Volume 25 • January/June 2019 • Number 1, 2 •
ISSN (print) 1512-5866
ISSN (online) 2232-8

MEDICAL JOURNAL
MEDICINSKI ŽURNAL

Journal of the Discipline for Research and Development
Clinical Center University of Sarajevo
Online first - www.kcus.ba

KLINIČKI CENTAR UNIVERZITETA SARAJEVO

DISCIPLINA ZA NAUKU I NASTAVU

KLINIČKI CENTAR UNIVERZITETA SARAJEVO

U SLUŽBI VAŠEG ZDRAVLJA

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 !

Bosnia and Herzegovina version of HeartScore is developed on the languages of the people of Bosnia and Herzegovina i.e. Bosnian, Serbian and Croatian! Program is easy to use and accessible at www.heartscore.org/eu !

Verzija za Bosnu i Hercegovinu razvijena je na jezicima naroda Bosne i Hercegovine, bosanskom, srpskom i hrvatskom! Program je jednostavan za upotrebu preko web stranice www.heartscore.org/eu !

Bosnia Herzegovina	France	Russian Federation
Croatia	Germany *	Spain *
Cyprus *	Greece *	Sweden *
Czech Republic *	Poland *	Slovakia *
Estonia	Romania	Turkey

Novi Centralni medicinski blok - Klinički centar Univerziteta u Sarajevu
New Central Medical Building - Clinical Center University of Sarajevo

Novi Evropski vodič za prevenciju tromboembolizma kod A Fib

CHA_2DS_2-VASc skor za procjenu rizika od tromboembolizma kod A Fib!

Risk factor-based point-based scoring system - CHA_2DS_2 -VASc

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

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

EUROPEAN SOCIETY OF CARDIOLOGY®

Major i non-major riziko fakori 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

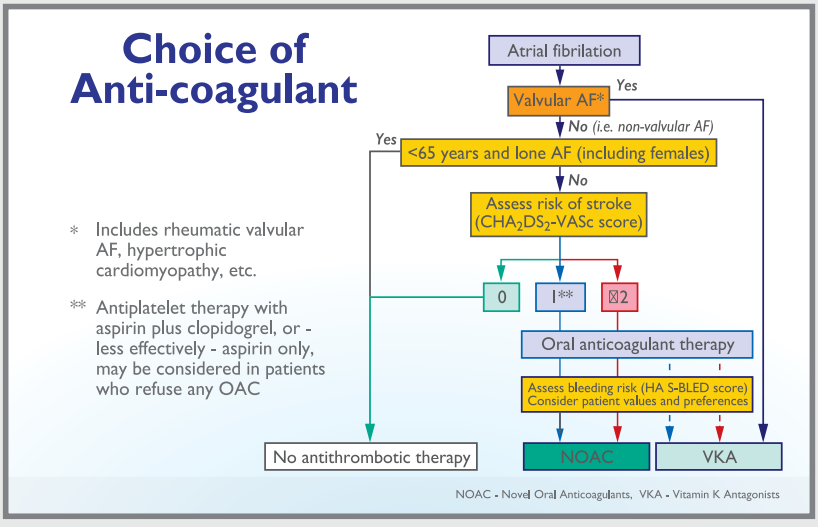
Clinically relevant non-major risk factors
CHF or moderate to severe LV systolic dysfunction [e.g. LV EF 40%]
Hypertension
Diabetes mellitus
Age 65-74 years
Female sex
Vascular disease

AF = atrial fibrilation; EF = ejection fraction (as documented by echocardiography, radio nudide ventriculography, cardiac catheterization, cardiac magnetic resonance imaging, etc.); LV = left venticular; TIA = trasient ischaemic attack.

EUROPEAN SOCIETY OF CARDIOLOGY®

Algoritam antikoagulantne terapije nakon procjene CHA_2DS_2VASc i major risk faktora!

Choice of Anti-coagulant



* 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

NOAC - Novel Oral Anticoagulants, VKA - Vitamin K Antagonists

PUBLISHER:
Discipline for Research and Development
Clinical Center University of Sarajevo
71000 Sarajevo, Bolnička 25
Bosnia and Herzegovina

For publisher:
Sebija Izetbegović, MD, PhD
General Manager
CCUS

Publishing editor:
Mirza Dilić, MD, PhD

AIMS AND SCOPE

The Medical Journal is the official quarterly journal of the Discipline for Research and Development of the Clinical Center University of Sarajevo and has been published regularly since 1994. It is published in the languages of the people of Bosnia and Herzegovina i.e. Bosnian, Croatian and Serbian as well as in English.

The Medical Journal aims to publish the highest quality materials, both clinical and scientific, on all aspects of clinical medicine. It offers the reader a collection of contemporary, original, peer-reviewed papers, professional articles, review articles, editorials, along with special articles and case reports.

EDITORIAL OFFICE

Address:
Medical Journal, Discipline for Research and Development
Clinical Center University of Sarajevo,
71000 Sarajevo,
Bolnička 25,
Bosnia and Herzegovina,
Phone: +387 33 668 415 +387 33 297 264
Email: institutnir@bih.net.ba
Web. www.kcus.ba
Technical secretariat: svjetlana.barosevcic@kcus.ba

SUBSCRIPTION

Annual subscription rates: Bosnia and Herzegovina € 50; Europe € 80; and other € 100.

SUPPLEMENTS, REPRINTS AND CORPORATE SALES

For requests from industry and companies regarding supplements, bulk articles reprints, sponsored subscriptions, translation opportunities for previously published material, and corporate online opportunities, please contact;
Email: institutnir@bih.net.ba

PRINT

KOPIKOMERC, East Sarajevo
Printed on acid-free paper.

TECHNICAL DIRECTOR

KOPIKOMERC, East Sarajevo

CIRCULATION

500 copies

Content

Original articles

Review articles

Case reports

The incidence of major airway injuries in thoracic trauma and the treatment outcome

Učestalost povreda velikih dišnih puteva u torakalnoj traumi i rezultat njihovog zbrinjavanja

Ilijaz Pilav[1]*, Safet Mušanović[1], Alma Alihodžić-Pašalić[1], Orhan Čustović[1], Meho Dapčević[1], Kenan Kadić[1], Kenan Karavdić[2]

[1]Clinic of Thoracic Surgery, Clinical Center University of Sarajevo, Bolnička 25, Sarajevo, Bosnia and Herzegovina
[2]Clinic of Pediatric Surgery, Clinical Center University of Sarajevo, Bolnička 25, Sarajevo, Bosnia and Herzegovina

* Corresponding author

ABSTRACT

Introduction: major airway injuries are observed less common among patients suffering from thoracic trauma, with other injuries to the thorax often disguising their clinical presentation. Changes in the incidence of major airway injuries over the time are attributed to advances in medicine and higher rates of pre-hospital survival among the patients on one hand, and the increased number of traffic injuries on the other. In rare circumstances, major airway injuries are diagnosed as isolated injuries. We investigated the frequency of major airway injuries, the cause, and the outcomes of treatment. Aim: to determine the frequency of major airway injuries in isolated thoracic traumas, as well as optimal methods of definitive treatment of patients with these injuries. Materials and methods: a retrospective study analyzed all patients admitted to Clinic of Thoracic Surgery of the Clinical Center University of Sarajevo, within a certain period, diagnosed with isolated major airway injury. The incidence, therapeutic modality, and outcome of treatment were established. Results: a total of 320 patients with isolated thoracic injury were hospitalized at the Clinic of Thoracic Surgery in the period from 1ST January 2013 to 1st January 2019, of which 16 had a tracheobronchial injury, which comprised 5% of all isolated thoracic injuries. Conservative treatment was the therapeutic choice in 18.75% of patients, and surgical treatment in 81.25%. Conclusion: major airway injuries are less common but life-threatening injuries. Early diagnosis is considered to be the most important factor associated with survival in these cases.

Keywords: bronchi, thoracic surgery, surgical treatment, trachea

SAŽETAK

Uvod: povrede velikih dišnih puteva u torakalnoj trauma su izuzetno rijetke i njihova dijagnoza je često prikrivena drugim povredama u sklopu torakalne traume. Stvarna incidenca ovih pacijenata se mijenja tokom godina, zbog napredovanja medicine i mogućnosti preživljavanja pacijenata do bolničkih ustanova, te povećanom broju sabraćajnih traumatizama. Veoma rijetko se postavlja dijagnoza izolovane povrede velikih dišnih puteva. Ovim istraživanjem utvrđena je incidenca traume velikih dišnih puteva, način i rezultati zbrinjavanja. Cilj rada: ustanoviti učestalost povreda velikih dišnih puteva u izolovanoj torakalnoj traumi i utvrditi optimalne metode definitivnog zbrinjavanja povreda velikih dišnih puteva. Pacijenti i metode: retrospektivnom studijom urađena je analiza svih pacijenata primljenih na Kliniku za torakalnu hirurgiju Kliničkog centra Univerziteta u Sarajevu u određenom vremenskom periodu sa dijagnozom izolovane povrede velikih disajnih puteva. Ustanovljena je incidenca, terapijski modalitet i ishod liječenja. Rezultati: ukupno 320 pacijenata sa izolovanom povredom grudnog koša je bilo hospitalizirano na Klinici za torakalnu hirurgiju tokom perioda od 01.01.2013. do 01.01.2019. godine, od kojih je 16 imalo povredu traheobronhalnog stabla, što izosi 5% svih izolovanih povreda grudnog koša. Konzervativni tretman bio je terapijski izbor kod 18,75% svih pacijenata, a hirurški kod 81,25% pacijenata. Zaključak: povrede velikih disajnih puteva su rijetke, ali životno ugrožavajuće povrede. Njihova rana dijagnoza je najvažniji faktor preživljavanja.

Ključne riječi: bronhi, torakalna hirurgija, hirurški tretman, traheja

INTRODUCTION

Major airway injuries are less common but life-threatening injuries (1). Injuries to the tracheobronchial tree within the chest may occur due to blunt, penetrating traumas, or gunshot wounds to the neck or chest. The most important factors associated with survival in these patients are prompt diagnosis and appropriate surgical intervention (2).

In general, 1-2% of patients with thoracic trauma have a penetrating tracheobronchial traumatic injury (3). The incidence of tracheobronchial injuries in blunt traumatic chest injuries is 2.8%. Most injuries caused by blunt trauma involve the thoracic part of the trachea and the main bronchi (4).

Tracheobronchial injuries occur as a result of blunt and penetrating traumas, causes such as iatrogenic injuries, burn, or less commonly caustic injuries. Three theories have been proposed

regarding the exact mechanism of blunt intrathoracic injuries to the tracheobronchial tree (5). One is the sudden and forceful anteroposterior compression of the thorax which is the most frequent mechanism of trauma that causes tracheobronchial avulsion and injuries. This can lead to an increase in the transverse diameter which pulls the lungs apart at the level of the carina. The second theory involves the compression of the chest and trachea while the glottis is closed, which in turn produces a rapid increase in airway pressure, principally in the trachea and the larger bronchi. When the airway pressure surpasses the elasticity of the tracheobronchial tree, the airway commonly ruptures at the membranous portion. The third one relates to rapid deceleration injuries where shearing forces occur at the relative fixation points, i.e. the cricoid cartilage and carina. Ruptures of the main bronchi occur on the right side more frequently than the left. Some researchers have found an equal frequency of right-sided and left-sided main stem bronchial injuries (6). Right-sided injuries may also be detected earlier because the left main stem bronchus is more protected by adjoining structures in the mediastinum (7).

The diagnosis has to be made on time and the first phase of treatment must be started promptly (7). Along with the general symptoms of trauma, symptoms of massive pneumothorax seem to dominate the clinical picture. Shortness of breath and respiratory distress are common symptoms and occur in 76% to 100% of cases (8). In the initial treatment, 60% of patients with tracheobronchial injuries have deep cervical emphysema and pneumomediastinum, over 70% of patients also have a pneumothorax (9). Complete bronchial transection leads to atelectasis; "absent hilum" or collapsing of the lung away from the hilum to the diaphragm known as the "fallen lung sign of Kumpe" (10). The standard radiographic examination of the chest is the initial diagnostic modality. Computed tomography (CT) of the neck and upper chest is decisive. Bronchoscopy offers a high diagnostic yield and provides a single definitive diagnostic study in patients with suspected airway injury (11).

The most important step in the treatment of major airway injuries is to secure and maintain an adequate airway. Surgery is the treatment of choice for tracheobronchial injuries, although minor tracheal injuries can be treated conservatively. The main purpose of surgical treatment is the debridement of devitalized tissue including cartilage and anastomoses as well as treatment of airway lesions using sutures (12).

AIM

To determin the frequency of major airway injuries in isolated thoracic traumas, as well as optimal methods of definitive treatment of patients with these injuries.

MATERIALS AND METHODS

This study included 320 patients hospitalized at Clinic of Thoracic Surgery of the Clinical Center University of Sarajevo, with isolated thoracic injuries, of which 16 were admitted with major airway injuries. Therapeutic procedures performed in these patients, depending on the type and severity of the injury, were: conservative treatment with observation and monitoring of the patient's health condition as well as surgical treatment, which included primary surgical treatment of the wound, pleural drainage, and thoracotomy with airway reconstruction.

The inclusion criteria: patients who had an isolated thoracic trauma with disorders of the pleural space and a suspected major airway injury.

Patients with polytrauma were excluded from the study.

RESULTS

A total of 320 patients with an isolated thoracic injury were hospitalized at the Clinic of Thoracic Surgery in the period from 1st. January 2013 to 1st. January 2019, of which 16 had a tracheobronchial injury, which comprises 5% of all isolated thoracic injuries. Out of the 16 patients with tracheobrochal injury, 13 (81.3%) were male, while three (18.8%) were female. Figure 1 depicts the age distribution of patients with tracheobronchial injuries. The largest number of injuries in a single age group was among people aged 19-35. Moreover, 93.8% of all patients with tracheobronchial injuries were over 18.

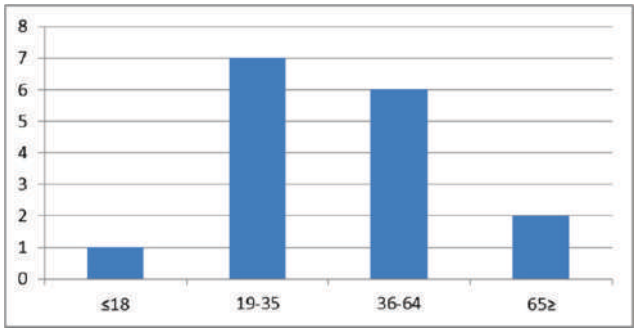


Figure 1 The incidence of tracheobronchial injuries by age group.

Blunt trauma is the leading cause of injury and was recorded in 11 patients, i.e. 68.8% of all cases, followed by penetrating injuries (12.5%) and iatrogenic injuries (18.8%) (Figure 2).

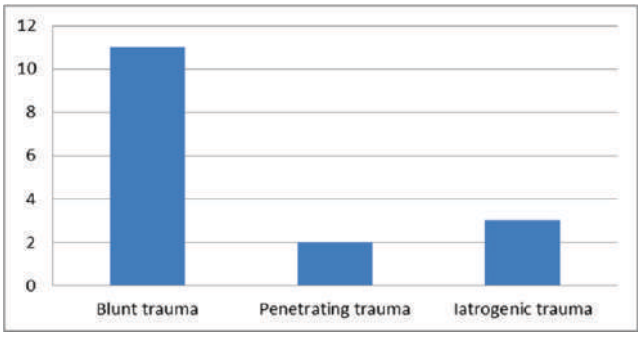


Figure 2 The etiology of tracheobronchial injuries.

According to their localization, most injuries were located in the thoracic part of the trachea, i.e. six patients (37.5%). The least common localization was the cervical part of the trachea (Table 1).

Table 1 **Anatomical localization of tracheobronchial injuries.**

Localization	Number of injuries	%
Cervical trachea	2	12.5
Thoracic trachea	6	37.5
Right main stem bronchus	2	12.5
Left main stem bronchus	3	18.75
Multiple injury to the TBT*	3	18.75
Total:	16	100

** TBT – Tracheobronchial tree*

Conservative treatment in our study was the therapeutic choice in three patients (18.75%) while 13 patients (81.25%) underwent surgical treatment.

We determined three-time intervals in which we observed survival rates. These intervals were: (1) the first day, (2) the first two weeks, and (3) more than two weeks since the admission to the Clinic. In both groups of patients, there were no deaths recorded on the first day and one death was registered within two weeks of the conservative treatment. One death was also reported in the group of patients who were treated surgically, with other patients surviving for more than two weeks (Table 2).

Table 2 **Survival rates after admission to the Clinic.**

Conservative treatment (8)	Died on the first day	0	0%
	Within two weeks	1	6.25%
	Survived more than two weeks	2	12.5%
Surgical treatment (13)	Died on the first day	0	0%
	Within two weeks	1	6.25%
	Survived more than two weeks	12	75%

The overall morbidity rate in the study was 12.5% (two out of 16 patients).

In the postoperative period during the stay at the Clinic, and after discharge, complications occurred in three out of 16 patients (18.75%). Stenosis, infection, and dehiscence were observed in each of these cases, as shown in Table 3.

Table 3 **Complications.**

Complication	Number of complications	
Infection	1 (1/16)	6.25%
Stenosis	1 (1/16)	6.25%
Dehiscence	1 (1/16)	6.25%
Total	3 (3/16)	18.75%

DISCUSSION

Tracheobronchial lesions are rare, occurring in 1% to 3% of patients with closed trauma and 2% to 9% of those who suffered penetrating cervical and/or thoracic injuries (13). Tracheobronchial injuries were considered very rare until the last three decades. Bertelsen and Howitz in an autopsy study in 1187 autopsies of traumatized patients concluded that only 33 patients (0.03%) died from tracheobronchial tree injuries.

The clinical picture varies according to lesion location and severity, and may not be immediately expressed, such as in closed trauma where it is believed to occur in up to two thirds of the tracheobronchial lesions, especially when on the left (14).

Subcutaneous and mediastinal emphysema were the most common signs. Pneumothorax occurred in all patients with intrathoracic airway lesions. These are non-specific signs, such as dyspnea, but should be particularly valued when they persist even after initial treatment such as chest drainage (15).

Radiological changes are nondiagnostic, but the presence of pneumomediastinum, persistent refractory pneumothorax, atelectasis and subcutaneous emphysema should raise the clinical suspicion of airway injury, and in this case, bronchoscopy should be the examination of choice, which should locate and characterize the lesion(16). The presence of blood in the airways or difficulty in visualizing the distal bronchial tree may compromise the exam power of resolution. Therefore, some authors recommend repeating the bronchoscopy in the face of clinical suspicion. In intubated patients, where possible, the tube should be removed for proper evaluation(17).

Regarding the approach to tracheobronchial lesions, it is believed that the majority can be treated by debridement and primary repair, both in penetrating and closed trauma (18). In some situations, end-to-end anastomosis may be necessary in both cervical and intrathoracic lesions, and tracheostomy is not mandatory. Small airways lacerations can be treated non-

operatively, in selected, hemodynamically stable patients without associated lesions (19).

The access of choice for the intrathoracic lesions is the right thoracotomy, which allows to approach the majority of the intrathoracic lesions, avoiding the aortic arch and better exposing the airway, leaving the left thoracotomy, and even the sternotomy, for more distal left lesions or more complex ones (20). Pulmonary resections are an alternative, especially in cases of vascular lesions associated with hemorrhage, which makes the bronchial repair difficult. The excellence of anesthesia is fundamental for the success of the procedure, both in terms of adequate positioning of the endotracheal tube and in the control of airways pressure (21). In the postoperative period, the correct positioning of the tube is also essential, preserving the suture line and reducing pressure on it. In special situations, particularly in complex and extensive lesions, the use of stents to avoid stenosis has been discussed and can be maintained for six to 18 months (22). We have no experience with the use of airway prostheses in trauma in our Service, and it is our conduct to operate the patient as soon as possible.

In this study, we collected data in the period from 2013 to 2019 and determined that 16 patients were admitted to the Clinic of Thoracic Surgery with tracheobronchial injuries. The ways and circumstances under which the injury occured determine the etiology of tracheobronchial injuries. Blunt and penetrating injuries constitute the vast majority of these injuries, but there were also iatrogenic injuries during endotracheal intubation, mediastinoscopy, and mechanical ventilation. Our data on etiology are consistent with the reference literature (23). Less common causes include injuries inflicted by a sharp object, strangulation, electrical injuries, burns, and caustic injuries. Cervical part of the trachea was the most common location of penetrating injuries (75%), followed by injuries to the thoracic part of the trachea (25%). Stab or gunshot wounds can cause damage to the main bronchi, and injuries to the main bronchi are almost always associated with other injuries, especially those that involve large vessels (24).

Analysis of the etiology of tracheobronchial tree injuries in this study shows that blunt trauma was the cause of injury in 11 patients, i.e. 68.8% of all cases, penetrating injuries were present in 12.5% of all cases, and iatrogenic injuries in 18.8% of all cases. The given data correspond to the reference literature. The least common sites of injuries were the cervical part of the trachea and the right main stem bronchus, i.e. only one injury each, while most injuries occurred in the thoracic part of the trachea, i.e. six (37.5%). In this research, anatomical localization of tracheobronchial injuries did not correlate with available epidemiological data and large studies on the frequency of tracheobronchial injuries. Due to the anatomical position, the cervical part of the trachea is more protected than the thoracic part of the trachea, which was injured in 12.5% of cases. Lesions of the cervical part of the trachea are generally caused by penetrating injuries, and rarely occur in the closed chest trauma, which predominantly causes lesions in the thoracic part of the trachea and main bronchi, 80% of which are found up to 2.5cm from the carina. Although most studies show a higher incidence of lesions in the right main stem bronchus, due to fact that it is less protected by mediastinal structures, three patients with closed chest trauma in our research had lesions in the left main stem bronchus. We determined three-time intervals in which we observed survival rates. These intervals were: the first day, the first two weeks, and more than two weeks since the admission to our Clinic. In both groups of patients, there were no deaths recorded on the first day and one death was registered within two weeks of the conservative treatment. One death was also reported in the group of patients who were treated surgically, with other patients surviving for more than two weeks Surgically treated patients have higher survival rates as compared to patients treated conservatively.

The overall estimated mortality for tracheobron-chial lesions is 30%. The overall morbidity rate in the our study was 12.5% The authors consulted suggest that early diagnosis and treatment of tracheobronchial lesions are associated with better results, with a greater possibility of primary repair, preserving as much as possible the functioning pulmonary parenchyma, and minimizing the risks of stenosis, empyema and other complications, more common in late repairs. We had three patients who evolved with Stenosis, infection and dehiscence of the anastomosis. The other patients had a good evolution.

We believe that the mechanism of trauma and clinical findings should be valued in the suspicion of airway injury and justify the insistence on early diagnosis.

CONCLUSION

Major airway injuries are less common but life-threatening injuries. Early diagnosis is considered to be the most important factor associated with survival in these cases. Tracheobronchial injuries constitute 5% of all isolated thoracic injuries. The least common injuries were in the cervical part of the trachea and the right main bronchus (12.5%), while the most common injuries were located in the thoracic part of the trachea (37.5%). The ooverall morbidity rate in our study was 12.5% (two out of 16 patients). Surgical treatment is the method of choice in the treatment of tracheobronchial injuries.

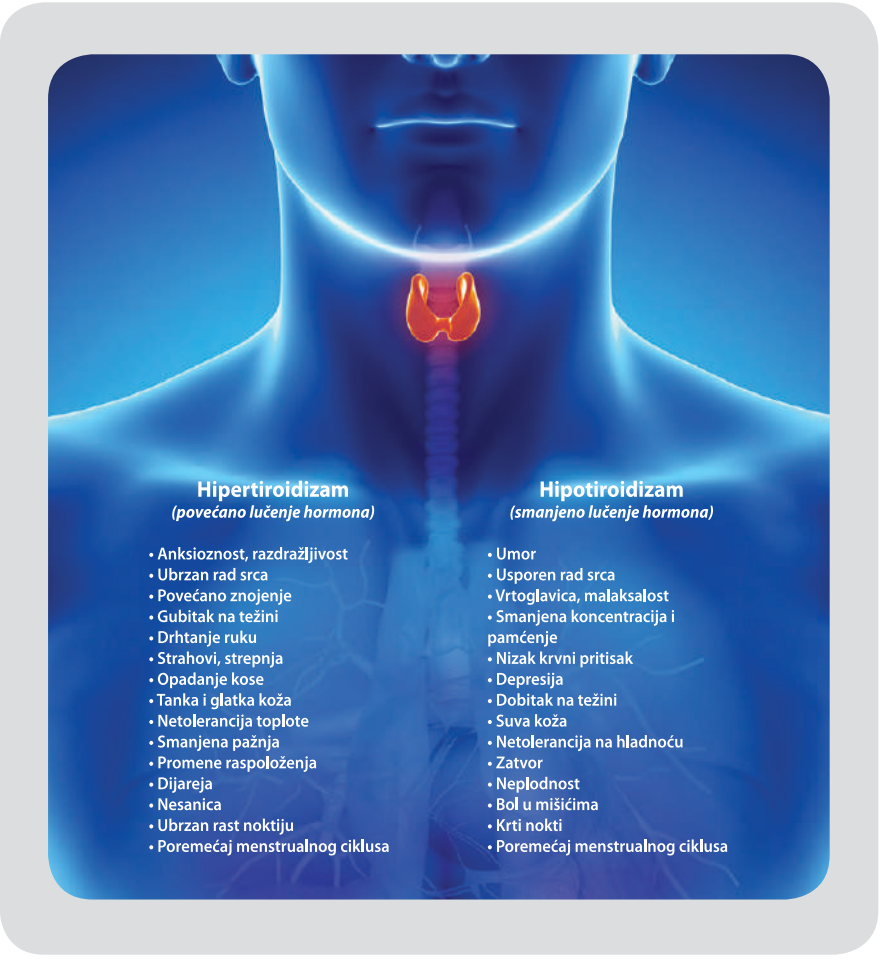
REFERENCES

1. Marsico GA. Lesões da traqueia e grandes brônquios. In: Marsico GA. Trauma torácico. 1a ed. Rio de Janeiro: Revinter. 2006. p.147-58.
2. Kiser AC, O`Brien SM, Detterbeck FC. Blunt tracheobronchial injuries: treatment and outcomes. Ann Thorac Surg. 2001;71(6):2059-65.
3. Chen JD, Shanmuganathan K, Mirvis SE, Kileen KL, Dutton RP. Using CT to diagnose tracheal rupture. AJR Am J Roentgenol. 2001;176(5):1273-80.
4. Noboru N, Fumio M, Shunsuke Y, Kichizo K, Masayuki Y, Sadaki, et al. Chest radiography assessment of tracheobronchial disruption associated with blunt chest trauma. J Trauma. 2002;53(2):372-7.
5. Rollins RJ, Tocino I. Early radiographic signs of tracheal rupture. AJR Am JRoentgenol. 1987;9:695-698.
6. Lee RB. Traumatic injury of the cervicothoracic trachea and major bronchi. Chest Surg Clin NAm. 1997;7:285-304
7. Karmy-Jones R, Wood ED. Traumatic Injury to the Trachea and Bronchus. Thorac SurgClin. 2007;17:35-46.
8. Le Guen M, Beigelman C, Bouhemad B, Wenjïe Y, Marmion F, Rouby JJ. Chest computed tomography with multiplanar reformatted images for diagnosing traumatic bronchial rupture: a case report. Crit Care. 2007;11(5):R94.
9. Kaewlai R, Avery LL, Asrani AV, Novelline RA. Multid etector CT of blunt thoracic trauma. Radiographics. 2008;28(6):1555-70.
10. Altinok T, Can A. Management of tracheobronchial injuries. Eurasian J Med. 2014;46(3):20915.
11. Wood DE. Tracheal Bronchial Trauma. In: Thoracic Trauma and Critical Care. Karmy-Jones R, Nathens A, Stern AJ (eds). Boston: Kluwer Academic Publishers; 2002. pp. 109-123.
12. Kiser AC, O'Brein SM, Dettrbeck FC. Blunt tracheobronchial injuries: treatment andoutcomes. Ann Thorac Surg. 2001;71:2059–65.
13. Rossbach MM, Johnson SB, Gomez MA, et al. Management of major tracheobronchialinjuries: a 28-year experience. Ann Thorac Surg. 1998;65:182-6.
14. Jones CM, Athanasiou T. Is virtual bronchoscopy an efficient diagnostic tool for the thoracicsurgeon Ann Thorac Surg. 2005;79:365-74.

15. Jougon J, Ballester M, Choukroun E, Dubrez J, Reboul G, Velly JF. Conservative treatment for postintubation tracheobronchial rupture. Ann Thorac Surg. 2000;69(1):216-20.
16. Gomez-Caro A, Ausín P, Moradiellos FJ, Diaz-Hellin V, Larrú E, Pérez JA, et al. Role of Conservative MedicalManagement of Tracheobronchial Injuries. J Trauma. 2006;61(6):1426-35.
17. Carbognani P, Bobbio A, Cattelani L, Internullo E, Caporale D, Rusca M. Management of postintubation membranoustracheal rupture. Ann Thorac Surg. 2004;77(2):406-9.
18. Bhojani RA, Rosenbaum DH, Dikmen E, Paul M, Atkins BZ, Zonies D, et al. Contemporary assessment of laryngotracheal trauma. J Thorac Cardiovasc Surg. 2005; 130:426-32.
19. Battistella FD, Benfield JR, Blunt and penetrating injuries of the chest wall, pleura. Andlungs. In Shields TW, Locicero III J, Ponn RB (eds). General thoracic surgery. 5th ed. Philadelphia: Williams& Wilkins. 2000:815-31.
20. Mahmodlou R, Sepehrvand N. Tracheobronchial injury due to blunt chest trauma. International journal of critical illness and injury science. 2015;5(2):116.
21. Balci AE, Eren N, Eren S, Ulkü R. Surgical treatment of post-traumatic tracheobronchial injuries: 14-year experience. Eur J Cardiothorac Surg. 2002;22(6):984-9.
22. Helmy N, Platz A, Stocker R, Trentz O. Bronchus rupture in multiply injured patients with blunt chest trauma. Eur J Trauma. 2002;28(1):31-4.
23. Faure A, Floccard B, Pilleul F, Faure F, Badinand B, Mennesson N, et al. Multiplanar reconstruction: a new method for diagnosis of tracheobronchial rupture? Intensive Care Med. 2007;33(12):2173-8.
24. Tamura M, Oda M, Matsumoto I, Fujimori H, Shimizu Y, Watanabe G. Double-barrel reconstruction for complex bronchial disruption due to blunt thoracic trauma. Ann Thorac Surg. 2009;88(6):2008-2010.

Reprint requests and correspondence:
Ilijaz Pilav, MD, PhD
Clinic of Thoracic Surgery
Clinical Center University of Sarajevo
Bolnička 25, 71000 Sarajevo
Bosnia and Herzegovina
Phone: +387 61 503 447
Email: ilijaz.p@dr.com
ORCID ID: 0000-0003-3117-2748

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: IP, SM, AA-P, OČ, MD, KK and KK, gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.



Analysis of changes in characteristics of severe traumatic injuries according to intention, mechanism and body localisation after the start of migrant crisis in Bosnia and Herzegovina

Analiza promjena karakteristika teških traumatskih povreda u odnosu na namjeru, mehanizam i zahvaćenost regija tijela nakon početka migrantske krize u Bosni i Hercegovini

Amela Ahmić*

Clinic of Emergency Medicine, Clinical Centre University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

Introduction: migrants suffering from injuries are everyday patients who require emergency services even from the start of migrant crisis in our country. It has become detectable that most of them have had similar pattern of injuries according to intention, mechanism, severity and localisation. This makes possible to create and implement injury prevention strategies and organize health providing system based on exact analysis of those patients injuries. That is especially important for life-threatening trauma. Materials and methods: this research included patients with life-threatening trauma ISS ≥ 16 with at least one physiological disorder treated at Clinic of Emergency Medicine of the Clinical Centre University of Sarajevo during the six months period (1 January to 31 June) of 2017 (n= 125) and 2019 (n= 132) with the purpose of making comparison between groups of patients before and after the migrant crisis. Data were collected retrospectively from electronic medical database, which were statistically proceesed, expressed as percentages and presented in figures and tables. Significance of data was evaluated by Chi-square and Fisher's tests where p-values lower than 0.05 ($p<0.05$) were considered statistically significant. Aim: to examine the contribution of migrants among severely injured patients, to analyse how they changed the figure of traumatism according to intention, mechanism and localisation of injuries, and consequently to indicate to the necessity of including prevention strategies and reorganisation of medical care services. Results: in 2019 there were 9.85% of all patients with life-threatening injuries identified as migrants. Proportion of intentional injuries significantly increased for 11.50% in 2019 in comparison to 2017 ($p<0.05$). All migrants suffered from intentional injuries (100%) and taking into account the said proportion of them in 2019, it was obvious that they contributed to this increase. Proportion of penetrating injuries between the observed years also significantly increased for 14.18% ($p<0.05$) while migrants with penetrating injuries took 9.09 % of all patients in 2019 and contributed to this increase. When talking about most severe injuries (leading injuries) per patient, there was a significant percentual increase in the chest and thoracic spine injuries by 9.1% in 2019 ($p<0.05$) and also insignificant percentual increase of the abdominal content and lumbar spine injuries by 5.36%, pelvic and extremities injuries by 2.13% and face injuries by 1.49% ($p>0.05$). Proportion of the head and neck injuries significantly decreased by 18.09% ($p<0.05$). Conclusion: migrant crisis was connected with significant increase of intentional and penetrating injuries and significantly higher incidence of severe injuries of chest and lower incidence of head and neck injuries. Systematic injury prevention strategies are required, but also improvement of health care system in offering faster and more organised response in emergency services and multidisciplinary approach. This was important especially if the number of migrants in our country would grow.

Keywords: migrants, life-threatening injury, injury prevention

SAŽETAK

Uvod: migranti sa povredama su svakodnevni pacijenti u urgentnim službama još od samog početka Migrantske krize u našoj zemlji. Primjećeno je da veliki broj tih pacijenata ima slične povrede u odnosu na intenciju, mehanizam, težinu i lokalizaciju. Zahvaljujući tome moguće je kreiranje i implementacija programa prevencije ozljeda i organizacija sistema pružanja zdravstvenog zbrinjavanja bazirano na ekzaktnoj analizi povreda kod ovih pacijenata. To je naročito važno kada se radi o životno ugrožavajućoj traumi. Materijali i metode: studija je uključila pacijente sa životno ugožavajućim povredama sa vrijednošću ISS ≥ 16 i poremećajem najmanje jednog vitalnog parametra koji su zbrinuti na Klinici urgentne medicine Kliničkog centra Univerziteta u Sarajevu u šestomjesečnom periodu (01.01-31.06.) u toku 2017. (n=125) i 2019. godine (n=132) sa svrhom poređenja grupa pacijenata prije i

poslije migrantske krize. Podaci su prikupljeni retrospektivo iz medicinske elektronske baze, statistički obrađeni, izraženi u postocima i prikazani u grafovima i tabelama. Značajnost rezultata je provjeravana putem Chi-square testa i Fischerovog testa tako da je p-vrijednost manja od 0.05 ($p<0.05$) smatrana statistički signifikantnom. Cilj: ispitati udio migranata u ukupnom broju pacijenata pacijenata sa teškom traumom, analizirati kako su oni promijenili sliku traumatizma u odnosu na intenciju, mehanizam i lokalizaciju povreda, te na osnovu dobivenih rezultata pokazati potrebu uvođenja sistemskih programa prevencije i reorganizaciju zdravstvenih ustanova koje vrše zbrinjavanje. Rezultati: udio pacijenata sa životno ugrožavajućim povredama identifikovanih kao migranti u 2019. je bio 9.85%. Udio nasilnih povreda je statistički signifikantno porastao u 2019. u odnosu na 2017. godinu za 11.50% ($p<0.05$). Svi migranti (100%) su imali nasilne povrede, a imajući na umu gore spomenuti udio tih pacijenata u 2019. godini očit je njihov doprinos porastu ovakvih povreda. Udio penetrantnih povreda je također imao statistički signifikantan rast od 14.18% ($p<0.05$) dok su migranti sa penetrantnim povredama zauzimali 9.09 % od svih pacijenata u 2019. godini, tako da je evidentno da su doprinijeli ovom rastu. Kada razmotrimo najteže (vodeće) povrede po pacijentu, došlo do statistički signifikantnog rasta udjela povreda regije grudnog koša sa torakalnom kičmom u 2019. godini za 9.1% ($p<0.05$) te nesignifikantnog rasta povreda regije abdomena sa lumbalnom kičmom za 5.36%, karlice sa ekstremitetima za 2.13%, te lica za 1.49% ($p>0.05$). Udio povreda regije glave i vrata je signifikantno opao za 18.09% ($p<0.05$). Zaključak: migrantska kriza je povezana sa značajnim rastom broja nasilnih i penetrantnih povreda. Također je povezana sa signifikantno povećanom incidencom teških povreda grudnog koša i smanjenom incidencom povreda glave i vrata. Zbog toga je provođenje sistemske strategije prevencije povreda potreba, zajedno sa usavršavanjem zdravstvenog sistema u cilju bržeg i organiziranijeg zbrinjavanja od strane urgentnih službi, ali također i multidisciplinarnog pristupa. Ovo je posebno važno ukoliko bi broj migranata u našoj zemlji nastavio da raste.

Ključne riječi: migranti, životno-ugrožavajuća povreda, prevencija povreda

INTRODUCTION

Since mid-2018 Bosnia and Herzegovina has been faced with growing number of migrants spending time in our country. Their presence is visible in everyday life. They have introduced different types of behavior and ways of living. That, along with lower socio-economic status has inevitably affected the medical service, not only based on the number of patients, but also based on certain specificities in diseases or healt conditions of these people. During the period of providing care for severely injured patients at Clinic of Emergency Medicine of the Clinical Centre University of Sarajevo (CCUS) it was evident that most migrants had similar injuries, according to intention, mechanism and affected body systems. Also, their number was not insignificant. It was necessary to collect data about injured patients, make exact analyses and answer the following questions: Does this represent burden for health system and is there a need for changes in medical services in order to improve providing helthcare? Is it possible and necessary to make plans for prevention of injuries of this group of people? This made sense especially if number of migrants would increase. Since decades ago injuries have been considered greatly preventable. Nowadays, making plans for prevention and health care improvement is based on epidemiology data, and has become a global trend and need (1,2). Collecting and analysing data help recognizing risk factors and endagered groups of people. Risk-control and behavioral strategies are basic parts of prevention programmes including multidisciplinary approach. Systematic prevention decreasis morbidity and mortality rates, makes better quality of life but also unburden health system and lowers the costs (2,3). This is especially important in preventing life threatening injuries with high mortality rate. By definition those are injuries with Injury Severity Score (ISS) $\geq$ 16 with at least one physiological disorder (4).

MATERIALS AND METHODS

The study included severely injured patients treated at Clinic of Emergency Medicine of the CCUS. Data were taken retrospectively from electronic medical database in the period from 2017 to 2019, in the six months period of each year (1 January to 31 June) for the purpose of making comparison between period before and after migrant crisis. It included patients with life-threatenig injuries with ISS $\geq$ 16 and at least one physiological disorder. All patients with incomplete data about causes of injury and final diagnoses were excluded. Patients without complete identity information were excluded, which made impossible to analyze injuries based on age. According to those criteria 125 patiens from 2017 and 132 patients from 2019 were observed.

AIM

To examine the contribution of migrants among severely injured patients; how they changed the figure of traumatism according to intention, mechanism and quality of injuries, and consequently to indicate to necessity of including prevention strategies and reorganisation of medical care services.

Statistical processing

All data were statistically proceesed, exspresed in percentages and presented in figures and tables. Significance of data was evaluated by the Chi-square and Fisher's tests where p-values lower than 0.05 ($p<0.05$) were considered statistically significant.

RESULTS

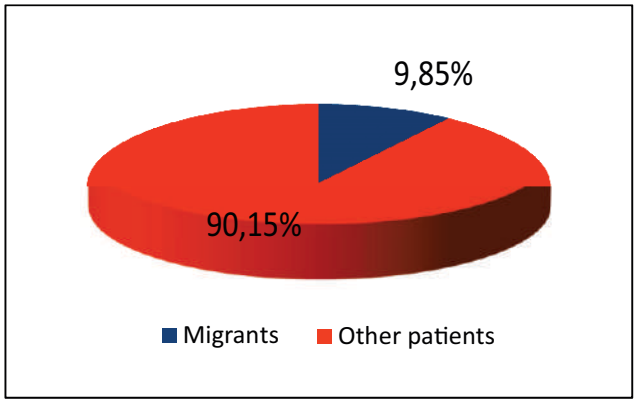


Figure 1 **Contribution of migrants among the observed patients in 2019.**

During the observed period in 2019, there were 9.85% of all patients with life threatening injuries identified as migrants (Figure 1) All of those patients were men (100%) and they were all suffering from intentional injuries (100%). Figure 2 shows injuries by intention. According to International Classification of External Causes of Injuries (ICECI) intent is one of the criteria for categorisation (5). For this research all kinds of intentional injuries were placed in one category, including intentional self-harm, assault and other violence. There was a detectable decrease of percentage ratio between unintentional and intentional injuries in 2019. Proportion of intentional injuries raised for 11.50% (from 10.04% in 2017 to 21.54% in 2019), which was statically singificant raise ($p<0.05$).

Consequently, unintentional injuries had statistically significant fall from 89.96% in 2017 to 78.46 % in 2019. All migrant had intentional injuries, and related to 9.85% of all analysed patients. It is obvious that they contributed to raise of these injuries in 2019, as without their participation it would be insignificant.

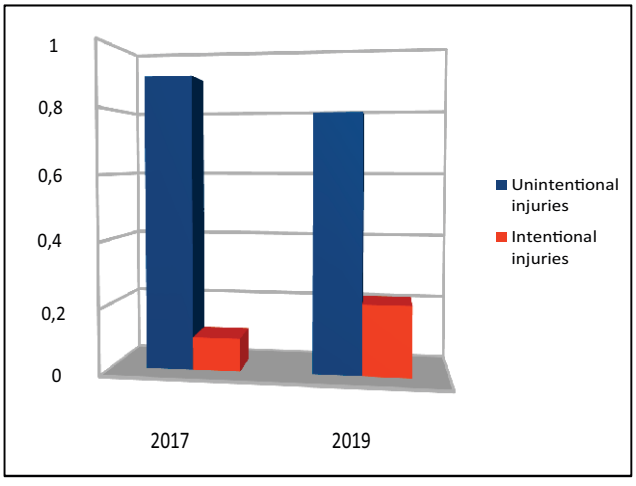


Figure 2 **Injuries by intention.**

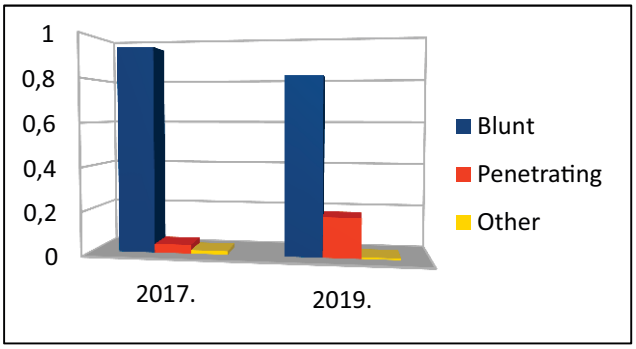


Figure 3 **Injuries by mechanism.**

Figure 3 shows the comparison of injuries' mechanism in two observed years according to ICECI. For this analysis all kinds of penetrating injuries, specified and unspecified, were included. Gunshots were also included. Thermal and chemical exposure, natural force, threat to breathing and (non)specific mechanical force damages although separate categories, for this analysis were put together and marked as "other". It is necessary to note that some of the multiply injured patients suffered two or more kind of force and had different injuries according to mechanism. In those cases, only one injury per patient, the life-threatening one, was considered.

In 2019 there was a statistically significant raise of penetrating injuries ($p<0.05$), related to significant fall of blunt injuries ratio ($p<0.05$). In 2017, 94.40% related to blunt injuries, but in 2019, that was 81.06% (13.34 % decrease). Penetrating injuries raised from 4.00% to 18.18%, which was 14.18% raise ($p<0.05$). Other kind of injuries didn't have significant change of percentage ($p>0.05$). Migrants with penetrating injuries took 9.09% of all patients in 2019 as presented in Table 1. Without their contribution, there would be no significant change of ratio among different types of injuries. This implicates the changes they made.

Table 1 **Distribution of injuries by mechanism between migrants and other patients.**

Type of injury	2017		2019	
	Migrants	Other patients	Migrants	Other patients
Blunt	0.00%	94.40%	0.76%	80.30%
Penetrating	0.00%	4.00%	9.09%	9.09%
Other	0.00%	1.60%	0.00%	0.76%

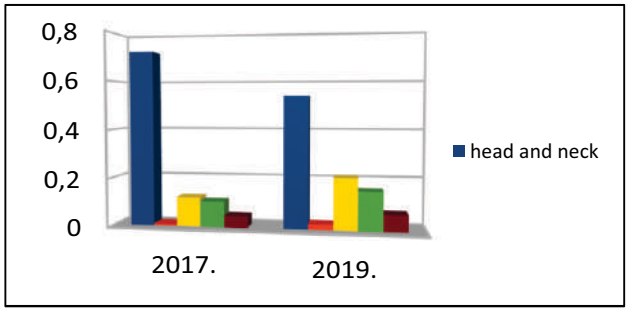


Figure 4 **Topographic distribution of the most severe injuries according to ISS body regions.**

According to definition, trauma maior is life threatening injury where either one or more body regions are affected. In multiple trauma there are two or more injuries from different regions, but one is the most affected and caused the most severe damages which are the potentional threat for survival. Figure 4 shows body regions according to ISS. Only one injury, and the most severe one from each of the observed patients was taken into consideration. It was evident that percentage of the head and neck injuries decreased by 18.09% (from 71.88% in 2017 to 53.79% in 2019), which was statistically significant ($p<0.05$). At the same time, there was a significant percentual increase in the chest and thoracic spine injuries by 9.1% (from 12.11% in 2017 to 21.21% in 2019), ($p<0.05$). There was also percentual increase in the abdominal content and lumbar spine injuries by 5.36% (from 10.55% in 2017 to 15.91% in 2019), which was not significant ($p>0.05$). Furthermore, percentage of injuries of other two body regions face and pelvic girdle with extremities insignificantly increased for 1.49% and 2.13% respectively ($p>0.05$).

DISCUSSION

Migrants contributed with 9.85% of all patients in 2019which made them noticeable in everyday care of severely injured people in emergency rooms. Poverty is considered as one of the main risk factors for intentional injuries (6). Therefore, the fact that all of the observed migrants suffered from intentional injuries was not surprising. Researches also showed that men exposed to stress had higher incidence of violent behavior and consequent injuries (7). In this research all of the observed migrants were men. Living in disorganised neighborhoods with disorder of social relationships encourages violent behavior (8). According to one of the researches history of homelessness is also connected with higher incidence of violent injuries (9). Migration and consequent changing the way of life may have impact to psychological condition of these people what also can be trigger for violent behavior and consequent injuries (10). Intentional injuries are recognised as preventable health problem (unintentional also), so worldwide there are continuous efforts to create and implement programs for prevention, either national or global (11,12) with the aim to minimise the morbidity and mortality, but also the costs of the health systems (13).

Analysis of observed patients and comparison between 2017 and 2019 showed significant raise of the number of penetrating injuries. Migrants contributed to that result, but even without them, raise was also evident in groups of other patients. This fact has impact to health care providers as there are different approaches to blunt and penetrating injuries, even from the first contact with the injured patient. Primary and secondary surveys are performed in emergency services and hospital emergency departments (Clinic of Emergency Medicine of the CCUS being one of them). Final treatment includes multiple hospital resources (14). Prompt and correct actions are necessary since these injuries are related to higher mortality rate. According to one of the researches in the USA prehospital mortality of penetrating injuries is raising despite the improvement of prehospital care (15) so increasing number of this kind of patients makes burden to emergency services and makes them obligated to improve, which may require costs enhancement. Time is one of the main factors of success in these cases. Not only the time of prehospital medical transport, but also the time spent in hospital emergency units before the prompt surgical intervention which is still considered crucial for rescuing patients with penetrating injuries (16). Increase of the number of these patients requires improvement of organisation and coordination between emergency departments and other, specially different surgical, departments inside hospitals to ensure multidisciplinar and early interventions. Improving the skils in everyday work with this kind of patients and making higher experience results in lowers mortality rate (17). If we go back to results of this analysis we can see significant difference in topographic distribution of the moste severe injuries. There was significance raise of chest injuries and insignificant raise of abdominal injuries as directly life-threatening. Stronger engagement of thoracic and abdominal surgeons and their mobilisation for prompt surgical response is required but adequate workspace, equipment and coordination are necessary for improving it. We must not forget that time has important role. All the human and material resources have to be organized to ensure fast and quality actions.

CONCLUSION

Migrants took a notable part (9.85%) of the patients with life-threatening injuries in 2019. Migrant crisis was related to significant increase of intentional injuries of 11.50% in 2019 in comparison to 2017, considering the fact that all of the migrants were suffering from intentional injuries (100%). According to mechanism it was connected with significant increase of penetrating injuries of 14.08%. Acccording to injury localisation it was connected with significant increase of severe chest injuries of 9.1%, insignificant increase of face, abdominal, pelvis with extremities injuries and consequent significant decrease of head and neck injuries of 18.09%. Injuries, especially intentional are considered preventable, so there is a need of creating and immediate implementing systematic injury prevention strategies in our country. Increase of penetrating injuries makes obligatory for health service to improve faster and to be more organised medical response in emergency services, but also multidisciplinary approach given the topografic distribution of the most affected body regions. This was specially important if the number of migrants in our country would increase.

REFERENCES

1. www.eurosafe.eu.com/home
2. Horan JM, Mallonee S. Injury Surveillance. Epidemiol Rev. 2003;25:24-42.
3. McClure RJ, Mack K, Wilkins N, Davey TM. Injury prevention as social change. Inj Prev. 2016;22(3):226-9.
4. Rau CS, Wu SC, Kuo PJ, Chen YC, Chien PC, Hsieh HY, et al. Polytrauma Defined by the New Berlin Definition: A Validation Test Based on Propensity-Score Matching Approach. Int J Environ Res Public Health. 2017;14(9):1045.
5. International Classification of External Causes of Injuries (ICECI) Available at: https://www.whofic.nl/sites/default/files/2018-05/ICECI%20in%20English.pdf
6. Laytin AD, Shumway M, Boccellari A, Juillard CJ, Dicker RA. Another "Lethal Triad"- Risk Factors for Violent Injury and Long term Mortality Among Adult Victims of Violent Injury. J Emerg Med. 2018;54(5):711-718.
7. Reidy DE, Berke DS, Gentile B, Zeichner A. Masculine discrepancy stress, substance use, assault and injury in a survey of US men. Inj Prev. 2016;22(5):3704.
8. Butcher F, Galanek JD, Kretschmar JM, Flannery DJ. The impact of neighborhood disorganization on neighborhood exposure to violence, trauma symptoms, and social relationships among at-risk youth. Soc Sci Med. 2015;146:300-6.
9. Jetelina KK, Reingle Gonzalez JM, Brown CVR, Foreman ML, Field C. Acute Alcohol Use, History of Homelessness, and Intent of Injury Among a Sample of Adult Emergency Department Patients. Violence Vict. 2017;32(4):658-670.
10. Poole GV, Lewis JL, Devidas M, Hauser CJ, Martin RW, Thomae KR.

Psychopathologic risk factors for intentional and nonintentional injury. J Trauma. 1997;42(4):711-5.
11. Cunningham R, Knox L, Fein J, Harrison S, Frisch K, Walton M et al. Before and After the Trauma Bay: The Prevention of Violent Injury Among Youth. Ann Emerg Med. 2009;53(4):490-500.
12. Rivara FP, Cummings P, Koepsell TD, Grossman DC, Maier RV. Injury Control: A Guide to Research and Program Evaluation. Cambridge University Press. 2001.
13. Coupet Jr E, Karp D, Wiebe DJ, Delgado MK. Shift in U.S. payer responsibility for the acute care of violent injuries after the Affordable Care Act: Implications for prevention. Am J Emerg Med. 2018;36(12):2192-2196.
14. Raja, AS and Zane, R. Initial Management of Trauma in Adults. In: Rose, BD (Ed), UpToDate. UpToDate, Waltham, MA. 2010.
15. Sakran JV, Mehta A, Fransman R, Nathens AB, Joseph B, Kent A, et al. Nationwide trends in mortality following penetrating trauma: Are we up for the challenge? J Trauma Acute Care Surg. 2018;85(1):160-166.
16. Nasser AAH, Nederpelt C, El Hechi M, Mendoza A, Saillant N, Fagenholz P, et al. Every minute counts: The impact of pre-hospital response time and scene time on mortality of penetrating trauma patients. Am J Surg. 2019;220(1)240-244.
17. Fu CY, Bajani F, Tatebe L, Butler C, Starr F, Dennis A, et al. Right hospital, right patients: Penetrating injury patients treated at high-volume penetrating trauma centers have lower mortality. J Trauma Acute Care Surg. 2019;86(6):961-966.

Reprint requests and correspondence:
Amela Ahmić, MD, MSc
Clinic of Emergency Medicine
Clinical Center University of Sarajevo
Bolnička 25, 71000 Sarajevo
Bosnia and Herzegovina
Email: amelatuco@gmail.com
ORCID ID: 0000-0002-7777-1204

Declaration of patient consent: The author certifies that she has obtained all appropriate patient consent forms.
Author's Contribution: AA gave substantial contribution to the conception or design of the article as well as in the acquisition, analysis, and interpretation of data for the work. She had a role in the drafting and revision of the article. Additionally, she gave final approval of the version to be published and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

Effects of video assisted toracoscopic pleurodesis on life quality of patients with malignant pleural effusions

Efekti videoasistirane torakoskopske pleurodeze na kvalitet života kod pacijenata sa malignim pleuralnim izljevima

Alma Alihodžić-Pašalić[1*], Veljko Marić[2], Ilijaz Pilav[1]

[1]Clinic of Thoracic Surgery, Clinical Center University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina
[2]Faculty of Medicine Foča, University of East Sarajevo, Studentska 5, 73300 Sarajevo, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

Introduction: malignant pleural effusions (MPE) indicate poor prognosis and quality of life. Treatment of MPE remains palliative with average survival of 3-12 months. Chemical pleurodesis (CP) controls effusion re-accumulation, alleviates pain, dyspnea and improves quality of life. Aim: to investigate which pleurodesis administration gives the best results. Materials and methods: sample of 180 patients was divided into three groups, 60 patients each. First group (G1) underwent VideoAssistedThoracoScopic (VATS) pleurodesis, second group (G2) pleurodesis via standard drainage and third group (G3) underwent thoracostomy with pleural catheter with subsequent pleurodesis. Karnofsky scale, dyspnea determining scale and ECOG performance scale were used to assess patients' condition**.** Results: the average value of Karnofsky score in G1 before pleurodesis was 74.83±8.924 and 94.33±8.71 after, and statistically significant increase of Karnofsky score was determined after intervention in G1 ($p<0.0001$), G2($p<0,0001$) and G3 ($p<0,0001$). Average intensity of dyspnea before and after pleurodesis was analyzed, and statistically significant reduction of symptoms' intensity was determined in all groups – G1 ($z=6.736$, $p<0.0001$), G2 ($p<0.0001$) and G3 ($p<0.0001$). ECOG performance scale was used to determine patients' level of functionality before and after pleurodesis, and statistically significant improvement was noted in all groups - G1 ($p<0.0001$), G2 ($p<0.0001$) and G3 ($p<0.0001$). Conclusion: patients treated with VATS pleurodesis experienced greatest alleviation of symptoms and signs of disease, improved functionality and were less dependent on others in preforming different activities.

Keywords: VATS, pleurodesis, quality of life

SAŽETAK

Uvod: maligne pleuralne efuzije su pokazatelj loše prognoze i kvaliteta života. Liječenje MPE je i dalje palijativno, sa prosječnim preživljavanjem od 3-12 mjeseci. Hemijska pleurodeza (HP) spriječava reakumulaciju efuzije, smanjuje bol, dispneju i povećava kvalitet života. Cilj: istražili smo koji postupak pleurodeze daje najbolje rezultate. Materijali i metode: uzorak od 180 pacijenata smo podijelili u tri grupe, od po 60 pacijenata. Prva grupa (G1) su bili pacijenti na kojima je rađena VideoAssistedThoracoScopic (VATS) pleurodeza, drugoj grupi (G2) je rađena pleurodeza preko standardne drenaže, a trećoj grupi je rađena torakostomija sa naknadnom pleurodezom kroz pleuralni kateter. Za procjenu stanja pacijenta koristili smo Karnofski skalu, dispneja determinantnu skalu i ECOG performans skalu. Rezultati: prosječna vrijednost Karnofski skora prije pleurodeze i nakon pleurodeze je pokazala statistički značajnu razliku u G1 ($p<0.0001$), G2($p<0,0001$) i u G3 ($p<0,0001$). Prosječan intenzitet dispneje je ispitan prije i poslije pleurodeze, i pronašli smo statistički značajno smanjenje simptoma u svim grupama: G1 ($p<0,0001$), G2 ($p<0,0001$) i G3 ($p<0,0001$). ECOG performans skalom se mjerio nivo funkcionalnosti pacijenata prije i poslije pleurodeze, i statistički značajno poboljšanje je pronađeno u svim grupama: G1 ($p<0,0001$), G2 ($p<0,0001$) i G3 ($p<0,0001$). Zaključak: pacijenti liječeni sa VATS pleurodezom su imali najveće olakšanje svih simptoma i znakova bolesti, poboljšanu funkcionalnost i bili su manje ovisni od trećih lica u obavljanju različitih aktivnosti.

Ključne riječi: VATS, pleurodeza, kvalitet života

INTRODUCTION

Patients with malignant pleural effusions (MPE) are treated mainly symptomatically, with palliation of dyspnea being the main objective of the therapy. Chemical pleurodesis (CP) is generally accepted palliative therapy for patients with recurrent MPE. The main objective of chemical pleurodesis is to create adhesions between the visceral and parietal pleura which eliminates the presence of pleural space preventing re-accumulation of fluid (1,2,3). Different methods of pleurodesis yield different results, some are more efficient than others, and improve health and quality of life of patients more. VATS (Video Assisted ThoracoScopy) pleurodesis is gradually replacing standard methods of pleurodesis and as such is being inaugurated as treatment of choice for MPI (2,3). However, despite VATS becoming a golden standard, other methods are still being used to this day, which are superseded and less beneficiary to the patients.

AIM

Primary goal of this study was to determine advantages of VATS pleurodesis on quality and comfort of life of the patients suffering from MPE, regulated by Karnofsky scale, dyspnea grading scale and ECOG performance scale over other conventional methods to incline physicians to perform more VATS pleurodeses' than other methods, where applicable.

MATERIALS AND METHODS

In the period from 1 October 2017 to 1 May 2019, randomized experimental study was conducted with the permission of Ethical Committee of the Clinical Center University of Sarajevo. Randomization was performed using MedCalc v12.6 as a triple blinded study, where each patient received an earlier assigned 4-digit number. First digit of the number determined the group where patient was placed. Inclusion criteria were: patients of both sexes over 18, with established recurrent pleural effusion due to previously established malignancy, and Karnofsky index ≥50%, life expectancy greater than 30 days. Based on the procedure they underwent, patients were randomly distributed in three groups. First group (G1) included 60 patients who underwent VATS pleurodesis, second group (G2) 60 patients who underwent standard thoracostomy and pleurodesis, and third group (G3) included 60 patients who underwent thoracostomy with pleural catheter and pleurodesis.

A basic criterion for estimating success of pleurodesis was monthly clinical and radiological control of pleural effusion during the first three months after pleurodesis. Success of pleurodesis was categorized as complete (no re-accumulation in three months), partial (lesser re-accumulation than amount before pleurodesis), and failed (same or greater re-accumulation). Patients' subjective parameters were compared, in relation to effect of pleurodesis on quality and comfort of life: Karnofsky scale, dyspnea grading scale and ECOG performance scale.

Statistical analysis of data was performed by SPSS (Statistical package for Social Sciences-Version 19) with application of Student t-test assuming equal variances, Mann-Whitney U-test of independent samples, Chi-Square and Wilcoxon test for paired samples. Determined level of significance was $p < 0.05$. The obtained results were compared to the data of relevant research in literature with the presentation of discussion and comments of individual results.

RESULTS

Out of the total number of participants included in the study, 40.5% (73/180) were men and 59.5% (107/180) women (F/M=1.465:1), divided into groups. Group G1 - 41.6% (25/60) men and 58.3% (35/60) women (F/M=1.40:1); G2 - 47.5% (29/60) men and 52.4% (31/60) women (F/M=1.06:1) and G3 - 31.6% (19/60) men and 68.3% (41/60) women (F/M=2.15:1).

The average age of the patients was 63.97±8.75 (31-80) years, and for groups: G1 - 63.92±8.53 (34-80), G2 - 64.56±6.45 (47-80) and G3 - 60.42±10.39 (31-80) years. There was no statistically significant difference among the participants compared to control G2 ($p=0.6424$) and G3 ($p=0.04$).

The average hospitalization of patients was 7.22±1.37 (5-13) days, and for groups: G1- 6.68±1.16 (5-12) days, G2 - 7.44±1.40 (6-13) G3- 7.52±1.41 (7-13) days. There was statistically significant difference in duration of hospitalization between the G1 and G2 ($p=0.0016$) and G1 and G3 ($p=0.0004$).

The average duration of thoracic drainage was 5.45±1.69 (3-12) days, and for groups: G1- 4.28±1.15 (3-10) days; G2 - 6.05±1.58 (5-12) days; G3 - 6.00±1.66, (5-12 days). Analysis showed statistically significant difference in duration of thoracic drainage between the G1 and G2 ($p<0.0001$), G1 and G3 ($p<0.0001$).

Success of pleurodesis after the first month pursuant to the chest x-ray showed no significant statistical difference in the outcome of the pleurodesis among the groups after the first month ($p=0.2089$). Success of pleurodesis after the second month showed statistically significant difference in efficiency of pleurodesis after second month among the groups G1 and G2 ($p=0.0011$) G1 and G3 ($p=0.0062$). Efficiency of pleurodesis after the third month was between G1 and G2 ($p=0.0006$) and between G1 and G3 ($p<0.0001$) (Figure 1).

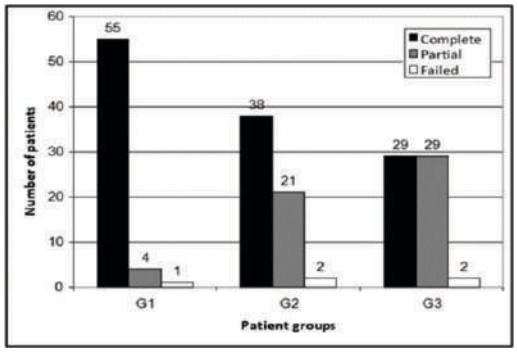


Figure 1 Success of pleurodesis after third month.

Average Karnofsky score in G1 was 74.83±8.924 before pleurodesis and 94.33±8.71 after pleurodesis and statistically significant increase of Karnofsky score was determined in G1 (before: 74.83±8.924, after: 94.33±8.71; $t=25.41$, $p<0.0001$), G2 (before: 70.98±8.70, after: 85.57±9.40; $p<0.0001$) and G3 (before: 68.00±9.53, after: 82.50±10.99; $p<0.0001$) (Figure 2). Statistically significant difference of Karnofsky score among the groups after pleurodesis was determined; between G1 and G2 ($p<0.0001$) and also between G1 and G3 ($p<0.0001$).

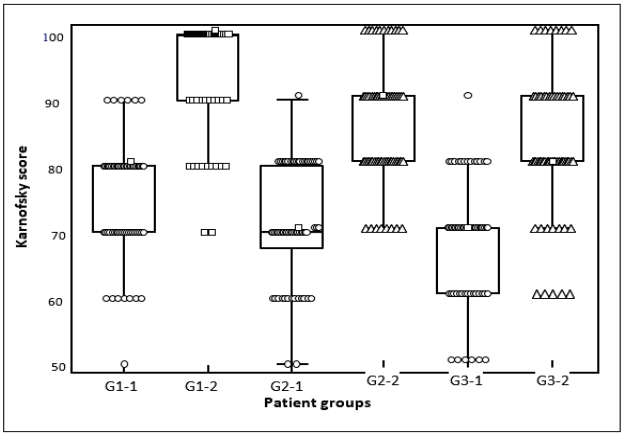


Figure 2 **Karnofsky score in groups, before (G#-1) and after pleurodesis (G#-2).**

The average degree of dyspnea in G1 prior to pleurodesis was 3.28±0.64, and afterwards 0.050±0.22 (p<0.0001) reduction of dyspnea. In G2 the average degree of dyspnea prior to pleurodesis was 4.10±0.68, and afterwards 0.62±0.76 (p<0.0001). In G3 the average degree of dyspnea prior to pleurodesis was 4.22±0.72, and afterwards 0.77±0.79 (p<0.0001). Statistically significant difference was determined in the degree of dyspnea after the pleurodesis between the G1 and G2 (p=0.0001), G1 and G3 (p=0.0001) (Figure 3).

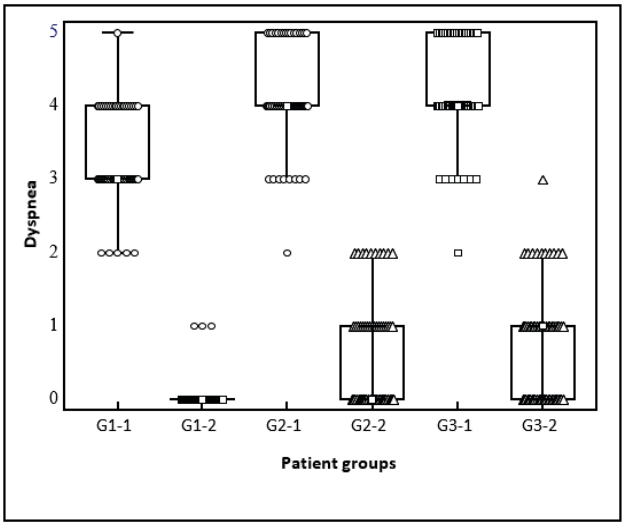


Figure 3 **Values of dyspnea scale in groups, before (G#-1) and after pleurodesis (G#-2).**

The average value of ECOG performance scale before and after pleurodesis for G1 was 2.15±0.70 and 0.03±0.18 after, for G2 was 2.87±0.56 and 0.59±0.74 after and for G3 was 2.85±0.73 and 0.70±0.74 after, which was statistically significant improvement of functional performance status after pleurodesis (G1: p<0.0001; G2: p<0.0001; G3: p<0.0001). Analysis of ECOG score before and after pleurodesis determined statistically significant difference in ECOG score values between G1 and G2 (before pleurodesis: p<0.0001; after pleurodesis: p<0.0001), and between G1 and G3 (before pleurodesis p<0.0001; after pleurodesis: p<0.0001). Post-operative complications were documented in 13.3% (24/180) of all patients (G1 -3.3% (2/60), G2- 15.0% (9/60) G3- 21.6% (13/60) (Figure 4)

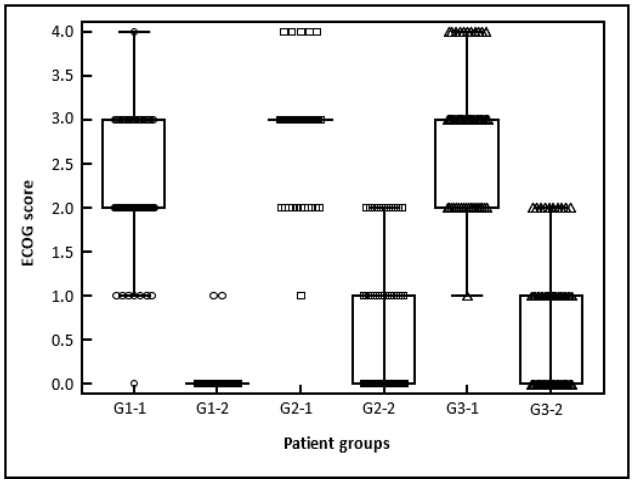


Figure 4 **ECOG score in groups, before (G#-1) and after pleurodesis (G#-2).**

DISCUSSION

Despite the achievements in the treatment of carcinoma, treatment of malignant pleural effusion remains palliative with average survival of patients being 3-12 months from the moment of diagnosis (1,2,3). Treatment of initial or recurrent MPE may be very simple and efficient but also very difficult and complex. Since patient survivability is limited, efficient symptom relief and reduction of hospitalization must be ensured as well as improved quality of life. Best therapeutical results are seen in patients with relatively good general condition, with localized disease and life expectancy of 6 months or more. Chemical pleurodesis can be performed by different medical procedures such as thoracentesis, thoracostomy-standard or with pleural catheter, VATS or thoracotomy with pleuroperitoneal shunt (1-9). Nowadays, VATS pleurodesis is used more often and it proved to be safe procedure with low rate of morbidity and mortality and as such it gradually replaces the standard modes of pleurodesis. In that manner, some authors try to inaugurate it as a procedure of choice in the treatment of MPE (9-13). Despite numerous similar studies being published, there is still no universal standard on these issues (11,14-20).

Abouzgheib, et al. (2009) reported that the average duration of hospitalization was 9 days after the VATS pleurodesis. Likewise, Fortin, et al. (2015) stated that the period of hospitalization was from 4 to 7 days for VATS pleurodesis (1). Troter, et al. (2005) and Mitrofan, et al. (2005) mention that the period of hospitalization for VATS talc pleurodesis was 7-10 days (3,4). The comparison of results related to duration of hospitalization obtained in this study (7.22±1.37 (5-13) days; Mann Whitney U-test - G1/G2: z=3.151, p=0.0016; G1/G3: z=3.518, p=0.0004) with the results obtained in the mentioned literature, suggests that in majority of cases those results do in fact correspond.

In this study, average duration of thoracic drainage for GI was 4.28±1.15 (3 -10) days which corresponds with other

authors (Khalil, et al. (2016.) - 4.73±0.3 days, Chen, et al. (2015) - 4.74±1.56 days, Verma, et al. (2016) - 4.5 (1-6) days, Basso, et al. (2012) - 9.4±4.1, Luh, et al. (2006) - 6.2±2.3 days) (7,8,9). Application of Mann-Whitney U-test of independent samples showed statistically significant difference in duration of thoracic drainage between the G1 and G2 ($z=7.574$, $p<0.0001$), G1 and G3 ($z=7.230$, $p<0.0001$), which corresponds to results from other authors. It may be concluded that such values are in similar ranges, whereby it is evident that duration of pleural drainage was shorter in case of VATS pleurodesis.

When comparing success of pleurodesis in this study with that of other authors, our success of pleurodesis after third month showed the statistically significant difference in the efficiency of pleurodesis, between G1 and G2 ($\chi^2=14.994$, $p=0.0006$) and also between G1 and G3 ($\chi^2=27.32$, $p<0.0001$). VATS pleurodesis was successful in 98.30% in the first two months and 91.60% after third month. This corresponds with results from other authors, who reported that pleurodesis was more successful when performed with VATS (Zarogoulidis, et al. (2013): 60-100% overall success; Chen, et al. (2015): 65.41% (694/1061) complete, 22.62% (240/1061) partial and 11.97% (127/1061) unsuccessful, of which, VATS pleurodesis was successful in 90-96% of cases) (6,10). However, results varied greatly in relation to individual techniques of pleurodesis.

Analysis of Karnofsky score in our study shows an increase of Karnofsky score regardless of procedure used, but remarkably for G1 (74:94). Other authors used Karnofsky score as a predictor of survivability, where Yoon, et al. (2016) and Steger, et al. (2007) noted that pre-operative Karnofsky score <60% corresponds to lower survival rate (11,12). Burrows, et al. (2000) noted that Karnofsky score ≥70 corresponded to an average patients' survival of 395 days (13). Combining results of our study with aforementioned study inferred that VATS pleurodesis improves quality of life as well as survivability.

When researching effect of VATS pleurodesis on dyspnea, Boujaoude, et al. (2015) used Borg's scale and they determined reduction of dyspnea score from 8.34 to 3.2 ($p<0.001$) after talc pleurodesis (14). Basso, et al. (2012) report dyspnea reduction from 4.2±0.8 to 2.7±1.0 before and after VATS pleurodesis (8). Koledin, et al. (2001) report that after pleurodesis 96% of patients did not experience dyspnea and Tremblay, et al. (2006) report partial or total improvement in 88.8% of patients after pleurodesis with pleural catheter (15,16). Van Meter, et al. (2011) determined symptomatic improvement of dyspnea in 95.6% of the patients after pleurodesis (17). Dhaliwal, et al. (2016) reported statistically significant ($p<0.0005$) improvement of dyspnea after pleurodesis (18). Reddy, et al. (2011) reported that before VATS talc pleurodesis Borg scale score in patients was 4.9 and 1.6, seven days after pleurodesis (19).

Analysis of result of ECOG performance scale in this study has shown statistically significant improvement of ECOG score after pleurodesis in G1 in relation to G2 and G3 ($p<0.0001$; 2:0). Other studies in available literature used ECOG performance scale as a predictor of survivability. As such, Yoon, et al (2016.) determined that after VATS pleurodesis, during follow-up course of two years, patients with poor performance status (ECOG 3 and 4) had negative predictive value on overall survivability of these patients (11). Zamboni, et al. (2015) report that patients with ECOG performance status of 0 had longest average survivability (55 months), while those who scored more had shorter survival period (1 - 22 months; 2 - 18 months; 3 - 7 months; 4 - 1 month) (20). Burrows, et al. (2000) and Anevlavis, et al. (2014) determined that ECOG performance score was significant predictive factor of survivability in patients with MPE (13,21). We can determine that ECOG performance scale in this study also had significant survivability prediction factor, since there is statistically significant improvement of ECOG score that due to time constraints (3 months) was not measured. However, during the follow-up period of this study, no lethal outcomes were documented.

The complications of thoracoscopy were usually moderate and included pain, dyspnea, procedure related respiratory insufficiency, hemorrhage, hypotension, heart arrhythmia, prolonged air leakage, subcutaneous emphysema, postoperative fever, pleural empyema, infection of operative wound and dissemination of malignancy along the thoracic wall (1-7). In this study, during the first three months of monitoring, there were no severe morbidities or lethal cases. The frequency of complications in patients included in this research corresponds to quotations of other authors form the available literature sources (1,13-18). Verma, et al. (2016) published that the complications occurred in 14.6% patients (7). VATS pleurodesis in comparison with other pleurodesis techniques is generally considered safe because complications are same or lesser compared to prior techniques.

CONCULSION

Patients treated with VATS pleurodesis experienced greatest alleviation of symptoms and signs of disease, improved functionality and were less dependent on others in performing different activities. It can be concluded that VATS pleurodesis should be used whenever applicable as it is best technique for managing of MPE.

REFERENCES

1. Abouzgheib W, Bartter T, Dagher H, Pratter M, Klump W. A prospective study of the volume of pleural fluid required for accurate diagnosis of malignant pleural effusion. Chest. 2009;135(4):999-1001.
2. Fortin M, Tremblay A. Pleural controversies: indwelling pleural catheter vs. pleurodesis for malignant pleural effusions. J Thorac Dis. 2015;7(6):1052-7.
3. Trotter D, Aly A, Siu L, Knight S. Video-assisted thoracoscopic (VATS) pleurodesis for malignant effusion: an Australian teaching hospital's experience. Heart Lung Circ. 2005;14:93-97.
4. Mitrofan C, Aldea A, Grigorescu C, Jitaru I, Losep G, Arama A, et al. Pleurodeza Toracoscopica in pleureziile maligne. [Thoracoscopic pleurodesis in malignant pleural effusions]. Rev Med Chir Soc Med Nat Iasi. 2005;109(4):799-803.
5. Khalil M, Shoukri AM. Thoracoscopic tetracycline poudrage for pleurodesis in malignant pleural effusion. Egypt J Bronchol. 2016;10:100-4.
6. Chen M, Wang X, Yu X. Pleural effusion as the initial clinical presentation in disseminated cryptococcosis and fungaemia: an unusual manifestation and a literature review. BMC Infect Dis. 2015;15:385.
7. Verma A, Dagaonkar RS, Marshall D, Abisheganaden J, Light RW. Differentiating Malignant from Tubercular Pleural Effusion by Cancer Ratio Plus (Cancer Ratio: Pleural Lymphocyte Count). Can Respir J. 2016;2016:7348239.
8. Basso SM, Mazza F, Marzano B, Santeufemia DA, Chiara GB, Lumachi F. Inproved quality of life in patients with malignant pleural effusion following videoassisted thoracoscopic talc pleurodesis. Preliminary results. Anticancer Res. 2012;32(2):5131-4.
9. Luh SP, Chen CY, Tzao CY. Malignant Pleural Effusion Treatment Outcomes: Pleurodesis via Video-Assisted Thoracic Surgery (VATS) Versus Tube Thoracostomy. Thorac Cardiovasc Surg. 2006;54(5):332-336.
10. Zarogoulidis K, Zarogoulidis P, Darwiche K. Malignant pleural effusion and algorithm management. J Thorac Dis. 2013;5(4):S413-S419.
11. Yoon DW, Cho JH, Choi YS. Predictors of survival in patients who underwent video-assisted thoracic surgery talc pleurodesis for malignant pleural effusion. Thorac Cancer. 2016;7:393-398.
12. Steger V, Mika U, Toomes H. Who gains most? A 10-year experience with 611 thoracoscopic talc pleurodeses. Ann Thorac Surg. 2007;83:1940-1945.

13. Burrows CM W. Mathews WC, Colt HG. Predicting Survival in Patients with Recurrent Symptomatic Malignant Pleural Effusions: An Assessment of the Prognostic Values of Physiologic, Morphologic, and Quality of Life Measures of Extent of Disease. Chest. 2000;117(1):73-78.
14. Boujaoude Z, Bartter T, Abboud M, Pratter M, Abouzgheib W. Pleuroscopic Pleurodesis Combined With Tunneled Pleural Catheter for Management of Malignant Pleural Effusion: A Prospective Observational Study. J Bronchology Interv Pulmonol. 2015l; 2(3):237-43.
15. Koledin M, Đurić D, Bijelović M, Baroš B. Pleurodeza talkom kod pleuralnih izliva maligne etiologije. Pneumon. 2000;38:37-43.
16. Tremblay A, Michaud G. Single-center experience with 250 tunnelled pleural catheter insertions for malignant pleural effusion. Chest. 2006;129(2):362-8.
17. Van Meter ME, McKee KY, Kohlwes RJ. Efficacy and safety of tunneled pleural catheters in adults with malignant pleural effusions: a systematic review. J Gen Intern Med. 2011;26(1):70-6.
18. Dhaliwal I, Mahdavian M, Asghari S, Chun To Wong B, Labelle R, Amjadi K. Management of Malignant Pleural Effusion with ASEPT® Pleural Catheter: Quality of Life, Feasibility, and Patient Satisfaction. Can Respir J. 2016; 2016:4273480.
19. Reddy C, Ernst A, Lamb C, Feller-Kopman D. Rapid Pleurodesis for Malignant Pleural Effusions: A Pilot Study. Chest. 2011;139(6):1419-1423.
20. Zamboni MM, da Silva CT, Jr, Baretta R, Cunha ET, Cardoso GP. Important prognostic factors for survival in patients with malignant pleural effusion. BMC Pulm Med. 2015;15:29.
21. Anevlavis S, Kouliatsis G, Sotiriou I, Koukourakis MI, Archontogeorgis K, Karpathiou G, Giatromanolaki A, Froudarakis ME. Prognostic factors in patients presenting with pleural effusion revealing malignancy. Respiration. 2014;87(4):311-316.

Reprint requests and correspondence:
Alma Alihodžić-Pašalić, MD, PhD
Clinic of Thoracic Surgery
Clinic Center University of Sarajevo
Bolnička 25, 71000 Sarajevo
Bosnia and Herzegovina,
Phone: + 387 61 216 245
Email: alma_ap68@yahoo.com
ORCID ID: 0000-0001-5950-4148

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: AA-P, VM and IP gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

Descriptive analysis of breast cancer sentinel lymph node biopsy use at Clinical Center University of Sarajevo

Deskriptivna analiza upotrebe biopsije stražarskog limfnog čvora kod karcinoma dojke na Kliničkom centru Univerziteta u Sarajevu

Emir Bičakčić[1*], Sadat Pušina[1], Mirhan Salibašić[1], Emina Bičakčić-Filipović[2]

[1]Clinic of General and Abdominal Surgery, Clinical Center University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina
[2]Oncology Clinic, Clinical Center University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

Introduction: the use of sentinel biopsy (SLNB) represents the standard of care in treating breast cancer. This method is routinely used in Department of Glandular surgery Clinical Center University of Sarajevo (CCUS), with the total of 75 patients. Aim: to represent the experience from the data we gathered in a year's experience and to compare it with the current literature. Materials and methods: a retrospective, clinically applied, descriptive study was conducted at Department of General Surgery of the Clinical Center University of Sarajevo in the period from January 2018 to December 2018. The data source was medical records of 75 patients with histopathologically verified breast cancer who were treated by using sentinel lymph node biopsy in 2018. The data were analyzed using descriptive statistical methodology and presented through tables, as well as compared with data from contemporary international studies Results: in our study we have analyzed data a total of 75 patients who were treated by using SLNB technique during 2018. Out of total number of patients in only one case SLN was undetectable. The median patient's age was 50.5 years. The most common T stage was T1 in 34 (45.9%) patients followed by T2 in 27 (36.4%) cases. In 45 patients (60.8%) number of retrieved sentinel lymph nodes was 1, whereas 2 sentinel lymph nodes were retrieved in 22 (29.7%) patients and 3 sentinel lymph nodes were harvested in 6 (8.1%) of patients. Seventeen patients (22.3%) were found to have a positive SN, out of which 15 (78.9%) were diagnosed with macrometastases and were treated with ALND. Total number of micrometastases that we've managed to retrieve was 4 (23.5%), out of which 2 were retrieved during the operative procedure and proceeded into an partial ALND and 2 were discovered in the permanent axillary specimen finding, with no further surgical treatment provided. In 9 (52.3%) out 17 nineteen positive cases, SLN were the only positive lymph nodes. Conclusion: SLN biopsy remains undoubtedly the method of choice in early-stage breast cancer, with false negative rate remaining an issue which could be resolved by increasing the number of sentinel lymph node harvested.

Keywords: breast cancer, SLN biopsy, axillary lymph nodes

SAŽETAK

Uvod: upotreba biopsije stražarskog limfnog čvora predstavlja standard u tretmanu pacijenata koje pate od raka dojke. Ova se metoda rutinski koristi na Odjeljenju za Glandularnu hirurgiju Kliničkog centra u Sarajevu, sa ukupnim brojem od 75 učinjenih procedura u 2018. Cilj: predstaviti iskustva iz prikupljenih podataka kao i usporedba istih sa suvremenom literaturom. Materijali i metode: retrospektivna, klinički potvrđena, deskriptivna studija je sprovedena na Odjeljenju glandularne hirurgije Kliničkog Centra u Sarajevu u periodu januar - decembar 2018. Izvor podataka je medicinska dokumentacija 75 pacijentica sa patohistološki potvrđenim rakom dojke i koje su tretirane biopsijom stražarskog limfnog čvora u 2018. Podaci su obrađeni koristeći deskriptivnu statističku metodologiju i prezentirani u obliku tabela, kao i usporedbom sa podacima iz suvremenim internacionalnim studijama. Rezultati: analizirani su podaci od ukupno 75 pacijentica tretiranih metodom biopsije stražarskog limfnog čvora tokom 2018. godine. Od ukupnog broja pacijentica u jednom slučaju stražarski limfni čvor nije bio detektabilan. Prosječna dob pacijentica je bila 50.5 godina. Najčešći T stadij je bio T1kod 34 (45.9%) pacijentica, te T2 stadij sa 27 (36.4%). Kod 45 (60.8%) pacijentica broj odstranjenih stražarskih limfnih čvorova je iznosio 1, dok je kod 22 (29.7%) pacijentice taj broj iznosi 2, a kod 6 (8.1%) pacijentica je bilo 3 čvora. Kod sedamnaest (22.3%) pacijentica je stražarski limfni čvor bio pozitivan, od kojih su kod 15 (78.9%) dijagnosticirane makrometastaze. Ukupan broj mikrometastaza koje smo ustanovili je 4 (21%), od kojih smo u 2 slučaja iste ustanovili tokom operativnog zahvata i potom učinili parcijalnu aksilarnu disekciju, dok su u 2 slučaja iste bile otkrivene u trajnom patohistološkom uzorku, gdje dalji hirurški tretman nije sproveden. U 9 (52.9%) od 17 pozitivnih slučajeva, stražarski limfni čvorovi su bili jedini pozitivni. Zaključak: biopsija stražarskog limfnog čvora neupitno predstavlja metodu izbora kod ranog stadija raka dojke.

Ključne riječi: rak dojke, SLN biopsija, aksilarni limfni čvorovi

INTRODUCTION

Axillary lymph nodes (ALN) status is the most powerful prognostic factor in patients with breast cancer and it determines along with the biological characteristics of the primary tumor, the prognosis and the subsequent adjuvant treatment (1).

Sentinel lymph node or the guardian node is being defined as the first lymph node or a group of nodes in which the spreading of cancer cells will start. Spreading of some forms of cancer usually has common progress, spreading at first into first regional lymph nodes, then into the next group of lymph nodes and so on, since the lymph flow is directed. The main basin of the lymphatic drainage flow from the breast is ipsilateral axilla (2).

Sentinel lymph node biopsy (SLNB) is associated with reduced arm morbidity, and better quality of life than standard axillary treatment and should be the treatment of choice for patients who have early-stage breast cancer with clinically negative nodes (3).

This method was routinely used at Department of Glandular Surgery of the Clinical Center University of Sarajevo (CCUS), with the total of 75 during 2018.

AIM

Aim of the study is to represent the data we gathered from a year's experience and to compare it with the current literature.

MATERIALS AND METHODS

A retrospective, clinically applied, descriptive study was conducted at Department of Glandular Surgery, Clinic of General Surgery of the CCUS in the period from January 2018 to December 2018. The data source are medical records of 75 patients with histopathologically verified breast cancer and who were treated by using sentinel lymph node biopsy (SLNB) in 2018. The data were analyzed using descriptive statistical methodology and presented through tables, as well as compared with data from contemporary international studies. We analyzed the demographic characteristics of the selected group of patients and pathologic features of the tumors, type of primary surgical procedure performed, as well as SLN histopathological characteristics.

RESULTS

In our study we have analyzed a total of 75 patients who were treated by using SLNB technique during 2018. Out of total number of patients in only one case SLN was undetectable. The median patient's age was 50.5 years. Fifty-four (72.9%) patients had invasive ductal carcinoma. We observed 44 (59.4%) cases where the left breast was the affected side, while in 30 (40.5%) cases it was the right breast. Grade 2 was noticed in 28 (37.8%) patients whereas grade 3 was observed in 27 (36.4%) patients. The most common T stage was T1 in 34 (45.9%) patients followed by T2 in 27 (36.4%) cases. Lymphovascular invasion and perineural invasion were seen in 16 (24.3%) and 15 (20.2%) patients, respectively. Breast conserving surgery was performed in 56 (75.6%) patients while radical mastectomy was the procedure of choice in 18 (24.3%) cases. 14 (18.9%) patients were treated with neoadjuvant chemotherapy. The patient's demographics, tumor characteristics and the primary breast surgical procedure are shown in Table 1.

Table 1 **Patient demographics, tumor features and primary breast surgical procedure.**

Characteristics	n (%)
Age in years, mean (standard deviation)	13.26
Age in years, median	50.5
Type of tumor	
Ductal	54 (72.9)
Lobular	11 (14.8)
DCIS	6 (8.1)
Affected breast side	
Right side	30 (40.5)
Left side	44 (59.4)
Pathologic T stage	
T0	8 (10.8)
Tis	4 (5.4)
T1	34 (45.9)
T2	27 (36.4)
T3	1 (1.3)
Tumor grade	
I	8 (10.8)
II	28 (37.8)
III	27 (36.4)
Primary breast surgical procedure	
Radical	18 (24.3)
Breast-conserving therapy (BCT)	56 (75.6)
Lymphovascular invasion	18 (24.3)
Perineural invasion	15 (20.2)
Received adjuvant chemotherapy before SLNB	14 (18.9)
Estrogen receptor positive	59 (79.7)
Progesterone receptor positive	34 (45.9)
Her2 receptor positive	7 (9.5)

Table 2 shows that in 45 patients (60.8%) number of retrieved sentinel lymph nodes was 1, whereas 2 sentinel lymph nodes were retrieved in 22 (29.7%) patients and 3 sentinel lymph nodes were harvested in 6 (8.1%) of patients. As for the number of positive lymph nodes we observed one positive sentinel lymph node in 9 (47.4%) of the total number of positive lymph nodes, while in 6 (31.6%) patients 2 sentinel lymph nodes were positive. In 2 (10.5%) cases we noticed positive lymph nodes in permanent pathological specimens, which were retrieved upon SLN biopsy, as a control group. In addition in 2 (10.5%) cases, micrometastases were diagnosed on a permanent pathological section. In these cases, also no further axillary involvement was performed.

Table 2 **Sentinel lymph node results.**

Number of sentinel lymph nodes harvested	*n (%)*
- One lymph node	45 (60.8)
- Two lymph nodes	22 (29.7)
- Three lymph nodes	6 (8.1)
- Four lymph nodes	1 (1.4)
Number of positive Sentinel Lymph Nodes	
- One lymph node	9 (47.4)
- Two lymph nodes	6 (31.6)
- Number of positive lymph nodes retrieved in permanent specimen	2 (10.5)
- Number of micrometastases found in permanent specimen	2 (10.5)

Table 3 shows that there were 75 mapping procedures. In only one procedure we were not able to identify SLN, so the ALND was immediately performed. Our identification rate was 98.7%. 77% were SN negative and required no further surgical treatment. Seventeen patients (22.9%) were found to have a positive SN, of which 15 (88.2%) were diagnosed with macrometastases and treated with ALND. Total number of micrometastases that we managed to retrieve was 4 (23.5%), of which 2 were retrieved during the operative procedure and proceeded into an partial ALND and 2 were discovered in the permanent axillary specimen finding, with no further surgical treatment provided. In 9 (52.9%) out of 17 positive cases, SLN were the only positive lymph nodes.

Table 3 **Sentinel lymph node (SLN) histopathology.**

Number of sentinel node mapping	75
Number of sentinel lymph node found	74
Identification rate	98.7%
Number of SLN negative	57/74 (77.0%)
Number of SLN positive	17/74 (22.9%)
Number of SLN macrometastases	15/17 (88.2%)
Number of SLN micrometastases	4/17 (23.5%)
SLN positive, ALND positive	7/17 (41.2%)
SLN positive, ALND negative	9/17 (52.9%)
Positive lymph nodes found in permanent specimen.	2/19 (10.5%)

DISCUSSION

SLN biopsy method is widely used and it has a high identification rate, at our institution we use radioisotope only and the identification rate was 98.7% which is in accordance with current literature (4).

Sentinel lymph biopsy is the standard of care for patients suffering from breast cancer, in our study we have observed 4 cases of positive lymph nodes retrieved in permanent pathological sections, out of which 2 were confirmed as micrometastases and 2 as macrometastases. We feel that the fore mentioned is due to the fact that we have one single SLN retrieved in 45 (60%) of cases. Removal of more than one SLN and avoidance of excisional biopsy are important variables in reducing the false negative rate (5).

In the study that we have conducted we have discovered that more than half of all positive SLN cases were limited to SLN only (9/17, 52.9%), which clearly points out the fact that even if we have positive SLN, ALND remains questionable, especially in cases where lymph nodes are not palpable and if they are localized in axillary level III (6).

In 15 cases patients were treated with neoadjuvant chemotherapy and in 14 (93.3%) cases SLN was successfully found whereas in one case in it was not possible. This data is in accordance with current international studies, emphasizing the fact that our institution follows the guidelines in which ALND is recommended in such cases (7). In the aforementioned case the axillary specimen was positive for metastasis with a pathologically determined poor response to neoadjuvant chemotherapy.

It was observed that this method allowed to achieve the similar result as the ALND, but it was associated with reduced arm morbidity and better quality of life than standard axillary treatment and should be treatment of choice for patients with early-stage breast cancer with clinically negative ipsilateral axillary nodes (3).

Regarding the treatment algorithm for the micrometastases, our institution is following recommendations that no further axillary clearance is needed in such cases, which is proven also by the fact that in 2 cases where the SLN were positive for micrometastases the remaining portion of axillary lymph nodes were found to be negative (8).

As for histological and molecular subtypes, breast side, all the data acquired is following the current data available (9).

CONCLUSION

SLN biopsy remains undoubtedly the method of choice in early-stage breast cancer, with false negative rate remaining an issue which could be resolved by increasing the number of sentinel lymph node harvested.

REFERENCES

1. AlSaif A. Breast cancer recurrence after sentinel lymph node biopsy. Pak J Med Sci. 2015;31(6):1426-1431.
2. Vural G, Sahiner I, Demirtas S, Efeturk H, Demirel BB. Sentinel lymph node detection in contralteral Axilla at initial presentation of a breast cancer patient: Case report. Mol Imaging Radionucl Ther. 2015;24(2):90-93.
3. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. J Natl Cancer Inst. 2006;98(9):599-609.
4. Bonnema J, van de Velde CJH. Sentinel node biopsy in breast cancer. Annals of Oncology. 2002;13:1531-1537.
5. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Ashikaga T, et al. National Surgical Adjuvant Breast and Bowel Project.Technical outcomes of sentinel-lymph-noderesection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. Lancet Oncol. 2007;8(10):881-8.
6. Kuerer MH. Kuerer's Breast Surgical Oncology. China: The McGraw-Hill Companies Inc. 2010;63:689.
7. Bear HD, McGuire KP. Sentinel Node Biopsy after Neoadjuvant Systemic Therapy for Breast Cancer: The Method Matters. Ann Surg Oncol. 2019;26:2316-2318.
8. Nowikiewicz T, Srutek E, Jankowski M, Las-Jankowska M, Klag M, Kozak D, Glowacka I, Zegarski W. Management and results of treatment of breast cancer patients having sentinel lymph node micrometastases. Neoplasma. 2014;61(3):299-304.
9. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. Breast Cancer (Dove Med Press). 2019;11:151-164.

Reprint requests and correspondence:
Emir Bičakčić, MD, MSc
Clinic of General and Abdominal Surgery
Clinical Center University of Sarajevo
Bolnička 25, 71000 Sarajevo
Bosnia and Herzegovina
Email: ebicakcic@gmail.com
ORCID ID: 0000-0001-5950-8667

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: EB, SP, MS and EB-F gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

Role of physicians in protecting children's rights during war conflicts and postwar migrations

Uloga ljekara u zaštiti prava djece u ratnim konfliktima i postratnim migracijama

Palikuća Adnan, Kamenica Amina, Duraković Senija, Mujanović Merjem, Mehić Asja, Ayse Yenisahal, Taylan Haskaya, Suada Heljić*

International University of Goražde, Medical Faculty, Ibrahima Čelika, 73000 Goražde, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

The history of warfare has shown that children are vulnerable group who have suffered various types of violence during armed conflicts. The United Nation Convention on the Rights of the Child from 1989 pointed to the necessity of children's protection during armed conflicts. 20th and 21th century have been marked by terrible suffering of children in armed conflicts worldwide. Severe suffering of children also marked Balkan wars during the nineties, especially in surrounded enclaves during aggression on Bosnia and Herzegovina. Except for killed and wounded children, invisible victims of the war were preterm and sick infants, without possibilities for survival due to lack of basic healthcare conditions. Children who have survived violence and cruelty during war conflicts worldwide suffer from posttraumatic stress disorder. Current war conflicts in the Middle East have brought a new mass phenomenon: migrations of the families with their children or children alone, without parental care. There are hundreds and thousands children refugees and migrants on Mediterranean route toward Europe which lasts for several years, without possibilities of schooling; investigations indicate that they show signs of deep psychologic trauma as a consequence of suffering experienced on their refugee route. Physicians can do a lot to ensure that children in the future have more chance for normal and fulfilled childhood, independent of birth place. Regardless of the fact that the triumph of pediatric medicine mostly refers to reduction of child mortality, eradication of some diseases like poliomyelitis, an important pediatric practice has been and will remains the care for children, war victims.

Keywords: children's healthcare rights, war-related injuries, physician's role

SAŽETAK

Istorija ratovanja je pokazala da su djeca vulnerabina skupina koja u ratnim konfliktima trpi različite vrste nasilja. Konvencija Ujedinjenih Naroda (UN) o pravima djeteta iz 1989. naglasila je potebu zaštite djece u oružanim konfliktima. Teško stradanje djece obilježilo je i balkanske ratove, osobito u opkoljenim enklavama za vrijeme agresije na Bosnu i Hercegovinu. Osim ubijene i ranjavane djece, postojale su i nevidljive žrtve rata, nedonoščad i bolesna djeca koja nisu imala uslove za preživljavanje zbog nedostatka osnovnih uslova za njihovu njegu. Djeca koja su preživjela nasilje i okrutnost u ratnim konfliktima širom svijeta pate od postraumatskog stresnog poremećaja. Tekući ratni konflikti na Bliskom istoku donijeli su novi masovni fenomen: migracije porodica sa djecom, ili same djece bez roditeljskog staranja. Stotine i hiljade djece izbjeglica i migranata na svom putu preko Mediterana prema Evropi koji traje i nekoliko godina, nema mogućnost školovanja, a ispitivanja pokazuju da ispoljavaju znake duboke psihološke traume kao posljedicu patnje koju su iskusili na svom izbjegličkom putu. Ljekari mogu dosta učiniti da se osigura da djeca u budućnosti imaju veće šanse za normalno i ispunjeno djetinjstvo, neovisno od mjesta rođenja. Bez obzira što se trijumf pedijatrijske medicine ponajviše odnosi na smanjenje smrtnosti djece, iskorjenjivanje nekih bolesti, kao npr. poliomijelitisa, važna praksa pedijatara sada i u budućnosti ostaje i briga o djeci, žrtvama rata.

Ključne riječi: pravo djece na zaštitu zdravlja, ozljede povezane sa ratnim konfliktom, uloga ljekara

INTRODUCTION

Children have not always been on the human rights agenda as a separate group (Declaration of the Rights of Man in 1780). European societies considered children as property of their parents, and not particularly valuable property at that. Human rights are generally relatively recent historical phenomenon (1). History of children's rights regulation has started in 1919, with the Declaration of Rights of Children (International Peace Union), taken over by the League of Nations in 1924 (Geneva Declaration of the Rights of the Child), and with some additions and amendments by the UN in 1959 (2). Modern era of international rights started with establishing of the UN system after the Second World War, especially with the Universal Declaration of Human

Rights from 1948. This declaration referred to children (Article 25, Paragraph 2): "Motherhood and children are entitled to special care and assistance. All children, whether born in or out of wedlock, shall enjoy the same social protection" (3). Other declarations and covenants, both of the UN and of other inter-governmental bodies, have echoed this concern about protection, which is based on the perceived developmental immaturity of young children (4). Indeed, all these declarations had seen children as objects requiring adult protection but not as subjects of rights. This actualized a question if human rights can be applied universally, bearing in mind that a childhood is not only defined by biological and physiological facts but also by culture or society integral to the history and culture of Europe and North America (1). Convention of the Rights of the Child was adopted by General Assembly UN in 1989. All programs of children's, rights protections provided by various agencies and non-governmental organizations were situated within the frame of this convention (5). The Convention recognizes children as human beings with their own perspectives, not as passive objects of care and charity. The Convention is widely accepted and ratified by 190 countries. The UNICEF was instrumental in promoting the widespread ratification of the UN Convention by organizing the 1990 World Summit for Children. The aim was to ensure that rights were enforced, but national plans had failed due to lack of resources for its implementation. The Convention on the Rights of the Child provides clear guidance and monitoring framework against which to evaluate progress towards the realization of children's right to health - from child mortality to combating disease and malnutrition, preventing violence and injury, ensuring rehabilitation and support for children with disabilities, or abolishing traditional practices that harm children such as early enforced marriage etc.

The Convention on the Rights of the Child (5) consists of 54 articles, but we wil l consider the content of articles 38 and 39, referred to the rights of children during war conflicts.

Children's rights in war

There is a phrase saying that in fact all wars are waged against the children. Article 38 of The Convention on the Rights of the Child reads: "Children have the right to be protected during war. No child under 15 can join the army or take part in war". Article 39 reads: Children have the right to get help if they have been hurt, neglected, treated badly or affected by war, so th ey can get back their health".

Over the past 500 years in Europe, Africa and Asia, there have been more years of war than of peace (6). The 20th century brought two world wars with millions of victims and suffering of children. Even the last year of the 1990 Cold war which was relatively peaceful year with annual conflicts, was responsible for 100.000 children deaths and for permanently impairing the health of approximately two million surviving children who were victims of war (6,7,8).

The Balkan wars of the 1990s, especially aggression on Bosnia and Herzegovina gave us a direct insight into various forms of child suffering, putting in focus health, social, legal and other aspects of the need to protect children (9,10). It is not known how many children were killed or disappeared during the Bosnian war. According to the "Research and Documentation Center" at least 3372 were killed, mostly in Sarajevo and Eastern Bosnia. Children were most often died from grenades and snipers or killed along with their parents. In Easter Bosnia the murdered children are still being searched for (10). In addition there is no data on how many were exhumed from mass graves. The investigation is still on going by relevant institutions.

„Every pediatrician needs to be a student of history" (6). Except for care of children wounded by grenades and snipers, health pediatricians have professional obligations to prevent and alleviate suffering of children war victims, especially since many of them were exposed to non-human behavior and barbarism of various kinds. The six grave violations are generally stated during arm conflicts: Killing and maiming of children; Recruitment and use of children by armed forces or armed groups; Sexual violence against children, especially girls; Attacks against schools and hospitals; Abduction of children and Denial of humanitarian access. During the Bosnian war in the 90ties we witnessed various types of suffering, including brutal examples of sexual violence against women and girls, and today visible, organized and aware „children of war". This research is still ongoing by appropriate institutions (9,10). Except for killed and wounded children, invisible victims during the 92-95 Sarajevo siege were preterm infants, whose incidence was doubled; they had no possibilities for survival due to lack of oxygen and other basic healthcare conditions. Prematurity and low birth weight is a very sensitive tool of physical and emotional impairment and inadequate health care with long term consequence. Perinatal mortality rate has increased for 70%, from 15.8%/1000 to 26.9/1000 live birth newborns, and the rate of stillborn has increased for 64%. The average birth weight was reduced for 20% (3700 to 3000 g) (11,12). Mortality rate of the youngest children has risen due to weakness, hypothermia, diarrheal and respiratory diseases, malnutrition (14,15).

Whether in uniform or serving as civilians, doctors who serve in conflicts do so as non-combatants. These doctors are enjoined to practice within the principles of the Geneva Conventions, both from the ethical traditions of medicine and from the explicit laws, both civilian and military, that govern the conduct of doctors who work in military and civilian disasters. The Geneva Conventions, together with less formal codes of chivalry and humanitarian behavior, form part of the broader theme of influence called the 'Laws of War'. Pediatricians are required to act within those laws, and offer some protection to the innocent and helpless.

The suffering of children from landmines

During armed conflicts and post conflict phase of war there is an additional suffering of children by landmines. This danger threatens to children in more than 26 post-conflict countries. No one knows how many children are killed and injured by landmines. The current best estimate places the death rate at some 800 people per month, with another 1000–2000 surviving each month with blast injuries and consequent disability (16,17) The medical consequences of landmines, as these affect children, are well known: avulsion of one or both feet or lower limbs, shrapnel fragmentation wounds to the pelvis and abdomen, blinding in one or both eyes, conductive deafness...

The death of children from landmines is one of 6 preventable causes of death in the world (pneumonia, gastroenteritis, malaria, measles, HIV and landmines). United Nations Convention 1997 (Vienna Convention) on antipersonnel landmines have been big steps forward to ensure the maintenance of a safer environment for the world's children.

'The mind in infancy is like the body in embryo; and receives impressions so forcible, that they are as hard to be removed by reason, as any mark with which a child is born". (18) Many children who have survived the war without physical disabilities inevitably carry the scars of war, natural disaster or refugee experience into their lives and sometimes to the next generations (19,20). Some studies of children in the aftermath of war and other catastrophic disasters have documented fear-conditioned responses to the experience of early violence. These include regressive or aggressive behavior, another long-term legacy of early exposure to the violence of armed conflict. Much has been written about the stress reactions of children trapped in the protracted periods between shelling or hand-to-hand assaults (20,21). Impact of stress existed from the birth. Research on the aftermath of the Bosnian war showed that the average birth weight of children and nutritional indices of those infants who continued to be breastfed were reduced during periods of continued immediate threat (11,12).

Children who have survived the violence and cruelty, when they outgrow childhood become more immune to horror and violence comparing to other children.

Post-traumatic stress disorder, with its morbidity of personal distress and agony, has been very much a featured disease of the late 20th and 21st centuries. Children are less likely than adults to talk about such episodes or to understand their genesis. Nevertheless, recurring obsessive thoughts of horror, flashbacks and recurring dreams either of stark reality or of symbolic illusion are some of the chronic symptoms of this childhood disorder (20-26). Because children do not write, while they are children about their traumatic experiences, it is easy to overlook the immediate effects of war on them. In the article published 1997 Godstein cites the data that almost 94% of the children with war related expirience after Bosnian war met Diagnostic and Statistical Manual of Mental Disorders, 4th ed, criteria for posttraumatic stress disorder.

Children-soldiers

A separate part of child abuse refers to children-soldiers, mostly boys between 8 and 18 years of age. Such abuse has been recorded through the history of warfare, since the time of ancient Greece. They are often orphans, unsocialized and illiterate, armed with automatic and cold steel, without developed ethical standards and morals, bonded into armed group of peers, ready to kill brutally, regardless of gender and age. With such brutal instrumentalization of children, additional drug and alcohol use is recorded. These child soldiers have become a phenomenon newly encountered in the 20th century and accruing with a tragic currency in the new millennium. (27) For the world that has become a global village, that imposed itself as an important and inevitable topic. The 1998 Statute of the International Criminal Court has defined as a war crime the conscription or enlistment of children under 15years of age into the armed forces for their use in combat. Child-soldiers are a vulnerable group with profound sequelae in their later life. Desocialization and dehumanization are consolidating in their young personality. The situation can be compounded by the fact that their parents or other close relatives are lost in massacres, bomb blasts or epidemics. Loss of childhood makes the schooling and subsequent rehabilitation very difficult. Long term sequelae includes inventible posttraumatic stress disorder, necessity of lifelong care fom appropriate social and psychiatric institutions, with a little chance of rehabilitation (6,27,28)

Children in movement - refugee and migrants

The twenty first century has brought a major problem due to new wars in the Middle East. On their refugee route children move with their families, but many of them are unaccompanied or separated. According UNICEF data among 100 000 refugee during last year, approximately 15% of them were children, usually boys aged 15- 17 years. They risk their lives in search of life better than the one they left behind, marked by suffering, loss of family members and poverty. Without other choice or legal alternative, children and adolescents take the destiny into their own hands, facing with the possibility of losing their lives or becoming the target of exploitation at the hands of immoral people. During brutal six-year' war in Syria, many refugee left along their refugee journey: more than 3 million live in the Turkey in the biggest migrants population on the world (half of them are children), several thousand are on Balkan Route. In December 2019, 1182 children (15% girls and 86% boys) were present in different accommodation centers in Bosnia and Herzegovina (29,30). Many of them have experienced terrible violence, sexual abuse, trafficking and emotional and psychological pressure and express signs of deep psychological trauma. UNHCR, the UN Refugee Agency, UNICEF, and IRC, the International Rescue Committee, issued a Roadmap for action to improve the situation of refugee and migrant children arriving and staying in Europe without their parents or care givers (31). The Roadmap* highlights the need to identify children, register them through child-friendly procedures, and build a relationship of trust with them as early as possible. Ensuring that a well-trained guardian takes immediate responsibility for the child, engaging cultural mediators, and mobilizing members of host communities are critical measures that can help build a trusting relationship and protect children from smugglers, traffickers or family pressure. Children need protection, proper health care including immunization, food, education, psychosocial help, and long-term solutions to these children based on their specific needs.

CONCLUSION

Pediatricians can do a lot to make sure that children in the future have more chance for normal and fulfilled childhood, independent of their birth place. No matter what the triumph of pediatric medicine mostly refers to reduction of child mortality, eradication of some diseases like poliomyelitis, an important pediatric practice now and in the future remains the care of children, war victims.

REFERENCES

1. Kosher H, Ben-Arieh A, Hendelsman Y. The History of Children's Rights. In Children's Rights and Social Work. 2016. Available from: https://www.researchgate.net/publication/315862642_The_History_of_Children's_Rights#fullTextFileContent DOI: 10.1007/978-3-319-43920-4_2
2. United Nations 1959. Declaration of the Rights of the Child, Humanium 1959. Available from: https://www.humanium.org/en/declaration-rights-child-2/
3. United Nations 2015. The Universal Declaration of Human Rights, 1948. Available from: https://www.un.org › udhrbook › pdf › udhr_booklet_en_web
4. Byrne I. The Human Rights of Street and Working Children. Intermediate Technology Publications London Print Book 1998. Available from: https://www.worldcat.org › oclc › editions
5. United Nations 1989. United Nations Human Rights. Convention on the Rights of the Child. Available from: https://www.ohchr.org/documents/professionalinterest/crc.pdf

6. Pearn J. Children and war. J Paediatr Child Health 2003 Apr;39(3):166-72. doi: 10.1046/j.1440-1754.2003.00124.x.
7. Last J. War and the health of children. Am J Prev Med. 1991;7:253.
8. Pearn JH. History, horror and healing. Health History. 1999;1:202-8.
9. Haseljić MA, Subašić-Galijatović S, Hajrić-Čaušević A. Srebrenica 1995-2015. Evaluating the legacy and long term consequences of genocide. University of Sarajevo, Institute for research for a crimees and International law Sarajevo, University of Tuzla, Memorial Center and cementary of the victims 1995 Srebrenica. Sarajevo – Tuzla – Srebrenica (Potočari): 9 – 11 July 2015.
10. Lakić M. Child Victims of Sarajevo Siege BIRN April 2018. https://balkaninsight.com/2018/04/04/rouses-for-children-killed-in-sarajevo-during-siege-04-04-2018/
11. Mann J, MPH; Drucker E; Tarantola D; and McCabe MP. Bosnia: The War Against Public Health 130 Medicine & Global Survival. 1994;1(3).
12. Simic S. Interviewed by Jerry Paccione, M.D. Sarajevo. November 22, 1993.
13. Schroll C.Letter to MPMcC. Zagreb: Nov 22, 1993. Sarajevo. November 22, 1993. 38. Bulletin of the Public Health Institute. Sarajevo: 1993;1 -40-134/93
14. WHO. Monthly report, WHO field office,Tuzl a. Geneva: October 28,1993.
15. WHO. Weekly epidemiological record 1993. Geneva: 1993;68:133 -140. Bulletin of the Public Health Institute.Sarajevo.1993;10-025/93
16. Andersson N, da Sousa CP, Paredes S. Social cost of land mines in four countries: Afghanistan, Bosnia, Cambodia and Mozambique. Br Med J. 1995;311:718-21.
17. Jeffrey SJ. Antipersonnel mines: who are the victims? J. Accid.Emerg. Med. 1996; 13:343-6.
18. Steele R. On recollections of childhood. In: Gross J, ed. The Oxford Book of Essays. Oxford University Press, Oxford, 1992;53 -6.
19. Freh FM. Psychological Effects of War and Violence on Children, J Psychol Abnorm 2015, S1 DOI: 10.4172/jpab.S1-e001
20. Liu M. War and Children. American Journal of Psychiatry Published Online: 2017https://doi.org/10.1176/appi.ajp-rj.2017.120702
21. Sheridan G, Kenning T. Trauma psychology. In: Sheridan G,Kenning T, eds. Survivors. Pan Books, London, 1993; vii–x,xiv–xix, 275–7.
22. Richard D. Goldstein, Nina S. Wampler and Paul H. Wise. War Experiences and Distress Symptoms of Bosnian Children. Pediatrics.1997;10(5); 873-878.
23. Hasanović M. Psychological consequences of war-traumatized children and adolescents in Bosnia and Herzegovina, Acta Medica Academica. 2011;40(1):45-66 DOI 10.5644/ama2006-124.8
24. Richter D, Verona E, Tjesic -Drinkovic D, Petricek I, Barisic N, Barisic I. Sending Croatian and Bosnian children for treatment abroad. JAMA. 1993;270: 574.53
25. Zivcic I. Emotional reactions of children to war stress in Croatia. J Am Acad Child Adolesc. Psychiatry. 1993;32:709-13.
26. Goldstein RD1, Wampler NS, Wise PH. War experiences and distress symptoms of Bosnian children Pediatrics. 1997;100(5):873-8.
27. Machel G. The impact of armed conflict on children. Proceedings of the International Conference on War-Affected Children; September 2000; Winnipeg, Canada. Government of Canada, Ottawa,
28. Pynoos RS, Nader K. Psychological first aid and treatment approach to children exposed to community violence: Research implications. J. Trauma. Stress. 1988;4:445-73.
29. UNICEF 2017. Unicef for every child, Geneva. Europe: new Roadmap to improve the situation of unaccompanied and separated refugee and migrant children 2017. Available from: https://www.unicef.org/eca/press-releases/roadmap-unaccompanied-separated-refugee-migrant
30. UNHCR, UNICEF & IOM. 2019. Refugee and Migrant Children in Europe in 2019- Accompanied, Unaccompanied and Separated. Available from: https://www.unicef.org/eca/media/12671/file
31. UNICEF 2019. Unicef for every child, Genava: Eight million children have been affected by war in Syria, which enters 9th year. Available from: https://www.infomigrants.net/en/post/15784/unicef-eight-million-children-have-been-affected-by-war-in-syria-which-enters-9th-year

Reprint requests and correspondence:
Suada Heljić, MD, PhD
International University of Goražde, Medical Faculty
Ibrahima Čelika, 73000 Goražde
Bosnia and Herzegovina
Email:heljicsuada@hotmail.com
ORCID ID: 0000-0003-3929-2541

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: PA, KA, DS, MM, MA, AY, TH and SH gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

Acute coronary syndrome - instructions to the patient after discharge from the hospital

Akutni koronarni sindrom - upute pacijentu nakon izlaska iz bolnice

Amer Iglica[1]*, Edin Begić[2], Nedim Begić[3], Amila Turalić[4], Nirvana Šabanović-Bajramović[1], Alen Džubur[1], Mirza Dilić[1]

[1]Clinic of Heart, Blood Vessel and Rheumatic Diseases, Clinical Center University of Sarajevo, 71000 Sarajevo, Bosnia and Herzegovina
[2]Department of Cardiology, General Hospital «Prim.dr. Abdulah Nakaš», Kranjčevićeva 12, 71000 Sarajevo, Bosnia and Herzegovina
[3]Department of Cardiology, Paediatric Clinic, Clinical Center University of Sarajevo, Jezero, 71000 Sarajevo, Bosnia and Herzegovina
[4]Department of Pharmaceutical Analysis, Faculty of Pharmacy, University of Sarajevo, Zmaja od Bosne 8, 71000 Sarajevo, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

After an acute cardiovascular incident, the patient has a question about how to return to daily life. All patients with acute myocardial infarction (AMI) need to be prepared to move on with their lives and self-aware enough to know that period after an AMI does not necessarily mean disability. The patient should gradually return to daily activities, with clear instructions for each week of recovery. Life after an AMI continues with a healthy lifestyle and a return to daily obligations. Life can still be of good quality, but the willingness and desire for life are of utmost importance. Patients' trust in their physician is essential, and the patient and the physician's cooperation is the only right way.

Keywords: myocardial infarction, secondary prevention, lifestyle

SAŽETAK

Nakon akutnog kardiovaskularnog incidenta, pacijent postavlja pitanje kako se vratiti svakodnevnom zivotu. Svi pacijenti sa akutnim infarktom miokarda trebaju biti spremni da nastave sa svojim životom, te dovoljno samosvjesni da znaju da preležani akutni infarkt miokarda ne znači nužno invalidnost. Pacijent se treba postepeno vraćati u svakodnevne aktivnosti, sa jasnim planom za svaku sedmicu oporavka. Život nakon akutnog infarkta miokarda se nastavlja, uz zdravi životni stil i vraćanje svakodnevnim obavezama. Život i dalje može biti kvalitetan, ali je važna volja i želja za životom samog pacijenta. Povjerenje u ljekara je jako bitno, a simbioza pacijenta i ljekara je jedini ispravni put.

Ključne riječi: infarkt miokarda, sekundarna prevencija, životni stil

INTRODUCTION

Ischemic heart disease occurs clinically in two forms: the chronic form of ischemic heart disease (stable angina pectoris) and acute form, acute coronary syndrome (ACS). The term ACS refers to any group of clinical symptoms compatible with acute myocardial ischemia. It includes unstable angina (UA), non-ST segment elevation myocardial infarction (NSTEMI), and ST-segment elevation myocardial infarction (STEMI) (1). The joint workgroup of the European Society of Cardiology (ESC), American College of Cardiology (ACC), American Heart Association (AHA), and World Health Organization (WHO), in 2018 defined myocardial infarction as the presence of acute myocardial injury, verified by an elevated level of enzymes of myocardial necrosis, the consequence of acute myocardial ischemia. Most severe forms of myocardial ischemia, if they are not momentary, can lead to myocardial infarction, which occurs distally from the place of critical stenosis of the coronary artery (2). Coronary reperfusion with the primary percutaneous coronary intervention (pPCI) improves outcomes in patients with STEMI. It is being used as the first and only reperfusion therapy if available. Discharge of stable patients with STEMI 72 hours after primary PCI is recommended, according to the results of the Second Primary Angioplasty in Myocardial Infarction (PAMI-II) clinical trial (2,3). Discharge on the same day apropos transfer of the patients on the lower healthcare level after successful primary PCI is routine practice (2,3). That can safely be done under appropriate supervision in haemodynamically stable patients who do not require vasoactive or mechanical support and not indicated for further revascularization (2,3). Every patient with STEMI should be subject to early or late risk stratification. Patients should gradually return to everyday activities, with a clear plan for every week of recovery.

First week

Patient can shave, have a shower or bath in lukewarm water, eat every meal at the table, go to the toilet, watch television, listen to the radio, read a newspaper, walk in the house, but not on the stairs, receive visits, and eat frequent and small meals (4). The patient should avoid smoking, excitement, obstipation (enough fruit juices, plums, figs), and effort (4). Patient should avoid plentiful meals that induce bloating, too spicy, and fatty foods (4). Patient should avoid sexual intercourse. It is recommended to sleep 8 to 9 hours in the night, and patient should lie down every forenoon and afternoon. Therapy should be taken regularly, according to the doctor's recommendation, at the recommended time, in addition to following tips regarding optimal nutrition.

Second week

The patient can be active in his apartment, help in lighter household chores, play favorite games, do sitting activities, reduce lying down and resting, and conduct important business interviews if they are not numerous, long or exciting (4).

Third and fourth week

Patient can go out if the weather is nice. He can walk to 500 meters a bit longer every day, so, until the end of the fourth week, the patient can walk around 2 kilometers a day. Gradually he can climb the stairs (at the beginning half floor, and gradually more and more) (1). Patient should avoid going out in the cold and windy weather, walking uphill, fatigue, exhaustion, and emotional excitements, walking, and effort immediately after meals, as well as carrying cargo (4).

Fifth to eight week

Patient can resume sexual intercourse, social activities, return to a job with part-time work hours (4). He should avoid overeating, weight gain, fatigue, tension, exhaustion, all sports. At the end of this period, it is recommended for patients to talk with their doctor about a possible workplace change, driving a car, and participating in various forms of recreation (4).

From the ninth week

Patient can do everything he has been doing before acute myocardial infarction. He should avoid sport competitions and work overtime. Fitness exercises are recommended.

Recommendations regarding symptoms in the thoracic region

The patient should contact his doctor if he feels intensive chest pain, if he feels shortness of breath, if his heart beats fast or irregularly, if he suddenly gains weight (one to two kg in day or two, or two to three kg in one week), if his legs are swelling, if he cannot lie on the flat surface, if he is constantly tired, down-hearted and if he sweats profusely or in case of any other unordinary symptoms (indeterminate difficulties in chest are usually nonsignificant, and disturbances in deep breathing and yawning attacks are common and doesn't mean much) (4).

Diet proposal

Changes in eating habits can have an influence on cardiovascular health (5). Mediterranean diet is recommended, which implies a diet rich with fruit, vegetables, whole grains, legumes, and stone fruits, in which olive oil is a leading source of fat in the diet (6). There is a moderate intake of fish, poultry, and milk products in this diet and low red meat intake (6). Vegetarian diet makes sense, with adequate energy intake supervision, and this diet has an effect on atherosclerosis process (7,8). In case of arterial hypertension, DASH (The Dietary Approaches to Stop Hypertension) diet is a good option (9,10). It consists of 4-5 daily fruit units, 4-5 daily units of vegetables, 2-3 daily units of milk products with lower milk fat content (9,10). Restriction of table salt is necessary on 4-6 g/day (less than 2.3 g of sodium) because salt intake is related to high blood pressure, higher risk of cardiovascular diseases, stomach cancer (9,10).

It is very important to have regular intervals of meal intake (skipping breakfast increases acute myocardial infarction incidence for 21-27%) (11). Consuming vegetables decreases the risk of cardiovascular diseases, and leafy green vegetables reduce diabetes mellitus (12,13). Fruit and vegetable intake reduces the risk of cardiovascular diseases (12). A larger intake of whole-grain cereals is correlated with a lower risk of cardiovascular diseases, diabetes mellitus, and colorectal cancer (14,15). Refined grains do not have this effect (16). Intake of sweet drinks is related to obesity, increased cardiovascular risk, and diabetes mellitus (15,17). Nuts, legumes, and vegetable proteins are related to a lower obesity rate and lower risk of diabetes mellitus (18). Red meat is associated with a higher risk of cardiovascular diseases, and fish is recommended due to its cardioprotective effect (omega-3 polyunsaturated fatty acids, including EPA - eicosapentaenoic acid and DHA - docosahexaenoic acid) (19,20).

Fluid intake should be restricted to 1.5 to 2 liter daily at patients with intensive diuretic therapy (in patients with reduced function of the left ventricle) (4,7,8). It is necessary to optimize energy intake in terms that 45-65% of daily intake should be carbohydrates and 20-35% of fat (10). An insufficient diet can lead to cardiac cachexia. Patients with chronic heart failure are at risk of malnutrition due to possible poor appetite, metabolic imbalance, liver congestion, malabsorption, and increased nutritional needs (4,6). Cardiac cachexia, like morbid obesity, are predisposing factors for increased mortality (1,3). Saturated fat intake should be limited and replaced with sources of unsaturated fatty acids, and oils reach with monounsaturated fatty acids (olive, fish) and products rich with omega fatty acids (fatty fish, some of the vegetable oils, nuts, flax seeds) (7,10). Intake of trans fatty acids should be reduced (snacks, fried food, different bakery products, cookies) (7,10).

Proteins should be 12-20% of energy intake (8,9,10,20). Daily needs in proteins are 0.8-1.0 grams per kg of body weight, although these needs vary depending on the patient's individual profile (10,11). Smoking termination is of essential value (21). Every cigarette alternative is undoubtedly the wrong option for patients with chronic heart failure. Food and drug administration (FDA) quotes that use of heating technology instead of burning, is less harmful alternative for the population that cannot stop smoking (22,23).

Alcohol should be reduced to the lowest possible amount due to the effect on the process of atherosclerosis. Clear cardioprotective effects of wine are not yet proven, despite traditional belief in the benefit of wine. Substances in the wine (resveratrol, katechin, epikatechin, kvercetin and antocyanin) have benefit in appropriate concentration (24). Caffeinated coffee should be avoided in patients with elevated blood pressure and

arrhythmias, although there is some evidence about the benefits of coffee (25).

Supplements like vitamin A, vitamin D, vitamin E, folic acid, B6, B12, and dietary fiber should be part of the overall diet pattern (26). Magnesium supplements (or consuming water rich with magnesium) should be a part of treatment of patients especially ones with reduced function of left ventricle, because it is believed that these patients have increased urine elimination of magnesium, decreased absorption, and decreased reabsorption due to diuretic therapy and therapy with digoxin (27). Selen and zinc have a cardioprotective effect (28,29). It is necessary to have sufficient amounts of potassium and calcium intake (1.000-1.200 mg daily), in the everyday diet, with the supervision of patients' kidney function and medicines that could disturb the balance of these electrolytes (30).

Physical activity (aerobic), rehabilitation with physical activity is recommended, with the gradual increase in exercise intensity (31). Dosed physical activity can have a protective effect on the heart muscle, on reduction and weight maintenance, on improving bone structure, decreasing the risk of fall in the older age, and incidence of fracture if fall occurs (31). Physical activity increases cognitive functions, decreases risk of dementia, including Alzheimer's disease (32). A sedentary lifestyle increases overall mortality, the mortality of cardiovascular diseases, the risk of newly developed diabetes mellitus, as well as the risk of colon cancer, cancer of endometrium, and lung cancer (31).

CONCLUSION

Self-discipline and motivation are extremely important, as well as good stress management. Environmental support is essential for overall patient well-being. Life after an acute myocardial infarction continues, with a healthy lifestyle and a return to daily obligations. Life can still be of good quality, but the willingness and desire for life are essential. Patients' trust in their physician is very important, and the mutual cooperation between the patient and physician is the only right way.

ACKNOWLEDGEMENTS

The authors express their thanks and gratitude to colleagues from the University Medical Center Sarajevo, 3rd Internal Medicine Clinic, who edited a short version of the recommendation back in 1980, under the title - *"Lifestyle after acute coronary syndrome. UMC Sarajevo:1980".*

REFERENCES

1. Kumar A, Cannon, CP. Acute coronary syndromes: diagnosis and management, part I. Mayo Clinic proceedings. 2009;84(10):917-38.
2. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax, JJ, Morrow DA, et al. Executive Group on behalf of the Joint European Society of Cardiology (ESC)/American College of Cardiology (ACC)/American Heart Association (AHA)/World Heart Federation (WHF) Task Force for the Universal Definition of Myocardial Infarction. JACC. 2018; 72(18):2231.
3. Stone GW, Marsalese D, Brodie BR, Griffin JJ, Donohue B, Costantini C, et al. A prospective, randomized evaluation of prophylactic intraaortic balloon counterpulsation in high risk patients with acute myocardial infarction treated with primary angioplasty. Second Primary Angioplasty in Myocardial Infarction (PAMI-II) Trial Investigators. J Am Coll Cardiol. 1997;29(7):1459-1467.
4. Urbinati S, Olivari Z, Gonzini L, Savonitto S, Farina R, Del Pinto M, et al. Secondary prevention after acute myocardial infarction: drug adherence, treatment goals, and predictors of health lifestyle habits. BLITZ-4 Investigators The BLITZ-4 Registry. Eur J Prev Cardiology. 2015;22(12):1548 -56.
5. Dontas AS, Zerefos NS, Panagiotakos DB, Vlachou C, Valis DA. Mediterranean diet and prevention of coronary heart disease in the elderly [published correction appears in Clin Interv Aging. 2008;3(2):397. Vlachou, Cleo [added]. Clin Interv Aging. 2007;2(1):109-115.
6. La Torre G, Saulle R, Di Murro F, Si liquini R, Firenze A, Maurici M. Collaborative group. Mediterranean diet adherence and synergy with acute myocardial infarction and its determinants: A multicenter case-control study in Italy. PLoS One. 2018;13(3):e0193360.
7. Tuso P, Stoll SR, Li WW. A plant -based diet, atherogenesis, and coronary artery disease prevention. Perm J. 2015;19(1):62-67.
8. Steinberg D, Bennett GG, Svetkey L. The DASH Diet, 20 Years Later. JAMA. 2017;317(15):1529-1530.
9. Maddock J, Ziauddeen N, Ambrosini GL, Wong A, Hardy R, Ray S. Adherence to a Dietary Approaches to Stop Hypertension (DASH)-type diet over the life course and associated vascular function: a study based on the MRC 1946 British birth cohort. Br J Nutr. 2018;119(5):581-589.
10. Segers VF, Lee RT. Protein therapeutics for cardiac reg eneration after myocardial infarction. J Cardiovasc Transl Res. 2010;3(5):469 -477.
11. Cahill LE, Chiuve SE, Mekary RA, Jensen MK, Flint AJ, Hu FB, Rimm EB. Prospective study of breakfast eating and incident coronary heart disease in a cohort of male US health professionals. Circulation. 2013;128(4):337-43.
12. He FJ, Nowson CA, Lucas M, MacGregor GA. Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies. J Hum Hypertens. 2007;21:717-28.
13. Carter P, Gray LJ, Troughton J, Khunti K, Davies MJ. Fruit and vegetable intake and incidence of type 2 diabetes mellitus: systematic review and meta-analysis. BMJ. 2010;341:c4229.
14. Mellen PB, Walsh TF, Herrington DM. Whole grain intake and cardiovascular disease: a meta-analysis. Nutr Metab Cardiovasc Dis. 2008;18:283-90.
15. Gonzalez CA, Riboli E. Diet and cancer prevention: contributions from the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Eur J Cancer. 2010;46:2555-62.
16. Sun Q, Spiegelman D, van Dam RM, Holmes MD, Malik VS, Willett WC, Hu FB. White rice, brown rice, and risk of type 2 diabetes in US men and women. Arch Intern Med. 2010;170:961-9.
17. Jiang R, Manson JE, Stampfer MJ, Liu S, Willett WC, Hu FB. Nut and peanut butter consumption and risk of type 2 diabetes in women. JAMA. 2002;288:2554-60.
18. Micha R, Wallace SK, Mozaffarian D. Red and processed meat consumption and risk of incident coronary heart disease, stroke, and diabetes mellitus: a systematic review and meta-analysis. Circulation. 2010;121:2271-83.
19. Mozaffarian D, Rimm EB. Fish intake, contaminants, and human health: evaluating the risks and the benefits. JAMA. 2006;296:1885-99.
20. Al Suwaidi J. Dietary patterns and their association with acute coronary heart disease: Lessons from the REGARDS Study. Glob Cardiol Sci Pract. 2015;2015(4):56.
21. Perneger TV. Smoking and risk of myocardial infarction. Statistical and biological interactions should not be confused. BMJ. 1998;317(7164):1017-1018.
22. Mallock N, Pieper E, Hutzler C, Henkler-Stephani F, Luch A. Heated Tobacco Products: A Review of Current Knowledge and Initial Assessments. Front Public Health. 2019;7:287.
23. FDA Authorizes Marketing of IQOS Tobacco Heating System with 'Reduced Exposure' Information. URL: https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-iqos-tobacco-heating-system-reduced-exposure-information (retrieved July 10, 2020)
24. Castaldo L, Narváez A, Izzo L, Graziani G, Gaspari A, Minno GD, et al. Red Wine Consumption and Cardiovascular Health. Molecules. 2019;24(19):3626.
25. van Dongen LH, Mölenberg FJ, Soedamah-Muthu SS, Kromhout D, Geleijnse JM. Coffee consumption after myocardial infarction and risk of cardiovascular mortality: a prospective analysis in the Alpha Omega Cohort. Am J Clin Nutr. 2017;106(4):1113-1120.
26. Rodrigo R, Hasson D, Prieto JC, Dussaillant G, Ramos C, León L, et al. The effectiveness of antioxidant vitamins C and E in reducing myocardial infarct size in patients subjected to percutaneous coronary angioplasty (PREVEC Trial): study protocol for a pilot randomized double-blind controlled trial. Trials. 2014;15:192.
27. DiNicolantonio JJ, Liu J, O'Keefe JH. Magnesium for the prevention and treatment of cardiovascular disease. Open Heart. 2018;5(2):e000775.
28. Benstoem C, Goetzenich A, Kraemer S, Borosch S, Manzanares W, Hardy G, Stoppe C. Selenium and its supplementation in cardiovascular disease--what do we know? Nutrients. 2015;7(5):3094-118.
29. Okabe T, Yakushiji T, Shimazu S, Saito J, Kimura T, Oyama Y, et al. Serum zinc concentration in patients with acute myocardial infarction in percutaneous coronary intervention era. PLoS One. 2018;13(8):e0203074.
30. Reid IR, Birstow SM, Bolland MJ. Calcium and Cardiovascular Disease. Endocrinol Metab (Seoul). 2017;32(3):339-349.

31. Ji H, Fang L, Yuan L, Zhang Q. Effects of Exercise-Based Cardiac Rehabilitation in Patients with Acute Coronary Syndrome: A Meta-Analysis. Med Sci Monit. 2019;25:5015-5027.
32. Gronek P, Balko S, Gronek J, Zajac A, Maszczyk A, Celka R, et al. Physical Activity and Alzheimer's Disease: A Narrative Review. Aging Dis. 2019;10(6):1282-1292.

Reprint requests and correspondence:
Amer Iglica, MD, MSc
Clinic of Heart, Blood Vessel and Rheumatic Diseases
Clinical Center University of Sarajevo
Bolnička 25, 71000 Sarajevo
Bosnia and Herzegovina.
E-mail: ameriglica@gmail.com.
ORCID ID: 0000-0002-4677-8489.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: AI, EB, NB, AT, NŠ -B, ADž and MD gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

Bosnia and Herzegovina versions of Guidelines for Patients!
Bosanskohercegovaka verzija Vodia za pacijente!

Energy drinks as a trigger for supraventricular tachyarrhythmia occurrence

Energetska pića kao triger za nastanak supraventrikularne tahiaritmije

Almin Handanagić[1*], Fuad Pajalić[1], Sadat Kurtalić[1], Edin Begić[2,3], Alma Handanagić[4], Nermina Kurtalić[4]

[1]Coronary Unit, Cantonal Hospital "Dr Irfan Ljubijankić" Bihać, Darivalaca krvi 67, 77000 Bihać, Bosnia and Herzegovina
[2]Department of Cardiology, General Hospital «Prim. dr. Abdulah Nakaš», Kranjčevićeva 12, 71000 Sarajevo, Bosnia and Herzegovina
[3]Department of Pharmacology, School of Medicine, Sarajevo School of Science and Technology, Hrasnička cesta 3A, 71210 Ilidža, Bosnia and Herzegovina
[4]Department of Dermatology, Cantonal Hospital "Dr Irfan Ljubijankić" Bihać, Darivalaca krvi 67, 77000 Bihać, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

Energy drinks (EDs) with substances in them (caffeine, taurine, guarana and L-carnitine) can induce the occurrence of cardiac arrhythmias, such as the supraventricular and ventricular ectopy, ventricular tachycardia and supraventricular tachyarrhythmias. The aim of this research was to present an 18-year-old patient with supraventricular tachyarrhythmia, which was pharmacologically converted to sinus rhythm, and after conversion underwent to cardiology examination.

Keywords: energy drinks, supraventricular tachycardia, treatment

SAŽETAK

Energetska pića, s obzirom na supstance u sastavu (kofein, taurin, guarana i L-karinitin) mogu indukovati pojavu poremećaja srčanog ritma, kao što je pojava supraventikularne i ventrikularne ektopije, ventrikularne tahikardije i supraventrikularnih tahiaritmija. Cilj rada je bio prikaz 18-godišnjeg pacijenta sa poremećajem ritma po tipu supraventrikularne tahiaritmije, koji je farmakološki konvertovan u sinusni ritam, te nakon konverzije i kardiološki obrađen.

Ključne riječi: energetska pića, supraventikularna tahikardija, tretman

INTRODUCTION

Energy drinks (EDs) have the effect of inducing cardiac arrhythmias (1,2). EDs with caffeine, taurine, guarana, and L-carnitine can lead to a proarrhythmogenic effect (1). They have been associated with the development of supraventricular and ventricular ectopy, ventricular tachycardia, atrial fibrillation, the development of seizures but also can induce neuropsychotic agitation, aggressive behavior and suicidal ideation (1). After consumption, they increase systolic blood pressure by 10 mmHg, diastolic by 7 mmHg, and heart rate by 20 beats per minute (bpm) (1).

AIM

The aim of this article was to present the occurrence of supraventricular tachyarrhythmia in an 18-year-old patient due to continuous consumption of EDs.

CASE REPORT

An 18 years old patient was admitted to the Emergency Centre in the early morning due to fast heartbeat, chest pain and shortness of breath. Cardiologist was called for examination. An hour before the attack of fast heartbeat, he vomited twice, and he drank half a liter of energy drink the night before. He did not take other stimulant substances.

He stated that he had consumed EDs daily, about half a liter per day. He denied previous existence of any cardiovascular pathology, existence of any disease, as well as previous hospitalizations. On the examination, he was cardiopulmonary compensated, heart rhythm was irregular, heart tones were clear, without heart murmur, with tension 120/80 mmHg and he was afebrile. The electrocardiogram (ECG) recorded on admission is shown in Figure 1. Carotid sinus massage and Valsalva maneuver did not lead to interruption of rhythm disturbances. Propafenone ampoule 150 mg intravenously was ordinated and after 20 minutes a sinus rhythm was obtained (Figure 2).

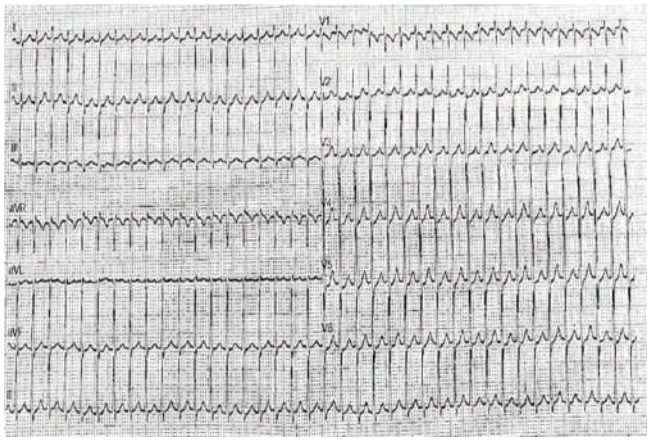


Figure 1 **ECG finding on admission - supraventricular tachycardia; 234 beats per minute.**

The patient was discharged, with magnesium effervescent (375 mg), along with monitoring of ECG and tension.

The day after echocardiography, normal-sized cardiac cavities, preserved systolic and diastolic function with trivial tricuspid and mitral regurgitation were. The 24-hour ECG-Holter monitoring verified the sinus rhythm, with attacks of sinus tachycardia and signs of respiratory arrhythmia. Ergometry was performed, which did not record significant ST segment and T wave changes, without rhythm disorders and with preserved tolerance to load. Laboratory findings verified normal complete blood count, mineralogram, thyroid hormones, with slightly elevated values of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma-glutamyltransferase (GGT).

Figure 2 **ECG finding after propafenon - sinus rhythm,**

DISCUSSION

EDs are used in everyday life, as a dietary supplement, especially in the younger population. Seifert et al. stated that 30-50% of young people in the United States of America use EDs on a daily basis (3). They are used for weight loss, to improve psychophysical performance, to reduce the effects of alcohol or to stimulate the effects of alcohol (4).

Mangi et al. state that EDs can induce supraventricular arrhythmias (atrial fibrillation, narrow complex tachycardia), ventricular arrhythmias (ventricular tachycardia, ventricular fibrillation, Torsade de points), prolonged QT interval, and even be a trigger for myocardial coronary ischemia (elevation of ST segment as sign of acute myocardial infarction), coronary vasospasm, cardiomyopathy and even for aortic dissection (4). Conen et al. denied that caffeine is associated with induction of atrial fibrillation (AF), as well as Shen et al. (5,6). Di Rocco et al. showed two cases of adolescents where EDs were the trigger of AF (7). Godlfarb et al. stated that consumption of EDs is associated with increased risk of AF, supraventricular arrhythmias, prolonged QT interval, Torsade de points, ventricular tachycardia, ventricular fibrillation and ST elevation (8).

Nagajothi et al. showed the case of 23-year old men with narrow complex tachycardia after consuming EDs, which was a refractory on carotid sinus massage and Valsalva maneuver, and was converted to sinus rhythm after adenosine administration (9).

In this case, sinus rhythm was obtained after the administration of propafenone, which was the first choice for treatment, due to the absence of adenosine in Institution. A case report suggests that continuous consumption of EDs could be associated with the onset of supraventricular arrhythmia. Patient will be controlled with frequent 24-hour ECG-Holter monitoring, with the prescribing of loading dose of propafenone 450 mg in case of new attacks.

CONCLUSION

In the case of newly developed supraventricular tachycardia in the younger population, it is necessary to review the anamnestic data, which may indicate the cause of the arrhythmia. EDs have a proarrhythmogenic effect, and should be considered as a possible cause of supraventricular tachyarrhythmia.

REFERENCES

1. Wassef B, Kohansieh M, Makaryus AN. Effects of energy drinks on the cardiovascular system. World J Cardiol. 2017;9(11):796-806.
2. Mattioli AV, Pennella S, Farinetti A, Manenti A. Energy Drinks and atrial fibrillation in young adults. Clin Nutr. 2018;37(3):1073-1074.
3. Seifert SM, Schaechter JL, Hershorin ER, Lipshultz SE. Health effects of energy drinks on children, adolescents, and young adults. Pediatrics. 2011;127:511–528.
4. Mangi MA, Rehman H, Rafique M, Illovsky M. Energy Drinks and the Risk of Cardiovascular Disease: A Review of Current Literature. Cureus. 2017;9(6):e1322.
5. Conen D, Chiuve SE, Everett BM, Zhang SM, Buring JE, Albert CM. Caffeine consumption and incident atrial fibrillation in women. Am J Clin Nutr. 2010; 92(3):509-514.
6. Shen J, Johnson VM, Sullivan LM, Jacques PF, Magnani JW, Lubitz SA, et al. Dietary factors and incident atrial fibrillation: the Framingham Heart Study. Am J Clin Nutr. 2011; 93(2):261-266.
7. Di Rocco JR, During A, Morelli PJ, Heyden M, Biancaniello TA. Atrial fibrillation in healthy adolescents after highly caffeinated beverage consumption: two case reports. J Med Case Rep. 2011; 5(1):18.
8. Goldfarb M, Tellier C, Thanassoulis G. Review of published cases of adverse cardiovascular events after ingestion of energy drinks. Am J Cardiol. 2014;113:168–172.
9. Nagajothi N, Khraisat A, Velazquez-Cecena JL, Arora R, Raghunathan K, Patel R, et al. Energy drink-related supraventricular tachycardia. Am J Med. 2008;121(4):e3-4.

Reprint requests and correspondence:
Almin Handanagić, MD
Coronary Unit, Cantonal Hospital "Dr Irfan Ljubijankić" Bihać
Darivalaca krvi 67, 77000 Bihać
Bosnia and Herzegovina
Email: almaalmin@hotmail.com.
ORCID ID: 0000-0002-6421-3668

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms
Author's Contribution: AH, FP, SK, EB, AH and NK gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.

Effect of chloropyramine in Brueghel's syndrome

Efekat hloropiramina u Bruegelovom sindromu

Muhamed Lepuzanović[3,4*], Admir Mehičević[1,2], Nevena Mahmutbegović[1,2], Enra Mehmedika-Suljić[1,2]

[1]Clinic of Neurology, Clinical Center University of Sarajevo, Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina
[2]Faculty of Medicine, University of Sarajevo, Čekaluša 90, 71000 Sarajevo, Bosnia and Herzegovina
[3]Department of Neurology, Cantonal Hospital „Dr Irfan Ljubijankić", Darivalaca krvi 67, 77000 Bihać, Bosnia and Herzegovina
[4]Faculty of Health Studies, University of Bihać, Pape Ivana Pavla II 2/II, 77000 Bihać, Bosnia and Herzegovina

*Corresponding author

ABSTRACT

This case reported chloropyramine's effect on focal dystonia, a variant of Meigs syndrome without blepharospasm also called Brueghel's syndrome. The patient, a 63-year-old man, was admitted to the Neurology Clinic due to the tongue's significant dystonic position and moderate dystonic positions of the oromandibular region. Swallowing was difficult, his speech was incomprehensible, the tongue was continuously protruding out of his mouth, and on attempting speech, the degree of protrusion would increase so that the tongue's root was visible. After administering chloropyramine in a dose of 10 mg, the dystonic movements were significantly reduced, his speech became more intelligible, and it became easier for the patient to consume food and drink. Characteristic of this case was the duration of symptoms and also good clinical response on chloropyramine, 25 years after the patient developed the symptoms. The results justify further studies of chloropyramine's effects in treating Brueghel's syndrome and other forms of focal dystonia.

Keywords: focal dystonia, Brueghel's syndrome, chloropyramine

SAŽETAK

U prikazu slučaja zabilježen je učinak hloropiramina na fokalnu distoniju, varijantu Meigsovog sindroma bez blefarospazma, koji se naziva i Bruegelov sindrom. Pacijent, 63-godišnjak je primljen na Neurološku kliniku zbog izraženog distoničnog položaja jezika, kao i umjerenog distoničnog položaja oromandibularne regije. Gutanje je bilo teško, govor je bio nerazumljiv, jezik je neprekidno virio iz usta, a pri pokušaju govora stepen protruzije jezika bi se povećao tako da se mogao vidjeti korijen jezika. Nakon primjene hloropiramina u dozi od 10 mg, znatno su bili manji distonični pokreti, govor je postao razumljiviji i pacijentu je postalo lakše jesti hranu i piće. Karakteristika ovog slučaja je trajanje simptoma, a također i dobar klinički odgovor na hlorpiramin, 25 godina nakon što je pacijent razvio simptome. Naši rezultati opravdavaju daljnja ispitivanja učinaka hloropiramina u liječenju Bruegelovog sindroma kao i drugih oblika fokalne distonije.

Ključne riječi: fokalna distonija, Bruegel sindrom, hloropiramin

INTRODUCTION

Dystonia can be defined as the adoption of abnormal postures, repetitive spasms occurring due to sustained muscle contractions. According to the site of spasm muscle, it can be classified into focal, multifocal, and generalized dystonia (1).

This case report presented a patient in whom, 25 years ago, developed focal dystonia of an unknown cause, which affected his tongue and oromandibular region. This type of dystonia is a variant of Meig's syndrome without blepharospasm, also referred to as Brueghel's syndrome.

CASE REPORT

A 63-year-old man was admitted to Neurology Clinic of the Clinical Center University of Sarajevo due to significant dystonic position of the tongue and moderate dystonic positions of the oromandibular region. The patient suffered from social stigma and shame due to the physical signs of his condition, namely the protrusion of the tongue. Due to this condition he rarely left home in the last 5 years prior to hospital admission, and his quality of life was significantly impaired. Swallowing was difficult, the speech was incomprehensible, the tongue was continuously protruding out of

the mouth, and on attempting speech the degree of protrusion would increase so that the root of the tongue was visible (Figure 1).

Figure 1 **Before administering chloropyramine.**

In an interview with a family member, it was discovered that in 1992, the patient's disorder was preceded by a period of vomiting and stomach problems. Subsequently, the patient received antiemetic therapy and 24 hours later, uncontrollable movements of the tongue appeared for the first time. Given that the patient symptoms occurred at time when there were specific conditions in Bosnia and Herzegovina, especially in the region where the patient comes from, his condition at that time was not recorded in any preserved written medical report. At that time, the only available antiemetic therapy was metoclopramide. The above information was recorded in a statement by a family member, but since it could not be substantiated by valid medical records, the use of metoclopramide could not be directly associated with dystonic movements in the patient.

According to his family, the pat ient was examined in 1994 at a Clinic in Germany and discharged in the same condition without being provided with an explanation for the etiological cause of dystonic movements. The family did not keep this medical record. In 2004, the patient was examined at Neurology Clinic of the Clinical Center University of Sarajevo, when explanation of the etiology of dystonic movements was not obtained. The aforementioned condition of the patient lasted for 25 years, with gradual progression of symptoms in terms of more pronounced dystonic movements and position of the tongue, and oromandibular region. Electroencephalography, neuroimaging, tumor marker studies, serum ceruloplasmin, and other biochemical tests were inconclusive.

After the administration of chloropyramine in a dose of 10 mg, the following improvements in the symptoms were documented: significantly fewer previously described dystonic movements. His speech became more intelligible and it became easier for the patient to consume food and drink (Figure 2).

Figure 2 **After administering chloropyramine.**

DISCUSSION

Dystonia has been characterized by persistent or intermittent muscular contractions, resulting in patterned abnormal repetitive movements and unexpected postures and can be accompanied by tremors. The focal dystonia is a subtype of dystonias, which manifests in specific regions of the body (2). The oromandibular dystonia is a specific type of focal disorder affecting the muscles of the lower facial region. It results from sustained, repetitive contractions of the tongue, chewing, and other lower facial muscles. It is caused by different types of pathologies mainly vascular, infective, toxins, drugs, and degenerative clinical disorders (3). Meige syndrome is a segmental craniofacial dystonia comprehending a preponderant blepharospasm and a variable involvement of other muscles supplied by the cranial nerves, both synchronous and symmetric (4). Paulson G, proposed the term "Meige syndrome" in 1972 for patients having facial muscle spasm, particularly blepharospasm and dystonia of oromandibular muscles. After several years, the term "Brueghel syndrome" was introduced, used by Gilbert, for a case of jaw dystonia. It is differentiated from Meige syndrome by the absence of blepharospasm (5,6,7).

Certain drugs can cause acute dystonia. These are substances that, by their mechanism of action, lead to the stimulation of dopamine receptors (D2) and the blocking of dopamine. Neuroleptics, antiepileptics, antipsychotics, antihypertensives, anesthetics, and antiemetic drugs are the offenders that can cause acute patterned abnormal repetitive movements and unexpected postures (7).

Common adverse drug reactions (ADRs) associated with metoclopramide therapy include restlessness (akathisia), and focal dystonia. Infrequent ADRs include hypertension, hypotension, hyperprolactinemia leading to galactorrhea, depression, headache, and extrapyramidal effects such as oculogyric crisis. Rare but serious ADRs associated with metoclopramide therapy include agranulocytosis, supraventricular tachycardia, hyperaldosteronism, neuroleptic malignant syndrome, akathisia, and tardive dyskinesia (8,9).

Metoclopramide may be the most common cause of drug-induced movement disorders (10). Dystonic reactions may be treated with benzatropine, trihexyphenidyl, or procyclidine. Symptoms usually subside with injected this drug intramuscularly

(11). Agents in the benzodiazepine class of drugs may be helpful, but benefits are usually modest and side effects of sedation and weakness can be problematic (12). The antiemetic effect is subserved by inhibiting the chemoreceptor trigger zone and area postrema in medulla oblongata due to blockade of dopamine receptors The acute dystonic reactions occur due to concomitant blocking of dopamine receptors (D2) in basal ganglia (13).

In this case, a patient with focal dystonia by type of Brueghel's syndrome was treated with the anticholinergic drug chloropyramine and received a good clinical response and improvement. Our results justify a further examination of the effects of chloropyramine in the treatment of the focal dystonia, and expression of dopamine D2 receptors on the somatodendritic side of the cholinergic interneurons in the central nervous system.

Twenty years ago, striatal cholinergic neurons were central figures in models of basal ganglia function. But since then, they have receded in importance. Recent studies are likely to lead to their re-emergence in our thinking. Cholinergic interneurons have been implicated as key players in the induction of synaptic plasticity and motor learning, as well as in motor dysfunction (13).

CONCLUSION

The case reported the effect of chloropyramine on focal dystonia, a variant of Meige's syndrome without blepharospasm, also called Brueghel's syndrome. The syndrome developed 25 years ago in a man who was exposed to antiemetic therapy (metoclopramide). After the administration of chloropyramine in a dose of 10 mg dystonic movements were significantly fewer, speech became more intelligible, and it became easier for the patient to consume food and drink. In addition to rarity, the characteristic of this case related to duration of symptoms and also a good clinical response on chloropyramine, 25 years after the patient developed the symptoms. The results justify further studies of the effects of chloropyramine in the treatment of Brueghel's syndrome and other forms of focal dystonia.

REFERENCES

1. Fahn S, Bressman SB, Marsden CD. Classification of dystonia. Adv Neurol. 1998;78:1-0.
2. Jinnah HA, Berardelli A, Comella C, Defazio G, Delong MR, Factor S, et al. The focal dystonias: Current views and challenges for future research. Mov Disord. 2013;28:926-43.
3. Tolosa ES. Clinical Features of Meige's Disease (Idiopathic Orofacial Dystonia): A Report of 17 Cases. Arch Neurol. 1981;38(3):147-151.
4. Khan J, Anwer HM, Eliav E, Heir G. Oromandibular dystonia: Differential diagnosis and management. J Am Dent Assoc. 2015;146:690-3.
5. Zhan S, Sun F, Pan Y, Liu W, Huang P, Cao C, et a l. Bilateral deep brain stimulation of the subthalamic nucleus in primary Meige syndrome. Journal of Neurosurgery. 2028;128(3):897-902.
6. Sellal F, Frismand S. Cervico-facial dystonia as depicted in sculpture before its scientific description. Rev Neurol (Paris). 2019;175(3):198-200.
7. Aires A, Gomes T, Linhares P, Cunha F, Rosas MJ, Vaz R. The impact of deep brain stimulation on health related quality of life and disease-specific disability in Meige Syndrome (MS). Clin Neurol Neurosurg. 2018;171:53-57.
8. Sherer J, Salazar T, Schesing KB, McPartland S, Kornitzer J. Diphenhydramine for Acute Extrapyramidal Symptoms After Propofol Administration. Pediatrics. 2017;139(2):e20161135.
9. Rossi S, ed. (2006). Australian Medicines Handbook. Adelaide: Australian Medicines Handbook. ISBN 978-0-9757919-2-3.
10. Hibbs AM, Lorch SA. Metoclopramide for the treatment of gastroesophageal reflux disease in infants: a systematic review. Pediatrics. 2006;118(2):746-52.
11. FDA requires boxed warning and risk mitigation strategy for metoclopramide-containing drugs" (Press release). U.S. Food and Drug Administration. 26 February 2009. Retrieved 11 June 2009. "Lay Summary - WebMD.
12. Olanow C, Schapira AV. Chapter 372. Parkinson's Disease and Other Movement Disorders. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson J, Loscalzo J. eds. Harrison's Principles of Internal Medicine, 18e. New York, NY: McGraw-Hill; 2012.
13. Pisani A, Bernardi G, Ding J, Surmeier DJ. Re-emergence of striatal cholinergic interneurons in movement disorders. Trends Neuros ci. 2007;30(10):545-53.

Reprtint requests and correspondence:
Muhamed Lepuzanović, MD
Department of Neurology
Cantonal Hospital „Dr Irfan Ljubijankić“
Darivalaca krvi 67, 77000 Bihać
Bosnia and Herzegovina
Email: muhamed.lepuzanovic@gmail.com
ORCID ID: 0000-0001-6920-3015

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.
Authors' Contributions: ML, AM, NM and EM-S gave substantial contribution to the conception or design of the article and in the acquisition, analysis and interpretation of data for the work. Each author had role in article drafting and in process of revision. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
Financial support and sponsorship: Nil.
Conflict of interest: There are no conflicts of interest.

INSTRUCTIONS TO AUTHORS

Journal **"Medical Journal"** publishes original research articles, professional, review and educative articles, case reports, criticism, reports, professional news, in the fields of all medical disciplines. Articles are written in-extenso in English, with the abstract and the title in English and Bosnian/Croatian/Serbian language.
Authors take responsibility for all the statements and attitudes in their articles. If article was written by several authors, it is necessary to provide full contact details (telephone numbers and email addresses) of the corresponding author for the cooperation during preparation of the text to be published.
Authors should indicate whether the procedures carried out on humans were in accordance with the ethical standards of medical deontology and Declaration of Helsinki.
Articles that contain results of animal studies will only be accepted for publication if it is made clear that ethics standard were applied.
Measurements should be expressed in units, according to the rules of the SI System.

Manuscript submission should be sent to Editorial Board and addressed to:
"MEDICINSKI ŽURNAL"
Disciplina za nauku i nastavu Kliničkog centra Univerziteta u Sarajevu
Bolnička 25
71000 Sarajevo
Bosna i Hercegovina
e-mail: institutnir@bih.net.ba; bibliotekanir@kcus.ba

COVER LETTER

Apart from the manuscript, the authors should enclose a cover letter, with the signed statements of all authors, to the Editorial Board of "Medical Journal" stating that:
1. the work has not been published or accepted for publication previously in another journal,
2. the work is in accordance with the ethical committee standards,
3. the work, accepted for publication, becomes ownership of "Medical Journal".

PREPARATION OF MANUSCRIPT

Article should be no longer than 10 computer pages, including figures, graphs, tables and references. The article may be submitted as a CD disk (Word Windows), or e-mail.
Spacing: 1,5: left margin: 2,5 cm; right margin: 2,5 cm; top and bottom margin: 2,5 cm.
Graphs, tables, figures and drawings should be incorporated in the text, precisely in the text, where these will be published, regardless of the program in which they are prepared. Articles are written in-extenso in English language.
The manuscript should be submitted on a good quality CD disc, or by e-mail, together with two printed copies (if possible). Sent CD disks will not be returned to the authors.

ARTICLE CONTAINS:

TITLE OF THE ARTICLE IN ENGLISH LANGUAGE
TITLE OF THE ARTICLE IN BOSNIAN/SERBIAN/CROATIAN (B/S/C) LANGUAGE
First and last name of the author/co-author(s)

Name and address of the institution in which author/co-authors is employed (same for all authors) in B/S/C and English language as well as the address of corresponding author at the end of the article.

Summary in B/S/C language with the precise translation in English. Abstract of approximately 200-250 words should concisely describe the contents of the article.
Key words (in B/S/C and in English language): up to five words should be listed under the Abstract.

ARTICLE BODY

The main body of the article should be systematically ordered under the following headings:
- **INTRODUCTION**
- **MATERIALS AND METHODS**
- **RESULTS**
- **DISCUSSION**

- **CONCLUSION**
- **REFERENCES**

INTRODUCTION

Introduction is a concise, short part of the article, and it contains purpose of the article relating to other published articles with the same topic. It is necessary to quote the main problem, aim of investigation, and/or main hypothesis which is investigated.

MATERIALS AND METHODS

This part should contain description of original or modification of known methods. If there is a method that has previously been described, it would be sufficient to include it in the reference list. In clinical and epidemiological studies the following should be described: sample, protocol and type of clinical investigation, place and period of investigation. Main characteristics of investigation should be described (randomization, double-blind test, cross test, placebo test), standard values for tests, time framework (prospective, retrospective study), selection and number of patients – criteria for inclusion and exclusion from the study.

RESULTS

Main results of investigation and level of its statistical significance should be quoted. Results should be presented in tables, graphs, figures, and directly incorporated in the text, at the exact place, with ordinal number and concise heading. Table should have at least two columns and explanation; figures clean and contrasted, graphs clear, with visible text and explanation.

DISCUSSION

Discussion is concise and refers to own results, in comparison with the other authors' results. Citation of references should follow Vancouver rules. Discussion should be concluded by the confirmation of the stated aim or hypothesis, or by its negation.

CONCLUSION

Conclusion should be concise and should contain most important facts, which were obtained during investigation and its eventual clinical application, as well as the additional studies for the completed application. Affirmative and negative conclusions should be stated.

REFERENCES – Instructions for writing references

References should follow the format of the requirements of **Vancouver rules**.

Every statement, knowledge and idea should be confirmed by reference. Each reference in the text is given its own sentence case in Arabic number in parenthesis at the end of the sentence according to the order of entering. Every further referring to the same reference, number of the first referring in the text should be stated. References are to be placed at the end of the article, and are to be numbered by ordinal numbers in the order of entering in the text (entering reference number). Journal's title is abbreviated using Index Medicus abbreviations. The names of the first six authors of each reference item should be provided, followed by "et al.".

It is very important to properly design references according to instructions that may be downloaded from addresses National Library of Medicine Citing Medicine http://www.ncbi.nlm.nih.gov/books/bv.fcg?rid=citmed.TOC&depth=2,

or International Committee of Medical Journal Editors Uniform Requirements for Manuscripts Submitted to Biomedical Journals:

Sample References http://www.nlm.nih.gov/bsd/uniform_requirements.html.

UPUTSTVA AUTORIMA

Časopis "Medicinski žurnal" objavljuje originalne naučne radove, stručne, pregledne i edukativne, prikaze slučajeva, recenzije, saopćenja, stručne obavijesti i drugo iz područja svih medicinskih disciplina. Rad *in-extenso* (cjelokupan) piše se na engleskom jeziku, uz sažetak i naslov rada koji uz engleski trebaju biti napisani i na našim jezicima (bosanski, hrvatski i srpski). Autori su odgovorni za sve navode i stavove u njihovim radovima. Ukoliko je rad pisalo više autora, potrebno je navesti tačnu adresu (uz telefonski broj i e-mail adresu) onog autora s kojim će uredništvo sarađivati pri uređenju teksta za objavljivanje.
Ukoliko su u radu prikazana istraživanja na ljudima, mora se navesti da su provedena u skladu s načelima medicinske deontologije i Deklaracije iz Helsinkija.
Ukoliko su u radu prikazana istraživanja na životinjama, mora se navesti da su provedena u skladu s etičkim načelima. Prilikom navođenja mjernih jedinica, treba poštovati pravila navedena u SI sistemu.
Radovi se šalju Redakciji na adresu:
"MEDICINSKI ŽURNAL"
Disciplina za nauku i nastavu Kliničkog centra Univerziteta u Sarajevu
Bolnička 25
71000 Sarajevo
Bosna i Hercegovina
e-mail: institutnir@bih.net.ba; bibliotekanir@kcus.ba

POPRATNO PISMO

Uz svoj rad, autori su dužni Redakciji "Medicinskog žurnala" dostaviti popratno pismo, koje sadržava vlastoručno potpisanu izjavu svih autora:
1. da navedeni rad nije objavljen ili primljen za objavljivanje u nekom drugom časopisu,
2. da je istraživanje odobrila Etička komisija,
3. da prihvaćeni rad postaje vlasništvo "Medicinskog žurnala".

OPSEG I OBLIK RUKOPISA

Radovi ne smiju biti duži od deset stranica na računaru, ubrajajući slike, grafikone, tabele i literaturu. CD zapis teksta je obavezan (Word of Windows), ili e-mail.
Prored: 1,5: lijeva margina: 2,5 cm; desna margina: 2,5 cm; gornja i donja margina: 2,5 cm.
Grafikone, tabele, slike i crteže unijeti/staviti u tekst rada, tamo gdje im je mjesto, bez obzira u kojem programu su rađene. Cijeli rad obavezno napisati na engleskom jeziku, a sažetak i naslov još i na našem jeziku.
Rad se dostavlja na CD-u, i/ili e-mailom, uz dva štampana primjerka (ako je moguće). CD se ne vraća.

RAD SADRŽI:

NASLOV RADA NA ENGLESKOM JEZIKU
NASLOV RADA NA NAŠEM JEZIKU

Ime i prezime autora i koautora

Naziv i puna adresa institucije u kojoj je autor-koautor/i zaposlen/i (jednako za sve autore), na engleskom jeziku, te na kraju rada navedena adresa kontakt-autora.

Sažetak na našem jeziku, kao i na engleskom - max. 200–250 riječi, s najznačajnijim činjenicama i podatcima iz kojih se može dobiti uvid u kompletan rad.
Ključne riječi - Key words, na našem jeziku i na engleskom, ukupno do pet riječi, navode se ispod Sažetka, odnosno Abstracta.

SADRŽAJ

Sadržaj rada mora biti sistematično i strukturno pripremljen i podijeljen u poglavlja i to:
- **UVOD**
- **MATERIJAL I METODE**
- **REZULTATI**
- **DISKUSIJA**
- **ZAKLJUČAK**
- **LITERATURA**

UVOD

Uvod je kratak, koncizan dio rada i u njemu se navodi svrha rada u odnosu na druge objavljene radove sa istom tematikom. Potrebno je navesti glavni problem, cilj istraživanja i/ili glavnu hipotezu koja se provjerava.

MATERIJAL I METODE

Potrebno je da sadrži opis originalnih ili modifikaciju poznatih metoda. Ukoliko se radi o ranije opisanoj metodi dovoljno je dati reference u literaturi. U kliničko-epidemiološkim studijama opisuju se: uzorak, protokol i tip kliničkog istraživanja, mjesto i vrijeme istraživanja. Potrebno je opisati glavne karakteristike istraživanja (npr. randomizacija, dvostruko slijepi pokus, unakrsno testiranje, testiranje s placebom itd.), standardne vrijednosti za testove, vremenski odnos (prospektivna, retrospektivna studija), izbor i broj ispitanika – kriterije za uključivanje i isključivanje u istraživanje.

REZULTATI

Navode se glavni rezultati istraživanja i nivo njihove statističke značajnosti. Rezultati se prikazuju tabelarno, grafički, slikom i direktno se unose u tekst gdje im je mjesto, s rednim brojem i konciznim naslovom. Tabela treba imati najmanje dva stupca s obrazloženjem što prikazuje; slika čista i kontrastna, a grafikon jasan, s vidljivim tekstom i obrazloženjem.

DISKUSIJA

Piše se koncizno i odnosi se prvenstveno na vlastite rezultate, a potom se nastavlja upoređivanje vlastitih rezultata s rezultatima drugih autora, pri čemu se citiranje literature navodi po važećim Vankuverskim pravilima. Diskusija se završava potvrdom zadatog cilja ili hipoteze, odnosno njihovim negiranjem.

ZAKLJUČAK

Treba da bude kratak, da sadrži najbitnije činjenice do kojih se došlo u radu tokom istraživanja i njihovu eventualnu kliničku primjenu, kao i potrebne dodatne studije za potpuniju aplikaciju. Obavezno navesti i afirmativne i negirajuće zaključke.

LITERATURA - Upute za citiranje - pisanje literature

Literatura se obavezno citira po **Vankuverskim pravilima**.

Svaku tvrdnju, saznanje ili misao treba potvrditi referencom. Reference u tekstu treba označiti po redoslijedu unošenja arapskim brojevima u zagradi na kraju rečenice. Ukoliko se kasnije u tekstu pozivamo na istu referencu, navodimo broj koji je referenca dobila prilikom prvog unošenja/pominjanja u tekstu. Literatura se popisuje na kraju rada, rednim brojevima pod kojim su reference unesene u tekst (ulazni broj reference), a naslov časopisa se skraćuje po pravilima koje određuje Index Medicus. Ukoliko je citirani rad napisalo više autora, navodi se prvih šest i doda "et al.".

Vrlo je važno ispravno oblikovati reference prema uputama koje se mogu preuzeti na adresama National Library of Medicine Citing Medicine http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=citmed.TOC&depth=2 , ili International Committee of Medical Journal Editors Uniform Requirements for Manuscripts Submitted to Biomedical Journals:

Sample References http://www.nlm.nih.gov/bsd/uniform_requirements.html.