and differences to the hemochorial placental species, they are most similar to mice. This has led to the use of many different terms to describe the components of the uteroplacental compartment [17]. The direction of the uteroplacental compartment is determined by the place where the blood enters the uterus. This area is called the mesometrial compartment and the other end is called the anti-mesometrial compartment. The mesometrial compartment of the uterus is composed of stromal cells, blood vessels (endothelial cells, smooth muscle cells), immune/inflammatory cells (macrophages), myometrial smooth muscle cells, and trophoblast cells [18]. The cellular composition of this compartment varies depending on the stage of gestation and species-specific characteristics. After implantation, natural killer (NK) cells proliferate and infiltrate into the mesometrial decidua adjacent to the developing chorioallantoic placenta. Decidual cells are derived from uterine stromal cells and have different functions depending on their location [19-21].

The development and function of decidual cells of rats and other species have been the subject of curiosity of researchers for many years. The decidua generally provides trophoblastic nutrition and serves as an immunological barrier, but its specific functions are not known. The cell division and cell cycle of the decidua have not been studied in detail. However, little is known about how decidua cells compensate for survival, stress, and other adverse conditions [22].

There are few morphological studies on the effects of vitamin A on the placenta and decidual layer. Therefore, we aimed to investigate the effects of doses of vitamin A, considered teratogenic and non-teratogenic to the fetus, on the placenta and decidual layer using stereological techniques.

Materials and Methods

This study was approved by the local animal experimentation ethics committee (#951-172). Female *Wistar* albino rats weighing 250-300 g were divided into 6 groups. Rats were housed in cages with a capacity of 5-6 rats and access to food and water ad libitum at constant room temperature (21°±3°C) and a cycle of 12 hours of darkness and 12 hours of light. All animals were obtained from Eskişehir Osmangazi University Medical and Surgical Experimental Animals Research and Application Center (TICAM). Menstruation of rats was determined by vaginal swabs. Females in estrus were kept with males for copulation. The next morning, females with sperm in the vaginal smears were considered pregnant and on the first day of gestation (P0).

On days P10-P12, the first group received 10.000 IU/kg, the second group 20.000 IU/kg, the third group 50.000 IU/kg, the fourth group 100.000 IU/kg, and the fifth group 200.000 IU/kg oral vitamin A (retinyl palmitate, Merck, Darmstadt-Germany) diluted in corn oil. [23]. 0.5 ml of the dose-adjusted vitamin A mixture was administered to the subjects with a gavage needle. The control group received 1 ml of corn oil on the same days. At P19, the rats were anesthetized, the placenta was removed by cesarean section, and the mothers were sacrificed. Ten placentas were randomly selected from each group. After histological procedures sections of 5 μm were stained with *Masson's trichrome* (Fig. 1). The volumes (Vp) of the placenta and the volume of the decidua basalis (Vd) were estimated using the *Cavalieri* volume estimation method, and their ratios to each other (Vd/Vp) were calculated.

The groups' data series were subjected to the *Kolmogorov-Smirnov* test, and after ensuring that the series were normally distributed, the groups were compared using a one-way ANOVA. Jamovi 2.3.21 software was used for the calculations.

Results

When the calculated placental volumes (Vp) were compared, it was found that the placental volumes of the experimental groups were higher than those of the control group. While this difference was significant when comparing with the 10.000 IU/kg group ($p < 0.05$), it was very highly significant when comparing the control group with the other groups ($p < 0.001$). When the volumes of the 10.000 and 20.000 IU/kg groups were compared with those of the other experimental groups, they were found to be smaller than the volumes of the 50.000 and 200.000 IU/kg groups ($p < 0.001$ resp. $p < 0.01$). At
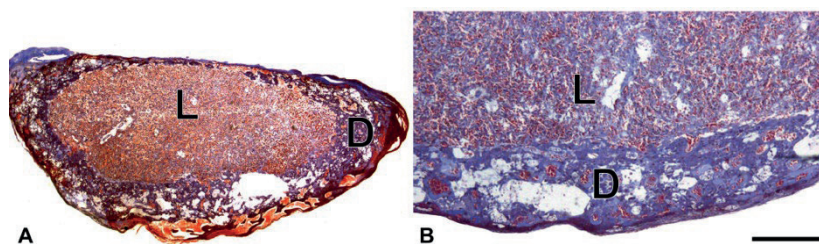
Figure 1. Massons's trichrome staining of rat placenta. The left image shows the placenta at low magnification (A). The red-brown area is the labyrinth, and the purple-red area is the decidua (scale 1.000 μm). The right image is a higher magnification of the left image (B). The red-purple area is the labyrinth, the purple area is the decidua (scale 160 μm). L: labyrinth, D: decidua.

the same time, it was calculated that the placental volume of the 100.000 IU/kg group was greater than that of the 10.000 IU/kg group ($p<0.05$) (Fig. 2).

When decidual volumes (Vd) were compared, it was found that the decidual volumes of the groups receiving retinyl palmitate at a dose of 50.000 IU/kg and more were higher than those of the control group. While this difference was significant when comparing the control group

and the groups receiving 200.000 IU/kg group ($p<0.05$), it was very highly significant when comparing the control group with the other experimental groups ($p<0.001$). When comparing the experimental groups with each other, the highest decidual volume was calculated for the 50.000 IU/kg group ($p<0.001$). While the decidual volume of the 10.000 IU/kg group, which was not different from the control group, was smaller than the decidual volumes of the 100.000 IU/kg

| Vp±SD | 42.4±1.2 | 51.3±0.3 | 54.2±6.9 | 63.8±1.6 | 60.1±13.8 | 58.5±3.1 | 62.6±0.9 |

Figure 2. Graph and table showing total placental volume and statistical significances between groups (n=10). The comparison of the control group with the other groups *; the comparison of the group given 10.000 IU/kg with higher doses + and the comparison of the group given 20.000 IU/kg with higher doses are represented by ×. One symbol means $p<0.05$, two means $p<0.01$, three means $p<0.001$.

| Vd±SD | 9.4±0.1 | 9.7±0.3 | 10.3±0.5 | 17.7±0.9 | 11.7±0.8 | 11.4±1.5 | 10.5±0.1 |
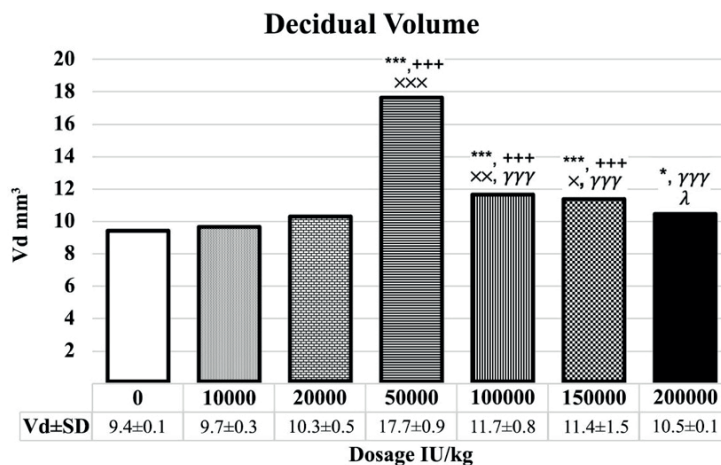
Figure 3. Graph and table showing decidual volumes and statistical significances between groups (n=10). The comparison of the control group with the other groups *; the comparison of the group given 10.000 IU/kg with higher doses +; the comparison of the group given 20.000 IU/kg with higher doses ×; the comparison of the group given 50.000 IU/kg with higher doses γ; and the comparison of the group given 100.000 IU/kg with higher doses are represented by λ. One symbol means $p<0.05$, two means $p<0.01$, three means $p<0.001$.

and 150.000 IU/kg groups ($p<0.001$), no difference was calculated for the 200.000 IU/kg group. Another group whose decidual volume did not differ from the control group was the 20.000 IU/kg group. While the decidual volume of this group was smaller than that of the 100.000 ($p<0.01$) and 150.000 IU/kg ($p<0.5$), there was no difference between the decidual volume of the 200.000 IU/kg group. No difference was calculated between the decidual volumes of the 100.000 and 150.000 IU/kg groups. However, although there was no difference between the decidual volume of the 200.000 IU/kg group and that of the 150.000 IU/kg group, the decidual volume of the 200.000 IU/kg group was smaller than that of the 100.000 IU/kg group ($p<0.05$) (Fig. 3).

When the ratio obtained by dividing the decidual volume by the placental volume (Vd/Vp) was examined, it was found that the ratio was significantly higher in the 50.000 IU/kg group in all groups ($p<0.001$). While no difference was generally observed between the other groups, the Vd/Vp ratio of the 200.000 IU/kg group was lower than that of the control group ($p<0.001$) and the 100.000 ($p<0.05$) group (Fig. 4).

Discussion

Our results show that placental volume increases with the dose of retinyl palmitate. A highly significant increase in placental volume is observed compared to the control group, especially above a dose of 20.000 IU/kg. Studies have shown that the placenta is a target organ for retinoids [24]. Wen et al (2011) noted that a large placental volume is an indicator of both low vascular resistance (low density) and placental insufficiency [25]. We are unable to obtain direct data on whether the increase in volume at doses below 50.000 IU/kg is related to placental insufficiency and whether it adversely affects fetal nutrition. Considering that the nervous system is the first organ affected by fetal malnutrition, our previous study may shed light on this problem. In this study, pregnant rats were given different doses of oral retinyl palmate, and it was observed in the study that the number of hippocampal neurons decreased from 20.000 IU/kg. However, an increase in the number of dividing cells was observed up to 50.000 IU/kg, while the number of apoptotic cells increased after this dose [26]. Also, in a study we conducted on the effect of vitamin A on the fetal liver, we observed that cell death
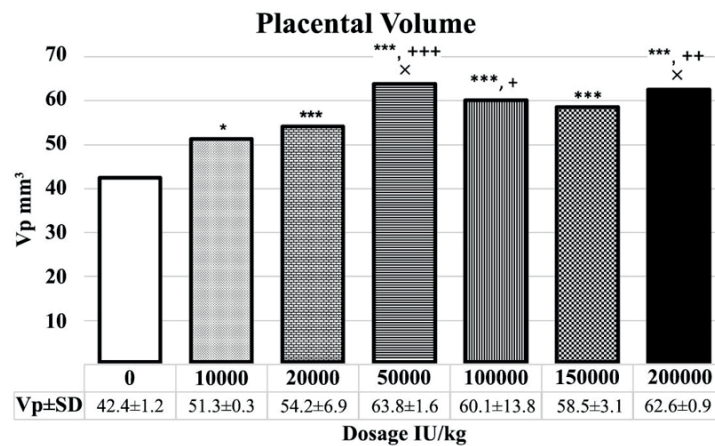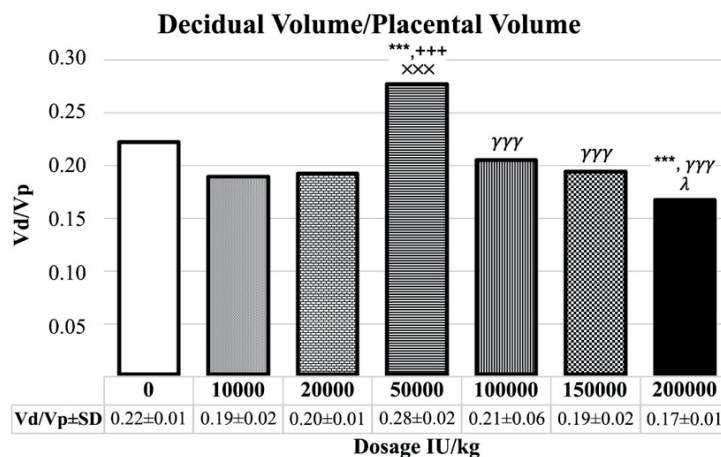

Figure 4. Graph and table showing the ratio of decidual volume and placental volume and statistical significance between groups (n=10). The comparison of the control group with the other groups *; the comparison of the group administered 10.000 IU/kg with higher doses +; the comparison of the group administered 20.000 IU/kg with higher doses ×; the comparison of the group administered 50.000 IU/kg with higher doses γ; and the comparison of the group administered 100.000 IU/kg with higher doses is represented by λ. One symbol means $p<0.05$, two means $p<0.01$, three means $p<0.001$.

in the liver increased at doses above 10.000 IU/kg [27] there are few studies on the microscopic effects of these doses on the organism. Based on the information in the above two articles, the increase in placental volume at doses of 10.000 and 20.000 IU/kg supports the notion that vitamin A promotes cell proliferation. However, when the effect of vitamin A on the fetal liver is examined, it is found that cell death increases above 10.000 IU/kg. It is not known whether this effect is due to compensation of a toxic effect of vitamin A or to malnutrition of the placenta. However, considering the results of the two studies, we think that the reason for the high placental volumes observed after 50.000 IU/kg could be placental insufficiency associated with vitamin A toxicity.

When examining the decidual volumes in our findings, the observed values support this suggestion. The decidual volumes peaked at 50.000 IU/kg and then abruptly decreased. However, decidual volumes were higher at doses higher than 50.000 IU/kg than in the control group. Ozaki et al (2017), concluded that decidual cells are very sensitive to retinoids. In their study, they showed that the amount of active retinoid in the placenta is kept under control by the RDH12 (retinaldehyde dehydrogenase 12) and DHRS3 (short chain dehydrogenase/reductase 3) genes of decidualized endometrial cells. The authors concluded that despite these compensatory mechanisms, high doses of retinoids are toxic to decidualized cells [28]. The fact that the volume of placental and decidual cells in our study was higher than in the control group, especially after 50.000 IU/kg, suggests that cells may have proliferated here to compensate for the high dose of retinoids. Comparing the volumes of decidual and placental cells determined in our study (Vd/Vp), the fact that this rate is lower in the 200.000 IU/kg group, supports the view that this dose is toxic to decidual cells. However, to support this view, stains with markers for cell division and cell death must be used.

Lee et al (2012), observed that high doses of RA caused the same malformations in some organs as RA deficiency. They attributed this effect to the increase in levels of enzymes that degrade retinoids in teratogenic doses of RA [29]. A study three years later showed that high doses of retinoids increase the synthesis of molecules that degrade retinoids in the placenta and embryo [30]. A study on the effects of vitamin A deficiency on the placenta found that deficiency of this vitamin induces cell death in the placenta. They concluded that this effect is caused by infiltration of neutrophils [31]. Deepak et al (2019), concluded that low placental levels of RA downregulate the vascular endothelial growth factor-1 (VEGF-1) receptor. They also showed that this increased TFAP2 (transcription factor AP-2-alpha [activating enhancer-binding protein 2 alpha]) levels [32] It was concluded that increased TFAP2 levels contributed to preeclampsia and inadequate placental development [33]. In our study, the decrease in Vd/Vp at doses higher than 50.000 IU/kg and especially in placental volume at a dose of 200.000 IU/kg suggests that this decrease in placental volume is due to cell death, especially due to the increase in enzymes that degrade retinoids.

Conclusion

As can be seen from the literature, the effect of retinoids on the placenta is complex and multifactorial. Our study showed that oral retinyl palmitate at different doses caused an increase in placental volume, except for the decidual volume of the 200.000 IU/kg group, which was even lower than the decidual volume of the control group. Although an increase in placental volume was observed from 10.000 IU/kg, the ratio between the decidual volume and the placental volume differed from that of the control group after 50.000 IU/kg, suggesting that the placenta began to lose its optimal functionality from this dose.

Conflict of interest

The authors have no competing interests to disclose.

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ORIGINAL ARTICLE

Axial external fixator in humerus shaft fractures

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Abstract

The causes of humeral shaft fractures are mostly high-energy traumas such as falling, hitting, traffic accident, and gunshot wounds. It may also occur as a result of simple falls due to osteoporosis in elderly patients. In surgical treatment, there are options such as intramedullary nail, plate-screw fixation and external fixator treatment. External Fixator Treatment it is the primary treatment option for soft tissue damage, open fractures, gunshot wounds, segmental bone loss, pseudoarthrosis, nonunion, and major vascular injuries. The purpose of the present study was to present the functional results of Axial External Fixator Treatment, which we often apply in humerus shaft fractures in our clinic. A total of 30 patients, who had gunshot wounds, multisystem injuries, open fractures, and advanced age comorbid problems, and who underwent Axial External Fixator Treatment due to humerus shaft fracture between January 2016 and January 2019 were included in the study. Disabilities of the Arm, Shoulder, and Hand (DASH) scores were used in clinical evaluations. Visual Analogue Scale (VAS) was used to evaluate the pain intensity in patients subjectively. Also, the results of patients with advanced age comorbid problems were compared with other patients. After a 12-month follow-up, significant improvements were detected in DASH scores. Although fracture union was later in patients with advanced age comorbid problems than in other patients, no differences were detected between union rates, clinical outcomes, and the surgical processes.We think that it is a more appropriate surgical technique than other surgical methods, due to its shorter surgical time and less invasiveness in patients with advanced age, high comorbidity and multisystem damage.

Keywords: Humerus, fracture, axial fixator, fixation

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Introduction

Humerus fractures are detected at an average rate of 6.9% in Türkiye [1]. Proximal humerus fractures are most commonly detected, and the less detected fractures are in the shaft area. These fractures are more common in high-energy trauma in younger patients. It can be seen in elderly patients as a result of simple falls [2]. Conservative treatments yield successful results in most cases and surgical methods are required in some patients [3]. Surgical treatment is usually performed when there are open fractures, unstable fractures, pathological fractures, fractures resistant to conservative treatment, multiple trauma patients, floating shoulder or elbow, bilateral fractures, progressive deficits of the radial nerve, brachial plexus problems, and vascular injuries [3]. There are options, such as intramedullary nail, plaque-screw fixation, and external fixator treatment in surgical treatment. The surgical treatment option in humerus shaft fractures varies according to the age, bone quality, condition of fracture, mechanism of occurrence, and to the presence of injuries in the surrounding soft tissue in patients.

External Fixator Treatment is one of the bedside treatment modalities for humerus fractures. It is the primary treatment option when there is soft tissue damage, open fractures, gunshot wounds, segmental bone losses, pseudoarthrosis, non-union, and significant vascular injuries [4,5]. The aim of our study is to present the functional results of patients who underwent Axial External Fixator Therapy for humeral shaft fractures in our clinic.

Materials and Methods

The study received ethical committee approval from Turgut Özal University Clinical Research Ethics Committee (2021/16). Our study was planned retrospectively. A total of 30 patients treated between January 2016 and January 2019 for humerus shaft fractures were included in the study.

Inclusion criterias

- Patients between the ages of 25 and 90

- Humerus shaft fracture

- Minimum follow-up period is 24 months.

Exclusion criteria

- Pregnancy

Surgical method

When the anesthesia, patient preparation stages, fracture reduction, and sequencing control were achieved, considering the stabilization and the distance of the radial nerve to the fracture area, two or three 3-mm pins were sent with drills to the proximal area of the axillary nerve and to the distal area of the radial nerve accompanied by scope. The surgery was terminated after controlling the reduction, bone sequencing, and stabilization with scope.

Post-operative evaluation

Clinical evaluation was performed in postoperative 2nd year by the same observer. Active elbow range of motion (ROM) was measured using a standard goniometer. Flexion, extension, internal and external rotation angles were recorded. Functional evaluation was performed with Disability of the Arm, Shoulder and Hand (DASH) Score, according to which patients were given scores between 0 (no obstacles) and 100 (maximum injury). Visual Analogue Scale (VAS) was used to evaluate the pain intensity in patients subjectively (scores 0 = no pain and 10 = worst possible pain). Postoperative complications and revision surgeries were recorded and compared.

Statistical Analysis

The IBM SPSS 19 Program was used in statistical analyses (IBM SPSS Statistics 19, SPSS Inc., an IBM Co., Somers, NY). Clinical data were expressed as numbers, percentages, or Mean ± SD. Two-way Chi-Square (χ2) test was used to evaluate the relationships between two categorical variables. Student's t test was used for continuous variables. $p \leq 0.05$ was considered statistically significant.

Results

Thirty patients treated with external fixator were included in our study. Demographic data of the patients are given in Table 1.

Significant improvements were detected in DASH score after 12 months of follow-up. Union was achieved in patients in an average of 13.7 weeks. Although fracture union was later in patients with advanced age comorbid problems than in other patients, no differences were detected between union rates, clinical results and the surgical processes; and 86.7% of these patients had bone union. There was superficial infection, which recovered with 1-week oral antibiotic treatment in 3 patients, and no patients developed nerve problems.

Discussion

Axial fixator is often used especially in the treatment of humerus shaft fractures depending on the injury, patient morbidity-mortality, and fracture type. We achieved successful results with axial fixator treatment, which we used to treat humerus shaft fractures, in our study in patients who had gunshot wounds, comorbid problems due to advanced age, multisystem injury, and open fractures. We obtained similar results in patients with comorbid problems because of advanced age and in other patients.

External fixator is used more frequently in orthopedic surgery with each passing day. The advantages of it are not requiring surgical incision, less damage to soft tissues, opportunity of dynamization, and allowing natural union [6]. Although union rates were reported to be lower in previous studies in humerus shaft fractures, 89-100% union rates are reported in recent studies with increased experience and implant development [7]. The mean union time varied between 11-24 weeks in these studies. In our study, we did not require additional surgical procedures because union was achieved in 26 patients (86.7%). We achieved union in 13.7 weeks on average. Union rates were similar in

Table 1. Demographic features of study group.

Gender (Male/Female)	17 (56.7%) / 13 (43.3%)
Side (Right/Left)	14 (46.7%) / 16 (53.3%)
Age	54.43±17.6
Injury Mechanism-Fracture Type	
☐ **Gunshot Wound**	2 (6.7%)
☐ **Multisystem Injury (High energy trauma)**	4 (13.3%)
☐ **Open Fracture**	8 (26.7%)
☐ **Patients with Advanced Age Comorbidity**	14 (46.7%)
☐ **Other**	2 (6.7%)

Data are given as mean ± standard deviation / Median / Minimum-Maximum or frequency, percent.

Table 2. General characteristics of study group.

Variables	Total	Young Patients	Elderly Patients	p
DASH scores	22.1±7.9	21.9±7.3	22.4±8.9	0.436
Scope Shot	9.5±2.5	9.0±0.9	10.0±3.6	0.158
Surgery Duration (min)	26.7±12.0	28.0±14.0	25.2±9.6	0.264
Union of fracture (week)	13.7±3.2	12.8±3.2	14.9±2.9	0.036
Reoperation	4 (13.3%)	2 (12.5%)	2 (14.2%)	

Data are shown as mean ± standard deviation / Median / Minimum-Maximum or frequency, percentage.
p: Independent sample t-test or chi-square test was used.
p: Comparison between subjects

our study to previous studies in the literature. Union times were higher than in studies in the literature. We believe that these high rates occurred due to the differences in age and indication distribution in the patients who were included in our study. In our study, 46.7% (14 patients) had high comorbid conditions over the age of 65. In fact, when these patients were compared with other patients, the union times were long because the potential for union was low in patients over 65 years of age. When we compared patients with gunshot wounds, open fractures, or multiple injuries, we found similar union rates. These results achieved in our study show that external fixator can be applied with the same safety and success in patients who have closed fractures and high comorbid conditions over the age of 65, as in similar age group and similar inductions reported in the literature.

In previous studies, complication rates of 8-36% were reported. Deep infection, pseudoarthrosis, and faulty union are common complications reported in previous studies [8]. In our study, 3 patients developed a superficial infection, which recovered with oral antibiotic treatment for 2 weeks and pseudoarthrosis in 4 patients. We had a low rate of complications in our study when compared to others, such as the recent study conducted by Azevedo et al. [7]. We believe that this may be because of the developing implant technology and accumulated experience.

Many methods have been described in the literature for the treatment of humeral shaft fractures. Many authors have reported that union is easy in humeral shaft fractures, and many conservative methods have been described showing that simple surgical methods can be used in the case of pseudoarthrosis [9,10]. In the literature, plate-screw fixation, intramedullary nail and external fixators are the main applications in surgical methods. Different success rates have been reported with these methods [11-13]. Many studies using plate and screw osteosynthesis have reported union rates of 96% and 100% [13]. Union rates in patients with anterograde intramedullary nails are 71-100% [14]. Patients had gunshot wounds, open fractures, pseudoarthrosis after conservative treatments, or elderly patients

with high morbidity and surgical indications were included in our study. For this reason, we applied Axial External Fixator Treatment to our patients, which we believe to be the simplest surgical procedure and in which we had high clinical experience. We achieved boiling rates almost the same as in open surgical methods in our patients.

External fixators, which were considered not to produce full stable reduction in emergency fracture fixation such as open fractures and multi-system injury patients in the past, are now used in simple closed fractures with the increased experience and developments in implant technology providing union rates similar to open methods with more stable fixation [7]. It is considered to cause less damage to the surrounding tissue, provide recovery of fracture hematone with less surgical duration contributing more to fracture recovery [7]. In this context, we believe that this will provide effective fracture recovery in external fixators when stable fixation is achieved with increased experience and appropriate implant selection. In this respect, as well as external fixator indications reported in the literature, we applied external fixators to elderly patients who could not be improved by closed methods or who had surgical indications. We achieved 86.7% union in these patients; and found no differences between the union rates of this group and the union rates of other patients. For this reason, we believe that this method is an applicable method in these patients.

The retrospective study design, lack of a control group, limited number of patients, and short follow-up times were among the limitations of the present study. Studies with more patients and higher effect size are required in this respect.

Conclusion

External fixator (EF) treatment is less invasive than other surgical treatment methods and the surgical time is shorter. EF treatment is a surgical method that is frequently applied in open fractures seen in high-energy traumas such as firearm injuries and traffic accidents. In conclusion, we think that it is a more appropriate surgical technique than other surgical methods, due to its shorter surgical time and less

invasiveness in patients with advanced age, high comorbidity and multisystem damage.

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ORIGINAL ARTICLE

Evaluation of skin disease patterns in a tertiary dermatology outpatient clinic in Türkiye

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Abstract

Skin diseases are among the reasons for frequent hospital admissions and bring a significant burden. The aim of this study is to determine the pattern of skin diseases in our dermatology outpatient clinic in a tertiary care hospital in T**ürkiye**. Pediatric and adult patients evaluated in our dermatology outpatient clinics for the first time were included in this cross-sectional observational designed study between January and March 2023. The characteristics of the patients, including age, gender, duration of disease, anatomic localization of the disease, and complaint counts, were recorded in the data collection form. Diagnoses were grouped according to gender, age, and complaint counts. A total of 1381 patients with 1772 skin problems were included in the study. 62.3% of the patients were female (n=860), and 37.7% (n=521) were male. The age range was between 0 and 98 years. The most common diseases were acne (18%), dermatophytosis (8.1%), viral warts (6.5%), seborrheic dermatitis (4.8%), other dermatitis (4.8%), follicular disorders (4.6%), pruritus (3.7%), scabies (3%), benign neoplasms (3%), and urticaria (3%), respectively. 23.4% of the patients (n=324) had at least two complaints. The maximum number of complaints at one visit was 5. The probability of reporting more than one complaint was higher in women and those whose first complaint was on the scalp. In this analysis to determine the patterns of skin diseases, acne, dermatophytosis, and viral warts were found to be important problems. The number of complaints at one visit may vary according to gender and localization.

Keywords: Skin diseases, epidemiology, prevalence, Türkiye

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Introduction

The skin is the largest organ of the human body and has some important fundamental functions such as protection against mechanical effects and chemical threats, taking part in adaptive and natural immune response, ensuring thermoregulation, and vitamin D production. Due to these properties of the skin, skin diseases are frequently encountered during hospital visits. According to the Global Burden of Disease 2013 report, skin diseases were the fourth leading cause of nonfatal disability worldwide [1]. Also, numerous studies contain data on the negative effects of skin diseases on quality of life [2].

The frequency of skin diseases can be affected by geographic conditions, ethnicity, socio-economic and socio-cultural status, and various environmental factors. Determining the distribution pattern of skin diseases in a population allows for determining treatment methods and taking preventive measures for some diseases. Until now, various studies have investigated the frequency of skin diseases in the literature. There are also studies in which special populations such as different age groups, gender, occupations, prisoners, and military personnel are examined regarding skin diseases, generally using hospital records [3-7]. However, to the best of our knowledge, there is no study in the literature that evaluates the priority order of the complaints of patients admitted to dermatology outpatient clinics and the average number of complaints in a visit. The aim of this study is to determine the frequency of dermatological diseases in patients who admit to our outpatient dermatology clinics, as well as to evaluate whether the priority order of complaints in individuals who apply for more than one complaint is related to conditions such as age, gender, and disease localization.

This study was carried out in the only tertiary central hospital in the province of Uşak, located in the Aegean region of Türkiye. This province, which has a population of approximately 375.000 people, has an altitude of 906 meters and a temperature range between -24°C and +39.8°C throughout the year.

Materials and Methods

The approval of the Institutional Review Board was received. In this cross-sectional observational study, pediatric and adult patients who were admitted to our dermatology outpatient clinics for the first time were included between January and March 2023. The clinical and demographic characteristics of the patients, including age, gender, duration of the disease, anatomic localization of the disease, and complaint counts, were recorded in the data collection form. The patients were diagnosed based on anamnesis, clinical findings, and dermatologic examination. The clinical diagnoses were confirmed using laboratory and histopathological examination if necessary. Patients who were followed up in our outpatient clinics due to chronic dermatological diseases and repetitive referrals were excluded from the study. The diagnoses were classified according to the International Classification of Diseases (ICD-10). The ages of the patients were grouped as 0-9, 10-19, 20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and ≥ 80 years. The anatomic localizations of the lesions were determined as the scalp, face, neck, chest-abdomen, back, forearm-arm, hand, thigh-tibia, foot, palmoplantar, fingernail, toenail, genital, and oral mucosa.

The statistical analysis was carried out using IBM SPSS Statistics 28.0. Continuous data were given as mean ± standard deviation (SD) and median ± Interquartile Range (IR). Categorical data were given as a percentage. *Pearson* Chi-Square analyses were performed in the analysis of the cross tables. For statistical significance, $p<0.05$ was accepted as the criterion. Informed consent was obtained from all patients.

Results

Demographics

A total of 1381 patients with any dermatological complaint were examined at our dermatology outpatient clinic between January 2023 and March 2023. 62.3% of all patients were female (n=860), and 37.7% (n=521) were male. The patients' ages ranged between 0 and 98 years. The median age was 33 years (IR 34). According to the age groups, the greatest number of patients was in the 10-19 years age group (n=301; 22.1%),

and the second most common age group was 20-29 (n=269; 19.7%). There was no statistically significant difference between genders in terms of age group distribution (*p*=0.166).

Table 1. Demographic characteristics of the patients.

Number of patients, n (%)	1381 (100%)
Gender, n (%)	
Female	860 (62.3%)
Male	521 (37.7%)
F:M	1.65
Age (year), median (IR)	33 (34)
Age groups (years), n (%)	
0-9	46 (3.4%)
10-19	301 (22.1%)
20-29	269 (19.7%)
30-39	204 (15%)
40-49	158 (11.6%)
50-59	145 (10.6%)
60-69	161 (11.8%)
70-79	77 (5.6%)
≥ 80	2 (0.14%)
Total	1363 (100%)
Complaint count, n, (%)*	
1	1381 (100%)
2	324 (23.4%)
3	61 (4.4%)
4	5 (0.36%)
5	1 (0.07%)
Disease duration (month), median (IR)	
First complaint	1.2 (34)
Second complaint	1.2 (46)
Third complaint	3.6 (108)
Fourth complaint	8.5 (27.2)

*By least number of complaints

The total number of complaints was 1772. 23.4% of the patients (n=324) had at least two complaints. The maximum number of complaints evaluated at one visit was 5. There was no statistically significant difference between the age groups and complaint number (*p*=0.53), but the difference between the number of complaints by gender is statistically significant (*p*=0.009). 25.8% of female patients had at least two complaints, while this rate was 19.3% for males.

The median disease duration for the first complaints of patients was 1.2 months (IR 34, minimum 1 day and maximum 600 months) and 1.2 months (IR 46, minimum 3 days and maximum 480 months) for the second complaints. There was only one patient with five complaints, and the duration of the fifth complaint was one month. Demographic characteristics according to gender, age, complaint numbers, and disease durations are shown in Table 1. The numbers of complaints by gender are shown in Table 2.

Distribution of skin diseases

The most common disease groups were "skin disorders of appendages" (30.8%); "dermatitis and eczema" (16.8%); "other disorders of skin and subcutaneous tissue" including vitiligo, other disorders of pigmentation, seborrheic keratosis, callus, xerosis cutis, connective tissue disorders, and insect bites (13%); "mycosis" (10%) and "viral infections" (6.8%), respectively. The frequency of the diseases and their distribution by gender are shown in Table 3. The most common diseases were acne (18%), dermatophytosis (8.1%), viral warts (6.5%), seborrheic dermatitis (4.8%), other dermatitis (4.8%), follicular disorders (4.6%), pruritus (3.7%), scabies (3%), benign neoplasms (3%), and urticaria (3%), respectively.

Table 2. The number of complaints according to the gender.

	Number of complaints						
Gender	1	2	3	4	5	Total	*p* value
Female (n, %)	637 74.1%	173 20.1%	46 5.4%	3 0.3%	1 0.1%	860 100%	0.009
Male (n, %)	420 80.6%	90 17.3%	10 1.9%	1 0.2%	0 0%	521 100%	

Table 3. The frequencies of the diagnoses of patients by gender.

Diagnosis	Female (n, %)	Male (n, %)	Total (n, %)
Infectious and parasitic diseases	192 (16.8)	171 (26.9)	363 (20.5)
Mycosis	90 (7.9)	91 (14.3)	181 (10.2)
Dermatophytosis	71 (6.2)	76 (12)	147 (8.3)
Pityriasis versicolor	15 (1.3)	14 (2.2)	29 (1.6)
Candidiasis	4 (0.35)	1 (0.15)	5 (0.28)
Viral infections	70 (6.2)	59 (9.3)	129 (6.3)
Viral warts	56 (4.9)	47 (7.4)	103 (5.8)
Herpes zoster	10 (0.87)	4 (0.62)	14 (0.79)
Herpes simplex infections	2 (0.17)	4 (0.62)	6 (0.33)
Molluscum contagiosum	1 (0.1)	2 (0.31)	3 (0.17)
Others	1 (0.08)	2 (0.31)	3 (0.17)
Scabies	32 (2.8)	21 (3.3)	53 (3.2)
Neoplasms	62 (5.5)	35 (5.5)	97 (5.5)
Malign neoplasms (non-melanoma)	8 (0.7)	9 (1.4)	17 (0.95)
Benign neoplasms*	54 (4.7)	26 (4.1)	80 (4.5)
Diseases of the oral cavity, salivary glands and jaws	8 (0.7)	3 (0.47)	11 (0.62)
Diseases of the skin and subcutaneous tissue	875 (77)	426 (67)	1301 (73.4)
Infections of the skin and subcutaneous tissue	16 (1.4)	18 (2.7)	34 (1.9)
Cutaneous abscess, furuncle and carbuncle	2 (0.17)	2 (0.31)	3 (0.17)
Cellulitis	1 (0.06)	6 (0.94)	19 (1.1)
Other local infections	13 (1.1)	0 (0)	1 (0.05)
Bullous disorders	1 (0.08)	121 (19)	299 (16.9)
Dermatitis and eczema	178 (15.7)	7 (1.1)	12 (0.67)
Atopic dermatitis	5 (0.43)	31 (4.9)	85 (4.8)
Seborrheic dermatitis	54 (4.7)	13 (2)	41 (2.3)
Contact dermatitis	28 (2.5)	3 (0.47)	11 (0.62)
Lichen simplex chronicus	8 (0.7)	30 (4.7)	65 (3.7)
Pruritus	35 (3)	37 (5.8)	85 (4.8)
Other dermatitis	48 (4.2)	28 (4.4)	65 (3.7)
Papulosquamous disorders	37 (3.3)	22 (3.5)	50 (2.8)
Psoriasis	28 (2.5)	3 (0.47)	7 (0.39)
Pityriasis rosea	4 (0.35)	2 (0.31)	6 (0.33)
Lichen planus	4 (0.35)	1 (0.15)	2 (0.11)
Pityriasis rubra pilaris	1 (0.08)	17 (2.7)	60 (3.4)
Urticaria and erythema	43 (3.8)	13 (2)	53 (3)
Urticaria	40 (3.5)	4 (0.62)	7 (0.39)
Other erythematous conditions	3 (0.26)	22 (3.5)	53 (3)
Radiation related disorders of the skin and subcutaneous tissue	31 (2.7)	10 (1.6)	22 (1.2)
Polymorphous light eruption	12 (1)	12 (1.9)	31 (1.7)
Actinic keratosis	19 (1.7)	153 (24.1)	545 (30.7)
Skin disorders of appendages	392 (34.5)	2 (0.31)	16 (0.9)
Nail disorders	14 (1.2)	4 (0.62)	11 (0.6)
Eccrine sweet disorders	7 (0.61)	15 (2.4)	24 (1.4)
Alopecia areata	9 (0.79)	10 (1.6)	22 (1.2)
Androgenetic alopecia	12 (1)	3 (0.47)	35 (2)
Telogen effluvium	32 (2.8)	79 (12.4)	311 (17.5)
Acne	232 (20.4)	7 (1.1)	45 (2.5)
Rosacea	38 (3.3)	33 (5.2)	81 (4.6)
Follicular disorders	17 (1.5)	67 (10.5)	244 (13.8)
Other disorders of the skin and subcutaneous tissue	48 (4.2)	10 (1.6)	22 (1.2)
Vitiligo	177 (15.6)	5 (0.78)	58 (3.3)
Other disorders of pigmentation	12 (1)	12 (1.9)	43 (2.4)
Seborrheic keratosis	53 (4.7)	14 (2.2)	37 (2)
Callus	31 (2.7)	6 (0.94)	28 (1.6)
Xerosis	23 (2)	5 (0.78)	15 (0.84)
Connective tissue disorders**	22 (1.9)	7 (1.1)	16 (0.9)
Insect bites	10 (0.9)	8 (1.3)	25 (1.4)
Other disorders of the skin and subcutaneous disorders (not elsewhere classified)	9 (0.79)	5 (0.78)	58 (3.3)
Total	1137 (64.1)	635 (35.9)	1772 (100)

*Including melanocytic naevi, Becker's nevus, skin tag, benign lipomatous neoplasm, cherry angioma, spider angioma, dermatofibroma.

**Including scar conditions and fibrosis, atrophic and hypertrophic disorders of skin, lupus erythematosus, localized scleroderma, other localized connective tissue disorders, vasculitis limited to skin.

When we evaluated the frequency of diseases according to gender, acne was the most common disease in both genders. While dermatophytosis was seen approximately two times, and viral warts and pruritus were approximately 1.5 times more in men than in women, urticaria was seen approximately 1.5 times more in women than in men. This difference in the distribution of disease frequencies by gender was statistically significant (*p*=.000). The distribution of the 10 most common diseases by gender is shown in Table 4.

When the frequencies of the most common 10 diseases according to age categories were evaluated, acne, viral warts, seborrheic dermatitis, and other dermatitis were most common in the 10-19 age group. Follicular disorders and scabies were most common in the 20-29 age group. Benign neoplasms and urticaria were the most common in the 40-49 age group and, dermatophytosis and pruritus were most common in the 60-69 age group. The distribution of the 10 most common diseases by age categories is shown in Table 5. Also, the distribution of disease frequencies by age categories was statistically significant (*p*=.000).

When we look at the frequency of the diseases according to the order of complaints, the three most common diagnoses according to the first complaint were acne (19.4%), dermatophytosis (6.9%), and viral warts (5.9%). According to the second-order complaints, the three most common diagnoses were dermatophytosis (13.3%), acne (11.4%), and follicular disorders (7.4%), while dermatophytosis (14.8%) benign neoplasms (11.4%) and acne (9.8%) were the

Table 4. The distribution of the 10 most common diseases by gender.

Disease	Female (n, %)	Male (n, %)
Acne	232 (20.4)	79 (12.4)
Dermatophytosis	71 (6.2)	76 (12)
Viral warts	56 (4.9)	47 (7.4)
Seborrheic dermatitis	54 (4.7)	31 (4.9)
Other dermatitis	48 (4.2)	37 (5.8)
Follicular disorders	48 (4.2)	33 (5.2)
Pruritus	35 (3)	30 (4.7)
Scabies	32 (2.8)	21 (3.3)
Benign neoplasms	54 (4.7)	26 (4.1)
Urticaria	40 (3.5)	13 (2)

Table 5. The distribution of the 10 most common diseases by age categories.

Disease	0-9 (n)	10-19 (n)	20-29 (n)	30-39 (n)	40-49 (n)	50-59 (n)	60-69 (n)	70-79 (n)	≥80 (n)
Acne	1	168	107	30	5	0	0	0	0
Dermatophytosis	3	7	13	25	22	24	37	11	0
Viral warts	4	26	26	25	11	6	3	4	0
Seborrheic dermatitis	2	28	21	12	4	6	6	2	0
Other dermatitis	4	15	11	12	12	10	12	1	0
Follicular disorders	0	15	26	14	8	10	7	6	0
Pruritus	3	6	6	5	8	8	16	9	1
Scabies	3	5	15	9	9	6	4	1	0
Benign neoplasms	3	11	8	7	22	11	6	4	0
Urticaria	0	8	8	6	11	6	10	6	0

three most common diagnoses among the third complaints, respectively. The diagnoses related to the complaints mentioned in the fourth order were viral wart (n=1), benign neoplasm (n=1),

Table 6. The frequencies of diagnosis according to the complaint order.

Diagnosis	Complaint 1 (n, %)	Complaint 2 (n, %)	Complaint 3 (n, %)
Infectious and parasitic diseases	273 (19.8)	76 (23.5)	13 (21.3)
Mycosis	123 (8.9)	47 (14.5)	11 (18.0)
Dermatophytosis	95 (6.9)	43 (13.3)	9 (14.8)
Pityriasis versicolor	24 (1.7)	3 (0.92)	2 (3.3)
Candidiasis	4 (0.29)	1 (0.30)	0 (0.0)
Viral infections	102 (7.4)	24 (7.4)	2 (3.3)
Viral warts	81 (5.9)	19 (5.9)	2 (3.3)
Herpes zoster	13 (0.94)	1 (0.30)	0 (0.0)
Herpes simplex infections	2 (0.14)	4 (1.2)	0 (0.0)
Molluscum contagiosum	3 (0.21)	0 (0.0)	0 (0.0)
Other	3 (0.21)	0 (0.0)	0 (0.0)
Scabies	48 (3.4)	5 (1.5)	0 (0.0)
Neoplasms	64 (3.5)	24 (7.4)	8 (13.1)
Malign neoplasms (non-melanoma)	14 (1.0)	2 (0.61)	1 (0.16)
Benign neoplasms*	50 (3.6)	22 (6.8)	7 (11.4)
Diseases of the oral cavity, salivary glands and jaws	10 (0.72)	1 (0.30)	0 (0)
Diseases of the skin and subcutaneous tissue	1034 (74.9)	223 (68.8)	40 (65.6)
Infections of the skin and subcutaneous tissue	30 (0.22)	2 (0.61)	2 (3.3)
Cutaneous abscess, furuncle and carbuncle	10 (0.72)	1 (0.3)	1 (1.6)
Cellulitis	3 (0.21)	0 (0)	0 (0)
Other local infections	17 (1.2)	1 (0.3)	1 (1.6)
Bullous disorders	1 (0.07)	0 (0)	0 (0)
Dermatitis and eczema	239 (17.3)	50 (15.4)	9 (14.8)
Atopic dermatitis	11 (0.8)	1 (0.3)	0 (0)
Seborrheic dermatitis	64 (4.6)	17 (5.3)	3 (4.9)
Contact dermatitis	38 (2.8)	2 (0.61)	1 (1.6)
Lichen simplex chronicus	10 (0.72)	1 (0.3)	0 (0)
Pruritus	53 (3.8)	11 (3.4)	1 (1.6)
Other dermatitis	63 (4.5)	18 (5.5)	4 (6.6)
Papulosquamous disorders	60 (4.3)	5 (1.5)	0 (0)
Psoriasis	46 (3.3)	4 (1.2)	0 (0)
Pityriasis rosea	7 (0.51)	0 (0)	0 (0)
Lichen planus	6 (0.43)	0 (0)	0 (0)
Pityriasis rubra pilaris	1 (0.07)	1 (0.3)	0 (0)
Urticaria and erythema	57 (4.1)	2 (0.61)	1 (1.6)
Urticaria	50 (3.6)	2 (0.61)	1 (1.6)
Other erythematous conditions	7 (0.51)	0 (0)	0 (0)
Radiation related disorders of the skin and subcutaneous tissue	48 (3.5)	4 (1.2)	1 (1.6)
Polymorphous light eruption	20 (1.5)	1 (0.3)	1 (1.6)
Actinic keratosis	28 (2)	3 (0.92)	0 (0)
Skin disorders of appendages	430 (31.1)	98 (30.2)	16 (26.2)
Nail disorders	11 (0.8)	5 (1.5)	0 (0)
Eccrine sweet disorders	7 (0.51)	3 (0.92)	1 (1.6)
Alopecia areata	21 (1.5)	2 (0.61)	1 (1.6)
Androgenetic alopecia	15 (1.1)	6 (1.9)	0 (0)
Telogen effluvium	17 (1.2)	15 (4.6)	3 (4.9)
Acne	268 (19.4)	37 (11.4)	6 (9.8)
Rosacea	38 (2.8)	6 (1.9)	1 (1.6)
Follicular disorders	53 (3.8)	24 (7.4)	4 (6.6)
Other disorders of the skin and subcutaneous tissue	169 (12.2)	62 (19.1)	11 (18)
Vitiligo	19 (1.4)	3 (0.92)	0 (0)
Other disorders of pigmentation	41 (3)	15 (4.6)	2 (3.3)
Seborrheic keratosis	24 (1.7)	15 (4.6)	3 (4.9)
Callus	24 (1.7)	13 (4)	0 (0)
Xerosis	14 (1)	9 (2.8)	4(6.6)
Connective tissue disorders**	13 (0.9)	1 (0.3)	1 (1.6)
Insect bites	14 (1)	2 (0.61)	0 (0)
Other disorders of the skin and subcutaneous disorders (not elsewhere classified)	20 (1.4)	4 (1.2)	1 (1.6)
Total	1381 (100)	324 (100)	61 (100)

*Including melanocytic naevi, Becker's nevus, skin tag, benign lipomatous neoplasm, cherry angioma, spider angioma, dermatofibroma.

**Including scar conditions and fibrosis, atrophic and hypertrophic disorders of skin, lupus erythematosus, localized scleroderma, other localized connective tissue disorders, vasculitis limited to skin.

androgenetic alopecia (n=1), seborrheic keratosis (n=1), and xerosis cutis (n=1). There was only one patient with 5 complaints, and the diagnosis was seborrheic dermatitis for the fifth complaint. Disease frequencies according to the order of complaints were shown in Table 6.

When we evaluated the anatomic localizations according to the order of complaint, the most common localizations reported for the first complaint were face (34.2%), chest-abdomen (21.3%), arm-forearm (11.6%), back (11.1%), and thigh-tibia (10.8%) regions. The anatomic localization according to the order of complaints is shown in Table 7.

When the number of complaints was compared according to the localization of the first complaints, 32.8% (n=42) of those with scalp involvement stated at least two complaints, while this rate was 22.2% (n=278) in those without scalp involvement. This difference was statistically significant (*p*=0.026). No relationship was found between other anatomical localizations for the first complaints and the number of complaints.

Discussion

The literature shows different results about the most common skin disease groups and skin diseases in various studies reported from different countries. However, the three most common disease groups are seen as dermatitis and eczema, skin disorders of appendages, and mycosis, similar to our study, although their order varies [8-10]. In a study from Türkiye, the most common disease group was identified as dermatitis and eczema (21.8%) [8]. Dermatitis and eczema were also the most frequently reported group of skin diseases in previous studies conducted in Greece, Iraq, Japan, Saudi Arabia, and South Africa [11-15]. In this study, the most common disease group among the 1772 skin diseases diagnosed was the disorders of skin appendages (30.7%). The most likely reason for this difference may be the age distribution of the patients in the study group. In our study, most of the patients were in the 10-19 age group (22.1%) and the most common disease was acne (17.5%). Acne accounted for more than half of skin disorders of appendages. On the other hand, although acne is the most common disease in both gender, it was proportionally more common in women than men (20.4% versus 12.4%), and the female-to-male ratio in our study was 1.65. For these reasons, the disorders of the skin appendages group are at the top of the list in our study. In addition, although the most frequently reported disease group in some of these studies was dermatitis and eczema, the most frequently reported disease was acne, which was in the skin disorders of appendages group, similar to our study [8,10]. Also, "dermatitis and eczema" is the most second disease group in our study (16.9%).

Evaluating the distribution of the most common diseases by gender, acne, dermatophytosis, and viral warts were the first three most common skin diseases in both groups in our study. When

Table 7. The anatomic localizations according to the order of the complaints.

Anatomic localizations	Complaint 1 (n, %)	Complaint 2 (n, %)	Complaint 3 (n, %)
Scalp	128 (9.3)	51 (15.7)	6 (9.8)
Face	473 (34.2)	100 (30.9)	18 (29.5)
Neck	41 (3)	10 (3.1)	1 (1.6)
Chest-abdomen	295 (21.3)	28 (8.6)	14 (22.9)
Back	154 (11.1)	29 (8.9)	12 (19.6)
Forearm-arm	160 (11.6)	26 (8)	7 (11.5)
Hand	133 (9.6)	24 (7.4)	4 (6.5)
Thigh-tibia	149 (10.8)	30 (9.3)	8 (13.1)
Foot	126 (9.1)	58 (17.9)	7 (11.5)
Palmoplantar	17 (1.2)	0 (0)	1 (1.6)
Finger nail	6 (0.43)	0 (0)	0 (0)
Toe nail	36 (12.6)	3 (0.92)	1 (1.6)
Genital	42 (3)	8 (2.5)	1 (1.6)
Oral mucosa	11 (0.79)	2 (0.61)	0 (0)

we look at the frequency rates of these three diagnoses, acne was more common in women (20.4% versus 12.4%). However, dermatophytosis was seen about 2 times more frequently in men (12% versus 6.2%), and viral warts were about 1.5 times more frequently (7.4% versus 4.9%). In a study from Türkiye, acne was the most common diagnosis, slightly more common in women than men, similar to our study (14.6% versus 14.1%). Also, dermatophytosis was the second most common disease in males and was slightly more common in men than women, similar to our study (10.2% versus 8.7%). Nevertheless, the most common second disease was contact dermatitis in females, which differs from our study. Also, the most common third disease was urticaria in both genders, and the frequency of viral warts was in lower order in their list [8].

Regarding the distribution of the most common diseases according to age groups, acne was most common in the 10-19 age group in our study. This result was consistent with some studies in the literature [8,10]. In a study among pediatric patients aged between 0 and 16 years from Türkiye, the most prevalent disease was acne [16]. In a study from the similar geographic region to our study, the most common diagnosis were encountered as acne as well [17]. However, in another study from Türkiye, the most common skin was reported as eczema in the 6-17 age group [18]. In another study in which patients aged 0-15 were evaluated, viral infections took the first place [19]. The differences might be due to the geographic localizations of the studies conducted and not including only 10-19 age group patients. Also, in our study, viral warts, seborrheic dermatitis, and other dermatitis were the most common other diseases in the 10-19 age group, consistent with the mentioned studies. In our study, the most common age group of dermatophytosis, the second most common diagnosis, was 60-69 years. Similar to our study, in a study in which the second most common diagnosis was dermatophytosis, it was stated that the most common age group for this diagnosis was 20-29 years [8]. However, in this study, while the 60-69 age group comprised 7.2% of the population, this proportion was 11.8% in our study. The difference in this result

might be due to the difference in the number of patients according to age distributions. In two different studies on geriatric patients, fungal infections were among the three most common diagnoses, similar to our study in the 65-74 age group [20,21]. According to our study, the most common age groups of viral warts, which are the third most common diagnosis, were 10-19 and 20-29 years. This result was consistent with the results of other studies evaluating the age groups [8,10].

No study focusing on the number of complaints of patients at one visit has been found in the literature. In our study, those with at least 2 complaints were 23.4% of the patients, and those with at least 3 were 4.4%. Almost one out of every four patients reported more than one complaint in a single visit. Considering the time that can be allocated for a patient in our outpatient clinics, it can be predicted that this situation may impose a significant burden on physicians, and the time required for diagnosis as well as treatment planning will be shortened. The three most frequent diagnoses based on the first complaint were acne (19.4%), dermatophytosis (6.9%), and viral warts (5.9%). The three most frequent diagnoses based on second-order complaints were dermatophytosis (13.3%), acne (11.4%), and follicular disorders (7.4%). Dermatophytosis (14.8%), benign neoplasms (11.4%), and acne (9.8%) were the most common diagnoses for the third complaint. Acne may be the first complaint, as it occurs in more visible anatomic localizations and may cause negative cosmetic results.

When we analyzed the factors affecting the number of complaints, it was determined that the rate of stating more than one complaint was higher in women than in men. 25.8% of female patients had at least two complaints, while this rate was 19.3% for males, and the difference was statistically different. However, there was no statistical difference between complaint number and age categories. When we look at the anatomical localizations of the complaints, the most common anatomical localization for all the complaints mentioned in the first three orders was the face. Chest-abdomen was the second most common localization for first and third complaints. The foot was the most

common second localization for the second complaint. When we look at the relationship between anatomic localizations and the number of complaints, the rate of having more than one complaint was significantly higher in patients with the first complaint site on the scalp than those without as an interesting result. In line with this information, it may be helpful to consider the possibility of a patient who has any complaints about the scalp making an additional complaint.

There are some limitations of our study. Our results cannot be generalized as it is not a population-based study. The timing of the study is short. The educational status and occupation of the patients included in the study might also be questioned, and it might be evaluated whether it affects factors such as the pattern of diseases, the number, and anatomic localizations of the complaint.

Conclusion

In conclusion, skin diseases are common in society of all ages and genders, and determining disease patterns can play an essential role in treatment planning and preventive measures. In addition to determining the distribution of skin diseases by age and gender, determining the number of complaints expected to be diagnosed at one visit will also enable dermatologists to be prepared in treatment planning and time management.

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Conflict of interest

The authors have no relevant financial or non-financial interests to disclose.

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Determination of the cost of prolonged hospitalization in cardiovascular surgery intensive care unit to the institution

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Abstract

In the provision of health services, health institutions should be perceived as an enterprise to use limited resources most effectively and efficiently, evaluate them optimally and ensure production efficiency. Therefore, cost information enables the most efficient utilization of resources in hospital enterprises and allows managers to use decision-making mechanisms most accurately. This study was conducted to determine and compare the costs of prolonged hospitalizations in the cardiovascular surgery intensive care unit of a university hospital. Our study was descriptive and retrospective. The hospitalizations in the cardiovascular surgery intensive care unit of the hospital were analyzed according to the prolonged hospitalization criteria determined by the social security institution. 29 extended hospitalization patient bills were determined in three years. The mean age of the prolonged hospitalization of patients was 67 years, the duration of hospitalization was 680 days, and the mean hospitalization day was 18.64. The items with the highest expenditure in prolonged hospitalization of patients were determined as drug costs, general applications and intervention costs, medical consumables costs, and laboratory costs. The increase in costs during the hospitalization and treatment process is mainly due to medication, general practices, interventions, and medical consumables. Related decision-makers should make root-cause analyses, and plans should be made to reduce costs.

Keywords: Hospital management, cost control, prolonged hospitalization

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Introduction

A healthy life is considered a constitutional and the most fundamental human right in many national and international documents. Regardless of the economic and political structures, it is the responsibility of the states to protect the health of individuals in social terms, treat sick individuals, create environments suitable for the living standards of disabled citizens and improve the level of social health [1]. Health is the source of life and underpins the need for all people to be healthier and the demand for health services [2]. Health is a need that affects all of us, regardless of our economic or cultural status, age, gender, or social status, and that we encounter throughout our lives. In 2012, Kızılçeç defined health economics as *"the application of economic rules to health services"* [3]. In addition to the formulation of health policies and the realization of legal regulations, it also covers the arrangements for activities such as production, division, distribution, and financing of health services and their economic results [2].

Despite the increasing demand for health services worldwide, the limited resources available in service delivery have brought the quantitative aspect of hospital management to the forefront. One of the significant steps to ensure cost control is to determine current costs [4,5]. The provision of health services by using limited resources most efficiently is the reason for the emergence of health institution management and is among the main objectives [6]. Although the primary purpose of hospital enterprises is not to make a profit, the calculation of costs has a strategic significance in terms of the effective use of resources [7]. In hospitals, which are institutions aiming to achieve the highest service quality with scarce resources, the first step in achieving this goal is to carry out detailed cost analysis studies [8].

Healthcare organizations are increasingly focusing on the determinants and variations of hospital length of stay to improve the quality of healthcare services and the management of hospital costs [9]. Today, determining the cost structure of the whole hospital and calculating the cost per patient, the costs of a unit or department are also within the scope of the applications. The aim at this point is to make the evaluation, planning, and auditing processes of the costs of different working departments and, accordingly, the financial situation effective [10]. Cost calculations in hospitals can be carried out appropriately and thus be effective in management decision processes only if the costs per unit can be calculated and determined regularly and associated with cost points [11]. Determining the costs of goods and services produced in hospital enterprises is a very comprehensive, attention-demanding, and time-consuming process. In the provision of health services, it is only possible to set the price to be demanded in return for the service with cost calculations. Our study aimed to determine and compare the costs of prolonged hospitalizations in the Cardiovascular Surgery (CVS) Intensive Care Unit.

Materials and Methods

In this study, a cost study was carried out on a total of 29 extended hospitalization patient invoices between 2012, 2013, and 2014 in the CVS intensive care unit at Karadeniz Technical University Farabi Hospital.

Research design

Our study is a retrospective, descriptive study. The data were collected from the hospital costs of the prolonged hospitalization of patients in the CVS intensive care unit of Karadeniz Technical University Farabi Hospital between 01.01.2012-31.12.2012 in 2012, between 01.01.2013-31.12.2013 in 2013, and between 01.01.2014-20.05.2014 in 2014 retrospectively by using of existing records and documents. In addition, cost data were obtained by comparing patient records, accounting department, and data processing records.

Research sample/Study group/Participants

The sample of our study consisted of a total of 29 prolonged hospitalization of patients who received treatment in the CVS intensive care unit in the relevant years.

Research instruments and processes

Data collection tools:

The following documents for the years 2012, 2013, and 2014 were utilized.

● Invoices for prolonged hospitalization in the Cardiovascular Surgery (CVS) Intensive Care Unit for the years 2012, 2013, and 2014 (including May),

● Financial and income statements,

● Inventory accounting records and tables,

● Hospital information system records.

Data collection process:

The data were collected from the medical, administrative, financial, and technical records of the hospital. Organizational charts and workflow charts were used to identify activities and create activity pools. Patient records in the ward, accounting department, and data processing records were compared, and cost data were used.

The determination and billing of costs in hospital enterprises are determined within the scope of the Communiqué on Health Practices (CHP), which is constantly revised by the Social Security Institution (SSI), and the prices to be paid for these services are determined by the Health Services Pricing Commission (HSPC). For prolonged hospitalizations, the date of the diagnostic procedure is considered the first day, and the health services provided by the same health service provider within the periods specified below concerning this procedure are considered within the scope of the diagnostic procedure. [12].

● Group A (Specialized operations and interventions) for diagnostic procedures; 15 days,

● Group B (Special operations and interventions) in diagnostic procedures; 10 days,

● Group C (Major operations and interventions) in diagnostic procedures; 8 days,

● Group D (Intermediate operations and interventions) in diagnostic procedures; 5 days,

● Group E (Minor operations and interventions) is 3 days for diagnosis-based procedures.

Within the scope of our study, the data for each year regarding the hospital costs of patients with prolonged hospitalization in the CVS intensive care unit for the years 2012, 2013, and 2014 were analyzed separately, and the Average Inpatient Patient Days (AID), Unit Cost of Inpatient Day (UCID) and Inpatient Unit Cost (IUC) were calculated with frequency analysis method, and finally, the data of each year were evaluated and compared as a whole. Formulas were calculated by taking the unit cost calculations proposed within the scope of the Hacettepe University Research Project (HURP) as an example [13,14].

Average Inpatient Days (AID): It can be expressed as the average inpatient day of a patient. It is the number obtained by dividing the total (clinic-based) number of inpatient days within a certain period (month, three months, or one year) by the number of discharged and deceased patients.

AID = Number of inpatient days / Number of discharged and deceased patients

The rate must be low because the duration of inpatient treatment of a patient should be low.

Unit Cost of Inpatient Day (UCID): It is calculated by associating the expenses incurred for the services provided to inpatients in hospitals within an operating period with the total number of inpatient days. The following formula is used in its calculation:

UCID= Cost of Inpatient Services / Number of Inpatient Days

The unit cost of an inpatient day shows the cost to the hospital for a single hospitalization day of an inpatient in an operating period.

Inpatient unit cost (IUC): It is calculated by associating the expenses incurred due to the services provided to inpatients in hospitals within an operating period with the total number of inpatients. The following formula is used in its calculation:

IUC = Inpatient service expense / Number of inpatients

Inpatient unit cost is the operating cost incurred by a hospital for an inpatient in an operating period.

Statistical Analysis

The binary relationships between age and length of stay, age and death, age and total cost, length of stay and death, gender and death, length of stay, and total cost were analyzed using *Pearson* Correlation in SPSS Statistical Analysis Software. Firstly, data for the years 2012, 2013, and 2014 were analyzed, and *Pearson* Correlation analysis was used in SPSS Statistical Analysis Software. Statistical frequency analyses were performed for other variables. The analyses and findings are examined in detail in the results section.

Ethical Considerations

Since the data used in our study did not contain any patient information, only institutional and data processing center permission was obtained. The permission of the institution and data processing center is dated 24.10.2014 and numbered 48814514/200/.

Results

The mean length of stay of 29 prolonged hospitalization of patients in the CVS Intensive Care Unit of the hospital in 2012, 2013, and 2014 was 680 days. In our study, the mean age of the prolonged hospitalization of patients was 67 years, and 58.62% were male. Significant differences are observed in the rates of UCID over the years. The data for 2012, 2013, and 2014 showed that although there was a decrease in the number of patients in 2013 compared to 2012, there was a significant increase in total costs. AID was the highest in 2013 with 28.9 days, and the average of the three years was 18.64. The most important factors in the calculation

Table 1. Summary table of data analysis of prolonged hospitalization of patients in 2012, 2013, and 2014 in the CVS intensive care unit.

Years / Data	2012	2013	2014	Total / Average
Total costs	₺21,481.68	₺76,776.19	₺5,455.81	₺103,713.68
Number of patients	14	11	4	29
Length of hospitalization	302	309	69	680
Average age	65	70	66	67
AID	21.57	29.09	6.27	18.64
UCID	₺71.13	₺248.47	₺79.07	₺152.52
IUC	₺1,534.41	₺6,979.65	₺495.98	₺3,576.33

AID: Average Inpatient Days; **UCID:** Unit Cost of Inpatient Day; **IUC:** Inpatient Unit Cost

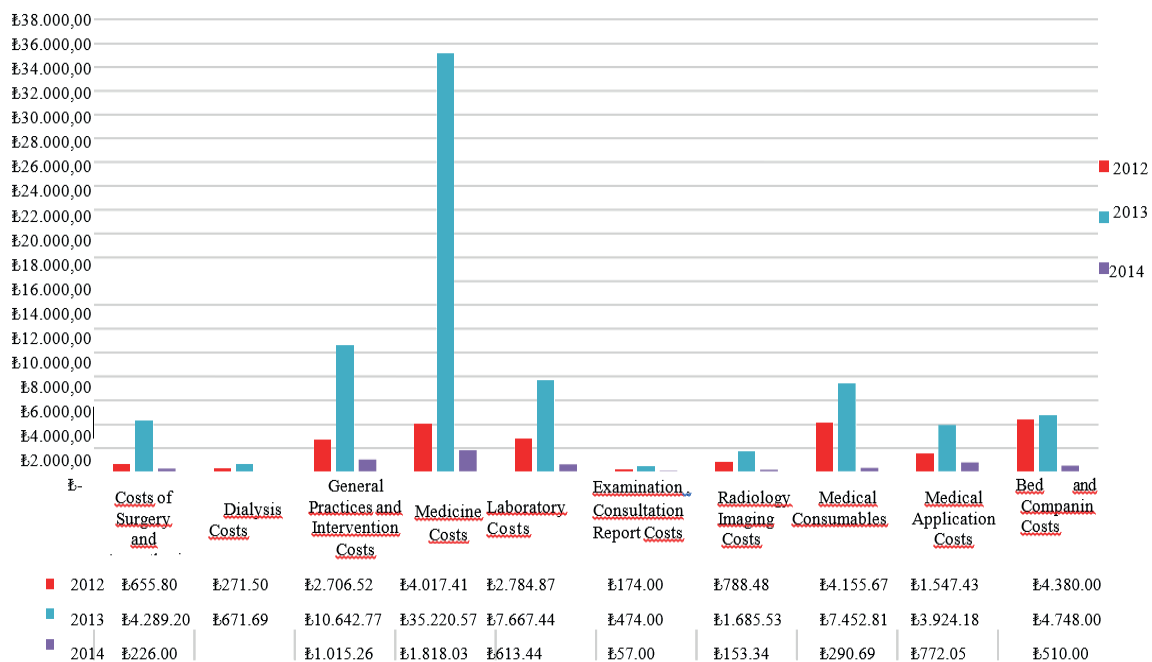|	Costs of Surgery and	Dialysis Costs	General Practices and Intervention Costs	Medicine Costs	Laboratory Costs	Examination Consultation Report Costs	Radiology Imaging Costs	Medical Consumables	Medical Application Costs	Bed and Companin Costs
2012	₺655.80	₺271.50	₺2.706.52	₺4.017.41	₺2.784.87	₺174.00	₺788.48	₺4.155.67	₺1.547.43	₺4.380.00
2013	₺4.289.20	₺671.69	₺10.642.77	₺35.220.57	₺7.667.44	₺474.00	₺1.685.53	₺7.452.81	₺3.924.18	₺4.748.00
2014	₺226.00		₺1.015.26	₺1.818.03	₺613.44	₺57.00	₺153.34	₺290.69	₺772.05	₺510.00

Figure 1. Prolonged hospitalization of patient costs in the CVS intensive care unit in 2012, 2013 and 2014.

of these rates are the total number of prolonged hospitalizations and days of hospitalization (Table 1). Determining the factors that increase the length of stay will provide important information on reducing costs and improving service delivery.

In our study, the cost items of prolonged hospitalization of patients were determined as medication, general applications and interventions, laboratory, radiology, medical consumables, dialysis, surgery and anesthesia, consultation, bed, and medical practice. The costliest expenses were drug costs Ł41,056.02, general practices and intervention costs of Ł14,364.55, medical consumables cost of Ł11,899.17, and laboratory cost of Ł11,065.75. The total cost of prolonged hospitalization was found to be Ł103,713.68 (Figure 1).

Pearson correlation test showed that there were positive changes in the significance level (0.018) of the relationship between age and total costs, the significance level (0.016) of the relationship between the length of stay and death, and the significance level (0.01) of the relationship between the length of stay, and total costs of patients with prolonged hospitalization in the CVS intensive care unit in 2012, 2013, and 2014. Especially since the significance level of the correlation coefficient is less than 0.01, the duration of hospitalization and total cost are directly related.

Table 2. Correlation analyses between Age / Length of stay, Age / Death, Age / Total cost, Length of stay / Death, Gender / Death, Length of stay / Death.

		Age	Length of hospitalization	Death	Total Cost	Gender
Age	Pearson Correlation	1	,237			
	Sig (2-tailed)		,216			
	N	29	29			
Length of hospitalization	Pearson Correlation	,237	1			
	Sig (2-tailed)	,216				
	N	29	29			
Age	Pearson Correlation	1		,261		
	Sig (2-tailed)			,171		
	N	29		29		
Death	Pearson Correlation	,261				
	Sig (2-tailed)	,171				
	N	29		29		
Age	Pearson Correlation	1			-,436*	
	Sig (2-tailed)				,018	
	N	29			29	
Total Cost	Pearson Correlation	-,436*			1	
	Sig (2-tailed)	,018				
	N	29			29	
Death	Pearson Correlation	1	,445*			
	Sig (2-tailed)		,016			
	N	29	29			
Length of hospitalization	Pearson Correlation	,445*		1		
	Sig (2-tailed)	,016				
	N	29		29		
Gender	Pearson Correlation	1		,133		
	Sig (2-tailed)			,491		
	N	29		29		
Death	Pearson Correlation	,133				1
	Sig (2-tailed)	,491				
	N	29				29
Length of hospitalization	Pearson Correlation	1			,882**	
	Sig (2-tailed)				,000	
	N	29			29	
Total cost	Pearson Correlation	,882**	1			
	Sig (2-tailed)	,000				
	N	29	29			

Discussion

Hospital enterprises have increasing importance due to the boosting demand for social and individual health services and the expectation of quality service. In addition to providing services mainly for the treatment of patients, hospitals are institutions where economically efficient and effective health care, education, research, and public health services are provided. Cost analyses provide the most objective information to decision-makers in evaluation and planning studies for the uninterrupted continuation, effectiveness, and efficiency of health services in hospital enterprises that are expected to provide services with limited resources. Cost information has strategic importance in following a realistic plan in all decision, implementation, and supervision stages. In this context, service production costs for hospital enterprises help to make healthy and sustainable decisions [15].

In hospitals, it is only possible to perform cost calculations in a healthy way and thus to be effective in management decision-making processes by regularly calculating the costs per unit and associating them with cost locations [10,16]. Evaluating the cost data of the unit ensures that the unit costs are realized at an optimal level by reducing costs and increasing efficiency. Thus, it is ensured that profit/loss amounts can be calculated on a divisional basis, shedding light on a more fair and realistic pricing study [14].

Differences are observed in the data of 2013 in the rates of unit cost inpatient day (UCID) by year. The data for the years 2012, 2013, and 2014 show that although there was a decrease in the number of patients in 2013 compared to 2012, there was a significant increase in total costs. The most significant factors in the calculation of these rates are the total number of prolonged hospitalization patients and hospitalization days, and the key factors in determining the costs were the length of hospitalization and drug costs. In the relevant cardiovascular surgery clinic, the ratio of drug costs to total costs was found to be quite high. This cost plan is confirmed by the relevant studies. Nosocomial infections are regarded as a global health burden in our country and the world. In addition to the increase in patient morbidity and mortality, it results in prolonged hospitalization,

the use of advanced antibiotic treatments, and higher additional costs [17]. Drug and especially antibiotic use and prolonged hospitalization are the best-defined parameters [18]. Drug costs can be significantly reduced through surveillance studies, training, and the use of evidence-based infection control measures, isolation methods, and rational antibiotic practices [19]. These measures will not only eliminate economic losses but will also contribute to the prevention of the increase in antibiotic resistance, albeit partially.

In the 3-year cost distribution of intensive care prolonged hospitalization bills, general practices, and intervention costs constitute the second largest cost after the high figures in drug costs. Patients with prolonged hospitalization are prone to systemic problems (hemodynamic variability during dialysis, pulmonary effusion, etc.) and metabolic disorders (metabolic acidosis, hyperkaliemia, hypoalbuminemia, etc.) as risk factors [20,21]. The interventions negatively affect the quality of life of patients and increase the consumption of resources [22].

Another noteworthy cost item is the cost of medical consumables. The cost of a patient day in intensive care is approximately three to six times higher than in normal wards. Some interventions and treatments applied to patients may bring increased costs and prolonged hospitalization risks [23]. Although frequent invasive interventions (central venous catheter, urinary catheter, intubation, and total parenteral nutrition) are necessary in cases of indication in the intensive care unit, they may also lead to nosocomial infections [24]. It should also be taken into consideration that the increase in the cost of the prolonged hospitalization process is caused by high medical equipment-related expenses. In patients with prolonged hospitalization, the increase in diagnostic examinations and the use of advanced diagnostic parameters such as laboratory and radiology may be associated with increased costs. It is concluded that the implementation of necessary measures and interventions can promote the quality of health care and save costs [19]. The conclusion that prolonged hospitalization patient costs are related to the hospitalization day in our study is consistent with the study of Bülüç and Ağırbaş, suggesting that prolonged hospitalization is a

critical factor affecting the cost of hospitalization [25]. Accordingly, we believe that our study will contribute to the cost accounting, planning, performance audit, quality, and development issues of health managers by revealing that the costs of procedures and applications of prolonged hospitalization patients can be determined objectively through statistical methods.

The benefits of determining costs in hospital organizations for managers in decision-making processes are as follows [26].

● Budgeting,

● Valuation of the difference between standard cost and actual cost,

● Profitability,

● Pricing policy,

● Estimation of future costs,

● Expansion or contraction of the services offered,

● Reduction of outsourced services or in-house fulfilment.

Identifying the factors that increase prolonged hospitalization is beneficial for improving the delivery of health services. Patient hospitalization days are a significant indicator of resource consumption. Determining the factors that increase the length of stay will provide valuable information on reducing costs and improving service delivery. The most effective factors in the calculation of these ratios are the total number of prolonged hospitalization of patients and hospitalization days.

According to the Pearson correlation test performed to determine the relationship between the age and total costs of patients with prolonged hospitalization in the CVS intensive care unit in 2012, 2013, and 2014, there was a statistically significant negative relationship between the age of patients and total costs (p=0.018). The total cost decreased as the age of the patients increased. The relationship between length of hospitalization and death was positive and statistically significant (p=0.016). The increase in the length of hospitalization increases the risk of death. There was a statistically significant positive relationship between length of hospitalization and total costs (p=0.01). Prolonged hospitalization increases total

costs [Table 2].

The fact that the cost information in the study was valid only for the relevant CVS intensive care unit of the hospital and cannot be generalized to other hospitals is considered a limitation of the study. In addition, the study covers the years 2012, 2013, and 2014, which is also considered a limitation in terms of time.

Conclusion

In our study, the costs of prolonged hospitalization of patients were analyzed and information sources that can be effective in understanding the structure and functioning of the hospital were obtained. The cost increase in the length of hospitalization and treatment process is mainly due to the costs of medication, general applications and interventions, and medical consumables. Therefore, it is recommended to take measures to shorten the length of hospital stay of the patients and reduce the cost of drugs, which constitute a significant cost item.

Conflict of interest

There is no conflict of interest.

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ORIGINAL ARTICLE

Inflammatory and infectious parameters in tension-type headache

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Abstract

Although tension-type headache (TTH) is the most common primary headache in the world, much fewer studies on its pathophysiology have been carried out in comparison to other primary headaches. Inflammatory processes are important in the pathophysiology of both peripheral and central pain. Studies on the role of inflammatory markers in TTH patients are limited. Therefore, in this study, it was aimed to examine the role of inflammatory parameters in TTH. 199 TTH patients and 154 control participants were involved in this study. C-reactive protein (CRP) and high-density lipoprotein (HDL) levels and neutrophil/lymphocyte (NLR), platelet/lymphocyte (PLR), monocyte/lymphocyte (MLR), HDL/monocyte and Immature/Total granulocyte ratios in all patients reviewed retrospectively. CRP value and immature/total granulocyte ratio were found to be significantly higher in the patient group when compared to the control group. No difference was found between NLR, PLR, MLR, and HDL/Monocyte ratios. There was no difference in NLR, MLR, immature/mature granulocyte ratios, and CRP values between the genders in the patient group. Median values of PLR, HDL, and HDL / monocyte were found to be higher in males. The fact that there is no difference in most of the inflammatory parameters in TTH and there is a significant difference in the immature/total granulocyte ratio is a new finding on this subject. There is no other study in the literature examining the immature/total granulocyte ratio in headaches.

Keywords: Neutrophil / lymphocyte ratio, platelet / lymphocyte ratio, immature / mature granulocyte ratio, tension-type headache

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Introduction

Even though tension-type headache (TTH) is the most common primary headache around the world, there are much fewer studies examining its pathophysiology when compared to other primary headaches. Although it is thought that genetic and environmental factors play a role together in its pathogenesis [1], the factors causing the attacks couldn't be clearly revealed yet. In recent years, it was claimed that the changes in both peripheral and central pain pathways played a role in pathophysiology [1,2]. The number of studies examining the role of inflammatory indicators in tension-type headache patients is limited. It was reported in the literature that some inflammatory indicators, which can be easily achieved from complete blood analyses, could be used in many diseases [2,4].

The present study aims to investigate the roles of neutrophil / lymphocyte (NLR), platelet / lymphocyte (PLR), monocyte / lymphocyte (MLR), HDL / monocyte, and immature / total granulocyte ratios and CRP values in tension-type headache.

Materials and Methods

In the present study, examining the files of patients aged 18 years or older who were followed and tested for headaches in the Neurology Department Polyclinic of the Medical Faculty of Sanko University and diagnosed with a tension-type headache by using the International Classification of Headache Disorders-III [5], complete blood, CRP, and HDL values were recorded. The control group who applied to our hospital for general medical examination, have no neurological disease or primary headache history known and were not diagnosed with any neurological disease during the neurological analyses and tests. For all cases, monocyte / lymphocyte ratio (MLR) is calculated by dividing monocyte and lymphocyte counts, neutrophil / lymphocyte ratio (NLR) is calculated by dividing neutrophil and lymphocyte counts, platelet / lymphocyte ratio (PLR) is calculated by dividing platelet and lymphocyte counts, monocyte / HDL ratio calculated by dividing monocyte and HLD values, and immature / total granulocyte ratio is calculated by dividing immature and total granulocyte counts were

statistically compared.

The present study was carried out in accordance with the principles of the Helsinki Declaration. Ethics committee approval was obtained from the Ethics Committee of the Medical Faculty of Sanko University on 2022/2.

Statistical Analysis

The data were analyzed using IBM SPSS V23. Fitness to normal distribution was tested using the *Kolmogorov-Smirnov* test. Comparison of categorical data by the groups was performed using the Chi-Square test. Comparison of non-normally distributed data by paired groups was performed using the *Mann Whitney-U* test, whereas samples *t*-test was used in comparing the normally distributed data. Statistical significance was set at $p<0.050$. In this study, the minimum sample size was found to be 102 when the sample size was calculated as alpha=0.05 and power=0.80 with 1 unit deviation.

Results

In the present study, 199 TTH patients having the mean age of 46.4 years (81 male patients) and 154 control cases having the mean age of 44 years (74 male participants) were involved. There was no statistically significant difference between the groups in terms of age and gender distribution ($p=0.380$ and $p=0.168$, respectively). There was no statistically significant difference between the patient and control groups in terms of NLR, PLR, MLR, and HDL / monocyte ratios but there was a statistically significant difference between the groups in terms of CRP and immature/total granulocyte ratios ($p=0.026$ and $p=0.004$, respectively) (Table 1). In the patient group, no statistically significant difference was found between the genders in terms of NLR, MLR, immature / total granulocyte ratios and CRP values. Considering the gender, PLR median value was found to be 108.7 among females and 118.4 among males; there was a statistically significant difference ($p=0.043$). By gender, HDL median value was found to be 47.0 among females and 50.0 among males; there was a statistically significant difference ($p=0.009$). HDL / Monocyte median value was found to be 0.080 among women and 0.090 among men and there was a statistically significant difference ($p<0.001$).

Discussion

The number of studies examining TTH and peripheral inflammation is limited [6,7]. The effects of systemic inflammation on tension-type headache are not clearly known. Differing from migraine, in which the role of neuroinflammation via trigeminovascular activation is accepted, the pathophysiology of TTH couldn't be understood yet [8]. Since it was found in several previous studies that proinflammatory cytokines were found to be at high levels in serum and cerebrospinal fluid in TTH, it was thought that inflammatory parameters might be considered for TTH pathophysiology [8-11]. In the present study, CRP value and immature/total granulocyte ratio were found to be higher in the patient group but there was no difference between NLR, PLR, MLR, and HDL / Monocyte ratios.

In a previous study, it was determined that TTH patients' thrombocyte counts and NLR, PLR, and CRP values were statistically significantly higher [7]. There also are studies relating these ratios to migraine [12,13]. In studies carried out, especially during migraine attacks, it was found that NLR and PLR were higher than in the control group [12]. In the literature, there also are studies reporting no significant difference between migraine patients and control groups in terms of NLR and PLR values [14].

Immature granulocytes were reported to be higher in peripheral blood mainly in diseases such as sepsis, acute infections, and acute appendicitis [15,16]. Immature granulocytes include metamyelocytes, myelocytes, and promyelocytes; they are precursors of neutrophils and they indicate increased bone marrow activity [17]. The immature/mature granulocyte ratio was reported to increase in some hematological and autoimmune diseases and be an important bioindicator [17,18]. Moreover, it was stated that it can be defined as both early diagnosis and prognosis bioindicator in sepsis and surgical diseases such as acute pancreatitis and acute appendicitis [15,19]. However, in the literature, there is no study examining this parameter in relation to headaches. İmmature/mature granulocyte values have just started to be studied in our laboratory. So we wanted to investigate this as a biomarker for tension-type headache. In the present study, both immature and mature granulocyte counts were found to be higher in TTH patients in comparison to the control group. Moreover, a statistically

Table 1. Comparison between peripheral blood parameters in patient and control groups.

Groups	Patient (n=199) (min-max) mean	Control (n=154) (min-max) mean	p
HDL (mg/dl)	(12-113) 49	(25-85.) 48.5	0.809
CRP (mg/L)	(0.09-28.1) 2.46	(0.2-26.1) 1.8	0.026
NLO	(0.22-24.49) 1.9	(0.54-7.37) 1.77	0.058
PLO	(44.9-517.8) 113.8	(45.9-308.3) 116.3	0.954
MLO	(0.07-0.97) 0.24	(0.11-0.89) 0.25	0.986
HDL / Monocyte	(0.02-0.34) 0.09	(0.03-0.26) 0.09	0.75
Immature / Total granulocyte	(0-0.02) 0.003	(0-0.02) 0.002	0.004

significantly higher immature/total granulocyte ratio suggests that immature granulocytes were higher than the total in the patient group.

The strengths of this study are as follows; it is known that the participants in the control group had no neurological disease and / or pain syndrome and the numbers of cases in the patient and control groups were enough. However, the limitations are that complete blood counts of TTH patients were obtained retrospectively and the results were not compared to clinical characteristics such as duration, frequency, and severity of headache.

Conclusion

In the present study, it is difficult to interpret the significantly higher immature / total granulocyte ratio by using the available data. To the best of our knowledge, there is no other study examining the immature / total granulocyte ratio in relation to headaches. In this study, the finding that patient and control groups were similar to each other in terms of NLR, PLR, and MLR values, which have been more widely studied in the literature, but different in terms of CRP and immature/total granulocyte ratio suggests that more useful information can be achieved from more detailed prospective studies examining clinical and laboratory data together.

Conflict of interest

The author declares no conflict of interest regarding this article.

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Factors affecting academic achievement of third-year students of Bursa Uludağ University Faculty of Medicine

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Abstract

The present study aimed to investigate the determinants of academic performance among third-year students in the Faculty of Medicine. A survey consisting of 45 questions was administered to 357 third-year students in the academic year 2017-2018, with a response rate of 233 participants. The academic achievement was assessed by evaluating the grade point average (GPA) scores, with a threshold of 3. The results revealed that several factors were significantly associated with a GPA score of 3 and above, including age ($p=0.011$), relationship with parents and positive parental attitude ($p=0.001$), staying with family ($p=0.015$), and school selection to "be a doctor" ($p=0.044$). The results also showed that negative parenting behaviors and smoking were associated with an increased risk of academic failure. However, no significant association was found between academic performance and gender, physical exercise, parents' education, and employment status. This study highlights the crucial factors impacting academic achievement in medical education. The results demonstrate the importance of age, relationship with parents, parental attitude, reasons for choosing a medical school, smoking habits, and extracurricular activities in determining GPA outcomes. The findings have important implications for the future planning of students, the development of education, and the formulation of new policies.

Keywords: Academic achievement, medical education, third-year medical student, Turkey

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Introduction

The universities aim to train "…*manpower suitable for the needs of the nation and the country in an order based on contemporary education and training principles*" that consist of different education periods and processes [1]. Universities primarily aim to provide education and training to individuals to prepare them for various careers and professions. This education is typically based on contemporary principles of teaching and learning, which may involve a combination of classroom instruction, laboratory work, fieldwork, internships, and other practical experiences. The ultimate goal of this education is to produce a skilled and knowledgeable workforce equipped to meet the needs of the nation and the country in various fields and industries. This may include training individuals for positions in healthcare, engineering, business, education, the arts, and many other areas [2].

University education can be both exciting and stressful for students, as it is a time of radical changes that can positively and negatively affect their lives. Students may struggle with various issues such as family problems, quality of education, economic difficulties, stress, communication problems, future anxiety, friend problems, learning problems, continuing an education that one does not want, academic achievement, etc. [3-7]. Academic achievement is one of the essential responsibilities of students who go through a challenging exam marathon to gain admission to the university, satisfy their families and plan the future [8,9].

Unlike "success", "academic success/ achievement", which also expresses/determines career choice and professional competence, is generally an essential output of universities to raise qualified personnel [10-12]. Academic achievement, which can be described with terms such as "Grade Point Average (GPA)", "Passing Grade", and "Cumulative Weighted Grade Point Average (CGPA)," is the most easily measurable output and is a determinant of the cognitive skills and proficiency and 'performance' shown in lessons [13,14]. This 'performance' is an essential indicator for families' and students' post-graduation career planning [15,16].

Although the factors determining the students' performance are discussed in many fields, the primary determinant is the GPA [17].

The faculty of medicine is known to have the longest education period among all the units in university education. This is due to the extensive training required to become a medical professional, including theoretical coursework and practical experience. The main purpose of education in medical faculties is to train good physicians to protect, develop and improve health. Medical education is a highly demanding and challenging process that requires significant commitment and dedication from students. As such, it is essential to understand the factors that influence the academic achievement of students in medical schools. There are discussions that the effects of the stress experienced by medical students on their success will indirectly impact the delivery of health services. This situation has led to the need to determine the reasons for students' academic success or failure, as well as the factors that influence them, resulting in the conduction of numerous studies. [15,18-21]. Although it has been examined under three main headings, cognitive, affective, and environmental, different classifications have been made, such as

• Age [13, 22-26],

• Gender [5,10,13,17,22,26-35],

• Socioeconomic Status [5,15,34,36-41],

• Parental Education [8,32,34,36,42,43],

• Parental Attitudes [14,43-46],

• Extracurricular Activity [25,33],

• Physical Activity [47-49],

• Work/Living Environment [10,22,33,34,36,50, 51],

• Stress/Depression [7,49,52-54],

• Learning Styles [55-57] *etc.*

Academic achievement, although it varies individually, can be a determining factor, especially in terms of the professional competencies of medical students after graduation, so it is essential to identify the factors that affect success. This study aims to identify

these factors, specifically in the pre-clinical period of medical school, to provide insights that can be used to improve medical education and develop new education policies. By exploring the factors, we can better understand how to support and promote academic achievement in medical schools. Additionally, the findings of this study may help develop interventions that can assist students struggling with academic or personal difficulties during their medical education.

This study is designed to investigate the factors that impact students' academic achievement in the pre-clinical medical school period. The main objective of the study is to evaluate these factors and their effects on the academic achievement of students of Bursa Uludağ Medical Faculty, which accepts the first 6000 students in the university entrance exam and allows approximately 300-350 students to graduate and join the healthcare sector every year.

Materials and Methods

This cross-sectional study was conducted with third-year students of Bursa Uludağ University Faculty of Medicine. Ethics committee approval was obtained from Uludağ University Clinical Trials Ethics Committee for the study (2017-1/19; 2020-10/23).

The research population comprises 357 students in the 2017-2018 academic year. The study was completed with 233 students (65.2%) who agreed to participate. The reasons for limiting the analysis to third-year students were;

• Implementation of a new and different education system (integrated education) at the faculty in the 1st and 2nd years,

• The potential of the adaptation process to medical education on suppressing other factors in the 1st and 2nd years,

• Continuation of classical medical education in 3rd year,

• And since the 3rd year was the last period of preclinical, it was possible to approach the factors affecting academic success more consistently.

Data and Data Collection Process

In the study, a survey form consisting of 45 questions, in which demographic, individual, and school-related factors are questioned, prepared by the researchers with the support of the literature, is used. Surveys were distributed to the students and collected by the researchers after filling them.

To evaluate academic achievement in the study, the general academic Grade Point Average (GPA) calculated at the end of the year, on which written, oral, and practice exams affect at different rates, has been used. The GPA scores of the 3rd year students participating in the study are calculated in the 4-point system. According to Bursa Uludağ University Associate and Undergraduate Education Regulation, students must have a GPA score of 3 and above to receive the honor/high honor award. Since academic success is the basis of the study, it is determined as the threshold value because it is included in the regulation and because the GPA scores are median 3. It is examined whether there was a difference between the students with a GPA score of 3 and above and those with a GPA below 3 in terms of the variables studied.

Statistical Analysis

The *Shapiro-Wilk* test examines whether the data showed normal distribution. Descriptive statistics are expressed as the mean and standard deviation for quantitative data and frequency and percentage for qualitative data. The *t*-test is used to compare two groups for normally distributed data. The *Pearson* Chi-square test and *Fisher's* Exact Chi-square test are used to analyze categorical data. The *Bonferroni* test was used as a multiple comparison test. Binary logistic regression analysis examines factors affecting the GPA score below 3. The significance level is determined as $\alpha=0.05$. Statistical analysis of the data is performed in the statistical package program IBM SPSS 28.0 (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp.).

Results

The mean age of the 233 third-year students participating in the study was 20.77±0.88 (19-25). Of the students, 134 (57.5%) were female, and 99 (42.5%) were male. While 148 (63.5%) students had a GPA score of 3 and above, 85 (36.5%) had a GPA below 3. A statistically significant

difference was found between the students with a GPA score of three and above and below three according to age (t(230)=2.557; p=0.011 (Table 1).

The effect size for the difference between the groups was calculated using Cohen's d, resulting in a value of 0.349, considered a small to medium effect. "The average age of students with a GPA score of 3 and above was lower than the others. However, there was no statistically significant difference when the students were compared regarding gender, whether the mother and father were alive, their relationship status, education level, and working status (p>0.05).

A statistically significant difference was found in comparing the students' GPA scores and their relationship with their parents (effect size w=0.252; p=0.001) (Table 2).

The rate of positive parental attitude (61.5%) was higher in students with a GPA score of 3 and above, while the rate of negative parental attitude was higher in students with a GPA score of less than 3 (58.5%). While there was a statistically significant difference in the comparison made according to the current place of residence, the rate of staying with a family (26.5%) of the students with a GPA score of 3 and above was found to be higher than those with a GPA below 3 (12.9%) (effect size w=0.159; p=0.015). There was no statistically significant difference between the two groups regarding the answers to whether a drug is used continuously and whether they do sports for 35 minutes a day, five days a week.

Table 1. Comparison of sociodemographic characteristics.

		GPA≥3 (n=148)	GPA<3 (n=85)	p
Age		20.66±0.82	20.96±0.94	0.011
Gender	Female	88 (59.5%)	46 (54.1%)	0.427
	Male	60 (40.5%)	39 (45.9%)	
Mother	Alive	145 (98%)	85 (100%)	0.556
	Dead	3 (2.0%)	0 (0%)	
Father	Alive	146 (98.6%)	84 (98.8%)	1.000
	Dead	2 (1.4%)	1 (1.2%)	
Parental coexistence status	Together	137 (94.5%)	80 (94.1%)	1.000
	Divorce / separated	8 (5.5%)	5 (5.9%)	
Mother's education level	High school graduate and below	101 (68.7%)	60 (70.6%)	0.883
	University graduate and above	46 (31.3%)	25 (29.4%)	
Father's education level	High school graduate and above	78 (53.4%)	42 (50%)	0.681
	University graduate and above	68 (46.6%)	42 (50%)	
Mother's job status	Having a job	50 (34.2%)	29 (34.1%)	0.984
	None	96 (65.8%)	56 (65.9%)	
Father's job status	Having a job	119 (81.5%)	72 (85.7%)	0.413
	None	27 (18.5%)	12 (14.3%)	

Descriptive statistics are expressed as mean ± standard deviation or n (%).

While the reason for choosing a medical faculty was statistically significant, students with a GPA score of 3 and above had a higher rate of choosing "to be a doctor".

In comparison, students with a GPA score below 3 had a higher rate of preferring to be a doctor (effect size w=0.133; p=0.044). A statistically significant difference was found when the students in the two groups were compared in terms of attending any course to improve their education, self-improvement, and smoking. The rate of attending the course (34.5%) and smoking rate (27.1%) were higher in students with a GPA

score below three than in students with a GPA score of 3 and above. "Which class hours are more productive for listening to the lesson?" No statistically significant difference was found in the answers to the question (p=0.094).

When the factors affecting the GPA score below three are examined as multivariate, the results are given in Table 3. According to this result, a 1-unit increase in the age variable increases the risk of a low GPA score by OR=1.554 times. When the student's relationship with their parents is examined, it is seen that students whose parents display positive behaviors have a lower risk of

Table 2. Comparison of the variables according to GPA level.

		GPA≥3 (n=148)	GPA<3 (n=85)	p
Relationship with parents	Negative parenting attitude	53 (35.8%)[a]	48 (58.5%)[b]	0.001
	Positive parenting attitude	91 (61.5%)[a]	29 (35.4%)[b]	
	Indifferent parents	4 (2.7%)	5 (6.1%)	
Current place of stay	With family	39 (26.5%)	11 (12.9%)	0.015
	Other	108 (73.5%)	74 (87.1%)	
Regularly drug use	No	139 (93.9%)	74 (87.1%)	0.072
	Yes	9 (6.1%)	11 (12.9%)	
Reason for choosing a medical school	Because I want to be a doctor	99 (67.3%)	67 (79.8%)	0.044
	Because my score is high	48 (32.7%)	17 (20.2%)	
Exercising for 35 minutes a day, five days a week	No	115 (77.7%)	74 (87.1%)	0.079
	Yes	33 (22.3%)	11 (12.9%)	
Attending any course for education and self-development	No	114 (78.1%)	55 (65.5%)	0.037
	Yes	32 (21.9%)	29 (34.5%)	
Smoking	No	135 (92.5%)	62 (72.9%)	<0.001
	Yes	11 (7.5%)	23 (27.1%)	
Which class hours are more productive in terms of listening to the lesson?	Between 8:00-11:00 hours	67 (45.9%)	27 (32.5%)	0.094
	Between 11:00-14:00 hours	63 (43.1%)	41 (49.4%)	
	Between 14:00-17:00 hours	16 (11%)	15 (18.1%)	

Descriptive statistics are expressed as frequency (n) with (%).

ab symbols were used to indicate groups that differed due to the *Bonferroni* test from multiple comparison tests following the identification of significant differences in overall comparison.

having a GPA score below three than students whose parents demonstrate negative behaviors (OR=0.249). Smoking increases the risk of having a GPA score below 3 (OR=5.079).

Discussion

In this study, conducted with third-year students at Bursa Uludağ University Faculty of Medicine during the 2017-2018 academic year, various factors affecting academic achievement were evaluated. The results showed a significant difference between age and academic achievement, with the average age of students with a GPA score above 3 being lower. This finding supports the idea that there is a negative correlation between age and academic achievement, which is consistent with the results of Nto et al [24]. However, other studies have found a positive relationship [22,25] or no relationship [13,23,52] between age and academic

achievement. This suggests that the relationship between age and academic achievement is complex and may be influenced by factors such as study habits, family support, and individual characteristics. Previous research suggests that female students tend to be more successful in terms of academic achievement when compared to male students [5,10,17,22,29-34]. However, our study did not find a significant difference in terms of gender, which is consistent with the results of Taşlıyan et al [13]. Furthermore, the literature suggests that socioeconomic level plays an essential role in shaping the outcome of a challenging and long-term medical education and its impact on success in terms of the psychological-social autonomy it brings [12,15,34,38,39,58]. But our study did not find a relationship between socioeconomic status and academic achievement. This result is in parallel with the studies conducted by Koç et al [5], and

Table 3. Examining the factors affecting the low GPA with binary logistic regression analysis.

		Beta	p	OR	95% CI	
Age		0.441	0.022	1.554	1.066	2.266
Relationship with parents	Positive vs. Negative	-1.390	<0.001	0.249	0.124	0.499
	Indifferent vs. Negative	-0.011	0.988	0.989	0.221	4.423
Current place of stay	Other vs. With family	0.776	0.084	2.172	0.901	5.235
Regularly drug use	Yes vs. No	0.585	0.308	1.796	0.583	5.531
Reason for choosing a medical school	My score is high vs. I want to be a doctor	-0.711	0.074	0.491	0.225	1.071
Exercising for 35 minutes a day, five days a week	Yes vs. No	-0.519	0.24	0.595	0.25	1.415
Attending any course for education and self-development	Yes vs. No	0.575	0.13	1.776	0.844	3.739
Smoking	Yes vs. No	1.625	0.001	5.079	2.016	12.796
Which class hours are more productive in terms of listening to the lesson?	11:00-14:00 vs. 8:00-11:00	0.736	0.052	2.088	0.994	4.387
	14:00-17:00 vs. 8:00-11:00	0.751	0.142	2.118	0.777	5.772

OR: Odds ratio; *CI:* Confidence Interval

Al Shawwa et al [40]. The literature suggests that parental education level and occupation can positively impact academic achievement [8,14,15,36], with some studies indicating that the father's educational status is more influential and others showing that the mother's educational status is more effective [32,33,43]. However, our study did not find a significant difference in parents' education levels or professions. This result is similar to previous studies such as those conducted by Ayyıldız et al [22], Yousif et al [36], and Al Shawwa et al [40].

Furthermore, the literature suggests that family relations can impact student education [43,44,58], but there is limited research on the specific effect of family relations on academic achievement in medical school students. Our study found that family relations significantly impact academic achievement (*p*=0.001). Specifically, students with positive family relationships have better academic success than those with negative or indifferent family relationships (Table 2). This result is consistent with previous research, such as a study by Kuzay [53] with health field students and Kaya et al [14] with Faculty of Education and Science and Letters students, which supports the idea that a positive and supportive family environment can contribute to academic success in medical school.

In our study, we investigated the impact of place of residence on academic achievement and found that students who stayed with their families had better academic success (*p*=0.015; Table 2). This finding is supported by previous research, such as a study by Bakouei et al [50] and Tiruneh et al [51], which also found that university students studying in Health Sciences faculties stayed with their families were more successful. However, there are differing opinions on the impact of place of residence on academic achievement in the literature. Al Shawwa et al argue that students with high GPAs have quiet and uninterrupted study habits [40]. On the other hand, Yıldırım et al [10] and Ogenler et al [34] found that students staying in the dormitory / hostels were more successful than students living alone and working alone in the library. The relations with family/friends can also explain these results. Dormitories are safe places for students who

must study away from their families after gaining admission to a university. However, many factors, such as the lack of single rooms for individuals, being in a crowded environment, and the physical and administrative features of the dormitory, can affect the student. In such overcrowded environments, a student used to studying quietly and calmly may not be able to find a particular area, which can hinder their quality of work and result in a decline in academic success.

On the other hand, a crowded working environment can positively affect students' success in the same faculty by allowing them to come together and work together. Similarly, in a family home prepared for the student in a supportive environment by parents, a good study environment can be created, whereas in unresponsive/uncommunicative or socioeconomically disadvantaged family homes, such an opportunity may not be available [10,31,34,46]. It is seen that more research is needed on this topic.

Our study found no significant relationship between participation in sports and academic achievement. In contrast, a study by Slade et al [48] showed that students who regularly participate in sports activities on campus have better academic performance, likely due to the stress-reducing effects of sports. However, our results differ from a study conducted in our country that found that students who engage in regular sports had higher academic success than those who do not or engage in sports only periodically. Additionally, our study found that smoking has a negative effect on academic achievement, with a statistically significant difference in the academic performance of smokers and non-smokers (27.1%). This finding is consistent with Ogenler et al [34], who also found a negative correlation between smoking and academic achievement.

Conclusion

Academic achievement is an important factor in determining the success of medical students. It is used to measure the student's knowledge, skills, and abilities in their field of study and is an indicator of their preparedness for future work

in the medical field. Additionally, academic achievement is essential for students and their families as it can influence their future job opportunities and earning potential. It is crucial to evaluate and track academic achievement throughout the medical education process to ensure that students are meeting the necessary standards and are on track to succeed in their future careers [43].

Medical education is an extensive and demanding process that requires not only a significant investment of time and effort from students but also support and guidance from their families. The academic achievement of medical students is paramount, as it indicates their preparedness for future work in the healthcare field. Furthermore, students' academic performance can significantly impact their future job prospects and earning potential. In light of this, it is imperative to consider the role of families in medical education, as their attitudes and support can significantly affect students' academic success. In this regard, it may be beneficial to hold seminars for families to educate them about appropriate attitudes toward students and provide support for students experiencing difficulties in their family relationships.

Furthermore, the physical environment in which medical students study and learn also plays a crucial role in their academic achievement. Providing new study spaces and redesigning lecture halls and classrooms can enhance the learning experience for students. Additionally, attention must be given to the accommodation conditions of students living in dormitories, as suitable living environments can positively impact students' academic success. In the end, identifying the factors that contribute to the success or failure of medical students during their education is crucial for advancing education and developing new educational policies.

Conflict of interest

There are no conflicts of interest in connection with this paper.

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Variable selection in gender and age decision-making for traumatic spine and thoracic pathologies after various accidents with Multivariate Adaptive Regression Spline (MARS)

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Abstract

Trauma is a condition that affects the body's structure and results from outside factors. After heart disease and cancer, it is the most common cause of death across all age categories. For a variety of causes, people are routinely exposed to traumatic vertebral, thoracic pathologies and rib fractures. Ribs can be harmed by simple falls, impacts, and blunt injuries as well as broken due to car accidents and falling from a height. Magnetic resonance imaging or computed tomography are used to diagnose these fractures. In this study, non-linear complex methods were used to categorize gender and age by utilizing thoracic pathologies, fractures or cracks in the body as a result of traffic accidents or falling from a height, which have the feature of being a case in forensic issues. The most important data in the classification of gender and age were determined by Multivariate Adaptive Regression Spline (MARS) method. Although autopsy should be utilized in these situations, complex regression methods is intended to have an impact on quick and accurate decision-making about events in order to speed up or direct the process in the field of forensic medicine. As a result, the effectiveness of the experts subsequent predictions will be increased by the preliminary findings produced by real-world data and artificial intelligence algorithms or complex non-linear regression problems.

Keywords: Thorax, vertebra, multivariate adaptive regression spline, variable selection, traffic collision, autopsy

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Introduction

For children and young adults between the ages of 5 and 29, traffic-related injuries are the main cause of death. An estimated 1.3 million people each year pass away in traffic-related incidents. Men are more likely than women to get in car accidents starting at a young age. Young men under the age of 25 account for nearly three times as many road traffic fatalities (73%) as young women [1].

As a result of 187 thousand 963 fatal and injury traffic accidents that occurred in Turkey in 2021, 2,421 people died at the accident site and 2,941 people died within 30 days due to the cause and effect of the accident after they were injured and transferred to health institutions. While 49.3% of the deaths and 72% of the injuries occurred within the residential area, 50.7% of the deaths and 28% of the injuries occurred outside the residential area [2]. Following a car collision, trauma is a condition that disturbs the body's structural order as a result of external forces [3]. 40% of all trauma cases involve thoracic trauma, the third most frequent type of injury overall [3-5]. Thoracic injuries make up one-third of all trauma emergency and hospital admissions [5-7]. A tomographic image of the vertebral and rib fractures is shown in Figure 1.

Ribs can be harmed by simple falls, impacts, and blunt injuries as well as broken due to car accidents and falling from a height. The crime scene is investigated as soon as the accident occurs on the road. Physicians are supposed to take part in gathering any biological evidence that may exist, assess if the incident was truly an accident, and decide whether an autopsy is necessary if a deceased person is present [8]. The Turkish Penal Code states in Article 280 that "if physicians, dentists, pharmacists, midwives, nurses and other healthcare providers fail to report the situation to the competent authorities or delay in doing so, despite discovering a sign that a crime has been committed while performing their duties, shall be punished with imprisonment of up to one year." Because of this, individuals who visit the emergency department or health facility; Situations including traffic accidents, falls, assaults, and work accidents should be treated as legal cases and reported in writing or verbally to the appropriate authorities [9].

However, in terms of both criminal and civil law, forensic medicine's determination of age and gender is significant. The least amount of mistakes should be used when defining anatomical features [10]. Identification will continue to be one of the most important aspects in forensic cases, according to studies done so far.

Since bone fractures pose a threat to world health, a comprehensive study of the density and burden of fractures was also carried out for the first time in 2019. This study showed the global fracture incidence rate for each anatomical region from 1990 to 2019 by age and sex [11].

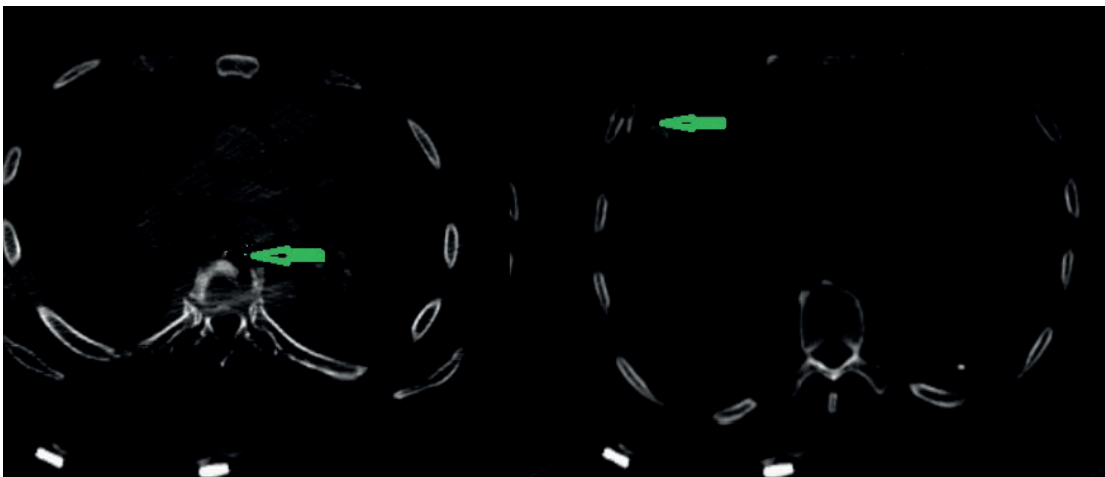In many traffic collisions, especially those

Figure 1. Tomography images of rib and vertebral fractures.

involving large cars, there are unrecognizably dead bodies [12,13].

To date, fractures have been found using techniques like magnetic resonance (MR) and computed tomography (CT) for a variety of causes. However, in this study, it has been proposed to estimate gender and age by looking for fractures or cracks in the body by combining deep learning and machine learning techniques. First, the variable selection was done, and then 150 features were chosen for both gender and age requirements. Making the data noiseless brought the feature reduction step before classification to a successful conclusion. For feature selection, a data collection with 251 samples overall was employed.

Materials and Methods

Thorax computed tomography scans were examined to determine which patients had spinal, rib fractures and thoracic pathologies. In forensic medicine, cases such as traffic accidents, falls, assaults, and work accidents are accepted as forensic cases. Therefore, the study included patients with rib fractures or thoracic vertebral fractures after a car collision and fall from a height. On a chest computed tomography, the degree of rib fractures, displacement, or non-displacement, were identified. Patients with thoracic vertebral fractures had their fracture levels, kinds (corpus fracture, transverse, and spinous process fractures) and thoracic pathologies identified. For statistical calculations, the R 4.0.2 environment was employed. Patients provided both written and verbal informed consents for the study, which were prepared in accordance with the Helsinki Declaration and approved by the local clinical research ethics committee of the Afyonkarahisar Health Sciences University (2022/16).

Feature Selection

A technique for identifying and removing unimportant participants from a data collection is feature selection. As a result of this procedure, the study moves forward using the information that best explains the topic under investigation. As a result, multidimensionality's complexity is eliminated. The literature describes three feature selection techniques: filtering, wrapping, and embedding. One of the wrapping approaches, MARS, was employed in this work to pick features [14].

Multivariate Adaptive Regression Spline

MARS is one of the new non-parametric regression methods. It was created in the early 1990s by Jerome H. Friedman [15], a statistician at Stanford University. MARS is a hybrid of Recursive Partitioning Regression (RPR) and Projection Pursuit Regression (PPR). This regression procedure is designed to accommodate both binary and continuous output variables. MARS is a versatile, precise, and quick technique. In contrast to linear methods, it considers subsets of variables [16]. This method, which is used for classification with a categorical output variable, has a wide range of applications because it is very flexible, accurate, and fast [17].

For $(x \in R)$, the following is the basis function:

$$(x - t)_+ = \{x - t, \; if \; x > t \quad 0 \; , otherwise \; and$$
$$(t - x)_+ = \{t - x, \; if \; x < t \quad 0 \; , otherwise \quad (1)$$

In the expression above, t represents the point at which every function becomes piecewise linear at the value t. A key part of MARS models are hinge functions taking the form. Figure 2 on the right shows a mirrored pair of hinge functions with a knot at 2. The goal of this inflection is to obtain the projected pair x_j via nodes with the value x_{ij} [18].

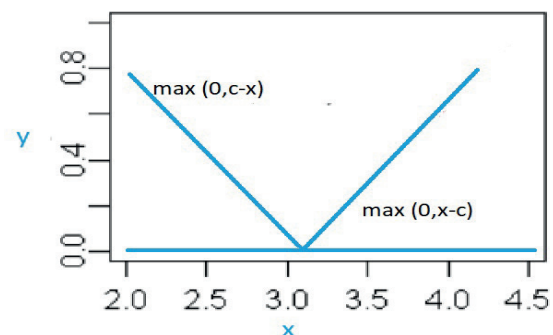$$C = \left\{ (x_J - t)_+, (t - x_J)_+ \right\} \quad (2)$$

Figure 2. A mirrored pair of hinge functions with a knot at x=c.

The maximum model obtained initially is cropped with the second step, the backtracking algorithm and the best model is discovered by

eliminating the least effective variables one by one in the MARS model construction process. The submodel with the best approximation is determined by comparing the submodels obtained in this process using the Generalized Cross-Validation (GCV) criterion. The GCV method is described below.

$$GCV = \frac{\sum_{i=1}^{N} \left(y_i - \hat{f}_\lambda(x_i)\right)^2}{(1 - M(\lambda)/N)^2}$$ (3)

$M(\lambda)$ and denote the number of effective parameters and the number of observations, respectively. $M(\lambda)$ is found in this expression as $M(\lambda) = r + cK$ where r and K denote the number of independent basis functions and the number of nodes chosen in the incremental part, respectively.

Results

251 patients who experienced various trauma cases traffic accidents and fall injuries were included in the study. In the model constituting the data set, 63.35% occurred as a result of falling from a height, and 36.65% as a result of traffic accidents. These patients had thoracic vertebral fractures as well as rib fractures or rupture, injury, bleeding, and other conditions in the lung. According to fracture or fracture status, it was shown that the degrees and types of fractures (corpus fracture, transverse, and spinous process fractures) in patients with spinal and/or rib fractures and in patients with thoracic vertebral fractures varied. 150 different variables were taken into account. Variable status was coded with a 1 rather than a 0.

For two variables in this investigation, feature reduction was done. Age and gender are these factors. A total of 150 features were reduced to 9 features using the MARS feature selection method for the age variable. These are Lung Parenchymal laceration, Lung left lower lobe atelectasis, right 7th rib displaced fracture, right 10th rib displaced fracture, left 6th rib displaced difference, left 8th rib non-displaced fracture, left 9th rib non-displaced fracture, C7 vertebra transverse process fracture, T10 vertebra transverse fracture.

A total of 150 features were reduced to 5 features using the MARS feature selection method for the gender variable. These were identified as right 3rd rib displaced fracture, right 7th rib displaced fracture, left 5th rib non-displaced fracture, left 9th rib non-displaced fracture, T2 vertebra corpus fracture.

Table 1 shows demographic data. Table 1 shows demographic data. Of the respondents, 148 were men and 103 were women. In the data

Table 1. Features of the population.

Variables		**Frequency**	**Mean**
Sex	Male	148	45,5
	Female	103	55,2
Age	16-44	97	
	45-70	114	49,25
	71 and above	40	
	Total	**251**	

Table 2. The treatment method according to the disease etiopathology.

Treatment method		Traffic accidents	Fall from height	Total
Surgical	n	54	113	169
	%	58.7%	71.1%	66.8%
Medical	n	38	46	84
	%	41.3%	28.9%	33.2%
	n	92	159	251

collection, there are 40 patients over the age of 71, 114 patients between the ages of 45-70 and 97 patients between the ages of 16-44.

Table 2 shows the treatment method applied according to the etiopathology of the diseases. As a result of traffic accidents, surgical methods were used in 58.7% and medical methods were used in 41.3%. As a result of falling from a height, 71.1% of the patients were treated with surgical methods, while 28.9% were treated with medical methods.

In the MARS feature selection, 150 features were reduced to 5 features for sex and 9 features for age, as shown in Table 3. Lung parenchymal laceration, Lung left lower lobe atelectasis, right

7th rib displaced fracture, right 10th rib displaced fracture, left 6th rib displaced difference, left 8th rib non-displaced fracture, left 9th rib non-displaced fracture, C7 vertebra transverse process fracture, T10 vertebra transverse fracture for age.

The features selected by the algorithms are given in Figure 3. Commonly selected are left 9th rib non-displaced and right 7th rib displaced fracture.

It is suggested in this study to increase the use of complex non-linear regression methods in the field of health management and services. In our study, we found that the physician's decisions are consistent with the outcomes of MARS. This

Table 3. Selected features performances for gender and age.

| Feature Selection Techniques	Number of Features Selected	Selected Features (MARS)
Sex	5	Right 3rd rib displaced fracture, right 7th rib displaced fracture, left 5th rib non-displaced fracture, left 9th rib non-displaced fracture, T2 vertebra corpus fracture
Age	9	Lung Parenchymal laceration, Lung left lower lobe atelectasis, right 7th rib displaced fracture, right 10th rib displaced fracture, left 6th rib displaced difference, left 8th rib non-displaced fracture, left 9th rib non-displaced fracture, C7 vertebra transverse process fracture, T10 vertebra transverse fracture.

Common Selected Features (MARS)
Left 9th rib non displaced
Right 7th rib displaced fracture
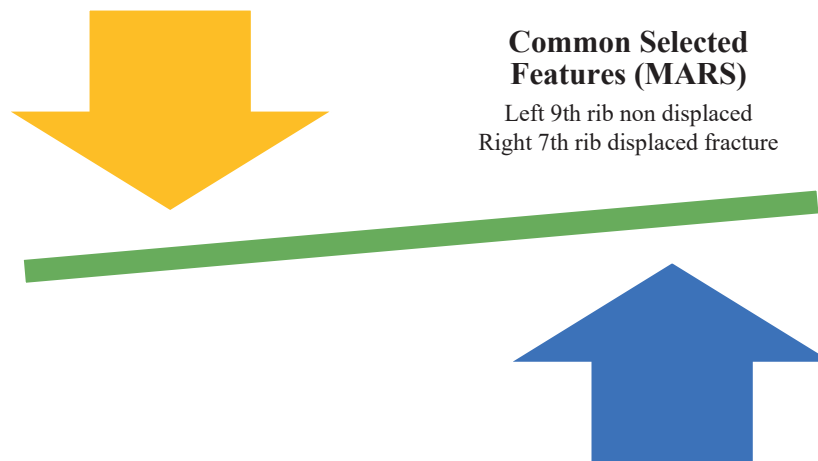
Figure 3. Commonly selected features.

demonstrates that complex non-linear regression can be used to reduce human-induced errors in diagnosis and treatment processes, as well as to aid in medical decision-making.

Discussion

It is very important to determine the age and gender of the corpses that are not recognized in the discipline of forensic medicine. Tülüce and Altuntaş [19] reported that traumatic pneumothorax is a very important pathology that requires early intervention due to rib fractures and contusion, Ergün and Topuz [20] reported that mortality is high in fracture patients accompanied by a chest injury, Dumanli et al [7] emphasized that the coexistence of vertebral and costal fractures in trauma patients should be kept in mind, and diagnosis and treatment planning should be made accordingly. In this study, in light of the literature, criteria such as fractures or cracks, bruises and injuries in the body were reviewed while determining the first criteria to be considered in the estimation of gender and age. Those who experienced trauma after a traffic accident and fell from a height were included in the study. These patients had rib fractures as well as possible thoracic vertebral fractures and thoracic pathologies. The factors seen in these patients were first reduced and then the most important variables were found. The basis of the data used in the study was traffic accidents and falls from height, which could be the subject of forensic medicine. In Table 2, as a result of the treatment method applied according to the etiopathology of the diseases, 58.7% of the traffic accidents were treated with surgical methods, 41.3% with medical methods, and as a result of falling from a height, 71.1% were treated with surgical methods and 28.9% with medical methods.

In this study, characteristics that should be considered in estimating age and gender were estimated using the regression curve technique. It has been suggested that deep learning, artificial intelligence and machine learning algorithms or complex nonlinear regression problems can be used in forensic applications.

Conclusion

A person may need recognition and separation from others for any reason. Both the government and the person's relatives attach great importance to this scenario. In these cases, forensic medicine institutions provide assistance. A person's identity consists of all the characteristics that allow identification and distinguish him from other people. A person may need recognition and separation from others for any reason. Using the complex nonlinear regression method on photographs of patients with spine and / or rib fractures and patients with thoracic vertebral fractures, this study identified the first features to consider when determining the age and sex of patients. X-rays were taken first. Patients with spine and/or rib fractures and patients with thoracic vertebral fractures were classified in a database by looking at these photographs. As a result, analysis of fractures or cracks seems to offer valuable information as a starting point for research. However, it is clear that the purpose of such a classification is to arrive at a general conclusion rather than a definitive answer. Accuracy rates are expected to serve as a guideline for the study to have appropriate evidential value. This research seeks to guide future research. As a result, machine learning algorithms or complex nonlinear regression problems used in forensics could help open the door to more experimental work in other disciplines. It is estimated that these people will be a new guide to the authorities when it is determined that the people who suddenly disappeared are buried in a place years later.

Conflict of interest

The authors declared no conflicts of interest.

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