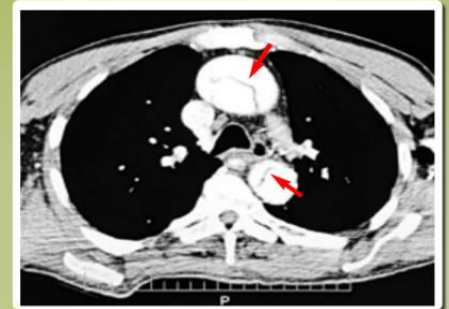
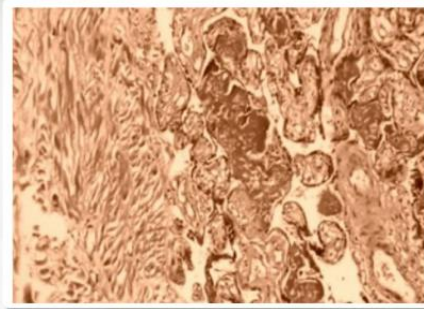
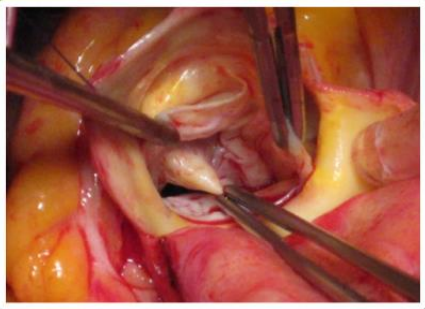




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Alternative cannulation techniques in surgical repair for acute type A aortic dissection

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In this issue of the *European Research Journal*, Yalcin *et al.* [1] reported an experience with ascending aorta cannulation for surgical repair in a case with acute type A aortic dissection (AAAD). This presentation raises many questions that should be answered by the authors. They reported direct true lumen cannulation of the ascending aorta under visual control but this technique has not clearly been explained in detail. How was the aortic cannula introduced? What was arterial systolic pressure before procedure? Was venous exsanguination from the right atrium performed? The answers to these questions have not been explicitly stated in the text. Another very important issue is cerebral protection. There is also no information about protection of the brain during the open distal anastomosis. The technique has not satisfactorily been discussed. Despite all these shortcomings, the authors are to be congratulated on their successful dissection repair with this technique and for bringing it to our attention. I would also like to share additional comments on alternative cannulation techniques for arterial inflow in these complicated patients.

AAAD is one of the life-threatening cardiovascular conditions and associated with an increased risk of mortality and morbidity. It requires immediate surgical intervention to avoid catastrophic complications such as aortic rupture or organ malperfusion (brain or visceral). The most important stages for successful surgical treatment of AAAD include the excision of the primary entry tear in the aorta, the elimination of aortic valve insufficiency, and the establishment of the

true lumen flow to correct the distal malperfusion [2].

The best arterial cannulation site for a prompt induction of CPB in surgical repair of AAAD remains controversial [3]. The most important objective for the arterial cannulation in this lethal condition is to allow antegrade blood flow through the true lumen. The choice of arterial inflow site is influenced by many factors including hemodynamic instability (cardiac tamponade or shock), the presence of malperfusion, the extent of dissection, possible involvement of the cannulation site, peripheral vascular disease, a history of stroke, the patient's age or the preference of the surgeon.

Many different inflow sites for arterial cannulation have been described. Possible access points for cannulation include the femoral artery, the axillary artery, the brachial artery, the innominate artery, the carotid artery, the subclavian artery, the ascending aorta, the transverse arch of the aorta, and the left ventricular apex. Each cannulation site has both the advantages and disadvantages [3].

In current cardiovascular practice, the femoral arteries and the axillary arteries are the most commonly used cannulation sites for repair of AAAD. Excellent results have been reported with these arterial inflow sites [4-6]. Femoral artery cannulation is the standard cannulation technique and allows for the rapid institution of CPB in hemodynamically unstable patients with AAAD. However, it has disadvantages of retrograde arterial perfusion such as an increased risk of retrograde cerebral embolization due to atherosclerotic debris or thrombus in the descending

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aortic lumen, stroke, critical organ malperfusion, false lumen enlargement, and the elevation of a dissected intimal flap [3]. Other complications of this technique are lower extremity ischemia, neurologic injury, lymphorrhea, and wound infection. Access site for femoral arterial cannulation is not suitable in the presence of atherosclerosis of the femoral vessels, severe peripheral occlusive disease, aorto-iliac aneurysms, and distal extension of the aortic dissection. In a retrospective study, Fusco *et al.* [4] cannulated the femoral artery for arterial access in 79 patients with AAAD. They reported that this cannulation technique is associated with a low malperfusion rate of 2.5%. The authors conclude that femoral artery cannulation is an appropriate choice and provides satisfactory postoperative outcomes.

The technique allowing antegrade perfusion is a good option, particularly in patients with AAAD. In contrast to femoral cannulation, axillary artery cannulation is a widely used approach for antegrade arterial perfusion to prevent cerebral and visceral complications in surgical repair of AAAD [5]. It also allows safely the extended utilization in aortic surgery and complex cardiac procedures [6]. The advantages of this cannulation technique include antegrade perfusion of the true lumen in aortic dissection, elimination of the risk of retrograde embolization, low risk of malperfusion, and the possibility to apply antegrade cerebral perfusion. However, the disadvantages of this approach are the necessity for an additional skin incision, and the possible small caliber of the axillary artery. Therefore, this technique is presumably more time consuming, especially in obese patients, and not always free from risk [7]. Although rare in experienced hands, it also has potential complications such as brachial plexus injury, axillary artery damage, axillary artery thrombosis, arm ischemia, lymphocele, and local wound infection [6]. This cannulation is not suitable in patients with hemodynamic instability. The patients with dissection extending into the innominate artery or the subclavian artery also have a risk of retrograde carotid dissection resulting in cerebral malperfusion [3]. The right axillary artery is rarely affected by the dissection process and may be cannulated either directly or interposing a vascular graft. In our institute we mostly prefer direct right axillary cannulation in patients with AAAD. In a study with direct axillary artery cannulation, we found no major complications regarding this technique [5]. Therefore, we think that

this cannulation procedure is easy to establish and may safely be used for arterial access in AAAD [3, 5].

The carotid artery may also be proposed for selected patients, as another possible alternative site for cannulation. Urbanski *et al.* [8] performed right carotid artery cannulation in 100 patients, including 27 with AAAD. This procedure offers the possibility of antegrade arterial flow during CPB and selective cerebral perfusion during aortic arch repair. However, it also carries the risk of cerebral malperfusion and local complications related to cannulation site. Innominate artery cannulation is also the preferred alternative cannulation technique for antegrade perfusion. This cannulation technique has a larger arterial access. It also does provide more central flow, does carry a low risk of neurological complications, and does not require an additional skin incision during surgery. Preventza *et al.* [9] cannulated the innominate artery with a side-graft in 263 patients undergoing the proximal aortic surgery. In their study, 27 (10.3%) patients had acute or subacute Type I aortic dissection. The mortality rate was 4.9% and postoperative stroke was 3.4% [9].

Ascending aorta cannulation, also referred to as central cannulation, is a challenging alternative technique for arterial cannulation in the complicated situations such as hemodynamic instability or when other cannulation options are not suitable for patients with AAAD [3, 10, 11]. It provides an advantage of antegrade perfusion but has the risk of the false lumen cannulation, which might lead to aortic rupture, or malperfusion [11]. This cannulation technique includes direct cannulation of the dissected ascending aorta [12-14] or transapical cannulation of the ascending aorta [10]. This technique is not recommended as the first cannulation option. Direct ascending aorta cannulation may be performed by the Seldinger technique (a guide-wire technique) under ultrasonographic guidance [12, 15-19] or direct true lumen cannulation of the dissected ascending aorta under direct visual control [20, 21].

Ascending aorta cannulation using the Seldinger technique is an attractive option for arterial inflow into the true lumen of the dissected ascending aorta to avoid malperfusion and retrograde embolization [19]. In this technique, a perfusion cannula through the guide-wire is inserted easily and safely into the true lumen of the aorta from the non-dissected portion of the aortic wall just beside the pulmonary artery under direct epiaortic ultrasound guidance [12, 19]. Yamada

et al. [19] did not use the purse-string suture for cannula fixation in the aorta to avoid hemorrhage. Ascending aorta cannulation is an appropriate option for rapid establishment of antegrade perfusion in hemodynamically unstable patients with AAAD [11, 12, 17, 18].

Reece *et al.* [15] applied the Seldinger technique for cannula insertion for surgical repair in 24 patients with AAAD. The eligible cannulation site was identified by transesophageal echocardiography and computed tomography. In their study, they did not utilize purse-string suture and the cannula was firmly held in position by hand during the cooling phase. They reported that there was no malperfusion in this series [15]. In addition to the femoral artery, Inoue *et al.* [12] routinely cannulated the ascending aorta using the Seldinger technique, also by epiaortic ultrasound guidance (6 patients), for arterial inflow in 32 patients with AAAD. The aortic perfusion cannula was introduced after aortic decompression by starting CPB with femoral arterial cannulation. Their technique was extremely complicated. CPB perfusion was retrogradely started by the femoral artery and then mean arterial pressure was reduced below 60 mmHg prior to the ascending aorta cannulation. Antegrade systemic perfusion was performed by aortic cannulation. These authors used purse-string suture for cannula fixation. In their study, the rate of false lumen cannulation was 12.5%, but they had satisfactory results with no clinical end-organ malperfusion [12].

Recently, Taguchi *et al.* [18] also used similarly a hybrid technique in 29 patients as described by Inoue *et al.* [12] with starting femoral arterial cannulation (retrograde flow) followed by ascending aorta cannulation (antegrade flow) using the Seldinger technique for cannula insertion. In both studies, reversing the blood flow before the repair can lead to adverse effects. The authors reported that all insertions (guide-wire or cannula) using this technique were only guided by transesophageal echocardiography. The authors also conclude that the proposed skills for this cannulation are careful evaluation of needle insertion site, feeling the resistance of needle insertion twice, and security of guide-wire in the aorta [18].

Ascending aorta cannulation is not an appropriate option in patients with thrombosed false lumen or intramural hematoma [15, 18]. In these situations, thrombosed false lumen dilatation during the insertion procedure is associated with possibility of complications such as disastrous thromboembolism.

In patients with circumferential dissection of the entire ascending aorta, the false lumen constitutes a large portion of the aortic lumen. Therefore, this technique may be difficult to enter the true lumen [19]. The risks related to cannulation of the dissected ascending aorta are false lumen cannulation, potential malperfusion, extension of the dissection, and aortic complete rupture as a result of tearing the fragile aortic wall. Therefore, Seldinger technique should be applied to the diseased aorta very gently [17, 18]. Ascending aorta cannulation has some advantages such as a low risk of malperfusion and retrograde cerebral embolism, ease of rapid induction of antegrade perfusion in hemodynamically unstable situations, and suitability in dissections extending into the innominate artery [18].

In a recent study of 14 cases, Gobolos *et al.* [17] reported an innovative ultrasound-guided direct true lumen cannulation on the concavity of the aortic arch at the level of Botallo's ligament by Seldinger technique. With their technique there was no need for purse-string suture for cannula fixation in the aorta. The cannula was attached to the skin incision with a suture. In this study, there were no operative mortality and permanent neurological deficits.

Direct cannulation of the dissected ascending aorta in 122 patients with AAAD was presented by Hannover group [13]. In contrast to other groups, their technique includes direct approach to the the aorta (conventional cannulation) in a less dissected or non-dissected area. This cannulation site was identified by preoperative computed tomography and intraoperative transesophageal echocardiography. They cannulated the ascending aorta at the site of the minimal distances of the dissected layers and used double purse-string sutures for cannula fixation. They showed that this technique is a safe option with malperfusion in 3 (2.5%) patients, aortic rupture in 1 (0.8%) patient, and hospital mortality in 18 (15%) patients [13].

Direct true lumen cannulation of the ascending aorta is another valid means as antegrade perfusion route in surgical repair of AAAD. This technique particularly may be recommended in patients with circumferential ascending aortic dissection, narrowed true lumen at the aorta, and the true lumen located on the posterior aspect of the aorta. Prevention of bleeding around the aortic cannula is provided either with a cross-clamp or with a snare passed around the aorta. The most important drawbacks of this cannulation technique is the possibility of rupture risk

of the aorta in this area during the separation between the adventitial layers of the ascending aorta and the pulmonary artery. Jakob *et al.* [20], in 2007, reported an experience with direct cannulation of the ascending aorta in 8 patients with AAAD. The technique consists of venous exsanguination, direct true lumen cannulation of the ascending aorta under direct vision (arterial systolic pressure at that time is 30 mmHg or less), controlled de-airing, followed by standard CPB after proximal aortic clamping. This technique process completes in less than ninety minutes [20]. Conzelman *et al.* [21] also reported their experience with 29 patients with AAAD using a similar technique as described by Jakob *et al.* [20]. The authors described that the ascending aorta was completely transected after venous exsanguination and the aortic true lumen was identified. An arterial cannula was directly inserted into the true lumen under direct visual control. Lastly, the arterial cannula was anchored with a ligature. In their report, the only minor technical difference was usage of the snare around the ascending aorta to fix cannula and to prevent bleeding around the cannula. There was no hospital mortality and temporary hemiplegia occurred in 4 (14%) patients. The authors conclude that direct true lumen cannulation is an encouraging technique with good results [21].

Tiwari *et al.* [22] reviewing 14 publications (the best evidence topic) compared ascending aorta cannulation and peripheral arterial cannulation for surgical repair of AAAD. The authors determined that central cannulation has a lower mortality rate but a higher stroke rate. They conclude that direct true lumen cannulation is a promising cannulation technique for quick and easy institution of CPB [22]. In contrast, artery cannulation was a remarkable choice according to all results when compared with central cannulation. Reece *et al.* [15] compared retrospectively the results of ascending aorta cannulation (n=24) versus peripheral arterial cannulation (n=46). They demonstrated that the peripheral cannulation group had a higher 30-day mortality rate than the central cannulation group (19.5% versus 4.2%; $p < 0.05$) [15]. From their experience of 235 patients on long-term survival, Kamiya *et al.* [23] analyzed the results of ascending aorta cannulation (82 patients) and femoral artery cannulation (153 patients) for AAAD. Although the 30-day mortality rate was lower in the aortic cannulation group (14% versus 23% in the femoral group), the difference was not statistically significant

($p = 0.07$). In this study, they also reported that the cannulation technique had no impact on long-term survival [23]. Suzuki *et al.* [16] compared central cannulation (n=26) and peripheral cannulation (n=51). In their study, an arterial cannula was inserted using the Seldinger technique under ultrasound guidance. The mortality rate was 4% in the central group and 8% in the peripheral group ($p = 0.45$). They showed that direct central cannulation has equal or superior clinical outcomes when compared to the peripheral cannulation.

In a recent study of 117 patients, Klotz *et al.* [11] analyzed the outcome after initial femoral arterial cannulation (53.1%) versus the central cannulation (46.9%) for AAAD in the last 10 years. In this study, there was no significant difference in term of the 30-day mortality and postoperative cerebral infarction between the cannulation groups (20% vs 17% , $p = 0.699$ in the central cannulation and 13% vs 9% , $p = 0.449$ in the peripheral cannulation). They reported similar results with both cannulation techniques for surgical repair of AAAD.

Wada *et al.* [24] retrospectively analyzed two different central cannulation techniques including direct ascending aorta cannulation (n=20) using the Seldinger technique and transapical aortic cannulation (n=6). They reported that excellent early results could be obtained by these cannulation techniques. There is no single best cannulation techniques. Therefore, the technique should be selected according to each patient's individual characteristics.

In ascending aorta cannulation, the relationship of the true and false lumens in the ascending aorta play an important role. In a study of 88 patients, Frederick *et al.* [14] classified three levels of distinct dissection anatomy. These anatomic variants affect the strategy of cannulation. A detailed examination of the preoperative computed tomographic angiogram shows the relationship of the true and false lumens in the ascending aorta and arch. This correlation is verified by visual inspection and intraoperative transesophageal echocardiography. The true lumen is localized anteriorly in the ascending aorta at Level 1, the true lumen is posterior and the false lumen is anterior at Level 2, and there is a free-floating ascending aortic true lumen at Level 3 [14]. The authors successfully underwent ascending aorta cannulation using the Seldinger technique guided by preoperative computed tomographic angiographic study and intraoperative transesophageal echocardiographic examination to assess guide-wire

access to the aortic true lumen [14].

Transapical aortic cannulation for establishing CPB is also a remarkable technique. The arterial cannula is inserted through an apical ventriculotomy (1 cm hole) into the left ventricle and then across the aortic valve directly into the true lumen of the ascending aorta guided by transesophageal echocardiography. Transapical aortic cannulation has some advantages including easy and fast procedure, adequate antegrade perfusion, and possible true lumen perfusion with low risk of cerebral embolization and organ malperfusion [10]. The disadvantages of this technique is the prolonged CPB time and the inability to additional procedures during cooling phase. This cannulation technique is not suitable in patients with severe aortic stenosis or undergoing redo median sternotomy. Another serious problem related to this technique is bleeding from cannulation site at the left ventricular apex. This problem might be overcome by performing simple stab-wound cannulation and closing the incision with interrupted sutures with pledgets. In a large cohort of 138 patients, including 129 patients with AAAD, Wada *et al.* [10] showed the safety and usefulness of transapical aortic cannulation for establishing CPB in surgical repair of AAAD. They reported good results without malperfusion events, but the hospital mortality rate was 18.8% (26 patients). In their study, these deaths were due to organ ischemia from malperfusion existing before the operation [10]. The cause of these deaths was the presence of preoperative malperfusion resulting in the organ ischemia.

As a cardiovascular surgeon, we must be familiar with alternative cannulation techniques in surgical repair for AAAD. It should be kept in mind that ascending aorta cannulation technique could be applied to provide antegrade flow for well-selected patients. It is more appropriate to wait the results confirmed by further studies in a larger group of patients for a general recommendation related to the best arterial cannulation technique in this complicated pathology.

Competing interests

The authors declare that they have no competing interests with respect to the authorship and/or publication of this article.

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The analysis of occupational satisfaction of resident physicians having emergency medicine education

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ABSTRACT

Objectives. The personnel of Emergency Service (ES) is under stress due to the intensity of the resulting from the very nature of the work to be performed in this department, which is characterized by the need of providing rapidly medical care to patients with often severe or even life-treating health problem and by though working conditions. In our study, we aimed to determine the satisfaction of resident physicians about choosing the emergency medicine, the factors affecting this satisfaction, and the plans of these resident doctors. **Methods.** In our study, we surveyed 66 resident physicians working in 4 emergency centres. The resident physicians completed the survey form given to them. **Results.** Regarding the occupational satisfaction of 66 resident physicians participating working in emergency medicine department, we obtained the following results: 54.5% (n=36) satisfied, 22.7% (n=15) not satisfied, 9.1% (n=6) more satisfied than expected, and 9.1% (n=6) neither satisfied nor not satisfied. When the opinions of residents were asked about how likely it was that they would be working in emergency medicine in 10 years hence, 40.9% (n=27) of the participants stated that they wanted to work there, 36.4% (n=24) stated that they were not sure, and 22.7% (n=15) stated that they didn't want to work. **Conclusions.** The encouraging legal regulations in regard to physicians' rights about working in emergency medicine branch should be revised, working conditions should be improved, and it is important to provide young doctors with carrier and educational opportunities. Otherwise, it is likely that we might lose our national and international achievements in emergency medicine branch.

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Keywords: Emergency medicine; burnout syndrome; resident physician education

Introduction

The personnel of Emergency Service (ES) is under stress due to the intensity of the department, the often severe health problems of the patients that receive the healthcare service there and the intense work schedules. Besides this pressure at work, the deteriorated social, familial and friendship

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relationships of the ES personnel are the main factors preparing the ground for burning out over the years[1]. The performed studies indicate that the rate of burn out in first ten years following the resident physician practice period is 1.5% [2]. According to the results of the research of Keller and Koenig, while still 53% of ES physicians stated that they were planning to work actively in ES after ten years, only 24% made this statement for 20 years later [3]. The major stressors affecting the resident physicians are seen to be too many patient examinations during the resident period, patient deaths, deterioration of the sleeping order, and long working hours [4]. In addition to them, working with difficult cases, problems in professional relationships, insufficient resources, and challenging and critical decisions also play a significant role in the development of burnout syndrome. It has been emphasized that 1 of every eight residents has significant stress syndrome and experiences emotional problems [5].

In our study, we aimed to determine the satisfaction of resident physicians, who are in emergency medicine education that has 20 years of history in our country, about choosing the emergency medicine, the factors affecting this satisfaction, and the future plans of these resident physicians. In addition, we wanted to determine the reasons for personnel problems in emergency healthcare services, an important problem in our country, and suggest possible solutions for it.

Methods

In our study, 66 resident physicians having emergency medicine education in 4 emergency medicine clinics (two university clinics and two education and research hospitals) have participated in our study. We reached the whole of the resident physician in study clinics. The resident physicians have filled the survey form given to them.

Statistical analysis

IBM Corp. (2012) IBM SPSS Statistics for Windows. Version 22.0 Armonk, NY: IBM Corp; 2012 Program was used for statistical analysis.

Results

In our study, 66 resident physicians having emergency medicine education in two university clinics and two education and research hospitals have participated in our study. The ages of participants varied between 25 and 45, with a mean age of 30.18. Among the participants, 65.2% (n=43) of the residents were male, and 34.8% (n=23) were female. In distribution by marital status, it was determined that 56.1% (n=37) were married, 6.1% (n=4) were engaged, and 37.9% (n=25) were single. In distribution by duration of working as resident physician, it was determined that 34.8% (n=23) of the participants had 25-36 month of experience, 25.8% (n=17) had 13-24 months, 21.2% (n=14) had 7-12 months, 9.1% (n=6) had 0-6 months, and 3% (n=2) had 49+ months. From the aspect of total years of experience in emergency service department, 39.4% (n=26) had been working in emergency service department for 3-6 years, 37.25% (n=25) for 1-3 years, 12.1% (n=8) for 0-1 year, 4.5% (n=3) for 6-10 years, and 4.5% (n=3) for 10 years or longer. While 45.5% (n=30) of resident physicians were working in a university hospital, 54.5% (n=36) were working in education and research hospitals. When the participants were asked about their emergency medicine choice in the medical specialty examination, 39.4% (n=26) stated that the rank was 5 or less. The portion of the ones that have chosen emergency medicine within first three preferences was 53% (n=35). The reasons for residents to choose emergency medicine specialty are presented in (Figure 1).

Accordingly, while 33.3% (n=22) stated that it was the branch, in which they wanted to work, 22.7% (n=15) said that they chose this branch because emergency medicine specialty was preferable for the future. While evaluating the satisfaction of working in emergency medicine branch, 54.5% (n=36) stated that they were satisfied (Figure 2).

Of the resident physicians, 40.9% (n=27) emphasized that their dissatisfaction was due to their hospital, 25.8% (n=22) stressed that the dissatisfaction would disappear after changing the hospital, and 25.8% (n=17) stated that changing the hospital would impact their level of dissatisfaction. Of the resident physicians, 27.3% (n=18) have emphasized that they were planning to work in 2nd step hospital in the future (Table 1).

The question about whether the emergency medicine residents are planning to work in emergency medicine branch in coming ten years was answered



Figure 1. Reasons to choose the field of emergency medicine resident

Table 1. The future plans of the emergency medicine residents

Future plans	n (%)
2 nd Step Public Hospital	18 (27.3)
2 nd Step Private Hospital	12 (18.2)
Staff at University Hospital	12 (18.2)
Staff at Training and Research Hospital	8 (12.1)
Not the Clinician	9 (13.6)
Work Outside the Health Sector	7 (10.6)

Table 2. Preferred choice other than emergency medicine?

Province	n (%)
Unanswered	12 (18.2)
Emergency Medicine	11 (16.7)
Forensic Medicine	1 (1.5)
Family Medicine	1 (1.5)
Anesthesia	4 (6.1)
Biochemistry	3 (4.5)
Dermatology	4 (6.1)
Physical Therapy and Rehabilitation	10 (15.2)
General Surgery	1 (1.5)
Ophthalmology	1 (1.5)
Obstetrics and Gynecology	1 (1.5)
Ear Nose Throat Surgery	1 (1.5)
Neurology	1 (1.5)
Orthopedics	3 (4.5)
Psychiatry	1 (1.5)
Radiological	11 (16.7)

positively by only 40.9% (n=27) of the participants. They also were asked about which branch they would be likely to choose if given that option According to their answers (see Table 2), 16.7% (n=11) responded that they would choose emergency medicine again.

Discussion

Work environment describes the whole of working conditions being effective on individual and his/her behaviours [6]. When evaluated together with night works, the working hours of the physicians, regarding working conditions, are seen to be risky, tiresome, and long when compared with other professions. A study carried out on healthcare personnel working in healthcare institutions in the city centre of Manisa showed that the working times increased the burnout. Within this context, the emotional exhaustion scores of the individuals having worked in cottage hospitals for ten years or longer were found to be higher [7]. In performed studies, the rate of exhaustion in first ten years following the resident physician period was found to be 1.5% per year [2]. According to the results of the research of Keller and Koenig [3], 53% of ES physicians stated that they would like to work actively in ES after ten years while only 24% made this statement for 20 years later. In our study, 63.6% of the residents seemed to be pleased about their choices. 25.8% of the residents thought that changing the hospital would not have effect regarding the

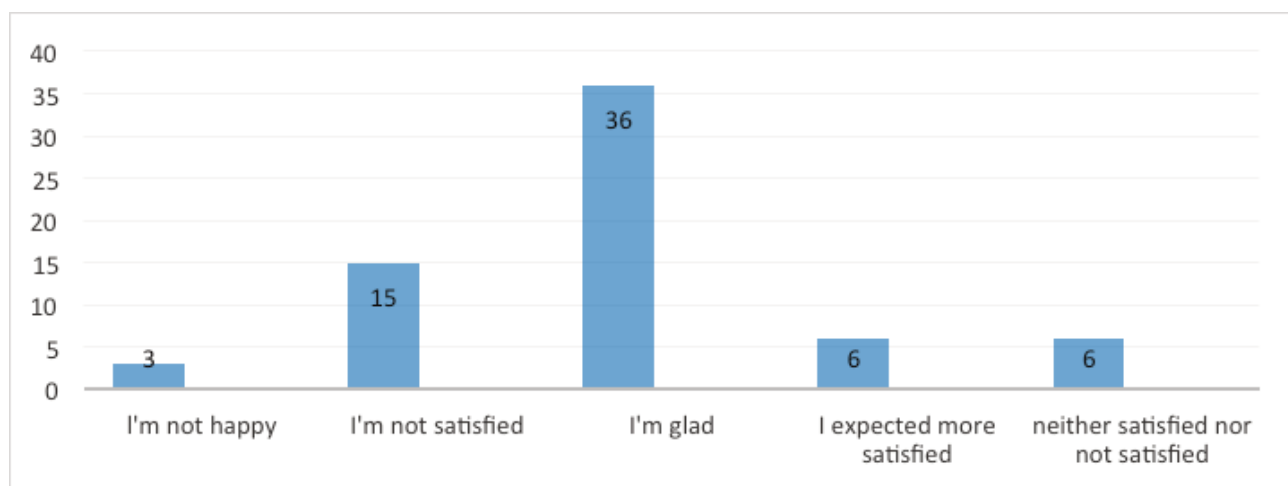


Figure 2. The satisfaction level of residents

dissatisfaction.

Moreover, 24.2% of the residents seemed to plan to quit working actively as physician or to work in professions that were not related to healthcare at all. In questioning the willingness of the emergency medicine residents about working in emergency medicine branch after ten years, only 40.9% of the residents considered this as likely. In a study of Keller and Koenig, the percentage of 54% found in the eagerness to work in emergency medicine branch after ten years is higher than the portion found in our study, and it indicated that the weight of the working conditions in emergency services are sufficient [3]. In the study of Sen J. et al., the emergency medicine positions' rate of being preferred in our country has been examined. In that study, the data of the period between years 2007 and 2012 were reviewed, and the rate of graduation from emergency medicine resident programs was found to be 66.1% [8]. Also, in a study carried out by the young physicians in Europe, was determined that 50% of the physicians felt disenchanted about their professional choice while 60% felt pleased and 33% felt significantly dissatisfied with the working conditions [9]. In a report prepared in 2012 upon request of the Ministry of Health, the reasons for the dissatisfaction of emergency medicine resident and the reasons for manpower shortage in many emergency departments were listed [10]. According to our study, the 54.5% of the satisfaction rate of our residents seems to be a lower satisfaction rate. The intensity of emergency services in our country and the workloads affect the level of the satisfaction of our residents, and only 1 out of every two persons seems to be satisfied. Interestingly, when

the future plans were examined, 24.2% answered that they either did not want to work as physician actively, or that they wanted work in professions outside the healthcare sector. In other words, it is interesting that one out of every four emergency medicine residents is planning not to have any active role in emergency medicine practice in future even if they would become a specialist in this branch.

Moreover, the portion of our residents planning to work in second stop public hospitals, where the employment and need of emergency medicine specialists are at highest level, is only 27.3%, and this portion corresponds with barely 1 out of every four residents. These values lead to the prediction that the problem of persisting shortage of emergency medicine specialists is unlikely to be resolved in short- or even in medium-term.

Consistently with this forecast, the question of "Would you like to choose another branch if you have an opportunity?" directed to emergency medicine residents was answered by only 16.7% residents that they would again choose the emergency medicine branch. The remaining 83.3% stated that they would prefer other branches that have less daily patient application have regular working hours and more quiet working environments. These statements indicate how our emergency department residents feel suffocated. It is seen that only 28.8% of the residents opted emergency medicine as one their first three preferences. in the examination for specialty in medicine (TUS).

Again, in another question, when asked about their reasons for choosing emergency medicine, 44% of the participants stated that selection was based on its

lower score requirement or the working conditions. It is sad to see that according to these data, the primary factor for choosing emergency medicine are at best practical rather than motivated by the willingness to work in this field. The actual conditions led the emergency medicine to become a branch that is chosen due to practical reasons rather than driven by any particular interest and eagerness, and we believe that this situation poses a significant risk for the emergency medicine community, since no abatement of manpower shortage is to be expected. In our study, the portion of those stating that they frequently read professional scientific studies (except while preparing presentations) was found to be only 4.5%. It is clear that this portion is very small. Despite that, 65.1% believe that their education is sufficient. In a study that is carried out on the knowledge level of emergency medicine residents in our country, up to 80% have stated that the knowledge of residents about topics such as cardiovascular emergencies, resuscitation, and trauma is sufficient [11]. The resident physicians' thought about education's sufficiency with the lack of literature reading habit is conflicting. But, even if the educational programs were comprehensive and academically excellent, it doesn't seem possible to gain professional competency without personal effort and habit of reading the publications.

Conclusions

Emergency medicine is still a relatively new medical branch in our country. Many physicians do still not know the limits of emergency medicine specialty. The chronic problems in our national emergency healthcare services and the increasing patient load have converted the need of qualified and enough personnel into a pressing priority. Despite this need in our country, no encouraging changes are made in this branch, and the number of burnouts of specialist-resident physicians working in emergency medicine system keeps increasing. The presence of drawbacks related to being in emergency medicine branch after ten years, even during having specialty education, emphasizes the difficulty of achieving the qualified and enough number of physicians in this branch. Unfortunately, resident physicians start to experience unwillingness about their emergency medicine choice even in their first years of residency program. It is required to make changes to encourage legal regulations towards physicians working in

emergency medicine branch as soon as possible, and to allow young physicians to choose emergency medicine eagerly and willingly. Otherwise, it is likely that we might lose our national and international achievements in emergency medicine that we gained in 20 years at a cost of significant efforts, or these accomplishments might decline.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Can QT dispersion predict multi-vessel coronary artery disease in patients with acute coronary syndrome?

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ABSTRACT

Objectives. This study was planned to evaluate the relation between QT dispersion (QTd) and multi-vessel coronary artery disease in acute coronary syndrome. **Methods.** Two hundreds and twenty-five consecutive patients with a diagnosis of non-ST segment elevation acute coronary syndrome were included. Three groups were defined as a single vessel, two vessels, and three vessels. Echocardiographic, biochemical and electrocardiographic parameters of the groups were compared. **Results.** QTd, corrected QT dispersion (QTcd) and corrected QT max values significantly increased in patients with the three-vessel disease compared to the patients in the single-vessel disease group (60 ± 27 vs. 45 ± 28 ms, 68 ± 32 vs. 50 ± 32 ms and 471 ± 52 vs. 443 ± 48 ms; $p=0.002$, $p=0.001$, and $p=0.001$, respectively). Also, QTd and QTcd were statistically more increased in patients with the two vessels disease than single-vessel disease group (57 ± 29 vs. 45 ± 28 ms; $p=0.045$, and 63 ± 32 vs. 50 ± 32 ms; $p=0.046$, respectively). **Conclusion.** In a patient with acute coronary syndrome and diffuse vessel disease, changes in the myocardial cells due to ischemia cause more of the QT dispersion in the patients with a multi-vessel disease than those with single-vessel disease.

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Keywords: Acute coronary syndrome, coronary artery disease, non-ST segment elevation, myocardial infarction, QT dispersion

Introduction

Ischemic heart disease is the leading cause of mortality worldwide [1]. In patients with multi-vessel coronary artery disease (CAD), hospitalized or not, ischemic events and other related complications may be frequently reported [2]. Therefore, multi-vessel CAD disease has to be defined, and a treatment plan should be made as soon as possible. QT dispersion (QTd) increase by ischemia is reported in various publications [3].

This study was planned to evaluate the relation

between QTd and multi-vessel CAD in acute coronary syndrome (ACS).

Methods

Following the permission of the Local Ethics Committee, the patient files of the Cardiology Department of Bursa Yuksek Ihtisas Training and Research Hospital were reviewed. Between January

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2013 and January 2014, all patients administered to the hospital due to ACS were enrolled in the study. Acute coronary syndrome was defined as presentation with symptoms of ischemia in association with electrocardiographic changes and positive cardiac enzymes. Patients diagnosed with non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA) were included in this study. Clinical information included data on systemic hypertension (HT), diabetes mellitus (DM), dyslipidaemia, smoking, previous history of CAD, including coronary angioplasty or myocardial revascularization, and early family history of CAD. DM was determined by physician report and was based on a fasting blood sugar level ≥ 126 mg/dl or use of antidiabetic medication. Hypertension was physician-reported for systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or use of antihypertensive agents. Hyperlipidaemia was physician reported for total cholesterol ≥ 200 mg/dl, low-density lipoprotein level ≥ 130 mg/dl, or use of cholesterol-lowering medication. Smoking included active or previous tobacco use over ten pack years.

Coronary angiographies were performed in our clinic using the standard Judkins technique [4]. Significant CAD was defined when $>70\%$ luminal diameter narrowing of a major coronary artery in any projection. Congestive heart failure, cardiogenic shock, valvular heart disease, left ventricular hypertrophy, severe HT, uncontrolled DM, serious arrhythmias with hemodynamic instability or heart failure, patients receiving class I or class III antiarrhythmic agents were excluded from the study.

Measurement of QRS Intervals from the 12-Lead ECG

Twelve-lead ECG was recorded using a Schiller AT2 PLUS at a paper speed of 50 mm/sec and a gain of 10 mm per mV with the patient lying supine. QT interval was measured manually from onset of the QRS complex to the end of the T wave, defined as the point of return of the T wave to the isoelectric line. QT interval was corrected for heart rate following Bazett's formula: $QTc = QT/\text{square root of RR}$. QT dispersion (QTd) was calculated as the difference between the longest (QT max) and the shortest QT (QT min) intervals recorded. Corrected QT dispersion (QTcd) was defined as the difference between the maximum and the minimum QTc for a given heart rate [5]. The study protocol was approved by the institutional review board of our Center, and informed consent was obtained from all patients.

Statistical Analysis

SPSS 16.0 statistical program (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. All values are given as mean \pm standard deviation. Mean values of continuous variables were compared between the groups using the Student t test or Mann–Whitney U test, according to whether normally distributed or not, as tested by the Kolmogorov–Smirnov test. A *p* value of less than 0.05 was considered as significant.

Results

During the above described period, a total number

Table 1. Comparison of biochemical variables of groups.

	Group I (n=76)	Group II (n=58)	Group III (n=91)	<i>p</i>
Age(Years)	58 \pm 12	61 \pm 13	60 \pm 12	0.94
Gender				
Male	57	44	66	0.73
Female	19	14	25	0.8
Height (cm)	168 \pm 6	168 \pm 6.5	168 \pm 7	0.61
Weight (kg)	79 \pm 12	77 \pm 11	76 \pm 10	0.82
BMI	28 \pm 4	27 \pm 4	27 \pm 3.5	0.34
Smoking	31 (40%)	24 (41%)	32 (35%)	0.25
DM	16 (21%)	17 (29%)	26 (28%)	0.8
HT	35 (46%)	29 (50%)	51 (55%)	0.35
Total cholesterol (mg/dl)	194 \pm 52	185 \pm 43	205 \pm 53	0.23
LDL (mg/dl)	120 \pm 44	117 \pm 40	127 \pm 46	0.22
HDL (mg/dl)	41 \pm 12	40 \pm 12	44 \pm 17	0.18
Triglyceride (mg/dl)	157 \pm 224	145 \pm 106	160 \pm 148	0.16

Data are presented as means \pm SD. BMI=Body mass index, DM=diabetes mellitus, HDL=High-density lipoprotein, HT=hypertension, LDL=Low-density lipoprotein

Table 2. Comparison of electrocardiographical features of groups.

	Group I (n=76)	Group II (n=58)	Group III (n=91)	p (I-II)	p (I-III)	p (II-III)
R-R (ms)	857±187	831±155	809±155	0.11	0.11	0.79
QTmax (ms)	405±42	411±50	421±52	0.14	0.56	0.9
QTc max (ms)	443±48	453±48	471±52	0.56	0.001	0.69
QTmin (ms)	360±35	353±40	361±45	0.19	0.10	0.74
QTcmin (ms)	393±35	390±36	403±40	0.88	0.19	0.31
QTd (ms)	45±28	57±29	60±27	0.045	0.002	0.34
QTcd (ms)	50±32	63±32	68±32	0.046	0.001	0.55

Data are presented as means ± SD. Max=maximum, Min=minimum, QTc=corrected QT, QTd=QT dispersion, QTcd=corrected QT dispersion

of 225 consecutive patients with a diagnosis of non-ST segment elevation ACS (NST-ACS) were hospitalized in our hospital. The study population was classified according to their number of lesions of coronary artery disease. Seventy-six patients with the single-vessel disease were defined as the group I, fifty-eight patients with the two-vessels disease were defined as group II and ninety-one patients with three-vessels disease were defined as group III.

The demographic, clinical, echocardiographic, biochemical, electrocardiographic and angiographic data of the three groups were compared (Table 1). There were no statistically significant differences in age, gender, weight, height, smoking, BMI, hypertension and diabetes mellitus among all three groups.

When ECG parameters are examined; comparison of group III to the group I, QTd (60±27 versus 45±28 ms; $p=0.002$), QTcd (68±32 versus 50±32 ms; $p=0.001$), QTc max (471±52 versus 443±48 ms; $p=0.001$) values seem significantly high. On the other hand, the comparison between group II and the group I shows us that group II's QTd (57±29 versus 45±28 ms; $p=0.045$) and QTcd (63±32 versus 50±32 ms; $p=0.046$) statistical values are obviously higher. When the three-vessels disease group compared with the two-vessels disease group, all ECG parameters didn't show a noticeable difference. And also, all three groups R-R, QT max, QT min, QTc min values did not have any difference (Table 2).

Discussion

Our study showed that QTd, QTcd, and QTc max values significantly increased in patients with the three-vessel disease compared to the patients with

single-vessel disease group. In addition to this, QTd and QTcd were more increased in patients with the two-vessel disease than single-vessel disease group.

Cardiovascular disease is the most significant cause of mortality and morbidity all around the world [1]. All ischemic events develop rapidly in the myocardial tissue and cause myocardial injury in ACS patients [6, 7]. Therefore, mortality, morbidity, and prognosis were mostly determined by the number of diseased vessels in acute coronary syndrome patients. In 2007, Mallika *et al.* [6] reported a study including modification of the classic ischemic cascade concept, demonstrating in 100% of cases studied that the earliest event in ischemia is QTc interval prolongation and its increased dispersion. The early appearance of QTc interval abnormalities is precisely one of its greatest advantages for ACS diagnosis since it provides evidence of the disease when, in many cases, ST-segment abnormalities have not yet been demonstrated [3].

QT interval shows the ventricle muscle repolarization and depolarization times. The difference between QT max and QT min interval named as QT dispersion. This term is used to describe heterogeneous ventricular repolarization, and an increase in QTd has been shown to heighten the risk of serious arrhythmias and sudden cardiac death. Some studies reported that patients with the triple-vessel disease had higher QTd [8]. A study in Buenos Aires, Argentina, involving patients with typical symptoms and enzyme abnormalities compatible with ischemia but without ST changes on EKG, found prolonged QTc interval and increased dispersion, primarily in cases with adverse clinical events [3].

Most clinical and experimental studies show that primary and secondary QT intervals constitute a substantial predisposition factor for ventricular

arrhythmia [9, 10]. Elongation of the repolarization time increases the risk of arrhythmia but not always cause ventricular arrhythmias. For the ventricular arrhythmia, main trigger factor is the repolarization's non-uniform character. For the first time, the relationship between the repolarization's non-uniform character and a decrease of the ventricular fibrillation threshold was shown by Han and Moe in 1964 [11]. In electrophysiological studies, the connection between heterogeneous repolarization and arrhythmia induction were supported [12, 13].

In the setting of cardiac ischemia, evidence suggests that QT prolongation in the surface ECG represents delayed and non-uniform recovery of repolarization in areas of ischemia or infarction. The underlying mechanism is due to elevation of extracellular potassium level, acidosis, and anoxia occurring during ischemia. These conditions cause a reduction in membrane excitability, shortening of action potential duration, and prolongation of excitability recovery following an action potential [14].

The Limitations of the Study

The weak points of our study include a small number of patients, lack of classification according to scoring systems (i.e. Syntax), and detailed measurements using digital devices.

Conclusions

In our study, we found that in patients with ACS and diffuse vessel disease, changes in the myocardial cells due to ischemia (ischemic damage, delay of the electrical message, elongation of the action potential) cause more change in the QT dispersion in patients with a multi-vessel disease than those with single-vessel disease. A thorough search of the English literature available to us revealed that our study is probably the first study concerning determining the number of diseased vessels and by using QT dispersion. Higher QTd values may alert the physician to possible multi-vessel disease and patients requiring prompt invasive measures.

We conclude that further studies with larger

number of patients may prove useful information concerning the value of QTd in treating ACS patients.

Conflict of interest

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Clinical importance of preoperative fine needle aspiration biopsy and computed tomography in parotid gland masses

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ABSTRACT

Objectives. To determine the diagnostic value of fine needle aspiration biopsy (FNAB) and computed tomography (CT) in parotid masses in the basis of postoperative histopathological results. **Methods.** The records of 68 patients diagnosed with a parotid mass and undergone parotid surgery between November 2004 and February 2011 were evaluated retrospectively. Preoperative FNAB and the CT findings were compared with postoperative histopathological findings. **Results.** The study included 36 (58%) female and 26 (42%) male patients. The mean age of the patients was 43.9 years. No statistically significant difference was detected with regards to the performances of both FNAB and the CT ($p=0.797$). When it was evaluated in a detail, the performance of parotid CT (81.82%) to diagnose a mass in parotid gland was relatively better than FNAB (72.73%). The performance of FNAB (94.12%) to detect healthy ones was also greater than parotid CT (90.2%). **Conclusion.** We emphasize that preoperative FNAB and parotid CT should be performed to the patients with a parotid mass. The use of these two tests together can minimize the risk rate have been proved.

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Keywords: Parotid tumors; computed tomography; fine needle aspiration

Introduction

Salivary gland benign and malignant tumours are responsible for 3% of all head-neck tumours and 80% of these tumours result from parotid gland [1].

Parotid salivary gland tumours are frequently observed by the clinician as a mass under the ear. Clinical history and physical examination are indispensable in the diagnostic course of diseases; however, it has a restricted role. It is essential that

parotid salivary gland masses be diagnosed pre-operatively regarding the development of appropriate therapy. If the pre-operative diagnosis is made, the surgeon will have information regarding the issues such as type, duration and limits of operation, even whether surgical treatment is needed or not; and the related patient will be informed. Furthermore, such problems result in unnecessary costs and time waste

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and exposing the patient to unnecessary morbidity, not being able to provide a health cure, and applying unnecessary diagnosis and treatment methods, can be prevented. Therefore, we studied the utilities of FNAB and parotid CT inspections, having a prominent place among pre-operative diagnostic methods, in the proper diagnosis of parotid masses.

In this study we evaluated efficacies and utilities of Fine-Needle Aspiration Biopsy (FNAB) and computed tomography (CT) imaging method, two important diagnostic methods, in parotid salivary gland masses, and to submit them in company with the existing literature by comparing the results of preoperative FNAB, and of CT to those of postoperative histopathological examination.

Methods

Sixty-eight patients, have been operated due to parotid masses, were retrospectively evaluated in our otolaryngology-head and neck surgery clinics between November 2004 and February 2011.

Six patients were excluded from the study due to lack of pre-operative parotid CT (4 patients) and FNAB (2 patients).

All CTs were performed with a "HITACHI Pronto" device. Their parotid CTs were received for consideration by a single senior radiologist, without knowing pathological results, so as to make an preoperative diagnosis FNABs of parotid salivary gland masses without USG assistance, without performing a local anaesthesia, performed by using an injector of 2 cc in 21 gauge (green end -0.8x38 mm injector nozzle) - 22 gauge (black end -0.7x32 mm), by primarily extracting 0.5 cc air into the injector and forwarding the nozzle through lesion fixed by means of free hands, by releasing the air into tissue, and after the nozzle is led inside the lesion with forward and backward movements, by applying negative pressure to the piston and leaving it, and by drawing back the injector. The area was cleaned by using Baticon and four eat least smears were prepared. Preparations were sent to the pathology laboratory in a form of being dried in the air. Preparations were stained with May Grünwald Giemsa.

Parotid salivary gland mass specimens of the cases were sent to the pathology laboratory inside 10% formaldehyde solution on the same day. On the following day, after their macroscopic investigations

were performed, pieces were taken to the tissue observation, and their histopathological examinations were carried out by being stained with Haematoxylin-Eosin.

Performances of diagnostics tests to determine benign-malign tumours were submitted together with sensitivity, selectivity, positive-negative estimation value, the ratio of positive-negative likelihood and the values remaining under the curve. For the performance comparison, P value belonging to whether or not there exists a statistically significant difference in Area under Curve (AUC) values was compared to 0.05. Analyses were performed using Med Calc 11.2.1.0 software.

Results

Sixty-two patients, having been operated due to parotid masses, were included in the study between the dates November 2004 and February 2011. Ages of cases varied from 16 to 66 and the average age were 43.9 ± 11.1 . Gender distribution was in a way of 36 (58%) females and 26 (42%) males.

When examined according to FNAB results, 33 (53.2%) patients were assessed as with pleomorphic adenoma, 12 (19.3%) patients as with Warthin tumour, 6 (9.6%) patients as with mucoepidermoid carcinoma, 4 (6.4%) patients as with adenoid cystic carcinoma, 2(3.2%) patients as with basal cell adenoma, 2 (3.2%) patients as with oncocytoma, 1 (1.6%) patients as with adipose tissue, 1 (1.6%) patients as with squamous cell carcinoma, and 1 (1.6%) patients as with infected cyst.

When parotid CT early diagnostics results were examined, 2 (3.2%) patients were, without giving any specific diagnosis, reported as with benign lesion, 1 (1.6%) patients, without giving any specific diagnosis, as with malign lesion, 25 (37%) patients as with pleomorphic adenoma (PMA), 17 (19.3%) patients as with Warthin tumour (WT), 8 (12.9%) as with mucoepidermoid carcinoma (MEC), 5 (8%) patients as with adenoid cystic carcinoma (ACC), 3 (4.8%) patients as with lymphadenopathy, and 1 (1.6%) patients as with lipoma.

When histopathological examination results were examined, 32 (51.6%) patients were founded as with PMA, 12 (19.3%) patients as with WT, 7 (11.2%) patients as with MEC, 4 (6.4%) patients as with basal cell adenoma (BCA), 3 (4.8%) patients as with ACC, 2 (3.2%) patients as with oncocytoma, 1 (1.6%)

Table 1. The correlation between FNAB results and histopathological results

FNAB RESULTS	HISTOPATHOLOGICAL RESULTS							
	PMA	WT	MEC	ACC	BCC	OC	SCC	Lipoma
PMA	28 (87.5%)	2 (16.6%)		1 (33.3%)	2 (50%)			
WT	2 (6.2%)	8 (66.6%)	2 (28.5%)					
MEC		1 (8.3%)	4 (57.1%)				1 (100%)	
ACC	2 (6.2%)			2 (66.6%)				
BCC					2 (50%)			
OC						2 (100%)		
SCC			1 (14.2%)					
Lipoma								1 (100%)
IC		1 (8.3%)						

PMA= pleomorphic adenoma, WT= warthin tumor, MEC= mucoepidermoid cancer, ACC= adenoid cystic carcinoma, BCC= basal cell cancer, OC= oncocytoma, SCC= squamous cell carcinoma, IC= infected cyst

patients as with squamous cell carcinoma (SCC), and 1 (1.6%) patients as with lipoma.

According to the FNAB results, 28 of 33 patients reported as PMA were diagnosed as with PMA, 2 of them as with BCA, 2 of them as with WT, and 1 of them as with ACC. Specimen results of 8 of the 12 patients called as with WT were as with WT, those of 2 of them as with PMA, and those of 2 of them as with MEC.

FNAB results of 6 patients diagnosed as with

MEC resulted as 4 MEC, 1 SCC, and 1 WT according to histopathological examination. FNAB results of 4 patients diagnosed as with ACC resulted as 2 PMA and 2 ACC. FNAB results of 2 patients diagnosed as with oncocytoma were as they had been diagnosed according to histopathological examination. FNAB results of 2 patients diagnosed as with basal cell adenoma were as they had been diagnosed. FNAB result of a patient diagnosed as lipoma was reported as with lipoma. FNAB result of a patient diagnosed as

Table 2. Parotid CT results and histopathological results correlation

PAROTID CT RESULTS	HISTOPATHOLOGICAL RESULTS							
	PMA	WT	MEC	ACC	BCC	OC	SCC	Lipoma
PMA	20 (62.5%)	3 (25%)			2 (50%)			
WT	8 (25%)	6 (50%)	1 (14.2%)	1 (33.3%)		1 (50%)		
MEC	1 (3.1%)	1 (8.3%)	3 (42.8%)	1 (33.3%)		1 (50%)	1 (100%)	
ACC	1 (3.1%)	1 (8.3%)	2 (28.5%)	1 (33.3%)				
LAP	1 (3.1%)				2 (50%)			
Lipoma								1 (100%)
BT	1 (3.1%)	1 (8.3%)						
MT			1 (14.2%)					

CT= computed tomography, PMA= pleomorphic adenoma, WT= warthin tumor, MEC= mucoepidermoid cancer, ACC= adenoid cystic carcinoma, BCC= basal cell cancer, OC= oncocytoma, SCC= squamous cell carcinoma, LAP=lymphadenopathy, BT= benign tumor, MT= malign tumor

with SCC was reported as with MEC, and a patient diagnosed as with infected cyst by FNAB was reported as with WT (Table 1).

Two patients only diagnosed as with benign lesion by not being able to establish an early diagnosis according to the result of parotid CT, one of them was reported as with PMA and the other one as with Warthin tumor according to the result of the histopathological examination. Histopathological examination result of one patient was resulted as with MEC, which was diagnosed as malign tumor by not being able to give an early diagnosis with CT evaluation. Of the 20 of 25 patients previously diagnosed as PMA, the histopathological evaluations of 3 and two specimens were reported as WT and BCA, respectively. Of the 17 patients previously diagnosed with WT according to the parotid CT evaluation 8, 6, 1, 1 and one specimens were histopathologically diagnosed as with PMA, WT, oncocytoma, MEC, and ACC, respectively. Of the three patients preoperatively diagnosed as lymphadenopathy, 2 were diagnosed as BCA, and the other was PMA. The histopathological result of one patient previously diagnosed as lipoma was the lipoma.

Specimen results of 8 patients diagnosed as with MEC were resulted as 3 MEC, 1 SCC, one oncocytoma, 1 WT and 1 PMA. Of the five patients previously diagnosed as ACC; 2, 1, 1 and 1 of specimens were diagnosed as MEC, ACC, PMA, and Warthin tumour, respectively (Table 2).

In a condition during which the histopathological results are evaluated as the golden standard,

performances of FNAB and parotid CT diagnostics tests to determine the difference between benign-malign were assessed through ROC (Receiver Operating Characteristic) Analysis, and compared. According to this, while (AUC-Area under Curve) value remaining under the curve indicating the performance of FNAB test was 0.834, that of parotid CT was founded as 0.86, notably close to the first value.

No statistically significant difference was detected with regards to the performances of both tests ($p=0,797$). When it is examined in a detailed way, while it can be seen that the performance of parotid CT to diagnose patients is relatively better than that of FNAB test (81.82-72.73), it can also be seen that the performance of FNAB test to detect healthy ones is, even if just a pinch, greater than that of parotid CT (94.12-90.2).

When the diagnostic test indicates as sick (malign), Positive Predictive Value (+PV), the probability of being really sick, is higher in FNAB test (72.7-64.3) whereas, when the diagnostic test indicates as healthy (benign), Negative Predictive Value (-PV), the probability of being really healthy, is, even if just a pinch, higher in parotid CT (95.8-94.1). Positive Likelihood Ratio (+LR) indicating how many wrong positive results FNAB test shows in response to each true positive result is high (12.36-8.35), at the same time, Negative Likelihood Ratio (-LR) indicating how many true negative results shown in response to each wrong negative result is also high (0.29- 0.20).

Values expressing the performances of the tests are shown in Table 3.

Table 3. Performances of the tests

	FNAB	Parotid CT
AUC (with 95% CI)	0.83 (0.718-0.917)	0.86 (0.748-0.935)
Sensitivity (%)	72.73	81.82
Specificity (%)	94.12	90.20
+PV (%)	72.70	64.30
-PV (%)	94.10	95.80
+LR (%)	12.36	8.35
-LR (%)	0.29	0.20

FNAB= fine needle aspiration biopsy, CT= computed tomography, AUC= area under curve, CI= confidence interval, +PV= positive predictive value, -PV= negative predictive value, +LR= positive likelihood ratio, -LR= negative likelihood ratio

Discussion

FNAB was first used in the diagnosis of salivary gland diseases in Radiumhemmet Stockholm in the year of 1953 [2, 3]. However, it's being accepted as a direct approach to the morphological diagnosis of salivary gland diseases could be possible after numerous researches during which cytology and biopsy results were correlated in the said field [4, 5]. Growing and increasing literature information every passing day has presented the importance of such diagnostic method, and indicated that the ratio of the establishment of the final diagnosis of the process varies between 80% and 98% [6]. Such ratio is a notable one for such a tissue as the parotid salivary gland, which is extensive enough to cause mistakes, and where different neoplastic and inflammatory lesions appear.

Basavanandswami *et al.* [7] stated that more than 70% of parotid lesions are benign tumours according to FNAB. In our study, benign cytology was found in 51 (82%) patients. CC Lin *et al.* [8] studied postoperative diagnosis of 276 patients with parotidectomy operations; and recognized 229 (85%) benign, 33 (12%) malign and 9 (3%) chronic inflammation diagnosis. Jose Granel *et al.* [9], reported the postoperative pathologic diagnosis of 52 patients with parotidectomy operation as 39 (75%) with benign, 13 (25%) with malign. In our study, histopathologic results were reported as 51 (82%) patients with benign and 11 patients (18%) with malign.

According to Cohen [10], FNAB has, in salivary glands, a sensitivity rate of 90% and more, and a specificity rate of nearly 95%. Again Cohen, Bottles, Rodriguez, and Zurida stated that accurate cytological diagnosis could be established in 90% of benign lesions, and nearly 75% of malignant lesions [13]. Some positive misdiagnoses were set in early periods of parotid FNAB. However, as the experience in this field increased, and salivary gland tumours and classifications started to be understood better, diagnostic accuracy rates increased as well [14]. In our series, correct and accurate diagnoses were able to be established in 6 of 8 cases, set proper cytological diagnoses, of 11 cases having malign histopathology, but wrong specific diagnoses were established in 2 of them. Real cytological diagnoses were confirmed for 46 of 51 cases, having benign histopathology, and correct specific diagnoses were established for 40 of

them. When accuracy rates of the values are examined, we can see that results of FNAB carried out recently can confirm truer and more accurate diagnoses. This shows us that experiences of both surgeon and cytopathologist in this field have developed over the years. It is essential that clinician and cytopathologist co-operate and increase their experience in this area for success in parotid FNAB.

In our study, sensitivity was calculated as 72.73% and specificity of 94.12% for FNAB. Rates of sensitivity and specificity for parotid FNAB were stated as 57-100% and 75-100% respectively, and utility rates as being 69-100% by various writers. In almost all of these series, specificity values were founded as higher than those of sensitivity.

There exists no evidence indicating that the risks, brought by surgical biopsy, also occur with FNAB. Facial nerve injury, fistula formation, and tumour implantation, as a result of FNAB, are extremely rare cases [10, 15]. In some instances, a minor hematoma can occur, and minor cellulitis responding to anti-biotherapy can happen few and far between as well [13]. No complication was developed in the patients included in our study.

CT is highly helpful, and very commonly used in the detection of parotid salivary gland tumours, the indication of tumour distribution, discrimination of solid/cystic and establishment of lipoma diagnosis depending on its specific density. X-ray exposure and having side effects which are subject to contrast agent as well as facial nerve navigation and its inadequacy in assessing its relation with mass are its disadvantages [17, 18].

Koyuncu *et al.* [19] compared CT and MRI efficiencies in 40 parotid mass patients during a study they performed in 2003. They found both imaging methods as similar with regards to tumour location and infiltration issues. MRI produced a better result with regards to tumour margin; even so this result did not change the operation strategy of the surgical team. They emphasize that it will be more reasonable to use CT method, costing less, since it is not possible to apply all methods in a pre-operative study, and since there exists no difference between the two methods. Moreover, it is emphasized that there exists no need for another imaging method in a patient apart from one of these two tests.

Urquhart *et al.* [20] studied the correlation between CT examinations and clinical assessment and post-operation results in their series of 29 patients, published in 2001, by starting from the idea that CT

examination should be applied to every parotid patient. Specifically, the growth, location, density, and whether it carries malignancy potential were inspected. Urquhart and his friend suggest that CT is used during the routine pre-operative inspection of parotid tumours.

Yalcin *et al.* [21] stated, in their study consisting of 40 patients during which they examined assistant, diagnostic methods in parotid tumours, that USG, CT, and sialography are helpful in pre-operative staging, but not in benign-malign discrimination. McGuirt *et al.* [22] suggest that pre-operative CT or MRI produced the appropriate response at a rate of 87% in benign-malign discrimination, and this rate was 69% in PET, and 78% in FNAB.

McGuirt suggests that MRI is primarily applied in sublingual gland tumours because of very high malignancy rate. Spiro suggests in his essay concerning salivary gland masses, published in 1995, that CT can be preferred to more expensive MRI [23].

Owen and his friends [21] stated, following their study in which they examined the usage of CT together with FNAB in parotid masses, as it is in our study, that both tests produced highly valuable information regarding preoperative histology and anatomy, and thus prevented occurrences of unnecessary procedures and complications.

In our study, the sensitivity of CT for benign-malign discrimination was calculated as 81.82%, and its specificity as 90.20%. That the number of patients having malignant tumour was small, and that 5 of total 11 malignant diseases were advanced might have increased the accuracy rate. Valid specific diagnoses were established for 31 of total 62 patients. This ratio can be drawn up to higher levels thanks to the developing technology and increase of experience of radiologist on this issue.

The establishment of pre-operative diagnosis in parotid salivary gland masses is not only of great importance regarding obtainment costs and time savings, but also is significant so as to both decreases the morbidity that patients suffer, and for physicians, to protect himself or herself regarding medico legal responsibilities. Although plenty of studies were carried out to determine inspections to be pre-operatively performed, not a complete consensus has been formed yet. Therefore, we executed this study based on this fact.

We consider that FNAB should be applied to any patient with parotid masses on account of the presence of high accuracy rates, and of minimum complication

risks with history and physical examination of patients.

Since parotid surgery includes substantial risks, it is essential that location, size, histological behaviour and relations with surrounding tissues, of pre-operative mass be well known to minimize the said risks. It is not possible for us to obtain all the mentioned information only through FNAB. Thus, we also consider that it is necessary to take benefit of the information that parotid CT, one of imaging methods, gives on these issues.

Conclusions

Results that we obtained from our study during which we researched utilities of FNAB and parotid CT tests, two of pre-operative assistant diagnosis tests, ended up as being compatible with the literature. We consider that these tests are indispensable for being a guide for surgeons during the pre-operative diagnosis process and formation of treatment, yet they are not alternatives one another. To perform new studies particularly on series in which the number of malignant diseases is high will make a contribution to the literature.

Conflict of interest

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The effect of surgery on functional outcomes of the elbow in adults with isolated capitellar fractures

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ABSTRACT

Objectives. The aim of this study was to evaluate the factors affecting the functional outcomes together with the clinical and radiological findings obtained from the treatment of adult capitellar fractures through open reduction and internal fixation. **Methods.** Patients who applied our clinic between 2008 and 2013 with a mean age of 37.5 (range: 17-77) were treated surgically. A total of 11 patients, seven male, and four female, were included in the study. In the study, fracture types of the patients were determined according to McKee modification of the Bryan and Morrey classification. After the operation, patients were followed for an average 26 (15-63) months. In the radiological and clinical evaluations, carrying angle of the operated elbow was compared with the carrying angle values of the healthy elbow. Clinical assessment was made of the Mayo Elbow Performance Index (MEPI). **Results.** Patients were clinically assessed according to the MEPI scoring over 100 points. It was seen that five patients got 100 points (excellent) while 6 got 85 points (good). No significant difference was observed between fracture types regarding elbow flexion. Type III fractures were found to be significantly more limited than type I and type IV fractures regarding elbow extension degrees ($p=0.040$). **Conclusions.** This study yielded inferences that we considered important. Degenerative changes observed in type III fractures only show that this fracture type poses the risk of osteoarthritis development. The fact that heterotopic ossification causes movement restriction affects clinical findings adversely. We believe that degenerative arthritis would decrease, joint range could be maintained better, and functional results will be better by avoiding challenging passive exercise and suggesting active practice instead.

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Keywords: Capitellum; elbow fractures; heterotopic ossification; osteoarthritis; elbow

Introduction

Capitellum fractures account for less than 1% of elbow fractures [1,2]. These fractures are observed particularly in adults and women [3,4]. The fracture may be accompanied by soft tissue injury, and it can be seen together with other elbow fractures including isolated capitellar fracture or radial head in particular [5-9]. They result from a certain degree of flexion of

the elbow and a fall onto the outstretched hand upon the transmission of force from the radial head to the capitulum. Capitellum fractures have long been classified as the thick fragment, thin fragment or comminuted fragment, and the most common of them (80%) appears to be the Hahn-Steinthal fracture (Type 1) [10]. The most frequent classification is Mc Kne

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modification of the Bryan and Morrey classification [11]. Most capitellar fractures are complex injuries that involve part of the trochlea [7, 12]. Different classifications have been offered to make fracture types more understandable, and studies have been carried out on the issue [13]. In the related literature, different approaches such as open reduction and internal fixation, excision and closed reduction can be seen in the treatment of capitellar fractures [9, 12, 14-18]. In the technically difficult procedure of closed reduction, cases of mal-union or avascular necrosis due to failure and often reduction loss have been reported [6, 17]. In excision cases, it is possible to observe valgus deformities, instability and joint stiffness and early joint degeneration resulting from joint compliance defect due to [6, 19, 20]. Lack of exercise and contractures in soft tissues may lead to joint stiffness. It is emphasized that angiogenesis mechanism is activated as a result of trauma; and with Platelet-Derived Growth Factor release, the increased vascularization in the damaged area is stated to cause heterotopic ossification development [21]. In elbow traumas, particularly those involving fractures and dislocations, one of the most important reasons for joint stiffness is heterotopic ossification [22-24]. All of these factors are effective in the functional results of the joint. Most studies in the literature include type I fractures, and the number of those carried out on the other types is limited, and most of them are case presentations. There are only a few studies examining all fracture types. The aim of the present study is to evaluate the functional results of our cases who had type I, II, III and IV fractures according to McKee modification Bryan and Morrey classification and were treated surgically for adult capitellar fractures and to specify the factors affecting results.

Methods

Patients who applied in our clinic between 2008 and 2013 with a mean age of 37.5 (range: 17-77) and were treated surgically. A total of 11 patients, seven male, and four female, were included in the study. All patients' pre-operational anterior-posterior radiographs were taken and to avoid inaccuracy in the classification of the fractures, computed tomography images were made for the operational plan before the operation. (Figure.1a-d).

Fracture types of the patients were determined

according to McKee modification of the Bryan and Morrey classification (Table 1) [12]. Three of the patients were classified as Type I, one patient with Type II, five patients as Type III and two of them as Type IV. Herbert screws, cannulated screws, conical headless compression screws, breakable pins and Kirschner wires were used as fixation materials. Surgical intervention was made with Kocher's lateral approach. Patients were included in a physical treatment and rehabilitation program following the operation.

After the surgery, patients were followed for 26 months (range: 15-63) on average. At the final examinations, comparative anterior-posterior and lateral radiographs were taken of both elbows. In the radiological and clinical evaluations, carrying angle of the operated elbow was compared with the carrying angle values of the healthy elbow, and radiological measurements were assessed [25]. Clinical assessment was conducted by the Mayo Elbow Performance Index (MEPI), which evaluates patients' pain, the range of joint motion, stability and daily functions.

Statistical analysis

IBM Corp. (2012) IBM SPSS Statistics for Windows. Version 21.0 Armonk, NY: IBM Corp; 2012 Program was used for statistical analysis. Since the types of fractures grouped in the analytical method were not normally distributed and the variances were heterogeneous, the analysis of the numeric data was done with Kruskal-Wallis test. Categorical data were analyzed by Chi-square test.

Results

When patients were clinically assessed according to the Mayo Elbow Performance Index scoring over 100 points, it was seen that five patients got 100 points (excellent) while six patients got 85 points (good). Joint range of two type IV patients and one type II patient were completed, whereas limitation was observed in the joint movements of two type I patients and all type III patients. No significant difference was seen between fracture types regarding elbow flexion and rotation. However, type III fractures were found to be significantly more limited than type I and type IV fractures regarding elbow extension degrees ($p=0.040$).

There were no complaints or complications that

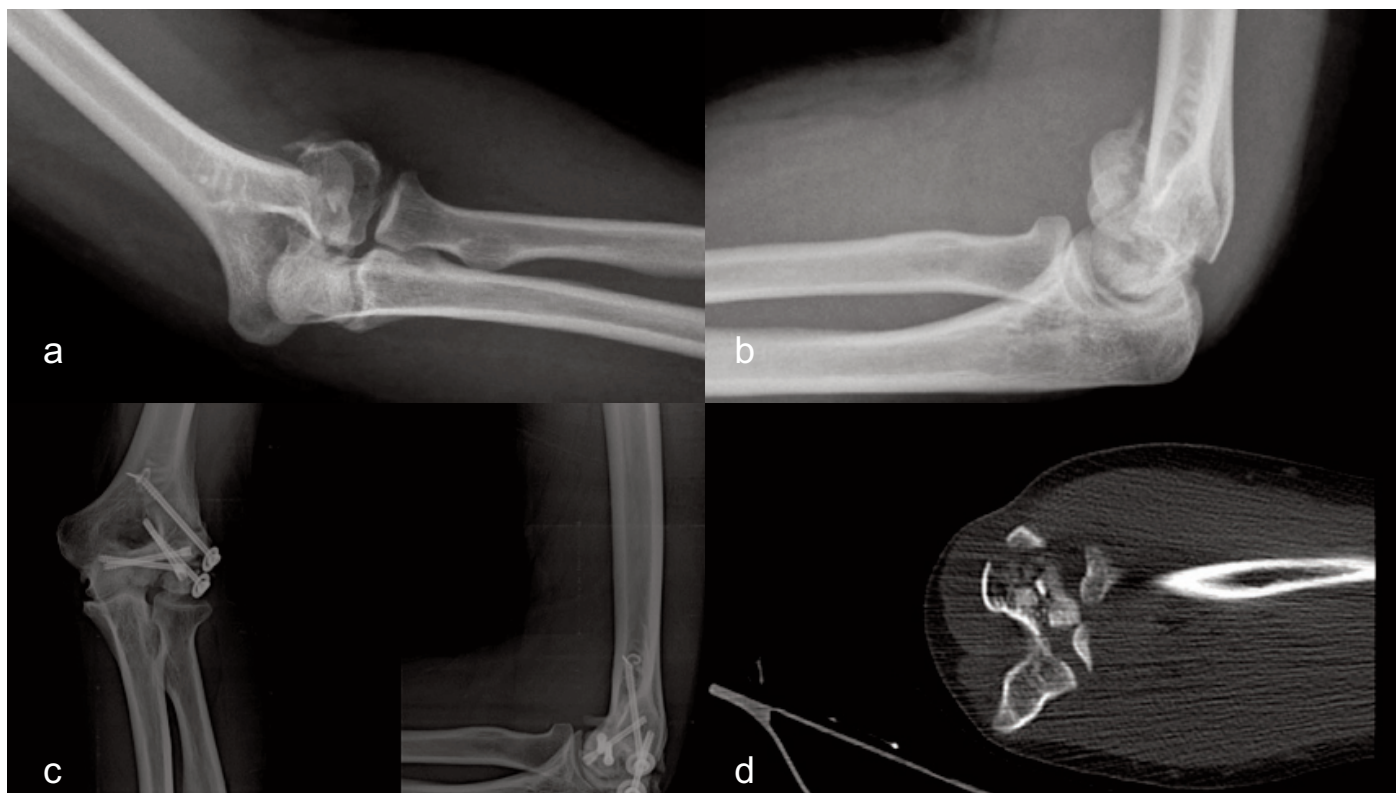


Figure 1. a) Preoperative radiography of elbow joint. b) Preoperative lateral radiography of elbow joint. c) Postoperative anterior-posterior radiography of elbow joint. d) Preoperative computerized tomography of elbow joint.

Table 1. Bryan and Morrey classification (McKee modification)

Type I	Hahn-Steinthal; large osseous fragment containing capitellum, may extend to trochlea.
Type II	Kocher-Lorenz; fracture of articular cartilage separation with very little subchondral bone attached.
Type III	Comminuted fracture.
Type IV	McKee modification; coronal separated fracture involving capitellum and trochlea.

would require removing the fixation material used in the patients. Heterotopic ossification was observed in five of the patients, and degenerative changes in five of them. None of them had avascular necrosis and nonunion. When the operated and healthy sides of the patients were compared, carrying angles were observed to have increased by 5.3° (1.1° - 12.0°) on average. In the range of joint motion evaluation, flexion-extension range was measured as 131.8° (85° - 145°) on average. Five patients were observed to have a rotation at non-significant levels.

No significant difference was found between heterotopic ossification and fracture types ($p>0.05$). Considering the degenerative changes, type III fractures were found to have a significantly higher risk than type I fractures ($p=0.018$) and type IV fractures ($p=0.048$) regarding osteoarthritis.

Discussion

Capitellar fractures usually occur as a result of falling onto the outstretched hand with the elbow at the extension. The accepted mechanism is the radial head's separation of capitellum by breaking it against proximal in the coronal plane with the force it axially transmits onto the capitellum [11].

Depending on this mechanism, formation of cubitus valgus or cubitus recurvatum in the normal elbow anatomy might make this injury more possible in the elbow [26]. It is stated that capitellar fractures occur more often in women than men because of the larger carrying angles of women [27]. However, no such relation was observed in our study.

Clinically, lateral elbow tenderness, pain, and minimal swelling are observed in capitellar fractures.

Table 2. Demographics and clinical results of the patients

Patients	Age	Gender	Side	Follow-up period (months)	Fracture type	MEPI	Flexion arc, range (angle)	Rotation arc	CAD	HO/DC
1	48	K	Left	37	Type 3	85 Good	10-145°	Full	+7.6°	-/+
2	18	E	Left	63	Type 4	100 Excellent	0-145°	25 Loss	+5.3°	-/-
3	55	E	Right	15	Type 3	85 Good	20-135	Full	+5.8°	+/+
4	77	E	Left	15	Type 1	100 Excellent	0-145°	20 Loss	+5.2°	-/-
5	17	E	Left	16	Type 1	100 Excellent	0-130°	Full	+4.8°	+/-
6	49	E	Right	21	Type 3	85 Good	10-145°	Full	+5.6°	-/+
7	28	K	Left	19	Type 2	100 Excellent	0-145°	20 Loss	+7.5°	-/-
8	27	K	Left	17	Type 3	85 Good	20-105°	20 Loss	+12°	+/+
9	24	E	Left	33	Type 1	85 Good	0-145°	25 Loss	+1.1°	+/-
10	18	E	Right	27	Type 4	100 Excellent	0-145°	Full	+2.3°	-/-
11	52	K	Left	26	Type 3	85 Good	20-145°	Full	+1.4°	+/+

MEPI=Mayo Elbow Performance Index, ROM=Range of motion CAD=Carrying angle difference, HO=Heterotopic ossification, DC=Degenerative changes, Rotation arc=Supination-Pronation arc

Diagnosis is usually made by the capitellum's semilunar displacement on the proximal found in the lateral elbow radiography. The fracture might not be noticed as the anterior-posterior radiography images may seem to be normal [28]. The importance of CT is emphasized particularly in the diagnosis of type IV capitellar fractures [29]. CT is recommended in the surgical planning of type III and type IV fractures [30]. All patients underwent CT scans together with the evaluations in the elbow anterior-posterior and lateral graphs to decrease errors in the classification of fractures and to make accurate surgical plans.

In these rare injuries, non-separated capitellar fractures may be followed up with plasters or immobilization. For separated fracture, on the other hand, closed reduction and plaster treatment are controversial as their anatomical reduction and fixation are tough [31]. However, in an 8-case study, which applied closed reduction in type I fractures, favorable results have been reported [32]. Similarly, three previous studies have produced promising results in closed reduction practices [15-17]. Those arguing the necessity of open reduction internal fixation have reported reduction loss and resulting avascular necrosis and malunion development. However, different clinical and radiological results in type I capitellar fractures given internal fixation are also controversial [7, 9, 12, 14]. The lateral Kocher approach is recommended for the surgical treatment of these fractures. Therefore, we employed the lateral Kocher approach for all our patients. Herbert screws and headless conical compression screws are claimed to be more stable as fixation materials in the literature. Their advantage over other materials is that they can

be applied because of the joint and do not require removing [33-35]. In one study, maxillofacial plates were used alternatively and yielded good results [36]. Most of our cases were operated using Herbert screws and Headless Conical Compression screws. When needed, they were combined with Kirschner wires and cannulated screws.

In the treatment of capitellar fractures, joint stiffness and limitation of movement occur at individual rates. It is also possible to observe keloid formation due to surgical scar, neurologic complications, avascular necrosis, infection, osteoarthritis, heterotopic ossification, non-union, malunion, fixation material incompetence or reduction [37]. Heterotopic ossification development and the degenerative changes seen only in patients with type III fractures are complications we have observed.

Some researchers have suggested that the excision of simple fracture fragments for which fixation is not possible [4, 18, 38]. Johanson and Rosman stated that they obtained good results from a case that they applied excision [38]. However, it is reported in another study that capitellar excision may lead to valgus instability [39].

Similarly, non-fixable fragments were excised in one of our cases and a good outcome was obtained according to the Mayo Elbow performance index. However, it has been stated that although a small fragment excision yields good results in the short term, joint stiffness and instability may develop in the future [4, 40, 41]. The defect in capitellum, radial head fracture, and accompanying coronoid defect may disrupt radio-capitellar stability seriously and lead to elbow instability [42]. Research has shown that

recurrent posterolateral instability may develop in the elbow due to radial head fractures [43, 44]. We performed fragment excision in one of our cases and did not observe instability. It is possible to see radial head fracture accompanying capitellar fracture and radial head posterior impaction [45]. However, sometimes there may not be fractures in these impaction injuries, but subchondral separation and lateral ulnar collateral ligament injury might be present. Therefore, magnetic resonance imaging is important for diagnosis and posterior bone marrow edema in the images indicate avulsion of the lateral ulnar collateral ligament [45, 46]. We did not use magnetic resonance imaging in our cases and did not observe elbow instability in the post-operative follow-ups. Since isolated capitellar fractures are rare instances, the small number of patients and the lack of extended follow-up results are the limitations of the present study.

It was seen in the evaluation of our cases that degenerative changes occurred only in type III fractures and that the functional results of type III fractures were worse than the other types. Studies in the literature also support this finding [30].

It is stated that careless surgical approach, insufficient irrigation of the surgical area and passive exercise may lead to heterotopic ossification [31, 47]. It is also reported that challenging passive exercise may result in soft tissue injuries and increase the risk of heterotopic ossification [48, 49]. Despite being a strong joint, tolerance of the elbow joint to trauma is weak and joint stiffness rates are high. One of the major reasons for this joint stiffness is heterotopic ossification. There are intrinsic, extrinsic or combined reasons for this stiffness in the elbow [50]. Non-steroidal anti-inflammatory drugs and radiotherapy are used to prevent heterotopic ossification. All our patients were given non-steroidal anti-inflammatory treatment after the operation. However, non-steroidal anti-inflammatory drugs have been shown to disrupt bone recovery [51]. Experimental studies have been conducted with recently developed medicines and favorable outcomes have been obtained [21].

In one of the studies, heterotopic ossification is reported to be located in the medial collateral ligament, ulna and radius proximal and most commonly in the distal humerus anterior [24]. In our cases, it was also observed in the elbow posterior and affected joint movement significantly (Figure 2).



Figure 2. Heterotopik ossification appearance in elbow joint at the last follow-up.

In some of our cases, we found heterotopic ossification in the elbow anterior, posterior, medial, or more than one location (Figure 1c). Cases with joint movement restriction due to degenerative changes or heterotopic ossification, it was seen that degrees of the extension were affected more than those of flexion and that there was more movement restriction particularly in type III fractures than type I and type IV fractures ($p=0.040$).

None of our case with complete flexion-extension range had degenerative changes and one of them developed heterotopic ossification. When the patients with restriction in the extension-flexion range were evaluated, it was seen that two patients were type I, and one patient was type III. Patients with complete flexion-extension range, two patients were type IV, one patient was type II and two patients were type I.

These findings show that movement restriction is one of the most important factors affecting functional results in capitellar fractures.

The finding that movement restriction is frequent in patients with heterotopic ossification and degenerative changes in the joint is significant. While heterotopic ossification could be seen in all fracture types, degenerative changes rather occurred in type III fractures in which joint surface is damaged more.

Conclusion

Since isolated capitellar fractures are rare cases and the number of patients is too small, it becomes harder to comprehend the phenomena thoroughly. There is an obvious need for studies with more series of patients. Nevertheless, in the present study covering all fracture types, we have made significant conclusions. Degenerative changes observed in type III fractures only show that this fracture type poses the risk of osteoarthritis development. The fact that heterotopic ossification causes movement restriction affects clinical findings adversely. We recommend excision of small undetermined pieces. In addition to the need for the development of preventive and therapeutic methods of treatment, we believe that degenerative arthritis would decrease, joint range could be maintained better, and functional results will be better by avoiding challenging passive exercise and suggesting active use instead.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Analysis of the cornea donor data: an eye bank study

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ABSTRACT

Objectives. To analyse 1.5-year data of our newly established eye bank and to evaluate the factors affecting donor quality. **Methods.** Our bank's donor cornea data between July 2013 and November 2014 were retrospectively analysed. The effects of donor age, sex, and time from death to harvesting on the findings of specular microscopy were assessed. **Results.** A total of 139 corneas retrieved from 70 donors. The mean age of donors was 34.2 ± 14.6 (5-64) years. The mean time from death to harvesting was 6.7 ± 2.9 (1-13) hours; the mean time from collection to transplantation was 5.2 ± 2.8 (1-14) days. Age had a significant negative correlation with mean endothelial cell count (ECC), a significant positive correlation between mean cell area (MCA) and standard deviation (SD). Time from death to harvesting had a significant negative correlation with cell count and 6A; it had a significant positive correlation with SD, the coefficient of variation, and MCA. **Conclusion.** According to the results of the present study, ECC, MCA, and SD levels were greater in younger donors. Endothelial morphology was altered as the time from death to harvesting was prolonged; however, the alteration in cell morphology was not severe enough to alter transplantation success with the corneas being harvested within the first 13 hours.

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Keywords: Eye Bank; cornea; specular microscopy; endothelial; donor

Introduction

Eye banks are special medical units responsible for harvesting donor corneal tissue required for the cornea transplantation from suitable donors, preserving harvested tissues under appropriate conditions, evaluating tissue quality for transplantation, transporting tissues to transplant centres under optimal conditions, registering patients who apply for keratoplasty procedure, as well as establishing and maintaining communication with the

patients. Donor suitability, time from donor death to tissue harvesting, cornea storage conditions, and time of harvesting to transplantation are vital factors for graft survival during the time of harvesting to transplanting corneal tissue. Corneal storage duration is dependent on corneal preservation methods (tissue culture medium, organ culture, moist chamber); corneal tissue should be transplanted as soon as possible before irreversible degeneration occurs after

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donor death and during storage [1].

As a result of continuously increasing the number of patients entering keratoplasty waiting lists and prolonged waiting durations, Turkish Ministry of Health has recently funded the establishment of new eye banks in various cities. As of the time of the writing this paper, there are 28 functioning eye banks in Turkey. Our eye bank was established in July 2013 by ministerial approval of Turkish Ministry of Health and supplied 139 donor corneal tissues between July 2013 and November 2014. In the following we want to assess the first donor data of our newly established eye bank.

Methods

Data of donor corneas harvested at Bursa Yuksek Ihtisas Training and Research Hospital Eye Bank between July 2013 and November 2014 were retrospectively reviewed. Data on donor age, sex, time of death to harvesting, time from collection to transplantation, serology results, specular microscopy (SM) results, and donor usage were recorded. In specular microscopy, the Centre Method was used to determine the corneal endothelial count and endothelial structure (polymegathism and pleomorphism) (Konan Eye Bank Kerato Analyzer, Konan Medical Inc., Japan). The effects of donor age, sex, and time from death to cornea harvesting on the findings of specular microscopy were analysed. The local ethics committee approved the study. After being harvested from the cadavers using the sclerocorneal button technique, donor corneas were preserved in the preservation solution (Eusol C, Alchimia, Italy) at 4°C; and endothelial photographs were taken to be examined for four times from all corneas by the same person using specular microscopy. For each donor cornea, endothelial cell count (ECC), mean cellular area (MCA), standard deviation (SD), hexagonality ratio (6A), and coefficient of variance (CV) were recorded. The donors were categorized into four age groups. Donor gender distribution, corneal side distribution, endothelial count, SD, CV, 6A, MCC, time from death to harvesting and time from collection to transplantation were compared across the four age groups.

Statistical analysis

Descriptive statistics included mean, standard

deviation, median, minimum, maximum, frequency, and percentage. The distribution of study data was tested with the Kolmogorov-Smirnov test. Quantitative data were analysed with ANOVA and Kruskal-Wallis (Mann-Whitney U) tests. Chi-Square test was used for the analysis of qualitative data. SPSS 22.0 software package was used for all statistical comparisons.

Results

Among 70 donors included in the study, 16 (23%) were female, and 54 (77%) were male. During our study period, 139 corneal tissues were retrieved from 70 donors. A pair of corneas was harvested from 69 donors and a single cornea from 1 donor. The mean age of the donors was 34.2±14.6 (5-64) years. The mean time from death to harvesting was 6.7±2.9 (1-13) hours; the mean time from collection to transplantation at different centres was 5.2±2.8 (1-14) days. The mean age of the transplant recipients was 45.8±25 (1-88) years at various centres. The obtained corneas were serologically tested using anti-HIV, HBsAg, anti-HCV and VDRL tests. Two corneas were HBsAg positive and were thus disposed of.

Another cornea was disposed of by a recipient centre due to suspected infection. The findings of specular microscopy, age and sex group distribution of corneal tissues were shown in Table 1.

There were no significant differences between the age groups on gender distribution and the distribution of corneal tissue side. The cell count was significantly greater in the first age group (5-19 years) compared with the second (20-34 years), third (35-49 years), and fourth (50-65 years) age groups ($p<0.001$). The cell count was significantly greater in the second age group compared to the 3rd and 4th age groups ($p<0.001$) (Table 2). The SD level was significantly lower in the first age group compared to the second, third, and fourth age groups ($p<0.001$). It was also significantly lower in the second age group compared to the fourth age group ($p<0.001$) (Table 2). There were no significant differences between the age groups on CV, 6A, time from death to harvesting, and time from collection to transplantation (Table 2). The first age group had a significantly lower MCA compared to the second, third, and fourth age groups ($p<0.001$) The MCA level was significantly lower in the second age group compared to the 3rd and 4th age groups ($p<0.001$)

Table 1. Specular microscopy, age and sex group distribution of corneal tissues

	Min-Max	Median	Mean ± SD
Donor Age	5-64	34	34.2 ± 14.6
Age Groups	5-19		34 (24.5%)
	20-34		37 (26.6%)
	35-49		43 (30.9%)
	50-65		25 (18.0%)
Cell Count	2008 – 3968	2857	2884.0 ± 457.3
SD	53.0 – 257.0	106.0	112.7 ± 36.2
CV	19.0 – 60.0	30.0	31.4 ± 6.7
6A	39.0 – 81.0	61.0	61.1 ± 8.6
MCA	252.0 – 498.0	347.0	354.3 ± 58.4

SD= Standart deviation, CV=coefficient of variance, 6A=hexagonality ratio, MCA=mean cellular area

(Table 2).

Cell count, SD, CV, 6A, and MCA levels were not significantly different between both genders (Table1). Time from death to harvesting had a significant negative correlation between cell count and 6A ($p=0.005$). It had a significant positive correlation with SD, CV ($p<0.001$ for both), and MCA ($p=0.011$) (Table 3). Twenty-nine (21%) of the harvested corneas were used at our hospital while the remaining 108 (79%) corneas were sent to other requesting institutions. Two corneas had HBsAg positivity and were thus disposed of.

Discussion

Today, there is an estimated 4.9 million patients with bilateral corneal blindness worldwide, especially in the developing countries, who may potentially

regain their visual ability with corneal transplantation. According to the World Health Organisation data, 120.000 keratoplasties (KP) operations were performed in 2000 worldwide [2, 3]. According to the data of the Turkish Ministry of Health, the numbers of keratoplasty operations were 1784 and 1921 in 2012 and 2013, respectively. The official number of patients who are in the cornea waiting lists is 4822, although unofficial estimates put the number at 10.000 [5, 6].

Evaluation of donor candidacy according to certain standards is vital to operational success and preventing complications. For this purpose, the European Eye Bank Association (EEBA) and the Eye Bank Association of America (EBAA) have set up the minimum medical standards for donor candidacy [7, 8]. FDA undertakes supervision and certification of the eye banks in the United States. The available standards are reviewed twice a year, published by the American Academy of Ophthalmology, and

Table 2. Age groups with the distribution of specular microscopy findings.

Age groups	5-19 Years	20-34 Years	35-49 Years	50-65 Years	p
Cell Count	3319 ± 361	2947 ± 358*	2685 ± 366*#	2518 ± 326*#	<0.001
SD	95.2 ± 42.6	113.7 ± 31.7*	114.9 ± 26.9*	133.0 ± 35.5*#	<0.001
CV	30.3 ± 8.9	32.7 ± 6.4	30.3 ± 5.0	32.6 ± 5.8	0.051
6A	63.9 ± 10.0	59.2 ± 6.9	59.9 ± 8.2	61.5 ± 8.5	0.111
MCA	304.8 ± 38.5	343.2 ± 41.5*	377.7 ± 52.9*#	403.8 ± 53.8*#	<0.001
Harvesting time (h)	6.1 ± 2.7	6.7 ± 3.2	6.7 ± 2.8	7.3 ± 3.0	0.504
Transplantation time (h)	4.7 ± 3.1	5.7 ± 3.2	4.8 ± 2.5	5.7 ± 2.4	0.212
Recipient Age	32.6 ± 25.6	42.6 ± 23.9*	55.4 ± 21.1*#	52.1 ± 20.7*	0.001

SD= Standart deviation, CV=coefficient of variance, 6A=hexagonality ratio, MCA=mean cellular area, Kruskal-Wallis / ANOVA, * $p<0.05$ vs. 5-19 years age group / # $p<0.05$ vs. 20-34 years age group

Table 3. Time from death to harvesting (Spearman Correlation)

		Cell Count	SD	CV	6A	MCA
Time from death to harvesting (Hour)	r	-0.240	0.349	0.394	-0.191	0.224
	p	0.005	0.000	0.000	0.031	0.011

SD= Standard deviation, CV=coefficient of variance, 6A=hexagonality ratio, MCA=mean cellular area,

distributed to eye banks that are members of EBAA [9].

A donor cornea having appropriate criteria for transplantation is one of the most important factors determining the keratoplasty success. Therefore, a harvested cornea should undergo a specular microscopic and serological evaluation before keratoplasty. Some studies using specular microscopy have shown that race, sex, and age of a person may alter morphological properties of the endothelium [10, 11]. It has also been reported that certain factors such as time of donor death to cornea harvesting and cause of donor death may also influence endothelial morphology [12, 13].

Some studies have reported that endothelial count is the most important factor for donor quality. Endothelial cell density is markedly reduced until early puberty, especially in the first couple of years after birth. Former studies have shown that the mean endothelial cell count is reduced, and pleomorphism is markedly increased after the age of 50 [14, 15]. Mean endothelial cell count is reportedly decreased by 0.3% to 0.6% each year while polymegathism and polymorphism simultaneously increase [16, 17]. Endothelial cell density is reduced between the second and eighth decades, dropping from 3000 to 4000 cell/mm² on average to as low as 2600 cell/mm² on average. The hexagonal cell percentage also drops from 75% to 60% [18], reducing the rate of usage of corneas obtained from elderly donors for transplantation. However, many studies have reported that corneas from advanced-age donors can also be sometimes used for transplantation, and thus donor age does not affect donor survival. Linke *et al.* [17] showed that 32.1% of corneas from donors aged over 80 years met the appropriate criteria for transplantation. Patel *et al.* [19] similarly demonstrated that 80% of corneas from advanced age donors had suitable standards for transplantation. According to EBAA criteria reported in 2006, donors should be between 10 and 75 years of age [20]. Besides, the minimum medical standards set by EBAA in 2013, as well as those set by EBAA in 2012, do not

specify an age limit for donor eligibility [7,8]. Kartal *et al.* [21] reported that ECC showed a significant negative correlation with age, being significantly greater in the first two decades of life. Likewise, our study revealed a negative correlation between ECC and age. Cell count was significantly higher in the first age group (5-19 years) compared with the second (20-34 years), third (35-49 years), and fourth (50-65 years) age groups. Cell count was significantly greater in the second age group compared to the third and fourth age groups (Table 3). Our study also demonstrated a positive correlation between age and MCA, SD values. SD and MCA levels were significantly lower in the first age group compared to the second, third, and fourth age groups. MCA was significantly lower in the second age group compared to the 3rd and 4th age groups, while SD was significantly lower in the second age group than the fourth age group. CV and hexagonality did not show any age-based differences. Some studies in the literature failed to show any age-associated differences in CV, MCA, and hexagonality, although some others have reported age-related differences in MCA [22, 23]. Kartal *et al.* [21] showed that CV and MCA were significantly lower in Group 1 and 2 (0-40 years of age). In our study, mean endothelial count was 2884.0±457.3, mean SD was 112.7±36.2, mean CV was 31.4±6.7, mean MCA was 354.3±58.4 and mean hexagonality was 61.1±8.6. Since our mean donor age was lower than those reported in the literature, specular microscopy findings were ideal for transplantation in all of our donors. Some studies investigated gender-based differences in endothelial cell morphology, some of them reporting ECC differences between both genders, but some others not [24, 25]. Kartal *et al.* [21] reported that female donors had a greater MCA, while a study from India, reported higher CV in female donors [26]. Our results did not reveal any significant difference between both sexes. Previous studies have shown a significant impact of time from donor death to cornea harvesting on endothelial count [17, 27]. EBAA recommends cornea harvesting within 20 hours in those aged less than 50 years, and within 18 hours in

those aged equal to or greater than 50 years of age [20]. As a general rule, it is recommended that corneal harvesting should be completed within 12 hours [28], although there is still no consensus regarding the upper limit of this time, and it may well be prolonged in some cases [29]. Kartal *et al.* [21] showed that ECC was greatest in the ≤ 3 hours group, although the difference was statistically non-significant. Our study showed a significant negative correlation between time from death to cornea harvesting and cell count, 6A. There was, however, a significant positive correlation between time from death to cornea harvesting and SD, CV, and MCA.

These results suggest that donor cornea quality is reduced as the time to the collection is increased. However, corneal endothelial structures did not undergo a degenerative process to preclude transplantation since corneas were harvested within maximum 13 hours. The harvested corneas should be serologically tested with anti-HIV, HBsAg, anti-HCV, and VDRL tests. Some domestic prevalence studies at different times have found a mean HBsAg positivity rate of 5% and a mean HCV positivity rate over 0.5% [30].

Kocazeybek *et al.* [31] reported corresponding figures of 6.6% and 0.9%. Our study revealed HBsAg positivity in two corneas, which were disposed of. One other cornea was disposed of by another centre due to suspected infection.

Of the donor corneas collected by our bank over a period of 1.5 years, 21% were used for transplantation by our hospital and 79% by other institutions. Various studies have reported that about 30% of donor corneas cannot be used owing to either serological results or an inappropriate endothelial morphology on specular microscopy examination [8]. We suggest that, we had a higher rate of cornea usage and we generally used high-quality corneas, because our eye bank preferred relatively younger donors, it rejected corneas with suspected infection due to prolonged stay at intensive care unit or the corneas which would be inappropriate for transplantation due their general appearance, and it harvested corneas at 6.7 ± 2.9 hours on average after donor death.

The harvested corneas were sent by our eye bank to other clinics as soon as possible when they were not to be used at our hospital. Time from harvesting to transplantation was 5.2 ± 2.8 (1-14) days on average at other clinics.

In conclusion, we revealed that ECC, MCA, and SD values were greater in younger donors; endothelial

morphology was altered as the time from death to harvesting was prolonged; however, the alteration in cell morphology was not too severe to alter transplant success with the corneas being harvested within first 13 hours. Eye banks should meticulously work in every step from donor harvesting to cornea transplantation. High-risk donor corneas should not be harvested. Harvested corneas should be examined serologically, as well as under specular microscopy, and they should be sent to centres of transplantation as soon as possible.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Efficacy of antibody levels in different post-exposure rabies vaccination programs

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ABSTRACT

Objectives. Rabies is a fatal acute viral zoonotic disease causing encephalomyelitis in humans and many other mammalian animals. Prophylaxis is vital since there is no treatment for rabies. This study was a comparison of antibody levels in patients who were vaccinated following different vaccination protocols. **Methods.** Eighty-five patients who were included in the rabies vaccination program who presented to the vaccination center of our clinic with the complaint of suspicious contact with rabies were included the study. In 61 (71.8%) patients a 2-1-1 vaccine program (Zagreb regimen) was implemented, and in 24 (28.2%) patients, a 5-dose rabies vaccine and rabies immune globulin (RIG) in a dose of 40 IU/kg (Essen regimen) was applied. **Results.** In patients on the 2-1-1 vaccine program, antibody levels on the 21st day were greater than 0.5 IU/ml in 49 (80.3%) patients. Antibody levels on the 28th day in the group that received the 5-dose rabies vaccine and rabies immune globulin administration was greater than 0.5 IU/ml in 17 (70.8%) patients. The difference between the two groups of vaccination programs was not statistically significant ($p=0.344$). Seroconversion rates for approximately one month after the last dose of vaccination in the serum samples were 90% and 75% in the groups with 2-1-1 vaccination, and RIG and 5-dose vaccinations, respectively. The differences were not statistically significant ($p=0.071$). **Conclusions.** Identification of similar seroconversion rates suggests that the 2-1-1 vaccination program may be a good alternative option to the standard vaccination program when RIG is unavailable.

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Keywords: Antibody; Immunization Schedule; Rabies

Introduction

Rabies is a viral zoonosis, preventable with the vaccine. The infection is transmitted from animals to humans with the virus in the saliva through lacerations, scratches, and bites, and proceeds with fatal encephalitis [1]. The incubation period usually ranges from 1 to 3 months after exposure, but can range from days to years. Approximately 10 million people worldwide receive prophylaxis due to animal

bites [2].

Rabies prophylaxis is administered through active and passive immunization. Prompt wound care and administration of rabies immune globulin (RIG) and vaccine are highly effective in prevention from human rabies following exposure. The World Health Organization (WHO) recommends human diploid cell vaccine + rabies immune globulin on initial, 3rd, 7th,

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14th, and 28th days. In 2009, the Center for Disease Control (CDC) provided new vaccine scheme recommendations. As an alternative to the Essen regimen (initial, 3rd, 7th, 14th, and 28th days), similar antibody levels were demonstrated with this regimen without applying the dose on the 28th day [3, 4].

The aim of this study was to determine the developing antibody levels after different vaccination applications and present data to define a preferable method for prophylaxis after contact.

Methods

This study was designed as a single centre. The patients using any drugs, age of under 15 and had chronic diseases were excluded from the study. Patients who presented themselves to the Rabies Vaccine Center of the Department of Infectious Diseases and Clinical Microbiology of the Ankara Education and Research Hospital with the complaint of suspicious contact with rabies, who consented the drawing of blood samples were included in the study. Patients were evaluated and included in the prophylaxis program according to the Rabies Prevention and Control Guidelines of the Republic of Turkey, Ministry of Health, General Directorate of Basic Health Services and WHO recommends [5, 6]. Abhayrab® vaccine (Human Biologicals Institute, India), licensed for active immunization procedures (Wistar rabies PM/WI 38-1503-3M strain), was used at 2.5 IU/dose, applied intramuscularly in 0.5 ml in the deltoid muscle.

For passive immunization, Equirab (Bharat Serums and Vaccines Ltd. India), which is a horse origin rabies antiserum containing 1000 IU/5 ml was applied at 40 IU/kg (Rabies immune globulin, RIG). According to the study design, venous blood samples were obtained twice in each group, such as on the 21st and 28th days of the 2-1-1 scheme and the RIG + 5-dose vaccine plan, respectively, and an average of four weeks after vaccination in both groups. Sixty-one (71.8%) patients received the 2-1-1 vaccine program. The 5-dose rabies vaccine and rabies immune globulin at a dose of 40 IU/kg were applied to 24 (28.2%) patients. Second blood samples were obtained in all patients 31.3 days (range 25-41 days), on average, after the last dose of the vaccination. Blood samples were centrifuged at 3000 rpm for four minutes, and serums were separated. Serums were placed in sterile

Eppendorf tubes and frozen and stored at -20°C. All samples were analysed simultaneously. Human Rabies Virus Antibody (IgG) ELISA Kit (Cusabio Biotech, China) was used for the rabies antibody assays.

Antibody levels were analysed in all patients. The serum antibody level, which has been accepted by WHO was 0.5 IU/ml, was taken as the lower limit of protection [6].

Statistical Analysis

Statistical analysis of data obtained was performed using SSPS for Windows 15.0 package program. The descriptive analysis was performed, was data was expressed as a number, percentage, and mean \pm standard deviation. Using chi-square and Fisher's exact test, values with $p < 0.05$ was set for statistical significance.

Results

Eighty-five patients who were included in the rabies vaccination program and who consented for blood to be drawn were included in the study.

The mean age of the patients was 34.8 ± 13.16 years. Forty-six (54%) were male. The patients were grouped according to the location of the bite on the body or mucosal contact with the animal, and the appropriate prophylaxis was applied. No patient received five doses of vaccine without receiving RIG. Rabies and tetanus prophylaxes were administered together in 57 (67.1%) patients (Table 1).

Among the 85 patients, antibody levels were higher than 0.5 in 27 (69.2%) of female and 39 (84.8%) of male patient respectively. This difference was not statistically significant ($p = 0.086$). Antibody levels in the second blood samples taken after the vaccination were positive in 43 (93.5%) males and 30 (76.9%) females. Among the men three patients (6.5%) and nine (23.1%) patients among women were had lower antibody levels. The difference was statistically significant ($p = 0.029$).

Mean age in the groups, with and without protective antibody levels were 34.5 ± 12.7 years and 35.7 ± 14.9 years, respectively, with no statistically significant difference between the groups ($p = 0.754$). On the 21st day, the antibody levels were higher than 0.5 IU/ml in 49 (80.3%) patients of the 61 patients on the 2-1-1 vaccine program. Corresponding antibody levels were greater than 0.5 IU/ml in 17 (70.8%)

Table 1. Demographics of the patients

General Characteristics	Total n (%)	2-1-1 n=61 n (%)	RIG+ 5 dose n=24 n (%)
Age	34.8 ±13.16	36.6 ±13.5	30.2 ±12.09
Gender			
Female	39 (49.5)	25 (41)	14 (58.3)
Male	46 (54.1)	36 (59)	10 (41.7)
Contact with animal causing risk			
Dog	72 (84.7)	52 (85.2)	0 (83.3)
Cat	13 (15.3)	9 (14.8)	4 (16.7)
Body region of bite or mucosal contact			
Lower extremity	60 (70.6)	47 (77)	13 (54.2)
Upper extremity	19 (22.4)	10 (16.4)	9 (37.5)
Both extremity	5 (5.9)	4 (6.6)	1 (4.2)
Head	1 (1.2)	-	1 (4.2)
Tetanus Prophylaxis	57 (67.1)	43 (70.5)	14 (58.3)
Day of control blood draw	31.3±2.8	31.5±2.9	30.9±2.5

RIG: Rabies immunoglobulin

patients on the RIG and 5-dose rabies vaccine group on the 28th day of the program. This difference between the two groups was not statistically significant ($p=0.344$) (Table 2).

Antibody levels in the second blood samples taken at a mean 31.5 days after the last vaccination (range 25-41 days) were analysed. Protective antibody levels were detected in 55 (90.2%) patients on the 2-1-1 vaccine program. Protective antibody levels were positive in six (9.8%) patients among those who had lower antibody level during the first blood drawn after the last dose of vaccination (on the 21st day), while six (9.8%) continued to be negative. Three (66%) patients of them were male.

Among patients who received rabies immune globulin and 5-dose rabies vaccine, protective antibodies were positive in 18 of 24 (75%) patients from the second blood samples taken at a mean

30.9±2.5 days after the last dose of vaccine. Protective antibody levels were positive in only one (1.6%) patient among those who had lower antibody level during the first blood drawn after the last dose of vaccination (on the 28th day), while six (25%) continued to be negative. Four (66%) patients of them were male. Although protective antibody rate was higher in the 2-1-1 group, this difference was not statistically significant (OR: 3.06, 95% CI: 0.75-12.6, $p=0.071$). Distribution of antibody levels in different vaccination programs was showed in Figure 1.

When considering the effects of tetanus prophylaxis, applied simultaneously with rabies prophylaxis after contact on protection, no statistically significant difference was found between patients with and without tetanus prophylaxis. Among the 85 patients, 44 (77.2%) developed protective antibodies among those with additional tetanus prophylaxis,

Table 2. Antibody levels according to the vaccination programs

	2-1-1 n=61 n (%)	RIG+5 dose vaccination n=24, n (%)	<i>p</i>
After the last dose of vaccination			
Antibody>0.5 IU/mL	49 (80.3)	17 (70.8)	0.344
Antibody<0.5 IU/mL	12 (19.7)	7 (29.2)	
Approximately one month after the last dose of vaccination			
Antibody>0.5 IU/mL	55 (90.2)	18 (75)	0.089
Antibody<0.5 IU/mL	6 (9.8)	6 (25)	

RIG: Rabies immunoglobulin

while 13 (22.8%) had no protection. Among patients with no tetanus prophylaxis, 22 (78.6%) patients similarly developed protective antibodies and six (21.4%) patients had no protection ($p=0.886$). Among the 13 (22.8%) patients with no protection after the last vaccination, who had been administered simultaneous rabies and tetanus prophylaxis, 7 continued to be antibody negative.

Discussion

The rapid fluorescent focus inhibition test (RFFIT) is considered the gold standard assay for detecting rabies antibody. But many other serological techniques are currently used for detecting rabies antibody levels like fluorescent antibody virus neutralization (FAVN), enzyme-linked immunosorbent assays (ELISAs) for humans and animals [7, 8].

Protective antibody levels can be determined with less vaccination. In this way, both the patient visits and the cost of the vaccine can be reduced. A detailed review of the evidence in support of reduced, four-dose schedules for human post-exposure has been published. In the review 12 published rabies vaccination studies during 1976-2008 representing approximately 1000 human subject, all subjects developed rabies virus neutralizing antibodies on day

14 [9].

Literature suggests that age and gender do not statistically significantly affect protective antibodies development [10-12]. There was no statistical association between age and protective antibodies in this study in concordance with the literature. However, the higher rate of protective antibodies in male patients was statistically significant. We attributed this situation to the greater number of male patients in this study. Further research in a larger patient population is required.

Bites on the extremities were the most frequent types of bits in the studies [13-15]. In the current study, the region of the body in which the bites or mucosal contacts occurred was in the lower extremity in 60 (70.6%) patients and the upper extremity in 19 (22.4%) patients. It was in concordance with the literature. It was thought to be because contact between animals and humans occurs at a level close to the ground, corresponding to the head of the animal and the lower extremities of humans. The use of the upper extremity to protect oneself from the animal is thought to be another factor explaining the frequency of extremity bites.

Protective antibody levels in the literature vary between 27% and 100%, with differences according to the day of the assay of antibody titre and the method of vaccination. In this study, protective antibodies

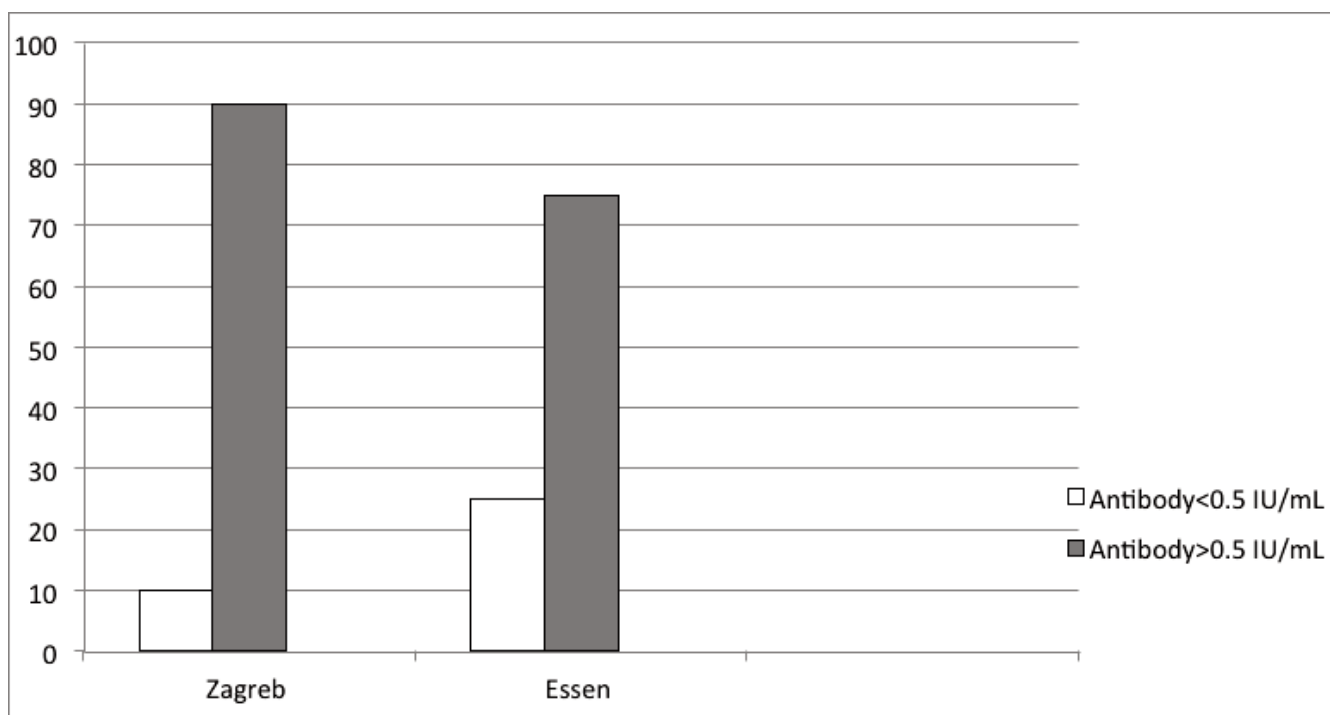


Figure 1. Distribution of antibody levels in different vaccination programs.

rates were determined as 80.3% and 90.2% for each vaccine program. It was compatible with the literature [16-22].

Protective antibodies rate in the late phase, approximately 28 days after the last dose of vaccine was 71% among patients who were administered the rabies immune globulin and 5-dose vaccine. It was in concordance with the literature [17, 18, 22, 23].

The 80% protective antibodies rate that was identified on the 21st day in patients in the 2-1-1 vaccine program was higher than the protective antibodies rate of 70% on the 28th day after RIG and five doses of rabies vaccine application. However, there was no statistically significant difference between the two groups in the protective antibodies rates. The lower rate of protective antibodies in the RIG-administered group was attributed to the differences in the immune responses among the patients, possibility of inappropriate storage conditions or improper application of RIG, or to the differences in the number of patients between the groups.

Serum samples were taken on the 21st and 28th days after the last dose of vaccination has been commonly evaluated in the literature with generally no evaluations after that. The protective antibodies rates developed in the first month, which were 90.2% and 75%, in the 2-1-1, RIG and 5-dose rabies vaccine programs, respectively were compatible with the literature [9, 22, 23]. The difference between the two applications was not statistically significant.

After three doses of vaccine, the protective antibody was detected in both groups. The follow-up period of the patients in the treated group 2-1-1 protective antibody positivity continued to be detected at a higher rate than the other group, but not statistically significant. However different results can be obtained in the other studies with long follow-up period and a large number of patients.

We determined that 12 patients in both groups had no protective antibody levels during the follow-up period. The age and sex have no effect on developing protective antibody, in this study. The patients, who had no protective antibody levels, were not examined for immunodeficiency. Because of being immunosuppression during the vaccination period can be the reason for lower protective antibody levels. Inappropriate storage conditions and applications of vaccine can cause this result also.

Simultaneous tetanus prophylaxis was identified to have been performed in 57 (67.1%) patients. This rate was 32% in a study by Hacibektasoglu *et al.* [24],

Torun [25] detected a 91.3% rate of tetanus prophylaxis. No study evaluating the association between the protective antibody rates and simultaneous tetanus prophylaxis could be found in the literature. In this study, protective antibody rates were not statistically significantly associated with tetanus prophylaxis rates. Further studies are required to be performed on this subject.

Conclusions

Application of prophylaxis after contact does not seem to be sufficient for rabies protection by itself. The percentages of antibody levels that are lower than the 0.5 IU/mL value accepted by the WHO as protective were 10% and 25% in the 2-1-1 and RIG + 5 dose vaccine applications, respectively.

When the lengthened incubation period in rabies is taken into account, the importance of appropriate and rapid wound cleaning is once more revealed. Patients who were bitten by an animal or who had mucosal contact with animals with a risk of rabies should present to health facilities as soon as possible.

The identification of antibody development rates of 75-90% in patients who completed the vaccination programs obligates an analysis of antibody titres again if the patients are exposed to the rabies virus again, and obligates re-vaccination if this value is lower than 0.5 IU/ml. The both regime show similar protective antibody rates and 2-1-1 rabies vaccination regimen is more cost effective. We recommend repeated vaccination in these situations if the period is more than one year after the first vaccination and if antibody titres could not be analysed.

Similar protective antibody rates identified after two different vaccination programs suggest that the 2-1-1 vaccination program can be a real alternative to the classic RIG and 5-dose vaccine applications.

Limitations of this study are ELISA, not gold standard test for detecting antibodies in rabies and the small number of patients.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Bilateral platelet rich plasma injections with assisted techniques for temporomandibular joint disorders

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ABSTRACT

Objectives. Temporomandibular joint (TMJ) disorders are frequently encountered in the population. Pain is the most common complaint. TMJ luxation needs surgical treatment which has many risks. The objective of this study was to treat TMJ disorders with a minimal invasive method, platelet rich plasma (PRP) injection, instead of surgery. **Methods.** The study included 7 female patients aged 15 to 42 years. Three ml (2 ml into the joint capsule and 1 ml into the pericapsular region) injections were applied in both sides. Two sessions of injections were planned. Three months after the last injection, a questionnaire was carried out. **Results.** Six of the subjects underwent two injections, and one of them underwent only one injection. Verbal analogue scale score was 7.66 ± 1.3 before the injections, 5.33 ± 2 after the first injection, and 3.33 ± 1.2 after the second injection. Pain decreased significantly after the first and more significantly after the second injection ($p=0.017$ and $p<0.001$, respectively). The mean total satisfaction rate was two at the first step ($p>0.05$) and four at the second step ($p=0.017$). **Conclusions.** Findings of our study indicate that PRP may be a useful technique for treatment of TMJ subluxations. The significant reduction in pain after either one or two injections suggests that it might be reasonable to investigate the efficacy and safety of this technique in larger study populations.

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Keywords: Platelet rich plasma, temporomandibular joint dislocation, temporomandibular joint pain

Introduction

Temporomandibular joint (TMJ) disorders like dislocation, pain, clicking, and inner ear pain are common in the general population. TMJ dislocation is defined as the movement of condyle out of the fossa and the advancement of the posterior surface of the condyle in front of the articular eminence. If this condition becomes chronic, surgical treatment is the only option. The goal of surgical treatment is to reposition the condyle and prevent further recurrences [1]. A new approach is different from surgery and is assisted with platelet rich plasma (PRP). Recent data

indicate that PRP injection into the ligaments supports connective tissue [2,3]. TMJ surgery is complicated and also has many risks. In this regard new and more minimally invasive treatment modalities would prove beneficial. In TMJ disorders, recurrent PRP applications may have positive regenerative effects, and may be coupled with conservative modalities like night splinting, anti-inflammatory drugs, and immobilization. We wanted to evaluate the effect of PRP injections into the TMJ on pain and patient satisfaction.

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Methods

This retrospective study included of 7 female patients aged 15 to 42 years, who were admitted to the plastic surgery outpatient clinic between July 2013 and August 2014 due to TMJ disorders. For acute conditions and first time occurring disorders, muscle relaxant, and anti-inflammatory medical therapy with night occlusal splint was started. Patients were queried for their complaints after one month follow-up time, and patients without a satisfactory response were recommended PRP treatment. PRP injection was applied twice in 6 patients and once in 1 patient who partially benefited from the injection and did refuse

the second injection. Minimum period between injections was one month.

PRP injection

50 ml of blood was drawn from the patients, and 6 ml of PRP was obtained using the Harvest's kit (Harvest Technologies Corporation, Munich, Germany) and advanced centrifuge technology (20 minutes at 200xg, Figure 1). Under sedative anaesthesia, three ml injections (2 ml into the joint capsule and 1 ml into the pericapsular region) were applied to both sides [4] (Figure 2). After PRP injection, patients' jaws were immobilized with an elastic bandage for three days during which just liquid

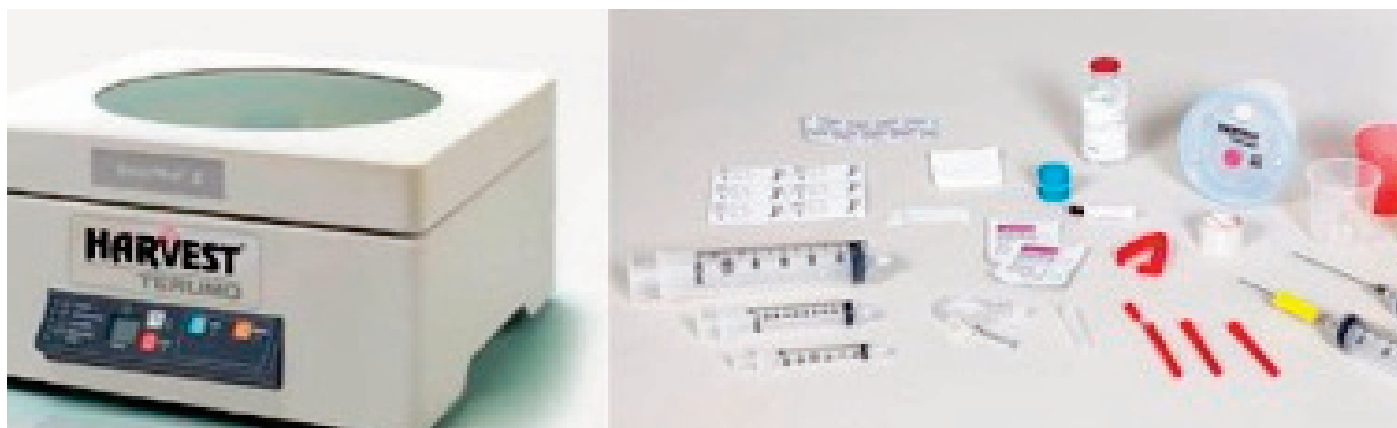


Figure 1. Harvest's kit and advanced centrifuge technology

diet was allowed. All patients were advised to restrict their joint movements and eat soft foods for one month.

Three months after the last injection, patients were asked to complete a questionnaire. The pain was assessed with verbal analogue scale (VAS) score, and using a 1 to 5 scale, satisfaction was determined in regard to clicking and dislocation before the injections and after the first and second injections. Maximal mouth opening (MMO) was estimated regarding millimetre before and after injections.

Statistical analysis

Normality of data distribution was assessed using Shapiro-Wilk test. Data with a normal distribution were expressed as mean \pm standard deviations while data with skewed distribution were expressed as median (minimum-maximum). Comparison of data was performed using Paired t-test or Wilcoxon test according to the distribution of the data.

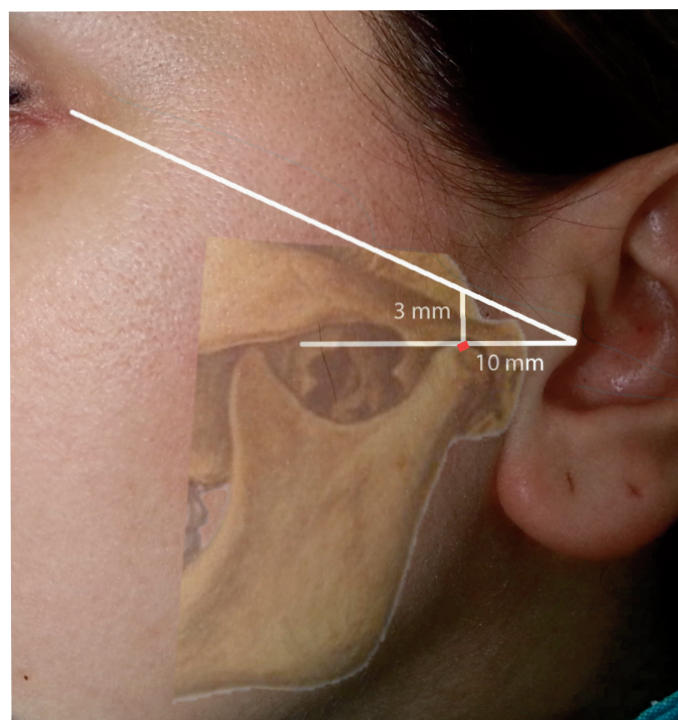


Figure 2. Anatomical landmarks for needle entry into the temporomandibular joint.

Results

Mean age was calculated as 23.14±9.3. The median time between the two injections was 38.5 days. Ages, VAS scores, and total satisfactions scores are listed in Table 1. Mean MMO was calculated as 45.14±4.7 mm before and 44.14±6 mm after two injections. Mean pain score was 7.66±1.3 before the injections, 5.33±2 after the first injection, and 3.33±1.2 after the second injection. Pain resolved significantly after the first and more significantly after the second injection ($p=0.017$ and $p<0.001$, respectively). There was also a significant improvement after the second injection compared to the pain score after the first injection ($p=0.021$).

The clicking was improved in one patient after the first injection was done. It was enhanced in another four patients after the second injection was done. Luxation developed in 2 patients after the first injection and in another four patients after the second injection. The difference was significant only after the second injection compared with the beginning ($p=0.03$). The total satisfaction rate was 2 (1-3) after the first injection ($p>0.05$) and 4±0.8 after the second injection ($p=0.017$). None of the subjects experienced significant complications associated with the procedure.

Discussion

The results of our study indicate that PRP injection may be a reasonable minimally invasive option in subjects unresponsive to conservative measures. We

observed a significant improvement in pain after both one and two injections and great satisfaction after two injections. There were no significant complications associated with the procedure.

Temporal and facial region pain is the most common complaint in TMJ disorders. Some patients also have TMJ luxation history, at least, one time. Common therapy for recurrent luxation is TMJ blockage with autologous grafts or biomaterials. However, those surgery methods have many risks like facial paralysis, foreign body reaction, hematoma, and abscess formation. Thus, novel minimally invasive treatment options are needed.

Platelet-rich plasma injection for strengthening the TMJ connective tissue is a rarely performed therapy but has positive results in bone, cartilage, ligament, and muscle tissue [5-10]. The popularity of this novel treatment method triggered an increase in studies. However, differences in application techniques, application regions, and PRP compositions make comparisons of efficacy results difficult. Potential complications following the procedures are mild; therefore, this method of treatment appears to be safer in comparison with surgical techniques [4]. PRP injection applied by orthopaedic surgeons and sport medicine physicians to the knee, ankle, and elbow joints [11, 12]. New studies suggest that PRP injection might be beneficial for TMJ ligament and cartilage healing [4].

In 1973, Schulz [13] was the first to report successful results using autologous blood injection (ABI) to treat chronic TMJ dislocation in ten patients. Daif [14] showed that injecting ABI into the superior joint space and pericapsular tissues was more

Table 1. Baseline and follow-up study variables

Patient No/Age	VAS Scores			Total Satisfaction Scores	
	Before	1 st injection	2 nd injection	1 st injection	2 nd injection
1/15	9	8	5	2	3
2/19	8	5	3	3	5
3/18	9	6	2	2	4
4/20	8	7	4	2	4
5/42	6	3	2	3	4
6/29	8	3	3	2	3
7/24	6	5	4	1	5

VAS= verbal analogue scale

successful compared to an injection into the superior joint space only (80 vs. 60%). Similarly, Machon *et al.* [15] reported an 80% success rate with ABI into the superior joint space and pericapsular tissue in 25 patients suffering from chronic recurrent TMJ dislocation.

Reduction in pain and clicking with PRP injection was showed in this study similar to Pihut's results [4]. Also, improvement in luxation was similar to the results of Candirli *et al.* [3]. To our knowledge, all previous studies used single injections for TMJ disorders. However, in this study, most of the patients underwent two injections. Our results show that after the second application, more significant pain reduction and patient satisfaction were observed.

Injection of PRP has the advantages of being repeatable, averting from tissue dissection, and less post-procedure complications [16]. The uncertain nature of the effect mechanism of the procedure is the primary disadvantage of the PRP technique [17]. Since the histopathological effects of PRP remain unclear, the fibrosis occurring after the procedure may not provide sufficient resistance to avoid dislocation in a frequently dislocated joints. Possible mechanisms underlying the effect of PRP injection on joint pain and function include platelets contain growth factors like platelet-derived growth factor, transforming growth factor beta, the vascular endothelial growth factor that is responsible for stimulating tissue generation and repair [18].

Our study has some limitations including the limited sample size and nonrandomized and open nature.

The results of our study indicate that PRP is practical and minimally invasive treatment of TMJ subluxations with favourable pain and satisfaction outcomes. The reduction in pain after recurrent applications suggests that it may be reasonable to investigate the efficacy and safety of this technique in prospective controlled trials with larger study populations.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Evaluation of Tp-e interval and Tp-e/ QTc ratio in patients with mild to moderate psoriasis

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ABSTRACT

Objectives. Many systemic diseases including cardiovascular disturbances have been described in psoriatic patients. In the previous studies, left ventricle (LV) subclinical myocardial dysfunction was reported in the psoriasis patients. The T-wave peak to end (Tp-e) interval is a relatively new marker for ventricular arrhythmogenesis and repolarization heterogeneity. Prolongation of this interval represents a period of potential vulnerability to ventricular arrhythmias. However, there is no information available assessing the Tp-e interval and related calculations in patients with psoriasis disease. The aim of this study was to evaluate ventricular repolarization in patients with psoriasis disease by using QT, corrected QT (QTc) and Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio. **Methods.** In this study, retrospective analysis of 30 patients who underwent the psoriasis treatment and of 30 healthy individuals was performed. The severity of the disease was evaluated by the "Psoriasis Area and Severity Index". QT, corrected QT (QTc), Tp-e interval and Tp-e/QT ratio were measured by means of the 12-lead electrocardiogram. Left ventricular function was evaluated by echocardiography. **Results.** Baseline characteristics and QT and QTc intervals were similar in both groups. No difference was detected between the groups with regards to Tp-e interval (83.0 ± 9 vs 82.3 ± 10 ; $p=0.81$), Tp-e/QT (0.22 ± 0.03 vs 0.23 ± 0.04 ; $p=0.3$) and Tp-e/QTc (0.20 ± 0.04 vs 0.19 ± 0.04 ; $p=0.77$). **Conclusions.** These findings suggest that ventricular repolarization in mild to moderate psoriasis patients might be unimpaired. Larger samples and severe degree psoriasis patients are needed to evaluate the arrhythmia risk in psoriasis patients.

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Keywords: Psoriasis; Tp-e interval; Tp-e/QT ratio

Introduction

Psoriasis is a chronic autoimmune skin disorder typically characterized by inflammatory plaques with a silver scale on the skin, scalp, nails and joints. Taking into account prevalence and incidence, psoriasis is thought to affect approximately 2-3% of the world

population [1]. Many systemic diseases including cardiovascular disturbances have been described in psoriatic patients [2-5]. In the previous studies, LV subclinical myocardial dysfunction was reported in the psoriasis patients especially in severe disease [6-8].

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Recent studies indicated that increased T-wave peak to end (Tp-e) interval and Tp-e /QT ratio might be a useful index to predict ventricular tachyarrhythmias and cardiovascular mortality [9,10]. However, there is no information available assessing the Tp-e interval and related calculations in psoriasis patients. The aim of this study was to evaluate ventricular repolarization in patients with psoriasis by using QT, corrected QT (QTc) and Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio.

Methods

The study population consisted of 30 patients with mild to moderate psoriasis (Group I, mean age 39 ± 13 years) and 30 control subjects (Group II, mean age 34 ± 8 years) were included.

Retrospective analysis of study patients was performed. All patients were diagnosed with Psoriasis Vulgaris based on clinical and histopathological findings. Patients with a right bundle or left bundle branch block, pacemaker implantation, coronary artery disease, valvular heart disease, heart failure, pulmonary hypertension and any medication for the prior six months including beta-blockers, antihypertensive drugs, and systemic anti-psoriatic treatment were excluded. All patients were observed to be in sinus rhythm. The ethics committee of our institute approved the study protocol.

The age, gender, height, body weight, as well as the presence of cardiovascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, and smoking) were recorded. Blood pressure was measured once after 15 min in the rest with the auscultatory method using a standard stethoscope and sphygmomanometer. Also, fasting blood glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) levels were measured.

Evaluation of the Patients

Clinical severity of the disease was assessed according to the psoriasis area and severity index (PASI). The PASI evaluates four body regions: the head, trunk, upper and lower extremities. For each region, the affected area is graded from 0 to 6, and each of the three variables (erythema, thickness, and scaling) is graded from 0 to 4, the scores from the regions were added to determine a PASI score ranging

from 0 to 72 [11]. Nail involvement of the patients was also noted.

Echocardiographic Measurements

A Vivid 7 echocardiographic unit (GE, Norway) with 3.5 MHz probe was used. All echocardiograms were performed by the same investigator. The echocardiographic study was performed in left lateral decubitus position, with parasternal long and apical 2- and 4- chamber views. Quantification by echocardiography was made according to the recommendations of European Association of Cardiovascular Imaging [12].

Measurement of Tp-e, QT and QRS intervals from the 12-lead ECG

All ECGs were scanned. The Tp-e interval was defined as the interval from the peak of T wave to the end of T wave (Figure 1). Measurements of Tp-e interval were performed from precordial leads as it was described [13]. T-wave peak to end interval, QT and RR intervals were measured by a computer based method. The QT interval was defined as extending from the beginning of QRS complex to where T waves descend onto the isoelectric baseline. When a U wave interrupted the T wave before returning to baseline, the QT interval was measured to the nadir of the curve between the T and U waves. The QTc interval was calculated using the Bazett formula: $QTc \text{ (ms)} = QT \text{ measured} / \sqrt{RR} \text{ (sec)}$. All measurements (Tp-e and other surface ECG related ones) were the mean value of three calculations. All the measurements were measured by a blinded investigator.

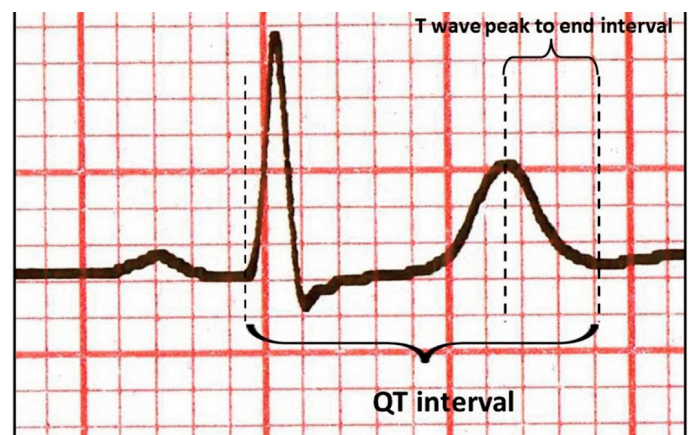


Figure 1. Demonstration of T wave peak to end and QT intervals

Statistical Analysis

SPSS version 13.0 (IBM Corporation, USA) was

used for statistical analysis. Data were summarized and organized into tables and analyzed using descriptive statistics which were given as mean±standard deviation. Categorical variables were compared via Fisher exact test. Normally distributed variables were compared across groups using student t-test whereas variables which did not normally distribute were compared using Mann-Whitney U test. $p<0.05$ was considered as statistically significant.

Results

The psoriasis group consisted of patients with a mild-to-moderate disease with a mean duration of 7.1 ± 5.3 years. Mean PASI score was 7.9 ± 4.3 . Nail involvement was detected in 30 % of patients with psoriasis (Table 1). None of the patients had psoriatic arthritis.

There were no statistically significant differences between the groups with regard to mean age, sex, heart rate, blood pressures, body mass index. There were no differences between the groups with regards to biochemical parameters (Table 2).

LV end-diastolic and end-systolic dimensions, LV

Table 1. Specific disease characteristics of patients with psoriasis vulgaris

Variables	Data
Duration of disease (years)	7.1±5.3
PASI score	7.9±4.3
Patients with nail involvement (%)	30

PASI= Psoriasis Area and Severity Index; Data are presented as means ± SD

Table 2. Characteristics of study population and biochemical parameters

	Group I (n= 30)	Group II (n= 30)	p
Age (Years)	39±13	34±8	0.116
Sex M/F	19 /11	19 /11	0.640
Body Mass Index (kg/m ²)	26.9±3	24.0±2.3	0.118
Systolic BP (mmHg)	117±12	112±9.8	0.073
Diastolic BP (mmHg)	75.5±8	71±7	0.116
Heart Rate (bpm)	75±11	76±10	0.745
WBC count (10 ³ /mm ³)	7.65±3.32	6.95±2.89	0.45
Glucose (mg/dl)	96±10	92±7	0.122
Total cholesterol (mg/dl)	168±45	160±40	0.234
LDL cholesterol (mg/dl)	97±22	92±18	0.135

LDL=Low density lipoprotein; HDL=High density lipoprotein. Data are presented as means ± SD

Table 3. Echocardiographic parameters between the patient group and the control group

	Group I (n=30)	Group II (n=30)	p
LVDD (mm)	46±3	45±3	0.193
LVSD (mm)	26±5	27.9±3	0.152
LVEF (%)	61.5±2.6	63±2	0.091
Ventricular septum thickness (cm)	0.9±0.2	0.91±0.1	0.915
LA diameter (cm)	3.6±0.2	3.46±0.3	0.113
E (m/s)	0.82±0.13	0.84±0.14	0.610
A (m/s)	0.74±0.12	0.72±0.11	0.522
E/A	1.1±0.3	1.18±0.2	0.610
Ea (cm/s)	16.3±0.9	16.9±0.4	0.836
E/Ea ratio	5.9±1.7	5.4±1,3	0.230

LVDD=left ventricle end-diastolic diameter, LVSD=left ventricle end-systolic diameter, LVEF=left ventricle ejection fraction, LA=left atrium, E=peak mitral flow velocity of early rapid filling wave, A=peak mitral velocity of late filling wave due to atrial contraction, Ea=peak early diastolic velocity. Data are presented as means ± SD.

ejection fraction, LA dimension, and diastolic Doppler indexes were not statistically different between two groups (Table 3).

Groups were compared for calculated Tp-e, QT and QTc intervals and Tp-e/QT and Tp-e/QTc ratios. We have not detected any significant differences between the groups for these calculations (Table 4). In correlation analyzes, there are no significant correlation between the PASI score and Tp-e interval ($r= -0.24, p=0.2$), QT interval ($r=0.11, p=0.54$) and QTc interval ($r=0.29, p= 0.14$) (Table 5).

The overall intraobserver variability in values for the assessment of Tp-e interval and QT interval were 0.95 and 0.90, respectively.

Discussion

Psoriasis Vulgaris is a T-cell-mediated chronic inflammatory disease characterized by the formation of inflamed plaques affecting the skin, scalp, nails and joints [14]. Despite the precise pathogenesis underlying psoriasis are not yet fully elucidated, systemic inflammatory response and oxidative stress are considered the most important mechanisms in the disease’s development [15, 16]. Many systemic diseases including diabetes, hypertension, cardiovascular disturbances have been described in psoriatic patients [2-5].

In the previous studies, LV subclinical myocardial dysfunction was reported in the psoriasis patients especially in severe disease [6-8]. However, there is

a scarcity of data on rhythm abnormalities and conduction disturbances in psoriatic patients. In the recent studies have showed that there is a tendency to atrial conduction disturbance in psoriasis patients [17, 18]. Recent studies have also demonstrated an inflammatory background of ventricular arrhythmias and atrial fibrillation [19-22]. Simsek *et al.* [17] reported that p wave dispersion and QTcD are increased in psoriasis patients. Proietti *et al.* [23] showed that increased sympathetic arm of the cardiac autonomic modulation in psoriasis patients by heart rate variability analysis. On the other hand, these studies include moderate to severe degree psoriasis patients. In the literature, there is no data about ventricular arrhythmia tendency in mild to moderate psoriasis patients.

Myocardial Repolarization has been evaluated by various methods including QT dispersion (QTd) and corrected QT dispersion (cQTd). Recent studies indicated that Tp-e interval, which is the interval between the peak and the end of T wave on electrocardiogram (ECG), can be used as an index of total (transmural, apicobasal, and global) dispersion of repolarization [24, 25]. Also, increased Tp-e interval might be a useful index to predict ventricular tachyarrhythmias and cardiovascular mortality [9]. Recently, a new index, the Tp-e/QT ratio has been suggested to be a more accurate measure of the dispersion of ventricular repolarization compared to QTd, cQTd, and Tp-e intervals which are independent of alterations in heart rate [10]. Also, these markers may be used as an electrocardiographic index of

Table 4. Electrocardiographic parameters between the patient group and the control group

	Group I (n=30)	Group II (n=30)	p
QT interval (msec)	377.4±30	356.1±38.0	0.47
QTc interval (msec)	415.1±22	431.3±31	0.64
Tp-e interval (msec)	83.0±9	82.3±10	0.81
Tp-e/ QT ratio	0.22±0.03	0.23±0.04	0.33
Tp-e/ QTc ratio	0.20±0.04	0.19±0.04	0.77

Tp-e= T wave peak to end, QTc= corrected QT, data are presented as means ± SD

Table 5. Correlations between the PASI score and ECG measurements in group I

Parameters	r	p
Tp-e interval	- 0.24	0.2
QT interval	0.11	0.54
QTc interval	0.29	0.14

ECG= electrocardiography, PASI= psoriasis area and severity index, Tp-e= T wave peak to end, QTc= corrected QT

ventricular arrhythmogenesis and sudden cardiac death [24]. The novel repolarization indexes Tp-e interval and Tp-e/QT ratio had not been studied in psoriasis patients before.

When two groups were compared in our study, QT, QTc, Tp-e interval and Tp-e/QT and Tp-e/QTc ratio were not different in mild to moderate psoriasis patients. According to the results of our study, the risk of ventricular arrhythmias in patients with mild to moderate psoriasis may not increase as much as expected. In our study, normal Tp-e interval and Tp-e/QT interval may be the following reasons: our patients to be younger. Also, they did not have any other cardiovascular risk factor. PASI Index alone is not enough for determining the severity of psoriasis. Several reports have shown that duration of psoriasis and nail involvement are necessary for establishing of psoriasis severity [26, 27]. Only 30% patients had nail involvement. So, we found normal Tp-e interval and Tp-e/QT interval because of the patients' disease severity may be milder than we assumed.

To the best of our knowledge, this is the first study to investigate Tp-e interval and Tp-e/QT interval in cases of mild to moderate psoriasis. In the present study, we demonstrated that patients with mild to moderate psoriasis had conserved normal ventricular myocardial repolarization.

There are some limitations of this study; our groups were too small for reaching definite conclusions, moreover disease severity was mild to moderate. Thus, measurement of Tp-e interval and Tp-e/QT interval in severe psoriasis patients needs to be studied in future research.

Conclusions

Patients with mild to moderate psoriasis had unimpaired myocardial repolarization. According to the results of our study, the risk of ventricular arrhythmias in patients with mild to moderate psoriasis may not increase as much as expected.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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Clinical and pathological evaluation of histopathological subtypes in patients with non-Hodgkin's lymphoma

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ABSTRACT

Objectives. Non-Hodgkin Lymphomas (NHLs) are tumours of the lymphoid system which originate from lymph nodes or extranodal lymphatic tissue. Since they represent a heterogeneous group of diseases, it is very important to determine prognostic factors apart from staging and identification of the patients with poor prognosis. The objective of our study is to investigate clinical characteristics, treatments applied, and their outcomes, survival rates, and prognostic factors which may be effective on survival. **Methods.** Clinical characteristics, treatments applied, and their outcomes, survivals, and prognostic factors which may be effective on the survival in 230 patients who were diagnosed as NHL, and consulted to our center between the years 2002, and 2015 were retrospectively evaluated. **Results.** Median age of our patients (male, 54.8 %, and female, 45.2 %) was 57 years. The most frequently seen histopathological subtype was diffuse large β cell lymphoma. We have seen that IPI score, β symptom, levels of LDH, albumin, β 2 microglobulin, and lymphocyte counts are significant prognostic factors. Stomach was the most frequently involved extranodal organ. Advanced stage, higher IPI score, extranodal organ involvement were found to be correlated with shorter survival times. **Conclusion.** Everyday developments occur in the diagnosis, classification, and treatment of NHL. Therefore, it is important for medical centres to evaluate their treatment outcomes, and prognostic factors affecting their survival rates.

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Keywords: Non-Hodgkin Lymphoma, survival rate, IPI score

Introduction

Non-Hodgkin's lymphoma (NHL) is a clonal proliferative disease of B, T or natural killer cells which originate from lymph nodes or extranodal lymphatic tissue [1]. NHL comprises 4% of newly diagnosed cancer, and 90 % of lymphomas. 90% of NHLs are β -cell lymphomas. Clinical features of NHL

demonstrate changes with geographical factors. Determination of the characteristics of the patients living in different regions, and definition of different prognostic parameters are very important [2, 3]. Since NHL represents a very heterogeneous disease group, determination of prognostic factors, and

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identification of patient groups with poor prognosis have a crucial importance [4].

Posttreatment complete response in NHL is around 60-80%, and median 5-year survival rate is over 55 percent [5]. Magnificent developments and innovations have been recorded in the diagnosis, classification, staging, and treatment of NHL. Evaluation of the treatment results of medical centres carries utmost importance.

The objective of our study is to investigate the importance of clinical characteristics, treatments applied, and their outcomes, survival rates, and prognostic factors which might affect survival rates of the patients who were referred to our Department of Medical Oncology and Haematology from any outpatient clinic of Mersin University Hospitals of Faculty of Medicine with the diagnosis of NHL.

Methods

A total of 278 patients were referred to the Department of Medical Oncology and Haematology with the established diagnosis of NHL between the years 2002 and 2015. In consideration of 20 % loss of data in medical files, we planned the study population to be at least 230 patients. Approval of the Mersin University Ethics Committee was obtained for the study. Clinical characteristics, treatments applied, and their outcomes, survivals, and prognostic factors which may be effective on the survival were retrospectively evaluated.

From patient files demographic, clinical, biochemical (albumin, lymphocyte counts, LDH, uric acid, β -microglobulin levels), histopathological findings, treatments applied, and their results, presence of extranodal involvement, and β -symptoms were recorded. For B symptoms, fever ($>38^{\circ}\text{C}$), marked night sweats, and $>10\%$ weight loss during the previous 6 months relative to baseline were taken as a basis. For clinical staging of the disease Ann Arbor classification was used. Histological classification was based on WHO (the World Health Organization) criteria. International Prognostic Index (IPI) scores were calculated. From patient files information about treatments of the patients, and follow-up periods were obtained. Living status of the patients who were lost to follow-up was learnt via phone contact with the patients. WHO criteria were considered for the evaluation of responses.

Statistical Analysis

Categorical data were summarized as numbers, and percentages, while using descriptive statistical methods continuous data were expressed as mean \pm standard deviation. In intergroup comparisons regarding patient ages independent two groups t test was used $p < 0.05$ was set as the level of significance.

In the present study which followed up patients with non-Hodgkin lymphoma, we aimed to calculate mortality, and survival rates. In survival analyses, the cause of failure was determined as mortality among other parameters (mortality, remission, recurrence etc.). Survival analysis was evaluated by means of Kaplan-Meier method. As an outcome of this analysis, in summary statistics, median survival times were used. In groups which demonstrated differences, the group under higher risk was determined, and interpreted using hazard ratio.

Results

A total of 230 patients (female, $n=104$; 45.2%, and male, $n=126$; 54.8%) were included in the study. General characteristics of the patients are given in Table 1.

At the time of diagnosis, mean ages of all cases, female, and male population were 57 ± 15.78 (16-87 years); 57 ± 14.69 , and 56 ± 16.66 years, respectively, without any statistically significant difference between genders ($p=0.467$).

At the time of diagnosis, mean IPI scores were 0 in 27 (11.8%), 1 in 57 (24.9%), 2 in 56 (24.5%), 3 in 60 (26.2%), 4 in 26 (11.4%), and 5 in 3 (1.3%) patients.

Fifty-nine (25.9%) patients underwent diagnostic surgery. Most frequently splenectomy (31.7%), tonsillectomy (20%), excision of the mass (16.7%), resection of small bowel/colon (10%), orchiectomy/ovarectomy (8.3%), and parathyroidectomy (5%) were performed.

At the time of diagnosis, based on Ann Arbor staging system, the patients were in Stages I ($n=39$; 17.4%), 2 ($n=42$; 18.8%), 3 ($n=53$; 23.7%), and 4 ($n=90$; 40.2%). In 98 (42.6%) cases β -symptom was seen. Splenic involvement in 36 (15.7%), and tonsillar involvement in 15 (6.5%) cases were seen.

The most frequently histopathological subtypes in order of decreasing frequency were as follows: diffuse large β -cell lymphoma (DLBCL, 43.2%), B-cell

lymphoma (15.4%), follicular lymphoma (FL, 9.7%), mantle cell lymphoma (MHL, 7.5%), T-cell lymphoma (5.3%). Based on WHO classification histopathological subtypes are given in Table 2.

Table 1. The data of the patients

Data	n (%)
Gender (Female)	104 (45.2)
Age (≥ 60 years)	115 (50)
IPI	
0	27 (11.8)
1	57 (24.9)
2	56 (24.5)
3	60 (26.2)
4	26 (11.4)
5	3 (1.3)
Stage	
I	39 (17.4)
II	42 (18.8)
III	53 (23.7)
IV	90 (40.2)
β -symptom (+)	98 (42.6)
Splenic involvement (+)	36 (15.7)
Tonsillar involvement (+)	15 (6.5)
Bone marrow involvement (+)	44 (32.8)
Extranodal involvement (+)	100 (43.9)
LDH (≥ 380 U/L)	43 (22.3)
Albumin (< 3.5 g/dL)	41 (21.5)
$\beta 2$ microglobulin (≥ 3000 ng/mL)	43 (36.4)
Uric acid (≥ 5.7 mg/dL)	62 (34.6)
Lymphocytes (≥ 1500 mm ³)	128 (60.3)

IPI= International Prognostic Index, LDH=lactate dehydrogenase

At the time of diagnosis bone marrow involvement was seen in 44 (32.8 %) cases. Albumin levels were ≥ 3.5 g/dL (n= 150; 78.5%) or below (n= 41; 21.5%) 3.5 g/dL. LDH levels were ≥ 380 U/L (n=43; 22.3%) or below (n=149; 77.7%) 380 U/L. $\beta 2$ microglobulin value was ≥ 3000 ng/mL in 43 (36.4%), and below this value in 75 (63.6%) cases. Uric acid levels were ≥ 5.7 mg/dL in 62 (34.6%), and < 5.7 mg/dL in 117 (65.4%) cases. Lymphocyte counts were ≥ 1500 /mm³ in 128 (60.3%), and lower that level in 84 (39.7%) cases.

Extranodal involvement was seen only in 100 (43.9%) cases. The distribution of extranodal involvement is given in Table 3.

Treatment Response Rates

The patients received cyclophosphamide+hydroxy

doxorubicin+vincristine (Oncovin®)+prednisone (CHOP) (n=18; 10%), rituximab-CHOP (R-CHOP) (n=134; 74.4%), and other chemotherapy (n=15; 8.3%) regimens.

Table 2. Distribution of patients' diagnosis according to histopathological subtypes

Histopathological Subtypes	n (%)
Diffuse large β -cell lymphoma	98 (43.2)
Mantle cell lymphoma	17 (7.5)
Follicular lymphoma	22 (9.7)
B-cell lymphoma	35 (15.4)
T-cell lymphoma	12 (5.3)
Small lymphocytic lymphoma	7 (3.1)
Lymphoblastic lymphoma	1 (0.4)
Malignant lymphoma	10 (4.4)
Marginal zone lymphoma	11 (4.8)
Burkitt lymphoma	2 (0.9)
Mixed type lymphoma	2 (0.9)
Anaplastic large B-cell lymphoma	7 (3.1)
MALT lymphoma	2 (0.9)
Natural Killer cell lymphoma	1 (0.4)

MALT= mucosa associated lenfoid tissue

Complete, and partial treatment response rates were achieved in 120 (62.5%), and 34 (17.7%) patients, respectively, while 37 (19.3%) patients did not respond to treatment. Hundred and seven patients (49.1%) exited, and 111 (50.9%) patients survived. R-CHOP or CHOP therapy achieved complete response rates in 86 (69.4 %), and 7 (41.2%) patients, respectively. Treatment response rates based on chemotherapeutic regimens are given in Table 4.

Table 3. Extranodal involvements

Affected organs	%
Stomach	15
Lungs	13.5
Small bowel/colon	13.5
Nasopharynx	12.4
Liver	9
Extremities	6.7
Vertebra	5.6
Brain	4.5
Parotid gland	3.4
Eyes	3.4
Ovary/ testis	3.4
Thyroid	3.4
Retroperitoneum	1.1
Breast	1.1
Kidney	1.1

Table 4. Treatment response rates according to chemotherapy regimens

Chemotherapy Protocols	Response	n (%)
R-CHOP	Complete response	86 (69.4)
	Partial response	18 (14.5)
	No response	20 (16.1)
CHOP	Complete response	7 (41.2)
	Partial response	3 (17.6)
	No response	7 (41.2)

CHOP= cyclophosphamide, hydroxy doxorubicin, vincristine (Oncovin[®]), prednisone, R-CHOP= rituximab + CHOP

Complete response rates were achieved in patients with IPI scores of 0 (n=17; 81%), 1 (n=38; 77.6%), 2 (n=31; 68.9%), 3 (n=23; 44.2%), and 4 (n=10; 47.6%). While in patients with IPI score of 5, one patient (33.3%) gave partial response, and 2 (66.7%) patients didn't respond to treatment. Treatment response rates based on IPI scores, and disease stages are shown in Tables 5, and 6.

Table 5. Response rates based on IPI scores

IPI Score	Response	n (%)
0	Complete	17 (81)
	Partial	1 (4.8)
	No	3 (14.3)
1	Complete	38 (77.6)
	Partial	3 (6.1)
	No	8 (16.3)
2	Complete	31 (68.9)
	Partial	5 (11.1)
	No	9 (20)
3	Complete	23 (44.2)
	Partial	17 (32.7)
	No	12 (23.1)
4	Complete	10 (47.6)
	Partial	7 (33.3)
	No	4 (19)
5	Complete	0
	Partial	1 (33.3)
	No	2 (66.7)

IPI= International Prognostic Index

Female patients gave complete (n=61; 68.5%) or partial (n=12; 13.5%) responses to treatment, while 16 (18%) female patients did not respond to the treatment

at all. Male patients gave complete (n=59; 57.3%) or partial (21.4%) response to treatment, while 22 (21.4%) male patients did not respond to treatment. Treatment response rates based on gender of the patients are given in Table 7.

Table 6. Response rates based on disease stage

Stage	Response	n (%)
I	Complete	0
	Partial	24 (82.8)
	No	5 (17.2)
II	Complete	31 (83.8)
	Partial	4 (10.8)
	No	2 (5.4)
III	Complete	19 (45.2)
	Partial	11 (26.2)
	No	12 (28.6)
IV	Complete	43 (54.4)
	Partial	18 (22.8)
	No	18 (22.8)

Table 7. Response rates according to gender

Gender	Response	n (%)
Female	Complete	61 (68.5)
	Partial	12 (13.5)
	No	16 (18)
Male	Complete	59 (57.3)
	Partial	22 (21.4)
	No	22 (21.4)

Patients with β -symptom gave complete (n=43; 51.8%) or partial (n=18; 21.7%) responses to treatment, while 22 (26.5%) of them did not respond

to the treatment at all.

Patients with albumin levels ≥ 3.5 g/dL gave complete (n=97; 74%) or partial (n=20; 15.3%) responses to treatment, while 14 (10.7%) patients did not respond to treatment at all.

In patients with LDH levels above 380 U/L, complete (n=23; 56.1%), and partial (n=9; 22%) response rates were achieved, while 9 (22%) patients were unresponsive to treatment.

In patients with $\beta 2$ microglobulin levels of ≥ 3000 ng/mL, complete (n=23; 57.5%), and partial (n=5; 12.5%) response rates were achieved, while 12 (30%)

patients did not respond to treatment. In patients with $\beta 2$ microglobulin levels of < 3000 ng/mL complete (n=55; 83.3%) and partial (n=9; 13.6%) response rates were achieved, while 2 (3%) patients did not respond to treatment.

Patients with uric acid levels ≥ 5.7 mg/dL gave complete (n=30; 57.7%) or partial (n=11; 21.2%) responses to treatment, while 11 (21.2%) patients did not respond to the treatment at all. Among patients with uric acid levels of < 5.7 mg/dL, complete or partial treatment response rates were achieved in 74 (72.5%), and 15 (14.7%) patients, respectively.

Table 8. Treatment response rates according to laboratory results

Test	Response	n (%)
Albumin ≥ 3.5 g/dL	Complete	97 (74)
	Partial	20 (15.3)
	No	14 (10.7)
Albumin < 3.5 g/dL	Complete	17 (47.2)
	Partial	8 (22.2)
	No	11 (30.6)
LDH ≥ 380 U/L	Complete	23 (56.1)
	Partial	9 (22)
	No	9 (22)
LDH < 380 U/L	Complete	90 (70.3)
	Partial	20 (15.6)
	No	18 (14.1)
Uric acid ≥ 5.7 mg/dL	Complete	30 (57.7)
	Partial	11 (21.2)
	No	11 (21.2)
Uric acid < 5.7 mg/dL	Complete	74 (72.6)
	Partial	15 (14.7)
	No	13 (12.7)
$\beta 2$ microglobulin ≥ 3000 mg/L	Complete	23 (57.5)
	Partial	5 (12.5)
	No	12 (30)
$\beta 2$ microglobulin < 3000 mg/L	Complete	55 (83.3)
	Partial	9 (13.6)
	No	2 (3)
Lymphocytes ≥ 1500	Complete	80 (69.6)
	Partial	22 (19.1)
	No	13 (11.3)
Lymphocytes $< 1500/\text{mm}^3$	Complete	40 (54.8)
	Partial	12 (16.4)
	No	21 (28.8)

LDH= lactate dehydrogenase

However, 13 (12.7%) patients did not respond to treatment at all.

Patients with lymphocyte counts of ≥ 1500 mm³ complete (n=80; 69.6%) or partial (n=22; 19.1%) respond rates were achieved, while 13 (11.3%) patients did not respond to treatment. Patients with lymphocyte counts of < 1500 mm³ complete (n=40; 54.8%) or partial (n=12; 16.4%) respond rates were achieved, while 21 (28.8%) patients did not respond to treatment.

Survival analyses

From a total of 230 study patients, 217 of them were included in the survival analysis. Median survival time of the patients was 60 months, while 5-year-survival rate was 48.1 percent.

A statistically significant difference was not found between the survival times of female, and male patients with non-Hodgkin lymphomas ($p=0.77$). Median survival times in female and male patients were 72, and 60 months, respectively. Five-year survival rates in female and male patients were 50, and 46%, respectively.

A statistically significant difference was found between patients with and without β symptoms as for survival times ($p=0.002$). Median survival times in patients with, and without β symptom were 48, and 72 months, respectively. The mortality risk in patients with β symptom was 1.93 times higher when compared with those without. Median 5-year survival rates were 35% and 57% in patients with and without β symptom.

A statistically significant difference was not found between survival times of those with, and without splenic involvement ($p=0.46$). A statistically significant difference did not exist between patients receiving radiotherapy or any other treatment ($p=0.55$). Median survival times in patients receiving radiotherapy and other therapies were 48 and 72 months, respectively. Median 5-year survival rate of those receiving radiotherapy was 32 percent.

A statistically significant difference was found between patients with serum albumin levels below 3.5 g/dL and above ($p<0,001$). Median length of the survival time was 72, and 36 months in patients with albumin levels of ≥ 3.5 g/dL, and $< 3,5$ g/dL, respectively. The patients with albumin levels of < 3.5 g/dL had 4.66 times higher risk of mortality. Median 5-year survival rate of the patients with serum albumin levels of ≥ 3.5 g/dL was 59%.

A statistically significant difference was found

between patients with and without LDH values of ≥ 380 U/L ($p=0.01$). Median survival times were 48, and 72 months for patients with LDH levels of ≥ 380 U/L and < 380 U/L, respectively. Patients with LDH levels over 380 U/L had a 1.96 times higher risk of death relative to patients with LDH levels below 380 U/L. Median survival rate of the patients with LDH levels of ≥ 380 U/L was detected to be 39%.

A statistically significant difference was found as for median survival times between patients with $\beta 2$ microglobulin levels of ≥ 3000 ng/mL (72 months), and < 3000 ng/mL (132 months, $p=0.03$). Patients with $\beta 2$ microglobulin levels of ≥ 3000 ng/mL had a 2.06 times higher mortality risk relative to patients with < 3000 ng/mL. Median survival rate of the patients with microglobulin levels of < 3000 ng/mL was estimated as 69%.

A statistically significant difference was not found between patients with serum uric acid levels of ≥ 5.7 and < 5.7 mg/dL regarding median survival times (60 vs 72 months) ($p=0.95$). Median 5-year survival rate in patients with serum uric acid levels below 5.7 mg/dL was 54%.

A statistically significantly difference in median survival times was found between patients with lymphocyte counts of ≥ 1500 mm³ and < 1500 mm³ (72 vs 36 months) ($p=0.003$). Patients with lymphocyte counts below 1500 mm³ had a 1.95 times higher risk of mortality relative to other group of patients. Median 5-year survival time was 56% in patients with lymphocyte counts ≥ 1500 mm³.

A statistically significant difference was not found between patients with and without bone marrow involvement regarding median survival times (48 months for both groups) ($p=0.36$). Median survival time in patients without bone marrow involvement was estimated as 45 percent.

A statistically significant difference was found between patients with and without extranodal involvement for overall survival rates ($p=0.03$). Median survival times for patients with and without extranodal involvement were 36, and 84 months, respectively. The patients with extranodal involvement had a 1.56 times higher risk of death. Median 5-year survival rate in patients without extranodal involvement was 56 percent. The patients were evaluated in stages 1-2, and 3-4. Survival times of stages 1-2, and 3-4 were statistically significantly different. ($p=0.048$). Median survival times in stages 1-2, and 3-4 were 72, and 48 months, respectively. Stage 3-4 patients had a 1.53 times higher risk of death

versus stage 1-2 patients. Median survival rates in stage 1-2 and 3-4 patients were 55, and 45%, respectively.

IPI scores of the patients were evaluated as 0 -1 (low), 2 (low-moderate), 3 (moderate-high), and 4-5 (high). A statistically significant difference was found between groups ($p=0.001$). Median survival times differed between IPI 0-1, vs 3; IPI 0-1 vs 4-5; IPI 2 vs 4-5. Median survival times of the patients were as follows: IPI 0-1, 96 months; IPI 2, 72 months, IPI 3, 48 months, and IPI 4-5, 36 months.

Discussion

In 1970s, and 1980s incidence of NHL, and related mortality rates demonstrated annual increase of 4 percent. From the year 1990 on, increase in the incidence rates of NHL decreased, however still an annual increase of 1-2% is detected. Although incidence of NHL increases in the whole world, incidence rates differ in diverse geographic regions, and vary with some etiological factors as environmental factors, and socioeconomic levels [6].

The American Cancer Society's most recent estimates for non-Hodgkin's lymphoma for 2016 are; about 72,580 people (40,170 males and 32,410 females) will be diagnosed with NHL. This includes both adults and children. About 20,150 people will die from this cancer [7].

Since NHL belongs to a very heterogeneous group of patients, determination of prognostic factors other than prognosis, and identification of patient groups with poor prognosis carry utmost importance [4].

Our study population mostly consisted of male patients. As seen in many other studies male/female (1.2 1/1) ratio represented male dominance. Male dominance rates differed among countries (USA, 1.43; Europe. 1.23; Austria, 1.52; Greece 1.16, and Korea, 1.6 [8-12].

Median age of our patients was 57 years (range, 16-87 years). Two studies performed in Turkey reported higher median ages of their patient population [2, 13]. However relative to Western society, median ages of our study and European estimates were similar [14, 15].

In our study incidence rates between genders as for mean age of its onset did not differ (women: 57±14.7 yrs, and men: 56±16.7 yrs). Based on literature data NHL is seen at an earlier age in men vs women. In all groups, incidence of NHL increases

with age. After 55 years of age, increase in incidence becomes marked irrespective of the gender of the patients [16, 17].

In our study the most frequently (43.2%) histopathological subtype of NHL was diffuse large β -cell lymphoma (DLBCL), followed by follicular lymphoma (9.7%), and mantle cell lymphoma (7.5%). Similarly, in the literature the most frequently reported histological subtype was also DLBCL. Some data have indicated follicular subtype as the most frequently seen histological subtype [2, 18, 19]. In our study 9.7% of our patients had follicular lymphomas. Recent increase in the incidence of follicular lymphoma has been presumably attributed to the all-encompassing definition of this subtype.

When data of the studies performed in USA, Europe, and Asia, using Ann Arbor staging system, 45-54 % of NHL patients were at an advanced stage of their disease at the time of diagnosis [20-23]. In our study, 63.9% of our patients were at an advanced stage of their disease (stage 3-4) at the time of diagnosis which is higher than those reported in various literature studies.

Still different definitions have been made for primary nodal, and extranodal (PEL) lymphomas. In some of these definitions involvements of Waldeyer ring, spleen or bone marrow are considered as primary nodal disease, while in other publications they are considered as forms of extranodal involvements. In a study by Arican *et al.* from Turkey performed on 464 patients, the incidence of PEL was indicated as 25%, while in other studies from Turkey its incidence was determined to range between 25 and 46 percent. In Western countries its reported incidence varies between 24, and 48 percent [24, 25]. In a study performed by Di-Amore *et al.* [26] in Denmark, and Economopoulos *et al.* [27] in Greece quite different incidence rates were reported (38 vs 45.6%). Such a wide spectrum of differences might stem from variations in the descriptions of primary extranodal lymphoma, and different geographic diversities. In our study extranodal involvement was detected in 43.9% of the cases, while in 56.1% the patients' nodal disease was found. Stomach was the most frequently seen site of extranodal involvement. Also as indicated in the literature, extranodal involvement was most frequently seen in the stomach in USA, and Asian countries. Followed by stomach, most frequently involvement of tonsils, small bowels, and skin has been reported [28-30]. In our study, lungs were the second most frequently involved organ. However, inclusion of

metastatic cases in this group might probably contribute to this higher incidence rates. Besides widespread use of PET in the diagnosis, and follow-up of lymphoma, might lead to misperception of pulmonary infections as cases of lymphoma which eventually contributed to erroneously higher rates of pulmonary involvement.

In our study we achieved complete (n=120; 62.5%), and partial response rates in 120, and 34 (17.7%) patients, respectively. More than an half (50.9%) of the patients survived. In a comprehensive meta-analysis of 2031 patients' complete response rate of 53 percent was reported [31].

According to 2007 data of a European study (EURO-CARE 4) 5-year survival rate was reported as 54.6 percent [32]. Based on data of SEER 13 study 5-year survival rate was reported as 69.1 percent [29]. In a study performed in Scandinavian countries between the years of 1964, and 2003, 5-year overall survival rate was reported to range between 50 and 60 percent [33]. In China average 5-year-survival rate was reported as 55.2 percent [30]. In our study, 5-year survival rate was 48.1 percent. This survival rate was lower than that of USA, and European survival rates, but at a similar level of China, and Scandinavian countries.

In an international organization (NHL Prognostic Factors Project) performed to develop a better prognostic model for NHL, 2031 patients with aggressive NHL were examined to formulate two indices namely IPI, and age adjusted IPI (sAAIPI). In this study age was detected to be a highly significant prognostic variable (>60, and ≤60 years) Seven factors were analysed, and only 5 of them were found to be significant including age, performance status, stage, number of extranodal involvements, and serum LDH levels [31, 34]. In our study complete response rates were detected in patients with IPI scores of 0 (n=17; 81%), 1 (n=38; 77.6%), 3 (n=23; 44.2%), 4 (n=10; 47.6%), and 5 (n=1; 33.3%). An inverse correlation was detected between IPI scores, and response rates. In the literature, higher IPI score, advanced stage, aggressive lymphoma subgroup according to WHO classification were observed to be poor prognostic parameters [31, 35].

In patients with NHL, various laboratory parameters have been analysed for their effects on treatment response, and overall survival rates. Prognostic values of sedimentation, and levels of LDH, CRP, albumin, uric acid, haemoglobin have been demonstrated in various studies [25, 36, 37]. In

our study complete treatment response rates were achieved in indicated percentage of 80 patients with serum levels of LDH <380 U/L (70.3%), β 2 microglobulin <3000 ng/mL (83.3%), uric acid <5.7 mg/dL (72.5%), albumin lymphocyte count of \geq 1500 mm³ (69.6%). In 97 patients with albumin levels of >3.5 g/dL complete response rate (74%) was achieved. In conclusion, similar to the literature, in our study prognostic values of the levels LDH, uric acid, β 2 microglobulin, albumin, and also lymphocyte counts have been also determined.

In our survival analysis, risk of mortality was higher in patients with β -symptom when compared with those without. A statistically significant difference existed between patients with and without β -symptoms. In patients who gave complete response to treatment a statistically significant difference was not detected as for the presence of β -symptom, however from clinical perspective, patients without β symptom had disease-free survival times longer than 36 months. In the literature, variable effects of the presence of β -symptom on the treatment response, and survival rates have been reported. In a study by Andrew *et al.* [38] presence of β -symptom was indicated as a prognostic factor which markedly effects survival time. In another study the effect of the presence of β -symptom on treatment response was not found, while its relationship with shorter survival time, and progression-free survival time was detected [14].

In the evaluation of overall survival, different from the literature data, a statistically significant difference was not found between survival times of the patients with affected bone marrow, spleen, and tonsils. In a study by Alici *et al.* [13] a statistically significant effect of bone marrow involvement on the treatment response, and survival rates was not detected.

In our study a statistically significant difference was found between patients with, and without extranodal involvement as for overall survival rates. A statistically significant difference was not detected between extranodal involvement, and disease-free survival. However, from clinical perspective, patients without extranodal involvement had 60-months longer survival time than those with nodal involvement. A significant difference has not been reported in the literature between patients with and without extranodal organ involvement [19, 30].

In studies performed after the year 2000, planning of the treatment has been recommended, and implemented based not only on the histology, and stage of the disease, but also on prognostic factors as

IPI. In especially high grade lymphomas individualization of the treatment is recommended based on IPI risk criteria [39]. Also in our study, IPI scores were graded as 0-1 (low risk), 2 (low-moderate risk), 3 (moderate-high risk), and 4-5 (high risk). Median survival times differed statistically significantly between IPI categories. In patients with complete response rates, median survival times did not differ between IPI categories.

In many studies performed unfavourable effects of higher serum LDH levels on treatment response, overall, and progression-free survival rates have been reported [34, 40]. In our study, patients with higher serum LDH levels had 2-times higher mortality risk. Overall survival rates were also significantly different.

Lower serum albumin levels have been associated with poor treatment response, and shorter survival times [34,40]. In our study a statistically significant difference was found between serum albumin levels, and overall survival rates. Patients with lower albumin levels had 4,5-fold higher mortality risk. However, a statistically significant difference was not found between albumin level, and disease-free survival. From clinical perspective, patients with higher albumin levels had a 48 month- longer disease-free life time.

In the literature lymphopenia has been demonstrated as a poor prognostic factor [41]. In our study lymphopenic patients had 2-fold higher mortality risk.

In recent years increases in $\beta 2$ microglobulin value in parallel with NHL stage have been demonstrated, which indicate that it is an important and independent prognostic factor by itself or in combination with serum NHL value [42]. Similar to literature findings, in patients with increased $\beta 2$ microglobulin values, 2-times higher risk of mortality was detected. In patients with higher $\beta 2$ microglobulin values overall survival and disease-free survival times were shorter with a worse treatment response when compared with the healthy individuals.

Conclusions

Clinical characteristics, treatments applied, and their outcomes, survival rates, and the importance of prognostic factors which may be effective on the survival were retrospectively evaluated.

Mean age of our patients was 57 ± 15.8 years. Our

study population consisted of relatively greater number of male patients in compliance with the literature. Patients in the advanced stage of the disease were more numerous than indicated in the literature. IPI score, β symptom, levels of LDH, albumin, $\beta 2$ microglobulin, and lymphocyte counts had prognostic value. Risky patient groups regarding this issue should be followed up more closely. Stomach was the most frequently involved organ. Advanced stage, higher IPI score, and extranodal organ involvement were associated with shorter survival times. Our study findings were comparable with literature data.

Every day new developments have been observed in the diagnosis, classification, and treatment of NHL. Therefore as an important issue, each centre should evaluate its own treatment outcomes, and prognostic factors effective on survival rates.

Conflict of interest

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A viable childbirth after correction of spontaneous uterine dehiscence

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ABSTRACT

We report a case of uterine dehiscence during pregnancy. Uterine dehiscence and rupture are serious complications of pregnancy. This situation takes place especially in women that prior uterine operation(s). We represent a 30-year-old woman diagnosed uterine dehiscence at 22nd gestation week. Uterine dehiscence treated surgically and then medical treatment was given to prevent preterm labour. At 34th gestation week, the patient was operated because of preterm labour and an alive foetus was born. The result of the pathologic examination of the placenta: Placental adhesion failure was detected. In conclusion women with prior caesarean delivery (one or more), ultrasound measurement should be recommended for measuring the lower uterine segment thickness in order to predict the possibility of uterine dehiscence and rupture.

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Keywords: Alive foetus; dehiscence; primary repair

Introduction

Nowadays uterine complication can be seen rather frequently because of increasing rate of caesarean section (C/S) operation. Uterine dehiscence and rupture are serious complications which could be considered in a patient who had prior caesarean operation(s) during pregnancy. While uterine dehiscence is defined as a situation in which myometrial layer is separated but amniotic sac is not ruptured, and foetus does not pass into abdominal cavity. Uterine rupture is defined as a condition in which uterine cavity combines with peritoneal cavity by the opening of the whole uterine wall including

serosa and integrity of the amniotic sac fails [1]. The overall incidence of uterine rupture and dehiscence has decreased significantly with the modern practice of obstetrics, but, in contrast, increasing the risk of pathologies like implantation anomalies and scar dehiscence are related to prior caesarean section scar. The incidence of uterine rupture is 0.07% in a developed country [2].

Severe abdominal bleeding could be seen mostly in uterine rupture. Also, it could be seen uterine dehiscence [3]. Regarding foetal heart rate monitoring with cardiotocography (CTG) is not a good predictor

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of adverse outcomes, however; late and variable decelerations could result in long-term foetal bradycardia and suddenly loss of foetal heart rate.

In some studies, uterine rupture cases constitute a significant portion of maternal and foetal deaths, especially in developing countries. In various studies, foetal mortality rates were reported as a range from 50% to 75 % [4].

We reported a rare case of uterine dehiscence and its management which was diagnosed and operated on 22nd gestation weeks.

Case Presentation

A 30-year-old woman who had prior caesarean section surgery was referred to a hospital with a lower side abdominal pain at 22nd gestational week. According to the physical examination, she had nausea and vomiting which was compatible with acute abdomen. There was no vaginal bleeding. The patient was hospitalized immediately. During the clinical observation, tachycardia and hypothermia rapidly progressed. According to ultrasonographic examination, foetal heart beat existed, amniotic fluid volume was sufficient, the placenta was observed as located anterior wall of the uterus, and there was no retroplacental pathology. But there was a complex structure with the diameter of 84x68 millimetres comprising a hypo-hyper echogenic area at the right adnexial location. The patient was operated with the diagnosis of acute abdomen; firstly diagnostic laparoscopy was applied to the patient then converted to laparotomy with median incision because of large coagulum in the abdominal cavity. Approximately 5-6 centimetres dehiscence covering with coagulum was found on the front face of the uterus which matched to prior caesarean scar area. When the coagulum was cleaned, maternal side of placenta was seen easily. Defective uterine scar was primarily repaired by suturing with polyglactin. After the successful operation, intravenous tocolytic treatment (ritodrine) was applied with until 13th postoperative day then tocolytic treatment used with magnesium citrate. The patient was followed up in the hospital until fetal birth. A fetus, whose APGAR score 8 was born by C/S because of preterm labor at 34th gestation week. Placenta, which was given purple halo seen on the isthmus of the uterus and front of the lower segment of corpus during operation. This 5-6 cm area on the

front wall of the uterus excised and primarily repaired. As a result, of pathological examination of the placenta, there was an adhesion abnormality (Figure 1). The patient was discharged from hospital without any complication.

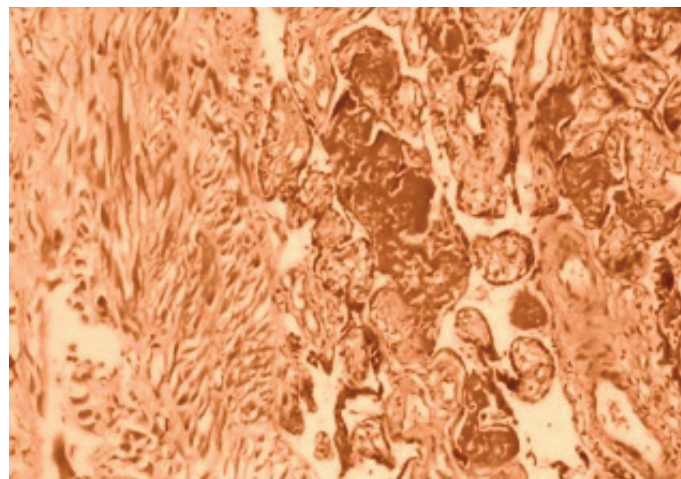


Figure 1. Pathology of placenta. Villi adhere directly to the myometrium without intervening decidua (HEEx200)

Discussion

Uterine scar dehiscence and rupture are serious complications of pregnancy. Spontaneous uterine ruptures also observed during labor. Risk factors for uterine rupture are given in Table 1 [5]. The settlement of the placenta on the cesarean scar and the presence of placental adhesion abnormalities can be defined as the main risk factors for the formation of spontaneous rupture especially in patients with prior CS. The majority of cases of spontaneous rupture occurs in the 3rd trimester of pregnancy. Obstetrical clinicians are very sensitive to uterine rupture and dehiscence especially in pregnant women who have a history of a prior caesarean section at weeks close to last period of pregnancy. But the most important point to keep in mind is uterine rupture and dehiscence also can be seen in the early weeks of pregnancy. Cases of uterine rupture in 2nd trimester are very rare. The main reason is medical evacuations in the 2nd trimester due to medical reasons or fatal anomalies of the foetus. It is known that placental adhesion abnormalities such as percreta etc. constitute the majority of cases of spontaneous rupture, and mostly they are observed at 23-28 weeks of pregnancy. In the study of Chapman and colleagues in which 606 cases of medical

Table 1. The risk factors for uterine rupture

Age between 31-35
Grand multiparity
Birth trauma
Neglected birth
Malpresentation
External or internal podalic version
Breech presentation
Manual cervical dilation
Use of oxytocin or prostaglandins
Placental adhesion abnormalities
Previous uterine surgery (myomectomy, cesarean section, cornual resection, hysteroscopic procedures, laparoscopic trochar injuries, abdominal penetrating injury)

evacuation were examined, uterine rupture was detected between 22-24 weeks in 4 women; prior caesarean delivery was found in three of them [6]. Cases of spontaneous uterine rupture occur more frequently in adhesion abnormality such as placenta percreata. The majority of these cases occur between 23-28 weeks of gestation. Spontaneous uterine ruptures can be seen even in primigravid women beside the more common case of the previous caesarean section. There are 3 cases found in the literature [7, 8]. Radiological imaging techniques could be insufficient in diagnosing such cases so that clinical diagnosis is also crucial to determine the cases of uterine rupture and dehiscence.

In this case, during the operation, uterine dehiscence diagnosed, amniotic sac was intact, and the foetus was alive. It is critical to diagnose this situation as early as possible. Unfortunately, most of such cases are diagnosed only after the complete uterine rupture with ripped amniotic sac and foetal expulsion partially or completely placed into the abdominal cavity. Also receiving the patient to the surgery within a few hours after the onset of symptoms is a vital prognostic factor for ongoing pregnancy like in our case.

Consequently; the possibility of uterine rupture and dehiscence should be considered during each period of pregnancy. It is important especially in pregnancies with a history of prior uterine surgery, C/S, and placental adhesion abnormalities.

In women with previous caesarean delivery(ies), ultrasound measurement has been used to study the lower uterine segment thickness and predict uterine dehiscence and rupture. Gotoh et al. [9] found no difference in lower uterine segment thickness at 19 weeks between women with or without a prior caesarean delivery, but lower uterine segment

thickness was significantly lower at 27 weeks in women with a previous caesarean delivery. Another study by Rozenberg *et al.* [10] also concluded that the risk of rupture was related to the thickness of the lower uterine segment at 37 weeks. Using a cut-off 3.5 millimetres (mm), they found that a thin lower uterine segment had a sensitivity of 88%, specificity of 73%, positive predictive value of 11.8%, and negative predictive value of 99.3% for prediction of uterine rupture. Therefore, ultrasound measurement of the lower uterine segment could be considered the standard diagnostic procedure that may assess the risk of uterine rupture and dehiscence.

On the other hand, if such cases could be diagnosed earlier and primary uterine repair could be performed on time with primary surgery can be a solution to the problem. Cases should be followed up more frequently so that it is possible to get a healthy baby as shown in our case with surgical repair.

Conclusions

Women with prior caesarean delivery (one or more), ultrasound measurement could be recommended for measuring the lower uterine segment thickness so that it may be helpful to predict the possible uterine dehiscence and rupture.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare that they have no competing

interests with respect to the authorship and/or publication of this article.

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Discrete subaortic stenosis in an adult patient

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ABSTRACT

Discrete subaortic stenosis is an unusual cause of the left ventricular outflow tract obstruction in the adults and characterized by a discrete subaortic membrane. A 52-year-old female patient presented with chief complaints of progressive dyspnoea, chest pain and fatigue. Echocardiographic study showed a discrete fibromembranous ridge located in the subaortic region, which resulted in severe subaortic stenosis, with a mild aortic regurgitation and a mean gradient of 65 mmHg. She underwent surgical resection of the subaortic membrane without any complications. The postoperative course was uneventful, and she was discharged from hospital on the 7th postoperative day. At one-year postoperative follow-up, the patient was doing well without recurrence on echocardiogram. A close follow-up is mandatory for a possible recurrence despite sufficient surgical resection.

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Keywords: Aortic valve; discrete subaortic stenosis; echocardiography; surgery

Introduction

Discrete subaortic stenosis (DSS) is a rare cause of left ventricular outflow tract (LVOT) obstruction in the adults. It is characterized by a membranous or fibromembranous tissue that partly or fully surrounds the subaortic region. This membranous shelf causing flow turbulence in the LVOT can result in progressive subaortic stenosis, concentric left ventricular hypertrophy, and secondary aortic regurgitation [1-3].

DSS is referred to as a congenital disease, but it is mostly considered to be due to an acquired disorder. However, the incidence, rate of progression, the treatment options including the timing and technique, and postoperative outcomes in adults have not been fully elucidated [3-6]. Surgical membranous resection, with or without septal myectomy in patients with DSS, is mostly a successful modality and may provide

sufficient relief of LVOTO with low morbidity [1, 7, 8].

Herein, we describe a case of a discrete subaortic membranous ridge in an adult female undergoing surgical intervention.

Case Presentation

A 52-year-old female patient had been suffering from complaints of exertional dyspnoea, chest pain and weakness for 2 years. One year earlier, she had been diagnosed with subaortic membrane using echocardiography, which was performed for the evaluation of cardiac murmur. The patient was strongly urged to consider surgical resection, which

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she refused. The patient was re-admitted to our hospital due to increasing complaints in the last 6 months and surgery was planned.

Physical examination revealed a grade III-IV/VI harsh ejection systolic murmur at the left sternal border. She had New York Heart Association (NYHA) functional classification II. She had hypertension and type 2 diabetes mellitus for 10 years and these disorders are under control with medication. There were no abnormalities in routine blood tests. An electrocardiogram showed sinus rhythm of 75 beats/min and left ventricular hypertrophy with a strain pattern. Chest radiography revealed mild cardiomegaly. There was no dilatation of the ascending aorta. Two-dimensional echocardiographic study including both transthoracic and transoesophageal echocardiography showed a discrete fibromembranous ridge located in the subaortic region, which resulted in severe subaortic stenosis, with mild aortic regurgitation and a mean transmembranous gradient of 65 mmHg. Coronary artery disease was ruled out by the normal coronary angiogram. The patient had no additional cardiac pathologies.

Surgery was performed with standard conventional cardiopulmonary bypass under moderate hypothermia. An oblique aortotomy was carried out and extended into the non-coronary sinus for subaortic resection. Aortic valve appeared tricuspid and aortic annulus was normal. Afterwards, the aortic valve leaflets were carefully retracted to explore the subaortic membrane. The discrete semilunar fibrous membranous structure of 5 x 20 mm was located about 10 mm below the aortic valve (Figure 1). Crescent-shaped fibrous membrane was carefully resected to

avoid injury to the conduction tissue and the anterior leaflet of the mitral valve (Figure 2). Residue fibromuscular tissues were also excised (Figure 3). Upon further inspection, interventricular septum was shown to be of normal anatomic structure.



Figure 1. Operative view of discrete membrane below the aortic valve, which is attached to the septum

Histopathological study revealed fibrous membranous tissue, collagen, fibrin tissue, and spindle-shape fibroblasts in haematoxylin-eosin staining. Early after surgery, postoperative echocardiography showed trivial aortic regurgitation. The postoperative course was uneventful, and she was discharged from hospital on postoperative day 7. She was doing well and there was no recurrence in her one-year postoperative follow-up echocardiogram.

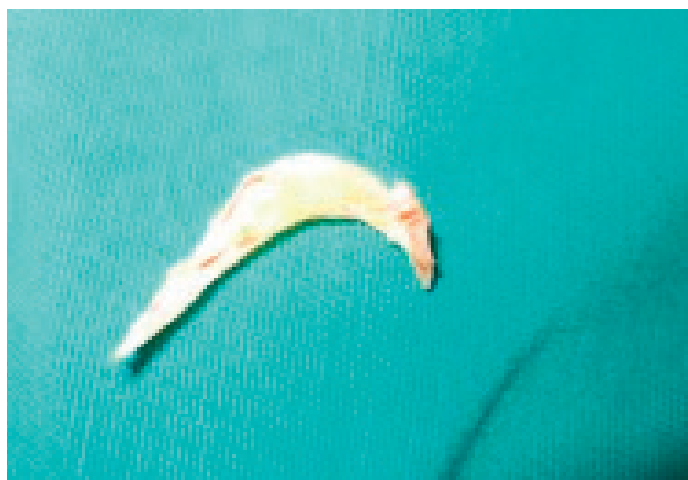


Figure 2. The resected specimen showing a crescent-shaped fibrous membrane.

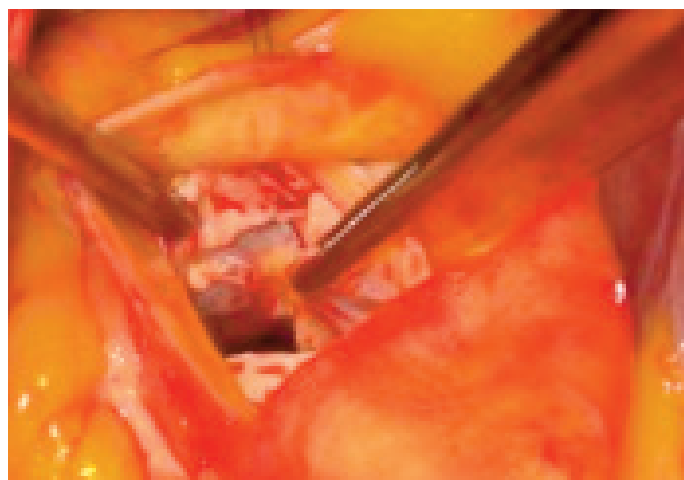


Figure 3. Excision of the residue fibromuscular membrane

Discussion

The prevalence, etiologic characteristics, therapeutic options, and postoperative outcomes for DSS in adults have not been well established [3-6]. DSS is more common in children and accounts for 8% to 20% of all cases of LVOT obstruction requiring surgery [6]. The prevalence of DSS has been increasing in adults with the development of diagnostic methods. In the largest series of 134 adult patients with DSS, Oliver *et al.* [4] reported that the prevalence was relatively frequent of 6.5% for all adults with congenital heart disease.

In adults, DSS is a rare pathology with an unknown aetiology. However, it is a well-described cause of isolated LVOT obstruction in children with its rapid haemodynamic progression and secondary aortic regurgitation. DSS is a progressive and probably acquired cardiac anatomical abnormality, in which the LVOT is characterized by the presence of the obstructing membrane immediately below the aortic valve [1, 8, 9]. This pathology can occur as a primary isolated lesion or in combination with additional subaortic anomalies such as abnormal septal attachments of mitral valve, accessory mitral valve tissue, abnormal left ventricular papillary muscle, anomalous muscular band, and muscularization of the anterior mitral valve leaflet [1]. The lesion is recognized as a result of an ongoing dynamic process and has obvious haemodynamic significance and consequences that reach far into adulthood [3-6].

DSS can also be associated with the presence of other congenital structural anomalies including ventricular septal defect, atrioventricular canal defects, bicuspid aortic valve, coarctation of the aorta, interrupted aortic arch, patent ductus arteriosus, double-outlet right ventricle, and persistent superior left vena cava [1, 8, 10, 11]. In a study, DSS has been determined in 44% of the cases associated with other congenital cardiac anomalies. Two most frequent lesions were ventricular septal defect and aortic coarctation [4]. The lesion may surprisingly appear as a secondary pathology year after the surgical repair of the associated congenital anomaly or mitral valve surgery for rheumatic heart disease [4, 6].

DSS is a manifestation of geometric abnormalities in the LVOT. These abnormal morphological arrangements including small LVOT, increased mitral-aortic fibrous distance, malaligned ventricular septal defect and steepened aorto-septal angle result in

altered flow patterns such as increased turbulence [4, 12]. These abnormalities increase septal shear stress producing local fibroproliferative reaction of the endocardium, eventually stimulating development of the subaortic membrane [3, 8, 9]. The high-velocity subvalvular systolic jet in the LVOT can result in progressive significant LVOT obstruction, concentric left ventricular hypertrophy, and aortic valve destruction, which may cause an aortic regurgitation. Patients with DSS are at increased risk to develop acquired aortic valve endocarditis [8, 10].

In a large cohort study of 149 adults at 4 centres, van der Linde *et al.* [3] evaluated the natural history of DSS and identified risk factors for DSS progression, aortic regurgitation progression, and the need for surgery. Interestingly, in contrast to children, longitudinal follow-up (median; 6.3 years) data showed that DSS progressed very slowly in adulthood. Their study demonstrated that the baseline LVOT gradient was 32.3 ± 17 mmHg, with <1 mmHg gradient increase per year. They also documented that, particularly the patients with associated congenital heart disease were at risk for faster progression ($p=0.005$), while progression did not influenced by the baseline LVOT gradient or age. In their study, mild aortic regurgitation was common (58%), but non-progressive over time ($p=0.701$). LVOT gradient ≥ 50 mmHg, LVOT gradient progression, and moderate to severe AR were independent predictors for surgery [3]. Another study by Oliver *et al.* [4] showed a similar slow progression rate (2.3 mmHg increase per year) during a mean follow-up of 4.8 years in only 25 patients with sequential echocardiographic studies. However, they suggested that DSS progression was influenced by the patient age and a significant relationship between age and LVOT gradient ($r=0.61$, $p<0.0001$) was found. Their data showed that aortic regurgitation detected by colour Doppler imaging in adults (81%) with DSS, but was hemodynamically significant (moderate to severe) in $<20\%$ of the patients [4].

DSS remains a clinically challenging diagnosis in the adults [8]. It may range from asymptomatic to varying degrees of symptoms such as syncope, chest pain, palpitations, weakness or exertional dyspnoea. The diagnosis is made by echocardiography in patients with LVOT obstruction with associated aortic regurgitation. Multimodality imaging is needed to distinguish DSS from hypertrophic cardiomyopathy with obstruction. Echocardiography assesses the

anatomy of the subaortic lesion, dimensions and function of the left ventricle as well as integrity of the aortic and mitral valves [8, 10]. Echocardiographic parameters that should be considered in patients with DSS include mitral-aortic separation, aorto-septal angle, LVOT width, aortic valve dextroposition, left ventricle wall and septal thickness, and indexed left ventricular end-diastolic and end-systolic diameters [10].

Surgery is the intervention of choice for the treatment in severe and symptomatic patients with DSS [8, 10, 13]. The optimal timing of surgical repair and proper surgical technique remains controversial [8, 10]. Surgical decision in adults should be based on the anatomic finding of the lesion, clinical evaluation, left ventricular hypertrophy, systolic function and aortic regurgitation [4]. To prevent damage to the aortic valve and rapid progression of LVOT obstruction, early surgical resection of the subaortic membrane may be recommended in patients with DSS. Indications for surgery include the mean LVOT pressure gradient greater than 50 mmHg and/or left ventricular systolic dysfunction, echocardiographic or angiographic evidence of progressive aortic regurgitation, and coexisting cardiac lesions that require surgery [8]. Definitive treatment for DSS consists of surgical correction of the subaortic obstruction, which may range from simple membrane excision to extensive ring resection, with or without myectomy [11]. Surgery allows sufficient relief of LVOT obstruction with low mortality and morbidity. In our case, she was diagnosed as DSS by patient's clinical status and echocardiography findings, and recommended for surgical intervention. She underwent surgical resection of the subaortic membrane with preservation of aortic valve without complications.

There are no data related to the benefits of early surgery in adults. Data from a study by Oliver *et al.* [4] showed that the benefits of early surgical repair in adults should be questioned. Recently, according to multicentre study by van der Linde *et al.* [3], early surgery in asymptomatic adults with DSS is not indicated solely to prevent rapid progression of the LVOT obstruction or progressive aortic regurgitation.

The surgery for DSS can lead to some complications such as incomplete relief of the obstruction or persistent gradient across the LOVT, an increase in the degree of aortic regurgitation, iatrogenic ventricular septal defect, mitral valve damage, bundle branch or complete heart block, and

risk of endocarditis. These early complications are usually associated with aggressive resection during circumferential myectomy. A postoperative transoesophageal echocardiographic examination is essential to identify any iatrogenic complication [5, 6, 8, 10, 11, 14].

Mortality following surgery for DSS is very low and survival is excellent, with 97% at 20 years [14]. Recurrent DSS requiring reoperation even after a successful repair still is an important problem, especially in the presence of a predisposing associated congenital heart abnormality and depending on the type of the preoperative lesion. Inadequate relief of the obstruction is a major factor in DSS recurrence. Therefore, concomitant selective myectomy is recommended to achieve complete relief of the LVOT obstruction [8, 10, 11, 14].

Surgery is associated with high DSS recurrence (20-30%) requiring reoperation. Recently, in a retrospective multicentre study, van der Linde *et al.* [14] identified risk factors for DSS recurrence, aortic regurgitation worsening and reoperation in a large cohort of 313 adult patients who previously underwent surgical intervention for DSS during the postoperative follow-up period of 12.9 years. They reported that 80 patients (25.6%) underwent at least one reoperation for recurrent DSS (1.76% per patient year). In this cohort, nearly all patients had adequate surgical relief. Mean LVOT gradient decreased from 76 mmHg preoperatively to 15 mmHg postoperatively ($p < 0.001$), and there was an overall increase of 1.3 mmHg per year in the gradient ($p = 0.001$). There was also mild aortic regurgitation in 68% of the patients, but generally did not progress over time ($p = 0.76$).

Predictors for reoperation included female sex (hazard ratio [HR]: 1.53) and progression of LVOT obstruction (HR: 1.45) [14]. In the same study, additional myectomy did not reduce the risk of reoperation ($p = 0.92$), but significantly increased the risk of complete heart block requiring pacemaker implantation (8.1% versus 1.7% of patients who underwent isolated enucleation; $p = 0.005$) [14].

Risk factors for DSS recurrence include younger age at initial surgery, increased age at the time of diagnosis (>30 years old), female sex, closer lesion proximity to the aortic valve (<7 mm), preoperative peak instantaneous LVOT gradient ≥ 80 mmHg, and intraoperative peeling of the membrane from the aortic or mitral valves [13-15]. These risk factors are associated with higher incidence of reoperation.

Conclusion

It would be important to keep DSS in mind as a cause of aortic stenosis in adults. It can be treated successfully with low mortality and morbidity, with or without concomitant septal myectomy. The anatomic findings of the lesion play an important role on the extent of surgical resection for DSS. The long-term outcome is not predictable in the adults. Therefore, meticulous follow-up is mandatory for DSS recurrence.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Tuberculosis: a rare cause of foot and ankle pain

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ABSTRACT

Skeletal tuberculosis is an uncommon infectious disease that occurs in 1-3 % of all tuberculosis cases. Apart from spine it can emerge in weight bearing joints. Tubercular involvement of the ankle is the most uncommon and infrequent amongst those of all joints. If imaging techniques and laboratory results are not sufficient while setting a precise diagnosis, this rare problem should be always taken into consideration just like other infections of the musculoskeletal system. In this paper we present a case of 83-year-old female patient who underwent conservative treatment for ankle tuberculosis.

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Keywords: Tuberculosis; foot; ankle; arthritis; treatment

Introduction

Tuberculosis is an infectious disease caused by the bacteria mycobacterium tuberculosis. It commonly occurs in lungs but can occasionally infect any part of the body. Bones and joints are involved in 1-3% of all tuberculosis cases and in 15% of extra-pulmonary tuberculosis cases [1]. According to dispersion and frequency range, bone and joints tuberculosis mainly infects the vertebra (50%), whereas occurrences in hips, knees, foot-ankle area (10%) are seldom observed [2-4]. The present paper describes a case of ankle and ankle area osteoarticular tuberculosis.

Case Presentation

An 83 years old woman presented with pain in her left foot and ankle. The pain in the foot area had been lasting for about 1 year and along with sensitiveness

it had been gradually intensifying for last months. The patient had not sustained any traumas. Apart from hypertension, she had not suffered from any systemic disease.

Examination findings included; short distance antalgic gait (as weight was not placed to the left lower extremity) and swelling in foot and ankle. By palpation, pain in areas near the ankle (especially in the distal crural region) was detected. Neurovascular examination seemed to be normal. Ankle movements seemed to be limited in all directions. (flexion-dorsiflexion 20-0-10, supination pronation 5-0-5).

The patient's inflammatory markers were normal as WBC = 6.03 mm³/ml (normal = 3.5-10.5), lymphocyte ratio = 22.2% (normal = 20-51.1), neutrophil ratio = 4.14 (normal = 1.7 -7), C-reactive protein (CRP) = 3.3 mg/l (normal = 0 - 5), erythrocyte sedimentation rate (ESR) = 47 mm/h (normal = 0- 20).

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Conducted Brucella Rose-Bengal test showed negative result.

Radiographs show severe osteopenia in anterior-posterior foot and ankle, significant sclerosis in subtalar joint, extensive osteoporosis and a bone cyst in talus and calcaneus (Figure 1).

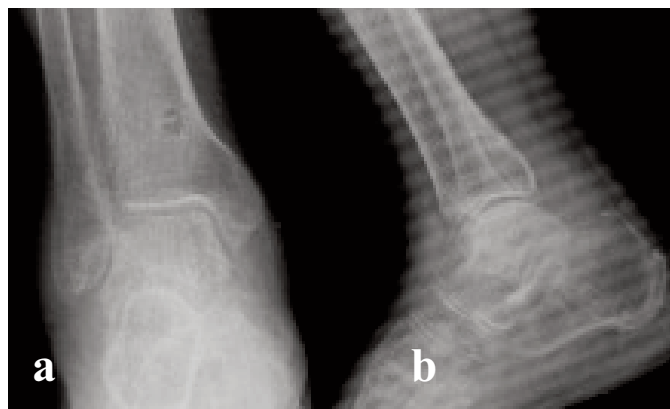


Figure 1. The graphy of anterior, posterior (a) and lateral ankle. Extensive osteopenia in bones, trabecular coarsening, narrowing in tibiotalar and talocalcaneal joint spaces, along with sclerosis (a, b). Radiolucent lesion, concordant with calcaneus sclerotic contoured cyst (b)

CT scan of left foot and ankle showed osteoporosis in the left foot and extensive radiolucency along with trabecular coarsening associated with fatty bone marrow degeneration. Moreover, in the central part of calcaneus a cystic cavity approximately 21 mm in diameter was detected. Inside of the cavity a 15 mm-sized hyperdense area was seen (Figure 2).

The magnetic resonance imaging show that minimal increasing signal intensity in the distal tibia,

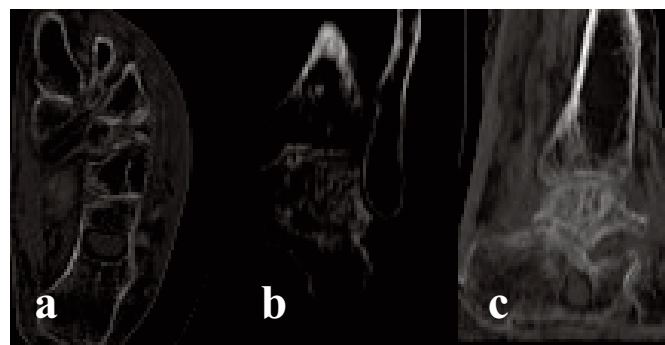


Figure 2. Ankle ct scan axial (a), coronal (b) and saggital (c) incisions: axial ct incision (a), coronal and sagittal ct reformat- ted images (b, c): generalized increased bone density, trabecular coarsening, along with bone thinning and disorders without peri- ost reaction in cortex. Sclerotic contoured cyst in 2 cm in dia- meter in calcaneus.

talus and calcaneus surfaces; sporadically developing cortical erosions; narrowing in talocalcaneal joint spaces which emerged along of existing inflammation; and cortical destruction-associated collapse (Figure 3).

Due to manifested symptoms the patient was thought to have developed osteomyelitis as a pre- diagnosis. Therefore an open biopsy had been planned. During the open biopsy samples were taken from talus, calcaneus and subtalar joints for culture and pathology examination. The culture examination revealed no growth. The histology showed granulomatous inflammation with epitheloid granuloma including multinucleate gaint cell and peripheral rim of lymphoid cells (Figure 4).

After histopathologic examination the diagnosis of ankle osteoarticular tuberculosis was given and anti-tuberculosis multi-modal therapy administered. For the first 2 months the patient had been prescribed rifampicin 300 mg/day oral, isoniazid



Figure 3. Magnetic resonance imaging of the ankle: axial – coronal – sagittal incisions. Sagittal t1 (a), stir (b), contrasted fs t1 (c), coronal stir (g) and contrasted fs t1 (h): hypointense in the distal tibia, the talus, the calcaneus and in the tarsal bones t1; hyperintense in stir; contrast retaining heterogeneous signal records in contrasted fs t1; bone disorders and erosions (osteomyelitis) in cortical bone. Contrast retention and thickening (synovitis, arthritis) in the ankle area and soft tissue. Hypotense in calcaneus t1, hypertense in stir, wall contrast retaining hypotense cystic lesion (necrotic cyst?) In contrasted fs t1.

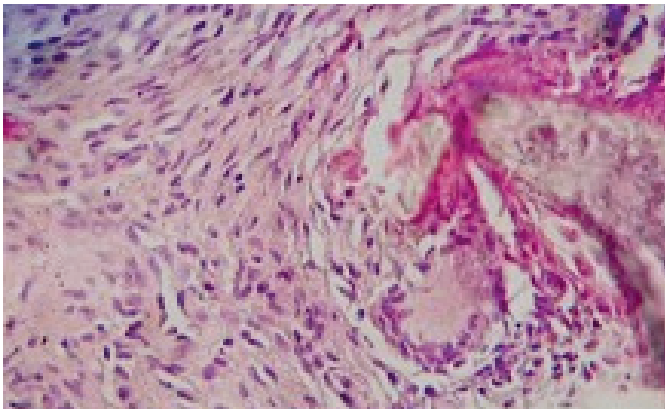


Figure 4. Granulomatous inflammation with epithelioid granuloma including multinucleated giant cell and peripheral rim of lymphoid cells

300 mg/day oral, pyrazinamide 500 mg/day oral, ethambutol 500 mg/day oral (ripe). Two months later, the treatment with ethambutol and pyrazinamide was discontinued; only isoniazid and rifampicin were administered for the following next 10 months. Thus, medication lasted 12 months. Three months after the anti-tuberculosis treatment started a regression of symptoms had been noticed. The patient's follow-up period was performed 6 months after completion of treatment. The patient reported that sensitiveness and ankle swelling had disappeared, nor did weight bearing still cause difficulties, and therefore she had been able to walk painlessly ever since.

Discussion

As skeletal tuberculosis occurs on rare occasions only, it is seldom considered for pre-diagnoses given by orthopaedic surgeons. Consequently, sometimes it can be difficult to make a precise diagnosis. The missing diagnosis and consequently inadequate treatment can cause an increase of inflammation and progressing bone and joint degeneration.

Skeletal tuberculosis generally disseminates via haematogenous spread from a primary focus to bone areas where more blood components are formed. After that it can leap to joints by nearby ways [5]. Less frequently the disease can spread through the lymphatic system [6]. Besides these, direct post-traumatic infections are reported to emerge in any bone or joint [7-8]. It is related to increasing vascularization or decreasing local resistance and connected to forming new foci which will cause reactivation of infection in post-traumatic areas [9-10].

Generally, the progression of skeletal tuberculosis is slow and insidious. Classical symptoms of pulmonary tuberculosis such as fever, night sweats and weight loss might not occur in the case of developing skeletal tuberculosis. Typically, symptoms such as swelling, sensitiveness, decreased range of joint motions, muscle spasms, malformations can be seen here.

In laboratory tests high levels of such parameters as WBC, CRP and sedimentation, which seem to become normal, prevent from giving the precise diagnosis. Normal levels of WBC, CRP and sedimentation complicate diagnosing as it draws orthopaedists away from infection diagnoses. However, in cases where radiological findings along with clinical findings substantiate chronic infections the possibility of emergence of bone and joint tuberculosis should be taken into consideration.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ascending aortic cannulation in acute type A aortic dissection: a frightening but lifesaving procedure

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ABSTRACT

Different cannulation sites (e.g., femoral artery, axillary artery, left ventricular apex, and ascending aorta) and perfusion techniques (anterograde or retrograde) have been used for treating acute type A aortic dissection. The patient's pathology and status determine the cannulation site. We present our experience with ascending aortic cannulation for acute type A aortic dissection.

Eur Res J 2016;2(1):74-76

Keywords: Aortic dissection; acute type A dissection; ascending aortic cannulation

Introduction

The ideal cannulation method for acute aortic dissection repair is usually described as “quick, easy and safe”. For arterial intervention, peripheral cannulation sites (femoral and axillary) have been used as standard approaches [1–3]. Some centres also use direct ascending aortic cannulation with good results [4–6]. We report a case in which we had to use direct true lumen cannulation of the ascending aorta.

Case Presentation

A 66-year-old man was admitted to our emergency service with the symptoms of chest and back pain and dyspnoea. A computed tomographic angiography (CTA) revealed type A aortic dissection (Figure 1). Bilateral femoral arteries were also affected. A transthoracic echocardiography showed a

mild aortic regurgitation and the ejection fraction was 55%. His arterial tension was 100/70 mmHg, and his pulse was 88/minute when he admitted to the hospital. He was taken to the operation room.

In our clinical experience, axillary artery cannulation is the first choice for the ascending aortic operations. Therefore, an infraclavicular incision was performed, and the right axillary artery was exposed. Although not observed in the CTA, the dissection had progressed to the axillary artery too. The bilateral femoral arteries were not intact either. We decided to cannulate the ascending aorta.

Following the median sternotomy, the pericardium was opened slowly. After careful dissection between the adventitial layers of the ascending aorta and the pulmonary artery, a clamp was passed around the ascending aorta and a tape placed.

An aortic cannula was inserted into the true lumen directly, and the ascending aorta snared tightly. A two-

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stage cannula was inserted into the right atrium, and a cardiopulmonary bypass (CPB) was established, and the patient started to cool down. The ascending aorta was then cross-clamped and the proximal part of the ascending aorta was opened. It was seen that the tear was beginning from supra-coronary part of the ascending aorta.

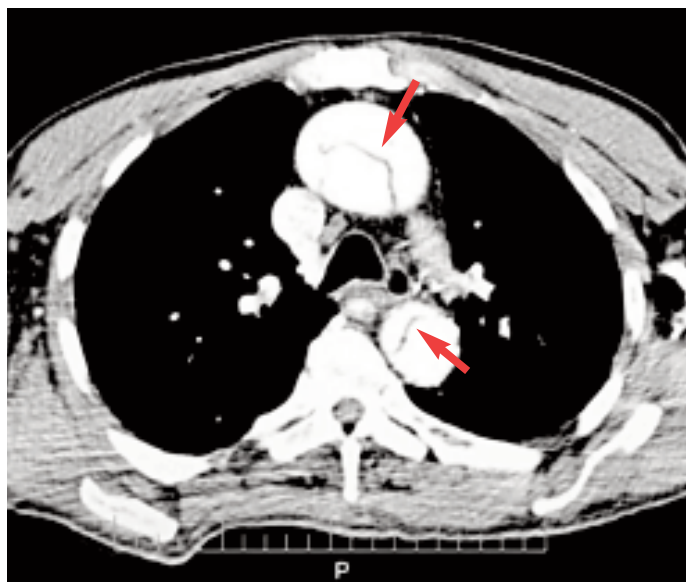


Figure 1. Preoperative computerized tomography image of dissected aorta; Arrows=intimal flaps.

The proximal anastomosis was done during the cooling period. At the desired temperature (18°C) CPB was stopped, and a deep hypothermic circulatory arrest started. The arterial cannula removed and the affected part of the ascending aorta was resected, and distal anastomosis was completed. A supra-coronary ascending aortic replacement with a 32 mm Dacron graft was performed. Then an aortic cannula was inserted into the graft and CPB started again. After rewarming to normothermia, the patient was weaned from CPB and the operation finished. (The cross clamp time, CPB time and total circulatory arrest time were 60 minutes, 130 minutes, and 24 minutes, respectively). His postoperative course was uneventful, and he was discharged on postoperative day 7. He recovered without complications following the surgery and today, i.e. three years later, he continues to feel well (Figure 2).

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His postoperative course was uneventful, and he was discharged on postoperative day 7. He recovered without complications following the surgery and, three years later, he continues to feel well today (Figure 2).

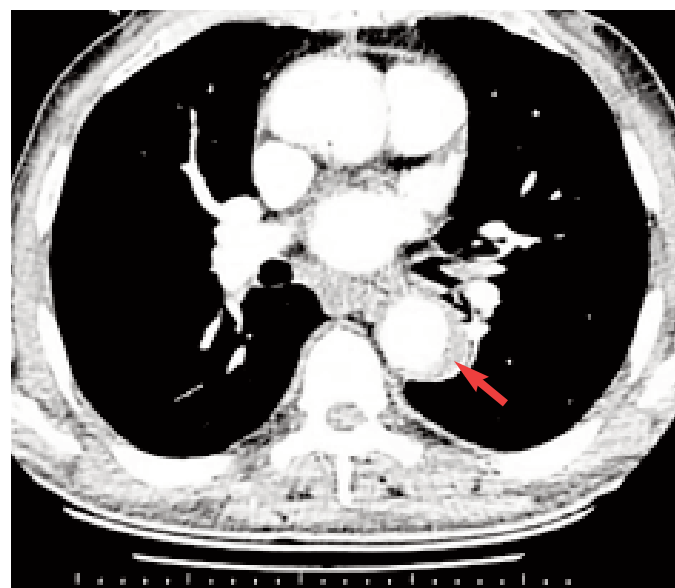


Figure 2. Postoperative computerized tomography image. Arrow shows regression of false lumen in repaired aorta

Discussion

Until the 1990s, the femoral artery was the most popular site for cannulation. Then to prevent the cerebral embolization and extension of dissection because of retrograde blood flow as well as to achieve selective anterograde cerebral perfusion during the hypothermic circulatory arrest, the femoral artery was replaced by the axillary artery. To minimize the risk of meal perfusion caused by retrograde flow during CPB femoral cannulation should be avoided and arterial perfusion through the axillary artery may be a useful alternative [7].

The axillary artery may be cannulated directly or through an 8 mm Dacron side-arm. We prefer to use

an 8 mm Dacron graft. However, while axillary artery cannulation is the preferred intervention, extension of the aortic dissection to the axillary artery remains a contraindication to its use [8]. Retrograde carotid dissection and cerebral meal perfusion complications may occur by the cannulation of the dissected axillary artery [9]. Blood flow into the false lumen at this level increases the risk of cerebral meal perfusion because of the proximity of the cerebral vessels. Borst *et al.* [10] first described the ascending aorta cannulation in the 1990s. It has been reported a few times since [11-15]. The Seldinger technique under epiaortic colour Doppler echography and transoesophageal echocardiography are used routinely in this cannulation procedure [16]. We believe that, because of the possible expanding aortic dissection that was affecting both axillary and femoral arteries, it clearly was mandatory to cannula the ascending aorta.

The ascending aorta offers several advantages as an alternative access for cannulation. First of all, if the patient is experiencing hemodynamic instability, this method is more suitable than others because there is no need to open another surgical area. There is no limitation on the diameter of inflow cannula so that a large-diameter cannula can be used. Also, ascending aortic cannulation does not require repair of the cannulation site. Finally, it is feasible when axillary and femoral arteries are dissected [17].

The risks of the ascending aortic cannulation are aortic rupture at the cannulation site and cannulation into the false lumen. Khalid *et al.* [5] found that only 1 (0.8%) of 122 patients had an aortic rupture caused by aortic cannulation.

Conclusion

Acute aortic dissection can present with various conditions, so there is no perfect cannulation side and method. Therefore, ascending aortic cannulation must be kept in mind as an appropriate choice of cannulation for CPB, mainly; in patients whom the peripheral arteries cannot be used.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Competing interests

The authors declare that they have no competing

interests with respect to the authorship and/or publication of this article.

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A pregnant woman with primary hyperparathyroidism: a case report

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ABSTRACT

Primary hyperparathyroidism is diagnosed with an increase of calcium levels and a decrease in phosphorus levels. Primary hyperparathyroidism is a rare condition in pregnancy. Calcium levels tend to be low in pregnant women, and high levels of calcium can point a primary hyperparathyroidism. Here, we report an original case of a pregnant woman with primary hyperparathyroidism who was fully healed after the surgery. A 30-year-old pregnant women (10th gestational week), admitted to the endocrinology department for management of thyrotoxicosis, when high calcium levels (11.8 mg/dL) were found in the laboratory tests. The parathyroid hormone level was 135 pg/ml. Ultrasound imaging revealed a parathyroid adenoma (12x7x27mm). She had maintained high calcium levels despite the medical treatment, for this reason, she had surgery in the second trimester. Our case was diagnosed early due to early recognition of calcium elevation. The mother and the foetus had not any complication. Pregnant women tend to have low calcium levels hence if a hypercalcemia situation appears in pregnant women; primary hyperparathroidism has to be suspected.

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Keywords: Pregnancy; hypercalcemia; hyperparathyroidism

Introduction

Parathyroid hormone (PTH) is a peptide hormone that regulates the calcium levels in blood and extracellular fluid in the human body. Primary hyperparathyroidism (PHP) is diagnosed with the increase of the calcium levels and the decrease of the phosphorus levels. The PTH measurement shows high levels in this situation. Urinary calcium excretion is also increased. Adenoma is detected in 85% of cases [1,2]. Calcium levels are detected low in pregnant

women due to hypoalbuminemia, passage of the calcium to the placenta and increased glomerular filtration rate [3]. High levels of calcium can point a PHP in pregnant women. PHP is a rare condition in pregnancy but causes complications for the mother and the foetus. Maternal complications include hyperemesis, muscle weakness, mental status changes, hypercalcemic crisis, bone disease, nephrolithiasis, and pancreatitis. Reported foetal complications

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include intrauterine growth retardation, low birth weight, preterm delivery, intrauterine foetal demise, neonatal postpartum tetany, and permanent hypoparathyroidism [4]. Fortunately, prompt diagnosis and effective management can improve outcomes for both. Here, we report an original case of pregnancy with primary hyperparathyroidism that was diagnosed in the course of routine laboratory examination and healed completely after the surgery.

Case Presentation

A 30-year-old pregnant women (10th gestational week) admitted to the endocrinology department for management the thyrotoxicosis that was determined during the routine laboratory tests that were performed by her gynaecologist. She had been diagnosed with hyperemesis gravidarum and was considered to have gestational thyrotoxicosis in the first step of the medical procedure, but high calcium levels (11.8 mg/dL) were noticed in the laboratory tests. There was no history of hypercalcemia and her family history also did not reveal any case of hypercalcemia or any endocrine tumours. The PTH and the calcium levels were tested again, but the results were high as same as the first test results. The results were 135 pg/ml and 11.6mg/dl respectively. Urinary calcium excretion rate was 456 mg/per day. Tubular phosphorus reabsorption rate was 91%, and the chlor-phosphorus ratio was 41.3. In the light of all these data, primary hyperparathyroidism was diagnosed.

Ultrasound imaging revealed a parathyroid adenoma (12x7x27mm) at the inferior of the right thyroid lobe (Figure 1).

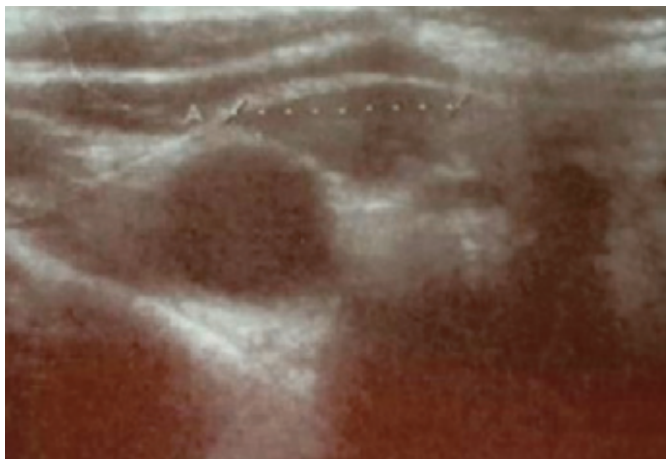


Figure 1. Ultrasound imaging revealed a parathyroid adenoma (12x7x27mm) at the inferior of the right thyroid lobe

The patient was treated with calcitonin and hydration during the first trimester. She had maintained high calcium levels despite the medical treatment, and underwent surgery for the parathyroid adenoma in the second trimester. Histopathological examination confirmed the diagnosis of a parathyroid adenoma (Figure 2-3).

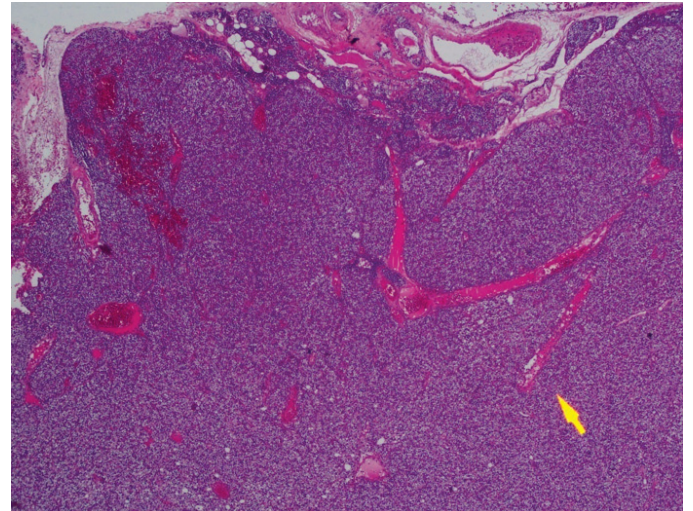


Figure 2. This parathyroid adenoma shows a rim of atrophic parenchyma at he periphery with only an attenuated capsule noted (H&E, x40)

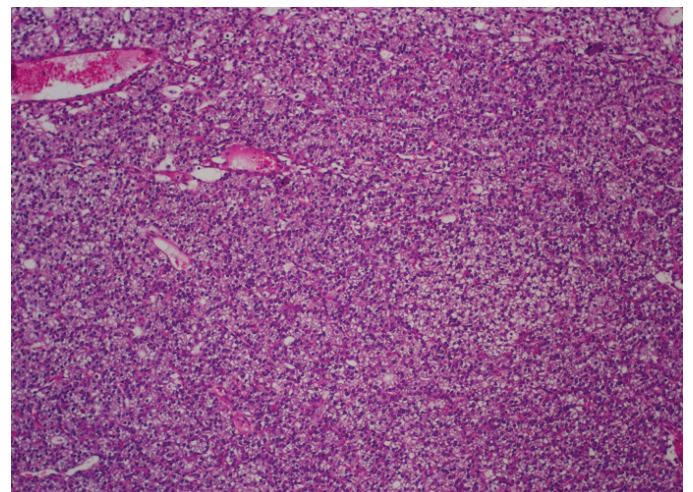


Figure 3. Chief cells compose this adenoma without any fat cells present. (H&E, x100)

The calcium levels turned to normal after the surgery, and the results were normal during the pregnancy. Similarly, the mother and the new-born did not have any complication associated with hypercalcemia after the birth.

Discussion

Primary hyperparathyroidism may cause complications for the mother and the foetus, because of this early intervention is vital during the pregnancy. The miscarriage rate is increased by 3.5-fold associated with this disease [5]. The abortions generally occur in the 2nd trimester. Surgical intervention is recommended in the 2nd trimester for patients whose calcium levels more than 11.4 mg/dL [5, 6]. If the patient approaches the 3rd trimester and has mild hypercalcemia, medical treatment is recommendable [7]. If severe hypercalcemia exists, diuretic therapy can be used [8]. Magnesium sulphate was reported to be effective in pregnant women with acute pancreatitis [9]. Phosphate was used to treat hypercalcemia in the past, but it is not suggested anymore [4, 10, 11]. Currently, there are case studies showing benefit from the calcitonin and cinacalcet. Both drugs are group C for pregnancy. Calcitonin therapy has limited efficacy and has a risk of tachyphylaxis [11-14]. Medical treatment that can be given to patients limited and we do not know all the adverse events. Therefore, early detection and surgical removal of adenoma in the second trimester is critical if it is necessary.

Calcium levels tend to be low during pregnancy. Unusually high levels of calcium can become an alert symptom in a pregnant patient. Thus, there will be a chance to prevent the development of complications for the mother and the foetus. Ultrasonography is a valuable imaging modality for detecting the parathyroid lesions when primary hyperparathyroidism is diagnosed. Our patient had her diagnose at early stages before the complications. She had no benefit from hydration and calcitonin. Surgery was performed in the second trimester. The abnormalities of calcium were not detected after the surgery during pregnancy and after the birth.

Conclusion

Our case is a patient who was diagnosed in time thanks to early recognition elevated calcium levels. The mother and the foetus had not any complication. Pregnant women tend to have low calcium levels

hence if a hypercalcemia situation appears in pregnant women, primary hyperparathyroidism has to be suspected.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Concurrent cases of bilateral anterior shoulder dislocation: our observations in three cases

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ABSTRACT

Bilateral anterior shoulder dislocations are rarely seen and usually occur due to the same mechanism arising from traumatic injuries. In here, we discussed three cases of traumatic bilateral anterior shoulder dislocation, one had an additional patella fracture, and the other one had bilateral tuberculum majus fracture. All of the patients were female and our first case that presented here was 65-year-old and given a closed reduction for isolated bilateral anterior shoulder dislocation that occurred as a result of falling due to an epileptic seizure. The second patient was 70-year-old and had bilateral shoulder dislocation and patella fracture (right leg) after of falling down the stairs due to syncope. Closed reduction was applied to the bilateral shoulder dislocation. Patella fracture on the right leg was fixated using open reduction internal fixation method. The third patient, who was 57-year-old, fell down from the stairs and had bilateral anterior shoulder dislocation accompanied by bilateral tuberculum majus fracture, and she was given closed reduction. For all three of the cases, Hippocrates method was used as the closed reduction method.

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Keywords: Bilateral, dislocation, shoulder, traumatic

Introduction

Bilateral anterior shoulder dislocations are quite rare. They frequently occur due to trauma. Three patients who had bilateral anterior shoulder dislocation- one because of falling off a chair and the other two down the stairs, were evaluated in company with the related literature. Unilateral anterior shoulder dislocations are the most frequent large joint dislocations coming to emergency services. In contrast, bilateral anterior shoulder dislocations are quite rare. It could be an isolated dislocation while it could also be accompanied by shoulder fractures and fractures in other areas. A majority of bilateral

shoulder dislocations occur in form of posterior shoulder dislocations, and the dislocations of the recorded cases occurred as a result of grand mal type epileptic seizures, electric shocks, and frequent contractions seen after electric shocks and hypoglycemia or voluntarily in psychic (mental) illnesses [1-6]. Anterior shoulder dislocations occur with extreme extension, abduction and external rotation force [7]. Since the forces causing dislocation have to affect both joints in a similar mechanism concurrently, they occur quite rarely. Therefore, they can easily be ignored [8, 9].

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Case Presentations

Case 1

A-65-year-old female falls down because of an epileptic seizure she had when trying to sit on a chair at home. In the medical examination, epaulette and motion restriction were observed. Neurovascular examination was natural. The graph of the patient showed a bilateral isolated anterior shoulder dislocation (Figure 1). Both dislocations were reduced closely with Hippocrates manoeuvre under sedation. In the control graphs, anatomic reduction was observed (Figure 2). Both shoulders were made

immobile for three weeks using velpau bandage. Afterwards, they were included in a rehabilitation program. In the examination 16 months later, shoulder joints were observed to be stable and no motion restriction was found. The dislocation did not recur in the meantime.

Case 2

Seventy years old female patient fell down and rolling from the stairs as a result of a sudden syncope. Subsequently, she was taken to emergency service with pain in her shoulders, motion restriction as well as pain and swelling in the right knee. In the physical

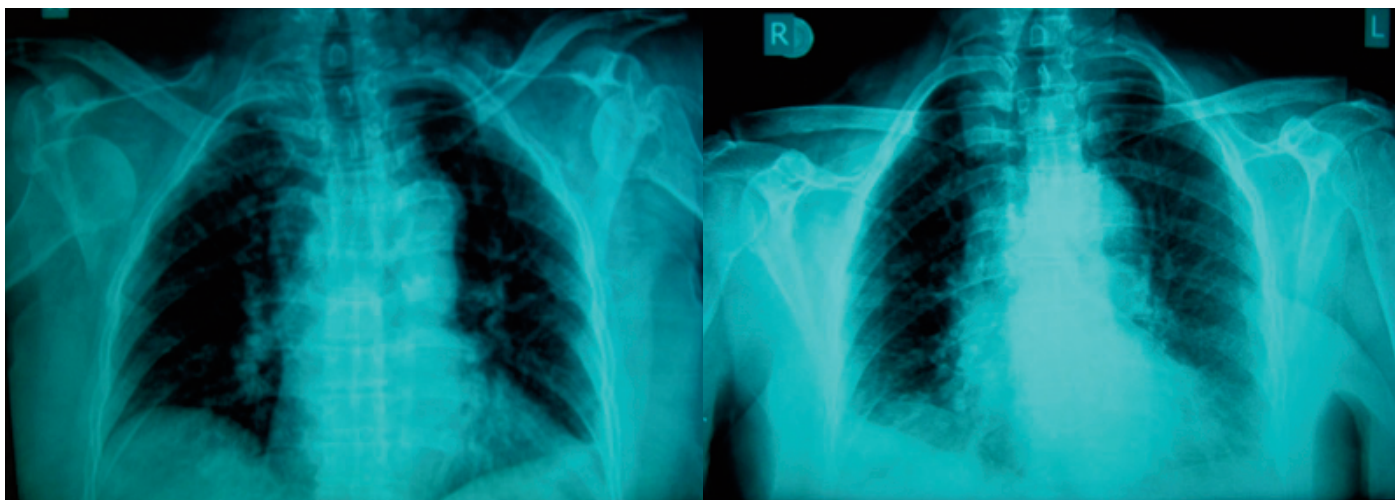


Figure 1. Case 1- Bilateral anterior shoulder dislocation radiograph

Figure 2. Case 1 radiograph after closed reduction

examination showed mild abduction and external rotation in both shoulders, findings of epaulette and motion restriction. The neurovascular examination was unremarkable. A swelling in the right knee, pain with palpation and patella deformity were observed. Graphs showed isolated anterior dislocation for both

shoulders (Figure 3). She was taken into operation under emergency circumstances, and a closed reduction was performed on both shoulders using Hippocrates manoeuvre under general anaesthesia. Control graphs were taken (Figure 4). Both shoulders were immobilized for three months with an arm sling.

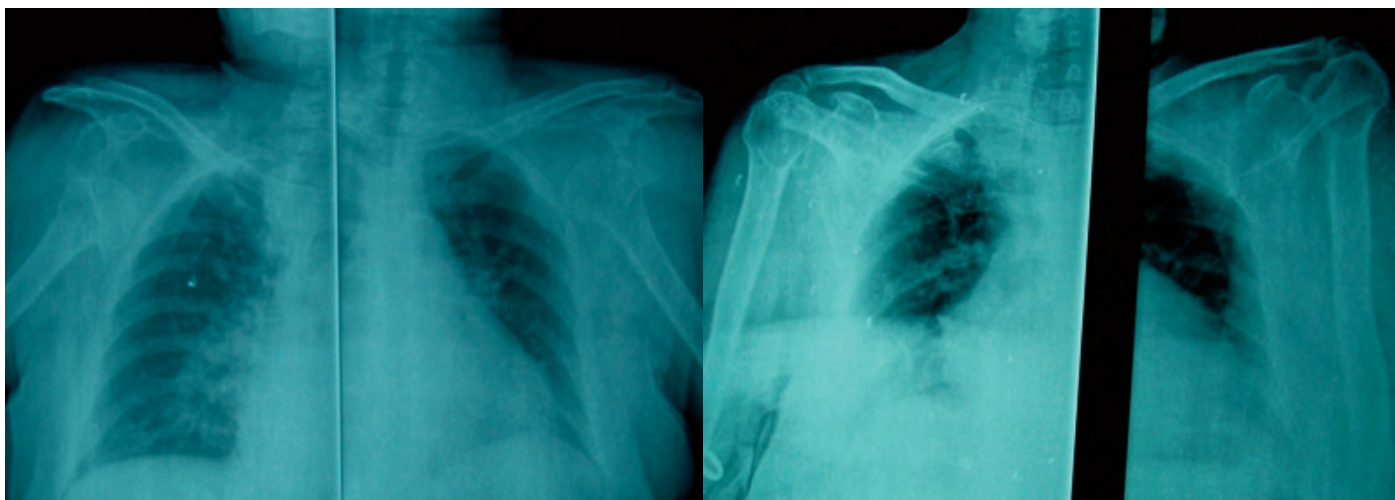


Figure 3. Case 2- Bilateral anterior shoulder dislocation radiograph

Figure 4. Case 2 - Bilateral shoulder radiograph after closed reduction

Afterwards, these received physical treatment and rehabilitation for four weeks. In the controls 16 months later, it was seen that union in the patella was full, movements of the left shoulder were close to perfect, and there were insignificant minimal restrictions in external rotation and abduction of the right shoulder and abduction of the right shoulder.

Case 3

A 53-year-old female patient admitted to the emergency service because of losing balance and falling when going down the stairs. She described to have fallen into open hands with both elbows in extension and rolled down 2 or 3 steps. In the physical examination, bilateral shoulder joint was deformed (epaulette sign) and the shoulder was observed to be in the mild abduction and external rotation.

Radiographs showed it was accompanied by a tuberculum majus fracture, and there was bilateral

anterior shoulder dislocation. However, shoulder graphs of the patient before reduction were not taken on the same cassette, so we had no chance to repeat (Figure 5, 6). Under general anaesthesia, closed reduction was performed using Hippocrates method. Both shoulders of the patient were immobilized for three months with velpau bandage. Later, she was included in the physical treatment program. In the controls 16 months later, it was seen that bilateral shoulders movements were close to perfect, and that union and reduction were complete (Figure 7).

Discussion

Glenohumeral dislocations are the most commonly observed ones among all large joint dislocations. They occur as a result of trauma in many young men. It is followed by dislocation in elderly



Figure 5. Case 3 -Bilateral shoulder dislocation right shoulder radiograph



Figure 6. Case 3- Bilateral shoulder dislocation left shoulder radiograph



Figure 7. Case 3-Bilateral shoulder dislocation and tuberculum majus fracture radiograph after closed reduction

women which occur due to the decrease in the number of crosslinks of collagen in the joint capsule and the increased risk of falling [10]. Bilateral shoulder dislocations occur rarely because of rotator muscles (*M. infraspinatus* and *M. teres minor*), which are weaker than the powerful internal rotator cuffs (*M. latissimus dorsi*, *M. pectoralis major* and *M. subscapularis*), dislocations frequently occur towards the posterior. Posterior shoulder dislocations most frequently occur as a result of grand mal type epileptic seizures, electric shocks, and frequent contractions seen after seizures due to alcohol deprivation and hypoglycaemia or voluntarily in psychic (mental) illnesses [1-6]. Contrary to posterior shoulder dislocations, bilateral anterior shoulder dislocations are seen very rarely, they usually occur following trauma.

Ozan *et al.* [12] reported 80 cases in the literature they review covering the period between 1902 and 2013. These dislocations have most often been accompanied by muscle tears, tuberculum majus or glenoid fractures and neurovascular complications [9, 11-15]. In the literature, among the etiological reasons of bilateral anterior shoulder dislocations, the rate of those occurrence caused by falls or strong extremity tractions is 50%, those occurring due to convulsive crises, electric shocks strong muscle contractions including physical exercises is 40%; and the rate of any cases other than trauma. such as neuromuscular diseases, hyperlaxity, and voluntary dislocations, is 10% [6, 11].

Anterior shoulder dislocation mechanisms can be of various nature. They mainly occur combined with abduction, extension and external rotation forcing. Movements such as falls on open hand at elbow extension fall at shoulder extension, abduction or internal rotation, pivot effect of acromion at hyperabduction position and traction cause shoulder displacement [6, 16, 17]. Since two of our cases had fallen because of an epileptic seizure and syncope, they could not recall the form and mechanism of the falls. We believe that this trauma mechanism resulted from falling on open hand at elbow extension as stated in the literature. The fact that the third and the last case was conscious when falling down the stairs and rolled down with two hands open at elbow extension supports the possibility that other cases had occurred in a similar mechanism as well. It was reported that 15% of these patients are accompanied by tuberculum majus fracture [18], 30% of those over 40 [19], and 54% of those older are accompanied by 54% rotator

cuff tears [20]. No glenoid or tuberculum fracture and cuff tears were observed to be accompanying shoulder dislocation in two of our cases. In the third case, a more distinct bilateral tuberculum majus fracture accompanied the dislocation. After early reduction and immobilization, there is a need for passive and active physiotherapy to be given efficiently [10]. For patients whose pain cannot be relieved and sufficient range of motion cannot be obtained despite rehabilitation, rotator cuff tear must be considered, and an MRI image must be taken. Since sufficient range of the movement was attained in our cases after rehabilitation, MRI was not taken. Formation of a fracture along with the dislocation is associated significantly because the patient was over 40, the dislocation occurred for the first time with the decreased bone density, ligamentous anatomy was strong, and it had occurred due to high energy trauma [21].

Especially after anterior displacement, there might be complications such as fractures, brachial plexus injury, vascular injury, soft tissue injuries and recurrent displacements. The possibility of recurrence after the first displacement is high in young patients. Our cases did not describe any prior shoulder displacement.

Another significant problem for these patients is the delay in the process of diagnosis. Dunlop [10] expressed more than 10% of them received delayed diagnosis. When patients apply to the emergency service following a seizure, very often they cannot remember the event in its entirety and complain most about the shoulder with pain. Unless careful examination is conducted, the dislocation of the other shoulder may remain undetected. Although it is the primary choice for treatment to prevent post shoulder dislocation recurrences, the priority is given to the treatment of complex structural injuries in elderly patients. The risk of rotator cuff injuries increases with the shoulder displacement at advanced age [18]. Even though the treatment of rotator cuff tears in these patients is controversial, first conservative treatment is given [20].

Post reduction fixation is usually done using Velpo bandage. Since Velpo bandage affects daily activities negatively in bilateral displacements, arm sling can be preferred. We fixated our first patient, who fell down due to a seizure of Grand mal epilepsy against the risk of having another seizure, with velpo bandage and the third patient due to bilateral tuberculum majus fracture; but we fixated the second patient with an arm sling which partly allows for shoulder movement. In

the literature, Kocher manoeuvre is usually preferred as the reduction method [3, 4, 6, 9, 16, 18]. Because of their elder age, we used Hippocrates manoeuvre for the reduction of the first two of our patients. It is because of the fracture risk during Kocher manoeuvre in osteoporotic patients. In the relatively younger third case, on the other hand, Hippocrates manoeuvre was used because of the tuberculum majus fracture. No serious complication was encountered in these three cases.

Conclusions

Although concurrent bilateral anterior shoulder displacements occur rarely, they can be seen about trauma in elderly patients; therefore, the neurovascular examination should not be ignored, and the possibility of fractures must be remembered.

Informed Consent

Written informed consent was obtained from the patient that was presented in this case.

Conflict of interest

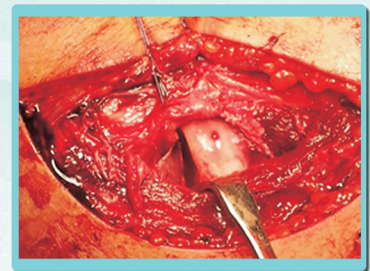
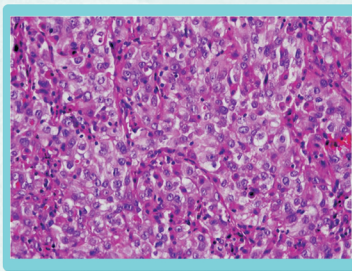
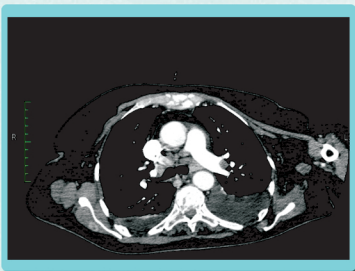
The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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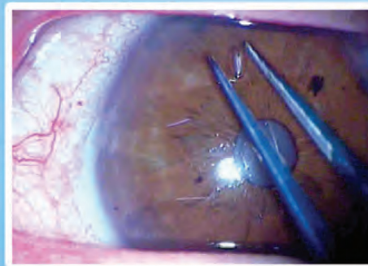
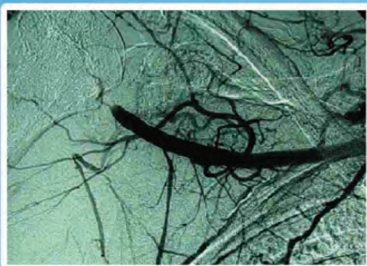


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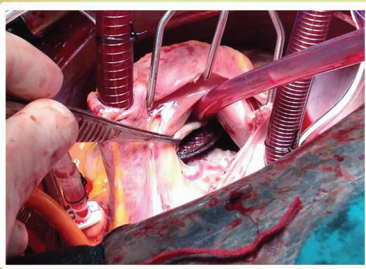


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