Bosnia and Herzegovina was the fourth country in Europe that developed National version of HeartScore program!

Bosna i Hercegovina je bila četvrta zemlja u Evropi koja je razvila Nacionalnu verziju HeartScore programa!
New Central Medical Building - University Clinical Center Sarajevo
Novi Centralni Medicinski Blok - Univerzitetski klinički centar u Sarajevu
Novi Evropski vodič za prevenciju tromboembolizma kod A Fib
CHA2DS2-VASc skor za procjenu rizika od tromboembolizma kod A Fib!

### Risk factor-based point-based scoring system - CHA2DS2-VASc

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure/LV dysfunction</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/thrombo-embolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease*</td>
<td>1</td>
</tr>
<tr>
<td>Age 65–74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category (i.e., female sex)</td>
<td>1</td>
</tr>
<tr>
<td><strong>Maximum score</strong></td>
<td><strong>9</strong></td>
</tr>
</tbody>
</table>

*Prior myocardial infarction, peripheral artery disease, aortic plaque. Actual rates of stroke in contemporary cohorts may vary from these estimates.

Major i non-major riziko faktori za procjenu tromboembolizma kod A Fib!

### Risk factors for stroke and thrombo-embolism in non-valvular AF

**Major risk factors**
- Previous stroke
- TIA or systemic embolism
- Age ≥75 years

**Clinically relevant non-major risk factors**
- CHF or moderate to severe LV systolic dysfunction [e.g., LV EF ≤40%]
- Hypertension
- Diabetes mellitus
- Age 65–74 years
- Female sex
- Vascular disease

AF = atrial fibrillation; EF = ejection fraction (as documented by echocardiography, radionuclide ventriculography, cardiac catheterization, cardiac magnetic resonance imaging, etc); LV = left ventricle; TIA = transient ischemic attack.

Algoritam antikoagulantne terapije nakon procjene CHA2DS2-VASc i major risk faktora!

### Choice of Anti-coagulant

- **Atrial fibrillation**
  - **Valvular AF**
  - **No** (i.e., non-valvular AF)

- **<65 years and lone AF (including females)**
  - **Yes**

- **Assess risk of stroke (CHA2DS2-VASc score)***
  - **0**
  - **1**
  - **≥2**

- **Oral anticoagulant therapy**
  - Consider patient’s values and preferences

- **No antithrombotic therapy**

NOAC - Novel Oral Anticoagulants, VKA - Vitamin K Antagonists

*Includes rheumatic valvular AF, hypertrophic cardiomyopathy, etc.
**Antiplatelet therapy with aspirin plus clopidogrel, or less effectively - aspirin only, may be considered in patients who refuse any OAC.
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Influence of various factors on the occurrence of postoperative seroma following breast cancer surgery .......................... 07
Sadat Pušina, Mirhan Salibašić, Emir Bičakčić, Amela Salibašić-Drnda

Absence of the national network for the primary treatment of acute coronary syndrome jeopardizes results of the surgical myocardial revascularization ........................................................................ 11
Sanko Pandur, Omer Perva, Faruk Custović, Edin Omerbašić, Enela Đonlić, Amina Mehić

Serum nitric oxide level in end-stage renal disease patients with different duration of dialysis therapy ..................... 16
Nesina Avdagić, Nermina Babić, Asija Začiragić, Anela Šubo, Amela Dervišević, Adnan Hadžimuratović, Sadeta Begić-Kapetanović, Amela Bećiragić; Izeta Aganović-Mušinović

The incidence and some characteristics of patients with hemophilia in Bosnia and Herzegovina .......................... 20
Edo Hasanbegović, Jelica Predojević-Samardžić, Nermana Čengić

Evaluation of surgical treatment of Achilles tendon rupture ......................................................................................... 23
Adnana Talić-Tanović, Fuad Džanković, Adnan Papović, Mehmed Zahirović

Benefits of cochlear implant speech processor upgrade ................................................................................................. 27
Sanja Špirić, Dmitar Travar, Predrag Špirić, Slobodan Spremo, Mirjana Gnjatić

Serum nitric oxide concentration in rheumatoid arthritis patients: the association with disease activity .................. 30
Amela Dervišević, Nermina Babić, Asija Začiragić, Nesina Avdagić, Šekib Sokolović, Almir Fajkić, Orhan Lepara, Anela Šubo, Jasminko Huskić

Defining the vascular skin territories of the septocutaneous blood vessels of the forearm with a special overview on their use in the fasciocutaneous flaps surgery .......... 34
Darko Jović, Aleksandar Jakovljević, Jovan Ćulm, Branislava Jakovljević, Ljiljana Latinović, Olivera Kosovac, Darko Lukić

Kinesiotherapy in early rehabilitation of patients after surgery of herniated cervical intervertebral disc ..................... 37
Ksenija Miladinović, Narcisa Vavra-Hadžiahmetović, Mirsad Muftić, Damir Čelik

Advantages of locking compresion plates in treatment of proximal humerus fracture .............................................. 41
Faruk Lazović, Ismet Gavrankapetanović, Adnana Talić-Tanović, Demil Omerović, Mehmed Jamakosmanović

Comparative advantages of VATS in relation to standard thoracic drainage in primary pleural empyema treatment ............................................................................................................ 45
Ilijaz Pilav, Safet Guska, Safet Mušanović

Review article

Exposure to ionizing radiation for medical purposes: effects on population, monitoring, management and reporting of radiation doses ........................................................................ 49
Sandra Vegar-Zubović, Spomenka Kristić, Irmina Sefić-Pašić

Instructions to authors ......................................................................................................................................................... 52

Uputstva autorima ............................................................................................................................................................... 54
Influence of various factors on the occurrence of postoperative seroma following breast cancer surgery

Uticaj različitih faktora na nastanak postoperativnog seroma nakon operativnih zahvata kod karcinoma dojke

Sadat Pušina1*, Mirhan Salibašić1, Emir Bičakčić1, Amela Salibašić-Drnda2

1Surgical Oncology Clinic, University Clinical Centre Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina; 2Faculty of Pharmacy, University of Sarajevo, Zmaja od Bosne 8, 71000 Sarajevo, Bosnia and Herzegovina

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ABSTRACT

Introduction: breast surgery and axilla are among the operational procedures of low morbidity and mortality unless associated with the simultaneous reconstructive breast surgery. Complications of breast cancer surgery may be non-specific (seroma, wound infection, bleeding, etc.) or specific for surgical procedures on the breast (fibrosis breast cancer lymphedema, cellulite, etc.) or in the axilla (seroma, lymphedema, neurosensory problems, limited mobility of upper extremity, etc.). The objective was to evaluate the impact of certain factors (size and histological type of tumor; state of axillary lymph nodes, hormone receptor status, type of surgery, number of drains, preoperative systemic adjuvant therapy) in the occurrence of postoperative seroma. Patients: a total of 168 patients with proven primary invasive breast cancer and defined-stage disease (TNM classification/AJCC), was included in the study, with or without applied neoadjuvant systemic therapy, aging between 18-75 years. Materials and methods: the study was retrospective, clinical-manipulative and descriptive-analytic. Clinical, radiological and histopathological findings were defined by the appropriate type of surgical treatment in the form of conservative breast surgery (wide local excision, quadrantectomy ) or radical breast surgery (modified radical mastectomy) with dissection of axillary lymph II level nodes (CALND) biopsy or axillary sentinel lymph node (SLNB). The postoperative seroma was defined as any clinically diagnosed accumulation of fluid in the axilla or under the skin incision treated with multiple needle aspirations. The appearance of seroma was analyzed in respect to the age of patients, preoperative chemotherapy, type of surgery, number of vacuum drains, type of hormone receptors, grade and tumor size and number of dissected positive axillary lymph nodes. Results: the results showed that there was a statistically significant difference in respect to the occurrence of postoperative seroma in patients who had undergone preoperative neoadjuvant chemotherapy ($\chi^2=17.818$, p=0.0001) and in respect to tumor size ($\chi^2=15.972$, p=0.0001). Results of the multivariate logistic regression analysis showed a statistically significant effect on postoperative seroma in patients who had preoperative neoadjuvant chemotherapy (OR=6.000 (2.370 to 15.19), p=0.0001, 95% CI 1.213 (1.069 - 1.660) and on tumor size [in patients with tumors ranging from 2 to 5 cm (stage T2) OR=2.115 (0.932 to 4.8); p=0.000; 95% CI 3.218 (1.84 to 7.17), while for tumors over 5 cm (stage T3 and T4) OR=11.8 (3.657 to 37.8) p=0.000, 95% CI 2.26 (2.26 to 2.26)]. Conclusion: the research showed that there was a statistically significant difference in the occurrence of postoperative seroma in relation to conducted preoperative neoadjuvant therapy and tumor size. It was also revealed that factors such as the age of patients, histological type and degree of tumor differentiation, state of the axillary lymph nodes, hormone receptor status, type of surgery and number of drains were not associated with the postoperative seroma development.

Key words: breast cancer surgery, complications, postoperative seroma

SAŽETAK

Uvod: hirurgija dojke i aksile spada u grupu operativnih procedura niskog morbiditeta i mortaliteta izuzev ako nisu udružene sa istovremenim rekonstruktivnim zahvatima na dojci. Komplikacije hirurgije karcinoma dojke mogu biti nespecifične (serom, infekcija, krvarenje itd.) ili specifične za operativne procedure na dojci (fibroza dojke, lymphedem dojke, celulitis itd.) ili u aksili (serom, limfedem, neurosenzorni problemi, ograničena pokretljivost ruke itd.). Cilj: evaluacija uticaja pojedinih faktora (veličina, histološki tip i stepen diferenciranosti tumora, stanje aksilarnih limfnih čvorova, status hormonskih receptorima, vrsta operativnog zahvata, broj drenova, sistematska adjuvantna terapija) na nastanak postoperativnog seroma. Pacijenti: analizirano je 168 pacijenica sa dokazanim primarnim invazivnim karcinomom dojke i definisanim stadijem oboljenja (TNM klasifikacija/AJCC), sa ili bez primjenjene neoadjuvantske intervencije, dobi između 18-75 godina, operisanih u periodu od januara 2014. do januara 2015. godine. Materijali i metode: istraživanje je bilo retrospektivno, kliničko-manipulativno i deskriptivno-analitičko. Prema kliničkom, radiološkom i patohistološkom nalažu definisana je intervencija tip operativnog tretmana u vidu poštivnih operativnih procedura (segmentektomija, kvadrantektomija ili hemimastektomija) i radikalnog operativnog zahvata (modificirane radikalne mastektomije) sa disekcijom II nivoa aksilarnih limfnih čvorova (CALND) ili biopsijom aksilarnog sentinel limfnog čvor (SLNB). Postoperativni serom je definisan kao bilo koje klinički dijagnosticirano nakupljanje tečnosti u aksili ili ispod kože operativnog reza tretirano sa mul-
Breast cancer is the most common malignancy in women and as a cause of death associated with malignant disease is the second among the most common, immediately after lung cancer (1).

Thanks to a widespread screening program for early detection of breast cancer and the use of non-invasive (ultrasound, mammography and magnetic resonance breast) and invasive radiological methods of the breast and axilla examination (tissue biopsy of the breast and axillary controlled by ultrasound) an increasing number of patients having breast cancer reveals the early stages of the disease when surgical treatment of breast cancer is the method of choice (2).

Breast and axillary surgery are operational procedures of low morbidity and mortality given that they are not associated with the simultaneous breast reconstructive surgery. Due to the increasing number of people affected by breast cancer at old age, we can still expect a variety of postoperative complications that can lead to increased morbidity producing additional costs of treatment and delaying the application of postoperative adjuvant therapy.

Complications of breast cancer surgery may be nonspecific (seroma, wound infection, bleeding, etc.) or specific operational procedures on the breast (fibrosis breast cancer lymphedema, cellulitis, etc.) or in the axilla (seroma, lymphedema, impaired neurosensitivity, limited mobility of upper extremity, etc.) (3).

The occurrence of complications could depend on various factors such as the patient age, type of surgical treatment, the extent of axillary lymph node dissection, the use of neoadjuvant chemotherapy, comorbidities, etc. The objective of the research was to evaluate the impact of certain factors (size and grade of tumor, the condition of axillary lymph nodes, hormone receptor status, type of surgery, number of drains, systemic adjuvant therapy) to the occurrence of postoperative seroma.

A total of 168 patients of the Clinic of Oncology Surgery, University Clinical Center Sarajevo (UCCS), diagnosed with primary invasive breast cancer and defined-stage disease (TNM classification / AJCC) with or without applied neoadjuvant systemic therapy, age between 18-75, surgically treated during the period from January 2014 to January 2015.

The study was retrospective, clinical-manipulative and descriptive-analytic. According to the clinical, radiological and histopathological findings, the appropriate type of surgical treatment was defined in the form of conservative breast surgery (wide local excision, quadrantectomy) or radical breast surgery (modified radical mastectomy) with dissection of axillary lymph II level nodes (CALND) biopsy or axillary sentinel lymph node (SLNB). After surgical removal of breast cancer simultaneous reconstructive procedures were not performed. Demographic and clinical information were obtained from the patients’ histories.

The postoperative seroma was defined as any clinically diagnosed accumulation of fluid in the axilla or under the skin incision treated with multiple needle aspirations.

The emergence of seroma was analyzed in relation to the age of patients, administering preoperative chemotherapy, type of surgery, number of vacuum drains, type of hormone receptors, grade and tumor size and number of dissected positive axillary lymph nodes.

Histopathological analysis of breast tumors and lymph nodes was carried out at the Institute of Pathology and Cytology of the UCCS based on the corresponding protocol.

From the obtained data given variables we calculated individual relative risk (odds ratio) using univariate regression analysis, and statistical significance by using chi-square test with a significance level, p <0.05. Multivariate logistic regression analyzes was performed to assess the independent risk factors for seroma. All variables in the course of study were considered as independent predictive factors and the formation of seroma was observed as a dependent variable in the multivariate analysis. Results of the analysis were presented in tables, and compared to the results of modern relevant researches in this field.

The study which was conducted in the period from January 2014 to January 2015 included 168 patients diagnosed with primary invasive breast cancer, average age of 58.87 ± SD (20-83), and surgically treated at the Clinic for Oncology and Glandular Surgery of the UCCS. Preoperative neoadjuvant chemotherapy was performed on 14.3% (24/168) of patients.
Radical breast surgery (RBS) was performed on 71.4% (120/168) of patients, while conservative breast surgery (CBS) was performed on 28.5% (48/168) of patients. Conservative breast surgery patients were drained with one active drain while two drains were used in radical breast surgery patients.

Regarding the lymph nodes, five positive lymph nodes were found in 80.09% (139/168) of patients, 6 to 10 positive lymph nodes in 6.5% (11/168) of the patients, whereas 10.7% (18/168) of patients had over 10 positive lymph nodes. The postoperative seroma was observed in 30.9% (52/168) of patients.

In 70.2% (118/168) of patients, breast cancer was estrogen and progesterone positive, in 13.1% (22/168) of patients breast cancer was Her-2 positive, and in 16.7% (28/168) of patients it was „triple negative”. In relation to tumor differentiation, grade II was recorded in 43.5% (73/168), grade III in 32.7% (55/168) and grade I in 13.1% (22/168) of patients. „Carcinoma in situ” was recorded in 10.7% (18/168) of patients. With respect to T-stage tumors, the most frequent was T2 stage which occurred in 51.8% (87/168) of patients, followed by TC1 and T1 stage tumors registered in 33.9% (57/168) of patients, whereas the minimum percentage of tumors related to stages T3 and T4, recorded in 14.3% (24/168) of patients.

Results of univariate analysis compared to the variables studied in relation to the occurrence of postoperative seroma are shown in Table 1.

A statistically significant difference in relation to the occurrence of postoperative seroma was recorded in patients who went through preoperative neoadjuvant chemotherapy ($\chi^2=17.818$, $p=0.0001$) and in relation to the size of the tumor ($\chi^2=15.972$, $p=0.0001$).

Results of multivariate logistic regression analyzing the influence of independent factors on the occurrence of postoperative seroma are shown in Table 2.

DISCUSSION

Breast cancer is the most common malignancy in women where the radical or partial surgical treatment with CALDN or SLNB is performed as the most common treatments for breast cancer. A large number of post surgical complications can occur after breast cancer surgery being mostly caused by the occurrence of postoperative seroma which incidence after breast and axillary surgery ranges between 2.5 to 60% (4).

It describes several factors that can be involved in the formation of seroma such as extentiveness of dissection of lymph nodes, number of drains, hormone receptors, the grade and size of tumor, size of tumor (cm), number of post surgical complications can occur after breast cancer surgery being mostly caused by the occurrence of postoperative seroma which incidence after breast and axillary surgery ranges between 2.5 to 60% (4).

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the axillary, supraclavicular and internal mammary lymph nodes, tending to create seroma formation in any enclosed space after surgical interventions on the breast (5,6,7,8,9,10).

In this research, the percentage of postoperative seroma was 30.9% (52/168). According to certain authors, the percentage of postoperative seroma varies from 2 to 51%, which corresponds to the results of our study (4,5,6). Other authors quoted lower incidence of seroma collection after breast and axilla surgery, ranging from 15 to 18% (7,8).

All these authors stated that the postoperative seroma was mostly an early postoperative complication of breast cancer surgery (4,5,6,7,8).

According to the prospective randomized study conducted by Petrek et al. the most striking factors for seroma are the extensiveness and the number of affected dissection of axillary lymph nodes (11). Gonzalez and Hashemi et al. in two separate studies disclosed that the only statistically significant factor influencing development of seroma is type of surgery (radical opposite conserving), explaining that extensive dissection with radical mastectomy and modified dissection of axillary lymph nodes leads to the damage of a number of blood and lymph vessels, and consequent “leak” of blood or lymph fluid with large areas of surgical wound leading to the occurrence of seroma (12,13,14).

In our survey, the appearance of postoperative seroma did not show significant association with the type of surgery and the number of dissected lymph nodes.

In the previously mentioned studies, factors such as the patient age, thickness, size of the tumor and neoadjuvant therapy, have no effect on the formation of seroma. However, our study revealed that tumor size showed statistical significance in connection to development of postoperative seroma ($\chi^2=15.972$, $p=0.0001$). Specifically, the ratio of tumor size and the size of the breast was one of the main parameters in choosing surgery type (radical or conserving). This is supported by a recent study conducted by Lumachia et al. who showed that tumor size and the total amount of fluid drained are main factors for seroma formation after axillary dissection in patients who have undergone breast cancer surgery (15).

In addition to tumor size, preoperative neoadjuvant chemotherapy had significant influence on the postoperative seroma development in our research ($\chi^2=17.818$, $p=0.0001$), which corresponds to the results of studies conducted by Woodworth et al. who described the association between adjuvant chemotherapy and seroma formation (4).

This research has not established statistical significance between the number of placed drains, age of patients, tumor size, histological grade and type of hormone receptors in the appearance of postoperative seroma.

**CONCLUSION**

The various complications of breast cancer surgery depend on various factors (age of the patient, the type of surgical treatment, the extent of dissection of axillary lymph nodes, the use of neoadjuvant chemotherapy, comorbidity, etc.) which importance varies in the genesis of postoperative complications. The occurrence of postoperative seroma is the most common complication which does not endanger breast cancer operated patients’ life, but may affect the cost of treatment, length of hospitalization and the start of systemic adjuvant therapy. The research has shown that there is a statistically significant difference in the occurrence of postoperative seroma in relation to conducted preoperative neoadjuvant therapy and tumor size. It was also noted that factors such as the age of patients, size and grade of tumor, number of the positive axillary lymph nodes, hormone receptor status, type of surgery, number of drains, are not associated with the development of postoperative seroma.

**Conflict of interest:** none declared.

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Absence of the national network for the primary treatment of acute coronary syndrome jeopardizes results of the surgical myocardial revascularization

Odsustvo nacionalne mreže primarnog zbrinjavanja akutnog koronarnog sindroma ugrožava rezultate hirurške revaskularizacije miokarda

Sanko Pandur1*, Omer Perva1, Faruk Ćustović2, Edin Omerbašić1, Enela Đonlić1, Amina Mehić1

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ABSTRACT

Left ventricular dysfunction with reduced ejection fraction and heart failure is the most common result of ischemic heart disease and a reflection of the devastating effects of myocardial infarction on the viability of the cardiac muscle mass. The aim of the study was to show that there is a large part of cardio surgery patients with impaired ejection fraction in our clinical practice, to compare the results with advanced European countries and establish the basis for monitoring the performance of percutaneous coronary interventions in terms of candidates for coronary revascularization. Materials and methods: we analyzed 120 coronary surgical patients divided into two groups. Out of the total number of patients 60 had stenosis of the left main coronary artery and affected other coronary systems, whereas 60 patients had changes in coronary arteries of all three systems except on the main stem of the left coronary artery. All patients underwent an echocardiography for preoperative estimation of the left ventricle ejection fraction. Afterwards, we compared the group of 120 patients with 466 isolated coronary surgery patients in four-year casuistry (2012-2015). Results: there was no statistically significant difference between the groups with a reduced ejection fraction (below 50 %) where $\chi^2$ test was 5.175 and $p=0.0752$. In the group of 120 patients with EF 35% and less there were 23.33% patients. In a four year casuistry of 466 patients, we found out that in 22.53% of patients ejekcione frakcije ispitivane grupe od 120 bolesnika sa četverogodišnjom kazuistiku 466 izoliranih koronarnih hirurških bolesnika operiranih u našoj ustanovi. Rezultati: nije utvrđena statistički signifikantna razlika među grupama G1: G2 sa sniženom ejekcionom frakcijom ispod 50% gdje je $\chi^2$ test 5.175, a $p=0.0752$. U grupi od 120 bolesnika ejekcione frakciju 35% i manje imalo je 23.33% bolesnika. U četverogodišnjoj kazuistici od 466 bolesnika EF 35% i manje imali smo u 22.53% bolesnika. Poređenjem grupe sa ejekcionom frakcijom 35 % i manje nije utvrđena signifikantna razlika, $p=0.948$. Zaključak: naši smo izrazito veliki broj bolesnika sa oštećenom ejekcionom frakcijom. Upoređujući grupu od 120 bolesnika sa četverogodišnjom kazuistikom nismo našli signifikantnu razliku, što upućuje na nedostatnost primarnog zbrinjavanja akutnog infarkta miokarda i urgira mrežu primarnog zbrinjavanja akutnog koronarnog sindroma.

Key words: coronary surgery, left ventricle dysfunction, PPCI network

SAŽETAK

Disfunkcija lijeve komore sa sniženom ejekcionom frakcijom i srčano popuštanje najčešća je posljedica ishemijskih bolesti srca i odraz je devastirajućih efekata miokardnog infarkta na vijabilnu mišićnu masu. Cilj rada je pokazati veliki udio kardiohirurških koronarnih bolesnika sa oslabljenom ejekcionom frakcijom u našoj kliničkoj praksi, komparirati rezultate sa naprednim Evropskim zemljama i utvrditi osnovu za praćenje uspješnosti perkutanih koronarnih intervencija sa aspekta kandidata za hiruršku revaskularizaciju miokarda. Materijali i metode: analizirali smo 120 koronarnih hirurških bolesnika od kojih je 60 sa stenozom glavnog stabla lijeve koronarne arterije (G1) i 60 elektivnih koronarnih bolesnika (G2). Bolesnicima je preoperativno procjenjivana ehokardiografski ejekciona frakcija. Zatim smo uporedili ejekcione frakcije ispitivane grupe od 120 bolesnika sa četverogodišnjom kazuistikom 466 izoliranih koronarnih hirurških bolesnika operiranih u našoj ustanovi. Rezultati: nije utvrđena statistički signifikantna razlika među grupama G1: G2 sa sniženom ejekcionom frakcijom ispod 50% gdje je $\chi^2$ test 5.175, a $p=0.0752$. U grupi od 120 bolesnika ejekcionu frakciju 35% i manje imalo je 23.33% bolesnika. U četverogodišnjoj kazuistici od 466 bolesnika EF 35% i manju našli smo u 22.53% bolesnika. Poredenjem grupe sa ejekcionom frakcijom 35 % i manje nije utvrđena signifikantna razlika, $p=0.948$. Zaključak: naši smo izrazito veliki broj bolesnika sa oštećenom ejekcionom frakcijom. Upoređujući grupu od 120 bolesnika sa četverogodišnjom kazuistikom nismo našli signifikantnu razliku, što upućuje na nedostatnost primarnog zbrinjavanja akutnog infarkta miokarda i urgira mrežu primarnog zbrinjavanja akutnog koronarnog sindroma.

Ključne riječi: koronarna hirurgija, disfunkcija lijeve komore, PPCI mreža
INTRODUCTION

Left ventricular dysfunction after acute myocardial infarction is the most serious long-term complication due to the devastating effects on the viability of myocardial muscle mass (1).

Left ventricular dysfunction (DLV) is defined as a reduced myocardial contractility with a consequent reduction in ejection fraction (EF) of the heart. Arbitrary, lowering EF of 40-50% is considered to be moderately reduced EF and below 40% of severely depressed EF. It depends on the severity of coronary atherosclerosis, atherosclerotic lesion location, extent of infarction, re-infarction, time between acute myocardial infarction and surgery.

Pre-existing risk factors such as diabetes, hypertension, smoking, peripheral vascular disease, chronic renal failure, obstructive pulmonary disease burden further course of the disease and complications of treatment.

Patients with left ventricular dysfunction, triple-vessel coronary artery disease with or without involvement of the left main coronary artery and patients with diabetes are preferred candidates for coronary bypass grafting according to the current guidelines for revascularization (2). Three important randomized multi-centre trials: STICH (3), SYNTAX and FREEDOM led to these conclusions.

Methods of surgical treatment is coronary artery bypass grafting with the use of extracorporeal circulation, or off-pump beating heart techniques and techniques of creating a bypass on the beating heart but with the use of extracorporeal circulation. Usage of the internal mammary artery is a golden standard for LAD territory revascularization. For other territories other arterial or venous grafts are used (4).

Despite the promising results of coronary surgery, patients with reduced EF of the LV remain the subject of intense medical care (5) because of heart failure, malignant arrhythmias and sudden cardiac death. Long-term survival of these patients is significantly less than in patients undergoing coronary artery surgery with preserved EF (6).

The role of percutaneous coronary intervention in acute coronary syndrome was revolutionary, because it changed the course of coronary patients by preserving the viability of myocardial mass.

A developed national network of interventional cardiology in advanced countries changed the rate of patients with preoperative impaired left ventricular function and improved long-term results of surgical myocardial revascularization (7).

MATERIALS AND METHODS

We analyzed 120 operated coronary patients of whom 60 patients (group G1) with left main stenosis and inclusion of other coronary arteries evaluated in the period from 1 June 2011 to 30 September 2013, and 60 patients (group G2) without signs of left main stenosis but with advanced coronary artery disease of other vessels with indication for operative treatment, evaluated in the period from 1 December 2012 to 31 March 2013. We designed a prospective study. We put this group of patients in a four year casuistic context of coronary surgery in the period from 1 January 2012 to 31 December 2015.

Criteria for inclusion in the study included patients of both sexes, regardless of age, patients with indication for coronary artery bypass due to primary ischemic heart disease and patients with a defined heart failure and previous interventional procedures.

Criteria for exclusion from the study included valvular patients with coronary artery disease, patients with affected ascending aorta and coronary artery disease and valvular patients with the need for creating one coronary bypass other than the left anterior descending artery and the right coronary artery.

Methods of research

This was a clinical, prospective, descriptive-analytical and manipulative study. The results are shown in text and graphics. Demographic information was drawn from personal documents and history of the disease. Forms of clinical manifestations among defined groups were done on the basis of medical records. Preoperative ejection fraction of patients was estimated by echocardiography – Simpson’s method and by defining the wall kinetics. The diagnostic ECHO check-up was performed on the same device, GE Vivid 7, by two echocardiographers with almost uniform criteria.

Statistics

Statistical analysis was performed using MedCalc for Windows, version 12.6, MedCalc Software, Ostend, Belgium. All variables were examined using standard statistical analysis methods. Parametrical data were tested with Student T test, Chi square test and the comparison between the groups was also performed throughout correlation tests. The level of significance alfa, p value of less than 0.05 was considered as statistically significant.

RESULTS

Analysis of demographic parameters and risk factors

The study included a total of 120 patient, of whom 60 patients with left main stenosis (Group 1-G1) and 60 electively selected patients (Group 2-G2) who did not require urgent surgical treatment (Table 1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>G1 (n=60)</th>
<th>G2 (n=60)</th>
<th>ALL (n=120)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>46 (77%)</td>
<td>32 (87%)</td>
<td>98 (82%)</td>
<td>NS**</td>
</tr>
<tr>
<td>F</td>
<td>14 (23%)</td>
<td>8 (13%)</td>
<td>22 (18%)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.55 ± 8.98</td>
<td>58.03 ± 9.3</td>
<td>59.79 ± 9.30</td>
<td>0.0377*</td>
</tr>
</tbody>
</table>

The average age of all subjects was 59.79 ± 9.30 years (ranging from 31 to 80 years). The average age in Group 1 (G1) was 61.55 ± 8.98 years (ranging from 36 to 80 years), and 58.03 ± 9.34 years (ranging from 31 to 77 years) in Group 2 (G2) (Table 1). There was a statistically significant difference in age between the groups of subjects (t(118)=3.5167, p=0.0377 (mutually).
Comparison of patients with preoperative ejection fraction (preoperative ejection fraction was estimated by echocardiography – Simpson’s method).

Using the student T test for independent samples the results of ejection fraction of both groups (preoperatively and postoperatively) were compared. There was no significant difference in the results between the groups before surgery in G1 (M=45.12, SD=9.61) and G2 (M=44.13, SD=9.04), t (120) = -0.378, p=0.1708 (mutually) or postoperatively in G1 (M=42.83, SD=10.89) and G2 (M=41.75, SD=9.56), t (120) = -1.403, p=0.1631 (mutually) (Figure 1).

The analysis done through Chi-square test of independence showed no significant difference in the distribution of the frequency of patients with lower preoperative values of ejection fraction (EF% ≤35%) between the groups, χ^2 (2, N=120) = 5.175, p=0.0752 (Figure 2).

Overview of ejection fractions in patients who were treated surgically in the 2012 - 2015 period and results of comparison between the groups of patients who had EF 35% or less (120 patients vs. 4-year casuistry of 466 patients) showed no significant statistical difference (Table 2).

### Table 2 The 2012-2015 casuistry of isolated CABG and comparison results between the two groups of patients with EF 35% or less.

<table>
<thead>
<tr>
<th></th>
<th>2012 – 2015 (466 pts)</th>
<th>G1+G2 (120 pts)</th>
<th>Comparison results G1+G2 vs 4 year casuistry (only EF 35% or less)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M F Total</td>
<td>M F Total</td>
<td>Total</td>
</tr>
<tr>
<td>EF ≤35%</td>
<td>155 48 203</td>
<td>42 35%</td>
<td></td>
</tr>
<tr>
<td>EF 36-49%</td>
<td>128 30 158</td>
<td>33.9%</td>
<td></td>
</tr>
<tr>
<td>EF ≥50%</td>
<td>88 17 105</td>
<td>23.3%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>371 (79.62%)</td>
<td>95 (20.38%)</td>
<td>466 100% 120 100%</td>
</tr>
</tbody>
</table>

**DISCUSSION**

As part of the preoperative preparation all patients underwent echocardiographic assessment of ejection fraction (EF) of the left ventricle using the Simpson method. In the group with LM stenosis average EF was 45.41% ranging from 20% to 60%. In the elective group the average value was 44.13% ranging from 20% to 55%. There were no statistically significant differences in the mean value of EF between the groups and p = 0.1708. However, there was a significant difference between the groups in the number of patients with impaired EF below 35%.

The group of patients with LM stenosis patients with EF below 35% consisted of 9 patients, or 15%, and in the elective group, the number of patients with an EF below 35% was 18 or 30%. The total number of patients with impaired EF was 77 or 64.17%. In the group with LM disease the number of patients with impaired EF was 35 or 58.33%, and in the elective group the number was 42 or 70%. These high values motivated us to look at them in the context of four-year casuistry in the period 2012 - 2015, where we concluded that there was a little difference in the comparison, and that the number of patients with a reduced EF was extremely high. A particular problem was the quota of patients with an EF of 35% or less. Preoperative dysfunction of the left ventricle is a known risk factor for early and late mortality after myocardial revascularization (8). In patients with low EF CABG surgery has proved to be a superior therapeutic option in comparison to other types of treatment, and it is proved that those patients have better significant clinical improvement and long-term survival. In patients with low EF - CABG is also associated with higher postoperative morbidity and mortality compared to patients with near-normal EF. In a large Dutch study (2010) conducted by Hamada et al, (9) based on 10285 patients treated with CABG surgery followed patients who were divided into three groups according to the EF /≤35%, 36-49% and 50% and more/ and compared them to general population in terms of Dutch estimates of survival. The study found that the ejection fraction below 50% was associated with relatively poor outcome for all monitored patients in comparison to those which EF was above 50% in which the results were better than expected. The group with EF below 35% consisted of 364 patients or 3.53%. The total number of patients with impaired EF was 2,081 or 20.22%. These values indicate the outstanding early care of acute coronary syndrome and myocardial mass rescue from definitive destruction.

Early mortality in the group with poor fraction was 10.5%, and late mortality after 10 years was 22.4%. Finland study conducted
by Hakonen et al. (10) and published in 2014 demonstrated an incredible 18% of patients-candidates for surgical revascularization with reduced EF (below 50%). An Italian study by Gatti & Associates (2015) showed that the amount of patients with reduced EF (35% and less) was 6.85%. If we compare these facts with ours we will see that our operating casuistry with low EF is 6-8 times higher than in developed European countries with consequent complications, early and late mortality. Care of ACS in our institution has been made for the last 8 years, but unsystematically. We can see the results of the trial care from the 2012-2015 period, but an established network of care for ACS on national level surely can provide better results in the preservation of myocardial function, a smaller number of surgical candidates for revascularization who have reduced EF, and better early and late survival. Study reports about patients with ejection fraction of the left ventricle of 35% or less.

Credo - Kyoto study (2) showed better five-year outcomes of patients with LVD treated with coronary surgery in comparison to PCI. The improvement in the ejection fraction of 10 % compared to the pre-operative in the first 6 months is considered a predictor of patient functional improvement. Hospital mortality of patients with EF below 35% varies from 5.3-10% according to reports of Hammad and Gatti, (11) and operative mortality in the last 5 years has a dramatic fall in the early postoperative period (30 days) and ranges from 2-4%. These results can be incorporated in our operating results. Late mortality, five and ten year survival is much worse in these patients compared to those with good EF. Report from Velasquez et al. (2015) (12,13) talks about five and ten year survival of patients with LVD and reduced EF. A five year survival was recorded in 61% of patients, and a ten year survival in 42% of operated patients (14). Average survival in coronary surgery is between 15 and 17.5 years. This data show the PCI contribution on preservation of the viability of muscle mass after AMI A, improvement of perioperative complications and survival. The most common causes of death in these patients were heart failure (15) and sudden cardiac death due to malignant arrhythmias. According to electrophysiologists all patients with reduced LV EF (less than 35%) and NYHA functional class II and III were recommended for ICD implantation (Class 1, Level A). The ICD implantation was also recommended to patients with LVD after AMI who had an EF of less than 30% and belonged to NYHA class I and to patients who survived cardiac arrest due to VF (16). Only under these criteria 50% of patients are candidates for the implantation of an internal cardioverter defibrillator. Our economic situation and the economical participation of patients in the acquisition of the ICD do not allow widespread use of ICD in these patients.

Assessment of viability and postoperative impact on the viability of the anterior wall is of great importance, because an improvement of the viability of the anterior wall is a powerful predictor of improvement of ejection fraction after CABG. We often forget the role of the right ventricular function in the estimation of the coronary patients. One of the important factors in early and late readmission to hospital is also right ventricular dysfunction (17).

**CONCLUSION**

In the above study we presented a large number of coronary surgical patients with moderately and severely reduced ejection fraction of the left ventricle. These patients represented a therapeutic challenge. Compared to the advanced European countries (Italy, Netherlands, Finland), we found that there was a 3-7 times higher incidence of these patients in our clinical material. Improving care for acute myocardial infarction with percutaneous Coronary intervention in the „golden hour“ can save the viability of the myocardial muscle mass, reduce future operating risk, improve quality of life and early and late survival of these patients. It is an urgent requirement to establish a national network for PCI to timely help to larger number of patients, and to reduce a number of those with impaired left ventricular function as candidates for surgical intervention. This research can be the basis for future comparisons of progress in managing ACS and reducing the number of patients with left ventricular dysfunction.

**Conflict of interest:** none declared.

**REFERENCES**


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Absence of the national network for the primary treatment of acute coronary syndrome jeopardizes results of the surgical myocardial revascularization

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Prestanite pušiti odmah!
Serum nitric oxide level in end-stage renal disease patients with different duration of dialysis therapy

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*Corresponding author

ABSTRACT

A deficiency of endogenous vasodilator nitric oxide (NO) has been implicated as a potential cause of increased blood pressure in end-stage renal disease (ESRD) patients. The aim of this study was to investigate the changes in serum NO concentrations in hemodialysis (HD) patients related to hemodialysis duration. The 60 ESRD patients of both genders were divided in two equal groups (n=30) based on the hemodialysis therapy duration: HD group < 5 years and HD group ≥ 5 years. Control group consisted of 30 age and gender matched apparently healthy individuals. The serum NO level was determined by classic colorimetric Griess reaction. The serum NO concentration was statistically different (p=0.001) between the HD group < 5 years and HD group ≥ 5 years, and healthy controls. No significant difference (p=0.17) in serum NO level was observed between HD patients with different duration of dialysis therapy. Serum NO level had fair diagnostic accuracy (AUC=0.603; p=0.017) in distinguishing HD patients from healthy controls, while in differentiating HD patients with different duration of dialysis therapy serum NO level had a poor diagnostic accuracy (AUC 0.716; p=0.001) in HD group < 5 years, HD group ≥ 5 years and control groups. No significant difference (p=0.17) in serum NO level was observed between HD group < 5 years and HD group ≥ 5 years, and healthy controls.

Key words: nitric oxide, end-stage renal disease, hemodialysis

INTRODUCTION

It is already well known that nitric oxide (NO), free radical gas, is an important cellular signaling molecule involved in many physiological and pathological processes (1). NO is synthesized enzymatically from amino acid L-arginine by three distinct isofoms of the enzyme, nitric oxide synthase (NOS). Two of these isofoms are expressed in constitutive manner, predominantly in the vascular endothelium (eNOS) and in the nervous system (nNOS). Under normal physiological condition these isoforms of NOS generate...
low, transient levels of NO in response to increases in calcium concentrations. These low levels of NO contribute to blood pressure regulation, platelet aggregation and adhesion, gastrointestinal motility and neurotransmission (2,3,4). However, third isoform inducible NOS has a special role. When it is induced by endotoxine and/or cytokines, it generates high sustained levels of NO. In certain condition, NO would produce peroxynitrite contributing to cell cytotoxicity and tissue damage and up-regulation of the inflammatory response. In fact an excess of NO is involved in pathophysiology of numerous diseases, including cardiovascular and metabolic diseases (5), kidney disease (6), inflammatory bowel disease (7), neurological diseases (8), many tumors (9) etc.

In the resting state, basal release of NO by endothelial cells contribute to the vasodilatation and maintenance of normal blood pressure. Conversely, relative NO deficiency leads to a rise in blood pressure (10,11). It has already been demonstrated by experimental evidence that NO plays an important role in the pathophysiology of hypertension (12,13). Furthermore, there is evidence that vascular endothelial NO production may be defective in some patients with primary and secondary hypertension (14). Hypertension is prevalent in patients with end-stage renal disease (ESRD), irrespective of the etiology of their renal failure. Previous studies have reported that hypertension is associated with endothelial dysfunction characterized by impaired NO synthesis, angiogenesis and reduced activation of coagulations factors, cell proliferations with increased adhesion on the vessel wall (12).

In the past decades there is clinical and experimental evidence that chronic renal disease (CRD) and end-stage renal disease (ESRD) are associated with NO deficiency (15,16,17). This could result from arginine deficiency caused by a loss of functional renal mass, increased endogenous NO synthase inhibitors that accumulate in renal failure, and/or other causes, such as increased oxidative stress (17). The aim of this study was to determine whether there were changes in serum NO levels in the ESRD patients with different duration of hemodialysis therapy.

**MATERIALS AND METHODS**

**Subjects**

The cross-sectional study included 60 patients with end-stage renal disease (ESRD), of both sexes. Based on the duration of hemodialysis therapy the study groups were divided into two equal subgroups (n=30): a group of subjects who were on hemodialysis therapy between three months and five years (HD group < 5 years), and a group of subjects who were on hemodialysis therapy for five or more years (HD group ≥ 5). Control group (n=30) consisted of age and gender-matched, apparently healthy individuals. All subjects involved in the study went through detailed anamnestic questionnaire, medical history, physical examination, standard laboratory analyses and blood pressure measuring. Recommended value for blood pressure in ESRD population - consistently <140 mm Hg systolic and <90 mm Hg diastolic (18). Written informed consent was obtained from all of the study participants. The study was carried out at the Hemodialysis Clinic of the University Clinical Center Sarajevo, with the approval of the Local Ethics Committee.

**RESULTS**

Table 1 summarizes baseline characteristics of HD patients with different duration of dialysis therapy and the control subjects.

A significant difference in age, gender and pre-dialysis systolic blood pressure was found when HD patients with different duration of dialysis therapy were compared to the control group (p<0.05). Patients from HD group ≥ 5 years had significantly lower pre-dialysis diastolic blood pressure compared to the control group (p=0.04). No significant difference in age, gender, pre-dialysis systolic and diastolic blood pressure was observed between HD patients with different dialysis therapy duration. There was no statistically significant difference between BMI and smoking between the study participants.
Serum NO concentrations of the three studied groups are shown in Figure 1. Median serum NO concentration was statistically different (p=0.001) between HD group < 5 years 7.98 µmol/L (6.15 µmol/L – 9.98 µmol/L), HD group ≥ 5 years 9.58 µmol/L (6.69 µmol/L – 12.21 µmol/L) and healthy controls 6.82 µmol/L (4.87 µmol/L – 8.74 µmol/L). Comparison of the serum NO level of HD group < 5 years with healthy controls showed a significant difference (p=0.03). A significant difference in serum NO level was also found when HD group < 5 years with healthy controls showed a significant difference (p<0.0005). No significant difference (p=0.17) in serum NO level was observed between HD group < 5 years and HD group ≥ 5 years.

### Table 1 Baseline characteristics of HD patients with different duration of dialysis therapy and the control group.

<table>
<thead>
<tr>
<th>Variables</th>
<th>HD group &lt;5 years (n=30)</th>
<th>HD group ≥5 years (n=30)</th>
<th>Control group (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages (years)</td>
<td>60.4 ± 2.1**</td>
<td>58.1 ± 2.2**</td>
<td>52.1 ± 1.4</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.9 ± 0.81**</td>
<td>26.1 ± 0.74*</td>
<td>26.6 ± 0.80</td>
</tr>
<tr>
<td>Sex</td>
<td>female</td>
<td>14 (46.7%)**</td>
<td>12 (40.6%)*</td>
</tr>
<tr>
<td></td>
<td>male</td>
<td>16 (53.3%)**</td>
<td>26 (85.7%)*</td>
</tr>
<tr>
<td>Pre-dialysis SBP (mmHg)</td>
<td>140.0** (128.7 – 160.0)</td>
<td>140.0* (130.0 – 150.0)</td>
<td>120.0 (110.0 – 130.0)</td>
</tr>
<tr>
<td></td>
<td>80.0 (70.0 – 90.0)</td>
<td>70.0 (60.0 – 82.5)</td>
<td>80.0 (75.0 – 90.0)</td>
</tr>
<tr>
<td>Smoking</td>
<td>yes</td>
<td>5 (16.7%)**</td>
<td>3 (10%)*</td>
</tr>
<tr>
<td></td>
<td>no</td>
<td>25 (83.3%)**</td>
<td>27 (90%)*</td>
</tr>
</tbody>
</table>

Data is presented as mean ± SEM; median (25th and 75th percentiles); n (%). HD - hemodialysis; BMI - body mass index; SBP - systolic blood pressure; DBP - diastolic blood pressure; NS - not significant; p-probability

* p<0.05 compared to healthy control
** p=0.005 compared to healthy control
NS - not significant in comparison to HD group < 5 years NO – nitric oxide; HD - hemodialysis patients.

The ROC curve for serum NO level for differentiation between HD patients and healthy controls.

### Table 2 Optimal cut-off, area under the curve with 95% confidence interval (AUC, 95% CI), sensitivity, specificity, positive and negative predictive value, overall accuracy of serum NO level in differentiating between HD and healthy controls.

<table>
<thead>
<tr>
<th>Variable and cut-off values</th>
<th>Diagnosing measures</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemodialysis patients vs. healthy controls</td>
<td>NO (≥ 9.23 µmol/L)</td>
<td>0.716 (0.61-0.83)</td>
</tr>
</tbody>
</table>

AUC - Area under the curve; CI - Confidence Interval; NO - nitric oxide; SEN - sensitivity; SPE - specificity; PPV - positive predictive value; NPV - negative predictive value; p-probability

**DISCUSSION**

The effect of end-stage renal disease on NO metabolism is incompletely understood. Both increased and decreased activities of L-arginine-NO pathway have been suggested in ESRD patients (20,21). In this regard, several studies have pointed to the possible reduction of NO production in ESRD (16,17,24). For instance, it has been shown that renal insufficiency causes accumulation of endogenous NOS inhibitors, which can potentially depress NO production in ESRD (1,20,21). Although the above observations point to impaired local or systemic NO production in ESRD, a number of other studies have offered evidence for increased vascular NO production in ESRD (15,16,17,24).

This study was carried out to determine whether duration of hemodialysis therapy influenced the serum NO level in the ESRD patients.

The results of our study showed that the serum NO level was significantly higher in both HD group < 5 years (p=0.03) and HD group ≥ 5 years (p<0.0005) as compared to the healthy controls. Although the serum NO concentration was higher in the HD group ≥
The present study demonstrates that serum NO production is low in ESRD, and concluded that this NO deficiency may contribute to hypertension and disease progression in ESRD. The same authors conducted a third study (24) to determine whether 24-hour NOX (NO2 and NO3) excretion (a qualitative index of total NO production) was reduced in patients with chronic renal disease. They conducted a study with controlled low-NOX intake and found that low 24-hour NOX output in ESRD patients suggested that total systemic NO production was low in humans with impaired renal function, as well as inadequate plasma clearance.

Meenakshi et al. (15) conducted a study to determine whether there were any changes in the levels of NO in chronic renal failure (CRF), as the disease progresses. These authors have demonstrated that CRF patients on maintenance hemodialysis have markedly increased NO concentration compared to the controls, and suggest that measurement of NO level in the peripheral blood may be used as an indicator of prognostic follow-up in the CRF patients on dialysis. This finding was in accordance with the report of Dejanova et al. (25) who also observed significantly higher serum NO level in HD patients compared to controls. However, with regard to hemodialysis duration these authors did not find statistically significant difference in serum NO concentration, which is in accordance with our results. In their opinion, the increased nitric oxide values observed in HD patients is probably due to the induction of hemodialysis membrane and/or a lack of renal excretion.

We further investigated the ability of serum NO concentration in differentiating HD patients from healthy controls as well as HD patients with different duration of dialysis therapy. In our study, based on the selected optimal cut-off value by ROC curve analysis, serum NO values showed a low sensitivity (43%) and excellent specificity (93%) in distinguishing HD patients from healthy controls. The results of our study demonstrate that the serum NO level displays a fair diagnostic accuracy in distinguishing hemodialysis patients from healthy controls (AUC=0.716; p=0.001) and poor diagnostic accuracy in distinguishing hemodialysis patients with different duration of dialysis therapy (AUC 0.603; p=0.17).

CONCLUSION

Up-regulation of systemic nitric oxide synthesis may play a key role in the modulation of complex hemodynamic disorders in ESRD patients. The present study demonstrates that serum NO production is high in ESRD patients on hemodialysis therapy as compared to the controls. The obtained results support the hypothesis that serum NO level measurement in ESRD patients can be used as independent marker only to distinguish hemodialysis patients from healthy control, but not in differentiating hemodialysis patients with different duration of dialysis therapy. However, due to small sample size, our findings are warranted for further confirmation in larger studies.

Conflict of interest: none declared.

REFERENCES


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The incidence and some characteristics of patients with hemophilia in Bosnia and Herzegovina

Incidenca i neke karakteristike pacijenata sa hemofilijom u Bosni i Hercegovini

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ABSTRACT

Introduction: hemophilia is a rare coagulation disorder, characterized by a tendency to bleed. The transmission of the disease is linked to a sex chromosome X, and it usually affects only males, while females are carriers. Objective: the aim of this study is to show the structure of patients with blood coagulation disorders in B&H, distribution of hemophilia A to the severity of the disease, age and developed inhibitors in patients. Materials and methods: we retrospectively analyzed the medical records of patients with congenital bleeding disorders in the largest children’s hospitals in the two entities of Bosnia and Herzegovina: Pediatric Clinic of the University Clinical Center Sarajevo, in the Federation of Bosnia and Herzegovina (FB&H) and the University Children’s Hospital Banja Luka, in the Republic of Srpska (RS). We also analyzed data from the Health Insurance Funds in both entities, in terms of annual consumption of coagulation factors in 2015. Results: the study showed that most people registered with coagulation disorders were with hemophilia A, 146 (68%), hemophilia B was in the second place with 35 (16%) patients, and there were 28 (13%) patients in the third place with Von Willebrand disease (VWD). There were 6 (3%) patients with other blood coagulation disorders. Majority of patients suffered from severe hemophilia A, 61 (42%). Moderate hemophilia A was associated with 48 (33%) patients and 37 (25%) patients suffered from mild form of hemophilia. There were 52 (36%) patients with hemophilia A under the age of 18 and 94 (64%) patients over 18 years of age. Low titre inhibitors <5 BU were developed in 6 (4%) patients with hemophilia A and high titre inhibitors ≥ 5 BU in 3 (2%) patients. Hemophilia B patients did not develop inhibitors. Conclusion: according to the World Federation of Hemophilia a comprehensive treatment of patients with hemophilia is realized at tertiary level centers. The introduction of home treatment and regular prophylaxis is a priority for all children with severe hemophilia, and for most adult patients.

Key words: hemophilia, inhibitors, prophylaxis

SAŽETAK

Uvod: hemofilija je rijedak poremećaj koagulacije, koju karakteriše sklonost krvarenju. Ovaj poremećaj se prenosi vezano za polni hromozom X, te uglavnom oboljevaju samo muškarci, dok su žene prenosioci. Cilj rada: da se prikaže struktura oboljelih od poremećaja koagulacije krvi u BiH, rasprostranjenost hemofilije A prema težini bolesti, starosnu dob i razvijene inhibitore kod oboljelih. Ispitanici i metode: retrospektivno su analizirane historije bolesti pacijenata s urođenim poremećajima krvarenja u najvećim dječjim bolnicama u dva entiteta Bosne i Hercegovine: Pedijatrijska klinika Univerzitetskog kliničkog centra u Sarajevu (UKCS), u Federaciji Bosne i Hercegovine (FBiH) i Univerzitetska Dječja bolnica Banja Luka u Republici Srpskoj (RS). Također su analizirani i podatci iz Fonda zdravstvenog osiguranja oba entiteta u pogledu godišnje potrošnje faktora koagulacije u 2015. Rezultati: istraživanje je pokazalo da najviše registрованиh osoba sa poremećajem koagulacije otpada na hemofiliju A 146 (68%), hemofilija B je na drugom mjestu sa 35 (16%) oboljelih, a na trećem mjestu sa 28 (13%) bilo je oboljelih od Von Willebrandove bolesti (VWD). Na ostale poremećaje krvarenja otpada 6 (3%) oboljelih. Najviše pacijenata je obolilo od teške forme hemofilije A, 61(42%). Na umjereni oblik hemofilije A otpada 48 (33%), a na blage forme 37 (25%). Broj oboljelih od hemofilije A ispod 18 godina je 52 (36%), a broj oboljelih iznad 18 godina je 94 (64%) pacijenata. Blagi oblik razvijenih inhibitora sa titrom < 5BU imalo je 6 (4%) pacijenata sa hemofilijom A, a sa visokim titrom ≥ 5BU, 3 (2%). Kod hemofilije B nije bilo pacijenata sa razvijenim inhibitorima. Zaključak: sveobuhvatan tretman osoba oboljelih od hemofilije prema standardu Svjetske federacije za hemofiliju, obavljaju centri na terciarnjoj razini. Uvođenje kućnog liječenja i redovna profilaksu predstavljaju prioritet za svu djecu s teškom hemofilijom i za većinu odraslih pacijenata.

Ključne riječi: hemofilija, inhibitori, profilaksu
INTRODUCTION

Hemophilia is a rare recessive hereditary disorder of blood clotting, which is characterized by a tendency to bleed. The word hemophilia has Greek roots haima (blood), phlein (love) and represents the earliest described hereditary disease.

The transmission of the disease is linked to a sex chromosome X, and it usually affects only males, while females are carriers. In about 30% of patients with hemophilia, family history was negative, indicating a spontaneous mutation of recessive gene for FVIII or transfer of the mutated genes for several generations. These are sporadic hemophilias. Hemophilia is characterized by a lack of specific coagulation factors, and classified into hemophilia A, or classic hemophilia related to the lack of factor VIII, hemophilia B (Christmas disease) related to the lack of factor IX, and hemophilia C related to the lack of factor XI. Hemophilia A occurs in 80% of all cases and is five times more common than hemophilia B, while hemophilia C is even less likely to occur (1,2).

It is assumed that the history of hemophilia is old as the history of man. The Talmud, sacred book of the Jews, written 1.500 years ago, stated that young Jew should not be circumcised, because the two sons of the same mother and three sons of her sister bled and died after circumcision.

Hemophilia is sometimes called ‘the royal disease” because the Queen Victoria transferred the gene for this disease to courts across Europe through her daughters (2,3,4).

The diagnosis of hemophilia is set based on personal and family medical history, clinical and laboratory findings. Hemophilia should be suspected if there is a history of hemophilia in the family, bruising and bleeding in the first years of life, spontaneous bleeding in joints and muscles, bleeding that is difficult to stop after injuries, tooth extraction or surgery. In hemophilia is lower F VIII, prolonged the coagulation time and active partial thromboplastin time (APTT). The platelet count is normal and the bleeding time is regular (4,5,6).

The clinical presentation mainly depends on the degree of deficit factor, F VIII level less than 1% indicates a serious condition, where occurs spontaneous bleeding not related to trauma. In moderate hemophilia with the values of F VIII 1-5%, bleeding occurs with a blow or fall, and patients with F VIII activity of 10-15%, bleed only after strong trauma (mild form). Most newborns do not show signs of the disease in the newborn period. With the development of motor functions (crawling, rising to the feet, walking) bleeding in joints and muscles appears in the form of large hematomas. Dentition or circumcision in the infant period may sometimes be the first bleeding in children suffering from hemophilia. The disease has a tendency to repeated bleeding into the same joint, which often results in degenerative changes, ankylosis of joints, osteoporosis and muscle atrophy. Rarely, there is bleeding in the CNS after head trauma or in the gastrointestinal tract (7,8,9).

The aim of this study is to show the structure of patients with blood coagulation disorders in B&H, distribution of hemophilia A to the severity of the disease, age and developed inhibitors in patients.

MATERIALS AND METHODS

We retrospectively analyzed the medical records of patients with congenital bleeding disorders in the largest children’s hospitals in the two entities of Bosnia and Herzegovina: Pediatric Clinic of the UCCS, in the Federation of Bosnia and Herzegovina (FB&H) and the University Children’s Hospital Banja Luka, in the Republic of Srpska (RS). We also analyzed data from the Health Insurance Funds in both entities, in terms of annual consumption of coagulation factors in 2015.

The analysis was done according to the type of blood coagulation disorder, distribution of hemophilia, age structure, level of inhibitors and therapeutic options.

RESULTS

Table 1 shows the most common congenital blood coagulation disorders in Bosnia and Herzegovina. The majority of patients were registered with hemophilia A, 146 (68%), hemophilia B was in the second place with 35 (16%) patients, and Von Willebrand disease (VWD) was in the third place with 28 (13%) patients. 6 (3%) patients had other blood coagulation disorders.

Table 2 shows the distribution of hemophilia A to the severity of the disease. Majority of patients suffered from severe hemophilia A, 61 (42%). Moderate hemophilia A was associated with 48 (33%) patients and 37 (25%) patients suffered from mild form of hemophilia.

Table 3 shows the age structure of patients with hemophilia A. There were 52 (36%) patients with hemophilia A under the age of 18, and 94 (64%) patients over 18 years of age.

Table 4 shows the level of developed inhibitors in hemophiliacs. A total of 9 (6%) patients developed inhibitors. Low titre inhibitors...
<5 BU were developed in 6 (4%) patients with hemophilia A and high titre inhibitors ≥ 5 BU in 3 (2%) patients. Hemophilia B patients did not develop inhibitors.

**DISCUSSION**

Hemophilia is a rare coagulation disorder characterized by a tendency to bleed. It is estimated that according to the last census Bosnia and Herzegovina has 3,791,662 inhabitants. The number of patients with hemophilia A and B is 181. Since Bosnia and Herzegovina is a European country, the priority health care of people with hemophilia is to achieve European protection principles for hemophilia. The introduction of home treatment and delivery of coagulation factors in the local pharmacies are the most important tasks to be achieved along with the introduction of regular prophylaxis for all children with severe hemophilia, and for most adult patients. With regard to congenital blood coagulation disorders in Bosnia and Herzegovina, majority of patients were registered with hemophilia A, 146 (68%), hemophilia B was in second place with 35 (16%) patients, and Von Willebrand disease (VWD with 28 (13%) patients. The data show a much smaller percentage of developed inhibitors. Out of all patients with hemophilia, 9 (6%) of them developed inhibitors. Low titre inhibitors < 5 BU were developed in 6 (4%) patients with hemophilia A and high titre inhibitors ≥ 5 BU in 3 (2%) patients. Hemophilia B patients did not develop inhibitors.

The distribution of hemophilia A to the severity of the disease in B&H show that the majority of patients suffer from severe hemophilia A, 61 (42%), 48 (33%) patients suffer from moderate hemophilia A, while 37 (25%) of patients has a mild form of the disease. Similar results have been described by other authors (9, 10).

The age structure of patients with hemophilia A showed that there was 52 (36%) patients with hemophilia A under the age of 18, and 94 (64%) patients over the age of 18.

Out of all patients with hemophilia, 9 (6%) of them developed inhibitors. Low titre inhibitors < 5 BU were developed in 6 (4%) patients with hemophilia A and high titre inhibitors ≥ 5 BU in 3 (2%) patients. Hemophilia B patients did not develop inhibitors (12, 13, 14).

The data show a much smaller percentage of developed inhibitors compared to other countries in the world.

**CONCLUSION**

According to the World Federation of Hemophilia a comprehensive treatment of patients with hemophilia is realized in tertiary level centers. In developed countries, patients with hemophilia live a normal life with proper treatment. The problem relates to unregistered patients. The most important priorities would be the establishment of the National Center for Hemophilia, the National Registry of patients with hemophilia and development of orthopedic surgery for patients with joints disability.

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**REFERENCES**


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Evaluation of surgical treatment of Achilles tendon rupture

Evaluacija operativnog liječenja rupture ahilove tetive

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ABSTRACT

Achilles tendon or heel tendon is the strongest tendon in human body, and is around 15 cm long. The tendon is an extension of muscle threads of the three-headed muscle consisting of gastrocnemius muscle (m.gastrocnemius), soleus muscle (m.soleus) and plantar muscles (m.plantaris), and attaches to the heel bone. Name tendon comes from Greek mythology, the Greek hero Achilles (Achilles' heel).

Rupture of the Achilles tendon usually occurs during recreational and sports activities, and the highest rate is reported in former athletes aged 40 years (football players, skiers, athletes). Ruptured tendon damage the surrounding tissue - usually occurs muscle contusion, hematoma develops that infiltrates the muscle tissue and damage contractility. Traumatized healed tendon rarely achieves the strength of a healthy tendon and is subject to new injuries of less effort.

Diagnosis of rupture is made by the clinical examination, positive Thompson’s sign and mandatory ultrasound examination. The aim of the work is to show the principles of surgical treatment and priority for emergency surgical treatment of fresh Achilles tendon rupture in relation to the delayed surgery. With surgical treatment the ends of the tendon should be smooth, thus the ends of the tendons that are torn or crushed get refreshed. Regardless of the type of stitches used, the tendon must not be under tension so that the suture does not dehiscence, and again achieves the physiological length. The study included total of 58 patients, of which 17 patients (45.71%) had an emergency surgery, and 31 (54.29%) delayed operative treatment. The average age of patients was 39 years. All patients were male and were surgically treated by open and percutaneous sutures method. The obtained results showed that in the group of urgently operated patients there was no case of rerupture and splicing, and were surgically treated by open and percutaneous sutures method. The obtained results showed that in the group of urgently operated patients there was no case of rerupture and splicing, and were surgically treated by open and percutaneous sutures method. The obtained results showed that in the group of urgently operated patients there was no case of rerupture and splicing, and were surgically treated by open and percutaneous sutures method. The obtained results showed that in the group of urgently operated patients there was no case of rerupture and splicing, and were surgically treated by open and percutaneous sutures method. The obtained results showed that in the group of urgently operated patients there was no case of rerupture and splicing, and were surgically treated by open and percutaneous sutures method. 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The tendon is named after the Greek hero Achilles, who according to the legend was bathed in the river Styx by his mother Thetis, holding him by the heel. Achilles was vulnerable only in that place, and was killed when Paris’ poisoned arrow (directed by Apollo) hit his heel. In medical literature the name Achilles tendon (tendo Achillis) was introduced by professor of anatomy from Loewen and the first work related to the Achilles tendon rupture was published by Ambrose Pare in 1633 (1,2). Achilles tendon is part of a three-headed muscle of the lower leg that starts with condyle thigh and head of the fibula and ends with tendon that attaches to the heel bone. The muscle bends the lower leg and foot, taking part in all the movements while walking, standing on tiptoe, squat, run, jump and landing.

The factors leading to increased incidence of rupture are the association between weight and strength of athletes, increased intensity of training, increased use of unnatural substances (eg. creatine), and the use of corticosteroids, growth hormones and testosterone. An increase Achilles tendon rupture is proportional to the increase in recreational sports activity in both young and elderly - even top athletes are not spared. The cause of the rupture is the combination of existence of relative hipovascularized zone and repeated microtraumas which cause the inflammatory reparative process, which due to poor vascularization is not able to oppose the stresses (4,5). Recently, there is a reported trend of an increased interest in sports and recreational activities among the people of mid-life ages (6,7). It is more common among men than women, the ratio being 9:1. The mechanism of Achilles tendon rupture is most often eccentric contraction in the ankle dorsiflexion and knee extension when m.soleus and m.gastroknemius are at their maximum tension (7,8).

Achilles tendon allows standing on toes, running, jumping, walking normally, climbing up and down the stairs. According to the action, m. triceps surae raises the heel and the entire body on your toes. It strongly raises the rear part of the foot, separating it from the ground and throws forward (1,6). When ruptured (torn) tendon clinical picture is typical. On the site of the rupture, two to three fingers wide above the heel, it can be seen clearly and touched the recess length of 2-3 cm, because the tendon is not toned, an broken ends are stretched. The patient feels a strong pain as a „shot with a rock” in the heel area, and sometimes hears the sound phenomenon called „the bang/the burst”. Clinical signs are palpable, painful „hollow” in the Achilles tendon and a partial or complete loss of plantar flexion. Positive Thompson („squeeze”) test, or lack of plantar flexion of the foot to manual compression in the quadriceps is a sure sign of the rupture (2,3,9).

Non-operative treatment is indicated in the elderly and in patients who have contraindications from anesthesiological aspect. In that case upper-knee circulatory cast with foot is placed in equines of about 20 degrees and the knee in flexion of 15-20 degrees for a period of 3 weeks, followed by another 3 weeks tibia plaster immobilization gravity equinus foot, and the last 3 weeks of immobilization with the foot in a neutral position and the ability to support (3 + 3 + 3). Partial joint stiffness (contracture) follows this treatment and the healing tendon requires a long period of physical therapy for satisfactory movement in the ankle joint. The scar at the site of ends growing together over the tendon is stiff and rigid, not more resilient as the rest of the tendon and should avoid efforts with that foot, because there is a re-rupture tendon on earlier place (8,9,10).

Tendon rupture is associated with muscle contusion, and hematoma developing which infiltrates the muscle tissue and impairs contractility. Hematoma and swelling puts pressure on the posterior tibial artery and other neurovascular elements. Any late recognition and delayed surgery can cause complications. If we do not recognize tendon rupture or postpone surgery and treat the injured with conservative methods, a larger scar develops between the ends of broken parts, twice weaker than the rest of the healthy part of the tendon. The action of the lower leg muscles is impaired which is very important when walking, climbing stairs and up the slope and standing on tiptoe. The tendon significantly weakens and develops disability (1,2,11).

The Achilles tendon rupture is most common 2-6 cm from its grips on the calcaneus bone, which is the zone of tendon hipovascularization, thus in larger defect the healing time is largely extended. Rehabilitation after surgery is very gradual and dosed and controlled strictly by physiatrist and surgeon. The result of such treatment is successful return to sport and other activities. Operative treatment has advantages for anatomic restitution of tendons and the preservation of its length, reducing scar tissue surgically (except in patients who for other reasons are unable to operate) given that an open access to tissues enables reconstruction of the tendon.

The aim of this paper is to demonstrate the principles and benefits of emergency surgical treatment of fresh Achilles tendon rupture in comparison to elective surgery.

**MATERIALS AND METHODS**

The study included a total of 58 patients treated at the Clinic of Orthopedics and Traumatology of the University Clinical Centre Sarajevo in the period from 1 January 2013 to 31 December 2014. Patients were divided into two groups: group I comprising 17 patients (45.71%) operated immediately (emergency surgery treatment) and group II consisting of 31 patients (54.29%) treated with elective surgery treatment. Before the start of treatment both groups of patients were subjected to a thorough clinical examination, X-ray of the lower leg with the ankle, and the ultrasound of Achilles tendon with linear probe of 7 MHz - 10 MHz. Operative treatments were carried out by the open method and percutaneous sutures. The patient is placed in ventral decubitus, with the foot in plantar flexion of about 15 degrees, which is important in order to bring the cut ends of the tendon into direct contact. Absorbable suture is used. When the thread ends are tightened, the ends of the tendon chords come into direct contact. Once the ends of the Achilles tendon were connected, defect on the site of rupture was not palpable and Thompsons’ sign had to be negative in order to achieve a the foot stability in pronation and supination, and active performance of movements.

While the patient was on the operating table, upper-limb plaster was placed with foot in equines of about 15 degrees and the knee in flexion. After 2-3 weeks the popliteal plaster was set, where certain surgeons retain the position of the foot in equines position for 2 more weeks, then plaster for travel lasting more than 2 weeks. All patients from the time of admission to the Clinic received thromboprophylaxis. Following the plaster removal, physical therapy was carried out.
RESULTS

The average age of patients was 38.8 ± 2.79 years (23-57 years old), whereas the average age in the group of patients treated with emergency surgery was 37.1 ± 3.98 years, and 40.2 ± 2.39 in the group treated with elective surgery with the statistically significant difference (t = 3.59; p = 0.0010, p <0.05) as shown in Figure 1.

The work results showed that there were no cases of reruptures and no healing in the group of operated patients. In the group treated with elective surgery, 1 rupture and 1 no healing of rupture was recorded, thus in both cases we performed surgery. In emergency operated patients no infection was detected, but 1 pulmonary thromboembolism was registered (2.85%). Thus it can be concluded that most of the patients did not have complications, which was statistically significant ($\chi^2$ test, p <0.1) as compared to the total number of study patients (Figure 2).

Emergency surgery of the Achilles tendon rupture was made within 12 hours of the injury, and elective surgeries was done on the fourth day after injury on average. Achilles tendon rupture of patients occurred in 33% of cases during basketball play, in 17% during football plays, in 13% it occurred during slips, in 9% while jogging, tennis 3%, and during other activities 25%.

It is observed that in the examined patients the rupture occurred on the right side in 28 cases (60.86%), while the left side of the rupture occurred in 18 (39.14%) of cases (Figure 3).

There were no signs of deep infection, whereas a superficial wound infection occurred in one case, which was repaired by regular wound bandaging and guided antibiotic treatment based on swab wound finding (highly sensitive to Staphylococcus aureus).

Immobilization of the injured limb lasted 47.26 ± 1.69 days on average; 42.68 ± 1.01 days in the group of urgently operated patients, and 46-54 days in the group of patients with delayed operation, with statistically significant difference (p = 9.493; p = 0.0001, p <0.05) as shown in Figure 4.

DISCUSSION

The tendon is a solid elastic structure made of fibrous connective tissue that connects muscle to bone. Under the control of muscle it directs movements, carries and resists the force of muscle contraction, and protects the muscle against external forces. When the load forces are greater than the threshold of tendon endurance, the tendon rupture occurs. The strong force that overloads the tendon can cause rupture. Permanent microtrauma, which are the result of incorrect or excessive load during sports activities, create morphological changes in connective and supportive tissue. In that way, morphologically altered tendon has an excessive burden which leads to its rupture. Similar methods of injury are reported in our study patients (1,2,3).

Injuries may result from more predisposing factors such as: anatomical variations and biomechanical abnormalities, difference in leg length, disorder shaft of the lower extremities in the hip, knee angular deformities (O or X legs), excessive rotation of the lower leg to the outside, and lowered the hollowed foot lead to changes and the tension in the string (3,4,5). Inflammation, and subsequent rupture of the Achilles tendon occurs after a sudden increase in activity of play, including change in playing pads from hard surfaces (concrete) to a softer (land), as well as due to prolonged repetitive microtrauma to the tendon due to inadequate equipment or no efficient training (6,7).

Ruptures are more common in older recreational athletes over the age of forty and occur in sudden acceleration where the incidence reaches 5.5% (12). The incidence of injury is about 0.2% in the general population. In the US the incidence is 18 per 100 000 inhabitants. Ruptures are more common in the male population, which is shown in our research, as well as in research work of other authors. This injury is more common in men than in women who practice recreational sports (1,7). The average age of patients is between 38 and 40 years, corresponding to the results of other authors and research works on this topic (12,14).
Main tendon blood supply is carried out through its mesotendon, with the richest supply through the front mesentery. As it turned out, the increase in the patient age that mesenteric supply decreases. With aging there is a loss of viscosity and elasticity as a result of changes in the collagen. This loss of elasticity and increased stiffness of the tissue predispose the injury. Repeated microtrauma in this area prevent reparative processes and degenerative exhaustion like this may be responsible for many of Achilles tendon ruptures (4,6,7).

In our study, all ruptures were located in the area of 2-6 cm proximal to the attachment of the calcaneus bone, relatively avascular zone. The tendon is the thinnest in that place and blood supply scarcest. Angiographic studies of Lagergena and Lindholm carried out in this „sensitive zone” between the 2 and 6 cm above the Achilles tendon insertions to calcaneus bone, showed a link between the hypovascular zone and tendon rupture (4). During the injury, the injured often continues walking and can no longer run. There is a possibility that the injury to the tendon is mistakenly replaced with the compromising ankle and muscle injury. Such injury requires a thorough clinical examination, X-ray, and lower limb Echo. All patients were examined by ultrasound which was important for the diagnosis confirmation and measurement of the defect length (1,2,3).

The skin in the front part of the lower limb is the only covering the bone which makes it exposed to direct impact of trauma, especially the front-inner part of lower-limb. Vascular internal network of the skin is poor, it quickly becomes ischemic and bulls/lumps are quickly formed. According to literature data, 12% of bulls occurs three hours after injury, and 43% after 24 hours which is consistent with our research results (12,14).

Out of the patients studied in the group of urgently operated, complications occurred in only 2.85% of patients, and they related to thromboembolism resulting from the plaster cast immobilization, not from the operation, as described in the literature (12,13,14).

Wound dehiscence, or divergence of its edge was reported in the group of patients with elective operation treatment. This complication depends on the type of thread used for stitching, local findings of the skin. Furthermore, the persistent presence of subcutaneous hematoma affects the postoperative wound and scar results. Material used in sewing after implantation act as a foreign body which causes the local tissue reaction (10,14). Operative treatment by percutaneous suture is rarely used at our Clinic. In five patients from our study excellent results were reported. According to Wallace RG et al. the percutaneous treatment of Achilles tendon is more successful than open surgery. This method turns a possible treatment in a small operating room, under local infiltrative anesthesia. Complications are rare and less extensive compared to other methods. The duration of cast immobilization and lack of sports activities are shorter than in those treated with other surgical and nonsurgical methods. That is a simple surgical technique performed under local anesthesia in a small operating room, outpatient surgery or with one-day hospital stay (0.4 days). It involves wearing a short cast immobilization (7.5 weeks on average), early mobilization and physical therapy, a shorter period of injury to full healing, and start of normal sports activities and the establishment of normal functions (mean 4.52 months), no postoperative scars, more improved aesthetic appearance, and minimal complications.

Bartelli R, Gaiani L, Palmonari M have presented a successful treatment with percutaneous sutures even with „outdated” ruptures of Achilles tendon.

CONCLUSION
This study does not show statistically significant difference between these two types of treatments, but highlights the following conclusions: emergency surgery of Achilles tendon rupture is a standard procedure at the Department of Orthopedics and Traumatology, UCCS; emergency surgery procedure yields a lower risk of infection, reduces the time of cast immobilization and the time of hospitalization, rehabilitation is faster, and thus the return to sports and other daily activities.

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REFERENCES

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ABSTRACT

Objectives: the upgrade from TEMPO+ and OPUS I to RONDO single-unit processor is easily acceptable and beneficial in children implanted before five years of age. Materials and methods: all our participants were prelingually hearing impaired children. They were implanted before 5 years of age and used MED-EL cochlear implant. We divided patients into two groups, 10 with TEMPO+ and 11 with OPUS I processor. We analyzed the results of speech recognition tests in quiet and in noise before upgrade, on the same day following the upgrade and 6 weeks later. Results: average age at the implantation was 2.7 for all participants. There were no significant differences in mean score for open field audiometry between the groups. The mean score for polysyllables in quiet at 60 dB was 71.9% in TEMPO+ and 58.6% in OPUS group (p=0.148) and increased in both groups up to 74.1% for TEMPO+ and 61.9% for OPUS I group on the same day following the upgrade. Six weeks later the score for polysyllables in quiet was 80.2% in group I and 65.9% in group II. There was no significance in the dynamics of the improvement between the groups (Mann-Whitney U test p=0.943). Speech recognition in noise was significantly better in TEMPO+ group (68.7%) on the day following the upgrade in comparison to previous OPUS I users (46.7%) (p=0.44). Improvement in speech recognition in noise was significantly better for both groups (TEMPO+ from 63% to 84% and OPUS I from 33% to 67%) six weeks later (p=0.008 and p=0.016). Conclusion: speech understanding in quiet and noise significantly improved with RONDO in children with Tempo+ and Opus I processor. Improvement with RONDO can be achieved immediately after upgrade with additional benefit after 6 weeks of adaptation. Significant benefits were demonstrated with RONDO processor when tested in background noise particularly for previous Tempo+ users.

Key words: cochlear implants, speech understanding, children, processor upgrade

SAŽETAK

Ciljevi: zamjena govornog procesora TEMPO+ i OPUS sa RONDO-single unit procesorom se lako prihvata i korisna je kod djece implantirane prije pete godine starosti. Materijali i metode: svi naši pacijenti su bili djeca sa prelingvalnim oštećenjem sluha. Implantirana su prije pete godine starosti, a ugrađen je implant kompanije ME-DEL. Pacijente smo podijelili u dvije grupe: 10 je bilo sa TEMPO+ a 11 sa OPUS I procesorom. Analizirali smo rezultate govorne razumljivosti u tišini i buci prije zamjene, na dan zamjene i 6 mjeseci poslije zamjene procesora. Rezultati: prosječna dob u trenutku implantacije je bila 2,7 godina za sve pacijente. Nismo uočili značajnije razlike u prosječnim vrijednostima govorne razumljivosti u otvorenom polju među grupama. Prosječna vrijednost razumljivosti za višešložne riječi na 60dB je iznosila 71% za grupu sa TEMPO+ a 58,6% za OPUS I grupu (p=0,148). Procenat govorne razumljivosti na dan zamjene se povećao na 74,1% kod prve grupe, a 61,9% kod druge grupe. Nakon 6 nedjelja rezultat kod prve grupe je bio 80,2%, a kod druge grupe 65,9%. Nije bilo razlike u dinamici poboljšanja među grupama (Mann-Whitney U test p=0.943). Rezultat govorne razumljivosti na dan zamjene u buci je bio statistički sigurno bolji u grupi TEMPO+ (68,7%) u poređenju sa grupom koja je upotrebljavala OPUS I (46,7%) (p=0,44). Poboljšanje govorne razumljivosti u buci kod obe grupe je bilo sigurno bolje nakon 6 nedjelja adaptacije (TEMPO+ sa 63% na 84% a OPUS I sa 33% na 67%) (p=0,008 i p=0,016). Zaključak: govorna razumljivost u tišini kao i u buci se značajno popravila nakon zamjene procesora TEMPO+ i OPUS I sa RONDO-single unit procesorom. Poboljšanje rezultata sa RONDO procesorom se uočava neposredno nakon zamjene sa dodatnim učinkom nakon šest nekoliko nedelja postupnom adaptacijom. RONDO processor je pokazao značajne prednosti pri testiranju u pozadinskoj buci naročito kod osoba koje su prethodno koristile TEMPO+ processor.

Ključne riječi: kohlearni implant, govorna razumljivost, djeca, napredni procesor

INTRODUCTION

Speech recognition abilities of cochlear implant patients have improved in recent years using new implant speech processors (1,2). According to other studies benefits for speech comprehension after speech processor upgrade are significant in background noise (3).
OPUS I to RONDO single-unit processor.

MATERIALS AND METHODS

Our study included 22 prelingually hearing impaired children implanted before 5 years of age. All of them used MED-EL cochlear implant with TEMPO+ or OPUS I processor and upgraded to RONDO single-unit processor. We analyzed results of open field audiometry before (with TEMPO+ or OPUS I processor) and after upgrade (with RONDO processor). We compared speech perception abilities using open set with polysyllables in quiet and in noise before the upgrade, on the day of the upgrade and 6 weeks after later.

RESULTS

Average age at the time of implantation was 2.7 years for all participants. There was no significant difference between the groups (TEMPO+ 2.9 and OPUS I 2.6 years) (p=0.608). All participants used MED-EL cochlear implants, 10 of them had TEMPO+ and 12 had OPUS I processor. The average length of experience was 6.6 years for all children without significant difference between TEMPO+ (8.40 years) and OPUS I (5.0 years) users (p<0.001). Open field audiometry was 30 dB for all patients without significant difference as compared to TEMPO+ (29.50 dB) and Opus I (30.45 dB) users (p=0.722). Open field audiometry with RONDO processor immediately after the upgrade was 29.05 dB and 28.57 dB six weeks later without significant difference as compared to results before the upgrade (p=0.377 and p=0.266). Speech understanding in quiet has increased for all participants from 65% to 68% immediately after the upgrade and 72.7% six weeks later, without significant difference (p=0.318 and p=0.115). Speech understanding abilities in quiet increased from 71.9% (TEMPO+) and 68% (Opus I) to 72.7% (RONDO) without significant difference between the groups (p=0.943).

Speech understanding in noise increased significantly from 49.6% to 57.2% immediately after the upgrade for all participants (p=0.333) (Table 1).

Speech understanding in noise significantly increased six weeks after the upgrade with RONDO processor vs. result immediately after switch on (p=0.001) (Table 3).

Speech understanding in noise significantly increased six weeks after the upgrade with RONDO processor vs. result immediately after switch on (p=0.001) (Table 3).

Table 1 Speech understanding in noise before and after upgrade.

<table>
<thead>
<tr>
<th>All participants</th>
<th>Speech understanding in noise before upgrade</th>
<th>Speech understanding in noise (RONDO)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Aarithmetic mean</td>
<td>49.62</td>
<td>57.19</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>23.74</td>
<td>26.87</td>
</tr>
<tr>
<td>Standard error of arithmetic mean</td>
<td>5.62</td>
<td>5.86</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>Lower limit</td>
<td>38.61</td>
</tr>
<tr>
<td></td>
<td>Upper limit</td>
<td>60.63</td>
</tr>
<tr>
<td>Minimum</td>
<td>10.0</td>
<td>15.0</td>
</tr>
<tr>
<td>The first quartile: Q1</td>
<td>30.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Median: Q2</td>
<td>51.0</td>
<td>60.0</td>
</tr>
<tr>
<td>The third quartile: Q3</td>
<td>67.0</td>
<td>82.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>97.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mann-Whitney U test for independent samples p<0.001

Table 2 Speech understanding in noise immediately after upgrade.

<table>
<thead>
<tr>
<th>Group</th>
<th>Speech understanding in noise (RONDO - immediately after upgrade)</th>
<th>Speech understanding in noise (RONDO - 6 weeks after upgrade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Aarithmetic mean</td>
<td>68.70</td>
<td>46.73</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>27.93</td>
<td>22.11</td>
</tr>
<tr>
<td>Standard error of arithmetic mean</td>
<td>8.83</td>
<td>6.67</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>Lower limit</td>
<td>51.39</td>
</tr>
<tr>
<td></td>
<td>Upper limit</td>
<td>86.01</td>
</tr>
<tr>
<td>Minimum</td>
<td>21.0</td>
<td>15.0</td>
</tr>
<tr>
<td>The first quartile: Q1</td>
<td>48.0</td>
<td>30.0</td>
</tr>
<tr>
<td>Median: Q2</td>
<td>82.0</td>
<td>50.0</td>
</tr>
<tr>
<td>The third quartile: Q3</td>
<td>85.0</td>
<td>70.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>100.0</td>
<td>85.0</td>
</tr>
</tbody>
</table>

Mann-Whitney U test for independent samples p=0.044

Table 3 Speech understanding in noise with Rondo immediately and six weeks after switch-on.

<table>
<thead>
<tr>
<th>All participants</th>
<th>Speech understanding in noise (RONDO - immediately after upgrade)</th>
<th>Speech understanding in noise (RONDO - 6 weeks after upgrade)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>Aarithmetic mean</td>
<td>57.19</td>
<td>65.90</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>26.87</td>
<td>22.94</td>
</tr>
<tr>
<td>Standard error of arithmetic mean</td>
<td>5.86</td>
<td>5.01</td>
</tr>
<tr>
<td>95% confidence interval</td>
<td>Lower limit</td>
<td>45.70</td>
</tr>
<tr>
<td></td>
<td>Upper limit</td>
<td>68.68</td>
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<tr>
<td>Minimum</td>
<td>15.0</td>
<td>20.0</td>
</tr>
<tr>
<td>The first quartile: Q1</td>
<td>30.0</td>
<td>45.0</td>
</tr>
<tr>
<td>Median: Q2</td>
<td>60.0</td>
<td>70.0</td>
</tr>
<tr>
<td>The third quartile: Q3</td>
<td>82.0</td>
<td>80.0</td>
</tr>
<tr>
<td>Maximum</td>
<td>100.0</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Mann-Whitney U test for independent samples p<0.001

DISCUSSION

Speech understanding in quiet and noise significantly improved with RONDO in children with Tempo+ and Opus I processor. Improvement with RONDO can be achieved immediately after upgrade with additional benefit 6 weeks following the adaptation. According to other investigators, speech perception improvement in noise could not be immediate but is significant after a few weeks with further improvement over the time. Significant benefits were demonstrated with RONDO processor when tested in background noise particularly for previous Tempo+ users. Updated cochlear implant technology with new speech processors could have a substantial impact on speech perception abilities in cochlear implanted children (6).
CONCLUSION

RONDO speech processor upgrade supports the expectations of increased benefit in speech understanding abilities in cochlear implanted children. Improvement is significant in condition of background noise with additional benefit after certain adaptation time.

Conflict of interest: none declared.

REFERENCES


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Serum nitric oxide concentration in rheumatoid arthritis patients: the association with disease activity

Serumska koncentracija nitričnog oksida kod pacijenata s reumatoidnim artritisom: povezanost s aktivnošću bolesti

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ABSTRACT

The aim of this cross sectional pilot study was to determine and compare serum nitric oxide (NO) concentration in 63 patients with rheumatoid arthritis (RA) and in 31 apparently healthy individuals. Based on the Disease Activity Score (DAS28 score), RA patients were divided into three subgroups: low stage of disease activity (DAS28 ≤3.2; n=19); moderate stage of disease activity (3.2<DAS28≤5.1; n=19) and high stage of disease activity (DAS28>5.1; n=25). Serum NO concentration was determined by classic colorimetric Griess reaction. Elementary zinc was used for the conversion of nitrate (NO32-) into nitrite (NO22-). Median serum NO concentration was not statistically different (p=0.36) between the control group [9.23 µmol/L (8.34 µmol/L-10.39 µmol/L)] and the group of RA patients [8.70 µmol/L (8.16 µmol/L-10.30 µmol/L)]. There was no significant difference (p=0.27) between NO concentration in serum of RA patients with high disease activity [9.59 µmol/L (8.43 µmol/L-11.02 µmol/L)], moderate disease activity [8.70 µmol/L (7.81 µmol/L-9.59 µmol/L)], low disease activity [8.52 µmol/L (8.16 µmol/L-10.30 µmol/L)] and the control group. Results of this study indicate that serum NO concentration measured by classic colorimetric Griess reaction is not associated with RA disease activity. Larger prospective studies are needed in order to access potential use of serum NO concentration in the evaluation of RA disease activity.

Key words: nitric oxide, rheumatoid arthritis, disease activity

INTRODUCTION

Nitric oxide (NO) is an unique gaseous signalling molecule with wide variety of functions in numerous physiological and pathological processes (1). Several studies confirm important roles of nitric oxide (NO) in regulation of blood vessels tone, platelet function, neurotransmission, immune regulation, mitochondrial functions and apoptosis (2,3).

This free-radical with short life-time is generated endogenously from L-arginine by the enzyme NO synthase (NOS). There are three distinct isoforms of NOS: endothelial NOS (eNOS), neuronal NOS (nNOS) and inducible NOS (iNOS) (4).
Serum nitric oxide concentration in rheumatoid arthritis patients: the association with disease activity

Endothelial and neuronal NOS are dependent upon intracellular calcium level and generally produce low levels of NO involved in normal physiologic processes. Inducible NOS is calcium-independent isoform of NOS and is present mainly in monocytes/macrophages, neutrophil granulocytes and other immunology cells. Upon stimulation of these cells by certain pro-inflammatory cytokines in inflammatory reactions or by endotoxin in bacterial infection high amounts of NO are produced. These high amounts of NO produced by iNOS perform important functions for host defense, but excess of NO production is also associated with various malignancies and inflammatory conditions including juvenile diabetes, multiple sclerosis, arthritis and ulcerative colitis (5,6).

Due to the short half-life of NO, usually its end products nitrate (NO32-) or nitrite (NO22-) are measured as an index of NO production.

Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease, mainly manifested by damage, deformity and dysfunction of multiple joints. Besides the joints, the disease also affects multiple other organs and systems. The extra-articular manifestations of RA include damage of exocrine lacrimal and salivary glands, vasculitis, anemia and peripheral neuropathy. RA affects 0.5-1% of the adult population worldwide and is more common in women than men at a ratio of approximately 3:1. It is a multifactorial disease in which a combination of genetic and environmental factors contributes to the disease progression (7,8).

Primary pathological process in RA is happening in the area of synovial membrane of a joint which becomes thicker, edematous and infiltrated with mononuclear cells (9).

Considering the heterogeneous presentation of the disease among different individuals, the ability to predict the progression of disease in patients with RA is of great importance in everyday clinical practice.

Experiments in animal models of arthritis and studies in patients with RA have reported important role of NO in inflammatory joint diseases. NO mediates many different cell functions at the site of synovial inflammation, including cytokine production, signal transduction, mitochondrial functions and apoptosis (10).

Thus, the objective of this study was to explore whether serum NO concentration measured by classic colorimetric Griess reaction is associated with RA and disease activity in laboratory diagnostics.

**MATERIALS AND METHODS**

This cross-sectional study included all eligible RA patients (n=63), hospitalized at the Cardiology Clinic of the University Clinical Center Sarajevo (UCCS) in the period between 1 January 2011 and 30 June 2011, who met the 1987 American College of Rheumatology (ACR) revised criteria for the RA classification. Based on the stage of disease activity evaluated by Disease Activity Score (DAS28 score), RA patients were divided into three subgroups: low stage of disease activity (DAS28<3.2; n=19), moderate stage of disease activity (3.2≤DAS28≤5.1; n=19) and high stage of disease activity (DAS28>5.1; n=25). The control group consisted of 31 healthy individuals. Upon careful explanation of the study procedure, all subjects gave their informed consent to answering the questionnaire and provided residual blood for analysis. The study was approved by the Ethical Committee of the UCCS.

The exclusion criteria for the studied group of RA patients included other rheumatic diseases, malignancy, active local or systemic inflammation caused by bacterial and viral infections, and pregnancy. During the study the use of tobacco products was prohibited.

Subjects of the control group had no history of RA or other rheumatic, autoimmune and inflammatory diseases, hyperlipidemia, hypertension or coronary heart diseases. None of the control subjects received any medication and they were not current smokers or alcohol consumers. Detailed history was taken from patients using specially prepared questionnaire that included questions relevant to RA such as disease duration, morning stiffness and drug taking history. All patients underwent thorough clinical examination with special attention to articular examination. The disease activity in RA patients was determined by experienced physician with the use of DAS28 score.

DAS28 is a mathematical formula with four variables:

\[
DAS28 = 0.56x\sqrt{(TEN28)} + 0.28x\sqrt{(SW28)} + 0.70x\ln(ESR) + 0.014x(GH).
\]

(TEN28: 28 joint count for tenderness, SW28: 28 joint count for swelling, Ln(ESR): the natural logarithm of Westergren’s erythrocyte sedimentation rate (ESR); GH: general health or patient’s global assessment of disease activity on the visual analog scale (VAS) of 100 mm).

After overnight fast, venous blood samples were collected early in the morning and allowed to coagulate. After coagulation, the serum samples were centrifuged for 5 minutes at 2000 g and deproteinized by adding 0.75 ml of distilled water and 0.05 ml of 30% zinc sulfate solution to 0.25 ml of each sample. Several minutes later, the samples were centrifuged for 10 minutes at 2000 g and separated supernatant was stored at -200C.

**NO measurement**

The NO level in obtained supernatant was determined by measuring nitrite concentrations, a stable metabolic endproduct of NO. Conversion of nitrate (NO32-) into nitrite (NO22-) was done with elementary zinc. Nitrite concentration in serum was determined by classic colorimetric Griess reaction (11).

Briefly, equal volumes of samples and Griess reagent were mixed at room temperature. After 5 minutes, the absorbance was measured at 570 nm using Perkin Elmer 550 S spectrophotometer. The concentration of nitrite was determined by a standard curve prepared with sodium nitrite (1-200). The results were expressed as µmol/L.

Determination of NO concentration in serum of RA patients and control individuals was done at the Department of Human Physiology of the Sarajevo University Medical School.

**Statistical analysis**

The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine normality. Due to the non-normal distribution, non-parametric tests, such as Mann-Whitney U and Kruskal-Wallis, were chosen for reporting significance. Correlation coefficient between variables was assessed by the Spearman’s test.

Statistical significance was set at p<0.05. All statistical analyses...
were conducted with Statistical Package for the Social Sciences (SPSS) version 13.0 for Windows (Chicago, IL, USA).

RESULTS

The mean age of healthy subjects in the control group was 49.7 ± 7.9 years and 87.1% were females, whereas mean age of RA patients in RA group was 54.3 ± 12.2 years and 93.7% were females (Table 1).

Median serum NO concentration was not statistically different (p=0.36) between the control group of healthy individuals, 9.23 µmol/L (8.34 µmol/L - 10.39 µmol/L) and the group of RA patients, 8.70 µmol/L (8.16 µmol/L - 10.30 µmol/L) (Figure 1).

There was no significant difference (p=0.27) between NO concentration in serum of RA patients with high disease activity [9.59 µmol/L (8.43 µmol/L - 11.02 µmol/L)], moderate disease activity [8.70 µmol/L (7.81 µmol/L - 9.59 µmol/L)], low disease activity [8.52 µmol/L (8.16 µmol/L - 10.30 µmol/L)] and control group [9.23 µmol/L (8.34 µmol/L - 10.39 µmol/L)] (Figure 2).

Also, we did not find significant correlation between serum NO concentration and DAS28 score in patients with RA (rho=0.19; p=0.98).

DISCUSSION

The results of our study showed that patients with RA had lower, but not statistically significant, serum NO concentration compared to the healthy subjects of the control group. The results also showed that determined distinction in serum NO concentration between RA patients with different stages of disease activity was not significant. Moreover, in overall sample of RA patients we did not find a significant association between serum NO concentration and the stage of disease activity evaluated by DAS28 score.

In contrast to our findings, other studies showed increased production of NO in the serum of patients with rheumatoid arthritis (12), osteoarthritis (13) and experimentally induced arthritis in animals (14).

Ersoy et al. (15) reported higher concentrations of nitrate and nitrite in the serum of patients with RA compared to the healthy subjects. These authors also observed a statistically significant positive correlation between serum concentrations of nitrate and nitrite and markers of systemic activity of disease in RA patients. However, in their study the amount of nitrate which patients entered into the body through food during the study was not taken into account. Choi et al. (16) have put examinees on twelve hour fasting period before performing the investigation and have also reported increased NO production in RA patients but without any correlation between serum NO concentration and laboratory parameters of disease activity. Conversely, Onur et al. (17) conducted a study in RA patients which demonstrated a statistically significant positive correlation between serum concentration of nitrite, stable end product of NO and the stage of disease activity. These authors also reported statistically significant positive correlation between serum concentration of nitrite and radiographic changes in the joints of patients with RA. Similar to the above findings, Ueki et al. (13) demonstrated a significant relationship between serum NO levels and disease activity in patients with RA.

The findings of our study could be explained in different ways. One of the possible explanations could relate to increased production of asymmetric dimethylarginine (ADMA) in these patients. ADMA is endogenous inhibitor of all three isoforms of NOS discovered in 1992. Since its discovery, many of ADMA properties have been investigated but inhibition of NO synthesis remains most prominent feature of this compound (18). ADMA in healthy individuals does not accumulate in the blood because it is rapidly eliminated through the urinary system. However, if renal function is altered, as it is often the case in RA patients (19,20), the natural elimination of ADMA is reduced or stopped, resulting in inhibition of NOS and decreased NO synthesis. Nevertheless, we can only speculate that underlying mechanisms for similar serum NO concentration in our sample of RA patients compared to healthy subjects is a consequence of increased ADMA production given that its serum concentration was not measured in the present study.

The use of various therapeutics such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and disease-modifying
anti-rheumatic drugs (DMARDs) may also reduce the activity of NOS and affect NO production (21). In the present study, out of the total of RA patients, 58.7% were taking methotrexate (MTX) as the most commonly used DMARD for the treatment of RA. Methotrexate blocks the synthesis of tetrahydrobiopterin, one of the essential cofactors of NO syntheses, which could be another reason for the reduced serum NO levels (14).

Moreover, observed similar NO levels in RA patients and the control group could also be a result of endothelial dysfunction, a condition primarily characterized by decreased production and bioavailability of NO. In patients with RA according to the research of Vaundo et al. (22), systemic inflammation is a reason of endothelial hyper-reactivity, caused by increased production of pro-inflammatory cytokines, mostly TNF-α with consequent increase of C-reactive protein (CRP) synthesis. Earlier study by Verma et al. (23) reported that increased levels of CRP induce decreased expression of eNOS with consequent decrease of NO production. It has also been demonstrated that some infectious microorganisms including cytomegalovirus, which is considered to be one of the etiological causes for RA, can induce endothelial dysfunction and lead to decrease of NO production in RA patients (24).

CONCLUSION

Results of the present pilot study indicate that serum NO concentration in patients with rheumatoid arthritis measured using Griess reaction is not associated with RA disease activity. Longitudinal studies with larger sample of RA patients are needed in order to fully clarify the role of NO in the pathogenesis of RA.

Conflict of interest: none declared.

REFERENCES

Defining the vascular skin territories of the septocutaneous blood vessels of the forearm with a special overview on their use in the fasciocutaneous flaps surgery

Definisanje vaskularnih kožnih teritorija septokutanih krvnih sudova podlaktice sa posebnim osvrtom na njihovu primjenu u hirurgiji fasciokutanih režnjeva

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*Corresponding author

ABSTRACT

The research of the septocutaneous forearm blood vessels created by radial, ulnar and the posterior interosseous arteries, as well as the size of certain skin territories they vascularise, has been performed on fifty cadaver forearms. Thirty forearms were injected with shower gelatine and precise dissection was performed. Remaining part of the research was conducted on twenty selected forearms, four of which were tested with the use of corrosive method. Average skin territory vascularised by the radial artery is 163.57 cm$^2$, while the average skin territory vascularised by the ulnar artery is 190.36 cm$^2$. The posterior interosseous artery vascularises the smallest skin territory in the forearm area, the average being 107.48 cm$^2$. These results clearly show that vascularised skin territories are directly proportional to the size and calibre of the main blood vessels supplying them, as well as with number of septocutaneous perforators they create. This means that the largest number of perforators per artery is created by radial artery (8.1% on average), followed by ulnar artery (5.6% on average) while the posterior interosseous artery creates the smallest amount of perforators (4.9% on average). The purpose of this research was to make contribution to the accuracy of the fasciocutaneous forearm flap surgery. Likewise, our aim was to clarify the skin territories which are vascularised by specific septocutaneous perforators making the surgical procedure safer.

Key words: vascular skin territories, reconstruction, septocutaneous perforators

SAŽETAK

Istraživanje septokutanih krvnih sudova podlaktice, koji nastaju od magistralnih krvnih sudova (arterija radialis, ulnaris i interossea posterior), kao i veličine pojedinih kožnih teritorija koje su vaskularizovane od istih, obavljeno je na 50 kadaveričnih podlaktica. Na 30 podlaktica izvršena su ispitivanja iniciranjem tuš-želatina, te precizna disekcija na lešnom obducijskom materijalu. Preostalo istraživanje sprovedeno je na 20 izdvojenih podlaktica, od kojih je na četiri podlaktice sprovedena korozivna metoda. Prosječna površina kože, izražena u kvadratnim centimetrima, koju vaskularizuje arterija radialis je 163,57 cm$^2$, dok je prosječna vrijednost kožne površine koju vaskularizuje arterija ulnaris nešto veća i iznosi 190,36 cm$^2$. Arterija interossea posterior vaskularizuje najmanju kožnu površinu u predjelu podlaktice, koja u prosjeku iznosi 107,48 cm$^2$. Iz ovih rezultata jasno se vidi da su vaskularizovane kožne površine u direktnoj srazmjerni sa veličinom i kalibrom samih magistralnih krvnih sudova koji ih ishranjuju, kao i sa brojem septokutanih perforatora koji od njih nastaju. Tako najveći broj perforatora po arteriji (u prosjeku 8,1%) nastaje od arterije radialis, nešto manji broj od arterije ulnaris (u prosjeku 5,6%), a najmanje od arterije interossea posterior (u prosjeku 4,9%). Ovim ispitivanjem smo željeli doprinjeti preciznosti same hirurgije podlaktičnih fasciokutanih reženjeva, razjasniti kožne teriotrije koje pojedini septokutani perforatori vaskularizuju, te učiniti na taj način sam operativni zahvat sigurnijim.

Ključne riječi: vaskularne kožne teritorije, rekonstrukcija, septokutani perforatori
INTRODUCTION

When it comes to reconstruction of the forearm and hand defects, fasciocutaneous forearm flaps are of great importance, and based on the Cormack and Lamberty classification the most common are fasciocutaneous flaps type C. The best known are posterior interosseous flap, radial forearm flap (Chinese flap) and ulnar forearm flap. These are fasciocutaneous forearm flaps through which forearm main blood vessels flow, out of which septocutaneous blood vessels branch out and vascularise corresponding forearm skin and hypodermis territories (1-5). Number, size, topography and the places where the septocutaneous blood vessels of the forearm’s main arteries branch out are of extreme importance during clinical implementation of aforesaid flaps. This means that in the procedure itself, apart from the radial, ulnar and the posterior interosseous arteries, at least one septocutaneous perforator must be used. The exact places where the perforators are separated from the main blood vessels along with their topography (blood flow) make the precise dissection and elevation of the fasciocutaneous flaps easier. Skin territories which are vascularised by specific septocutaneous blood vessels, including their boundaries, are of particular significance since that is the manner in which safe territories of skin for particular flaps are defined. Extensive knowledge of the topography and the size of the skin territories based on the vascularisation of the forearm’s septocutaneous blood vessels reduce the possibility of making a mistake during the elevation of the fasciocutaneous flaps, thus making the surgical procedure safer. Reverse-Flow Posterior Interosseous Flap was for the first time described in 1986 by Laijin (6) in Chinese literature, in English literature by Penteada in 1986 (7) and by Zancolli in 1988 (8). Chinese flap, or fasciocutaneous forearm flap, was for the first time described in China in 1981 by Yang Guofan et al. (1, 9, 10).

MATERIALS AND METHODS

Research of septocutaneous perforator artery branches of the forearm was performed on fifty cadaver forearms. Thirty forearms were injected with shower gelatine and precise dissection was performed. Remaining part of the research was conducted on twenty selected forearms, of which four forearms were used for the corrosive method. We used the method of injecting shower gelatine into the artery system, and after colouring, a precise microsurgical dissecting was performed which included all measurements (number, place of occurrence, calibre, as well as the topography of septocutaneous perforators). Corrosive method was performed by injection of methyl methacrylate into the very posterior interosseous artery, after which the corrosion of the forearm tissue was performed in 40% solution of NaOH, resulting in plastic casts of posterior interosseous artery with its septocutaneous perforators.

Segregation of vascularized cutaneous perforators of the ulnar, radial and posterior interosseus arteries was preceded by an elongated cut, 10cm long, in the area of cubital fossa and the dissection of the brachial artery and its ending branches. Through the cut on the brachial artery we were able to place two catheters, one in the ulnar and one in the radial artery, after which we fastened them from the outside with a tightening loop. After rinsing the arteries with warm water, we selectively injected 20ml of 5% melted gelatine coloured in blue and red ink. The separated forearms were entered through the common interosseous artery with a thin catheter and the area of vascularization was separated with green dyed gelatine. The injection lasted until the area was coloured without the overlap of vascular cutaneous territories. After 10 minutes, which were necessary for the gelatine to solidify, the dissection started. We measured the obtained coloured skin territories with a planimeter.

RESULTS

The vascular skin territory of the septocutaneous forearm blood vessels.
Table 1 shows the results of the average value of skin territories vascularised by septocutaneous perforators of radial, ulnar and posterior interosseous arteries.

<table>
<thead>
<tr>
<th></th>
<th>Skin surface (cm²) of the radial artery</th>
<th>Skin surface (cm²) of the ulnar artery</th>
<th>Skin surface (cm²) of the posterior interosseous artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min.</td>
<td>110</td>
<td>125</td>
<td>63.1</td>
</tr>
<tr>
<td>Max.</td>
<td>212.5</td>
<td>261.2</td>
<td>175</td>
</tr>
<tr>
<td>Middle value</td>
<td>163.57</td>
<td>190.36</td>
<td>107.48</td>
</tr>
<tr>
<td>Standard deviation</td>
<td>45.62</td>
<td>56.71</td>
<td>39.60</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 2 shows the number of septocutaneous arteries: radial, ulnar and posterior interosseous artery by the thirds of the forearm.

<table>
<thead>
<tr>
<th>Number of perforators</th>
<th>Radial artery</th>
<th>Ulnar artery</th>
<th>Posterior interosseous artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal third</td>
<td>2</td>
<td>1.2</td>
<td>0.7</td>
</tr>
<tr>
<td>Medial third</td>
<td>3.7</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>Distal third</td>
<td>2.4</td>
<td>2.4</td>
<td>2.1</td>
</tr>
<tr>
<td>Total number</td>
<td>8.1</td>
<td>5.6</td>
<td>4.9</td>
</tr>
</tbody>
</table>

Figure 1 shows skin territory in different colours after the injection of shower gelatine in some of the main blood vessels. Radial artery was injected with red, ulnar artery with blue and posterior interosseous artery with green shower gelatine, based on which the skin territory vascularised by certain arteries could be measured.

Figure 2 shows the posterior side of the forearm where the field injected with green shower gelatine represents the skin territory vascularised by the posterior interosseous artery.
DISCUSSION

The results of the research show that the skin territory vascularised by septocutaneous perforators of radial artery is mainly in the radial part of the forearm and the border which separates it from the vascular skin territories of adjacent blood vessels is unclear.

Average skin territory vascularised by the radial artery is 163.57 cm², while the average skin territory vascularised by the ulnar artery is 190.36 cm². The posterior interosseous artery vascularises the smallest skin territory in the forearm area, the average being 107.48 cm². These results clearly show that vascularised skin territories are directly proportional to the size and calibre of the main blood vessels which supply them, as well as with number of septocutaneous perforators they create. This means that the largest number of perforators per artery is created by radial artery (8.1% in average), followed by ulnar artery (5.6% in average), whereas the posterior interosseous artery creates the smallest amount of perforators (4.9% in average).

Cormack states that the skin territory of radial artery includes the lateral half of the anterior side and the lateral edge of the forearm, but not the area above extensor pollicis brevis muscle and abductor pollicis longus muscle, which are vascularised by the posterior interosseous artery (1). The border between radial and ulnar territory varies and depends on the size of the cubital artery. The lateral border between the skin territories of radial and the posterior interosseous arteries correspond to the lateral edge of the extensor digitorum muscle (11,12,13). Ulnar artery vascularises the skin territory of the posterior part of the forearm. The furthest border of the ulnar skin territory is located in the level of the posterior part of the humerus, while the closest border is in the area of the anterior forearm’s medial line. Skin territory of the posterior interosseous artery lies mainly in the area of lateral edge of the extensor digitorum muscle and borders with the radial territory to the rear area of ulna, where it borders with the ulnar territory (1). According to Costa the skin territory of the posterior interosseous artery lies in the posterior part of the forearm, 4 cm beneath the intercondylar line, all the way to the wrist joint (11, 14, 15, 16).

CONCLUSION

On the basis of the aforementioned, we may conclude that the largest area of the forearm, placed at the anterior and posterior part is vascularised by ulnar artery; somewhat smaller skin territory placed at the posterior side of the forearm is vascularised by radial artery, and the smallest territory of the forearm is vascularised by the posterior interosseous artery which lies in the central part of the posterior part of the forearm. The number of perforators is not correlated with the size of skin territories. radial artery has the largest number of septocutaneous perforators, even though it vascularises the smaller skin territory than ulnar artery. This means that the size and calibre of the septocutaneous perforators themselves has an impact on the vascularised skin territories of the forearm. The borders between the skin territories are irregular, which implies an unclear border and the existence of numerous anastomosis between some of the septocutaneous blood vessels.

Conflict of interest: none declared.

REFERENCES


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Kinesiotherapy in early rehabilitation of patients after surgery of herniated cervical intervertebral disc

Kinesiterapija u ranoj rehabilitaciji pacijenata nakon operacije hernije cervikalnog intervertebralnog diskusa

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ABSTRACT

Background: surgery of herniated cervical intervertebral disc is not completed if not followed by rehabilitative kinesiotherapeutical program, which should complete the effect of surgical intervention and prevent relapses of herniation. Objective: to analyze effect of different kinesiotherapeutical programs in early postoperative rehabilitation of cervical intervertebral disc herniation. Materials and methods: a retrospective study included 120 patients rehabilitated after surgical treatment of herniated cervical intervertebral disc, done by anterior discectomy and fusion, during the period from May 2012 to May 2014. Depending on type of kinesiotherapeutical program, made based on severe pain occurring during certain type of exercises, patients were divided in 3 groups: the first group, 40.0% (N=48), was performing isotonic and isometric exercises, the second group, 25.8% (N=31), was performing only isotonic exercises, and the third group, 22.5% (N=27), was performing only isometric exercises. All groups were included in the occupational therapy program. In 11.7% (N=14) of patients kinesiotherapy was not indicated. Effects of kinesiotherapeutical programs were evaluated by Manual Muscle Test and Barthel Index. Results: women were represented with 71.7% (N=86), and men with 28.3% (N=34). The average age of patients was 51.7±10 years, ranging from 28-77. The median time period between the surgery and the beginning of rehabilitation was 20.1 day. The most common level of operated disc was C5/C6 (37.1% n=13). In total sample (18.5±2.9 vs. 17.5±4.2) as well as of Manual Muscle Test (4.27±0.59 vs. 3.93±0.75). The first group of patients had significant increase of Barthel Index (19.5±1.0 vs. 18.3±2.1), and improvement of Manual Muscle Test (4.27±0.59 vs. 3.93±0.75). Prva grupa pacijenata je imala signifikantno povećanje Barthel Indeksa (19.5±1.0 vs. 18.3±2.1), i poboljšanje Manuelnog mišićnog testa (4.27±0.59 vs. 3.93±0.75). Prva grupa pacijenata je imala signifikantno povećanje Barthel Indeksa (19.5±1.0 vs. 18.3±2.1). Kliničke riječi: postoperativna rehabilitacija, cervical disc surgery.

SAŽETAK

Uvod: operativni tretman hernije cervikalnog intervertebralnog diskusa je nepotpun ako nije popraćen rehabilitacijskim kineziterapeutskim programom koji će kompletirati efekte hiruške intervencije i prevenirati relaps hernijacije. Cilj: analizirati efekat različitih kineziterapeutskih programa u ranoj postoperativnoj rehabilitaciji hernije cervikalnog intervertebralnog diskusa. Materijali i metode: retrospektivna studija uključila je 120 pacijenata stacionarno rehabilitiranih nakon hiruškog tretmana hernijacije cervikalnog intervertebralnog diskusa, urađenog prednjom discektomijom i fuzijom, u periodu od maja 2012. do maja 2014. godine. Ovisno o tipu kineziterapeutskog programa, određenog pojavom jakog bala za vrijeme testnog izvođenja pojedinih vrsta vježbi, pacijenti su bili podijeljeni u tri grupe: prva grupa, 40.0% (N=48), izvodila je izotonične i izometrijske vježbe; druga grupa, 25.8% (N=31), izvodila je samo izotonične vježbe, a treća grupa, 22.5% (N=27), izvodila je samo izometrijske vježbe. Sve grupe su bile uključene u program okupacione terapije. U cijelom uzorku je došlo do signifikantnog poboljšanja Barthel Indeksa (18.5±2.9 vs. 17.5±4.2), kao i Manuelnog mišićnog testa (4.27±0.59 vs. 3.93±0.75). Prva grupa pacijenata je imala signifikantno povećanje Barthel Indeksa (19.5±1.0 vs. 18.3±2.1), i poboljšanje Manuelnog mišićnog testa (4.5±0.6 vs. 4.15±0.53). Druga grupa pacijenta takodje je pokazala signifikantno povećanje Barthel Indeksa (15.7±4.5 vs. 14.3±3.2), i poboljšanje Manuelnog mišićnog testa (4.0±0.55 vs. 3.6±0.62). Poboljšanje Barthel indeks u trećoj grupi nije bilo signifikantno (19.5±0.9 vs. 18.6±1.2). Kliničke riječi: postoperativna rehabilitacija, cervical disc surgery.
INTRODUCTION

Cervical spine surgery is a major undertaking, and early rehabilitation is an important part of helping patients to get the most possible benefit from their surgery.

Spine fusions which require the placement of plates and screws tend to last much longer than simple discectomies. Patients often report improvements in the way they feel immediately after they awake after surgery. However, strengthening the weakened muscles and soft tissue surrounding and supporting the neck requires a longer-term program of exercise and therapy. Although many patients see and feel immediate benefits, they need the benefits of a comprehensive rehabilitation program for several months to get the total benefit (1).

Essentially, rehabilitation program can help patients recover from spine surgery as quickly and completely as possible. Controlling pain is an important first step in allowing patients to regain their strength, as it is very difficult to complete a rehabilitation program if one is in a great deal of pain.

Kinesiotherapy is vital to getting better after cervical spine surgery. In addition to pain control, exercises aim to strengthen key muscles in charge of preserving proper postural relations and the elimination of pressure on the spinal nerve roots.

It is the key to eliminating fatigue, getting patients back to activity safely, and avoiding re-injury, e.g. reherniation or new disc herniation. Ultimately, exercise is critical both in helping the body heal from the original injury and in preventing (or minimizing) future episodes of cervical pain (2).

Depending on the severity of pain and the type of surgery exercises are programmed individually. Exercise therapy focuses on:
- muscles in the incision area;
- muscles that may have been weakened by nerve problems before the surgery;
- small muscles that work around each vertebra and help stabilize the spine.

Most people (even those without spine problems) do not use small muscles very often. However, if these muscles are trained properly, they can provide excellent stabilization that can protect the spine and newly operated area to prevent future problems.

Early postoperative rehabilitation after anterior cervical discectomy and fusion starts with posture education for daily activities, which means patient education for conducting protective ergonomic positions for cervical spine in activities of daily living, in order to improve stabilization and reduce pain. That is achieved by occupational therapy program. Also, the task of occupational therapy is to achieve patient’s adherence to long-term regular performance of exercises and protective ergonomics position in order to avoid or manage chronic pain and other symptoms connected to degenerative diseases of cervical spine.

Occupational therapy in early postoperative rehabilitation is followed by diaphragmatic breathing and relaxation exercises.

Isometric and isotonic exercises are introduced in postoperative rehabilitation program as soon as possible, in order to decrease swelling, pain and inflammation, prevent stiffness, encourage wound healing and increase activity tolerance.

Isometric exercises are applied on all cervical muscle groups with progressive resistance, performed first by physiotherapist and then by patient. Session time progressively increases from 5 to 15 minutes. Resistance is also progressive from mild to stronger. These exercises are applied on both upper and lower extremities.

Isotonic exercises in early postoperative rehabilitation program after anterior cervical discectomy and fusion are applied to shoulder region without overhead movements, and to other joints of upper extremities. These exercises prevent stiffness and increase tolerance to daily activities. Collar use is estimated individually.

It is very important to determine an individual exercise program for each patient in early stage of rehabilitation after operation of cervical intervertebral disc, otherwise they may lead to unwanted adverse effects.

MATERIALS AND METHODS

A retrospective study included 120 patients rehabilitated at the Clinic for Physical and Rehabilitation Medicine of the University Clinical Centre Sarajevo, in the early stage after surgical treatment of herniated cervical intervertebral disc, done by anterior fusion and discectomy, during the period from May 2012 to May 2014.

Depending on type of kinesiotherapeutical program, which was made based on pain occurrence during certain type of exercises, patients were divided in 3 groups: the first group, 40.0% (N=48), was performing isotonic and isometric exercises. Isotonic exercises were applied to shoulder region without overhead movements, and to other joints of upper extremities. Isometric exercises were applied on all cervical muscle groups with manual resistance given by physiotherapist. Resistance was progressive from mild to stronger. Isometric exercises were applied on both upper and lower extremities. Exercises from this group were performed in two daily sessions in duration of 20 minutes. The second group, 25.8% (N=31), was performing only isotonic exercises in two daily sessions in duration of 15 minutes. In this group of patients isometric exercises provoked pain. The third group, 22.5% (N=27), was performing only isometric exercises in two daily sessions in duration of 15 minutes. In this group of patients isotonic exercises provoked pain.

All groups were included in the program of occupational therapy which main task was to educate patient how to perform daily activities conducting protective ergonomic spine positions. All patients were performing exercises of diaphragmatic breathing and relaxation.

In 11.7% (N=14) of patients kinesiotherapy was not indicated at all, given that all types of exercises provoked severe pain. They were rehabilitated through occupational therapy and daily activities.

Effects of kinesiotherapeutical programs were evaluated by the Manual Muscle Test (MMT) and Barthel Index (BI).

RESULTS

Out of the total of 120 patients, 71.4% (N=86) were females and 28.6% (N=34) males (Figure 1).

Mean age of patients in the sample was 51.69±10.6 years, median 53 years. The youngest patient was 28 and the oldest 77 years of age. The most frequent age group was from 45-65 year, including 65.8% (N=79) of patients, whereas the least number of patients, 2.5% (N=3) was at 66-75 age group (Figure 2).
The median time period between the surgical treatment of intervertebral discus at the level of cervical spine and the beginning of the physical rehabilitation was 20.1 days with interquartile range from 14.1 to 21.0 days.

Cervical intervertebral disc herniation was most frequently located at the level C5/C6 in 37.5% (N=45) of patients, followed by level C5/C6 - C6/C7 in 25.8% (N=31), and at level C4/C5 in 20.0% (N=24) of patients. The least percent of affected disc in the tested sample was observed at the level C3/C4 in 2.5% (N=3) of patient (Figure 3).

From the baseline, 40.0% (N=48) of patients were involved in kinesiotherapy which included isotonic and isometric exercises, 25.8% (N=31) of patients were performing only isotonic exercises, while 22.5% (N=27) of patients were performing isometric exercises only (Figure 4). In 11.7% (N=14) of patients kinesiotherapy was not indicated.

Mean value of the Manual Muscle Test at discharge was 4.27±0.59 which represents a significant increase compared to the admission with mean value of 3.93±0.75 (p<0.001). Also, the values of the Barthel Index was significantly higher (p<0.001) at discharge with mean value of 18.5±2.89 compared to admission with mean of 17.5±4.15 (Table 1).

The first group of patients had significant increase of the Manual Muscle Test (4.5±0.6 vs. 4.15±0.53). The second group also showed significant improvement of the Manual Muscle Test (4.0±0.55 vs. 3.6±0.62), as well as the third group (4.2±0.6 vs. 4.0±0.52) (Table 2).

The first group of patients had significant increase of the Barthel Index (19.5±1.0 vs. 18.3±2.1). The second group also showed significant improvement of the Barthel Index (15.7±4.5 vs. 14.3±3.2). Improvement of the Barthel Index in the third group was not statistically significant (19.5±0.9 vs. 18.6±1.2) (Table 3).
DISCUSSION

Patients with cervical disc disease (herniation and/or spondylotic changes) often present complex symptomatology. The symptoms include disc specific and non-specific neck pain, distinct, intense arm pain, sensory loss, motor loss, and reflex abnormalities. Furthermore, the symptoms are often followed by physical and psychological disability, illness, long periods of sick-leave, and difficulty returning to work. Surgeries aimed to decompress the spinal nerve root and/or medulla have been established worldwide for managing radiculopathy (annual incidence is about 0.8%) due to cervical disc disease. Surgery on one or a few segmental levels is expected to cure cervical disc-specific pain and reduce neurological deficits, but not non-specific neck pain or related illnesses. These patients are often considered to have chronic pain. These circumstances have resulted in the need for a structured physiotherapy program designed to improve physical and psychological function, facilitate performance of daily activities, and teach pain management (3).

Our study analyzed effects of different rehabilitation programs in early stage after the cervical intervertebral disc surgery, which included isometric exercises for neck and extremities, isotonic exercises for shoulder region without overhead movements, isotonic exercises for upper extremities, and occupational therapy, which task was to inform the patient about movements to avoid during the first weeks after the surgery and the importance of good posture and ergonomic thinking in daily life. There was no similar study to compare the results. There is ongoing prospective, randomized, controlled multi-centre study with an independent, blinded investigator to compare two alternative rehabilitation programs. After inclusion, the patients will be randomized to receive either (A) customary treatment, including information and advice at the Neurosurgery clinic, or (B) customary treatment plus a standardized, structured, behavioral medicine program. The medical exercise therapy focuses on sensorimotor training, neck stabilization, neck muscle endurance, and strengthening the muscles that stabilize the scapula. Additionally, throughout the program, the patient will work on postural correction and ergonomics. Based on a well-defined frame of exercises that provide a standardized, structured progression, the experienced physiotherapist will adjust the program by selecting exercises and dosages appropriate for each patient (after a clinical examination and functional behavioral analysis) (4).

The third group of patients from our study did not show significant improvement of the Barthel Index score. It could be explained by fact that this group did not have isotonic exercises in their program, which affected the activities of daily life.

The importance of early involvement of kinesiotherapeutic program after surgery for cervical intervertebral disc has been reviewed in several studies.

Study of Greenfield et al. demonstrated that a 4 week postoperative exercise program can improve pain disability and spinal function in patients who undergo microdiscectomy. A brief course of active based therapy provided long-term (up to 1 year) benefits to patients following microdiscectomy. These exercise induced benefits augmented the outcomes provided by surgery. The authors expound on the long-term reconditioning that likely precedes surgery. Moreover, if properly applied, aggressive spinal strengthening performed presurgically may have not only improved surgical outcomes, but helped many patients avoid surgery altogether (5). Positive effects of isometric exercises are very well known. Study of Highland et al. included ninety patients participated in an 8 week training study. Diagnostic groups included patients with the following: degenerative disc (n=6), herniated disc (n=14), and cervical strain (n=70). Full-range isometric strength tests were performed at eight equidistant positions in a device that constrained all motion with the exception of cervical flexion and extension. Post tests were performed following training. Significant gains were seen in strength as well as range of motion. Perceived pain was significantly reduced (6).

Study of McFarland showed that both early physical therapy intervention and usual care resulted in the same amount of improvement at 6 weeks after anterior cervical fusion surgery (ACF). Addition of cranio cervical flexion (CCF) exercises (deep flexors) was not more effective than usual care for the first 6 weeks after ACF surgery. Long term follow up to examine the carry over effects of CCF training may reveal a different outcome (7).

Exercise program of our study did not include cranio cervical flexion in early rehabilitation after anterior cervical fusion and microdiscectomy.

CONCLUSION

All kinesiotherapeutical programs showed positive effects in early rehabilitation of patients after surgical treatment of cervical intervertebral disc, done by anterior fusion and microdiscectomy. There was no significant difference in the improvement of the Manual Muscle Test between the groups with different kinesiotherapeutical program, or improvement of the Barthel Index between the first two groups. The third group of patients, that performed only isometric exercises, did not show significant improvement of the Barthel Index score.

Conflict of interest: none declared.

REFERENCES

2. Kurz Larry. Understanding rehabilitation and care following anterior cervical fusion. www.understandspinesurgery.com/Articles/Read/Understanding-Rehabilitation-Care
7. McFarland C, Wang S. Comparison of Clinical Outcomes Between Early Physical Therapy Intervention and Usual Care in Individuals following Anterior Cervical Fusion. Texas Woman’s University, School of Physical Therapy, Dallas, TX, 2012.

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Advantages of locking compression plates in treatment of proximal humerus fracture

Prednosti upotrebe ugaono stabilnih ploča u tretmanu proksimalnog okrajka humerus

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ABSTRACT

Introduction: fractures of the proximal humerus account for 5-9% of injuries to the appendicular skeleton and are mostly stable, minimally-displaced osteoporotic fractures in the elderly as the result of low-energy trauma. Most of the fractures are without displacement and therefore operative treatment is not necessary. Open reduction with internal fixation (ORIF) is the most common operative method. Among the ORIF methods, osteosynthesis with plate is the most common treatment at the Clinic of Orthopedics and Traumatology of the University Clinical Center Sarajevo (UCCS). The most common plates are conventional T plates and locking compression plates. Aim: to define and determine types of fractures which require the treatment with ORIF method and among them to define those that need to be treated with conventional plate or with locking compression plate; to determine complications after treatment with conventional plate, and complications after the locking compression plate treatment. Materials and methods: a retrospective, clinical, epidemiological, descriptive-analytical analysis was performed. Results: the study included 65 patients divided in two groups [first (LCP plate); control (T-plate)]. Out of the total number of patients 37 were treated with LCP while 28 were treated with conventional T-plate [32 male, 33 female (χ²=2.613; p=0.087); mean age in the first group was 56.9±15.85, and 60.39±15.91 in the second group, F=0.912; p=0.343]. The most common cause of injury in both groups was fall (first group 54.1%; control 71.4%) and there was no significant difference between the groups (χ²=6.546; p=0.088). There was no difference between two groups in the number of fracture fragments (first group 2 parts 16.22%, 3 parts 35.14%, 4 parts 48.65%; control group 2 parts 14.81%, 3 parts 33.33%, 4 parts 51.85%). Analysis of postoperative x-ray showed better results in the first group (χ²=11.990; p=0.002). Analysis of x-ray images 6 weeks after the surgery provided better results in the first group (χ²=7.787; p=0.020), and the same results of the x-ray analysis 3 months after the surgery (χ²=7.583; p=0.043). Based on HSS score, results 3 months after the surgery were better in the first group (76.89) as compared to control group (66.32) (F=9.022; p=0.007). HSS score in 2 part fractures group was 80.15%, good or excellent: in the control 76.3% and 84% in the first group (p=0.311). In 3 part fractures, HSS score was 68.75% good or excellent: 59.3% in the control, 78.2% in the first group (p=0.041). In 4 part fractures, HSS score was 52.5% good or excellent: 36.2% in control, 68.8% in the first group (p=0.003). Analysis of x-ray images 3 months after the surgery showed better results in the first group in patients with 4 part fractures, and the results were satisfactory in both groups in 2 and 3 part fractures. Four minor complications were determined. There were 7 mayor complications in the control group and two in the first group. Conclusion: conventional T-plates can be used in the treatment of two part fractures. Locking compression plates are superior in treatment of three and four part fractures.

Key words: proximal humerus fractures, conventional plate, locking compression plate

SAŽETAK

Uvod: većina preloma proksimalnog okrajka humerusa su stabilne, minimalno dislocirane osteoporotske frakture kod starih osoba i rezultat su djelovanja slabijih sile. U velikom broju slučajeva ova vrste preloma je bez veće dislokcije i operativni tretman nije potreban. Utkrivena redukcija i unutrašnja fiksacija je metoda koja se najčešće primjenjuje. Najčešće upotrebljavane ploče za osteosintezu su Klinici za ortopediju i traumatologiju Univerzitetskog kliničkog centra (UKCS) su konvencionalna T ploča i ugaono stabilna ploča. Ciljevi istraživanja: definisati i odrediti vrstu preloma proksimalnog okrajka humerusa koje treba liječiti sa metodom utvrdjene redukcije sa unutrašnjom fiksacijom, te u okviru toga definisati prelome koje treba liječiti sa ugaono stabilnim pločom i sa konvencionalnim pločom. Utvrditi učestalost komplikacija nastalih nakon liječenja sa obje vrste ploča. Materijali i metode: istraživanje je bilo retrospektivno, kliničko, epidemiološko, deskriptivno-analitičko. Rezultati: istraživanje je obuhvatilo ukupno 65 pacijenata koji su podijeljeni u dvije grupe [37 LCP pločom (ispitivana), 28 T pločom (kontrolna)]. Kod najvećeg broja pacijenata u obje grupe uzrok povrijedavanja je bio pad sa istog nivoa (LCP- 54.1%; T-71.4%) i nije bilo statistički značajne razlike između dvije grupe (χ²=6.546; p=0.088). Analizom rtg nalaza urađeni post operativno (χ²=11.990; p=0.002). Sest sedmica nakon operacije (χ²=7.787; p=0.020) i tri mjeseca nakon operacije utvrdjeno je da je stanje ispitavana ispitivane grupe bolje i da postoji statistički značajna razlika...
INTRODUCTION

Fractures of the proximal humerus account for 5-9% of injuries to the appendicular skeleton (1). Most are stable, minimally-displaced osteoporotic fractures in the elderly, and occur as a result of low-energy trauma. There are more common in women than in men and their incidence increase with the age (>50). Fractures occurring in the elderly are usually result of low-energy injury (1,2). Neer’s classification system is based on six groups and four main fracture segments (parts) comprising the head, greater tuberosity, lesser tuberosity and shaft. Displacement is defined as more than 1 cm of translation or 45 degrees of angulation (3).

The aims of this study were:

- To define and determinate type of proximal humerus fracture that should be treated with ORIF method and within them to define those that should be treated with locking compression plate and conventional plate;
- To define the rate of complications after the treatment with locking compression plate; and
- To define the rate of complications after the treatment with conventional plate.

MATERIALS AND METHODS

A retrospective study was performed on 65 patients with proximal humerus fracture who were surgically treated at the Clinic of Orthopedics and Traumatology of the UCCS in the period from 1 July 2008 to 1 July 2013. Inclusion criteria involved all adult patients with proximal humerus fracture treated with ORIF (open reduction with internal fixation) method. Exclusion criteria were as follows: pathological fractures, patients with metabolic and endocrinologic disease, impact on bone quality, malignant processes, Neer I and VI types of fractures and bilateral proximal humerus fractures.

We analyzed: demographic data, anamnesis and clinical findings, pre and postoperative x-ray, x-ray and clinical findings 6 weeks and 3 months post operatively, and clinical findings after the physiotherapy. Hospital for special surgery (HSS) score was used for clinical findings.

According to the type of plates patients were divided in two groups:

- patients treated with locking compression plate; and
- patients treated with conventional plate.

RESULTS

The study included 65 patients divided in two groups. Patients treated with LCP plate were in the first group (37 i.e. 56.7%) and patients treated with conventional plate were in control group (28 i.e. 43.1%).

The study included 32 males and 33 females ($\chi^2=2.613; p=0.087$). In the first group 40.5% of patients were males and 59.5% females. In the control group 60.7% of patients were males and 39.3% females. Mean age in the first group was 56.59±15.85 and in a control group it was 60.39±15.91 ($F=0.912 p=0.343$). The most common cause of injury in both groups were falls (first group 54.1%; control 71.4%) and translation or 45 degrees of angulation ($\chi^2=6.546; p=0.088$). There was no difference between the groups in the number of fracture fragments ($\chi^2=18.140; p=0.782$).

Table 1 Types of fractures in both groups.

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Control</td>
</tr>
<tr>
<td>Two - part</td>
<td>Number</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>16.22</td>
</tr>
<tr>
<td>Three - part</td>
<td>Number</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>35.14</td>
</tr>
<tr>
<td>Four - part</td>
<td>Number</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>48.65</td>
</tr>
<tr>
<td>TOTAL</td>
<td>Number</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>100.00%</td>
</tr>
</tbody>
</table>

Analysis of postoperative x-ray showed better results in the first group ($\chi^2=11.990; p=0.002$) as compared to the control group. Analysis of x-ray images 6 weeks after the surgery showed better results in the first group ($\chi^2=7.787; p=0.020$), and the same results after x-ray...
Advantages of locking compression plates in treatment of proximal humerus fracture

Table 2 HSS score, follow-up and outcomes of the two groups.

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Controle group</th>
<th>First group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-part</td>
<td>76.3%</td>
<td>84.0%</td>
<td>0.311</td>
</tr>
<tr>
<td>Three-part</td>
<td>59.3%</td>
<td>78.2%</td>
<td>0.041</td>
</tr>
<tr>
<td>Four-part</td>
<td>36.2%</td>
<td>68.8%</td>
<td>0.003</td>
</tr>
</tbody>
</table>

There were no differences between the two groups after analysis of x-ray images right after the surgery, but results were better in the first group including patients with 3- and 4-part fractures ($\chi^2=8.192$; p=0.017). X-ray analysis conducted 6 weeks after the surgery, showed better results in the first group including patients with 3- and 4-part fractures. Analysis of x-ray images 3 months postoperatively, showed better results in the first group in patients with 4- part fractures.

Table 3 X-ray 3 months postoperatively.

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Groups</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>First</td>
<td>Controle</td>
</tr>
<tr>
<td>Good</td>
<td>Number</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Bad</td>
<td>Number</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>15.4%</td>
</tr>
<tr>
<td>Good</td>
<td>Number</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>84.6%</td>
</tr>
<tr>
<td></td>
<td>3- parts</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>Number</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>55.6%</td>
</tr>
</tbody>
</table>

Four minor complications were determined. In the first group we noticed one case of heterotrophic ossification and one superficial infection, whereas two cases of subacromial impingement were recorded in the control group. There were 7 major complications in the control group (two failures of fixation, two AVN and three malunions) and 2 in the first group (one failure of fixation and one malunion).

DISCUSSION

In our study we found no differences in gender structure between the two groups ($\chi^2=2.613$; p=0.087). In the study of Kummar et all. conducted on 52 patients, male to female ratio was 25/16 (4). In the study of Hussain et all. (2014) conducted on 25 patients, no difference was found in the gender structure (5). In the study of Jost et all. (2012) conducted on 121 patients, female to male ratio was 67/54 (6).

We found no differences in the age distribution. According to Teppas et all. (2013) proximal humeral fractures increase exponentially in patients after the age of 40, with approximately 70% of the patients over 60 years and female (7). According to Maier et all. (2015) in the United States, the incidence of proximal humeral fractures within the Medicare population (sixty-five years of age or older) was approximately 250 per 100,000 in the period from 1999 to 2005 (8).

In adults, the incidence of proximal humeral fracture was lowest in the third decade of life and increased in both sexes until the age of 50 years. In young patients the most common were sport related injuries while in older patients the most common were falls. The largest number of fractures in adult men occurred during the active ages between 30 and 60 years, whereas in women a dramatic increase was noted after menopause.

We found that functional outcome was better in young patients with less comminuted fractures. According to Browner (2014) although the fractures of proximal humerus may occur in any age group, an increased frequency occurs in older middle-aged and elderly individuals, because of the age-related increase in osteoporosis. In the study of Berkes et all. (2013) one of the conclusions was that regardless of the method of fixation utilized, functional outcomes are dependent on anatomic reduction, restoration of the medial column, and a patient’s ability to participate in their postoperative rehabilitation course (9).

According to Denglu Yan et all. (2012.) study conducted on 91 patients, the HSS score in two-part fractures was 80.8% good or excellent: 77.8% in the T-plate group (16 excellent, five good, four general, and two poor), and 84% in the locking-plate group (14 excellent, seven good, three general, and one poor) (10). In three-part fractures, the HSS score was 66.7% good or excellent: 55% in the T-plate group (four excellent, seven good, six general, and three poor), and 78.9% in the locking-plate group (10 excellent, five good, three general, and one poor). There was no difference between the two methods in two-part fractures ($P=0.975$); however, in three-part fractures, patients with locking plates tended to have a higher HSS score than patients with T-plates ($P=0.034$).

Based on interpretation of x-ray images after the surgery we found that patients with 3- and 4-parts fractures treated with LCP had better results as compared to those treated with conventional T-plate. According to the study of Hussain et all. (2014) fixation of 2- and 3-part fractures with conventional plate has good functional outcome but is not recommended in 4-part fractures.
with locking plates had less complications as compared to those participate in adequate and early rehabilitation. Patients treated greater tuberosity and medial column, and also when patient can be applied when it is possible to reduce articular surface, reduces risk of complications. Open reduction with internal fixation fractures. Rigid fixation with locking plates provides sufficient primary compression plates had much better results in three- and four-part fractures. Functional outcome in three-part and four-part fractures were good for both plates based analysis of x-ray images, but locking plate osteosynthesis for the proximal humeral region (11). Therefore locking can possibly contribute to regain early joint function and thus reduce impairment of motion, particularly in difficult cases. In addition, with stable fixation, revascularization of the humeral head may be possible reducing the need for joint replacement.

Jo et all. (2012) conclude that conventional plating may still be used in the case of a young patient with good bone quality, or for the treatment of simple two-part greater tuberosity fractures (12).

In the study of Ricchetti et all. (2014) conducted on 54 patients treated with locking compassion plate, minor complications related to one patient who had a superficial wound hematoma in the early postoperative period and two patients had complaints of subacromial plate impingement (13).

Out of major complications, AVN developed in 1 patient. Five patients healed with varus malunion (one 2-part fracture, three 3-part, one 4-part), but none were symptomatic enough to require additional surgery. One of the patients was also considered as a failure of fixation due to fracture displacement following the plating. This patient developed a varus malunion after the proximal locking screws were partially pulled out of the humeral head in the early postoperative period. The fracture continued to heal in this position and the patient was not symptomatic enough to require additional surgery. There was another case of failure of fixation due to nonunion. No cases of hardware failure occurred. The nonunion underwent revision of ORIF using a longer locking plate and iliac crest bone grafting and the fracture continued to heal.

Berkes et all. (2014) conclude that locking plate technology has improved fixation of these fractures and decreased the risk of screw pull-out from the humeral head. Complications of fracture fixation remain despite the use of locking plates and plate augmentation (9).

CONCLUSION

Proximal humerus fractures are most commonly seen in the elderly population (>50 years old). There were no differences in the incidence of fractures according to age distribution. The most common cause of injury was fall, while the fall from the heights had the lowest incidence. Functional outcome was better in young patients with less comminuted fractures. In 2-part fractures results were good for both plates based analysis of x-ray images, but locking compression plates had much better results in three- and four-part fractures. Functional outcome in three-part and four-part fractures was better in patients treated with locking compression plate, while the result in two- part fractures was the same in both groups. Conventional plates can be used in treatment of two-part fractures. Locking plates were superior in fixation of three-part and four-part fractures. Rigid fixation with locking plates provides sufficient primary stability to allow early functional treatment and rehabilitation which reduces risk of complications. Open reduction with internal fixation should be applied when it is possible to reduce articular surface, greater tuberosity and medial column, and also when patient can participate in adequate and early rehabilitation. Patients treated with locking plates had less complications as compared to those treated with conventional plates. Complications of fracture fixation remain despite continuous improvement of surgical materials and methods. Appropriate screw and plate placement are crucial. Screw penetration of humeral head and varus malreduction should be avoided. Functional outcome depends on anatomic reduction, reconstruction of soft tissues, reestablishment of the medial column and early post operative physiotherapy.

Conflict of interest: none declared.

REFERENCES


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Comparative advantages of VATS in relation to standard thoracic drainage in primary pleural empyema treatment

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*Corresponding author

ABSTRACT

Until recently Video-assisted thoracoscopic surgery (VATS) has an important place in surgical treatment of primary pleural empyema (PPE). Patients with anamnesis shorter than 4 weeks have a good opportunity to be cured only by the VATS. As it is not easy to precisely define the beginning of the disease, it is difficult to say to which period the VATS method will be strictly successful in the PPE treatment. Materials and methods: The study involved 100 patients with findings showing PPE in the period of four years who based on the applied surgical procedure were divided into two groups of 50 patients; control and test group. Results: significant difference in the total length of treatment of the test (13.56 ± 7.98) and the control group (19.37 ± 10.07) was found, as well as difference in the length of hospitalization after surgery for the test (9.90 ± 3.315) and the control group (18.46 ± 9.52). Duration of thoracic drainage in the test group was 8.06 ± 3.005, and 17.3 ± 9.98 days in the control group. Treatment was completed by primary procedure without additional interventions in the test group in 94% of patients, and in the control group in 58% of patients. Based on the final outcome all patients in the test group were discharged from the Clinic as cured. Regarding the control group 88% of patients were discharged from the Clinic as cured and 12% of patients as recovered. Significant difference was found between the final results in both groups. Conclusion: the best time to indicate surgical treatment by using the VATS method is history of disease in duration of four weeks. Debridement or the VATS decortication method is safe and efficient surgical procedure, especially in the first two stages. This method is recommended as the first surgical option for patients in early stages of the disease.

Key words: VATS, thoracic drainage, pleural empyema, disease stage

INTRODUCTION

Method of active thoracic drainage is the most frequently used procedure in the treatment of pleural empyema. In the recent years pleural empyema video assisted thoracoscopic surgery within surgical treatment (VATS) has been increasingly applied. VATS is defined as minimal invasive surgery carried out by coordination of surgeon’s hand and eye supported by video link.

Literature shows that the results of this method are much better compared to standard pleural drainage techniques, especially in I and II stage of pleural empyema (1,2,3,4,5,6). Although the literature state procedure of decortication using VATS technique, it is not entirely clear if some authors are using this method in late stages of disease (III stage.) Some papers state the VATS decortication procedure, but it cannot be said for sure that it is proved that standard Fowler-Delorme procedure has been carried out

SAŽETAK

VATS u novije vrijeme zauzima značajno mjesto u hirurškom liječenju primarnog pleuralnog empijema (PPE). Pacijenti čija je anamnesa kraća od 4 sedmice imaju dobru priliku da se izliječe samo VATS-om. Kao što nije lako precizno definisati početak oboljenja, teško je sa striktnom preciznošću kazati do kojeg će to perioda metoda VATS-a u liječenju PPE biti uspješna. Materijali i metode: istraživanjem je obuhvaćeno 100 pacijenata sa nalazima odgovarajućim za PPE u periodu od četiri godine, koji su u odnosu na primjenjenu hiruršku proceduru u liječenju podijeljeni u dvije grupe od po 50 pacijenata, kontrolna i ispitvana. Rezultati: utvrđena je značajna razlika u ukupnoj dužini liječenja ispitanice (13,56 ± 7,98) i kontrolne grupe (19,37 ± 10,07), kao i razlika u dužini bolničkog liječenja nakon izvedenog operativnog zahvata za ispitivanu (9,90 ± 3,315) i kontrolnu grupu (18,46 ± 9,52). Dužina trajanja torakalne drenaže u ispitanoj grupi je iznosila 8,06 ± 3,005, a u kontrolnoj 17,3 ± 9,98 dana. Liječenje je završeno prvim proceodrom bez dodatnih intervencija u ispitanu grupu kod 94%, a u kontrolnoj kod 58% pacijenata. Na osnovu konačnog ishoda svi pacijenti ispitane grupe su otklonjeni kao izlječeni. U kontrolnoj grupi 88% pacijenata je otklonjeno kao izlječeni, 12% pacijenata su otklonjeni kao oporavljeni. Ustanovljena je značajna razlika između konačnog ishoda u obje grupe. Zaključak: idealno vrijeme u kome treba indicirati hirurški tretman VATS metodom jeste povijest oboljenja u dužini trajanja do četiri nedjelje. Debridement ili dekortikacija VATS metodom je sigurna i efikasna hirurška procedura, pogotovo u prva dva stadija. Može se dati preporuka da se ova metoda primjenjuje kao prvi hirurški izbor za bolesne u ranim fazama bolesti.

Ključne riječi: VATS, torakalna drenaža, pleuralni empijem, stadij oboljenja
Success rate of procedures carried out by VATS technique is from 68% to 93%, and it seems that it is in close correlation with careful choice of group of patients. Patients whose history is shorter than 4 weeks have a good opportunity to be cured only by VATS method (10,11,12,13,14) while patients with a history of over 5 weeks (presumed stage III) usually require decortication (15,16,17).

MATERIALS AND METHODS

The study involved 100 patients with clinical, laboratory and radiologic findings corresponding to PPE, divided into two groups of 50 patients as follows:

- Group 1 (test group) consisting of patients treated by VATS method, and
- Group 2 (control group) consisting of patients treated by standard thoracic drainage

RESULTS

The study was carried out in the period from 1 January 2008 to 31 December 2011 on the sample of 100 patients with primary pleural empyema treated at the Clinic of Thoracic Surgery of the University Clinical Centre Sarajevo (UCCS). The patients were divided into two groups. Average age of patients in the test group was 53.82 ± 14.14 (26 to 76) and 56.06 ± 14.46 (21-82) in the control group. Regarding gender structure, 82% (41/50) of patients in the test group were men, and 18% (9/50) were women, with the male/female ratio 4.55:1, whereas 76% (38/50) of patients in the control group were men and 24% (12/50) were women, with ratio 3.17:1. The length of symptoms duration in the pre-clinic stage of disease established by anamnesis, i.e. until admission to the Clinic was in the range from 3 to 43 days for the test group and from 5 to 40 days for the control group. Average duration of symptoms in the test group was 19.2 ± 7.77, and 15.98 ± 8.79 days in the control group (Table 1, Figure 1).

There were 6% (3/50) of patients in the test group in the first stage of the disease and 12% (6/50) in the control group. In the second stage of the disease there were 78% (39/50) of patients in the test group and 86% (43/50) of patients in the control group, whereas in the third stage of the disease there were 16% (8/50) of patients in the test group and 2% (1/50) in the control group.

On the basis of microbiological analysis, which was performed in all patients, positive culture of pleural puncture was found in 64% (32/50) of patients in the test group, and in 58% (29/50) of patients in the control group. The average length of total treatment at the Clinic was 13.56 ± 7.98 days in the test group and 19.37 ± 10.07 days in the control group. The average length of staying at the Clinic following the admission for the surgical procedure was 2.86 ± 0.82 days for the test group and 0.54 ± 1.32 days for the control group, whereas the length of treatment after the surgery was 9.90 ± 3.315 days for the test group and 18.46 ± 9.52 days for the control group (Table 3).

The treatment completed by primary procedure without any additional intervention was carried out in 94% (47/50) of patients in the test group and in 58% (29/50) of patients in the control group. In 6% (3/50) of patients in the test group the conversion into thoracotomy and decortication of lungs was carried out. In the control group, addi-
tional surgical procedures were performed in 42% of patients, whereas the conversion to thoracotomy was performed in 2% (10/50) of patients, conversion in VATS in 8% (4/50) of patients, and in 14% (7/50) of patients additional drainage (re-drainage) was carried out.

<table>
<thead>
<tr>
<th>Table 5 Comparison of VATS method and standard drainage procedure efficiency.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment completed by primary procedure</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Conversion to thoracotomy</td>
</tr>
<tr>
<td>Conversion to VATS</td>
</tr>
<tr>
<td>Re-drainage (additional drainage)</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
</tbody>
</table>

Recorded complications in post-operative period were manifested only in the form of prolonged drainage due to prolonged secretion and air loss through drains (Table 6).

<table>
<thead>
<tr>
<th>Table 6 Post-operative complications.</th>
</tr>
</thead>
<tbody>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Duration of symptoms</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>Prolonged drainage ≥ 2 weeks</td>
</tr>
<tr>
<td>Discharge from the Clinic with H valve</td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
</tr>
</tbody>
</table>

Prolonged drainage was found in 56% (28/50) of patients in the control group and in 8% (4/50) of patients in the test group. Due to prolonged secretion and loss of air through the drain due to presence of pleural fistula, 8% (4/50) of patients in the control group were discharged from the Clinic with placed Haimlich valve, whereas there were no such patients in the test group.

Based on the final outcome, all patients within the test group left the Clinic as cured. In the control group, 88% (44/50) of patients left the Clinic as cured and 12% (6/50) as recovered (with Haimlich valve due to pleural fistula and prolonged drainage). Cases of mortality were not recorded in this study (Table 7).

<table>
<thead>
<tr>
<th>Table 7 Outcome of treatment.</th>
</tr>
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<tr>
<td>-------------------------------------------------------</td>
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<td>OUTCOME OF TREATMENT</td>
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<td>Died</td>
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Analysis of standard radiogram in PA and corresponding lateral position in the test group, carried out on discharge of patients from the Clinic, and follow-up control 1 hour after discharge, and comparison with standard radiograms from the same phase of the control group is given in Table 8. Analysis of pulmonary radiograms was carried out according to Rx score 5% scale. Standard radiogram on discharge from the Clinic in the test group was normal and without radiological verified sequelae with full restitution and Rx score 5% = 100 in 68% (34/50) of patients, and during follow-up control one month later in 84% (42/50) of patients.

In the control group only 20% (10/50) of patients had normal chest radiogram on discharge, and at the follow-up control 30 days later 32% (16/50) of patients was radiologically without sequelae. Significant post-therapeutic and post-operative changes radiologically confirmed as a sequelae in the form of obliterator fc sinus, Rx score 5% = 50 on the control radiogram after a month in the test group were found in 10% (5/50) of patients, and in 32% (16/50) of patients in the control group.

Severe form of sequelae verified radiologically at follow-up control in the form of fibrotorax Rx score 5% = 25 was found in only 2% (1/50) of patients in the test group and even in up to 24% (12/50) of patients in the control group. Rest kavum Rx score 5% = 0, was falling behind in 4% (2/50) of patients in the control group, whereas it was not recorded in the test group (Table 8).

<table>
<thead>
<tr>
<th>Table 8 Analysis of lungs X-ray on discharge from the Clinic and follow-up control after 30 days.</th>
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<td>Duration of symptoms</td>
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<td>Lungs X-ray</td>
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<tr>
<td>Clean (complete restitution)</td>
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<tr>
<td>Narrowed fc sinus</td>
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<td>Shadowed/Obliterator fc sinus</td>
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<tr>
<td>Incomplete reeksp/Fibrotorax</td>
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Mean values of Rx score 5% are shown in the Table 9. Analysis of standard chest radiogram was made during discharge of patients from the Clinic and during follow-up control one month later.

<table>
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<th>Table 9 Evaluation of standard chest radiogram.</th>
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<td>Mean values Rx score 5%</td>
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<tr>
<td>On discharge from the Clinic</td>
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<td>Follow-up control after a month</td>
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</table>

DISCUSSION

Recent approach in the treatment of pleural empyema is based on the need to start surgical treatment in the early stage of the disease. Almost general agreement has emphasized that VATS, as a minimally invasive method, has an important place in surgical treatment of pleural empyema in early stage (17,18). Key factor of effectiveness of VATS debridement is early diagnosis and indication for surgery. Several studies in literature have proven the assertion that VATS is effective in the early stages of empyema thoracic (stage I and stage II) (19,20). However, Waller and Rengarajan (2001) have proven that this method can also be effective in advanced stages of empyema (stage III). It seems that assertion that patients with anamnesis shorter than 4 weeks have a good chance to be cured only by VATS can already be defended, while chances of patients with history of disease longer than 5 weeks (stage III) are smaller (21). Sublimated conclusion of majority of papers published so far could be expressed in a way that debridement or decortication by VATS method is safe and efficient surgical procedure, especially in the first two stages, but that it
also has a role in stage III.

After research done in this work, it can be accepted without re-serve that in most cases debridement achieving complete enabling of lungs with full re-expansion is sufficient technical process with concur-rent satisfying result with regard to small pleural trauma and avoiding pleural fistula, which has direct impact on post-operative recovery in terms of shorter duration of thoracic drainage and the length of post-operative treatment.

According to results of this study the average length of total treatment at the Clinic in the test group was significantly shorter than in the control group. As an important indicator of efficiency of the methods applied, in addition to total length of treatment, the duration of thoracic drainage after surgical procedure was analyzed, and it was almost twice shorter when using the VATS method.

Using the VATS method reduces the need for other, more ag-gressive surgical procedures, such as a thoracotomy. Compared to the standard drainage, observed complications are less represented and milder in their scope. The final outcome of treatment of patients treated with the VATS method also show far better results in per-cent-age of healing, as well as the results based on radiologic analysis performed in the post-operative period Rx score by 5% method.

Analysis of the results gives a clear confirmation of assertion that the VATS method is superior and in every way more efficient than the standard procedure of thoracic drainage in the treatment of pleural empyema in the above mentioned stages of the disease.

Based on this research this method can be introduced as a part of standard protocol in the treatment of primary pleural empyema in patients whose history of disease is up to 5 weeks, and even in case of longer duration of the disease. It can be considered as an ideal surgical method for treatment of pleural empyema in patients whose history of disease is shorter than 4 weeks.

CONCLUSION

Based on the objectives of the research, conducted methodolog-ical treatment and obtained values of the research results, it can be concluded that: the best time to indicate the surgical treatment by the VATS method is the history of disease in duration of four weeks; de-bridement or decortication by the VATS method is safe and efficient surgical procedure, especially in the first two stages, but it also has its role in stage III; it is not necessary to insist on the classic procedure of decortication given that good results in radiological and functional terms can also be achieved by debridement; this method is extremely safe and efficient for patients with low rate of conversion to thoracot-omy, the type and frequency of mild complications; it is recommend-ed that this method is used as the first surgical option for patients in early stages of the disease.

Conflict of interest: none declared.

REFERENCES


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Exposure to ionizing radiation for medical purposes: effects on population, monitoring, management and reporting of radiation doses

Izlaganje jonizirajućem zračenju u medicinske svrhe: efekti na populaciju, praćenje, upravljanje i izvještavanje o dozi radijacije

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ABSTRACT

The use of ionizing radiation for diagnostic and therapeutic purposes has been constantly increasing. Mostly, the medical radiation exposure comes from computed tomography (CT) and nuclear medicine procedures, the examinations with potential risk of malignant diseases induction. By optimizing the dose, while avoiding unnecessary exposure, the side effects of medical radiation can be significantly reduced. Software CT solutions for dose management are one of the methods for dose exposure reduction. With the introduction of dose management software, monitoring of doses received by the patient can be done quickly, comprehensively and fully automatically. By reducing the average effective dose and the consequent reduction of the risk for the patient it is possible to achieve significant savings in the health system, which significantly exceeds the cost of installation of dose management software.

Key words: radiation dose exposure reduction, dose management software solutions

INTRODUCTION

The use of ionizing radiation for diagnostic and therapeutic purposes has been constantly increasing in the world (1). To approve the use of diagnostic and therapeutic procedures using ionizing radiation, it should be sufficient to demonstrate the utility of the relationship of the total potential of diagnostic or therapeutic procedures, including the direct health benefits for the individual and for the society, and the potential damage that could be caused to health of the individual (2).

Some methods have shown more positive influence on the final outcome of the diagnostic and therapeutic procedures than the others. According to data from 2009, around 75% of the medical radiation exposure comes from computed tomography and nuclear medicine procedures (3).

In the UK, Germany and USA, CT represents more than 50% of the radiation exposure from diagnostic imaging (4) and computed tomography (CT) - related ionizing radiation exposure has been cited as the largest and fastest growing source of population-wide iatrogenic ionizing radiation exposure (5).

CT, since the introduction in the practical use in 1972 year, has witnessed a steady increase in the use in medical institutions, due to the extremely positive impact on the final outcome of the diagnostic and therapeutic procedures of the patient and reducing the time required for treatment of the patient.

As a result, the number of CT scans is growing at a rate of 10% per year in developed countries, whereas the growth in developing countries in recent years, is even faster. As an illustration, the number of CT scans in the USA in the 1996-2010 period has increased three times.

According to incomplete data for the period of 5 years (2009-2014), the number of CT examinations in Bosnia and Herzegovina
increased by around 75%. At the same time, the number of CT examinations at the Department of Radiology of the UCCS increased from 22,958 examinations to 38,050 - an increase of 67%. A similar trend is expected in the near future.

This fact poses some other challenges to a health system such as population exposure to ionizing radiation. Unfortunately, the impact of this type of radiation is not sufficiently documented. Studies on the biological effects of exposure to low doses of radiation on the human body are mainly based on the monitoring of the radiation effects on the survivors after the 1945 atomic bombings on Japan.

A small number of purely retrospective studies has been recently conducted, following the long-term effects of exposure to x-rays and all of them have shown that there is a correlation between exposure to radiation during CT examinations and an increased risk for the development of malignancies in children and young people. One of the studies has shown small but existing absolute risks of leukaemia and brain cancer after CT scanning (one case of leukaemia and one case of brain tumour per 10,000 head CT scans) (6).

Even smaller number of studies have analyzed the exposure of adults to diagnostic procedures using ionized radiation and related risk from malignant disease development. The reason for that is in the fact that CT-associated cancer risks in adults depend on study type, analyzed body region, patient age and sex, and also from the fact that it is very difficult to collect data on all conducted radiology procedures during the lifespan (7, 8).

Based on that considerations, the International Commission for Radiation Protection (ICRP) coefficients were elaborated to calculate the potential risk of developing malignant tumors after exposure to radiation. The nominal ICRP coefficient of risk, balanced by gender, age and type of examination, is about 5.5% for the received dose of 1 Sievert’s (Sv). However, an effective dose and with it related potential risk, if any of these parameters are calculated separately, can vary dramatically: for example, the potential risk for the patient to whom an X-ray of the foot was done is less than 10-9, and the potential risk for a young girl to whom CT examination of the trunk was performed (thorax, abdomen and pelvis) has increased to significant 10-3 (9).

United States National Academies in their report concerning radiation health effects called the Biologic Effects of Ionizing Radiation (BEIR) VII estimate that 1,050 cases of solid cancer and 85 cases of leukemia are expected to result in 100,000 persons exposed to 100 mSv (10).

Numerous authors have studied the practical application of nominal coefficients risk of malignant diseases development as a result of medical radiation. The study „Projected Cancer Risks From Computed Tomographic Scans Performed in the United States in 2007” (11) estimated that in the United States 29,000 new malignant diseases will develop as a result of 70 million CT examinations done in 2007 (increased risk compared to general population of about 0.041%). Similar studies in Bosnia and Herzegovina have shown projection of increased risk of about 0.05%, taking into account the dose of radiation to which patients were exposed (12). Therefore, it is realistic to expect that about hundred new cases of malignant diseases will be induced every year in Bosnia and Herzegovina.

The cost of a year of treatment, care and monitoring of a patient with cancer, depending on the type and stage of disease, ranges from several thousand to several hundred thousand BAM.

Based on the increase in the number of CT examinations and the potential risk of induction of malignant diseases there is a great responsibility of health professionals and regulatory authorities in terms of optimizing the radiation dose and implementing the principle of justification of diagnostic medical exposure (13). By optimizing the dose, while avoiding unnecessary exposure, the side effects of medical radiation can be significantly reduced.

In a study published in the New England Journal of Medicine in 2009 (Exposure to Low-Dose Ionizing Radiation from Medical Imaging Procedures in the United States) the author states: „In conclusion, our results suggest that a form of medical imaging in the United States resulting in significant exposure to a large number of younger people to ionizing radiation. It is necessary to encourage the development of new approaches to optimize and ensure the correct use of these procedures” (3).

Specific solutions in terms of optimization and proper utilization of medical equipment that generates ionizing radiation have already been adopted in the USA, but the new legislation and the EU in 2013 introduced innovations in terms of:

- Obligations to provide written protocols for each type of equipment and time for all relevant categories of patients;
- Mandatory documentation of the radiation dose that patients receive during each time (radiologists and clinical doctors);
- Referral guides for medical radiological examination, which include data on radiation, must be accessible to the reference institutions and individuals;
- The institution is obliged to keep data on individual and cumulative doses of radiation received by the patient (14).

Due to incomplete infrastructure, Member States were given a deadline until 1 January 2018 to fully adapt their systems with the mentioned legal solution.

Bosnia and Herzegovina on its path towards the EU, is obliged to adapt its legislation to the EU law. The existing legislation can be improved, for example, with implementation of more detailed rules regarding regulation of clinical audit, obligation to inform patients about potential risks of radiation etc. (15).

However, the adjustment process is very complex. It was shown on the example of number of institutions in the EU, which have spent significant resources (e.g. time for evaluation and training, funds for new equipment, etc.) without improving the patient’s safety. It is a time consuming process which have to be done constantly, in order that the team involved in it can periodically analyze collected data and suggest further improvements of the system.

With the increasing number of examinations using ionizing radiation, health care institutions, as seen in previous data, are faced with number of challenges:

1. Adjusting the legal regulation of radiation dose;
2. The application of the best practices in the management of radiation doses and documentation thereof;
3. Reducing costs.

Software solutions, by nature of CT diagnostics as a high-tech process, have been imposed as a possible solution. By the introduction of dose management software, monitoring of doses received by the
Conflict of interest: none declared.

In addition, the analysis of a large number of data can provide radiologists, engineers, physicists and control authorities access to CT dose distribution, productivity and capacity utilization (17, 18), and based on that data to plan the distribution of work and other activities to improve the quality and technological development.

Practice has shown that the institutions that introduced dose management software were able to reduce the average effective dose for CT procedures for 25-30% (19).

CONCLUSION

By reducing the average effective dose and the consequent reduction of the risk for the patient, in terms that the development of a large number of malignant diseases can be prevented, it is possible to achieve significant savings in the health system, which significantly exceed the cost of installation of dose management software.

Conflict of interest: none declared.

REFERENCES


15. Državna regulatorna/regulativna agencija za zaštitu od jonizirajućeg zračenja kod medicinske ekspozicije. Službeni glasnik BiH broj 13/11.


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