



**E Journal
of Cardiovascular
Medicine**

| Volume **5** | Issue **2** |

| April-June **2017** |

www.ejcvsmmed.org

E Journal of Cardiovascular Medicine

**The effect of enoxaparin on in vitro stimulated
platelet aggregation by elective percutaneous
coronary intervention patients**

Ebru İpek Türkoğlu, Nazan Bitir

Isolated ventricular septal defect in infants

Zeynep Eyileten, Adnan Uysalel

**Transcatheter successful palliation of a newborn
with ductal-dependent pulmonary circulation**

Tamer Yoldaş, Senem Özgür, Vehbi Doğan, Özkan Kaya, Utku Arman Örün, Selmin Karademir



E Journal of Cardiovascular Medicine
is a global e-journal targeting articles on:

- clinical cardiology,
- interventional cardiology,
- arrhythmia,
- cardiovascular surgery,
- vascular & endovascular surgery,
- vascular biology

Editor-in-Chief

Prof. Öztekin Oto

FESC, FACC / President, Heart and Health Foundation of Turkey / Izmir / Turkey

Asistant Editors

Prof. Ali Kutsal

*Sami Ulus Children Hospital Department of
Cardiovascular Sugery / Ankara / Turkey*

Prof. Erdem Silistreli

*Dokuz Eylül University, Department of Cardiovascular
Sugery / Izmir / Turkey*

Prof. Bektaş Battaloğlu

*İnönü University, Department of Cardiovascular Sugery
Malatya / Turkey*

Dr. Onur Saydam

*Karaman State Hospital Cardiovascular Surgery
Karaman / Turkey*

Dr. Emre Doğan

*Trabzon Ahi Evren Cardiovascular Surgery Hospital
Trabzon / Turkey*

Dr. Taylan Adademir

Kartal Koşuyolu Resarch Hospital / Istanbul / Turkey

Owner

© TÜSAV Heart and Health Foundation of Turkey

Administration Office

Şair Eşref Bulvarı, 1402 Sk. No. 2/2 Özbaş Apt.
Alsancak - Izmir / Turkey
Tel: + 90 232 464 19 63 / Fax: +90 232 464 24 70
e-mail: info@oztekinoto.com | info@tksv.org

Publishing Coordinator

Hüseyin Kandemir

huseyin@medikalakademi.com.tr

Publisher

Medikal Akademi Yayıncılık ve Prodüksiyon Tic. Ltd. Sti.
Halaskargazi Cad. No: 172, D: 134 - Şişli / İstanbul
Tel: +90 537 309 29 55, Faks: (0212) 233 90 61
www.medikalakademi.com.tr/hizmetlerimiz

International Scientific Advisory Board

Prof. Harald Kaemmerer

German Heart Centre / Munich / Germany

Prof. Marko Turina

University Hospital of Zurich / Zurich / Switzerland

Prof. Frank W. Selke

*Chief of Cardiothoracic Surgery at Brown Medical School
Rhode Island / USA*

Prof. Joseph E. Bavaria

*Hospital of the University of Pennsylvania
Philadelphia / USA*

Prof. Fausto Pinto

*Director of Lisbon Cardiovascular Institute / Portugal
& President of the European Society of Cardiology*

Prof. Lazar Davidovic

*Belgrade Medical School Cardiovascular Surgery
Belgrade / Serbia*

Prof. Stephan Schueler

*Tyne Freeman Hospital, Department for Cardiothoracic
Surgery Newcastle / United Kingdom*

Prof. Piotr Kasprzak

*University Hospital Regensburg, Director of Vascular
Surgery / Regensburg / Germany*

Prof. Jose Luis Pomar

*Hospital Clinico de Barcelona, Department of
Cardiovascular Sugery / Barcelona / Spain*

Prof. Mohamed Moustafa Abdelaal

*Kafrelsheikh University Hospital, Cardiothoracic surgery and
General Director / Kafr El Sheikh / Egypt*

Assoc. Prof. Barış Akça

*Inonu University School of Medicine, Department of
Cardiovascular Surgery / Malatya / Turkey*

Dr. Rezan Aksoy

*Siyami Ersek Training and Research Hospital,
Cardiovascular Surgery / Istanbul / Turkey*

Dr. Şafak Alpat

*Birmingham Children's Hospital Pediatric Cardiovascular
Surgery / Birmingham / UK*

Dr. Mustafa Aldemir

*Kocatepe University, Department of Cardiovascular
Surgery / Afyon / Turkey*

Dr. Elena Zapata-Arriaza

*Hospital Universitario virgen del Rocío, Instituto de
biomedicina de Sevilla, Vascular Medicine / Sevilla / Spain*

Dr. Mehmet Atay

*Bakırköy Sadi Konuk Research Hospital, Cardiovascular
Surgery / Istanbul / Turkey*

Assoc. Prof. Hakan Aydın

*Sami Ulus in Ankara Training and Research Hospital,
Cardiovascular Surgery / Ankara / Turkey*

Assoc. Prof. Ahmet Çağrı Aykan

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery / Trabzon / Turkey*

Assoc. Prof. Vedat Bakuy

*Bakırköy Sadi Konuk Training and Research Hospital,
Cardiovascular Surgery / Istanbul / Turkey*

Dr. Stefano Bartoli

*ASL Roma2, Cardiovascular Surgery
Rome / Italy*

Assoc. Prof. Elif Börekçi

*Bozok University Research and Application Hospital,
Internal Medicine / Yozgat / Turkey*

Dr. Tomasa Centella

*Hospital Ramón y Cajal, Cardiovascular Surgery
Madrid / Spain*

Assoc. Prof. Ahmet Çalışkan

*Dicle University School of Medicine, Cardiovascular Surgery
Diyarbakır / Turkey*

Dr. Gökhan Çavuşoğlu

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery, Radiology / Trabzon / Turkey*

Dr. Deniz Çevirme

*Kartal Koşuyolu Research and Education
Hospital, Cardiovascular Surgery / Istanbul / Turkey*

Prof. Ferit Çiçekçioğlu

*Bozok University, Training and Research Hospital,
Cardiovascular Sugery / Yozgat / Turkey*

Assoc. Prof. Ertan Demirdaş

*Bozok University Research and Application Hospital and
Cardiovascular Surgery / Yozgat / Turkey*

Assoc. Prof. Yüksel Dereli

*Necmettin Erbakan University, Meram Midical Faculty
Hospital, Cardiovascular Surgery / Konya / Turkey*

Assist.Prof. İnci Selin Doğan

*Karadeniz Technical University Faculty of Pharmacy
Pharmacology, Medicinal Chemistry / Trabzon / Turkey*

Dr. Vehbi Doğan

*Sami Ulus Training and Research Hospital, Pediatric
Cardiology / Ankara / Turkey*

Dr. Çağrı Düzyol

*Kocaeli Derince Education and Research Hospital
Cardiovascular Surgery / Kocaeli / Turkey*

Assoc. Prof. Hüseyin Ede

*Bozok University, Medical Faculty, Cardiovascular Surgery
Yozgat / Turkey*

Dr. İlker Ertuğrul

*Sami Ulus Training and Research Hospital, Pediatric
Cardiology / Ankara / Turkey*

Prof. Niyazi Görmüş

*Necmettin Erbakan University, Meram Medical Faculty
Hospital, Cardiovascular Surgery / Konya / Turkey*

Assist. Prof. Adem Güler

*Gulhane Military Medical Academy Department of
Cardiovascular Surgery / Ankara / Turkey*

Assoc. Prof. Mustafa Gülgün

*GATA Department of Pediatrics, Division of Pediatric
Cardiology / Ankara / Turkey*

Prof. Usama Ali M. Hamza

*Mansoura University Faculty of Medicine, Cardiothoracic
Surgery, Cardiovascular Surgery / Mansoura / Egypt /*

Dr. James B Hermiller

*St Vincent's Medical Group, Interventional Cardiology
Indianapolis / USA*

Dr. Akihiko Ikeda

*Tsukuba Medical Center Hospital, Cardiovascular
Surgery / Tsukuba / Japan*

Dr. Richard W Issitt

*Great Ormond Street Hospital, Cardiac Surgery -
Pediatric Cardiology / London / UK*

Dr. Mehmet Kalender

*Derince Training and Research Hospital, Cardiovascular
Surgery / Kocaeli / Turkey*

Dr. Ayşegül Karadeniz

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery, Radiobiology / Trabzon / Turkey*

Assoc. Prof. Osman Kayapınar

*Duzce University, Medical Faculty Department of
Cardiology / Düzce / Turkey*

Assoc. Prof. Alper Kepez

*Marmara University Training and Research Hospital Cardiol-
ogy Clinic / Istanbul / Turkey*

Assoc. Prof. Yasir Khan Khan

*Ch. Pervaiz Elahi Institute of Cardiology, Cardiovascular Sur-
gery / Punjab / Pakistan*

Assoc. Prof. Levent Korkmaz

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery / Trabzon / Turkey*

Assoc. Prof. Ulaş Kumbasar

*Hacettepe University Medical School Cardiovascular
Surgery / Ankara / Turkey*

Dr. Redha Lakehal

*Department of heart surgery, EHS Erriadh / Constantine
Algeria*

Dr. Wei-Chieh Lee

*Kaohsiung Chang Gung Memorial Hospital, Cardiology
Kaohsiung City / Taiwan*

Dr. José Luis Serrano Martínez

*University Hospital of Granada, Department of Internal
Medicine / Granada / Spain*

Assoc. Prof. Ümit Mentşe

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery / Trabzon / Turkey*

Dr. Nooredin Mohammadi

*Iran University of Medical Sciences, Cardiology, Demand
for Health Care, Determinants of Health / Tehran / Iran*

Dr. Vinod Namana

*Maimonides Medical Center, Department of Medical
Research / New York / USA*

Dr. Silvio Nocco

Sirai Hospital, Department of Cardiology / Carbonia / Italy

Assoc. Prof. Zeynep Tuğba Özdemir

*Bozok University School of Medicine, Internal Medicine
Yozgat / Turkey*

Dr. Tanıl Özer

*Kartal Koşuyolu Yüksek İhtisas Research and Education
Hospital / Istanbul / Turkey*

Prof. Murat Özeren

*Mersin University Medical School, Cardiovascular
Surgery / Mersin / Turkey*

Assoc. Prof. Emre Özker

*Başkent University School of Medicine, Department of
Cardiovascular Surgery / Ankara / Turkey*

Dr. Abdullah Özyurt

*Mersin Maternity and Children Diseases Hospital, Pediatric
Cardiology / Mersin / Turkey*

Dr. Recep Oktay Peker

*Hacettepe University, Department of Cardiovascular Surgery
Ankara / Turkey*

Dr. Hikmet Sahratov

*Gülhane Education and Research Hospital, Department of
Cardiovascular Surgery / Ankara / Turkey*

Dr. Gonzalo Luis Alonso Salinas

*Marcelo Sanmartín of Hospital Universitario Ramón y Cajal
Madrid / Spain*

Dr. Stefano Salizzoni

*Città della Salute e della Scienza, Cardiac Surgery,
Cardiac Surgery / Turin / Italy*

Dr. Gökhan Sargın

*Adnan Menderes University Medical School, Internal
Medicine / Aydın / Turkey*

Dr. Mustafa Seren

*Ankara 29 Mayıs State Hospital and Cardiovascular
Surgery / Ankara / Turkey*

Prof. Erdem Silistreli

*Dokuz Eylül University, Department of Cardiovascular
Surgery / İzmir / Turkey*

Assoc. Prof. Ömer Tanyeli

*Necmettin Erbakan University, Meram Medical Faculty
Hospital, Cardiovascular Surgery / Konya / Turkey*

Dr. İlker Tekin

*Antalya Medicalpark Hospital, Cardiovascular Surgery
Antalya / Turkey*

Assist. Prof. Dinçer Uysal

*Isparta Süleyman Demirel University, Department of
Cardiovascular Surgery / Isparta / Turkey*

Dr. Olivier Villemain

*IM3C Necker-Enfants Malades, AP-HP, Université Paris
Descartes, Pediatric Cardiology, Radiology / Paris / France*

Dr. Mustafa Esat Yamaç

*Ahi Evren University of Health Sciences, Thoracic and
Cardiovascular Surgery / Trabzon / Turkey*

Assoc. Prof. Ali Ümit Yener

*Canakkale Onsekiz Mart University Medical Faculty,
Department of Cardiovascular Surgery / Çanakkale / Turkey*

Dr. Dilek Yeşilbursa

*Uludağ University, Medical Faculty, Department of
Cardiology / Bursa / Turkey*

Dr. Mustafa Yılmaz

*Sami Ulus Training and Research Hospital, Pediatric
Cardiology / Ankara / Turkey*

| Volume **5** | Number **2** | April-June **2017** |

Research Articles

The effect of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients | 21

Ebru İpek Türkoğlu, Nazan Bitir

Review Article

Isolated ventricular septal defect in infants | 27

Zeynep Eyileten, Adnan Uysalel

Case Report

Transcatheter successful palliation of a newborn with ductal-dependent pulmonary circulation | 34

Tamer Yoldaş, Senem Özgür, Vehbi Doğan,
Özkan Kaya, Utku Arman Örün, Selmin Karademir

Dead sea like giant negative t wave associated with subarachnoid hemorrhage | 37

Recep Kurt, Hakan Güneş

Aortic valve replacement due to lactococcus lactis infective endocarditis | 41

Özgür Altınbaş, Erdal Ege, Ali Sarıgül

The effect of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients

Ebru İpek Türkoğlu¹, Nazan Bitir¹

¹ Izmir Northern Public Hospitals Association, Kemalpaşa State Hospital, Department of Cardiology, Specialist Dr., İzmir, Turkey

Abstract

Aim: The aim of the present study was to investigate the effects of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients.

Method: Twenty-two patients that scheduled for elective percutaneous coronary angioplasty (PTCA) were enrolled in the present study. The patients who had not been taking any antiaggregant agent other than aspirin and normal platelet account received enoxaparin (1 mg/kg IV bolus) as anticoagulant agent during PTCA. Two blood samples were obtained for every patient via femoral arterial sheath during the intervention before and 10 minutes after enoxaparin administration and stimulated platelet aggregation responses are investigated.

Results: The decrease in platelet aggregation responses to adenosine diphosphate (ADP), collagen and epinephrine before and after enoxaparin administration were statistically significant ($p < 0.05$). The decrease in platelet aggregation response to ristocetin before and after enoxaparin was not statistically significant ($p > 0.05$).

Conclusion: Enoxaparin may reduce platelet aggregation in elective PTCA patients pretreated with aspirin only. With the knowledge of the importance of the platelet inhibition, choice of the anticoagulant agent during PTCA may be beneficial.

Keywords: Enoxaparin, stimulated platelet aggregation, elective PTCA

Türkoğlu E. İ., Bitir N. The effect of enoxaparin on in vitro stimulated platelet aggregation by elective percutaneous coronary intervention patients EJCM 2017; 05 (2): 21-26. Doi: 10.15511/ejcm.17.00221

Introduction

Subcutaneous (SC) enoxaparin has been shown to be better choice than unfractionated heparin (UFH) in the medical treatment of unstable angina (UA) and non-ST- elevation myocardial infarction (NSTEMI).⁽¹⁻⁴⁾ Combined analysis of two studies, the Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events (ESSENCE) and Thrombolysis In Myocardial Infarction (TIMI) 11B, showed that enoxaparin reduced the risk of death and MI by 20% at 43 days without any significant increase of major hemorrhage.⁽⁵⁾ ESSENCE and TIMI 11B trials demonstrated superiority of enoxaparin over UFH at 43 days for end points death or myocardial infarction (MI) and death or MI or urgent revascularization in patients who did not undergo percutaneous coronary intervention (PCI).⁽⁵⁾

In this analysis, excluding events that occurred before PCI, there was also superiority of enoxaparin treatment over UFH measured at 1 year for both end points in patients who underwent PCI.⁽⁵⁾ Several studies have shown good outcomes with SC enoxaparin anticoagulation of patients with UA/NSTEMI underwent PCI on SC enoxaparin treatment.⁽⁶⁻⁸⁾ Intravenous (IV) low-molecular-weight heparins (LMWH) in elective PCI have been evaluated and shown to be safe and effective in various registries.^(3,9-11)

There are several studies that measure platelet reactivity in stable PCI patients using different methods.⁽¹²⁻¹⁴⁾ The aim of the present study was to investigate the effect of enoxaparin on in vitro stimulated platelet aggregation by using % aggregation test to certain agonists in elective coronary intervention patients and the clinical significance of aggregation response to enoxaparin.

Materials and Methods

Study Population

Study population comprised patients older than 30 years with stable angina pectoris and documented ischemia (positive treadmill exercise test or positive myocardial perfusion scan for ischemia), who underwent coronary angiography and scheduled for elective PCI.

Exclusion criteria were:

1. unstable state or acute coronary syndrome,
2. stable angina with an identified precipitating factor (e.g. severe anemia, heart failure, tachyarrhythmia, thyrotoxicosis, severe uncontrolled hypertension),
3. myocardial infarction or PCI in previous month or coronary bypass surgery in 2 months,
4. treatment with UFH or LMWH >24 hours of any cause before enrollment,
5. treatment with any other anti-platelet agent than aspirin (e.g. clopidogrel, ticlopidin, dipyridamol),
6. refusal of patient

22 patients, 16 males and 6 females were enrolled to the study. Mean age was 56.8 ± 1.6 years. Mean age for female patients was 57.4 ± 2.1 and for male patients 56.7 ± 1.4 . Seventeen patients (14 of males and 3 of females) were smoker. Only 3 patients (2 of males and 1 of females) had diabetes mellitus and none were under insulin treatment. Fifteen patients (11 of males and 4 of females) had hypertension and were under treatment. Seventeen patients (12 of males and 5 of females) were under statin treatment since their coronary angiography procedures.

Concomitant medication was similar in male and female patients. All of patients received daily aspirin (ASA) > 100 mg more than 7 days before procedure. Fifteen of males and 5 of females were taking beta-blockers. Fourteen of males and 5 of females were using nitrates. All hypertensive patients were taking ACE-inhibitors and all of hyperlipidemic patients were taking statins.

Blood Collection

Immediately after femoral sheath replacement the first blood sample was drawn through the sheath to determine the basal (before anticoagulant) platelet aggregation response. Enoxaparin was given 1 mg/kg (100IU/kg) IV bolus after PTCA-wire crossed the lesion as a single dose. Ten minutes after the administration of enoxaparin the second blood sample was drawn through the sheath.

In vitro Platelet Aggregation Measurement

Immediately after blood collection, platelet aggregation measurements were made. All blood samples were studied into 2 hours after their collection. In vitro platelet functions were evaluated in the hematology laboratory with aggregometer. Stimuli were adenosine diphosphate (ADP), collagen, epinephrine and ristocetin. PAP-4CD Bio-Data was used for platelet aggregation.

Statistical Analysis

A student-paired t-test was applied to assess the differences between pre- and post-enoxaparin platelet aggregation responses. Results are expressed as mean \pm standard error (SE). The level of significance was set at $p < 0.05$. SPSS 10.0 software was used for the statistical analysis.

The alteration in the platelet aggregation response with certain stimuli before and after enoxaparin is investigated in order to explore if enoxaparin has an additional antiaggregant effect.

Results

Baseline clinical characteristics of study population and concomitant medications are described in **Table 1 and 2**. Baseline platelet counts were within normal limits in the study population and were unchanged after the intravenous administration of enoxaparin ($212 \pm 48 \times 10^6$ before and $210 \pm 42 \times 10^6$ after enoxaparin). Not any major bleeding complication occurred. None of patients had required blood transfusion. Only 3 of patients had small hematoma on the femoral access site. In this study not any in-hospital complication (such as ischemic complications or infection) was experienced.

Stimulated platelet aggregation responses before and after enoxaparin are summarized in **Table 3**. Values are given as mean \pm SE of % aggregation. Platelet aggregation responses to ADP were 36.2 ± 4.6 before and 29.3 ± 3.4 after enoxaparin ($p=0.005$) and to epinephrine 41.4 ± 5.3 before and 30.5 ± 4.7 after enoxaparin ($p=0.02$). The difference was statistically significant. Platelet aggregation responses to collagen were 57.8 ± 5.0 before and

Table 1. Patient Demographics

Demographics	Male (N=16)	Female (N=6)
Age	56.7 ± 1.4	57.4 ± 2.1
Smoker	14	3
Diabetes Mellitus	2	1
Hypertension	11	4
Hyperlipidemia	12	5

N indicates number of patients. Age is given mean \pm SE in years.

Table 2. Concomitant medications of the study patients

Medication	Male (N=16)	Female (N=6)
ASA>7 days	16	6
β -blocker	15	5
Nitrate	14	5
ACE-I	11	4
Statin	12	5

N indicates number of patients.

Table 3. Stimulated Platelet Aggregation Responses

Stimuli	Before Enoxaparin (N=22)	After Enoxaparin (N=22)	P value
Adenosine diphosphate (ADP)	36.2 ± 4.6	29.3 ± 3.4	0.005
Collagen	57.8 ± 5.0	45.7 ± 6.0	0.05
Epinephrine	41.4 ± 5.3	30.5 ± 4.7	0.02
Ristocetin	75.0 ± 3.0	67.0 ± 4.3	0.07

N indicates number of patients. Data are given mean \pm SE of % aggregation. A value of $P < 0.05$ is considered statistically significant.

45.7 ± 6.0 after enoxaparin (p=0.05); to ristocetin 75.0 ± 3.0 before and 67.0 ± 4.3 after enoxaparin (p=0.07).

Discussion

Despite of new tools, new drugs and new techniques, clot formation remains still as an important issue in interventional cardiology. The UFH has been the primary anticoagulant agent for more than 30 years, but the optimal dosage, the monitoring of anticoagulation level and the interaction between UFH and platelets remain controversial.⁽¹⁵⁻¹⁷⁾ LMWHs offer a stable and predictable anticoagulant response and do not need for coagulation monitoring.⁽¹⁸⁾

Enoxaparin has shown its superiority to UFH in the medical treatment of UA and NSTEMI.^(1,2) There is also a meta-analysis revealing a better evolution in ST-segment elevation acute myocardial infarction patients, who received enoxaparin instead of UFH as an adjunctive therapy to the thrombolytic regimen.⁽⁴⁾ Several studies have also shown good results with enoxaparin on UA/NSTEMI patients who underwent PCI.⁽⁶⁻⁸⁾

There are some potential mechanisms, which may explain beneficial effects of enoxaparin.⁽¹⁸⁾ Because of the molecular features enoxaparin may permit more suppression of thrombin generation than UFH with a higher antifactor Xa: antifactor IIa (thrombin) ratio (3.8:1).⁽¹⁸⁾ Enoxaparin has a prolonged antifactor Xa activity and higher antifactor IIa activity than UFH because of better bioavailability, is less sensitive to the inhibitory effects of platelet factor 4, may release the tissue factor pathway inhibitor with greater capacity, has a lower tendency to increase activation and aggregation of platelets and shows potential antiplatelet effects while suppressing von Willebrand factor greater degree.^(18, 19-28)

The aim of this study was to investigate the aggregation response of stable patients to enoxaparin via platelet functions beyond its anticoagulation activity. To the best our knowledge, this is the first study that compared parameters of platelet aggregation before and after administration of enoxaparin during elective PCI in patients pretreated only with aspirin. All unstable patients were excluded to avoid the interaction between activated aggregation and coagulation cas-

cade and platelet aggregation response. In the present study, enoxaparin showed a slight decrease of % aggregation on platelet aggregation responses stimulated with collagen and ristocetin but it was statistically not significant. Enoxaparin significantly decreased platelet aggregation responses stimulated with ADP and with epinephrine in elective PCI patients. None of our patients experienced any ischemic or hemorrhagic complications neither in 72 hours nor in 30 days in follow-up.

Platelets play a key role in the development of thrombotic events during and after PCI.⁽²⁹⁻³¹⁾ There are multiple pathways of platelet activation and aggregation. Thrombin is the most potent agent, which activates platelets in subnanomolar concentrations via protease-activated receptors (PARs).^(31,32,33) PAR activation results ADP release from dense granules, which acts in an autocrine way on the platelet ADP receptors.^(31,34)

This endogenous ADP release may be reduced via enoxaparin resulting in significant decrease of ADP induced platelet aggregation. In a previous study Xiao et al. investigated platelet aggregation response to enoxaparin in patients taking only aspirin with UA and found a modest but not statistically significant increase in platelet aggregation with enoxaparin.⁽²⁵⁾ The conflict may be related to the study population. While UA patients have been included to the study of Xiao et al, all UA patients were excluded from the present study.⁽²⁵⁾ In another study, Aggarwal et al. have found that anticoagulation with enoxaparin during hemodialysis is associated with less platelet reactivity in a different study population.⁽³⁵⁾

The limitations of the present study were small number of patients and lack of unstable patients. In acute coronary syndromes and unstable patients, especially by the site of thrombus, antiaggregant effect of enoxaparin may be more critical, but further studies are needed. In conclusion, enoxaparin may reduce platelet aggregation in elective PCI patients treated with aspirin only. With the knowledge of the stronger the platelet inhibition, the lower the incidence of ischemic complications,⁽³⁶⁻³⁹⁾ choice of the anticoagulant agent or additional antiaggregant agents during PCI may be beneficial.

References

1. Antman EM, McCabe CH, Gurfinkel EP, Turpie AG, Bernink PJ, Salein D, Bayes de Luna A, Fox K, Lablanche JM, Radley D, Premmereur J, Braunwald E. Enoxaparin prevents death and cardiac ischemic events in unstable angina/non-Q-wave myocardial infarction (TIMI) 11B trial. *Circulation* 1999; 100: 1593-601
2. Goodman SG, Cohen M, Bigonzi F, Gurfinkel EP, Radley DR, Le Iouer V, Fromell GJ, Demers C, Turpie AG, Califf RM, Fox KA, Langer A. Randomized trial of low molecular weight heparin (enoxaparin) versus unfractionated heparin for unstable coronary artery disease: 1-year results of the ESSENCE Study. Efficacy and Safety of Subcutaneous Enoxaparin in Non-Q-Wave Coronary Events. *J Am Coll Cardiol* 2000; 36: 693-8
3. Choussat R, Montalescot G, Collet JP, Vicaut E, Ankri A, Gallois V, Drobinski G, Sotirov I, Thpmas D. A unique, low dose of intravenous enoxaparin in elective percutaneous coronary intervention. *J Am Coll Cardiol* 2002; 40: 1943-50
4. Theroux P, Welsh RC. Meta-analysis of randomized trials comparing enoxaparin versus unfractionated heparin as adjunctive therapy to fibrinolysis in ST-elevation acute myocardial infarction. *Am J Cardiol* 2003; 91: 860-4
5. Fox KA, Antman EM, Cohen M, Bigonzi F; ESSENCE/TIMI11B Investigators. Comparison of enoxaparin versus unfractionated heparin in patients with unstable angina pectoris / non-ST segment elevation acute myocardial infarction having subsequent percutaneous coronary intervention. *Am J Cardiol* 2002; 90: 477-82
6. Collet JP, Montalescot G, Lison L, Choussat R, Ankri A, Drobinski G, Sotirov I, Thomas D. Percutaneous coronary intervention after subcutaneous enoxaparin pretreatment in patients with unstable angina pectoris. *Circulation* 2001; 103: 658-63
7. Fergusson JJ, Antman EM, Bates ER, Cohen M, Every NR, Harrington RA, Pepine CJ, Theroux P; NICE Investigators. The use of enoxaparin and IIb/IIIa antagonists in acute coronary syndromes, including PCI: final results of NICE 3 study (abstr). *J Am Coll Cardiol* 2001; 37: 365A
8. Goodman SG, Fitchett D, Armstrong PW, Tan M, Langer A; INTERACT Trial Investigators. The Integrilin and Enoxaparin Randomized Assessment of Acute Coronary syndrome Treatment (INTERACT) trial (abstr). *J Am Coll Cardiol* 2002; 40: 5
9. Rabah MM, Premmereur J, Graham M, Fareed J, Hoppensteadt DA, Grines LL, Grines CL. Usefulness of intravenous enoxaparin for percutaneous coronary intervention in stable angina pectoris. *Am J Cardiol* 1999; 84: 1391-5
10. Kereiakes DJ, Kleiman NS, Fry E, Mwawasi G, Lengerich R, Maresh K, Burkert ML, Aquilina JW, DeLoof M, Broderick T, Shimshak TM. Dalteparin in combination with abciximab during percutaneous coronary intervention. *AM Heart J* 2001; 141: 348-52
11. Kereiakes DJ, Grines C, Fry E, Esente P, Hoppensteadt D, Midei M, Barr L, Matthai W, Todd M, Broderick T, Rubinstein R, Fareed J, Santoian E, Neidarman A, Brodie B, Zidar J, Ferguson JJ, Cohen M; NICE 1 and NICE 4 Investigators. Enoxaparin and abciximab adjunctive pharmacotherapy during percutaneous coronary intervention. *J Invasive Cardiol* 2001; 13: 272-8
12. Kabbani SS, Watkins MW, Ashikaga T, Terrien EF, Holoch PA, Sobel BE, Schneider DJ. Platelet reactivity characterized prospectively: a determinant of outcome 90 days after percutaneous coronary intervention. *Circulation* 2001; 104: 181-6
13. Kabbani SS, Watkins MW, Holoch PA, Terrien EF, Sobel BE, Schneider DJ. Platelet reactivity in coronary ostial blood: a reflection of the thrombotic state accompanying plaque rupture and J Thromb Thrombolysis 2001; 12: 171-6
14. Aggarwal A, Sobel BE, Schneider DJ. Decreased platelet reactivity in blood anticoagulated with bivalirudin or enoxaparin compared with unfractionated heparin: implications for coronary intervention. *J Thromb Thrombolysis* 2002; 13: 161-6
15. Eika C. Inhibition of thrombin-induced aggregation of human platelets in heparin. *Scand J Haematol* 1971; 8: 216-222.
16. Thomson C, Forbes CD, Prentice CRM. The potentiation of platelet aggregation and adhesion by heparin in vitro and in vivo. *Clin Sci Mol Med* 1973; 45: 485 – 494
17. Mascelli MA, Kleiman N, Marciniak S, Damaraju L, Weisman HF, Jordan RE. Therapeutic heparin concentrations augment platelet reactivity: Implications for the pharmacologic assessment of the glycoprotein IIb/IIIa antagonist abciximab. *Am Heart J* 2000; 139: 696-703.
18. Antman EM, Cohen M, McCabe C, Goodman SG, Murphy SA, Braunwald E; TIMI 11 B and ESSENCE Investigators. Enoxaparin is superior to unfractionated heparin for preventing clinical events at 1-year follow-up of TIMI 11B and ESSENCE. *Eur Heart J* 2002; 23: 308-14
19. Lane DA, Denton J, Flynn AM, Thunberg L, Lindahl U. Anticoagulant activities of heparin oligosaccharides and their neutralization by platelet factor 4. *Biochem J* 1984; 218: 725-32
20. Abildgaard U, Lindahl AK, Sandset PM. Heparin requires both antithrombin and extrinsic pathway inhibitor for its anticoagulant effect in human blood. *Haemostasis* 1991; 21: 254-7
21. Lindhout T, Hemker H. Anticoagulant mechanism of action of low molecular weight heparins. In: Doutremepuich C. ed. *Low Molecular Weight Heparins in Clinical Practice*. New York: Marcel Dekker, Inc. 1992: 23-50
22. Hoppensteadt DA, Jeske W, Fareed J, Bermes EW Jr. The role of tissue factor pathway inhibitor in the mediation of the antithrombotic actions of heparin and low molecular weight heparin. *Blood Coagul Fibrinolysis* 1995; 6 (Suppl): S57-64
23. Brieger D, Daves J. Long-term persistence of biological activity following administration of Enoxaparin sodium (clexane) is due to sequestration of antithrombin-binding low molecular weight fragments- comparison with unfractionated heparin. *Thromb Haemost* 1996; 75: 740-6
24. Agnelli G. Pharmacological activities of heparin chains: should our past knowledge be revised? *Haemostasis* 1996; 26:2-9
25. Xiao Z, Threoux P. Platelet activation with unfractionated heparin at therapeutic concentrations and comparisons with a low molecular weight heparin and with a direct thrombin inhibitor. *Circulation* 1998; 97: 251-6

26. Montalescot G, Philippe F, Ankri A, Vicaud E, Bearez E, Poulard JE, Carrie D, Flammang D, Dutoit A, Carayon A, Jardel C, Chevrot M, Bastard JP, Bigonzi F, Thomas D. Early increase of von Willebrand factor predicts adverse outcome in unstable coronary artery disease: beneficial effects of enoxaparin. French Investigators of the ESSENCE Trial. *Circulation* 1998; 98: 294-9
27. Antman EM, Handin R. Low molecular weight heparins: an intriguing new twist with profound implications. *Circulation* 1998; 98: 287-9
28. Montalescot G, Collet JP, Lison L, Choussat R, Ankri A, Vicaud E, Perlemuter K, Philippe F, Drobinski G, Thomas D. Effects of various anticoagulant treatments on von Willebrand factor release in unstable angina. *J Am Coll Cardiol* 2000; 36:110-4
29. Fuster V, Badimon L, Badimon JJ, Chesebro JH. The pathogenesis of coronary artery disease and acute coronary syndromes (1). *N Engl J med* 1992; 326: 242-50
30. Massberg S, Schulz C, Gavaz M. Role of platelets in the pathophysiology of acute coronary syndrome. *Semin Vasc Med* 2003; 3: 147-62
31. Sibbing D, Busch G, Braun S, Jawansky S, Schömig A, Kastrati A, Ott I, von Beckerath N. Impact of bivalirudin or unfractionated heparin on platelet aggregation in patients pretreated with 600 mg clopidogrel undergoing elective percutaneous coronary intervention. *Eur Heart J* 2008; 29: 1504-9
32. Kahn ML, Nakanishi-Matsui M, Shapiro MJ, Ishihara H, Coughlin SR. Protease-activated receptors 1 and 4 mediate activation of human platelets by thrombin. *J Clin Invest* 1999; 103: 879-87
33. Sambrano GR, Weiss EJ, Zheng YW, Huang W, Coughlin SR. Role of thrombin signaling in platelets in haemostasis and thrombosis. *Nature* 2001; 413: 74-8
34. Dorsam RT, Kunapuli SP. Central role of the P2Y12 receptor in platelet activation. *J Clin Invest* 2004; 113: 340-45
35. Aggarwal A, Whitaker DA, Rimmer JM, Solomon RJ, Gennari FJ, Sobel BE, Schneider DJ. Attenuation of platelet reactivity by enoxaparin compared with unfractionated heparin in patients undergoing haemodialysis. *Nephrol Dial Transplant* 2004; 19 (6): 1559-63
36. Mehta SR, Yusuf S, Peters RJ, Bertrand ME, Lewis BS, Natarajan MK, Malmberg K, Rupprecht H, Zhao F, Chrolavicius S, Copland I, Fox KA; the CURE investigators. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet* 2001;358:527-33
37. Patti G, Colonna G, Pasceri V, Pepe LL, Montinaro A, Di Sciascio G. Randomized trial of high loading dose of clopidogrel for reduction of periprocedural myocardial infarction in patients undergoing coronary intervention: results from the ARMYDA-2 study. *Circulation* 2005; 111:2099-106
38. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, Neumann FJ, Ardissino D, De Servi S, Murphy SA, Riesmeyer J, Weerakkody G, Gibson M, Antman M; TRITON-TIMI 38 Investigators. Prasugrel versus clopidogrel in patients with acute coronary syndromes. *N Engl J Med* 2007; 357:2001-15
39. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW, Scirica BM, Skene A, Steg PG, Storey RF, Harrington RA; PLATO Investigators. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *N Eng J Med* 2009; 361:1045-57

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Acknowledgements

We wish to thank to the Ege University, division of Hematology.

Received: 11/02/2017

Accepted: 17/05/2017

Published: 15/06/2017

Disclosure and conflicts of interest:

Conflicts of interest were not reported.

Corresponding author:

Dr. Ebru İpek Türkoğlu

Mail: dripek73@yahoo.com

Isolated ventricular septal defect in infants

Zeynep Eyileten¹, Adnan Uysalel¹

¹ Ankara University Faculty of Medicine, Department of Cardiovascular Surgery, Prof. Dr., Ankara, Turkey

Abstract

Ventricular septal defect is a hole in the interventricular septum and may be isolated or associated with other major defects involving patency of the arterial duct, coarctation of aorta, pulmonary stenosis, tetralogy of Fallot, double-outlet right ventricle, truncus arteriosus, and transposition, and account for over half of the patients with congenital heart disease. Isolated ventricular septal defect is the most commonly recognized congenital heart anomaly in children and accounts for about one-fifth of all congenital heart disease. In this chapter, we'll cover isolated ventricular septal defects.

Key words: Ventricular septal defect, isolated, infant.

*Eyileten Z., Uysalel A. Isolated ventricular septal defect in infants
EJCM 2017; 05 (2): 27-33. Doi: 10.15511/ejcm.17.00227.*

Classification

The interventricular septum (IVS) is commonly divided into four parts—the membranous septum and the inlet, trabecular, and outlet portions of the muscular septum. Depending on their location in the IVS, isolated ventricular septal defect (VSD) can be divided into four types;^(1,2,3)

Type I VSDs (Doubly committed/ Subarterial/ Outlet/ Infundibular/ Conotruncal/ Conal/ Juxta-arterial/ Supracristal) account for 5% to 10% of isolated VSDs. They are located below the semilunar valve and above the crista supraventricularis. The right aortic leaflet most commonly is sucked into the defect, resulting in aortic incompetence in 40% to 50% of conal defects. Atrioventricular conduction tissue is far away from the borders of this type of VSD.

Type II VSDs (Perimembranous/ Conoventricular) are the most common isolated VSDs, comprising about 70% to 80% in most series. These defects are located in the membranous septum and may extend into the inlet or outlet. They are usually bordered cranially by aortic valve and posteroinferiorly by anteroseptal commissure of the tricuspid valve and they can undergo partial or complete closure by apposition of the septal leaflet of the tricuspid valve, forming a tricuspid valve “pouch” or “aneurysm of the ventricular septum”. Less commonly the noncoronary aortic leaflet may prolapse through the defect, resulting in decrease of the defect as well as progressive aortic incompetence. Atrioventricular conduction axis penetrates directly through the posteroinferior border of the defect. These type of VSDs can be associated with malalignment of the aortopulmonary septum, as in the setting of tetralogy of Fallot (anterior malalignment) or interrupted aortic arch (posterior malalignment). A Gerbode-type defect is a communication between the left ventricle and right atrium through the membranous IVS.

Type III VSDs (Atrioventricular canal/ Inlet type) account for about 5% of isolated defects. They are situated beneath the septal leaflet of the tricuspid valve, with the tricuspid valve annulus forming their posterior border. They can be associated with primum type atrial septal defects and left atrioventricular valve

clefts. The conduction tissue is closely related to the posteroinferior border of the defect. They have a remarkably high prevalence in genetic conditions such as trisomy 18 and trisomy 21.

Type IV VSDs (Muscular/Trabecular) account for 10% to 15% of isolated VSDs. They have a rim totally made up of muscle and are divided into midmuscular (most common), apical (trabecular), and anterior muscular defects. The presence of multiple muscular defects is known as the “swiss cheese” septum. The conduction tissue is generally remote from the edges of a muscular defect.

The defects in the neonate are divided into 3 subgroups depending on their size;^(1,4)

- Small (restrictive) VSD is < 4 mm (or less than the 33% of cross-sectional diameter of the aortic root in catheterization), the pulmonary to systemic blood flow ratio ($Q_p:Q_s$) < 1.5.

- Moderate VSD is 4-6 mm (or between the 33-75% of cross-sectional diameter of the aortic root in catheterization), $Q_p:Q_s = 1.5 - 2.3$.

- Large (non-restrictive) VSD is > 6 mm (or larger than the 75% of cross-sectional diameter of the aortic root in catheterization), $Q_p:Q_s > 2.3$.

Patophysiology

In non-restrictive VSDs, the magnitude of the shunt depends on the relative pulmonary (PVR) and systemic vascular resistance (SVR). Since in a normal individual SVR is greater than PVR, in smaller defects, the blood flow is from the left to right ventricle. In patients with a large VSD, the systolic pressure in both ventricles is the same, with right sided pressures elevated to the same levels as those normally present on the left side of the heart. Large VSDs place two major hemodynamic loads upon the ventricles; increased pressure load on the right ventricle and increased volume load on the left ventricle.

PVR is high at birth and little flow across the defect may exist during this period. When PVR shows a sharp fall by 2-8 weeks of age, in patients with large VSD, pulmonary blood flow increases secondary to increased left-to-right shunt. The augmented blood flow returns through the left atrium to the left ventricle. To acco-

moderate the increased pulmonary venous return, the left ventricle dilates. If the left ventricle becomes greatly dilated, the myocardium can not develop sufficient tension to maintain the pressure volume relationship, causing congestive cardiac failure. Patients with large VSD, develop congestive heart failure and its symptoms of tachypnea, slow weight gain and poor feeding by 2 to 3 months of age.

As pulmonary vascular disease develops, PVR increases and left to right shunt reverses and the presence of a right to left shunt will result in cyanosis (Eisenmenger syndrome). Congestive heart failure lessens. These rarely present in children below age 5 with isolated VSDs and is usually seen in adolescents and adults. In a patient with high fixed PVR, the defect should not be closed.^(1,2,3)

Diagnosis

Patients with small VSDs usually are asymptomatic. A loud holosystolic murmur may be heard best at the left sternal border. Pulmonary arterial pressure and pulmonary vascular resistance is near normal. The normal decline in PVR can be delayed in infants with moderate and large VSDs. Thus, murmurs may not be detected in such infants until several weeks postnatally.

Infants with moderate or large VSDs may present with pallor, tachypnea, increased work of breathing, poor weight gain, or failure to thrive, and diaphoresis particularly with feeding at approximately two to eight weeks of age. Right ventricular impulse, felt at the lower left sternal border is prominent. A precordial trill may be palpable. As the degree of pulmonary hypertension increases, the intensity of the pulmonary component of S2 will increase. There will be holosystolic, midfrequency murmur. In patients with large VSDs, in addition to the systolic murmur, there will be a middiastolic mitral flow murmur as a result of increased volume of blood flowing from the left atrium to the left ventricle. As the PVR rises, the holosystolic murmur may disappear entirely, leaving a loud second heart sound due to closure of the pulmonary valve which is indicative of severe pulmonary hypertension.

The electrocardiogram; may be normal in small

VSDs. Moderate sized VSD's may be commonly associated with hypertrophy of right, left or both ventricle. In patients with large VSDs, left atrial dilatation, manifested by biphasic P waves in leads I, AVR, and V6 associated with right ventricular hypertrophy and left or right axis deviation may be seen. Patients with pulmonary hypertension, will exhibit evidence of right ventricular hypertrophy in electrocardiography

In chest radiography; patients with small defects often will have a normal cardiac silhouette and normal pulmonary markings, while moderate and large VSD patients will have increased pulmonary vascularity and cardiomegaly with biventricular enlargement. Lateral projections may show upward deviation of the left main bronchus due to left atrial dilatation in large defects. In patients with Eisenmenger syndrome, the heart may not be enlarged and the pulmonary vascular markings may not be increased. Only the main pulmonary artery is enlarged.

Transthoracic echocardiography is the mainstay for the definitive diagnosis of VSD. It allows delineation of the anatomic site of the VSD, associated cardiac lesions, pulmonary artery pressure, degree of cardiac dilatation. *Cardiac catheterization* is only indicated to determine; quantification of the ratio of systemic and pulmonary flows, the pulmonary artery pressure and accurate identification of smaller defects.⁽¹⁾

Natural history

The incidence of spontaneous closure of VSDs is highest during the first year of life (40%) but continues to a lesser degree up to about 5 years, after which spontaneous closure is rare. Most VSDs are restrictive and frequently become smaller or undergo spontaneous closure. Defects located in the muscular septum close with the growth and hypertrophy of the surrounding muscular septum. Small membranous defects may close through apposition of the septal leaflet of the tricuspid valve secondary to negative pressure created by the jet through the defect.

In patients with nonrestrictive VSD, congestive heart failure symptoms develop soon after birth, concomitant with the fall in the elevated neonatal pulmo-

nary resistance. Patients are at risk of developing irreversible pulmonary vascular disease after 1-2 years of age (earlier in children with trisomy 21). Generally, outcome is good in patients of all ages when preoperative PVR is only mildly or moderately elevated. Large VSDs in such children should be repaired by three to four months of age. Eisenmenger syndrome, appearing most frequently in the second and third decade of life and typically leading to death by the age of 40.

Some patients with isolated VSD develop subpulmonary stenosis due to right ventricular infundibular hypertrophy. These patients are not at risk of pulmonary vascular destructive disease. Prolapse of the leaflets of the aortic valve occurs most frequently with the defects opening directly into the outlet of the right ventricle, muscular outlet, or perimembranous defects opening to the right ventricular outlet with malalignment of the muscular outlet septum. Untreated prolapse of the aortic valvar leaflets results first, in a decreased left-to-right shunt because the involved leaflet often prolapses into the defect and reduces the shunt, and second, worsening aortic insufficiency.^(2,3)

Indication for VSD repair

- Large VSDs presenting in the first few months of life with severe congestive heart failure or inlet (AV canal) and outlet (supracristal) defects which do not generally close spontaneously are the VSD's in which surgical closure is indicated.

- An undesirable mechanism of spontaneous occlusion is prolapse of an aortic valvar leaflet into the defect, often causing aortic insufficiency. This is also an indication for surgical repair. It is preferable to identify the defects associated with this potential complication and close them before its development.

- Bacterial endocarditis is a rare complication. Following antibiotic treatment of the active infection, closure of VSD regardless of its size is indicated.

- All VSDs irrespective of size, if associated with another reason for cardiac surgery,

- All residual VSDs >3 mm or those associated with elevated pulmonary artery pressures have also indication for closure.^(2,5,6)

Early repair of congenital cardiac lesions with improved postoperative care is the best strategy to prevent the development of severe pulmonary vasculopathy in CHD. However, even in developed nations, some infants/children are older at presentation or have yet-undiscovered genetic abnormalities that predispose to increased pulmonary vasoreactivity or early development of pulmonary vascular remodeling. The decision to operate on these patients with an acceptable risk of early and late postoperative complications is not easy, and the current view is that it should be not be based on single parameters.

During the 5th World Symposium on Pulmonary Hypertension of the World Health Organization (Nice, France, February 2013), a PVR of 4 Wood units m² and PVR:SVR ratio < 0.3 was proposed as a limit for considering surgery, and a PVR of 4–8 Wood units m² as the range in which patients should be discussed case by case. The PVR of 6 Wood units m² and a PVR:SVR ratio of 0.3 as limits for considering operation in PAH-CHD was proposed and a 20% decrease in PVR from baseline during the acute vasodilator test is considered sufficient to define a positive response but not to characterize operability. There has been debate about what to do with patients with elevated PVR (e.g., PVR > 8–10 Wood units m² and PVR:SVR > 0.5), in particular since the answer will not be the same for patients at different ages.^(7,8,9)

Technique of surgical repairing of VSD

The progress in cardiopulmonary bypass, myocardial protection, improved skill, and surgical techniques and in the perioperative care has advanced so that standard corrective operation for ventricular septal defect closure in infant patients is now obtained with almost no mortality or major morbidity. Today pulmonary artery banding is not preferred except for only a very few specific lesions like multiple muscular (Swiss cheese) VSDs, multiple VSDs with coarctation, single ventricle with large VSD, for preparing left ventricle in late (after 6 weeks of age) presented transposition of great arteries (TGA) and for training left ventricle for a double switch in congenitally corrected transposition of great arteries.

The corrective operative approach varies according

to the type of VSD. Perimembranous and inlet VSDs are usually repaired through a right atrial approach. Doubly committed VSD's are approached through the pulmonary artery, aorta or right ventricle. Muscular VSDs are usually approached through right atrium or through limited right or left ventriculotomy.

Following aortic and bicaval cannulation, moderate hypothermia (28-32°C) is constituted. The aorta is clamped and the heart is arrested with cardioplegic perfusate. The right atrium is opened to expose the tricuspid valve orifice. The pump sump sucker is placed in the left ventricle through interatrial septum to keep the operative field dry. If atriotomy is not required, the sucker is placed via the right superior pulmonary vein or left atrial appendage.

The perimembranous VSD is identified by retracting the septal and anterior leaflets of tricuspid valve. In some instances, the VSD perimeter cannot be completely identified because of the overlying tricuspid valve tissue (tricuspid valve pouch). Tricuspid valve detachment may be required by incision on the septal leaflet, parallel to the tricuspid valve annulus. The next step is to inspect the VSD. The aortic leaflets may prolapsed into the defect and must be avoided during suture placement.

The technique of VSD closure that we have been using at Ankara University, Department of Cardiovascu-

lar Surgery, is to encircle the perimeter of the VSD with multiple, interrupted, pledget-based 5-0 polypropylene sutures (**Figure-1**). To avoid injury to the conducting system, the sutures should be placed superficially and carefully along the inferior and posterior margins of the defect and stay on the right ventricular side of the VSD. This closure begins from the area of the insertion of the muscle of Lancisi (medial papillary muscle of the conus) to the annulus of the tricuspid valve near the region of the triangle of Koch. Care must be taken when placing these sutures to avoid the aortic valve cusp.

The sutures are then sequentially placed through an appropriately sized patch (1.5 times the size of the actual hole in the septum), the patch is lowered into the defect, and the sutures are tied and cut. We commonly use Dacron patch. Alternatively, autologous pericardium, or polytetrafluoroethylene (Gore-Tex) patch material may be used. After the patch has been anchored by tying all the sutures, the tricuspid valve is repaired (usually with 6-0 prolene) if detachment was performed. The right ventricle can be irrigated with saline to identify tricuspid valve regurgitation. The completion of the VSD closure is accomplished by closing the atrium. Transesophageal echocardiography (TEE) is very important to assure the integrity of the repair after the closure by evaluating for residual intracardiac left-to-right shunting.

Figure 1. Dacron patch repair with interrupted sutures

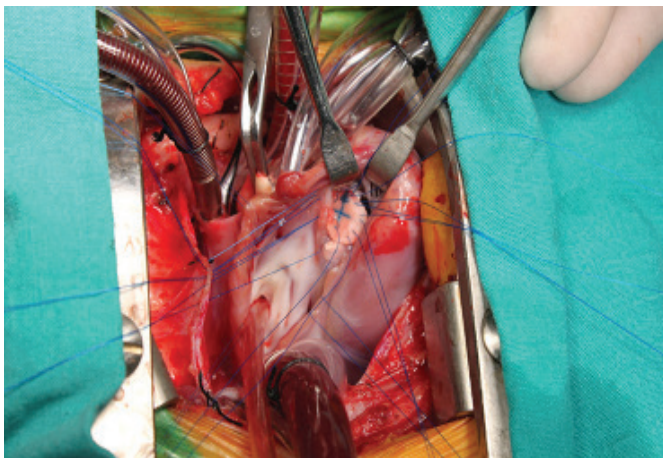
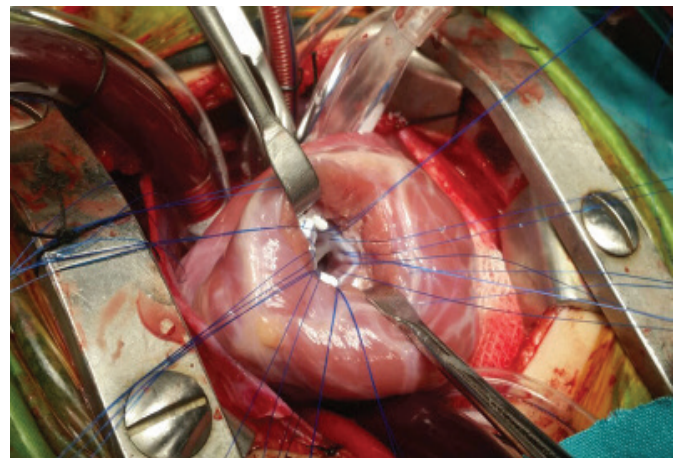


Figure 2. Left ventriculotomy for muscular VSD closure



The exposure of doubly committed VSD is usually accomplished through a vertical incision in the pulmonary artery. Pulmonary valve is gently retracted. A critical part of the closure involves placing sutures directly in the base of the pulmonary valve cusp. Pledged sutures are placed circumferentially around the perimeter of the VSD.

Certain muscular VSDs (Swiss cheese) may be easier to patch on the left ventricular side because of the relatively smooth septum. Left ventricular incisions, however is associated with significant long-term ventricular dysfunction and should be avoided whenever possible (**Figure-2**). Multiple anterior muscular defects may be closed through short vertical right ventriculotomy. The defects are sandwiched between two strips of felt or pericardium, one placed inside and the other outside the right ventricle parallel to the left anterior descending coronary artery. Interrupted horizontal mattress sutures are used. Midmuscular septal defects may be closed using a single composite patch to avoid injury to the conduction tissue.^(2,6,10,11,12)

If the PVR is moderately elevated: (1) partial closure of the communication; (2) leaving a small ASD open while repairing posttricuspid defects; (3) placing a band on the pulmonary artery should be considered.

Over the past decade or so, transcatheter techniques for closure of ventricular septal defects have been developed. These methods have been especially useful for muscular defects, which can be the most difficult to Access surgically. Much interest has been generated in development of transcatheter approaches to close perimembranous defects. At present, this technique is not undertaken in most units because of the unacceptably high rate of post-procedure heart block associated with currently available devices.⁽¹³⁾

Complications

Premature rate death occurs in less than 2.5% of patients when pulmonary resistance is low preoperatively. Repair of VSD during the first 1 or 2 years of life is curative for most patients, resulting in full functional activity and normal or near-normal life expectancy. Complications of surgical closure of VSD are generally related to injury to the anatomic structures, inadequate exposure and cardiopulmonary bypass.

Conduction system and the leaflets of tricuspid and aortic valves are at risk during VSD closure. Transient arrhythmias may be seen. Right bundle branch block (RBBB) is present late postoperatively in many patients in whom VSDs are repaired via right ventriculotomy. RBBB is less prevalent when the right atrial approach is used for VSD repair. Serious ventricular arrhythmias and sudden death late after repair of VSDs have been rare. Complete heart block requiring a pacemaker has been reported in 1-2 % of cases. Prevalence is slightly higher in patients undergoing repair of multiple VSDs. Inlet VSDs extending posteriorly to the crux, associated with straddling tricuspid valve, also have increased prevalence of heart block after repair.

During suture placement, aortic valve injury can occur and cause aortic insufficiency. Perimembranous VSD (rather than VSDs in the right ventricular outlet) and older age at operation contribute to presence of important aortic regurgitation after repair. VSD patch may rarely cause hemolysis. Tricuspid insufficiency can occur if the leaflets are retracted inappropriately or after tricuspid detachment for exposure. In experienced centers, reoperation for residual VSD should be 2% or less. Late postoperative cardiac function is essentially normal when repair is done during the first 2 years of life by modern techniques through the right atrium.^(2,10,14)

References

1. Rubin AE, Lewin MB. Ventricular septal defect. In Moss & Adams' Heart Disease in Infants, Children, and Adolescents, Including the Fetus and Young Adult. Eighth edition. Editors: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF. 2013. p. 713-722
2. Mavroudis C, Backer CL, Jacobs JP, Anderson RH. Ventricular septal defect. In Pediatric Cardiac Surgery. Fourth edition. Editors: Mavroudis C, Backer CL. 2013. p. 311-336.
3. Chaudhry TA, Younas M, Baig A. Ventricular Septal defect and associated complications. JPMA 2011;61(10):1001-4.
4. Van Praagh R, Geva T, Kreutzer J. Ventricular septal defects: how shall we describe, name and classify them? J Am Coll Cardiol 1989; 14:1298.
5. Up to date, 2015
6. Knott-Craig CJ. Ventricular septal defect. In Mastery of Cardiothoracic Surgery. Second edition. Editors: Kaiser LR, Kron IL, Spray TL. 2007. p.750-758.
7. Lopes AA, Rabinovitch M. Statements on the management of pulmonary hypertension associated with congenital heart disease. Cardiol Young 2009(Suppl. S1):1-53.
8. Beghetti M, Galie` N, Bonnet D. Can "inoperable" congenital heart defects become operable in patients with pulmonary arterial hypertension? dream or reality? Congenital Heart Dis 2012;7:3-11.
9. Lopes AA, Barst RJ, Haworth SG, et al. Repair of congenital heart disease with associated pulmonary hypertension in children: what are the minimal investigative procedures? Consensus statement from the Congenital Heart Disease and Pediatric Task Forces, Pulmonary Vascular Research Institute (PVRI) Pulm Circ 2014;4(2):330-341. DOI: 10.1086/675995.
10. van Doorn C, de Leval MR. Surgery for congenital heart defects. Third edition. Editors: Stark J, De Leval M, Tsang VT. 2006. p.355-371.
11. Ventricular septal defect. In Comprehensive Surgical Management of Congenital Heart Disease. Second edition. Editor: Jonas RA. 2014. p.331-345.
12. Ventricular septal defect. In Cardiac Surgery Safeguards and Pitfalls In Operative Technique. Fourth edition. Editors Khonsari S, Sintek CF. 2008. p. 256-265.
13. Penny DJ, Vick GW. Ventricular septal defect. Lancet 2011; 377: 1103-12.
14. Ventricular septal defect. In Kirklin/Barrat-Boyes Cardiac Surgery. Fourth edition. Editors: Kouchoukos NT, Blackstone EH, Hanley FL, Kirklin J. 2013. p. 1275-1319

Received: 16/11/2016

Accepted: 21/03/2017

Published: 15/06/2017

Disclosure and conflicts of interest:

Conflicts of interest were not reported.

Corresponding author:

Prof. Dr. Zeynep Eyileten

Mail: zeyileten@gmail.com

Transcatheter successful palliation of a newborn with ductal-dependent pulmonary circulation

Tamer Yoldaş¹, Senem Özgür², Vehbi Doğan¹, Özkan Kaya¹, Utku Arman Örün², Selmin Karademir³

¹⁾ Dr.Sami Ulus Maternity and Children Research and Training Hospital,Department of Pediatric Cardiology, Specialist Dr., Ankara, Turkey

²⁾ Dr.Sami Ulus Maternity and Children Research and Training Hospital,Department of Pediatric Cardiology, Assoc. Dr., Ankara, Turkey

³⁾ Dr.Sami Ulus Maternity and Children Research and Training Hospital,Department of Pediatric Cardiology, Prof. Dr., Ankara, Turkey

Abstract

We report a newborn who have congenital heart disease with duct-dependent pulmonary circulation and hypoplastic peripheral pulmonary arteries, was successfully palliated with ductal multiple stent implantation.

Key words: Pulmonary atresia, pulmonary hypoplasia, ductal stent implantation.

Yoldaş T., Özgür S., Doğan V., Kaya Ö., Örün U. A., Karademir S. Transcatheter successful palliation of a newborn with ductal-dependent pulmonary circulation. EJCM 2017; 05 (2): 34-36. Doi: 10.15511/ejcm.17.00234

Introduction

Conventional management of neonates with ductal-dependent pulmonary flow entails maintaining ductal patency using prostaglandin E1 infusion followed by surgical palliation with Blalock-Taussig shunt (B-T shunt). Nowadays, percutaneous transcatheter placement of a stent to maintain ductal patency has been used as an alternative method to provide a source of pulmonary blood flow.^[1,2] The potential advantages of ductal stenting include reduced procedure-related risks and improved distribution of pulmonary artery blood flow.^[3] Ductal stenting could be used as a bridge toward corrective surgery in neonates.^[4]

Case Report

A two-day-old boy was referred to our hospital for cardiac evaluation moderate to severe cyanosis (percutaneous oxygen saturation 60%). Echocardiography showed, situs solitus, levocardia, concordant atrioventricular connection, large outlet ventricular septal defect, pulmonary atresia, hypoplastic pulmonary artery branches, right aortic arch and vertical arterial duct. Cardiac catheterization was performed via right femoral vein. Pulmonary artery branches were hypoplastic (right and left pulmonary artery 3 mm) and supplied by a vertical, tortuous ductus with distal narrowing which arises from the inner curve of a right sided aortic

Figure 1. Vertical, tortuous ductus with distal narrowing.

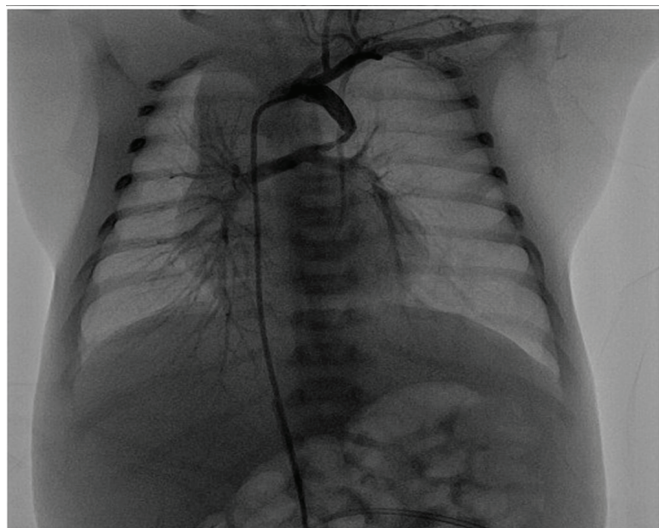


Figure 2. First stent implantation

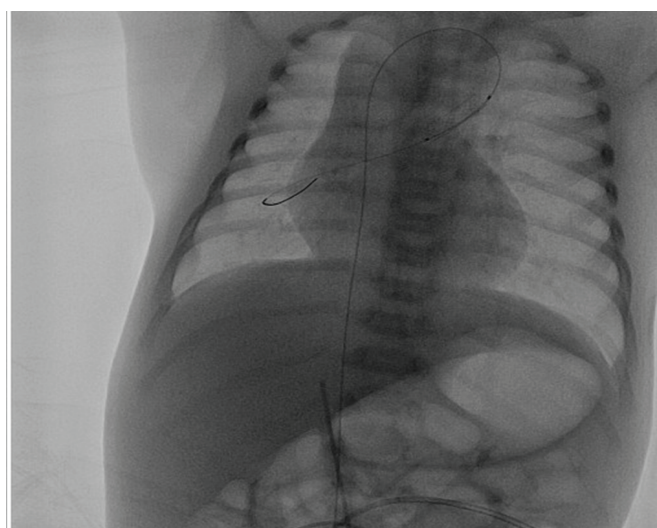


Figure 3. Second stent implantation

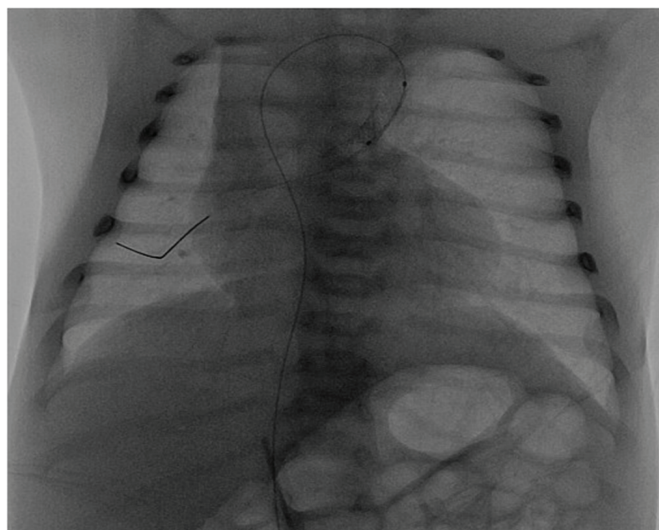
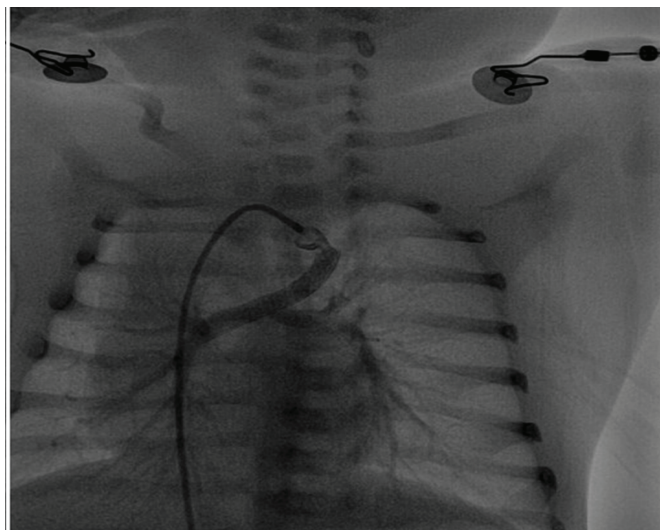


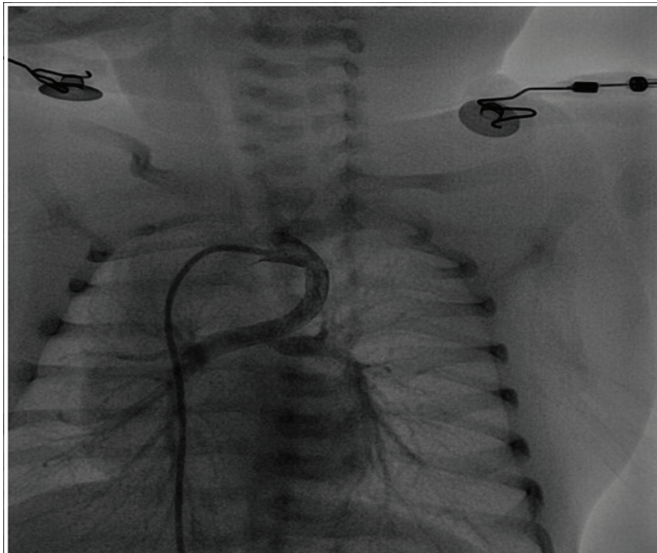
Figure 4. Critically stenotic aortic end of ductus arteriosus



(**Figure 1**). Firstly distal narrowed part of ductus arteriosus was stented with a coronary stent (4×15 mm) (**Figure 2**). After that a second coronary stent (4×15 mm) was implanted to cover most of the duct (**Figure 3**). The final oxygen saturation was 90% after two stent implantation. After cessation of prostaglandin infusion the patient' oxygen saturation gradually decreased up to the 55%. Second cardiac catheterization

showed critically stenosis in aortic end of ductus (**Figure 4**). A third coronary stent (4×15 mm) was placed to cover the aortic side entirely (**Figure 5**). The oxygen saturation was increased to 85% after third stent implantation. The patient was discharged with %85 oxygen saturation in the following days. During follow-up periods of to three months he had no problem clinically, weight gain and %88 percutaneous oxygen saturation.

Figure 5. Ductus arteriosus after three stent implantation



Discussion

Ductal stenting a reliable and more physiologic alternative to surgical systemic to pulmonary shunt in neonates. But the lack of stent coverage of the entire ductus (especially in long and tortuous duct) results duct constriction and cyanosis of the patient and causes re-intervention in most cases. It is well known that passing a catheter through the stent is technically very difficult and increases the risk of thrombosis and hemodynamic destabilization when compared with the primary intervention. Therefore stent long must be enough to cover entire ductus. But in some cases a small segment of the duct may be left uncovered and necessitating use of second or third stent. The full-length stenting of the duct without leaving any ductal tissue is important.

References

1. Alwi M, Choo KK, Haifa AL, Geetha K, Hasri S, Mulyadi MD. Initial results and medium-term follow-up of stent implantation of patent ductus arteriosus in duct-dependent pulmonary circulation. *J Am Coll Cardiol*. 2004;44:438–45.
2. Gewillig M, Boshoff DE, Dens J, Mertens L, Benson LN. Stenting the neonatal arterial duct in duct-dependent pulmonary circulation: New techniques, better results. *J Am Coll Cardiol* 2004;43:107–112.
3. McMullan DM, Permut LC, Jones TK, Troy Alan Johnston TA, Rubio AE. Modified Blalock-Taussig shunt versus ductal stenting for palliation of cardiac lesions with inadequate pulmonary blood flow. *J Thorac Cardiovasc Surg* 2014;147:397-403.
4. Santoro G, Gaio G, Castaldi B, et al. Arterial Duct Stenting in Low-Weight Newborns With Duct-Dependent Pulmonary Circulation. *Catheterization and Cardiovascular Interventions*. 2011; 78:677–685

Received: 08/10/2016

Accepted: 25/02/2017

Published: 15/06/2017

Disclosure and conflicts of interest:

The authors declare no conflict of interest.

Corresponding author:

Dr. Tamer Yoldaş

Mail: tameryoldas@gmail.com

EJCM 2017; 05 (1): 37-40

Doi: 10.15511/ejcm.17.00237

Dead sea like giant negative t wave associated with subarachnoid hemorrhage

Recep Kurt¹, Hakan Güneş¹

¹ Sivas Numune Hospital, Department of Cardiology, MD, Sivas, Turkey

Abstract

Subarachnoid hemorrhage is a catastrophic neurological event. Rupture of an aneurysm results it. In addition to neurological signs and symptoms ECG abnormalities reported. These ECG findings reported are prolonged QTc, ST segment abnormalities, T wave inversion, abnormal U wave, bradycardia, tachycardia, Premature ventricular complex, Premature atrial complex, atrial fibrillation, VT, AV blocks. We described a patient with subarachnoid hemorrhage showed giant inverted T wave.

Keywords: Subarachnoid hemorrhage, T wave inversion

Kurt R., Güneş H., Dead sea like giant negative t wave associated with subarachnoid hemorrhage. EJCM 2017; 05 (2): 37-40. Doi: 10.15511/ejcm.17.00237.

Introduction

Subarachnoid hemorrhage is a catastrophic neurological event. Rupture of an aneurysm results it. In addition to neurological signs and symptoms ECG abnormalities reported. These ECG findings reported are prolonged QTc, ST segment abnormalities, T wave inversion, abnormal U wave, bradycardia tachycardia, Premature ventricular complex, Premature atrial complex, atrial fibrillation, VT, AV blocks. We described a patient with subarachnoid hemorrhage showed giant inverted T wave. Generally inverted T waves are related with acute coronary syndromes. Additionally, T wave inversion occurs in patients with left ventricle hypertrophy, acute myocarditis, WPW syndrome, acute pulmonary embolism, pericarditis, electrolyte disturbances, on treatment with digoxin and Yamaguchi syndrome.

Case Report

64-year old woman admitted to the emergency department with sudden loss of consciousness and left hemiparesis. The blood pressure was 180/120 mmHg with a heart rate of 78 bpm. Her ECG showed global very widely splayed and very deeply inverted T-waves with prolonged QT (QTc: 640 ms) (**Figure 1**). Cranial CT showed subarachnoid hemorrhage.

Standard biochemical parameters were in normal

limits except serum potassium level of 3.1 mg/dL and leukocytosis on complete blood count. Bilateral basal crackling rales in the lungs were detected but the echocardiography, cardiac markers and the renal parameters were all in normal limits. The patient was intubated after a short period after admission and she died after a short time of deterioration.

Discussion

T wave is the electrocardiographic manifestation of ventricular repolarization. Any reason disrupting ventricular repolarisation just like acute coronary syndromes, left ventricular hypertrophy, pulmonary embolism, electrolyte disturbances and cerebrovascular events eventuate T wave abnormalities. Subarachnoid hemorrhage is usually accompanied by electrocardiographic abnormalities including the T-wave abnormalities and it's thought that these changes are caused by increased sympathetic and vagal tone leading to aberrant repolarisation, probably secondary to myocyte injury and contraction band necrosis.¹

Neurogenic ECG alterations are often transient. It causes diagnostic problems, ECG findings in neurogenic problems can mimic acute myocardial infarction. It is important to avoid inappropriate therapies. An imbalance of autonomic cardiovascular control and increased

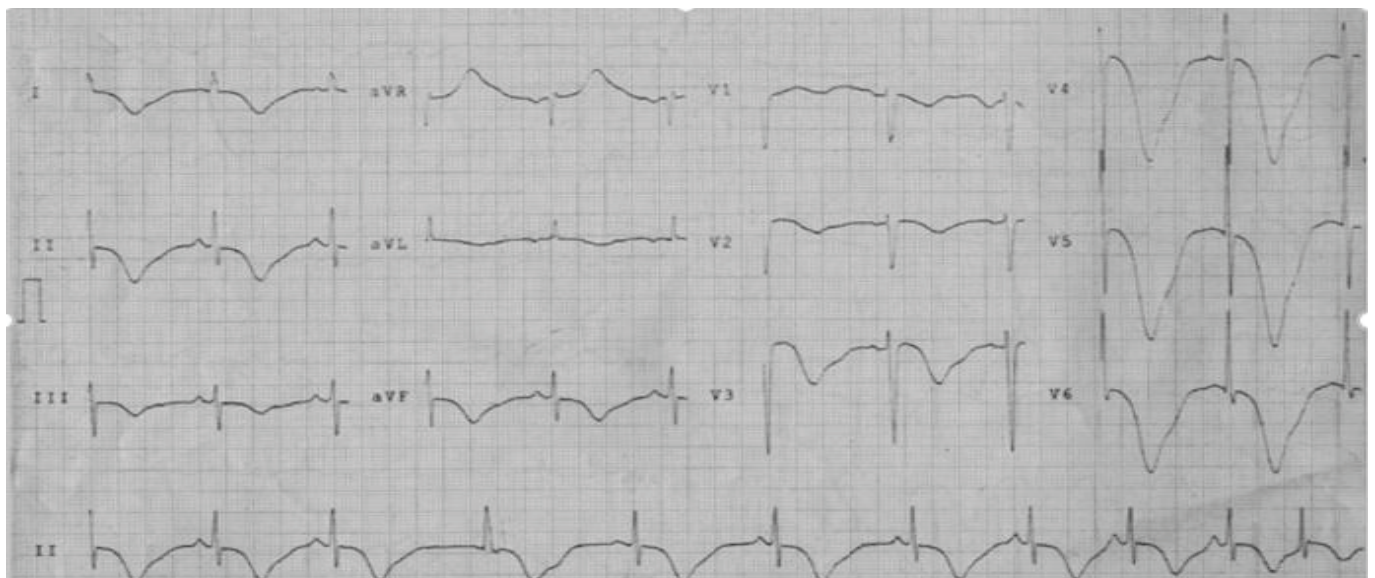


Figure 1: Her ECG showed global very widely splayed and very deeply inverted T-waves with prolonged QT

circulating local myocardial tissue catecholamines. Several experience investigation reported that a sudden increase in intracranial pressure occurs that a massive sympathetic discharge.^{2,3} Experimental studies suggest that a large amount of norepinephrin is released during sudden neurologic problems. Alterations in cardiac depolarisation and repolarisation reported 74% of patient with cerebrovascular events.⁴ Experimental studies implicates that insular cortex is responsible in cardiovascular control and heart chronotropik organisation.

Studies suggest that its involvement occurs neurogenic ECG alterations.⁵ Porter et al.⁶ found that stimulation of the posterolateral hypothalamus not only induced rhythm abnormalities but also caused repolarisation changes. Attar and colleagues found that stimulation of the anterior hypothalamus produced ST elevation and deepening of T waves.⁷ Thus, hypothalamic stimulation is capable of causing both arrhythmias and a variety of ECG changes which mimic acute myocardial injury or ischemia. In a study by Estanol et al.⁸ rhythm and repolarisation changes were created in dogs by introducing

blood into the subarachnoid space.

Rudehill et al.⁹ ECG s were prospectively studied on 406 patients with subarachnoid hemorragiae. Three hundred thirty one patients (82%) had an abnormal ECG. The predominant findings were U wave changes (47%). T wave abnormalities (32%), prolonged QTc interval (24%), and ST segment depression.(15%). Stober et al.¹⁰ showed that ECG abnormalities in patients with subarachnoid hemorragiae were interested in arterial spasm on the brain. Several studies revealed electrocardiographic abnormalities related with subarachnoid hemorragiae.¹¹⁻¹³

In conclusion; acute ischemic cardiac events show electrcardiographic abnormalities. T wave abnormalities also can often seems as a result of acute cardiac problems. On the other hand acute cerebrovascular events can mimic electrocardiographic abnormalities in patients with acute cardiac problems. As a result phsician must be aware about these ECG similarities. Otherwise, these ECG abnormalities can cause inappropriate therapies.

References

1. Hironosuke Sakamoto, Hiroshi Nishimura, Kouji Imataka. Abnormal Q Wave, ST-Segment Elevation, T-Wave Inversion, and Widespread Focal Myocytolysis Associated With Subarachnoid Hemorrhage. *Jpn Circ J* 1996; 60: 254-7.
2. Nathan MA, Reis DJ. Fulminating arterial hypertension with pulmonary edema from release of adrenomedullary catecholamines after lesions of anterior hypothalamus in the rat. *Circ Res*
3. Hoff JT, Nishimura M, Garcia Uria J, Miranda S. Experimental neurogenic pulmonary edema, Part 1: The role of systemic hypertension. *J Neurosurgery* 1986; 226-35.
4. Oppenheimer SM, Cechetto DF, Hochinski VC, Cerebrogenic cardiac arrhythmias, Cerebral electrocardiographic influences and their role in sudden death. *Arch Neurol* 1990; 47: 513-9.
5. Tokgözoğlu SL, Batur MK, Topçuoğlu MA. Effects of stroke localization on cardiac autonomic balance and sudden death. *Stroke* 1999; 30: 1307-11.
6. Porter RW, Kamikana K, Greenhoot JH: Persistent electrocardiographic abnormalities experimentally induced by stimulation of the brain. *Am Heart J* 1962; 64: 815-9.
7. Attar HJ, Gutierrez MT, Bellet S: Effects of stimulation of hypothalamic and reticular activating systems on production of cardiac arrhythmias. *Circ Res* 1963; 12: 14-21.
8. Estanol BV, Loyo MV, Mateos JH: Cardiac arrhythmias in experimental subarachnoid hemorrhage. *Stroke* 1977; 8: 440-8.
9. Rudehill A, Olsson GL, Sundquist K: ECG abnormalities in patients with subarachnoid hemorrhage and intracranial tumors. *J Neurol Neurosurg Psychiatry* 1974; 50: 1375-81.
10. Stober T, Kunze K. Electrocardiographic alterations in subarachnoid haemorrhage. Correlation between spasm of the arteries of the left side on the brain and T inversion and QT prolongation. *J Neurol* 1982; 227: 99-113.
11. van Bree MD, Roos YB, van der Bilt IA, Wilde AA, Sprengers ME, de Gans K, Vergouwen MD. Prevalence and characterization of ECG abnormalities after intracerebral hemorrhage. *Neurocrit Care*. 2010; 12: 50-5.
12. Brunninkhuis LG. Electrocardiographic abnormalities suggesting myocardial infarction in a patient with severe cranial trauma. *Pacing Clin Electrophysiol* 1983; 6: 1336-40.
13. Wittebole X, Hantson P, Laterre PF, Galvez R, Duprez T, Dejonghe D, Renkin J, Gerber BL, Brohet CR. Electrocardiographic changes after head trauma. *J Electrocardiol* 2005; 38: 77-81.

Received: 09/07/2016

Accepted: 30/03/2017

Published: 15/06/2017

Disclosure and conflicts of interest:

Conflicts of interest were not reported.

Corresponding author:

Dr. Hakan Güneş

Mail: drhakangunes83@hotmail.com

Aortic valve replacement due to lactococcus lactis infective endocarditis

Özgür Altınbaş¹, Erdal Ege², Ali Sarıgül²

¹⁾ Necmettin Erbakan University, Meram Medical Faculty, Department of Cardiovascular Surgery, Ass. Dr., Konya, Turkey

²⁾ Necmettin Erbakan University, Meram Medical Faculty, Department of Cardiovascular Surgery, Prof. Dr., Konya, Turkey

Abstract

Infective endocarditis characterized by microbial infection of the endothelial surface of the heart, has an estimated annual incidence of 3 to 9 cases per 100.000 persons in industrialized countries. Although common species causing infective endocarditis include streptococci, staphylococci, enterococci and fastidious gram negative coccobacilli, aortic valve replacement due to lactococcus lactis infective endocarditis seen in the literature, even if rarely. In this study we presented a 34 year old male patient underwent surgery, diagnosed with lactococcus lactis infective endocarditis.

Keywords: Infective endocarditis, Lactococcus lactis, Complication

Altınbaş Ö., Ege E., Sarıgül A. Aortic valve replacement due to lactococcus lactis infective endocarditis; Case report
EJCM 2017; 05 (2): 41-43. Doi: 10.15511/ejcm.17.00241.

Introduction

Endovascular, microbial infection of intracardiac structures facing the blood including infections of the large intrathoracic vessels and of intracardiac foreign bodies, called infective endocarditis. The early characteristic lesion is a different sized vegetation, although destruction, ulceration or abscess formation may be seen earlier by echocardiography.⁽¹⁾

The highest rates of the infective endocarditis are observed among patients with prosthetic valves, intracardiac devices, unrepaired cyanotic congenital heart diseases or a history of infective endocarditis, although 50% of cases of infective endocarditis develop in patients with no known history of valve disease. Other risk factors include chronic rheumatic heart disease, age-related degenerative valvular lesions, hemodialysis and coexisting conditions such as diabetes, human immunodeficiency virus infection and intravenous drug use. Diagnosis of endocarditis is usually based on clinical, microbiologic and echocardiographic findings.⁽²⁾

Indications for cardiac surgery are; heart failure, no control of infection, vegetations and embolic risk, perivalvar infection, valvar obstruction, unstable prosthesis, prosthetic infective endocarditis, fungal infective endocarditis, difficult-to-treat microorganisms and neurological complications. *Lactococcus lactis* is a mesophilic and microaerophilic fermenting bacteria, used for fermented food products production. It can be isolated even if rarely from oropharynx, intestines, or vagina as a part of normal flora. For a long time it was considered as nonvirulent with low pathogenicity in humans.⁽³⁾

Case Report

Thirty four year old male patient, previously healthy, sometimes presented with a high fever, cold and chills problems last one month. He had first applied to a health care center and oral antibiotherapeutic medication was started but his problems had continued to exist. And then patient was applied to a hospital and though there was a suspicious aspect in transthoracic echocardiography, he was referred to university hospital for transesophageal echocardiography. He was hospitalized in infectious diseases service and there was

no significant pathology in his physical examination. Four blood cultures were taken from patient and *Lactococcus lactis* was seen in one of them. 1,5*2,1 cm sized vegetations on the aortic valve were determined in transesophageal echocardiography. Ejection fraction was 60%. Aortic regurgitation was 2-3rd degree. Intravenous antibiotherapy included gentamicin and vancomycin started to the patient.

The patient was referred to us and because of the risk of embolisation due to vegetation, emergency operation was decided for him. He was interned to cardiovascular intensive care unit and aortic valve replacement was made with 25 mm SJ prosthetic valve. Aortic valve wall was fibrocalcific and approximately 1,6 * 2,2 cm sized vegetations were seen on the valve. There was no microorganism produced in valve culture.

Discussion

The incidence of IE continues to rise, with a yearly incidence of \approx 15 000 to 20 000 new cases. Although advances in antimicrobial therapy and the development of better diagnostic and surgical techniques have reduced the morbidity and mortality of infective endocarditis, it remains a potentially life-threatening disease.⁽⁴⁾ The most common cause of the endocarditis is the infection and endocarditis due to *Lactococcus lactis* is a rare clinical situation that most frequently occurs in immunocompromised patients or in those with impaired local defense mechanism in which this usually non-pathogenic microorganism may be cause of severe infection.⁽⁵⁾

Diagnostic work-up, including a complete transthoracic and transesophageal study, must be performed immediately in every patient admitted to an intensive care unit with embolism, heart failure, cardiogenic or septic shock of unknown cause, as the data presented here suggest that prompt surgical intervention can be life-saving in patients with infective endocarditis despite the presence of severe shock and the occurrence of multiorgan failure.⁽⁶⁾ Infective endocarditis caused by *Lactococcus lactis* is a rare clinical situation, so it must be considered as one of the factors of infective endocarditis. Early surgical intervention in *Lactococcus lactis* endocarditis can save lives.

References

1. Dieter Horstkotte, Ferenc Follath, Erno Gutschik, Maria Lengyel, Ali Oto, Alain Pavié et al. Guidelines on Prevention, Diagnosis and Treatment of Infective Endocarditis Executive Summary: The Task Force on Infective Endocarditis of the European Society of Cardiology. *Eur Heart J* (2004) 25 (3):267-276
2. Bruno Hoen, Xavier Duval. Infective Endocarditis. *N Engl J Med* 2013;368:1425-1433
3. Bshara Mansour, Adib Habib, Nazih Asli, Yuval Geffen, Dan Miron, Nael Elias. A Case of Infective Endocarditis and Pulmonary Septic Emboli Caused by *Lactococcus Lactis*. Case Report in Pediatrics. Volume 2016, Article ID 1024054, 4 pages
4. Diagnosis and Management of Infective Endocarditis and its Complications. Arnold S. Bayer, MD; Ann F. Bolger MD; Kathryn A. Taubert, PhD, et al. *Circulation* 1998;98:2936-2948
5. C. Rostagno, P. Pecile, P. L. Stefano. Early *Lactococcus lactis* endocarditis after mitral valve repair: a case report and literature review. *Infection* (2013)41:897-899
6. Complicated infective endocarditis necessitating ICU admission: Clinical course and prognosis
7. Georg Delle Karth, Maria Koreny, Thomas Binder... et al. *Critical Care* 2002,6:149-154

Received: 12/01/2017

Accepted: 04/05/2017

Published: 15/06/2017

Disclosure and conflicts of interest:

Conflicts of interest were not reported.

Corresponding author:

Dr. Özgür Altınbaş

Mail: ozgurinterpol@yahoo.com

E-Journal of Cardiovascular Medicine welcomes scientific contributions in the field of cardiovascular and thoracic surgery - all aspects of surgery of the heart, vessels and the chest in various article types: new ideas, brief communications, work in progress, follow-up studies, original articles, best evidence topics, case reports, reports on unexpected results etc. All manuscripts shall be reviewed by the Editor-in-Chief, Associate Editors, Invited Referees and a Statistician when appropriate. If accepted, articles will be posted online and opened up for discussion. Acceptance criteria are based on the originality, significance, and validity of the material presented.

All material to be considered for publication in E-Journal of Cardiovascular Medicine should be submitted in electronic form via the journal's online submission system. (<http://my.ejmanager.com/ejcm/>)

A cover letter should be enclosed to all new manuscripts (to be filled in online), specifying the name of the journal and the type of paper, and including the following statements:

- The manuscript should not be previously published in print or electronic form and is not under consideration by another publication.
- All authors should contribute to the content of the article.
- All authors should read and approve the submission of the manuscript to ICVTS.
- Subject to acceptance, authors will sign an exclusive license to publish.
- No ethical problem or conflict of interest should exist.

If your first language is not English, we recommend that you consult an English language editing service to ensure that the academic content of your paper is fully understood by journal editors and reviewers. Language editing does not guarantee that your manuscript will be accepted for publication.

Manuscripts should be prepared using a word-processing package (save in .doc, .docx or .rtf format). The font type and font size should preferably be Arial or Times New Roman 11 points. The manuscript should be double-spaced and should include line and page numbers. The lines of the reference list do not need to be numbered; include a section break before.

Manuscripts should be organized as follows:

(a) Title page; (b) Abstract and Key words; (c) Text with the following sections (not applicable for article types with unstructured abstracts): Introduction, Materials and Methods, Results, Discussion, Acknowledgement (optional), Funding statement, Conflict of interest statement, (d) Figure (and Video) legends; (e) Tables; (f) References.

Title page (1st page): Title: should be brief and descriptive (100 characters) - no abbreviations are allowed, even if well known.

Authors: list all authors by full first name, initial of or full middle name and family name. Qualifications are not required. Ensure the author names correspond (in spelling and order of appearance) with the metadata of the system

Institution(s): include the name of all institutions with the location

(department, institution, city, country) to which the work should be attributed (in English). Use superscript numbers to connect authors and their department or institution.

Corresponding author: The full name, full postal address, telephone/fax numbers and the e-mail address should be typed at the bottom of the title page.

Meeting presentation: If the manuscript was (or will be) presented at a meeting, include the meeting name, venue, and the date on which it was (or will be) read; also indicate if you have submitted an Abstract of this manuscript for the EACTS or ESTS annual meeting and whether it has been accepted (if known).

Word count: The total number of words of the whole article (including title page, abstract, main text, legends, tables and references) must be specified on the title page.

Abstract (2nd page): An abstract should be a concise summary of the manuscript. Reference citations are not allowed. The abstract should be factual and free of abbreviations, except for SI units of measurement.

Keywords: Following the abstract, 3-6 keywords should be given for subject indexing.

Introduction: Should state the purpose of the investigation and give a short review of pertinent literature.

Materials and methods: Should be described in detail with appropriate information about patients or experimental animals. Use of abbreviations renders the text difficult to read; abbreviations should be limited to SI units of measurement and to those most commonly used, e.g. VSD, ASD, CABG (abbreviations should not be included in headings and extensions should be included at first mention).

Results: Results should be reported concisely and regarded as an important part of the manuscript. They should be presented either in tables and figures, and briefly commented on in the text, or in the text alone. Repetition of results should be avoided!

Discussion: The discussion is an interpretation of the results and their significance with reference to pertinent work by other authors. It should be clear and concise.

Acknowledgement: Acknowledgements and details of non-financial support must be included at the end of the text before the references. Personal acknowledgements should precede those of institutions or agencies.

Tables: All tables must be included in the manuscript file, should start on separate pages and be accompanied by a title, and footnotes where necessary. The tables should be numbered consecutively using Arabic numerals. Units in which results are expressed should be given in parentheses at the top of each column and not repeated in each line of the table.

References: Authors are responsible for checking the accuracy of all references. If you use EndNote or Reference Manager to facilitate referencing citations (not required for submission), this journal's style is available for use. References should be numbered in order of appearance in the text (in Arabic numerals in parentheses) and must be listed numerically in the reference list. Journal titles and author initials should be properly abbreviated and punctuated.

GENERAL RULES

Files should be prepared as a Word document using font size 12 Times New Roman characters, double-spaced and with 2.5 cm margins on each side, top and bottom. Only standard abbreviations should be used; other shortened phrases should be indicated in parentheses as used in the text. Generic or chemical names of drugs should be used instead of trade names.

ETHICAL ISSUES

Publishing responsibilities of authors and Ethics

The publication of an article in a peer-reviewed journal is an essential building block in the development of a coherent and respected network of knowledge. It is a direct reflection of the quality of work of the author and the institutions that support them. Peer-reviewed articles support and embody the scientific method. It is therefore important to agree upon standards of expected ethical behavior.

Reporting standards

Authors of reports of original research should present an accurate account of the work performed as well as an objective discussion of its significance. Underlying data should be represented accurately in the paper. A paper should contain sufficient detail and references to permit others to replicate the work. Fraudulent or knowingly inaccurate statements constitute unethical behavior and are unacceptable. Review and professional publication articles should also be accurate and objective, and editorial 'opinion' works should be identified as such.

Hazards and human or animal subjects

If the work involves chemicals, procedures or equipment that have any unusual hazards inherent in their use, the author must clearly identify these in the manuscript. If the work involves the use of animal or human subjects, the author should ensure that the manuscript contains a statement that all procedures were performed in compliance with relevant laws and institutional guidelines and that the appropriate institutional committee(s) has approved them. Authors should include a statement in the manuscript that informed consent was obtained for experimentation with human subjects. The privacy rights of human subjects must always be observed.

Use of patient images or case details

Studies on patients or volunteers require ethics committee approval and informed consent, which should be documented in the paper. Appropriate consents, permissions and releases must be obtained where an author wishes to include case details or other personal information or images of patients and any other individuals in publication. Written consents must be retained by the author and copies of the consents or evidence that such consents have been obtained must be provided to us on request. Particular care should be taken with obtaining consent where children are concerned (in particular where a child has special needs or learning disabilities), where an individual's head or face appears, or where reference is made to an individual's name or other personal details.

Originality and plagiarism

The authors should ensure that they have written entirely original works, and if the authors have used the work and/or words of

others, that this has been appropriately cited or quoted. Plagiarism takes many forms, from 'passing off' another's paper as the author's own paper, to copying or paraphrasing substantial parts of another's paper (without attribution), to claiming results from research conducted by others. Plagiarism in all its forms constitutes unethical publishing behavior and is unacceptable.

Data access and retention

Authors may be asked to provide the raw data in connection with a paper for editorial review, and should be prepared to provide public access to such data (consistent with the ALPSP-STM Statement on Data and Databases), if practicable, and should in any event be prepared to retain such data for a reasonable time after publication.

Multiple, redundant or concurrent publication

An author should not in general publish manuscripts describing essentially the same research in more than one journal or primary publication. Submitting the same manuscript to more than one journal concurrently constitutes unethical publishing behavior and is unacceptable. In general, an author should not submit for consideration in another journal a previously published paper. Publication of some kinds of articles (e.g. clinical guidelines, translations) in more than one journal is sometimes justifiable, provided certain conditions are met. The authors and editors of the journals concerned must agree to the secondary publication, which must reflect the same data and interpretation of the primary document. The primary reference must be cited in the secondary publication.

Acknowledgement of sources

Proper acknowledgment of the work of others must always be given. Authors should cite publications that have been influential in determining the nature of the reported work. Information obtained privately, as in conversation, correspondence, or discussion with third parties, must not be used or reported without explicit, written permission from the source. Information obtained in the course of confidential services, such as refereeing manuscripts or grant applications, must not be used without the explicit written permission of the author of the work involved in those services.

Fundamental errors in published works

When an author discovers a significant error or inaccuracy in his/her own published work, it is the author's obligation to promptly notify the journal editor or publisher and cooperate with the editor to retract or correct the paper. If the editor or the publisher learns from a third party that a published work contains a significant error, it is the obligation of the author to promptly retract or correct the paper or provide evidence to the editor of the correctness of the original paper.

Authorship of the paper

Authorship should be limited to those who have made a significant contribution to the conception, design, execution, or interpretation of the reported study. All those who have made significant

contributions should be listed as co-authors. Where there are others who have participated in certain substantive aspects of the research project, they should be acknowledged or listed as contributors. The corresponding author should ensure that all appropriate co-authors and no inappropriate co-authors are included on the paper, and that all co-authors have seen and approved the final version of the paper and have agreed to its submission for publication.

Changes to authorship

This policy concerns the addition, deletion, or rearrangement of author names in the authorship of accepted manuscripts. Before the accepted manuscript is published in an online issue:

Requests to add or remove an author, or to rearrange the author names, must be sent to the Journal Manager by the corresponding author of the accepted manuscript, and must include:

The reason the name should be added or removed, or the author names rearranged

Written confirmation (e-mail, fax, letter) from all authors that they agree with the addition, removal or rearrangement. In the case of addition or removal of authors, this includes confirmation from the author being added or removed

Requests that are not sent by the corresponding author will be forwarded by the Journal Manager to the corresponding author, who must follow the procedure described above.

Note that:

- Journal Managers will inform the Journal Editors of any such requests
- Publication of the accepted manuscript in an online issue is suspended until authorship has been agreed
- After the accepted manuscript has been published in an online issue:

Any requests to add, delete or rearrange author names in an article published in an online issue will follow the same policies as noted above and may result in a corrigendum.

TYPES OF PAPERS

Original Articles

Original articles should consist of sections titled as “Abstract, Introduction, Materials and Methods, Results, Discussion and Conclusion”. For information about the abstract, refer to ‘Manuscript Formatting’ section.

The Introduction section of the manuscript should clearly state the purpose of the manuscript and include a brief summary of the most relevant national and international literature stating the main purposes and research question of the study. Contradictory aspects of the research, if present, should be mentioned. The expected contribution of this study to family medicine and practice should be highlighted.

The Materials and Methods section should describe the study population and the study design, with adequate information on the

techniques, materials and methods used. The section should include information of the study type, population, sample, sample size and selection of the sample. Validity and reliability of scales and questionnaires used also should be referred to. A clear description of the statistical methods should also be given.

The Results section should include a detailed report on the findings of the study. All figures, tables and illustrations should be used in this section. Results should be presented either as text or figures and/or tables and not be replicated.

The Discussion section of the study should emphasize the importance of the results and compare them with the results of other authors with relevant citations from the most recent literature. Study limitations and strengths should be specified. Suggestions for further studies in this area should be added.

The Conclusion should include the main conclusions based on the results of the research, emphasize the contributions of the study to family practice and propose original suggestions. A brief revision of all the results and the discussion should be avoided.

Original articles excluding case reports and systematic reviews should not exceed 3000 words excluding the abstract, references and tables. Case reports should not exceed 1000 words excluding the abstract, references and tables. There are no restrictions for systematic reviews.

Short Reports

Short Reports are accepted when the research topic, aim and results of the study are limited in scope and in cases that do not require writing a full original article. Short Reports can be described as a summarized version that have been prepared according to the structure of research articles. Publishing an article as a short report does not reflect a lower quality. The same rules as relevant to original articles apply to preparing a short report, but structured abstracts are not mandatory references and tables should not exceed 6 and 2 in number, respectively. Abstracts should not exceed 100 words and the text should be restricted to a maximum of 1000 words.

Reviews

Reviews are evidence-based articles about a specific topic using relevant citations from the most recent literature with the authors’ conclusions on this subject. The author is expected to have conducted research on the subject and to have experience in order to discuss and analyze the subject. There is no obligation to follow a particular format and may contain subtitles depending on the subject. The text should not exceed 4000 words excluding the title, abstracts, references and tables. E Journal of Cardiovascular Medicine, only publishes review articles solicited by the editors.

Letters to Editor and Comments

Letters to the editor or comments can be sent to provide commentary and analysis concerning an article published in the journal, to give information about ongoing research, to provide informa-

tion in cardiology and cardiovascular-vascular-endovascular surgery, cardio-metabolic and vascular sciences. Letters to the editor or comments may include an optional title, tables and references. These articles should not exceed 1000 words.

What Would You Do?

These are brief articles discussing cases and situations encountered in cardiology and cardiovascular surgery with a biopsychosocial approach. If necessary, photographs (with permission from the patient/owner) may be added. Sections should consist of a title, case report, discussion, questions and answers. Brief comments can be sent to provide commentary on previous articles and case reports written by other authors. Comments should include the number of the journal the article was published in. The text should not exceed 1000 words.

International Reprints

Translations of important documents, declarations and guidelines prepared by international organizations in the field of cardiology and cardiovascular surgery, may be published in the journal. Presubmission Inquiry to the Editorial Board of the Journal before submitting the article is recommended. It is the translator's responsibility to obtain permission from the owner of the original manuscript for publication and translation.

News

These articles focus on advances and innovations in clinical topics relevant to cardiology and cardiovascular surgery. There is no obligation to follow a particular format. The text should be limited to 1000 words.

Editorials

Editorials usually provide information about the editorial policy of E Journal of Cardiovascular Medicine, give commentary and feedback on articles published in the journal, draw attention to topics of current interest and give information related to and discuss the development of cardiology and cardiovascular surgery in the world. They are mainly written by the members of the Editorial Board. Editorials are limited to 2000 words with some exceptions and may include a title and references when necessary.

MANUSCRIPT FORMATTING

Manuscripts should be designed in the following order:

Title page

Abstract

Main text

References

Tables, figures and illustrations

Title Page

The title page of the manuscript should include: The title, first

and last names of each author. Complete affiliation and title for each author, with the name of department (s) and institution (s) to which the work should be attributed.

The corresponding author should be clearly identified with name, address, telephone- facsimile number and email address for correspondence about the manuscript. Authors should clearly indicate if the article has previously been presented at a congress or scientific meeting. The title should be concise and informative without abbreviations and not exceed 10 words.

Abstract

Abstracts should be exact in English, with a minimum of 150 and maximum of 350 words. Abstracts of original research articles should be structured under subheadings as follows: objectives, methods, results and conclusion. A maximum of 3 key words should be added to English abstracts.

Text

The text contains the rest of the manuscript. It is structured differently according to the type of manuscript (original research article, review, etc.). For example, original research articles should consist of aim and objectives, methods, results, discussion and conclusion.

References

References should be cited in consecutive numerical order as first mentioned in the text and designated by the reference number in parentheses. If the number of authors for the reference is more than 6 authors, list the first three authors and add "et al".

Journal names should be abbreviated as used in Index Medicus. References should be cited in the Vancouver style. For detailed information please visit the relevant link

Examples:

For research articles follow the example below:

– Verschuren WM, Jacobs DR, Bloemberg BP, et al. Serum total cholesterol and long-term coronary heart disease mortality. JAMA 1995; 274(2): 131–6.

For book chapters follow the example below:

– Rakel RE. The family physician. In: Rakel RE, editor. Textbook of family practice. 5th ed. Philadelphia: W.B. Saunders; 1995. p. 3-19.

For web pages follow the example below:

– Guidance for clinicians. An International Benchmarking Study. <http://www.who.int/topics/surgery/> accessed: 29/09/2002.

Tables and Figures

Legends should take place on the top of the page for tables, and bottom of the page for figures and placed on separate pages. Explain all nonstandard abbreviations in footnotes.



E Journal of Cardiovascular Medicine
is a global e-journal targeting articles on:

- clinical cardiology,
- interventional cardiology,
 - arrhythmia,
- cardiovascular surgery,
- vascular & endovascular surgery,
- vascular biology