ISSN: 2148-4724
E-ISSN: 2548-0030

TMSJ

TURKISH MEDICAL STUDENT JOURNAL

Volume: 5 Issue: 1 Feb 2018

http://tmsj.trakya.edu.tr/

TMSJ

TURKISH MEDICAL STUDENT JOURNAL

THE OFFICIAL JOURNAL OF
TRAKYA UNIVERSITY FACULTY OF MEDICINE

Citation Abbreviation: Turkish Med. Stud. J.

VOLUME 5 - ISSUE 1 - FEB 2018

Published three times a year

Free access to the Journal's web site: *http://tmsj.trakya.edu.tr*

Manuscript Submission*: tmsj@trakya.edu.tr*

Editorial Office
Address: Trakya Universitesi Tıp Fakültesi 22030 Edirne, Turkey
Phone: +90 (284) 235-7653
E-mail: dekanlik@trakya.edu.tr

Printing at: Trakya Üniversitesi Basımevi
Edirne Teknik Bilimler M.Y.O Sarayiçi Yerleşkesi, 22020 Yeni İmaret, Edirne, Turkey
Phone: +90 (284) 224 02 83
Printing Date: Febuary 2018
ISSN: 2148-4724 E-ISSN: 2548-0030

TMSJ
TURKISH MEDICAL STUDENT JOURNAL

Editor-in-Chief
Koray DEMİRCİ
Trakya University Faculty of Medicine, Edirne, Turkey

Deputy Editor-in-Chief
Öznur YUMURTACI
Trakya University Faculty of Medicine, Edirne, Turkey
Furkan YİĞİTBİLEK
Trakya University Faculty of Medicine, Edirne, Turkey
Nur Gülce İŞKAN
Trakya University Faculty of Medicine, Edirne, Turkey

English Editor
Aslıhan AKŞAR
Trakya University Faculty of Medicine, Edirne, Turkey

Editorial Board

Ahmet EMİN
Trakya University Faculty of Medicine, Edirne, Turkey
Alperen ŞİRİN
Acıbadem University Faculty of Medicine, Istanbul, Turkey
Aslı GÖZTEPE
Trakya University Faculty of Medicine, Edirne, Turkey
Batuhan AKSOY
Istanbul University Faculty of Medicine, Istanbul, Turkey
Begüm SÖYLEYİCİ
Trakya University Faculty of Medicine, Edirne, Turkey
Berfin TAN
Trakya University Faculty of Medicine, Edirne, Turkey
Berk TOY
Marmara University Faculty of Medicine, Istanbul, Turkey
Berkay KEF
Okan University Faculty of Medicine, Istanbul, Turkey
Cansu KURT
Trakya University Faculty of Medicine, Edirne, Turkey
Çağrı GİRİT
Trakya University Faculty of Medicine, Edirne, Turkey
Ece ŞENYİĞİT
Trakya University Faculty of Medicine, Edirne, Turkey
Fatih Erkan AKAY
Trakya University Faculty of Medicine, Edirne, Turkey
Hasan Orkun İPSALALI
Bahçeşehir Faculty of Medicine, Istanbul, Turkey
Hilal Sena ÇİFCİBAŞI
Trakya University Faculty of Medicine, Edirne, Turkey
Kubilay ELMACI
Trakya University Faculty of Medicine, Edirne, Turkey
Mahmut Alper GÜLDAĞ
Trakya University Faculty of Medicine, Edirne, Turkey
Ozan ÖNER
Trakya University Faculty of Medicine, Edirne, Turkey
Pelinsu Elif HÜNKAR
Trakya University Faculty of Medicine, Edirne, Turkey

Indexed In
Türk Medline
Science World Index
Science Library Index
Academic Keys

Publisher
Trakya University

TMSJ
TURKISH MEDICAL STUDENT JOURNAL

Editorial Advisory Board

Prof. Ahmet Muzaffer DEMİR, MD
Trakya University, Edirne, Turkey (Hematology)
Prof. Ahmet ULUGÖL, MD
Trakya University, Edirne, Turkey (Pharmacology)
Prof. Ahmet YILMAZ, MD
Trakya University, Edirne, Turkey (Forensic Medicine)
Prof. Ali AYDINLAR, MD
Uludağ University, Bursa, Turkey (Cardiology)
Prof. Ali İlker FİLİZ, MD
Okan University, İstanbul, Turkey (General Surgery)
Prof. Ali YILMAZ, MD
Trakya University, Edirne, Turkey (Anatomy)
Assoc. Prof. Andrea Mario Pompeo ROMANI, MD, PhD
Case Western Reserve University, Cleveland, OH, USA (Physiology & Biophysics)
Prof. Atakan SEZER, MD
Trakya University, Edirne, Turkey (General Surgery)
Assoc. Prof. Ayşe ÇAYLAN, MD
Trakya University, Edirne, Turkey (Family Medicine)
Assist. Prof. Ayşe Gülsen CEYHUN PEKER, MD
Ankara University, Ankara, Turkey (Internal Medicine)
Prof. Babürhan GÜLDİKEN, MD
Trakya University, Edirne, Turkey (Neurology)
Prof. Berna ARDA, MD
Ankara University, Ankara, Turkey (History of Medicine and Ethics)
Prof. Berrak Çağlayan YEĞEN, MD
Marmara University, İstanbul, Turkey (Physiology)
Assoc. Prof. Beste Melek ATASOY
Marmara University, İstanbul, Turkey (Radiation Oncology)
Prof. Betül Ayşe ACUNAŞ, MD
Trakya University, Edirne, Turkey (Pediatrics)
Prof. Cem UZUN, MD
Trakya University, Edirne, Turkey (Otolaryngology)
Assoc. Prof. Dumrul GÜLEN, PhD
Namık Kemal University, Tekirdağ, Turkey, (Tumor Biology and Immunology)
Prof. Erbuğ KESKİN,MD
İstanbul Universit,İstanbul,Turkey(Pediatric Urology)
Prof. Ersan TATLI, MD
Sakarya University, Sakarya, Turkey (Cardiology)
Assist. Prof. Ertan ŞAHİN, MD
Namık Kemal University, Tekirdağ, Turkey (Nuclear Medicine)
Prof. Fatih ÖZÇELİK, MD
Trakya University, Edirne, Turkey (Cardiology)
Prof. Galip EKUKLU, MD
Trakya University, Edirne, Turkey (Public Health)
Prof. Gülay DURMUŞ ALTUN, MD
Trakya University, Edirne, Turkey (Nuclear Medicine)
Prof. Hakan KARADAĞ, MD
Trakya University, Edirne, Turkey (Pharmacology)
Prof. Hakan TUNA, MD
Trakya University, Edirne, Turkey (Physical Medicine and Rehabilitation)
Prof. Hakkı Mete ÇEK, MD
Trakya University, Edirne, Turkey (Urology)
Prof. Hanefi Yekta GÜRLERTOP, MD
Trakya University, Edirne, Turkey (Cardiology)
Prof. Hasan YAZICI, MD
Academic Hospital,İstanbul,Turkey (Rheumatology)
Assist. Prof. Hilmi TOZKIR, MD
Trakya University, Edirne, Turkey (Medical Genetics)
Prof. Hüsniye Figen KULOĞLU, MD
Trakya University, Edirne, Turkey (Infectious Diseases)
Prof. Hüseyin Ahmet TEZEL, MD
Trakya University, Edirne, Turkey (Gastroenterology)
Assoc. Prof. Işık GÖRKER, MD
Trakya University, Edirne, Turkey (Child Psychiatry)
Prof. İlknur ERDEM, MD
Namık Kemal University, Tekirdağ, Turkey (Infectious Diseases)
Prof. Kenan SARIDOĞAN, MD
Trakya University, Edirne, Turkey (Orthopedics)
Prof. Levent ÖZTÜRK, MD
Trakya University, Edirne, Turkey (Physiology)
Assoc.Prof. Merter YALÇINKAYA,MD
İstinye University, İstanbul,Turkey (Orthopedics)
Prof. Murat AKSU, MD
Acıbadem University, İstanbul, Turkey (Neurology)
Prof. Mustafa ERTAŞ, MD
Istanbul, Turkey (Neurology)
Prof. M. Erkan KOZANOĞLU, MD
Çukurova University, Adana, Turkey (Physical Medicine and Rehabilitation)
Prof. Mustafa İNAN, MD
Trakya University, Edirne, Turkey (Pediatric Surgery)
Prof. Necdet SÜT, PhD
Trakya University, Edirne, Turkey (Biostatistics and Informatics)
Prof. Nermin TUNÇBİLEK, MD
Trakya University, Edirne, Turkey (Radiology)
Prof. Nurettin AYDOĞDU, PhD
Trakya University, Edirne, Turkey (Physiology)
Prof. Okan ÇALIYURT, MD
Trakya University, Edirne, Turkey (Psychiatry)
Prof. Osman Nuri HATİPOĞLU, MD
Trakya University, Edirne, Turkey (Pulmonology)
Assist. Prof. Ozan SALİM, MD
Akdeniz University, Antalya, Turkey (Hematology)
Assoc. Prof. Rahime Nida ERGİN BAYIK
Bahçeşehir University, İstanbul, Turkey (Gynecology and Obstetrics)
Prof. Sedat ÜSTÜNDAĞ, MD
Trakya University, Edirne, Turkey (Nephrology)
Prof. Selma Süer GÖKMEN, PhD
Trakya University, Edirne, Turkey (Biochemistry)
Prof. Sevgi ESKİOCAK, MD
Trakya University, Edirne, Turkey (Biochemistry)
Prof. Sibel GÜLDİKEN, MD
Trakya University, Edirne, Turkey (Endocrinology)
Prof. Şaban GÜRCAN, MD
Trakya University, Edirne, Turkey (Microbiology and Clinical Microbiology)
Prof. Tammam SİPAHİ, PhD
Trakya University, Edirne, Turkey (Biophysics)
Assoc. Prof. Tarkan YETİŞYİĞİT, MD
Namık Kemal University, Tekirdağ, Turkey (Internal Medicine)
Assist. Prof. Tayfur TOPTAŞ, MD
Marmara University, İstanbul, Turkey (Hematology)
Prof. Ufuk TALU,MD
American Hospital,İstanbul,Turkey (Orthopedics)
Prof. Ufuk USTA, MD
Trakya University, Edirne, Turkey (Pathology)
Assoc. Prof. Volkan İNAL, MD
Trakya University, Edirne, Turkey (Intensive Care)
Assoc. Prof. Volkan YÜKSEL, MD
Trakya University, Edirne, Turkey (Cardiovascular Surgery)
Prof. Yekta Altemur KARAMUSTAFAOĞLU, MD
Trakya University, Edirne, Turkey (Thoracic Surgery)
Prof. Zafer KOÇAK, MD
Trakya University, Edirne, Turkey (Radiation Oncology)
Assist. Prof. Zehra Nihal DOLGUN, MD
Trakya University, Edirne, Turkey (Gynecology and Obstetrics)
Assoc. Prof. Zeynep Banu DOĞANLAR, PhD
Trakya University, Edirne, Turkey (Medical Biology)

Owner
Prof. Ahmet Muzaffer DEMİR, MD
Dean, Trakya University Faculty of Medicine
Responsible Manager
Koray DEMİRCİ
Trakya University Faculty of Medicine, Edirne, Turkey

MISSION & SCOPE

Turkish Medical Student Journal (TMSJ) is an independent, non-profit, peer-reviewed, international, open access journal; which aims to publish articles of interest to both physicians and scientists. TMSJ is published three times a year, in February, June and October by Trakya University. The language of publication is English.

TMSJ publishes original researches, interesting case reports and reviews regarding all fields of medicine. All of the published articles are open-access and reachable in our website. The primary aim of the journal is to publish original articles with high scientific and ethical quality and serve as a good example of medical publications for stimulating students, doctors, researchers. Our mission is to feature quality publications that will contribute to the progress of medical sciences as well as encourage medical students to think critically and share their hypotheses and research results internationally.

The Editorial Board and the Publisher adheres to the principles of International Council of Medical Journal Editors (ICMJE), Committee on Publication Ethics (COPE).

Turkish Medical Student Journal is indexed in Google Scholar, Science World Index, Science Library Index and Academic Keys. Turkish Medical Student Journal is available as hard copy. In addition, all articles can be downloaded in PDF format from our website (http://tmsj.trakya.edu.tr), free of charge.

EDITORIAL PROCESS

All manuscripts submitted for publication are reviewed for their originality, methodology, importance, quality, ethical nature and suitability for the journal by the editorial board and briefly revised by the advisory board whose members are respected academicians in their fields. Well-constructed scheme is used for the evaluation process. All manuscripts are reviewed by two different members of the editorial board, followed by peer revision from at least two professors, belonging to different institutions, who are experts in their areas. The editors assist authors to improve the quality of their papers. The editor-in-chief has full authority over the editorial, scientific content and the timing of publication.

ETHICS

Turkish Medical Student Journal depends on publication ethics to ensure all articles published in TMSJ are acceptable in terms of scientific ethical standards and do not include any kind of plagiarism. TMSJ expects authors and editorial board to adhere the principles of Committee on Publication Ethics (COPE). To reach the highest standards, TMSJ has an advisory board member who is a professional in ethics.

All original articles submitted to the TMSJ have to be approved by an ethical committee and include the name of ethics committee(s) or institutional review board(s), the number/ID of the approval(s). Additionally, informed consent documents obtained from patients involving case reports is required for the submission.

All received manuscripts are screened by a plagiarism software (iThenticate). Similarity percentage more than 25 (or more than 5 for one paper) and six consecutive words cited from an another published paper in the same order are the causes of immediate rejection.

MATERIAL DISCLAIMER

All opinions, reports and results within the articles that are published in the TMSJ are the personal opinions of the authors. The Editorial board, the editorial advisory board, the publisher and the owner of the TMSJ do not accept any responsibility for these articles.

INSTRUCTIONS TO AUTHORS

CATEGORIES OF ARTICLES

The Journal publishes the following types of articles:

Original Research Articles: Original prospective or retrospective studies of basic or clinical investigations in areas relevant to medicine.

Content:

- Abstract (average 400 words; the structured abstract contain the following sections: aims, methods, results, conclusion)
- Introduction
- Material and Methods
- Results
- Discussion
- References

Review Articles: The authors may be invited to write or may submit a review article. Reviews including the latest medical literature may be prepared on all medical topics.

Content:

- Abstract (average 400 words; without structural divisions)
- Titles on related topics
- References

Case Reports: Brief descriptions of a previously undocumented disease process, a unique unreported manifestation or treatment of a known disease process, or unique unreported complications of treatment regimens. They should include an adequate number of photos and figures.

Content:

- Abstract (average 200 words; the structured abstract contain the following sections: introduction, case report, conclusion)
- Introduction
- Case presentation
- Discussion
- References

Editorial Commentary/Discussion: Evaluation of the original research article is done by the specialists of the field (except the authors of the research article) and it is published at the end of the related article.

Letters to the Editor: These are the letters that include different views, experiments and questions of the readers about the manuscripts that were published in this journal in the recent year and should be no more than 500 words.

Content:

- There's no title and abstract.
- The number of references should not exceed 5.
- Submitted letters should include a note indicating the attribution to an article (with the number and date) and the name, affiliation and address of the author(s) at the end.
- The answer to the letter is given by the editor or the author(s) of the manuscript and is published in the journal.

Scientific Letter: Presentations of the current cardiovascular topics with comments on published articles in related fields.

Content:

- Abstract (average 200 words; without structural division)
- Titles on related topics
- References

What is Your Diagnosis? : These articles are related with diseases that are seen rarely and
show differences in diagnosis and treatment, and they are prepared as questions-answers.

Content:

- Titles related with subject
- References

MANUSCRIPT PREPARATION

Authors are encouraged to follow the following principles before submitting their material.

-The article should be written in IBM compatible computers with Microsoft Word.

ABBREVIATIONS: All abbreviations in the text must be defined the first time they are used, and the abbreviations should be displayed in parentheses after the definition. Authors should avoid abbreviations in the title, abstract and at the beginning of the first sentences of the paragraphs.

FIGURES, PICTURES, TABLES AND GRAPHICS:

-All figures and tables should be cited at the end of the relevant sentence. Explanations must be placed at the bottom of figures, whereas at the top of tables.

-Figures and tables must be added to the e-mail as attachments in .jpg or .tiff formats.

- The name of the file should be named as: last name of the first author_Table/Figure_No.TIFF/JPEG. For example: Sancar_Figure_1.JPEG.
- All abbreviations used, must be listed in explanation which will be placed at the bottom of each figures and tables.
- For figures and tables to be reproduced relevant permissions need to be provided. This permission must be mentioned in the explanation.
- Pictures/photographs must be in color, clear and with appropriate contrast to separate details.

TITLE PAGE: A concise, informative title, should be provided. All authors should be listed with academic

degrees, affiliations, addresses, office and mobile telephone and fax numbers, and e-mail and postal addresses. If the study was presented in a congress, the author(s) should identify the date/place of the congress of the study presented.

ABSTRACT: The abstracts should be prepared in accordance with the instructions in the "Categories of Articles" and placed in the article file.

KEYWORDS:

-They should be minimally three.

- Keywords should be appropriate to "Medical Subject Headings (MESH)"

(Look: www.nlm.nih.gov/mesh/MBrowser.html).

ACKNOWLEDGEMENTS: Conflict of interest, financial support, grants, and all other editorial (statistical analysis, language editing) and/or technical assistance if present, must be presented at the end of the text.

REFERENCES: References should be numbered in the order they are cited. Only published data or manuscripts accepted for publication and recent data should be included. Inaccessible data sources and those not indexed in any database should be omitted. Titles of journals should be abbreviated in accordance with Index Medicus- NLM Style (Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007 - [updated 2011 Sep 15; cited Year Month Day] (http://www.nlm.nih.gov/citingmedicine). All authors should be listed if an article has three or less authors; first three authors are listed and the rest is represented by "ve ark." in Turkish articles and by "et al." in English articles. Reference format and punctuation should be as in the following examples.

Journal: Muller C, Buttner HJ, Peterson J et al. A randomized comparison of clopidogrel and aspirin versus ticlopidine and aspirin after placement of coronary artery stents. Circulation 2000;101:590-3.

Book Section: Sherry S. Detection of thrombi. In: Strauss HE, Pitt B, James AE, editors. Cardiovascular Medicine. St Louis: Mosby; 1974.p.273-85.

Books with Single Author: Cohn PF. Silent myocardial ischemia and infarction. 3rd ed. New York: Marcel Dekker; 1993.

Editor(s) as author: Norman IJ, Redfern SJ, editors. Mental health care for elderly people. New York: Churchill Livingstone; 1996.

Conference Proceedings: Bengisson S. Sothemin BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Piemme TE, Rienhoff O, editors. MEDINFO 92. Proceedings of the 7th World Congress on Medical Informatics; 1992 Sept 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992.p.1561-5.

Scientific or Technical Report: Smith P. Golladay K. Payment for durable medical equipment billed during skilled nursing facility stays. Final report. Dallas (TX) Dept. of Health and Human Services (US). Office of Evaluation and Inspections: 1994 Oct. Report No: HHSIGOE 169200860.

Thesis: Kaplan SI. Post-hospital home health care: the elderly access and utilization (dissertation). St. Louis (MO): Washington Univ. 1995.

Manuscripts accepted for publication, not published yet: Leshner AI. Molecular mechanisms of cocaine addiction. N Engl J Med In press 1997.

Epub ahead of print Articles: Aksu HU, Ertürk M, Gül M et al. Successful treatment of a patient with pulmonary embolism and biatrial thrombus. Anadolu Kardiyol Derg 2012 Dec 26. doi: 10.5152/ akd.2013.062. [Epub ahead of print]

Manuscripts published in electronic format: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis (serial online) l995 Jan-Mar (cited 1996 June 5): 1(1): (24 screens). Available from: URL:http://www.cdc.gov/ncidodlElD/cid.htm

EDITORIAL

Dear readers,

As William Osler –one of the founders of the Johns Hopkins Hospital- said: "Medicine is a science of uncertainty and an art of probability". Enlightening unknown mechanisms, discovering new approaches, achieving findings that contribute to advances in medicine are the goals of many researchers around the world. Medical students, who have the passion of being part of the scientific world, carry out studies continuously. As TMSJ, we are proud of having carried out the task to create an opportunity for medical students to publish their manuscripts internationally since 2014. Growing up as a journal each year, we believe each issue that is published will reach more readers, sharing valuable information obtained by the recent studies in our journal with them, also encouraging many to take part in researches.

In the first issue of 2018, you can find 3 original articles, 2 case reports and 1 letter to the editor. Akay et al. shared their data of 552 patients focusing on the risk of hepatitis B virus reactivation in patients receiving immunosupressive therapies. Söyleyici et al. found out that T wave amplitude in lead aVR can be used to evaluate the prognosis of ICD implanted hypertrophic cardiomyopathy patients, while Tekwani et al. investigated the use of the antiseptic chlorhexidine to prevent premature rupture of membranes in pregnant women with varicose disease.

As we are beginning a new year, there have been changes in our editorial board. 10 new editors from different institutions joined us and have done great contributions so far. Having new editors from different universities increased the diversity of our editorial board, thus, enabled us to reach more readers and evaluate manuscripts more efficiently. We are grateful to them for adjusting to our teamwork in a very short time with great motivation.

There are also great organizations around the world that aim to provide a platform for medical students to present their researches internationally and create a good scientific atmosphere. Biomedical Congress University of Porto (AEICBAS, 15-18 March 2018), Bukovinian International Medical Congress (BIMCO, 4-6 April 2018), Medical International Conference for Students (MEDICS, 19-22 April 2018), 4th McMaster International Review Course in Internal Medicine (MIRCIM, 10-12 May 2018), and International Congress of Medical Sciences (ICMS, 10-13 May 2018) are among those amazing medical student congresses. As TMSJ, we are going to attend them representing our journal. We kindly invite all of our readers to be a part of these events!

Hope to meet you again in our next issue.

Koray DEMİRCİ
Editor-in-Chief

CONTENTS

ORIGINAL ARTICLE

1 ***RISK FACTORS AND MANAGEMENT OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS WITH HEMATOLOGICAL DISORDERS***

Fatih Erkan Akay, Berfin Tan, Mahmut Alper Güldağ, Sena Çifcibaşı, Kubilay Elmacı, Elif Gülsüm Ümit

5 ***IMPACT OF T WAVE AMPLITUDE IN LEAD aVR ON PREDICTING APPROPRIATE THERAPIES IN HYPERTROPHIC CARDIOMYOPATHY PATIENTS WITH AN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR***

Begüm Söyleyici, Pelinsu Elif Hünkar, Çağrı Girit, Cansu Kurt, Fatih Mehmet Uçar

9 ***NEW APPROACHES IN PREVENTING PREMATURE RUPTURE OF MEMBRANES IN PREGNANT WOMEN WITH VARICOSE DISEASE***

Vinisha Tekwani, Varahabhatla Vamsi, Gaidai Nataliya

CASE REPORT

14 ***PERIOSTEAL CHONDROMA OF THE FEMUR: A CASE REPORT***

Ece Şenyiğit, Nur Gülce İşkan, Mert Çiftdemir

18 ***A CASE REPORT OF SPONTANEOUS CORONARY ARTERY DISSECTION***

Yusuf Can Özdemir, Kubilay Elmacı, Fatih Özçelik

LETTER TO THE EDITOR

22 ***EUROPEAN STUDENT RESEARCH NETWORK (EUROSURG) IMAGINE PROJECT***

Bahadır E. Baki, Bahar B. Ozkan, Başak Yüksek, Arif Y. Sen, Melik K. Aktas

TMSJ
Turkish Med. Stud. J. 2018; 5: 1-4 DOI: 10.4274/tmsj.2018.05.01.0001

Received: 18.12.2017 - Accepted: 28.12.2017

RISK FACTORS AND MANAGEMENT OF HEPATITIS B VIRUS REACTIVATION IN PATIENTS WITH HEMATOLOGICAL DISORDERS

Fatih Erkan Akay[1], Berfin Tan[1], Mahmut Alper Güldağ[1], Hilal Sena Çifcibaşı[1], Kubilay Elmacı[1], Elif Gülsüm Ümit[2]

[1] Trakya University School of Medicine, Edirne, TURKEY
[2] Department of Hematology, Trakya University School of Medicine, Edirne, TURKEY

ABSTRACT

Aims: The aim of this study is to evaluate hepatitis B virus serological status and to categorize the risks of our treatment modalities in patients with both benign and malignant hematological disorders.

Methods: This was a retrospective study of 552 patients who were admitted to the Trakya University Hospital Hematology unit between 01.01.2017 and 31.12.2017. All data regarding the diagnosis, treatment and HBV serological status were collected from patient files. Data were analyzed with IBM SPSS V.20 using descriptive statistical analysis.

Results: Hepatitis B surface antigen was positive in 45 (8.2%) patients, antibody to the hepatitis B surface antigen was positive in 279 (50.5%) patients and antibody to the hepatitis B core antigen was positive in 247 (44.7%) patients. According to these results, 32 patients were found to be vaccinated for hepatitis B virus. Reactivation was observed in 4 (0.7%) patients who have been hepatitis B surface antigen positive and have received adequate duration of antiviral prophylaxis with tenofovir. These 4 patients have received monoclonal antibody for immunosuppressive treatment.

Conclusion: To conclude, although the rate of hepatitis B surface antigen reactivation is quite low, as many patients as possible should be vaccinated to reduce the costs of antiviral treatments and monitorization. If there is no time to vaccinate, patients should be categorized according to guidelines by their hepatitis B surface antigen serological status and by the planned immunosuppressive treatments.

Keywords: Hepatitis, hematology, immunotherapy

INTRODUCTION

The course of hepatitis B virus (HBV) infection depends on the interplay between host's immune status and response and viral replication. In all patients, HBV persists within the body even after sereological recovery. The suppression of immune system with certain treatments brings a risk for reactivation and flare of HBV infection (1). This interplay of HBV and altered immune status of the patient may cause delay in immunosuppresive treatment for the underlying hematological disease or even lead to fulminant hepatic failure and/or death (1).

According to guidelines, before the initiation of immunosuppresive treatment, all patients should be screened for HBV infection (2). Screening test for HBV should include HBV surface antigen (HBsAg) and HBV core antibody (Anti-HBc) which demonstrate the encounter with HBV (3). Depending upon these results, if the patient is HbsAg positive, baseline HBV DNA levels should be measured. In patients who are HBsAg negative but Anti-HBc positive, HBV DNA testing is also recommended depending on the risk of the planned immunosuppressive treatment (4). It is recommended that patients with a positive HBsAg result should also be tested for HBeAg and Anti-HBe. All patients, who are negative for HBV screening and will undergo immunosuppresive treatment, should be vaccinated, preferably before the immunosuppresive treatment (2-5).

Patients who are positive for HBV serology (HbsAg and/or anti-HBc positive) are at risk for HBV reactivation if they receive immunosuppressive treatment. This immunosuppresive treatment may be either for an autoimmune disorder such as immune thrombocytope-

Adress for Correspondence: Fatih Erkan Akay, Trakya University School of Medicine, Edirne, TURKEY - e-mail: erkanfatih48@gmail.com

nia (ITP), autoimmune hemolytic anemia (AHA) or a hematological malignancy like leukemia, lymphoma or myeloma including stem cell transplantation (6).

The aim of our study is to evaluate HBV serological status and to categorize the risks of our treatment modalities in patients with both benign and malignant hematological disorders.

MATERIAL AND METHODS

This study was approved by Scientific Research Ethics Committee of Trakya University Medical Faculty. Patients who were admitted to Trakya University Hospital Hematology unit between 01.01.2017 and 31.12.2017. All data of 552 patients were screened in a retrospective manner. All patients who are older than 18 years of age were included in the study. All data regarding the diagnosis (bening or malign hematological disorders), treatment (immunomodulatory threapies that the patients received), HBV status (HBsAg, Anti-HBs, Anti-HBc test results) were collected from the files of patients. With the data obtained, the number of patients, who are vaccined for HBV and the reactivation rate among patients were planned to be determined, in order to establish the risk of HBV reactivation in patients recieving immunomodulatory therapies.

Data were analysed with IBM SPSS V.20 using descriptive statistical analysis. Numbers, percentages, arithmetic mean, minimum, maximum were used as descriptive statistics.

RESULTS

Total number of inpatient admission during a whole year period was 552. Out of all patients, 234 (42.3%) of them were female, while 318 (57.7%) of them were male. Mean age was 59,12 years and minimum age was 18 years, whereas maximum age was 93 years. Regarding diagnosis of patients, 114 (20.7%) patients had benign hematological disorders including ITP, AHA and hemostatic disorders; 231 (41.8%) patients had lymphoma, 97 (17.6%) had multiple myeloma and 110 (19.9%) patients had leukemia. 108 (19.6%) patients were observed to receive non-immunomodulatory treatment while 131 (23.7%) patients received monoclonal antibodies including rituximab and brentuximab, 253 (45.8%) patients received conventional chemotherapy, 49(8.9%) patients received hypomethylating agents and 11 (2%) patients received targeted therapy containing regimens. Patients who are receiving monoclonal antibodies may also receive conventional treatment. Within combination, 246 (44.6%) patients received anthracycline category of immunosuppression and 359 (65%) patients received corticosteroids.

HBsAg was positive in 45 (8.2%) patients, Anti-HBs in 279 (50.5%) patients and Anti-HBc was positive in 247 (44.7%) patients. From these results, it was deduced that 32 patients were vaccinated for HBV.

Among the patients, 119 of them were observed to receive antiviral treatment with lamivudine, tenofovir or entecavir. Those patients were observed to receive conventional low dose chemotherapy, hypomethylating agent or short duration of corticosteroids. Of patients receiving corticosteroids, 138 were categorized as long-term and high-dose therapy group and all were on adequate antiviral treatment. Patients who were on low-dose and short-term corticosteroids were either on antiviral treatment or on close monitorization, depending on the patient-physician decision and concerns.

Reactivation was observed in 4 patients (0.7%) who have been HBsAg positive and have received adequate duration of antiviral prophylaxis with tenofovir, initiated 2 weeks prior to chemotherapy. All 4 patients had received monoclonal antibody (rituximab) for immunosuppressive treatment.

DISCUSSION

As high as 70% of HBsAg positive patients receiving conventional chemotherapy for solid/hematological tumors were reported to develop HBV reactivation. For patients with assumably resolved HBV infection defined as HBsAg negative but AntiHBc positive, reactivation prevalence was reported as 0.3-9% (1). Any immunosuppresive treatment has a potential to cause HBV reactivation. However, certain regimens are related with more pronounced risk of activation. The American Gastroenterological Association (AGA) and the American Association for the Study of Liver Diseases (AASLD) have attempted to categorize the level of risk for HBV reactivation among individuals receiving certain immunosuppressive agents (1, 2). In the Table 1, the treatments with rated risks of HBV reactivation are summarized. To be pointed out is that with the development of high technology treatment options, the list of treatments that are associated with HBV reactivation is constantly expanding. Almost all immunosuppressive and immunomodulatory drugs including traditional chemothe-

Table 1: Immunosuppressive Agents and Risk Classification of HBV Reactivation.

Very High Risk (20% risk of reactivation) HBsAg positive patients	High risk (11-20% risk of reactivation) HBsAg positive patients	Moderate Risk (1-10% risk of reactivation) HBsAg positive patients	Low Risk (<1% risk of reactivation) HBsAg positive patients	Very low risk
Rituximab	High dose corticosteroids (≥20 mg/day, at least 4 weeks)	Cytotoxic chemotherapy without corticosteroids	Methotrexate	HBsAg negative and anti-HBc positive patients receiving cytotoxic chemotherapy without glucocorticoids, anti-TNF therapy, methotrexate, or azathioprine.
Ofatumumab	Alemtuzumab	Anti-TNF therapy	Azathiopurine	
Obinutuzumab		Anti-rejection therapy for solid organ transplantation	HBsAg negative and AntiHBc positive patients receiving high dose (≥20 mg/day) corticosteroids or alemtuzumab	
Hematopoietic stem cell transplantation				

rapeutic agents and glucocorticoids, as well as biologic agents (e.g. anti-CD20 and anti-TNF agents), and new classes of drugs, such as targeted treatments like tyrosine kinase inhibitors ans mechanistic target of rapamycin inhibitors, bring the risk of HBV reactivation (3, 4).

The major determinant of HBV reactivation in a patient is the HBV serological status. Patients who are HBsAg positive have a greater risk than patients who are HBsAg negative. Among patients who are HBsAg positive, particularly those who are also HBeAg positive have a much greater risk for HBV reactivation. HBsAg negative patients are likely to have a resolved infection. Nevertheless, patients who are HBsAg negative but Anti-HBc positive are at risk for HBV reactivation if immunosuppressive treatment is initiated. Reactivation may occur even in those who are anti-HBs-positive but with a low risk (6).

For patients who are HBsAg negative and receiving rituximab, cyclophosphamide, doxorubicin and prednisone (RCHOP, the gold standart regime for B-cell lymphomas) HBV reactivation prevalence ranges from 3% to 41%. The risk for patients who are receiving rituximab for collagen tissue disorders are even lower. This decreased risk may be explained with the underlying immunological condition and concomitant treatments (7, 8).

The risk of corticosteroids depends on the dose and duration of treatment. High-dose, prolonged treatments are related with higher risk while it should be stated that low-dose treatment with prolonged use may also bring risk. HBV replication increases in the presence of corticosteroids. This effect may be due to the stimulation of replicative activity with steroids. However, during the replication of HBV, necroinflammation of hepatocytes are suppressed with steroids, and as a result, serum transaminase levels are low. Once the glucocorticods are stopped, viral replication is controlled with active immunity but a necroinflammation develops and transaminase levels increase. The peak increase of transaminases typically occurs 4-6 weeks after withdrawal. Corticosteroids are commonly used within combination regimes and are frequently ignored as a major treatment agent. However, it should be kept in mind that even within combination regimens, the use of corticosterods increases the risk of HBV reactivation (9). In our study, we observed that patients receiving corticosteroids for a short duration (less than 4 weeks) may be just monitorized without antiviral treatment.

Most patients with HBV reactivation are asymptomatic, but in patients with increased transaminase levels, an acute hepatitis infection manifestation may be observed. Jaundice, hepatic failure and even death may be certain.

The diagnosis of HBV reactivation is based on the increase in HBV DNA levels. A detectable HBV DNA level in a corticosteroids for a short duration undetectable HBV DNA; a rise of more than 2 log10 international units/mL compared to baseline or a reverse seroconversion (previously HBsAg negative then HBsAg positive) (1).

Treatment of HBV reactivation is generally supportive measures and antivirals. Tenofovir or entecavir may be used in a treatment-naive patient, decision depending upon the renal functions. These agents should be preferred to lamivudine since lamivudine is related with increased risk of resistance. A patient who previously received lamivudine should be treated with tenofovir due to entecavir monotherapy resistance in lamivudine refractory patients.

The main goal of management in patients with HBV seropositivity should be based on prevention. Patients who will undergo immunosuppressive treatment and are HBsAg positive or HBsAg negative, anti-HBc positive (regardless of anti-HBs positivity), should be evaluated for antiviral prophylaxis. According to the risk category defined by AASLD and AGA and summarized in Table 1, patients should be evaluated according to HBV serological status and the planned immunosuppressive treatment for the underlying hematological disorder. For patients who have a moderate to very high risk, antiviral therapy should be started concurrently and preferably

prior to immunosuppression. The duration of antiviral prophylaxis is one year after the last dose of immunosuppression especially, in patients receiving anti-CD20. For patients with low and very low risk, decision to start antiviral therapy may be postponed with close transaminase and HBV DNA monitoring. Lastly, in patients with uncertain risk, the decision to start prophylactic antiviral treatment depends on the physicians' concern (1-5). In our study group we observed a good monitorization in patients with low risk without reactivation.

General approach for the choice of antiviral treatment is tenofovir or entecavir over lamivudine. Lamivudine is recommended only when the first line agents are not available since lamivudine resistance is not rare.

Although the reactivation rate of HBV was found to be quite low in our study, vaccinating as many patients as possible is advantagous because of its role in reducing costs of antiviral treatments and monitorization. If we do not have time to vaccinate, we shall categorize the patients according to guidelines with their HBV serological status and the planned immunosuppressive treatments.

Ethics Committee Approval: This study was approved by Scientific Researches Committee of Trakya University School of Medicine.
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Author contributions: Concept: FEA, BT, MAG, HSÇ KE, EGÜ. Design: FEA, BT, MAG, HSÇ KE, EGÜ. Supervision: FEA, BT, MAG, HSÇ KE, EGÜ. Resources: FEA, BT, MAG, HSÇ KE, EGÜ. Materials: FEA, BT, MAG, HSÇ KE, EGÜ. Data collection and/or processing: FEA, BT, MAG, HSÇ KE, EGÜ. Analysis and/or Interpretation: FEA, BT, MAG, HSÇ, KE, EGÜ. Literature Search: MAG, HSÇ, KE, EGÜ. Writing Manuscript: FEA, BT, MAG, HSÇ, KE, EGÜ. Critical Review: FEA, BT, MAG, HSÇ KE, EGÜ.
Financial disclosure: The authors declared that this study received no financial support.
Editor-in-chief's Note: Five of the authors of this article, Fatih Erkan Akay, Berfin Tan, Mahmut Alper Güldağ, Sena Çiftçibaşı and Kubilay Elmacı are members of the editorial board of Turkish Medical Student Journal. However, they did not take place in any stage on the editorial decision of the manuscript. The editors who evaluated this manuscript are from another institutions.

REFERENCES

1. Reddy KR, Beavers KL, Hammond SP et al. American Gastroenterological Association Institute guideline on the prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. Gastroenterology 2015;148:215-9.

2. European Association For The Study Of The Liver. EASL clinical practice guidelines: management of chronic hepatitis B virus infection. J Hepatol 2017;67(2):370-98.

3. Di Bisceglie AM, Lok AS, Martin P et al. Recent US Food and Drug Administration warnings on hepatitis B reactivation with immune-suppressing and anticancer drugs: just the tip of the iceberg? Hepatology 2015; 61:703-11.

4. Hwang JP, Somerfield MR, Alston-Johnson DE et al. hepatitis B virus screening for patients with cancer before therapy: American Society of Clinical Oncology provisional clinical opinion update. J Clin Oncol 2015; 33:2212-20.

5. Perrillo RP, Gish R, Falck-Ytter YT. American Gastroenterological Association Institute technical review on prevention and treatment of hepatitis B virus reactivation during immunosuppressive drug therapy. Gastroenterology 2015; 148:221-4.

6. Perrillo RP, Martin P, Lok AS. Preventing hepatitis B reactivation due to immunosuppressive drug treatments. JAMA 2015;313:1617-8.

7. Mozessohn L, Chan KK, Feld JJ et al. Hepatitis B reactivation in HBsAg-negative/HBcAb-positive patients receiving rituximab for lymphoma: a meta-analysis. J Viral Hepat 2015;22:842-9.

8. Huang H, Li X, Zhu J et al. Entecavir vs lamivudine for prevention of hepatitis B virus reactivation among patients with untreated diffuse large B-cell lymphoma receiving R-CHOP chemotherapy: a randomized clinical trial. JAMA 2014;312:2521-30.

9. Hui CK, Cheung WW, Au WY et al. Hepatitis B reactivation after withdrawal of pre-emptive lamivudine in patients with haematological malignancy on completion of cytotoxic chemotherapy. Gut 2005;54:1597-603.

TMSJ
Turkish Med. Stud. J. 2018; 5: 5-8 DOI: 10.4274/tmsj.2018.05.02.0001
Received: 06.12.2017 - Accepted: 22.12.2017

IMPACT OF T WAVE AMPLITUDE IN LEAD aVR ON PREDICTING APPROPRIATE THERAPIES IN HYPERTROPHIC CARDIOMYOPATHY PATIENTS WITH AN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

Begüm Söyleyici[1], Pelinsu Elif Hünkar[1], Çağrı Girit[1], Cansu Kurt[1], Fatih Mehmet Uçar[2]

[1] Trakya University School of Medicine, Edirne, TURKEY
[2] Department of Cardiology, Trakya University School of Medicine, Edirne, TURKEY

ABSTRACT

Aims: Although implantable cardioverter defibrillator reduces mortality in hypertrophic cardiomyopathy patients, inappropriate implantable cardioverter defibrillator shocks are related to increased mortality. The aim of this study is to investigate whether a new electrocardiographic marker of T wave amplitude in lead aVR can be used to predict appropriate therapy of implantable cardioverter defibrillator (shock or anti-tachycardia pacing) in hypertrophic cardiomyopathy patients.

Methods: Thirty-six hypertrophic cardiomyopathy patients, who were admitted to the outpatient clinic for pacemaker control, with implantable cardioverter defibrillator were retrospectively examined (mean age: 51 ± 10.2 years, 72.2% male). The primary endpoint was appropriate implantable cardioverter defibrillator therapy. All hematological, biochemical and electrocardiogram parameters were measured before implantable cardioverter defibrillator was implanted.

Results: Over a median follow-up period of 33 months, 9 (25%) patients experienced appropriate implantable cardioverter defibrillator therapy. Heart rate and QRS interval were similar between groups. QT and QTc values were higher in patients that received appropriate shocks. Patients who have T wave inversion were higher in therapy positive group. T wave amplitude in lead aVR values were significantly associated with appropriate therapy.

Conclusion: Using simple ECG parameters, we may predict arrhythmic episodes before ICD implantation and an improvement of the medical antiarrhythmic therapy might be protective for HCM patients with ICD.

Keywords: Hypertrophic cardiomyopathy, defibrillator, electrocardiography

INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most frequent hereditary cardiovascular disease in general population and seen in 1 in 500 equally on both sexes (1). It is characterized by increased ventricular wall thickness. HCM is associated with increased risk of atrial fibrillation, cardiac insufficiency and myocardial ischemia (2). Clinical manifestation of HCM might be shortness of breath, tachycardia, syncope, ischemia or abnormal vascularity. It is the prior cause of sudden death at early ages, with a 0.5-1% occurrence per year and 2.8% mortality rate in the follow-up (3-5).

Implantable cardioverter defibrillator (ICD) is a device which is implanted inside the body in order to provide cardioversion, defibrillation and pacing of the heart. ICD is remarkably effective in reducing the rate of sudden cardiac death due to ventricular tachyarrhythmia. It is used for several indications such as HCM, ischemic-nonischemic cardiomyopathy, Brugada syndrome and Long QT syndrome (6).

Nevertheless, inappropriate ICD therapy, which is caused by a failure of differentiating between supraventricular and ventricular tachyarrhythmia or non-cardiac oversensing (e.g. myopotentials), has possibly life-threatening side effects. Inappropriate ICD therapy

Adress for Correspondence: Begüm Söyleyici, Trakya University School of Medicine, Edirne, TURKEY - e-mail: begumsoyleyici96@gmail.com

(inappropriate anti-tachycardia pacing and inappropriate shocks) or electrode displacement and dysfunction have been associated with myocardial damage and increased mortality. Additionally, inappropriate ICD therapy, especially inappropriate shock therapy, has been related to psychological distress and reduced quality of patients' life (6-8). Therefore, evaluating the adequacy of ICD therapy is highly important for patients. Besides, the association between TAaVR (T wave amplitude in lead aVR) and proper therapy of ICD in HCM patients is not known.

The aim of this study is to reveal the association between a simple electrocardiogram (ECG) parameter, T wave amplitude, on aVR derivation and appropriate ICD therapy (shock or anti-tachycardia pacing) in HCM patients.

MATERIAL AND METHODS

This study was approved by Scientific Research Ethics Committee of Trakya University Medical Faculty. The study is carried out according to the World Health Organization Helsinki Declaration and international ethical standards. Informed consent was obtained from all of the subjects. Patients over 18 years old who are diagnosed with hypertrophic cardiomyopathy, have implantable cardioverter defibrillator and were hospitalized in the cardiology clinic of Trakya University Hospital in between January 2017- 2018 constitute the universe of this retrospective research. 36 subjects were included in the study. Electrocardiograms and discharge reports of these patients are collected from the archive of Trakya University Faculty of Medicine through patients' medical record numbers. T wave amplitudes in the aVR lead of the selected patients' electrocardiograms are examined for the most suitable ICD treatment. All of the measurements were made by the same cardiologist in order to standardize the results.

The 12-lead ECG was recorded at the 50 mm/s speed (Nihon Kohden, Tokyo, Japan) in the supine position and at rest. During the evaluation of the patients, resting heart rate was measured from the ECG. To minimize the incorrect measurements, QT and QRS intervals were measured manually with calipers and magnifying glass. ECG measurements of QT and QRS intervals were done by two cardiologists who were blinded to the patient data. Measurement was done in lead II and lead V5 and the longest QT interval was chosen for the analysis. The QT interval was measured from the beginning of the QRS complex to the end of the T wave and was corrected using the Bazett's formula. T wave inversion was defined as a negative T wave (T amp <0 mV) in at least two contiguous leads except for aVR, V1, and V2 (9). The T wave amplitude was defined as the maximum deviation from the PR isoelectric baseline and/or the first deflection after the QRS complex (10).

The patients were divided into two groups regarding having an appropriate ICD therapy or not. The first group consisted of 27 patients, who had not recieved ICD therapy; while the second group included 9 patients.

After data collection, all of the data was analyzed by using SPSS software version 17.0. A p-value of <0.05 was evaluated as statistically significant. Continuous variables included median with interquartile range or mean ± standard deviation of the data and categorical variables included numbers and percentages of the data. Chi-square test or Fisher's exact test was performed to associate the categorical variables. Data were analysed for normal dissemination using Mann-Whitney U test, Kolmogorov-Smirnov test or Student's t-test and was used for continuous variables, when appropriate. Pearson's correlation test was used for correlational analysis.

RESULTS

The mean age of the subjects was 51 ± 10.2 years; baseline clinical characteristics and laboratory parameters of the patients are shown in Table 1. The baseline clinical and demographic characteristics of the patients were similar between groups (p>0.05).

The ECG and echocardiographic results are shown in Table 2. There was no contrast between the two groups with regard to left ventricular ejection fraction (p=0.22) and left ventricular diameters (p=0.44 and 0.36, respectively). QTs interval and heart rate corrected QT (QTc) intervals were longer in patients who have appropriate therapy (p<0.01 and p<0.001, respectively.). QRS duration was similar between groups (p=0.28). Number of patients with T wave inversion was higher in the appropriate therapy group (p= 0.005) and TAaVR values were significantly associated with appropriate therapy (p < 0.001).

Table 1: Baseline clinical and demographic characteristics, laboratory parameters and medications of the study subjects.

	Therapy (-) (n=27)	Therapy (+) (n=9)	P value
Male (%)	74 (20)	66 (6)	0.66
Age (years)	51 ± 10.9	49 ± 8.3	0.64
Diabetes, (%) n	33 (9)	11 (1)	0.19
Hypertension, (%) n	51 (14)	22 (2)	0.12
Atrial Fibrillation, (%) n	7 (2)	11 (1)	0.72
Glucose (mg/dL)	99 ±18.0	97 ±17.5	0.58
Creatinine (mg/dL)	0.87 ±0.23	0,85 ±0.13	0.85
Na (mEq/L)	132 ±24	137 ±2.1	0.66
K (mEq/L)	4.6 ±0.5	4.4 ±0.7	0.59
AST (mg/dL)	25 (11-49)	30 (16-65)	0.50
ALT (mg/dL)	24 ±13	25 ±11	0.85
LDL (mg/dL)	117 ±42	110 ±55	0.75
HDL (mg/dL)	39 ±13	44 ±33	0.64
Wight blood cell, x109/L	8.1 ±1.8	9.0 ±1.0	0.30
Hemoglobin (mg/dL)	13.0 ±1.7	13.4 ±1.0	0.57
Beta-blocker n (%)	85 (23)	88 (8)	0.78
ACEI-ARB, (%) n	85 (23)	55 (5)	0.08
Digoxin, (%) n	14 (4)	11 (1)	0.63
Spironolactone, (%) n	37 (10)	44 (4)	0.71

Na: Sodium; K: Potassium; AST: Aspartate aminotransferase; AST: Alanine transaminase; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker

Table 2: Echocardiographic and electrocardiographic results of the patients.

	Therapy (-) (n=27)	Therapy (+) (n=9)	P value
Ejection Fraction (%)	60 ± 2.9	62 ± 4.5	0.22
LVEDD (mm)	45 ± 4.8	46 ± 3.1	0.44
LVESD (mm)	30 ± 4.1	29 ± 3.9	0.36
Heart rate (bpm)	73 ± 11.3	79 ± 11.5	0.19
QT interval (ms)	378 ± 17.8	397 ± 19.5	0.01
QTc interval (ms)	404 ± 32.5	437 ± 55.5	<0.001
QRS interval (ms)	94 ± 11	99 ± 14	0.28
T wave inversion, (%)n	22 (6)	77 (7)	0.005
TaVR	- 0,04 ± 0.03	- 0,17 ± 0.04	< 0.001

Data are represented as mean values ±SD. LVEDD: Left Ventricle End Diastolic Diameter; LVESD: Left Ventricle End Systolic Diameter; mm: millimeters; bpm: beats per minute; TAaVR, T wave amplitude in lead aVR.

DISCUSSION

Hypertrophic cardimyopathy is a genetic cardiovascular disease and characterized by increased wall thickness in which left ventricle of the heart due to subaortic stenosis without a certain cause. HCM is a common disease with a prevalence of one in 500 people of both genders (1, 2).

Myocardial ischemia, atrial fibrillation and heart failure risks are increased in patients with HCM. Atrial fibrillation is seen in 20% of patients and is the most common arrhythmia in HCM (1). Atrial fibrillation affects patients with HCM by increasing the risk of embolic stroke and heart failure. Those risks are increased in patients with left ventricular outflow obstruction. Aging and left atrial enlargement are associated with susceptibility to atrial fibrillation. Atrial fibrillation has not been explained by a particular genetic substrate or mitral regurgitation or left-ventricular outflow obstruction but there is no evidence about an independent cause of sudden death in atrial fibrillation (2).

In this study, it is found that the frequency of patients with more negative TAaVR was significantly higher in the therapy positive group than the therapy negative group ($p<0.001$). For this reason, T wave amplitude in lead aVR can be used to predict and evaluate appropriate of ICD therapy in HCM patients.

The importance of the lead aVR is usually neglected. However, ST elevation in lead aVR has been reported in left main coronary artery disease prediction (11). Furthermore, aVR is important in the evaluation of Brugada syndrome and it can be used for risk stratification (12).

In other respects, T wave amplitude in lead aVR can be used to evaluate the prognosis of diseases. It was demonstrated in dialysis patients that, positive TAaVR was related to all-cause mortality (13). In addition, a research by Tanaka et al. (14) reported that TAaVR was used for prediction of cardiovascular events in ischemic and nonischemic cardiomyopathy patients with ICD.

In the end of the study, we concluded that a higher TAaVR is associated with appropriate therapies in HCM patients who have ICD implants. Using simple ECG parameters, we may predict arrhythmic episodes before ICD implantation and an improvement of the medical antiarrhythmic therapy might be protective for HCM patients with ICD.

Ethics Committee Approval: This study was approved by Scientific Researches Committee of Trakya University School of Medicine.
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Author contributions: Concept: BS, ÇG, PEH, CK, FMU. Design: BS, ÇG, PEH, CK, FMU. Supervision: BS, ÇG, PEH, CK, FMU. Resources: BS, ÇG, PEH, CK, FMU. Materials: BS, ÇG, PEH, CK, FMU. Data collection and/or processing: BS, ÇG, PEH, CK, FMU. Analysis and/or Interpretation: BS, ÇG, PEH, CK, FMU. Literature Search: BS, ÇG, PEH, CK, FMU. Writing Manuscript: BS, ÇG, PEH, CK, FMU. Critical Review: BS, ÇG, PEH, CK, FMU.
Financial disclosure: The authors declared that this study received no financial support.
Editor-in-chief's Note: Four of the authors of this article, Begüm Söyleyici, Pelinsu Elif Hünkar, Çağrı Girit and Cansu Kurt are members of the editorial board of Turkish Medical Student Journal. However, they did not take place in any stage on the editorial decision of the manuscript. The editors who evaluated this manuscript are from another institutions.

REFERENCES

1. Maroon BJ, Maroon MS. Hypertrophic cardiomyopathy. Lancet 2013; 81:242–55.

2. Liew AC, Vassiliou VS, Cooper R et al. Hypertrophic cardiomyopathy-past, present and future. J Clin Med 2017;6(12):118.

3. Spirito P, Autore C, Formisano F et al. Risk of sudden death and outcome in patients with hypertrophic cardiomyopathy with benign presentation and without risk factors. Am J Cardiol 2014;113:1550-5.

4. Veselka J, Zemanek D, Jahnlova D et al. Risk and causes of death in patients after alcohol septal ablation for hypertrophic obstructive cardiomyopathy. Can J Cardiol 2015;31:1245-51.

5. Maron BJ, Rowin EJ, Casey SA et al. Hypertrophic cardiomyopathy in adulthood associated with low cardiovascular mortality with contemporary management strategies. J Am Coll Cardiol 2015;65:1915-28.

6. Sears SF, Conti JB. Quality of life and psychological functioning of ICD patients. Heart 2002;87:488-93.

7. Moss AJ, Schuger C, Beck CA et al. Reduction in inappropriate therapy and mortality through ICD programming. N Engl J Med 2012;367:2275-83.

8. Özkartal T, Breitenstein A, Saguner AM et al. The subcutaneous implantable cardioverter defibrillator in daily clinical practice. Swiss Med Wkly 2017 9;147:w14518.

9. Konno T, Fujino N, Hayashi K et al. Differences in the diagnostic value of various criteria of negative T waves for hypertrophic cardiomyopathy based on a molecular genetic diagnosis. Clin Sci (Lond) 2007;112(11):577-82.

10. Tan SY, Engel G, Myers J et al. The prognostic value of T wave amplitude in lead aVR in males. Ann Noninvasive Electrocardiol 2008;13(2):113-9.

11. Kireyev D, Arkhipov MV, Zador ST et al. Clinical utility of aVR-The neglected electrocardiographic lead. Ann Noninvasive Electrocardiol 2010;15(2):175-80.

12. Babai Bigi MA, Aslani A, Shahrzad S. aVR sign as a risk factor for life-threatening arrhythmic events in patients with brugada syndrome. Heart Rhythm 2007;4(8):1009-12.

13. Matsukane A, Hayashi T, Tanaka Y et al. Usefulness of an upright T-wave in lead aVR for predicting the short-term prognosis of incident hemodialysis patients: a potential tool for screening high-risk hemodialysis patients. Cardiorenal Med 2015;5(4):267–77.

14. Tanaka Y, Konno T, Tamura Y et al. Impact of T wave amplitude in lead aVR on predicting cardiac events in ischemic and nonischemic cardiomyopathy patients with an implantable cardioverter defibrillator. Ann Noninvasive Electrocardiol 2017;22:1245-53.

TMSJ
Turkish Med. Stud. J. 2018; 5: 9-13 DOI: 10.4274/tmsj.2018.05.03.0001

Received: 29.12.2017 - Accepted: 05.01.2018

NEW TREATMENT APPROACHES TO PREVENT PREMATURE RUPTURE OF MEMBRANES IN PREGNANT WOMEN WITH VARICOSE DISEASE

Vinisha Tekwani[1], Varahabhatla Vamsi[1], Gaidai Nataliya[2]

[1] Zaporozhye State Medical University, Zaporozhye, UKRAINE.
[2] Department of Obstetrics and Gynecology, Zaporozhye State Medical University, Zaporozhye, UKRAINE.

ABSTRACT

Aims: To investigate modern methods to prevent premature rupture of membranes by the use of chlorhexidine in pregnant women with varicose disease.

Methods: The data of 39 pregnant women with varicose disease, who delivered between 2014 and 2016 at Maternity Hospital No. 3, Zaporozhye were analyzed using SPSS software. Patients were divided in 3 groups according to their medical history, complications during pregnancy, childbirth and postpartum period. The 1st group consisted of 13 pregnant women who did not receive prenatal vaginal douching with chlorhexidine; the 2nd group consisted of 13 patients with varicose disease, who received douching of birth canal with vaginal suppositories with chlorhexidine 1 time per day for 10 days before their delivery, but did not undergo a rehabilitation at the sanatorium; and the 3rd group had 13 pregnant women who received sanatorium rehabilitation at "Veliki lug" during the II. trimester of their pregnancy with the course of 1 chlorhexidine suppository per day for 10 days before delivery.

Results: In the 1st group, the percentage of premature death was 61.5%; anemia and significant ultrasound markers were present in 46.2%; the percentage for the presence of hematometra was 38.5%; premature rupture of membranes, anomalies of labor and polyhydroamniosis were 30.8%; chorioamnionitis 15.4%; and intrauterine infection of fetus was 7.7%. In the 2nd group, anemia was present in 35%, 23.1% showed anomalies of labor; premature rupture of membranes, ultrasound markers, premature death, and hematometra were present in 15.4%. Whereas in the 3rd group, anemia and anomalies of labor were present in 15.4%, premature rupture of the membranes and premature death were present in 7.7% of the patients.

Conclusion: With its broad antibacterial and antiviral effect, chlorhexidine in antiseptic form was found to be beneficial and it is found to promote the restoration of the vaginal microflora.

Keywords: Pregnancy, infection, membrane

INTRODUCTION

With the progress in modern obstetrics, the need for new approaches to problems concerning the protection of the fetus becomes evident. Preterm premature rupture of membranes (PROM) can be characterized as the rupture of the fetal membranes before the beginning of labor at any gestational age before 37th week (1-2). Complications such as PROM occur in nearly 8% percent of all term pregnancies (>37 weeks) and about 20% of these are prolonged by PROM, about 30% of these being preterm deliveries (3-5). Genital tract infections constitute an important risk factor for women of reproductive age (6). Intensive reproduction of microorganisms in the vagina flora and cervix leads to an entry into the uterine cavity. Furthermore, the microorganisms are colonized in the basal layer of the decidua through which the microorganisms can pass into the blood vessels of the fetus and subsequently cause choriovasculitis or can reach the amniotic layer causing bacterial amnionitis. Moreover, microorganisms penetrating the amniotic fluid contribute to the inactivation of local antibacterial systems.

Currently, bacterial vaginosis is considered as the most common cause of PROM. Recent studies indicate the number of neonates with signs of bacterial intrauterine infection (IUI) as 20-55%. Gram-negative mic-

Adress for Correspondence: Vinisha Tekwani, Zaporozhye State Medical University, Zaporozhye, UKRAINE - e-mail: vinishatekwani33@gmail.com

robacteria play an important role in the development of IUI's. PROM has been found to be associated with urogenital infections such as chlamydiosis, trichomoniasis, syphilis and gonorrhoea (6).

In neonates, PROM can increase the risk of intraventricular hemorrhage which can result in neurodevelopmental disability (cerebral palsy). PROM can lead to maternal infection, fetal deformation, low Apgar score, low birth weight, fetal infection, umbilical cord compression and prolapse, pulmonary hypoplasia, preterm delivery, and fetal demise (7). Pregnancies complicated by infections may constitute a difficulty in selection of the right antibacterial therapy due to its possible adverse effects on the developing fetus.

Risk factors for PROM include infections such as bacterial vaginosis, urinary tract infections, sexually transmitted diseases, PROM or preterm delivery in previous pregnancy, multiple gestations, bleeding episodes during the pregnancy, smoking during pregnancy, nutritional deficit, low socio-economic status, underweight, illicit drug use during pregnancy, polyhydramnios, invasive procedures such as amniocentesis, cervical insufficiency (7).

Chlorhexidine is an antiseptic which is active against bacteria (gram-positive and negative) and has no effect on clostridium spores (8). Chlorhexidine has a variety of usage, such as in surgical hand antisepsis, neonatal wiping, preoperative shower, vaginal wiping prior to delivery, cord care, dental and oral hygiene (9). Chlorhexidine is included under section 15.1, antiseptics by WHO Model Formulary 2009, 2011 (10, 11).

The Food and Drug Administration, in the early 1990's, granted clearance for 3 types of medical equipment that contain chlorhexidine: intravenous catheters, topical antimicrobial wound dressers, and antimicrobial surgical mesh implants.

The aim of this study was to investigate modern methods to prevent premature rupture of membranes by the use of chlorhexidine in pregnant women with varicose disease.

MATERIAL AND METHODS

This study was approved by Scientific Research Ethics Committee of Zaporozhye State Medical University. The data of 39 pregnant women with varicose disease, who have been delivered between 2014 and 2016 at Maternity Hospital No. 3, Zaporozhye were analyzed and evaluated retrospectively. Patients were divided into 3 groups according to the anamnesis, complications during pregnancy, childbirth and the postpartum period. The 1st group consisted of 13 pregnant women who did not receive prenatal vaginal douching with chlorhexidine; the 2nd group had 13 patients with varicose disease, who received douching of birth canal with chlorhexidine vaginal suppositories once per day for 10 days prior to delivery, but did not receive a rehabilitation at the sanatorium; and the 3rd group had 13 pregnant women who received sanatorium rehabilitation at "Veliki lug" during the II. trimester of their pregnancy with a course of chlorhexidine suppository once a day over a 10-day period prior to delivery.

Examination of pregnant women with varicose veins included a bacterioscopic and bacteriological study of the vaginal mucosa, cervical canal, urethra, general clinical, biochemical analysis, ultrasound determining the biophysical profile of the fetus, dopplerometry of the utero-fetoplacental complex.

After data collection, all of the data was analyzed by using SPSS software. Numbers, percentages, and arithmetic mean were used as descriptive statistics for this study.

RESULTS

Patients' ages were divided based on their reproductive age, anamnesis, gestational period and complications during their pregnancy. In the 1st group, there were 3 (23%) patients whose age were in between 16-25 years, 5 (38.4%) patients in between 26-30 years, 5 (38.4%) patients in between 31-40 years. According to gestation, 1 (7.7%) patient was pregnant for 28 weeks, 3 (23.1%) patients were pregnant for 34-37 weeks, 9 (69.2%) patients were pregnant for 38-41 weeks. In the 2nd group, 6 (46, 2%) patients were in the age group between 20-30 years, 7 (53.8%) patients were between 31-42 years. In terms of gestation: 3 (23.1%) patients were between 33-37 weeks of gestation, 10 (76.9%) patients were in between 38-40 weeks. In the 3rd group, 2 (15.4%) patients were in the age group between 21-29 years, 8 (64.5%) patients were in between 30-35 years and 3 (23.1%) patients were in the age group between 36-41 years.

Considering the results for the bacteriological study of the mucosa prior and after the rehabilitation and medical treatment in the 2nd group of patients, the data presented in Table 1 was acquired.

Table 1: Results from the bacteriological study of the mucosa prior and after the rehabilitation and medical treatment in the 2nd group of patients.

Vaginal Microflora	Cell count before treatment	Cell count after treatment
Gardnerella vaginalis (CFU/ml)	10^6	10^2
Candida albicans (CFU/ml)	10^5	10^2
Escherichia coli (CFU/ml)	10^7	10^3
Staphylococcus epidermalis (CFU/ml)	10^7	10^2
Mobiluncus spp (CFU/ml)	10^5	-
Klebsiella spp (CFU/ml)	10^8	10^3
Staphylococcus aureus (CFU/ml)	10^6	10^4

Almost 50% of the cases were associated with two or three microorganisms found in all groups. The data from the examination of the patients before sanitation are presented in Table 2.

Table 2: The data obtained from the examination of the patients before the sanitation and after the improvement in the local sanatorium "Veliki Lug".

Vaginal Microflora	Cell count before treatment	Cell count after treatment
Candida albicans (CFU/ml)	10^6	-
Staphylococcus aureus (CFU/ml)	10^5	10^2
Staphylococcus epidermalis (CFU/ml)	10^8	10^3
Gardnerella vaginalis (CFU/ml)	10^7	10^3
Streptococcus hemolyticus (CFU/ml)	10^6	10^2
Escherichia coli (CFU/ml)	10^6	10^2

Analysis of pregnancy, childbirth and postpartum period in patients from all the three groups of the study are presented in Table 3.

DISCUSSION

Currently, rehabilitation for pregnant women with varicose disease is not a popular research topic. It is a known fact that application of external heat source shows a positive effect by causing a regression of chronic venous insufficiency. The truth behind this is the reduction of vascular spasm, activation of immune

Table 3: Analysis of the pregnancies, childbirth and postpartum period of patients.

Complications during pregnancy, childbirth and the postpartum period	1st Group	2nd group	3rd group
PROM (%)	30.8	15.4	7.7
Grade 1-2 anemia (%)	46,2	35	15.4
Polyhydroamnion (%)	30.8	-	-
Ultrasound markers of uterine infection (%)	46.2	15.4	-
The threat of premature birth (%)	61.5	15.4	7.7
Chorioamnionitis (%)	15.4	-	-
Anomalies of labor activity (%)	30.8	23.1	15.4
Hematometra (%)	38.5	15.4	-
Intrauterine infection (%)	7.7	-	-

responses, increase of the general tone and resistance of the organism (12-15).

Many researchers declared that douching of vagina and cervix with an active substance like chlorhexidine prevents peripartal infection of the mother and fetus by limiting bacterial growth (16). In addition, two studies using 0.25% chlorhexidine as a vaginal/neonatal disinfectant conducted in developing countries, including a hospital-based study in Malawi providing a second 1-month control period (16). After the therapy, there were compelling reductions in overall septic and newborn admissions, early neonatal mortality as a result of sepsis, as well as significant decrease in maternal hospital admissions (17).

A study conducted in Egypt with 4400 women showed that chlorhexidine treatment resulted in a decreased number of admissions at the neonatal and maternal hospital, with reduced newborn deaths due to infections as well as sepsis (18).

In 2006, Mullany LC et al. (19) stated that 4% chlorhexidine solution used during first 24 hours of delivery reduces the risk of umbilical cord infections.

The review of Lumbiganon et al. (20) indicated 3 studies with 3012 participants showing no benefits with chlorhexidine usage during labor in preventing neonatal and maternal infections (except HIV and streptococcal infections). However, they also stated that a well-designed randomized clinical trial is necessary for the prediction of an appropriate concentration and volume of chlorhexidine solution (20).

In the revised version conducted in 2014, Lumbiganon et al (21) included the same number of participants and assessed the efficacy and side effects of vaginal cleansing with chlorhexidine during labor, which revealed lowered neonatal and maternal infections excluding Guillain-Barré syndrome (GBS).

Christensen et al. (22) proposed a method for preventing GBS infection in term and preterm neonates using chlorhexidine as a vaginal disinfectant during labor in a study conducted between the years of 1983-1999.

Goldenberg et al. (16) conducted a systematic review in 2006, in which they identified the outcomes of each study where, chlorhexidine was used as vaginal irrigant, with or without washing the neonates. They found out that usage of chlorhexidine as vaginal or newborn disinfectant reduced bacterial count including transposal of GBS from mother to child excluding life-threatening maternal or neonatal infections (16).

A systemic review by Stade BC et al. (23) included five studies on 2190 infants both term and preterm, showed the reduction of group B streptococcal colonization with the usage of vaginal chlorohexidine excluding clinical infections. Therefore, the use of vaginal chlorohexidine is not supported by evidence (23).

Many studies have demonstrated that the usage of chlorhexidine as an antiseptic during surgeries as well for douching of the vagina (24, 25). However, none of them presented intensely on complications during the course of pregnancy like PROM.

The study conducted at "Veliki Lug" for the first time in Ukraine, concluded that the usage of sauna therapy with infrared thermos camera reduced chronic venous insufficiency in pregnant women with varicose disease (13). Thus, it averts the pharmacological burden usually acquired via the usage of traditional drug therapy.

In this study, the most substantial outcome of pregnancy, childbirth and postpartum period for the mother and the newborn were noted in the third group of women whose pregnancy preceded against the background of varicose disease with sanatorium rehabilitation as well as vaginal douching with antiseptic drug chlorhexidine. This study included the recovery stage of pregnant women with varicose disease at the local sanatorium 'Veliki Lug'. In addition, the treatment of choice for genital infections was chlorhexidine. Hence, it is inevitable that chlorhexidine meets all the requirements as an antiseptic, antibacterial and antiviral agent plays a crucial role in reducing maternal sepsis and newborn death rates.

Ethics Committee Approval: This study was approved by Scientific Researches Committee of Zaporozhye State Medical University.
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Author contributions: Concept: GNV. Design: GNV. Supervision: GNV, VT. Resources: GNV. Materials: GNV. Data collection and/or processing: GNV, VT, VV. Analysis and/or Interpretation: GNV, VT, VV. Literature Search: GNV, VT, VV. Writing Manuscript: VT, VV. Critical Review: GNV, VT, VV.
Financial disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Aaron BC, Julian NR, Errol RN et al. Contemporary diagnosis and management of preterm premature rupture of membranes. Rev Obstet Gynecol 2008;1(1):11–22.

2. Mackeen AD, Seibel-Seamon J, Grimes-Dennis J et al. Tocolytics for preterm premature rupture of membranes. Cochrane Database Syst Rev 2011;5(10):CD007062.

3. Cunningham F. Abnormal Labor. In: Cunningham F, Leveno KJ, Bloom SL et al, editors. Williams Obstetrics. New York: McGraw-Hill Education; 2014.

4. Roman AS. Late Pregnancy Complication, section: premature rupture of membranes. In: Decherney AH, Nathan L, Laufer N, editors. Current Diagnosis & Treatment: Obstetrics & Gynecology. New York: McGraw-Hill Medical; 2013.

5. Sarah N, Dan KK, Freddie B et al. Practice bulletins No. 139: premature rupture of membranes. Obstet Gynecol 2013;122(4):918-30.

6. Nakubulwa S, Kaye DK, Bwanga F et al. Genital infections and risk of premature rupture of membranes in

Mulago Hospital, Uganda: a case-control study. BMC Res Notes 2015;16(8):573.

7. Beckmann C. Premature Rupture of Membranes. In: Beckmann CRB, Ling FW, Barzansky BM, editors. Obstetrics and Gynecology. Baltimore: Lippincott; 2010.p.13–6.

8. World Health Organization. WHO guidelines on hand hygiene in health Care. WHO, 2009. Available from URL:http://www.who.int/gpsc/5may/tools/9789241597906/en/ (13 August 2012).

9. McClure EM, Goldenberg RL, Brandes N et al. The use of chlorhexidine to reduce maternal and neonatal mortality and morbidity in low-resource settings. International Journal of Gynecology and Obstetrics 2007;97(2):89–94.

10. World Health Organization. Model list of essential medicines for children, 3rd list. Geneva: WHO; March 2011.

11. World Health Organization Expert Committee on Essential Medicines. The selection and use of essential medicines. Geneva: WHO; 2009.

12. ZA Lupinskaya. Endothelium of blood vessels-the main regulator of local blood flow. Vest-nik KRSU 2003:34-7.

13. Lutsenko NS, Evtereva IA. Sanatorium-and-spa treatment as a factor of optimizing the out-come of pregnancy. Zaporozhye Medical Journal 2006:91-4.

14. Lutsenko NS, Gayday NV, Shapran NF. Ways to optimize hemodynamics in the fetoplacen-tal pool, as a factor in influencing the perinatal outcome. Porto Biomed J 2017;2(5):245.

15. Makarov OV, Kozlov LV. Ways of preventing perinatal morbidity and mortality in preterm pregnancy. Women's Health 2012;72:91-5.

16. Goldenberg RL, McClure EM, Saleem S et al. Use of vaginally administered chlorhexidine during labor to improve pregnancy outcomes. Obstet Gynecol 2006;107(5):1139–46.

17. Taha TE, Biggar R, Broadhead RL et al. Effect of cleansing the birth canal with antiseptic solution on maternal and newborn morbidity and mortality in Malawi: clinical trial. BMJ 1997;315:216–9.

18. Bakr AF, Karkour T. Effect of predelivery vaginal antisepsis on maternal and neonatal morbidity and mortality in Egypt. J Womens Health 2005;14:496–501.

19. L C Mullany, J M Tielsch, G L Darmstadt et al. Topical applications of chlorhexidine to the umbilical cord for prevention of omphalitis and neonatal mortality in southern Nepal: a communi-ty-based, cluster-randomised trial. The Lancet 2006;367(9514):910-8.

20. Lumbiganon P, Thinkhamrop J, Thinkhamrop B et al. Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV). Cochrane Database Syst Rev 2004;18(4):CD004070.

21. Lumbiganon P, Thinkhamrop J, Thinkhamrop B et al. Vaginal chlorhexidine during labour for preventing maternal and neonatal infections (excluding Group B Streptococcal and HIV). Cochrane Database Syst Rev 2014;14(9):CD004070.

22. Christensen KK, Christensen P, Dykes A et al. Chlorhexidine for the prevention of neonatal colonization with group B streptococci. I. In vitro effect of chlorhexidine on group B streptococ-ci. European Journal of Obstetrics & Gynecology and Reproductive Biology 1983;16:157-65.

23. Stade B, Shah V, Ohlssen A. Vaginal chlorhexidine during labour to prevent early-onset neonatal group B streptococcal infection. Cochrane Database Syst Rev 2004;3:CD003520.

24. Hemani ML, Lepor H. Skin preparation for the prevention of surgical site infection: which agent is best? Reviews in Urology 2009;11(4):190-5.

25. Shubair M, Stanek R, White S et al. Effects of chlorhexidine gluconate douche on normal vaginal flora. Gynecol Obstet Invest 1992;34(4):229-33.

Turkish Med. Stud. J. 2018; 5: 14-7 DOI: 10.4274/tmsj.2018.05.04.0001
Received: 25.12.2017 - Accepted: 03.01.2018

PERIOSTEAL CHONDROMA OF THE FEMUR: A CASE REPORT

Ece Şenyiğit[1], Nur Gülce İşkan[1], Mert Çiftdemir[2]

[1] Trakya University School of Medicine, Edirne, TURKEY
[2] Department of Orthopedics and Traumatology, Trakya University School of Medicine, Edirne, TURKEY

ABSTRACT

Aims: Periosteal chondroma is a rare and benign cartilage tumor seen mostly in long bones and in patients under 30 years of age. In this case report, it is aimed to present a 16-year-old female patient with a periosteal chondroma in the distal femur.

Case Report: A 16-year-old female patient was admitted to the hospital with the history of pain in her distal part of right thigh. A superficial cortical erosion with well-defined borders without any relation to the intramedullary area was seen in magnetic resonance imaging. The lesion was regarded as periosteal chondroma and marginal excision was performed.

Conclusion: This case report shows the importance of the differential diagnosis in cortical lesions. Periosteal chondroma may be considered when a patient has a history of long term pain in adolescent age group.

Keywords: Chondroma, thigh, adolescent, periosteum

INTRODUCTION

Periosteal chondroma is a rare and benign cartilage tumor. It is located on the surface of the cortical bone (1). It is seen mostly in long bones, particularly the proximal humerus (2). Its predominant region is metaphyses of long bones (3). In addition, it is seen mostly in younger than 30 years of age and the highest frequency is between 10 and 20 years (1, 4). Its diagnosis is mainly based on histological characteristics (1).

In this case report, a 16-year-old female patient with a periosteal chondroma in the right distal femur is presented. Written informed consent was obtained from patient's parents.

CASE REPORT

A 16-year-old female patient was admitted to Orthopedics Department of Trakya University Hospital with an eight-month history of pain in the distal part of her right thigh. The patient described the pain as gradually increasing at night and with exercise. Additionally, she could locate the pain with her finger. In physical examination, the thigh had no edema, erythema nor increase in warmth and the patient had no history of weight loss and limitation of the right knee range of motion. In physical examination, the pathologies which can be associated with these symptoms such as trauma or infection were excluded.

Further analysis was done by plain radiographs and magnetic resonance imaging (MRI). A cortical expansion was seen at the anterior cortex of the distal metaphysis of right femur in plain radiographs. In addition, a small osteolytic lesion at the apex of the expanded anterior femoral cortex with a narrow transition zone was seen. In MRI, there was a superficial erosion with well-defined borders at the apex of the expansion which is 6.4 mm X 4.3 mm in size and it has no relation with intramedullary area (Figure 1).

The lesion showed hypointense signal properties in T1 and hyperintense signal properties in T2 weighted sequences. Bone scintigraphy revealed a subcentimetric osteoblastic focus at the anterior cortex of right distal femur.

Adress for Correspondence: Ece Şenyiğit, Trakya University School of Medicine, Edirne, TURKEY - e-mail: ece_senyigit@hotmail.com

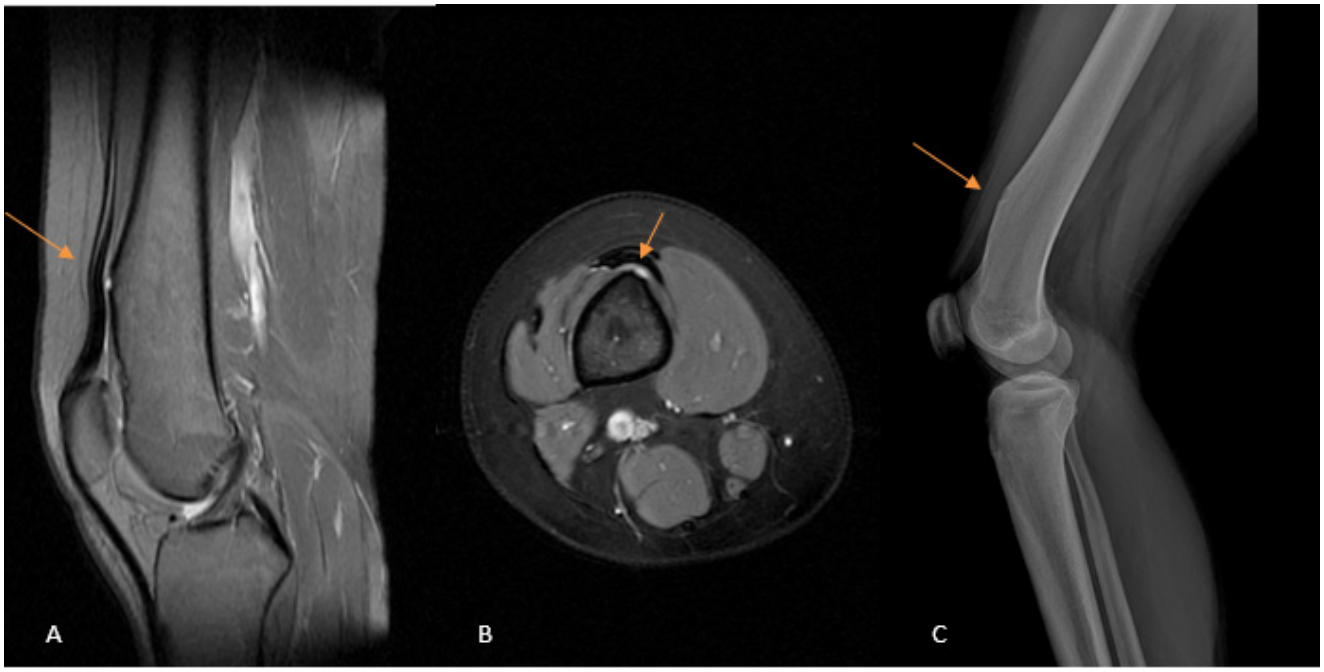

Figure 1: Sagittal and axial T2 Fat-Sat MRI views of right femur (A&B), Lateral plain radiograph of right femur (C).

Initially, the lesion was regarded as osteoid osteoma. In order to confirm the diagnosis, the patient's response to acetylsalicylic acid was tested, bone scintigraphy and MRI of the patient were examined. The result of acetylsalicylic acid test was negative. According to the test result and absence of a nidus and perilesional bone edema in the MRI, osteoid osteoma was excluded from the differential diagnosis list. The lesion was thought as a periosteal benign lesion such as periosteal chondroma, periosteal ganglion, subperiosteal giant-cell reparative granuloma, superficial aneurysmal bone cyst and surgical treatment had been decided to remove the lesion. In surgery, periosteally located lesion was observed and marginal excision was performed (Figure 2-3). Then the material was sent to the pathology department for further examination. Histopathological examination confirmed the diagnosis of periosteal chondroma (Figure 4-5). The patient was seen 3 months after the surgery and she had a full recovery. She had no pain or any other symptoms which were seen before. In MRI, there was no sign of relapse.

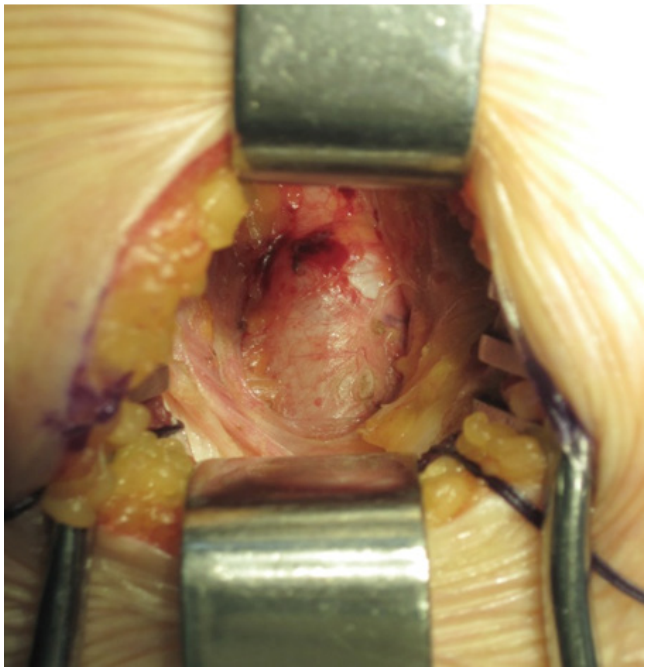

Figure 2: In surgery, the lesion is seen as a hump on the periosteum covering right femur.

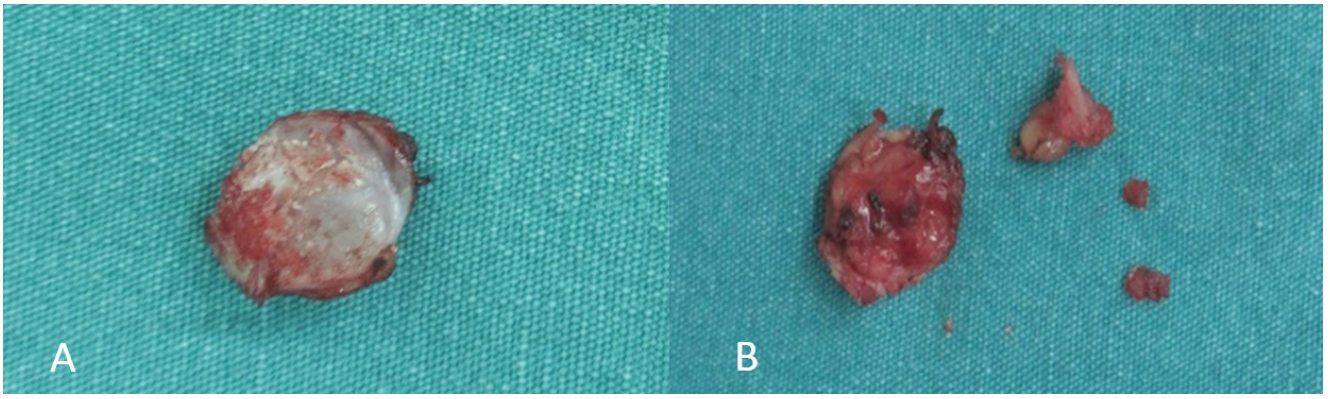

Figure 3: The dorsal aspect of the lesion after the excision (A), the ventral aspect of the lesion covered with periosteum after the excision (B).

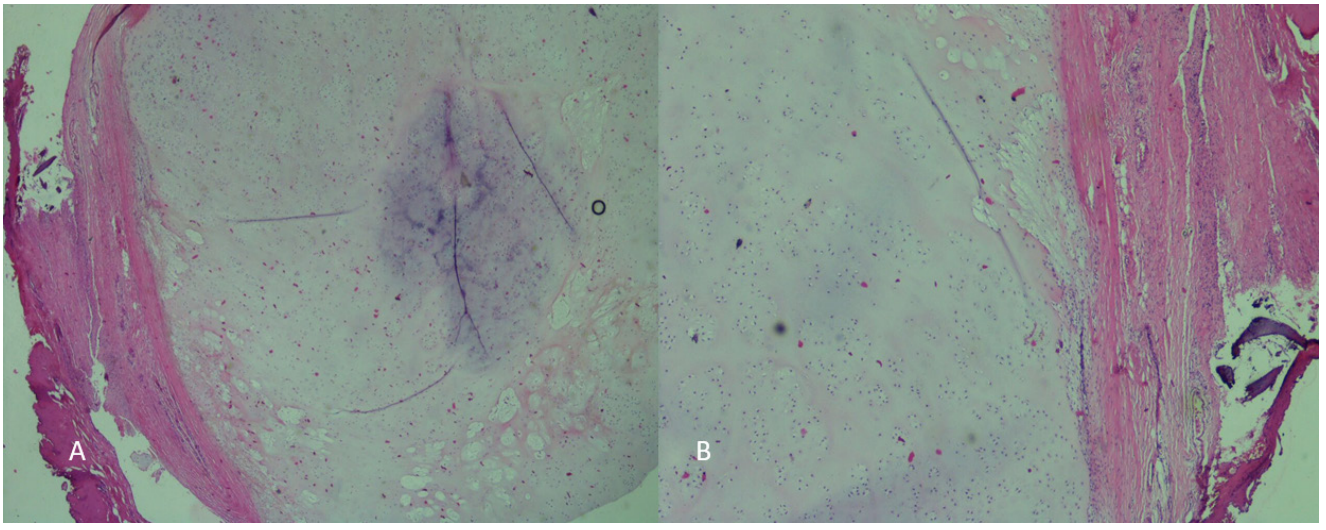

Figure 4: Benign chondroid tumor with a lobulated pattern, adjacent to fibrous periosteal tissue. (A: HEx40, B: HEx100).

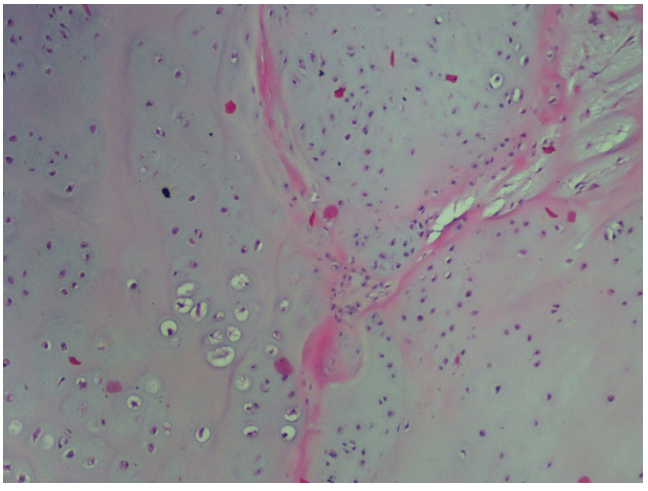

Figure 5: Benign chondroid lobular proliferation with surrounding ossified borders and septation (HEx100).

DISCUSSION

Periosteal chondroma is a slow-growing lesion of partial size arising within or under the periosteum (5). The lesion is seen mostly in patients younger than 30-year-old (6). Close collaboration between the surgeon, the radiologist, and the pathologist is needed to achieve the right diagnosis and treatment (4).

Our patient, who was 16 years old, consulted to the hospital with pain in her right knee. Because of the rest pain, three diagnoses were thought: tumor, infections or rheumatologic diseases. However, pain that increases with exercise is not a usual complaint for these diagnoses. Osteoid osteoma is characterized by night-time pain that may be reassured by acetylsalicylic acid or other non-steroid anti-inflammatory drugs (2, 7).

To support the diagnosis of osteoid osteoma, patient's response to acetylsalicylic acid was tested. It was expected to be positive but the result was negative. Osteoid osteoma was excluded from the differential diagnosis list after examining the radiological and clinical features of the lesion and the patient. Eventually, the diagnosis was thought as a benign periosteal lesion and surgical intervention was decided.

In the review and the case report of Kai Z et al. (1) 50% of the patients were male, which shows that the distribution of the lesion does not vary between genders. In addition, the mean of age was 14.67 years (1). In this aspect, our case is coherent with the literature.

Estimation of clinical course of periosteal chondroma can help in its diagnosis. Characteristically, the first symptom is localized swelling, followed by more than 6 months of continuous pain (4). In our case, the patient had 8 months history of pain and also night-time pain, but she did not have swelling.

Histopathologically, periosteal chondromas show a protuberant lobular organization of hyaline cartilage and extend from the periosteum toward the adjacent cortical bone. They are usually hypocellular (1). In pathology report of this patient, it is reported that the lesion is cellular and shows focal ossification.

The treatment of periosteal chondroma requires surgical management which consists of en bloc marginal excision and thorough curettage (2). In this case, en bloc marginal excision was preferred.

In conclusion, clinicians should think cortical lesions which are in osteolytic appearance when they face with these kinds of radiological findings as in our patient. Periosteal chondroma is one of them. For the treatment of these kinds of benign lesions, marginal excision provides successful results.

Acknowledgements

We would like to thank Prof. Ufuk Usta for his contributions.

Ethics Committee Approval: N/A
Informed Consent: Written informed consent was obtained from the patient's parents of this study.
Conflict of Interest: The authors declared no conflict of interest.
Author contributions: Concept: EŞ, NGİ, MÇ. Design: EŞ, NGİ, MÇ. Supervision: EŞ, NGİ, MÇ. Resources: EŞ, NGİ, MÇ. Materials: EŞ, NGİ, MÇ. Data collection and/or processing: EŞ, NGİ, MÇ. Analysis and/or Interpretation: EŞ, NGİ, MÇ. Literature Search: EŞ, NGİ, MÇ. Writing Manuscript: EŞ, NGİ, MÇ. Critical Review: EŞ, NGİ, MÇ.
Financial disclosure: The authors declared that this study received no financial support.
Editor-in-chief's Note: Two of the authors of this article, Ece Şenyiğit and Nur Gülce İşkan are members of the editorial board of Turkish Medical Student Journal. However, they did not take place in any stage on the editorial decision of the manuscript. The editors who evaluated this manuscript are from another institutions.

REFERENCES

1. Kai Z, Xiuchun Y, Songfeng X et al. Periosteal chondroma of the femur: a case report and review of the literature. Oncol Lett 2015;9(4):1637-40.

2. Fabbri N, Donati D. Periosteal chondroma. In: Picci P, Manfrini M, Fabbri N et al. Atlas of Musculoskeletal Tumors and Tumorlike Lesions. Switzerland: Springer; 2014.p.57-9.

3. Saraç K, Kaygusuz Akif, Elmalı N. Periosteal chondroma of the hand: two cases. Turgut Özal Tıp Merkezi Dergisi 1996;3(1):44-6.

4. Boriani S, Bacchini P, Bertoni F et al. Periosteal chondroma: a review of twenty cases. J Bone Joint Surg Am 1983;65:205-12.

5. Lewis MM, Kenan S, Yabut SM et al. Periosteal chondroma. A report of ten cases and review of the literature. Clin Orthop Relat Res 1990;256:185–92.

6. Akansu B, Atık E, Altintaş S et al. Periosteal chondroma of the ischium; an unusual location. Turk Patoloji Derg 2012;28:172–4.

7. Gökalp MA, Gözen A, Ünsal SŞ et al. An alternative surgical method for treatment of osteoid osteoma. Med Sci Monit 2016;22:580-6.

Turkish Med. Stud. J. 2018; 5: 18-21 DOI: 10.4274/tmsj.2018.05.05.0001
Received: 19.01.2018 - Accepted: 22.01.2018

A CASE REPORT OF SPONTANEOUS CORONARY ARTERY DISSECTION

Yusuf Can Özdemir[1], Kubilay Elmacı[1], Fatih Özçelik[2]

[1] Trakya University School of Medicine, Edirne, TURKEY
[2] Department of Cardiology, Trakya University School of Medicine, Edirne, TURKEY

ABSTRACT

Aims: Spontaneous coronary artery dissection is a random rupture of the coronary artery wall, which may lead to ischemia of the heart tissue. 30% of the cases are male patients. The aim of this article is to report a patient with spontaneous coronary artery dissection, raise awareness and extend the literature.

Case Report: A 43-year-old male patient was presented to Trakya University Hospital with a complaint of persistent chest pain. The patient underwent coronary angiography, revealing spontaneous coronary artery dissection in the left anterior descending artery and circumflex artery.

Conclusion: In this case report, we demonstrated the diagnosis of spontaneous coronary artery dissection with coronary angiography. Our patient had the most common dissection, left anterior descending artery, right coronary artery and left main coronary artery. Only medical therapy could be started for the patient due to his voluntary discharge.

Keywords: Coronary vessels, coronary artery disease, coronary angiography, chest pain

INTRODUCTION

Spontaneous coronary artery dissection (SCAD) is a random rupture of the coronary artery wall. SCAD is a rare defect, mostly affecting women. Especially in peripartum period, it can be fatal (1-3). The severity of SCAD is determined by obstruction ratio of blood flow and the diagnosis is generally made with coronary angiography (CAG) (4). Currently, management of SCAD is largely based on expert opinions (5). Medications may be administered to prevent coagulation and to reduce chest pain, blood pressure, cholesterol. Another treatment method for SCAD is percutaneous coronary intervention.

Spontaneous coronary artery dissection is not a newly discovered case. It was first reported by Pretty (1931) after the unexpected death of a patient who had symptoms such as vomiting, indicating coronary artery rupture (6). With the advances in imaging and diagnostic techniques, awareness of SCAD has raised greatly (7).

There is not consensus on categorizing SCAD. Traditionally, patients with SCAD are studied under four groups: patients with congenital connective tissue disorders that cause arterial wall defects, idiopathic SCAD, women in the peripartum period and patients suffering from atherosclerosis, particularly men at the age of 55 on average (8). However, on the contrary, modern definition of SCAD excludes patients with atherosclerosis (5).

There are two possible ways for the development of intramural hematoma with SCAD. The first one is intimal rupture causing blood flow into the intimal space, generating a false lumen within the artery; the second one is rupture of the vasa vasorum (9).

Three different monitoring methods can be used to diagnose SCAD. The first one is coronary angiography which provides a two-dimensional image limits the identification of the type of luminal obstruction (10). The second way is optical coherence tomography and intravascular ultrasound that gives information about the condition of the artery wall. Compared to CAG that only shows the lumen, which can be of advantage (11). The third way is cardiac computed tomography that is not common to evaluate SCAD due to its lower resolution (11). This method can only be used if the dissection is formed in a proximal segment of the artery (12).

Adress for Correspondence: Yusuf Can Özdemir, Trakya University School of Medicine, Edirne, TURKEY - e-mail: ysfcn1998@hotmail.com

The aim of this article is to report a patient with spontaneous coronary artery dissection, raise awareness and extend the literature.

CASE REPORT

A 43-year-old male patient presented to an outside facility complaining of chest pain, then was referred to Trakya University Hospital after his cardiac stress test results were found significant. The patient had a history of urinary tract infection; however a history of diabetes mellitus, hypertension, old myocardial infarction or coronary artery disease were not present. Continuous usage of tobacco and alcohol was noted. The drugs used by our patient were acetylsalicylic acid (ASA) and beta blockers. His blood pressure was 135 mmHg systolic and 70 mmHg diastolic on admission. His electrocardiogram (ECG) had negative T waves in V5-V6 (Figure 1). Physical examinations were normal in this case. Echocardiography that was performed before CAG revealed the following results: systolic dysfunction, global hypokinesia, ejection fraction deficiency, concentric hypertrophy and type 1 diastolic dysfunction in the left ventricle; mild mitral and aortal insufficiencies. An appointment was scheduled for coronary angiography and routine tests.

The patient was hospitalized in the cardiology unit one day before CAG and his usual medication was provided. Routine tests showed high platelet distribution width, high number of basophils, high levels of LDL-C, ALT, CRP, Ig-G, prothrombin time and low mean platelet volume and sodium levels.

Coronary angiography revealed spontaneous spiral diffuse dissection of circumflex artery (CX), starting from the proximal part and extending to the middle , dissection of the left anterior descending artery (LAD), starting from the proximal part and extending to S2 (Figure 2). Distal Thrombolysis in Myocardial Infarction (TIMI) 3 flow was detected in both CX and LAD. In ventriculography, anterior apical and inferior hypokinesia was found. The board diagnosed the case as coronary artery disease. Myocardial perfusion scanning (MPS) was considered necessary and scheduled.

Spironolactone, clopidogrel, perindopril, beta blockers and acetylsalicylic acid were given until his discharge. As a result of this medication regimen, angina disappeared and his systolic blood pressure decreased to 110 mmHg. While the patient was still being monitored in the cardiology service, another CAG was performed to check if any further operation is needed.

The second CAG revealed a dissection and 70% stenosis after the first diagonal branch (D1) and 70% stenosis in the ostium of D1; also, a 5 cm spiral dissection starting from proximal and extending to the distal part of CX. For the treatment decision (medication, stent implantation or coronary artery bypass grafting), the board decided to evaulate the MPS results.

The patient wanted to be discharged even when he was informed about all the risks of his condition before MPS was done. Perindopril, clopidogrel, ASA, atorvastatin, pantoprazole and metoprolol were given to the patient for regular use after his discharge.

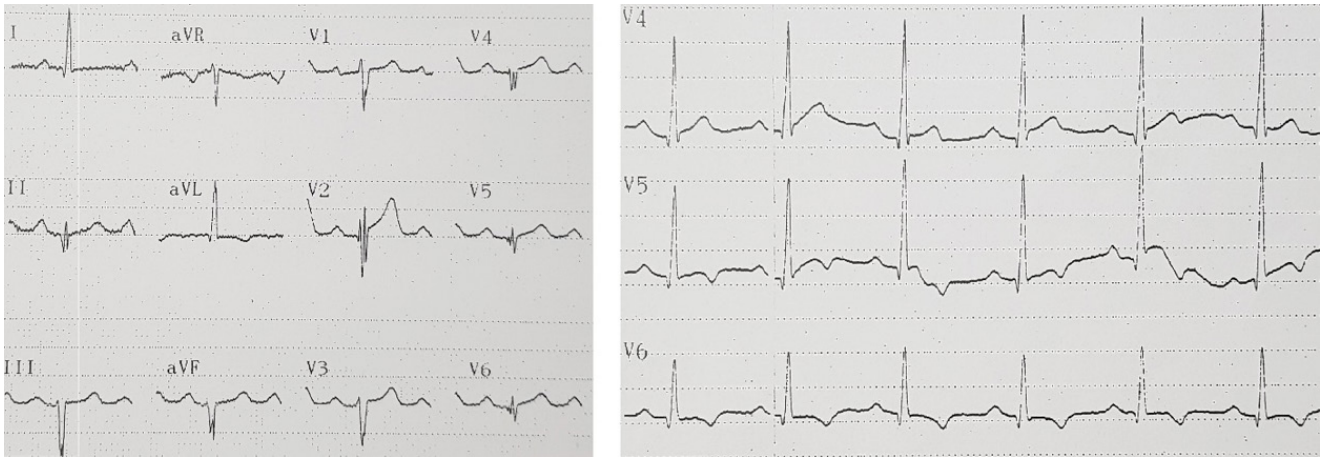

Figure 1: ECG findings of the patient, revealing negative T wave in V5-V6.

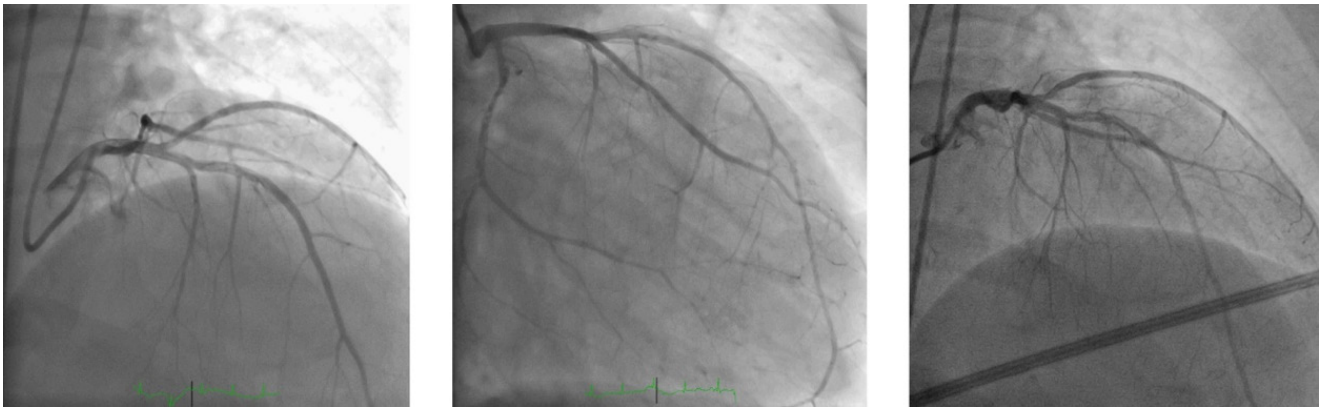

Figure 2: CAG findings of the patient, revealing dissections of LAD and CX, normal right coronary artery.

DISCUSSION

Gender distribution for SCAD is unbalanced. 30% of the SCAD patients are male, as in our case (13, 14). There were no risk factors present for our patient, apart from an intensive use of tobacco and alcohol. The most common three dissection areas are LAD, right coronary artery and left main artery, respectively (15). Our patient had a dissection of LAD, which is the most frequently involved coronary artery.

Depending on the severity of ischemia, culmination in acute coronary syndrome (ACS) and clinical findings, coronary reperfusion can be provided with stent implantation in spontaneaus dissections. Coronary artery bypass grafting can be offered to the patients with coronary anatomies that are unsuitable for stent implantation or in clinically stable patients without angina and ACS, medical therapy can be a choice.

In the management of SCAD, medical therapy plays an important role. Medication includes beta-blockers, angiotensin-receptor blockers, anticoagulants, thrombolytic therapies, antiplatelet therapies and lipid-lowering therapies (5). As our patient was clinically stable and did not have angina or ACS, the decision for a MPS analysis was made in order to determine if the dissections resulted in a serious ischemia. In our case, medical therapy was the only treatment as the patient denied MPS analysis and treatment, and wanted to be discharged, preventing us from making the analysis and completing the treatment.

To conclude, CAG is the current gold standard to diagnose SCAD. According to size and the type of the dissection, appropriate treatment should be determined by specialists.

Ethics Committee Approval: N/A
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Author contributions: Concept: FÖ, YCÖ, KE. Design: FÖ, YCÖ, KE. Supervision: FÖ. Resources: FÖ, YCÖ, KE. Materials: FÖ, YCÖ, KE. Data collection and/or processing: FFÖ, YCÖ, KE. Analysis and/or Interpretation: FÖ, YCÖ, KE. Literature Search: FÖ, YCÖ, KE. Writing Manuscript: FÖ, YCÖ, KE. Critical Review: FÖ.
Financial disclosure: The authors declared that this study received no financial support.
Editor-in-chief's Note: One of the authors of this article, Kubilay Elmacı is a member of the editorial board of Turkish Medical Student Journal. However, he did not take place in any stage on the editorial decision of the manuscript. The editors who evaluated this manuscript are from another institutions.

REFERENCES

1. Tweet MS, Hayes SH, Pitta SR et al. Clinical feature, management and prognosis of spontaneous coronary artery dissection. Circulation 2012;126:579-88.

2. Adlam D, Cuculi F, Lim C et al. Management of spontaneous coronary artery dissection in the primary percutaneous coronary intervention era. J Invasive Cardiol 2010;22:549-53.

3. Jorgensen MB, Aharonian V, Mansukhani P et al. Spontaneous coronary dissection: a cluster of cases with this rare finding. Am Heart J 1994;127:1382-7.

4. Mokhberi V, Bagheri B, Navidi S et al. Spontaneous coronary artery dissection: a case report. J Teh Univ Heart Ctr 2015;10(3):159-62.

5. Saw J, Mancini J, Humphries HK. Contemporary review on spontaneous coronary artery dissection. JACC 2016;68(3):297-312.

6. Pretty HC. Dissecting aneurysm of coronary artery in a woman aged 42: rupture. BMJ 1931;1:667.

7. Tweet MS, Gulati R, Aase LA et al. Spontaneous coronary artery dissection: a disease-specific, social networking community-initiated study. Mayo Clin Proc 2011;86:845-50.

8. Sabatine MS, Jaffer FA, Staats PN et al. Case records of the massachusetts general hospital. Case 28-2010. A 32-year-old woman, 3 weeks post partum, with substernal chest pain. N Engl J Med 2010;363:1164-73.

9. Yip A, Saw J. Spontaneous coronary artery dissection-a review. Cardiovasc Diagn Ther 2015;5(1):37-48.

10. Al Emam AR, Almomani A, Gilani SA et al. Spontaneous coronary artery dissection: one disease, variable presentations, and different management approaches. International Journal of Angiography 2016;25(3):139-47.

11. Saw J. Coronary angiogram classification of spontaneous coronary artery dissection. Catheter Cardiovasc Interv 2014;84(7):1115-22.

12. Wain-Hobson J, Roule V, Dahdouh Z et al. Spontaneous coronary artery dissection: one entity with several therapeutic options. Cardiovasc Revasc Med 2012;13(3):203.

13. DeMaio SJ Jr, Kinsella SH, Silverman ME. Clinical course and long-term prognosis of spontaneous coronary artery dissection. Am J Cardiol 1989;64:471-4.

14. Thompson EA, Ferraris S, Gress T et al. Gender differences and predictors of mortality in spontaneous coronary artery dissection: a review of reported cases. J Invasive Cardiol 2005;17:59-61.

15. Zampieri P, Aggio S, Roncon L et al. Follow up after spontaneous coronary artery dissection: a report of five cases. Heart 1996;75:206-9.

Turkish Med. Stud. J. 2018; 5: 22-3 DOI: 10.4274/tmsj.2018.05.06.0001
Received: 29.12.2017 - Accepted: 04.01.2018

EUROPEAN STUDENT RESEARCH NETWORK (EUROSURG) IMAGINE PROJECT

Bahadır E. Baki[1], Bahar B. Ozkan[2], Başak Yüksek[3] , Arif Y. Sen[4], Melik K. Aktas[5]

[1]Karadeniz Technical University School of Medicine, Trabzon, TURKEY
[2]Department of General Surgery, Ankara University School of Medicine, Ankara, TURKEY
[3]Düzce University School of Medicine, Düzce, TURKEY
[4]Dokuz Eylül University School of Medicine, Izmir, TURKEY
[5]Çukurova University School of Medicine, Adana, TURKEY

To the Editor,

European Student Research Network (EuroSurg) collaborative was founded by medical students and surgeons at the European Society of Coloproctology (ESCP) congress in 2015 with the aim of running multi-center international studies (1). Due to purpose of collaboration, it has gained active members from many countries all across Europe in very short time.

Turkey is one of the founder members of EuroSurg Collaborative. In the first project called "EuroSurg-1 Major Gastrointestinal Surgery", EuroSurg Turkey took part with more than 120 collaborators from 20 faculties (2). Projects like these will provide opportunities for medical students in Turkey to take part in an international project and take an important step for their future academic careers. EuroSurg Turkey National Management Team consists of local leads from attending universities.

EuroSurg collaborative provides opportunities for students who are willing to improve research skills, to contribute to international studies. It also supports education for evidence-based research. All collaborators who contribute to EuroSurg projects will gain important research methodology skills throughout the study process (3). All students' names who contribute to EuroSurg projects will be listed as PubMed-citable co-authors.

Postoperative ileus is known as temporary bowel motility dysfunction after abdominal surgery or abdominal trauma. After major abdominal surgery, paralytic period lasts 0-24 hours for the small intestine, 24-48 hours for the stomach and 48-72 hours for the colon. The absence of intestinal motility after these periods is called postoperative ileus (4).

Ileus Management International (IMAGINE) project is a cohort study which will assess postoperative ileus incidence and treatment protocol at different centers around the world. Besides this main aim, this project also focuses on the effects of nonsteroidal anti-inflammatory drugs (NSAIDs) on the recovery of intestinal functions when used for postoperative analgesia, also the safety and risks of NSAIDs (including acute kidney damage and anastomosis leakage) will be assessed (5). People who contribute to this cohort study as medical students, interns, residents will prospectively collect data of patients undergoing elective colorectal surgery over a 14-day period.

EuroSurg Turkey aims for the collaboration of medical students, surgical trainees and consultant surgeons in Turkey and their engagement in international research projects. In this manner, Turkish medical students who are willing to take part in a study will have a more effective role in the medical research world.

REFERENCES

1. EuroSurg Collaborative. EuroSurg: a new European student-driven research network in surgery. Colorectal Dis 2016;18(2):214-5.

2. Özkan BB, Özbalcı GS, Tavuz Aİ et al. EuroSurg: cerrahide, öğrenci odaklı Avrupa çapında yürütülen alışılmışın dışında yeni bir çalışma grubu. Turk J Surg 2016;32(2):155-6.

3. Chapman SJ, Glasbey JC, Kelly M et al. Promoting research and audit at medical school: evaluating the educational impact of participation in a student-led national collaborative study. BMC Med Educ 2015;13:15-47.

Adress for Correspondence: Bahadır E. Baki, Karadeniz Technical University School of Medicine, Trabzon, TURKEY - e-mail: bahadir61baki@gmail.com

4. Liu S, Carpenter RL, Neal JM. Epidural anesthesia and analgesia,their role in postoperative outcome. Anesthesiology 1995 Jun;82(6):1474-506.

5. Chapman SJ, EuroSurg Collaborative. Ileus Management International (IMAGINE): Protocol for a multicentre, observational study of ileus after colorectal surgery. Colorectal Dis 2018 Jan;20(1):17-25.

Authorship Contributions Form

Manuscript No. :

……

……

Manuscript Title :

……

……

Corresponding author :

……

1. Authorship requires at least 3 contributions listed in the table below, including critical review of the manuscript, which is a mandatory contribution for all authors.
2. All authors are required to contribute to manuscript draft preparation, and critical review of its important intellectual content.
3. All authors are responsible for approval of the final proofs of the article
4. Those authors who do not fulfill the required number of contributions or do not meet criteria should be listed in the Acknowledgement section at the end of the manuscript.
5. These rules are set in frame of Council of Science Editors (CSE) and International Committee of Medical Journal Editors (ICMJE) guidelines for authorship.

Contribution	Explanation	Contributing Authors
CONCEPT	The idea for research or article/hypothesis generation	
DESIGN	Planning the methods to generate hypothesis	
SUPERVISION	Supervision and responsibility for the organization and course of the project and the manuscript preparation	
RESOURCES	Supplying financial resources, equipment, space, and personnel vital to the project	
MATERIALS	Biological materials, reagents, referred patients	
DATA COLLECTION AND/OR PROCESSING	Responsibility for conducting experiments, management of patients, organizing and reporting data	
ANALYSIS AND/OR INTERPRETATION	Responsibility for presentation and logical explanation of results	
LITERATURE SEARCH	Responsibility for conducting literature search	
WRITING MANUSCRIPT	Responsibility for creation of an entire or the substantial part of the manuscript	
CRITICAL REVIEW	Reworking the final, before submission version of the manuscript for intellectual content, not just spelling and grammar check	
OTHER	For novel contributions:	

CORRESPONDING AUTHOR :

……

SIGNATURE : …… DATE : ……

TMSJ Form for Disclosure of Potential Conflicts of Interest

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information.
* The form is in four parts.

1. Identifying information.
Type your full name. If you are NOT the corresponding author please check the box "No" and type the name of the corresponding author. Provide the requested manuscript information.
*If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare under Sections 2, 3, or 4 below, you can check "Nothing to disclose" (see Section 1, line 7, page 2). In this case only, the disclosure applies to all authors, and the form is complete.

2. The work under consideration for publication.
This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party—that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation, or commercial sponsor, check "Yes". Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.
This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work.
Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.
For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations, or academic institutions, need not be disclosed here (but can be acknowledged on the title page of the manuscript). For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships.
Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.
*If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare under Sections 2, 3, or 4 below, you can check "Nothing to disclose" (see Section 1, line 7, page 2). In this case only, the disclosure applies to all authors, and the form is complete.

Section 1. Identifying Information
Complete by providing the requested information in the white boxes.

1. Given Name (First Name):		2. Surname Last Name):		3. Current Date:	
4. Are you the corresponding author?	___Yes	___No	If "No", name of corresponding author:		
5. Manuscript Title:					
6. Manuscript Identifying Number (if you know it):					
7. If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare, check here:				___**Nothing to Disclose**	

TMSJ Form for Disclosure of Potential Conflicts of Interest

The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. The form is designed to be completed electronically and stored electronically. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information.
* The form is in four parts.

1. Identifying information.
Type your full name. If you are NOT the corresponding author please check the box "No" and type the name of the corresponding author. Provide the requested manuscript information.
*If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare under Sections 2, 3, or 4 below, you can check "Nothing to disclose" (see Section 1, line 7, page 2). In this case only, the disclosure applies to all authors, and the form is complete.

2. The work under consideration for publication.
This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking "No" means that you did the work without receiving any financial support from any third party—that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation, or commercial sponsor, check "Yes". Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

3. Relevant financial activities outside the submitted work.
This section asks about your financial relationships with entities in the bio-medical arena that could be perceived to influence, or that give the appearance of potentially influencing, what you wrote in the submitted work. You should disclose interactions with ANY entity that could be considered broadly relevant to the work.
Report all sources of revenue paid (or promised to be paid) directly to you or your institution on your behalf over the 36 months prior to submission of the work. This should include all monies from sources with relevance to the submitted work, not just monies from the entity that sponsored the research. Please note that your interactions with the work's sponsor that are outside the submitted work should also be listed here. If there is any question, it is usually better to disclose a relationship than not to do so.
For grants you have received for work outside the submitted work, you should disclose support ONLY from entities that could be perceived to be affected financially by the published work, such as drug companies, or foundations supported by entities that could be perceived to have a financial stake in the outcome. Public funding sources, such as government agencies, charitable foundations, or academic institutions, need not be disclosed here (but can be acknowledged on the title page of the manuscript). For example, if a government agency sponsored a study in which you have been involved and drugs were provided by a pharmaceutical company, you need only list the pharmaceutical company.

4. Other relationships.
Use this section to report other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work.
*If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare under Sections 2, 3, or 4 below, you can check "Nothing to disclose" (see Section 1, line 7, page 2). In this case only, the disclosure applies to all authors, and the form is complete.

Section 1. Identifying Information
Complete by providing the requested information in the white boxes.

1. Given Name (First Name):		2. Surname Last Name):		3. Current Date:	
4. Are you the corresponding author?	___Yes	___No	If "No", name of corresponding author:		
5. Manuscript Title:					
6. Manuscript Identifying Number (if you know it):					
7. If you are the corresponding author, and neither you nor your co-authors have any disclosures to declare, check here:				___**Nothing to Disclose**	

Section 2. The Work Under Consideration for Publication

Did you or your institution at any time receive payment or services from a third party for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc...)?

Complete each row by checking "No" or providing the requested information in the white boxes. Add rows as needed.

The Work Under Consideration for Publication

Type	No	Money Paid to You	Money to Your Institution*	Name of Entity	Comments
1. Grant					
2. Consulting fee or honorarium					
3. Support for travel to meetings for the study or other purposes					
4. Fees for participation in review activities such as data monitoring boards, statistical analysis, end point committees, and the like					
5. Payment for writing or reviewing the manuscript					
6. Provisions of writing assistance, medicines, equipment, or administrative support					
7. Other					

*This means money that your institution received for your efforts this study.

Section 3. Relevant financial activities outside the submitted work.

Please indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. You should report relationships that were present during the 36 months prior to submission.

Complete each row by checking "No" or providing the requested information in the white boxes.

Relevant Financial Activities Outside the Submitted Work

Type of Relationship (in alphabetical order)	No	Money Paid to You	Money to Your Institution*	Name of Entity	Comments
1. Board membership					
2. Consultancy					
3. Employment					
4. Expert testimony					
5. Grants/grants pending					
6. Payment for lectures including service on speakers bureaus					
7. Payment for manuscript preparation					
8. Patents (planned, pending or issued)					
9. Royalties					
10. Payment for development of educational presentations					
11. Stock/stock options					
12. Travel/accommodations/ meeting expenses unrelated to activities listed**					
13. Other (err on the side of full disclosure)					

*This means money that your institution received for your efforts.

**For example, if you report a consultancy above there is no need to report travel related to that consultancy on this line.

Section 4. Other Relationships

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

____No other relationships/conditions/circumstances that present a potential conflict of interest.

____Yes, the following relationships/conditions/circumstances are present (explain below):

At the time of manuscript acceptance, we ask that you update your disclosure statements if anything has changed. On occasion, we may ask you to disclose further information about reported relationships.

This form is adapted from the Author Disclosure Form created by the International Committee of Medical Journal Editors (ICMJE). The ICMJE has not endorsed nor approved the contents here. The official version of the ICMJE Author Disclosure Form is located at http://www.icmje.org/coi_disclosure.pdf

CONSENT FORM for CASE REPORT

Title of Project:_____

1. I have read, and understood the Participant Information Sheet dated _____
2. I freely agree to the use of my medical records for the purpose of this study.
3. I understand that the case report will be published without my name attached and researchers will make every attempt to ensure my anonymity. I understand, however, that complete anonymity cannot be guaranteed.
4. I have been given a copy of the Participant Information Sheet and Consent Form to keep.

Name of Participant_____

Signature of Participant _____ Date _____

The participant was informed through phone call and a verbal consent was obtained.

The following section regarding the witness is not essential but may be appropriate for patients where the research teams feel that the participant should have a witness to the consent procedure.

Name of witness (if appropriate)_____

Signature of witness_____ Date _____

Name of Researcher_____

Signature of Researcher_____ Date_____

Name of Researcher

Signature of Researcher_____ Date_____


bimco_2018
BIMCO - your way to self-improvement!
DEADLINE : 31-JAN-2018
FREE publication & online participation
JOIN US NOW !
BIMCO
Bukovinian International Medical Congress
+380 (66) 18 254 81
bim.co.ua/eng
Chernivtsi, Ukraine
4th-6th of April 2018
@bimcochernivtsi


Your education is too important to be left in the hand of others - own it.
MEDICS
2018
Medical International Conference for Students
19 - 22 April | Bucharest, Romania
Join us and discover inspiring Keynote Speakers and interactive Workshops, which you can now book in seconds
Abstract Submission is open!
Send your abstract before 18 March 2018
Register now at www.soms-medics.com !
Regular fee deadline: 19 March 2018
Organised by
SOMS
PARTNERS:
MEDICS is accredited to provide continuous medical education (CME) for physicians. The exact number of CME credits will be announced on our website.


ICMS
FOR STUDENTS & YOUNG DOCTORS
Your Science. Our Future.
XVII
International Congress of Medical Sciences
10th-13th May 2018
Sofia, Bulgaria
Abstract Submission
Deadline: 10th March 2018


MIRCIM 2018
McMaster International Review Course in Internal Medicine
Kraków, Poland
10-12 May 2018