Časopis Udruženja kardiologa Srbije

SRCE i krvni sudovi

Heart and Blood Vessels

Journal of the Cardiology Society of Serbia

1955 UKS CSS
UDRUŽENJE KARDIOLOGA SRBIJE
CARDIOLOGY SOCIETY OF SERBIA
www.uksrb.org

Harvesting, ex vivo manipulation and clinical use of mononuclear and CD34+ cells in the treatment of myocardial ischemia

Percutaneous Coronary Interventions over the last three decades: the adjunctive devices (role, development and perspectives)

"Tip-In" method: a novel, wire randez-vous method in need of retrograde CTO PCI

Percutaneous repair of mitral regurgitation with the Mitraclip system: clinical indications and first slovenian experience

Most relevant complications of transcatheter aortic valve implantation related to the site of implantation: results of slovenian national registry

Endovascular treatment of severe aortic stenosis in high and intermediate surgical risks patients

Prevention of adverse ischemic events with Watchman device in non-valvular patients with atrial fibrillation and contraindications for long-term anticoagulation therapy

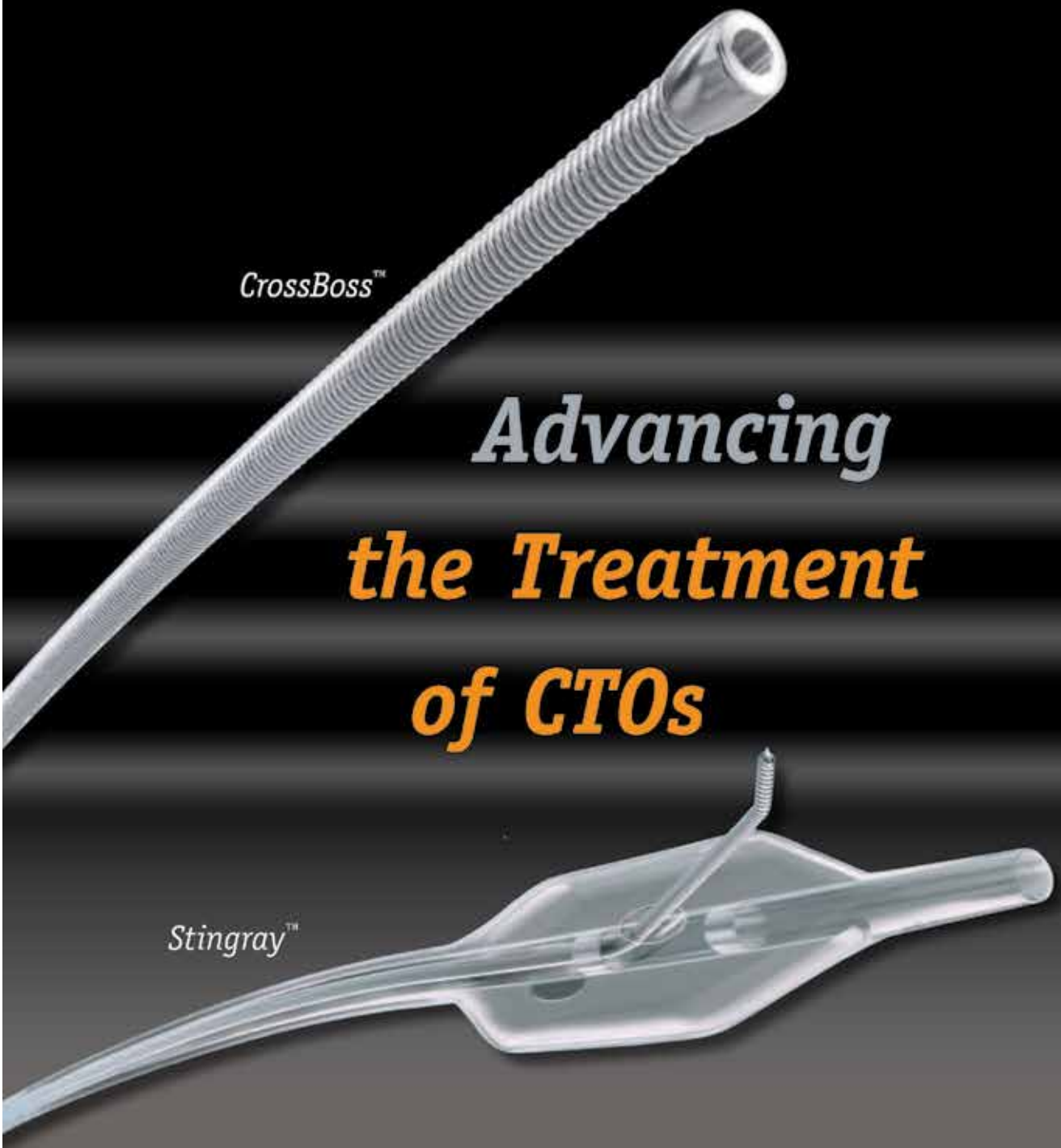
Volumen 34 Broj 1
2015. godina

Ovaj broj časopisa je posvećen BASICS 9 kongresu koji se održava od 22-25 aprila 2015. godine u Beogradu

CrossBoss™ & Stingray™

Coronary Crossing and Re-Entry Devices

Boston Scientific
Advancing science for life™



Advancing the Treatment of CTOs

UDRUŽENJE KARDIOLOGA SRBIJE
CARDIOLOGY SOCIETY OF SERBIA

SRCE I KRVNI SUDOVI

Volumen 34 Broj 1 2015. godina

ADRESA UREDNIŠTVA
EDITORIAL OFFICE

Udruženje kardiologa Srbije
Višegradska 26
11000 Beograd
Email: srceikrvnisudovi.urednistvo@gmail.com
www.uksrb.org

* Data pismena saglasnost za članstvo u odborima.
Uredništvo ostaje otvoreno za sve promene i dopune uređivačkih odbora.

UPUTSTVO AUTORIMA

„Srce i krvni sudovi" je časopis Udruženja kardiologa Srbije koji objavljuje originalne radove, prikaze bolesnika, kardiovaskularne slike ("cardiovascular images"), pregledne i specijalne članke. Uz rukopis obavezno priložiti pismo koje su potpisali svi autori, a koje treba da sadrži:

- izjavu da rad prethodno nije publikovan i da nije istovremeno podnet za objavljivanje u nekom drugom časopisu,
- izjavu da su rukopis pročitali i odobrili svi autori.

Rukopis rada i sve priloge uz rad dostaviti elektronskom putem na adresu: srceikrvnisudovi.urednistvo@gmail.com i branko.beleslin@gmail.com, naslovljeno na: prof. dr Miodrag Ostojić, glavni urednik časopisa „Srce i krvni sudovi". Prispele rukopise uređivački odbor šalje recenzentima radi stručne procene. Ukoliko recenzenti predlože izmene i dopune, tada se recenzirani rukopis dostavlja autorima s molbom da tražene izmene unesu u tekst ili pak u protivnom da argumentovano izraze svoje neslaganje sa datim primedbama recenzenta. Konačnu odluku o prihvatanju rada za štampu donosi glavni i odgovorni urednik zajedno sa uređivačkim odborom.
Za objavljene radove se ne isplaćuje honorar, a autorska prava se prenose na izdavača.
Časopis se štampa na srpskom jeziku, sa kratkim sadržajem prevedenim na engleski jezik. Inostrani autori mogu svoje članke, u celini, poslati na engleskom jeziku.
Molimo saradnike da svoje radove za časopis „Srce i krvni sudovi" pišu jasno, koncizno, racionalno, gramatički ispravno i u skladu sa sledećim uputstvima.

UPUTSTVA ZA PISANJE RADA

Tekst rada kucati u programu za obradu teksta Word, latinicom, fontom Times New Roman i veličinom slova 12 tačaka (12pt). Sve margine podesiti na 25 mm, veličinu strane na format A4, sa levim poravnanjem i uvlačenjem svakog pasusa za 10 mm. Ukoliko se u tekstu koriste specijalni znaci (simboli), koristiti font Symbol. Stranice numerisati redom u okviru donje margine desno, počev od naslovne strane. Podaci o korišćenoj literaturi u tekstu označavaju se arapskim brojevima u običnim zaokruženim zagradama, i to onim redosledom kojim se pojavljuju u tekstu. Rukopis rada dostaviti urađen po sledećem redosledu:

- naslovna strana,
- sažetak na srpskom jeziku,
- sažetak na engleskom jeziku, sa naslovom i institucijom odakle dolazi rad takođe na engleskom jeziku,
- tekst rada,
- tabele,
- opisi slika,
- posebno slike (grafikoni) ili fotografije.

Naslovna strana. Na posebnoj, prvoj stranici treba navesti sledeće:

- naslov rada bez skraćenica
- puna imena i prezimena autora (bez titula)
- kratak naslov rada
- zvaničan naziv i mesto ustanova u kojima autori rade. Ukoliko su u radu autori iz različitih institucija, indeksirati autore iz raličitih institucija arapskim brojevima
- na dnu stranice navesti kontakt osobu, odnosno ime i prezime, adresu, broj telefona, faksa i e-mail adresu radi korespodencije

Kratak sadržaj na srpskom i engleskom jeziku. Na sledećoj strani priložiti kratak sažetak rada obima do 250 reči. Za originalne radove kratak sadržaj rada treba da sadrži: uvod, metod, rezultati i zaključak.
Prikazi bolesnika, pregledni i specijalni članci treba da imaju nestrukturisan sažetak obima do 150 reči.
Na kraju sažetka dostaviti i 2-4 ključne reči.
Svaki sažetak, sa naslovom i institucijom, mora biti preveden na engleski jezik.

Tekst rada. Tekst treba da sadrži sledeća poglavlja: uvod, metodi, rezultati, diskusija, zaključak, literatura. Svi podnaslovi se pišu malim slovima i boldovano. U radu koristiti kratke i jasne rečenice. Za nazive lekova koristiti isključivo njihova internacionalna nezaštićena imena. U radu se mogu koristiti određene skraćenice, ali samo kada je to neophodno. Za svaku skraćenicu koja se prvi put javlja u tekstu treba navesti i pun naziv. Sve rezultate navoditi u metričkom sistemu prema Međunarodnom sistemu jedinica (SI).
Originali rad ne treba da prelazi 4000 reči.
Prikaz bolesnika čine: uvod, prikaz bolesnika, diskusija, literatura. Prikaz bolesnika ne treba da prelazi 1500 reči.
Kardiovaskularne slike (cardiovascular images) ne treba da bude struktuirane i ne treba da prelaze 500 reči.
Pregledni i specijalni članci ne moraju da budu struktuirani po prethodnom modelu. Pregledni i specijalni članci ne treba da prelazi 5000 reči.

Literatura. Reference numerisati rednim arapskim brojevima prema redosledu navođenja u tekstu. Broj referenci ne bi trebalo da bude veći od 30, a broj citiranih originalnih radova mora da bude najmanje 80%. Izbegavati korišćenje abstrakta kao reference. Reference članaka koji su prihvaćeni za štampu označiti kao ,,u štampi" (in press) i priložiti dokaz o prihvatanju rada. Reference se citiraju prema Vankuverskim pravilima, koja su zasnovana na formatima koja koriste National Library of Medicine i Index Medicus. Naslove časopisa takođe treba skraćivati prema načinu koji koristi Index Medicus (ne stavljati tačke posle skraćenice).
Ukoliko rad koji se navodi ima više od 6 autora, onda navoditi tako što se posle trećeg autora staviti: et al. Stranice se citiraju tako što se navode početna i krajnja stranica (npr. 134-138).
Primer za navođenje reference iz časopisa: Leal J, Ramon Luengo-Fermnandes R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. Eur Heart J 2006;27:1610-1619.
Primer za navođenje reference iz knjige: Nichols A, Rourke MH. Aging and hypertension. U knjizi: Hypertension. Urednici: Nichols A, Rourke MH. Lea and Febiger; London/Melbourne, 1990:257-299.

Tabele se označavaju arapskim brojevima po redosledu navođenja u tekstu. Tabele raditi u programu Word, koristiti font Times New Roman, veličinu slova 12 pt, sa jednostrukim proredom i bez uvlačenja. Tabela mora da ima naslov i ukoliko se u tabeli koriste skraćenice, iste treba objasniti u legendi ispod tabele. Svaku tabelu dati na posebnom listu papira.

Slike (grafikoni) se označavaju arapskim brojevima po redosledu navođenja u tekstu. Na posebnom listu dati naslov sa opisom slika (grafikona) i ukoliko se koriste skraćenice, iste treba objasniti u nastavku. Svaki grafikon treba dati na posebnom listu papira. Slike (grafikone) dati u formatu ppt, ai ili eps.
Fotografije se označavaju arapskim brojevima po redosledu navođenja u tekstu. Primaju se isključivo originalne fotografije (crno-bele ili u boji) na sjajnom, glatkom (a ne mat) papiru. Na poleđini svake fotografije treba napisati redni broj. Fotografiju moraju da budu u tif, eps ili ai formati, najmanje rezolucije 300dpi.

Napomena. Rad koji ne ispunjava sve gore navedene tehničke uslove neće biti poslat na recenziju i biće vraćen autorima da ga dopune i isprave.
Glavni urednik i uređivački odbor zadržavaju pravo da radove, za koje smatraju da ne zadovoljavaju osnovne kvalitete i interesovanja publikovanja u časopisu, ne pošalje recenzentima i vrati autorima.

INSTRUCTIONS FOR AUTHORS

Heart and Blood Vessels is the official journal of the Serbian Cardiology Society and publishes Original articles, Case reports, Cardiovascular images, Review articles and Special articles. It is mandatory to enclose, along with the manuscript, a letter to the Editor-in-chief stating that the manuscript:

- has not been previously published or is currently submitted for review to another journal
- was read and approved by all authors

The manuscript with all appendices should be addressed to:
Prof. Miodrag Ostojic, MD, PhD
Editor-in-Chief, Heart and Blood Vessels
and mailed to srceikrvnisudovi.urednistvo@gmail.com, branko.beleslin@gmail.com and mostojic2003@yahoo.com.

The Editorial Board will send it to reviewers for evaluation. Reviewers' comments will be forwarded to the author to either correct the original manuscript in accord with the suggestions or to express their opinion with adequate arguments in a letter to the Editor-in-chief explaining why they refrained from doing as reviewers deemed appropriate. The final decision will be made by the Editor-in-Chief together with the Editorial Board whether to accept the manuscript for publishing or not. For published manuscripts authors don't get fees, while copyright is transferred to the publisher. The journal is published in Serbian with summaries in English. Foreign authors can submit their manuscripts entirely in English.
We kindly request authors to keep their manuscripts for Heart and Blood Vessels clear, concise, rational, grammatically correct and in accord with the following instructions.

GENERAL INSTRUCTIONS

Manuscript text should be prepared using a Word processing package, in Times New Roman font size 12. All margins set at 25mm of an A4 page, with no alignment and 10mm tab at the beginning of each paragraph. In case special signs are used, please use Symbol font. Keep page numbering in the footer, starting from the Title page. References should be marked by order of appearance in the text in Arabic numerals in round brackets. The manuscript should be submitted in the following order:

- Title Page,
- Abstract,
- Body of the text,
- Tables, Figures' descriptions,
- Figures or photographs.

Title page. A separate, first page should encompass the following:

- the title
- the name(s) of authors,
- the institution(s) and location of all authors (Please, index in Arabic numerals the different Institutions by order of appearance),
- short title,
- at the bottom of the page cite the corresponding author with his contact address, phone, fax number and email address.

Abstract. Next page should contain a 250 words abstract. Original papers should encompass: Introduction, Methods, Results and Conclusion. Structured form of abstracts is not mandatory for case reports, review and special articles, but should not exceed 150 words.

The text should encompass: Introduction, Methods, Results, Discussion, Conclusions, and References. Subtitles should be typed in regular font and bold. Short and simple sentences are advised. For medication, it is recommended not to use trade names, but their generic names. Abbreviations can be used in the text, but only when necessary and properly introduced. All results should be cited in standard SI units.
An original paper should be up to 4000 words.
A Case Report consists of an Introduction, Case presentation, Discussion and References. A Case Report should be up to 1500 words. Cardiovascular Images shouldn't be structured and should be up to 500 words.
Review and Special Articles don't have to be structured and shouldn't exceed 5000 words.

References. References should be marked in order of appearance in Arabic numerals. The number of quoted references shouldn't exceed 50 out of which 80% should be original articles. It is advised to avoid abstracts as references. When quoting papers that are accepted for publishing, however, not yet published, mark them as in press and enclose a printed proof of the manuscripts' acceptance. References are quoted according to Vancouver style based on the formats used by National Library of Medicine and Index Medicus. Journals' titles should be shortened in accord with Index Medicus (no full stops after the abbreviation). If the paper quoted has over 6 authors, after the third one, et al. should be used Pages are quoted as first and last (i.e. 134-136).
Article citation example: Leal J, Ramon Luengo-Fermnandes R, Gray A, Petersen S, Rayner M. Economic burden of cardiovascular diseases in the enlarged European Union. Eur Heart J 2006;27:1610-1619.
Book citation example: Nichols A, Rourke MH. Aging and hypertension. In: Hypertension. Editors: Nichols A, Rourke MH. Lea and Febiger;London/Melbourne, 1990:257-299.

Tables are marked in order of appearance in Arabic numerals. Tables should be prepared using a Word processing package, Times New Roman font size 12, single spaced with no indent. Each Table should have a title. If abbreviations are used in the Table, they should be defined in the explanatory footnote below. Each table should be presented on a separate page.
Figures are marked in order of appearance in Arabic numerals. Please, provide on seprate page Figure legends. Each Figure should be prepared on a separate page using following format: ppt, ai or eps.
Photographs are marked in order of appearance in Arabic numerals. Only original photographs are accepted (black and white or color) on glossy paper. The back of each photograph should have the number and an arrow marking the top. The photograps should be prepared in following format: tip, eps, or ai, with minimal resolution of 300dpi.

Note. A paper not fully compliant with all aforementioned rules and regulations, will not be forwarded to reviewers, but returned to authors for correction. The Editor-in-Chief and the Editorial Board can reject any manuscript they deem not in the scope of the journal or not acceptable in terms of baseline quality of publishing material, even prior seeking reviewers' opinion.

1955 UKS CSS
UDRUŽENJE KARDIOLOGA SRBIJE
CARDIOLOGY SOCIETY OF SERBIA

SRCE I KRVNI SUDOVI

Volumen 34 Broj 1 2015. godina

Sadržaj

CIP - Katalogizacija u publikaciji
Narodna biblioteka Srbije, Beograd

Srce i krvni sudovi: Časopis Udruženja kardiologa Srbije
Heart and blood vessels: Journal of Cardiology society of Serbia
Editor in-chief Miodrag Ostojić, Godina 5,
Volumen 34, Broj 1
Beograd, Koste Todorović 8: Udruženje kardiologa Srbije
2015-Beorad: Newassist doo
Tromesečno-Broj 1 izašao 2011. god.

ISSN 182-4835=Srce i krvni sudovi
COBISS.SR-ID 174253580

Pozdravni govor

Poštovane koleginice i kolege,

Veliko nam je zadovoljstvo da Vas pozdravim na početku **„Devetog beogradskog samita interventnih kardiologa (BASICS+)“**, koji se održava od 22-25. aprila 2015. godine u Hotelu M „Best Western“ u Beogradu. Ovaj naš tradicionalni kongres nastavlja sa realizacijom ideja koje smo imali od početka i koje obuhvataju prenose uživo kompleksnih procedura na koronarnim arterijama, inovacije sa uvođenjem novih procedura na srčanim zaliscima (od prošle godine krenuli smo sa implantacijama aortne valvule perkutanim putem i zatvaranjem aurikule leve srčane pretkomore), praćenje i predstavljanje savremenih tendencija putem predavanja renomiranih interventnih kardiologa, a sve u cilju unapređenja kvaliteta rada interventne kardiologije u Srbiji. Uz rukovodstvo i inicijativu Kliničkog centra Srbije, ove godine imamo podršku svih centara interventne kardiologije u Srbiji, kao i mnogih centara iz regiona, tako da ovaj kongres evoluira u najznačajniji i najposećeniji kongres interventne kardiologije u jugoističnom delu Evrope. I ove godine očekujemo veliki broj inostranih gostiju koji su ujedno i operateri i predavači, a pre svega prijatelji srpske kardiologije.

Velika zahvalnost, kao i svih ovih godina, ide prema industriji potrošnog i ugradnog materijala u interventnoj kardiologiji, farmaceutskoj industriji, Prvoj televiziji koja svih ovih godina realizuje prenose i tehničku podršku događaja, Telekomu Srbija kojim nam obezbeđuje linkove za video i audio prenos, i Hotelu M „Best Western“ koji je omogućio sve tehničke uslove za ostvarivanje kvalitetnog prenosa kao i održavanje kongresa.

S poštovanjem,
Prof. dr Milan A. Nedeljković
Predsednik Radne grupe za kateterizaciju srca i perkutane koronarne intervencije Udruženja kardiologa Srbije

Dear Colleagues,

It is my great pleasure to greet you at the beginning of the **“Ninth Belgrade Summit of Interventional Cardiologists (BASICS+)”** that is being held from April 22-25, 2015, at the Hotel M “Best Western” in Belgrade. This traditional interventional congress continues with the implementation of ideas that we had from the beginning and that includes live transmissions of complex coronary procedures, innovations with the introduction of new procedures for the structural heart disease (last year we performed first percutaneous aortic valve implantations and closure of the left atrial auricle), following of contemporary cardiology through lectures of world famous interventional cardiologists, with the aim of improving the quality of interventional cardiology in Serbia. With the leadership and initiative of the Clinical Center of Serbia, this year we have the support of all interventional cardiology centers in Serbia, as well as many centers in the region, so that this congress is evolving into the most important and most influential interventional cardiology meeting in the South-eastern Europe. This year we expect great number of foreign guests who are also operators and lecturers, and primarily friends of Serbian cardiology.

We greatly appreciate support of the industry in interventional cardiology, pharmaceutical companies, “Prva” television that organize recording of procedures, transmission, and technical support of the event, to “Telekom Srbija” that provides us high-quality audio-video links required for the transmission, and Hotel M “Best Western” which contribute us all the technical conditions needed for the transmissions as well as for conference realization.

Sincerely yours,
Professor Milan A. Nedeljkovic, MD, PhD, FESC, FACC
The president of the Working group for cardiac catheterization and percutaneous coronary intervention of the Cardiology Society of Serbia

Srce i krvni sudovi 2015; 34(1):2-3

Proširen apstrakt

Harvesting, ex vivo manipulation and clinical use of mononuclear and CD34+ cells in the treatment of myocardial ischemia

Bela Balint[1,2], Vladimir Kanjuh[3], Milena Todorovic-Balint[4], Slobodan Obradovic[1], Zoran Trifunovic[1], Saso Rafajlovski[1], Mirjana Pavlovic[5]

[1]Military Medical Academy, Belgrade, Serbia; [2]Institute for Medical Research, University of Belgrade, Serbia; [3]Serbian Academy of Sciences and Arts, Belgrade, Serbia; [4]Clinic for Hematology of CCS, Belgrade, Serbia; [5]Department of Computer and Electrical Engineering and Computer Science, FAU, FL, USA

The study objective was to recapitulate developing research frontiers in the mononuclear and stem cell (MNC and SC) biology and clinical use in the regenerative medicine. The preliminary results of the therapy of our patients with acute cardiac infarction (intracoronary infusion) and coronary artery bypass (intramyocardial application) – treated by intracoronary infusion or intramyocardial application of the steady state vs. activated (primed) autologous BM derived SCs – are also summarized.

Concisely, "autopoiesis" refers to ability of a biological system to reproduce and maintain itself. Within that, cytogenesis or cytopoiesis involve the origin and development of different cells. This is a multipart cyclic event in which from a small quantity of toti/pluri/multipotent (immature) SCs – through proliferative and differentiative processes – a spectrum of mature cell populations is produced. The complex network of interactive cytokines and other mediators regulates SC survival and functions. Therefore, SCs – having well-balanced self-renewal, proliferative and differentiation potential – could be predictive of "steady-state homeostasis" in tissue-generating systems and BM repopulation or organ regeneration/repair after therapeutic use.

The SC compartment can be divided into embryonic and adult cells. Embryonic SCs are, reasonably, capable to differentiate into all cell types of human body. Immature adult SCs have also a potential to trans-differentiate into numerous somatic cell types (plasticity) – such as osteocytes, chondrocytes, hepatocytes, myocytes, cardiomyocytes and even endothelial cells (plasticity). Thus, they improve tissue/organ healing or repair due to their "regenerative-potential". Thanks to this ability, immature SCs and mesenchymal progenitors are clinically applicable in the treatment of patients with myocardial, brain, vascular, liver, pancreas and some other tissue damages. The application of SCs has positive effects on myocardial ischemic damages, including prevention of post-infarction cardiac remodeling following acute myocardial infarction (AMI).

Immature SCs are applicable in the regenerative medicine, being capable of colonizing different tissues due to homing and lineage-plasticity potentials, despite the fact that the ideal type and source of cells have not yet been defined. In practice, SCs can be collected from BM or harvested from peripheral blood after mobilization (chemotherapy/rHuG-CSF). Peripheral blood transplant can be characterized by the absence of the risk of bone infections and anesthesia, with faster hematopoietic reconstruction. During the last decades, peripheral blood is used for more than 70-80% of allogeneic and almost for all autologous "conventional" transplants. On the contrary, BM is the most frequent source of cells used in the fields of regenerative medicine, especially for cardiac repair.

Our (pre)clinical study – is one decade practice by using of native SCs and progenitors, harvested from steady state vs. activated/primed BM – included cardiologic patients (≤ 71 years) with a large first infarction of anterior wall (EF: ≤ 41%, but ≥ 19%). The angioplasty and followed stent placement were performed using percutaneous coronary access. Cells from BM were harvested by multiple aspirations from the iliac crests – collections were performed under sterile conditions in the operation room, while the patents were in general anesthezia. For BM priming, rHuG-CSF was used (3 – 5 μg/kgbm, subcutaneously) 24 hours before cell harvesting. The BM aspirate was initially filtered and then processed by Cobe-Spectra (TerumoBCT, USA) and resuspended in serum-free culture medium up to an optimized hematocrit level (Hct = 0.30). The total nucleated cells (TNCs) and MNCs were quantified by Advia-2120 (Bayer, Germany). Using triple staining, CD34 and CD45, as well as immature ($CD34^+/CD90^+$) vs. mature ($CD34^+/CD90^-$) CD34 subset antigens by EPICS-XL (Coulter, USA) were tested. The quantity of applied cells for MNCs and $CD45^+/CD34^+$ cells was: $8.4x10^9 \pm 6.1x10^9$ and $10.4 \pm 7.54x10^6$ per treatment, respectively. Results obtained for cell viability (determined by 7-aminoactinomicin D or 7-AAD testing) were: $7\text{-}AAD_{viability}$ = 95.42%

(for $CD34^+$ cells) and 7-$AAD_{viability}$ = 95.42% (for $CD90^+$ cells). Obtained cells (MNCs enriched with native SCs) were administered as an intermittent infusion into the affected artery across coronary catheter (cardiology) or directly into myocardium during coronary artery bypass grafting (cardiosurgery).

In this study, an effective protocol for cell harvesting and processing was verified. Results obtained indicate positive outcome of the clinical use of BM (especially rHuG-CSF primed) derived cells – such as improvement of systolic function (evaluated 6 months after treatment in the 50% of patients): (a) ejection fraction (EF) improvement ≥5%; (b) affected infarct region reduction ≥5%; and (c) decreased left ventricular remodeling. Patients tolerated the use of cell-mediated treatment well, without any adverse effects. Although the mechanisms by which SCs can be trans-differentiated are still poorly understood, the presented results and facts suggest that appropriate populations of BM derived cells could be used as a way of recovery of damaged myocardium.

Srce i krvni sudovi 2015; 34(4):4-8

Pregledni rad

Percutaneous Coronary Interventions over the last three decades: the adjunctive devices (role, development and perspectives)

Leo Finci

Dr Leo Finci
Membre de la Société Suisse de Cardiologie,
Fellow of the American College of Cardiology,
Founding Fellow of the European Society of Cardiology.

Abstract Percutaneous coronary interventions (PCI) performed on large-scale basis in routine practice with documented long-term clinical benefit for the patient are balloon angioplasty introduced in 1977 and coronary stenting since 1986. Other coronary devices, so-called "adjunctive", have triggered a great admiration at the time of its initial clinical application but showed to be less successful at the long-term follow-up. However, many adjunctive devices are still necessary in 1-2% of all PCI procedures for complex cases. This article is a short, comprehensive review retracing the conception and destiny of these devices. Coronary balloon catheters, a standard device with advance "therapeutic" features comprise: cutting, drug eluting and high pressure non-compliant balloon catheters. Atherectomy devices can be directional for lesions "debulking", rotational (Rotablator) for calcified, long lesions and recently Orbitral supposed to have less no-reflow phenomenon. Excimer Laser angioplasty for treatment of "uncrossable" lesion was claimed much in the past. Brachytherapy is used almost exclusively for in-stent restenosis. A numerous thrombectomy and embolic protection devices exist but none has shown a proven clinical benefit in randomized studies. With an advancement in medical technology adjunctive devices will play more important role in the future, especially for recanalization of chronic total occlusion and during acute myocardial infarction.

Key words percutaneous coronary interventions, stents, adjunctive devices.

Introduction

Coronary balloon angioplasty (PTCA) introduced in 1977, followed by coronary stenting in 1986 represent the only two percutaneous interventions (PCI) that have documented and confirmed clinical benefit for the patient and are being performed in current practice at the large-scale basis[1]. Many other coronary devices, still remaining as a part of interventional cardiologist's arsenal, have triggered a great admiration at the time of initial clinical application but turned out to be less successful at the long-term follow-up. The author of this article has been in the field of interventional cardiology from the begging of its routine application and believes that these so-called "adjunctive" devices need to be mentioned. It is like reading a medical paper that shows negative result - but from it, one can learn a lot, sometimes even more than reading a study with positive, significant result. During last three decades, the level of performed PCI has progressively increased reaching currently a steady usage level while new device technologies are still in progress (Figure 1). For this analysis, Switzerland was chosen as sample country for comparisons due to its stable politi-

Corresponding author: Cardiology Champel, Marignac 13, 1206 Geneva, Switzerland, e-mail: leo.finci@bluewin.ch

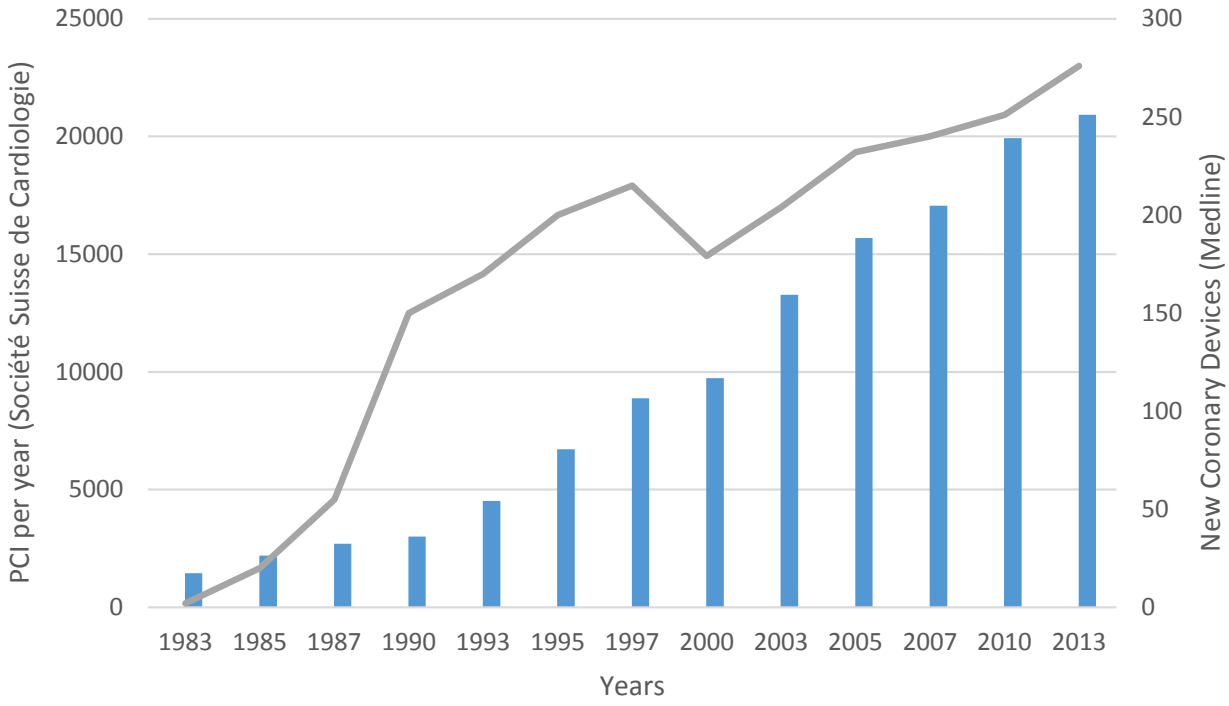


Figure 1. Correlation of PCI performed in Switzerland with publications on new coronary devices (number per year) during last three decades

cal and medical situation that had no variations over the examined time period, unlike the rest of the Europe, where creation of the European Union, reunification of Germany and other variables made an impact on the interventional cardiology statistics. New coronary devices were analyzed through the PubMed-Medline research coupled with clinical experience. Furthermore, over the last several years, more attention has been paid by the international cardiology community to their organized development and introduction of special events taking place in the course of congresses such as the Innovation session during the European congress of Cardiology[2]. The purpose of this article is to make a short comprehensive review of the conception and destiny of adjunctive devices. Coronary devices are classified according to their mechanism of action and none of the devices that are used for pure diagnostic purpose (e.g. intravascular ultrasound) is mentioned.

Balloon catheters

The idea to perform more interventions inside the coronary vessel using a simple balloon catheter with advance "therapeutic" features is still very accurate. Since 1992 "cutting" balloons have been developed to challenge complex lesions resistant to conventional balloon angioplasty[3]. Different types exist, using either single or multiple microsurgical blades bonded longitudinally to its surface, suitable for creating discrete longitudinal incisions in the targeted atherosclerotic coronary segment which are being activated during balloon inflations. Its current use is for "high-pressure balloon resistant lesions" including de novo lesions and in-stent restenosis (AngioSculptTM Scoring Balloon, Angioscore, USA). However, compared to PTCA there were no significant differences at 6-month follow-up in angiographic and clinical results. The high-pressure non-compliant balloons that can tolerate the pressure of 40 bars are now available (OPN NC®, high pressure balloon catheter, SIS Medical AG, Winterthur, Switzerland). Drug eluting balloon (DCB) combines features of active drug and balloon inflation. The low rates of adverse clinical outcomes makes DCB a feasible treatment option in small vessel coronary artery disease, diffuse disease and bifurcation lesions. Their superiority has been proven only for the indication of the in-stent re-stenosis, as shown in a recent meta-analysis[4] , where the need for TLR was significantly reduced compared to other treatments. As a novel strategy, DCB still has a long way to ride before its full implementation. The only commercially available drug for DCB is Paclitaxel.

Atherectomy

There are three different types of atherectomies: Directional (DCA), Rotational (RA) and recently introduced Orbital Atherectomy. The DCA is probably the greatest deception of all coronary devices. Developed by John Simpson in 1984, just a few year after clinical introduction of his movable coronary guide-wire, DCA was supposed to decrease the high restenosis rate observed after PTCA (30-50%). The device, called AtheroCath™ (Abbott Vascular, Redwood City, CA, USA) consists of a cylindrical metal housing with a lateral side window cutter and a low pressure balloon on the contralateral side. Low pressure balloon inflation assures for proper tissue-cutter apposition.

The plaque is gently displaced into the window housing and "shaved-off", using the cutter, into the collecting nose cone at the distal tip of the device. In an early multi-center registry, DCA was successful in 85% of cases, and as such was subsequently comparable to success in balloon angioplasty. After having been approved by FDA, it gained confidence worldwide as an alternative to balloon angioplasty, and by 1990's accounted for approximately 10% of PCI procedures in the United States. In the following years several non-randomized studies showed an improved intraluminal coronary gain after DCA as compared to PTCA that generated an extreme enthusiasm for the device. However, in 1993 after publication of a randomized CAVEAT study showing higher restenosis (57 % versus 50%) and complication rates (11% versus 5%) with DCA compared to PTCA, the use of DCA rapidly decreased. The protagonists of atherectomy[5] welcomed the new multicenter USA clinical trial with Orbital atherectomy device on 443 consecutive patients with severely calcified coronary lesions[6] .

Rotablator TM (Boston Scientific USA) is the most known device of RA. It can effectively ablate calcified plaques, facilitating stent delivery and expansion. Practice guidelines recommend its use for preparation of heavily calcified or severely fibrotic lesion that cannot be crossed by a balloon or adequately dilated. However, late restenosis remains high when it is used as a stand-alone therapy or with bare-metal stents. Some observational study suggested a favorable long-term results of RA followed by DES implantation, but a randomized study including 240 patients showed that routine lesion preparation using RA did not reduce late lumen loss even after implantation of DES at 9 months follow-up[7].

Laser

The potential advantages of intracoronary laser angioplasty are to ablate the plaque material and vaporize all atherosclerotic plaque along the arterial wall. The bulk removal of plaque material could improve acute procedural success rates, decrease complication rates, take care of "untreatable" lesions, and decrease restenosis rates. Several types of lasers have been used in the past (Argon, Holmium), but only the excimer laser is still in practice (ELCA® Laser Ablation Catheter, Spectranetics USA). The coronary laser catheters are offered in sizes ranging from 0.9 to 2.0 mm in diameter and contain up to 250 small, flexible optical fibers mounted within a thin plastic tube.

The great enthusiasm to use the laser angioplasty for the treatment of coronary occlusions was raised in 1986 because laser energy can vaporize atherosclerotic plaque, and there may be no requirement for a pre-existing channel. However, high rate of complications, thermal injury and collateral miss have limited its application. A systemic literature search[8] performed in 2014 by McGill University in Canada, found no benefit even in patients with un-crossable coronary lesion. Occurrence of complications such as coronary dissection (up to 9%), myocardial infarction (0-10%), or major bleeding (0-6%) and increased procedure cost influenced the decision not to recommend its use in Canada.

Brachytherapy

The radiation is believed to inhibit the cellular proliferation. Radiation for treatment of in-stent restenosis has been using two sources: gamma and beta radiation. Currently approved are the Checkmate System (Cordis Corporation) that uses gamma radiation and the Beta-Cath System (Novoste Corporation) that uses beta radiation. Approval by the FDA in USA for both of these devices is limited their use in stents that had been implanted in the past, and then re-stenosed. In the years following 2000, the treatment of restenosis after bare metal stent implantation using brachytherapy raised a great hope, but rapid developments in drug eluting stents had progressively pushed the brachytherapy a side. A meta-analysis[9] in 2011 of 12 studies and comparing the outcomes of drug-eluting stents versus intracoronary brachytherapy for in-stent restenosis suggests that the use of drug-eluting stents for in-stent restenosis is associated with reduced occurrences of target-vessel revascularization and binary restenosis. The American College of Cardiology Guidelines (2011) do not recommend brachytherapy for the prevention of restenosis as the lower rates of restenosis occur with the use of drug-eluting stents in comparison to bare metal stents or vascular brachytherapy. Many technical limitations are present within brachytherapy, such as the operator's protection against gamma radiation, coronary lesion geographical miss (unwilling exposure of healthy tissue to the radiation) and the absence of distinguished long-term benefit.

Thrombectomy

A numerous devices with different mechanisms of action exist all having the same objective to reduce distal thrombus embolization and improve myocardial perfusion. In a meta-analysis there was a significant improvement in ST-segment resolution, myocardial blush and TIMI grade 3flow as parameters of myocardial perfusion, as well as clinical parameters such as reduction in mortality. Non-manual, mechanical thrombectomy may have a role in selected patients with large caliber vessels and heavy thrombus burden[10].

Catheter aspiration thrombectomy uses a catheter that is advanced over a guidewire to the thrombus whereby syringe suction is used to aspirate the debris. Devices used for this procedure include the DiverTM, Export®, ProntoTM, RescueTM, Thrombuster®, and TransVascular Aspiration Catheter®. Mechanical thrombectomy devices apply energy directed through

saline jets or a rotating catheter head to facilitate breakup of the thrombus prior to its active aspiration. These devices include the AngioJet® and X-Sizer®.

Embolic protection

Embolic protection devices can be proximal and distal, using either balloon or filters. Distal device employs an occlusion balloon advanced over a guide-wire distal to the thrombus in order to trap and aspirate thrombotic debris released during angioplasty and stenting procedures such as the PercuSurge GuardWire®, FilterWire EXTM, SpideRXTM, AngioGuardTM and Filtrap. A study concerning these devices conducted in 2011 by the USA Agency for Healthcare Research and Quality examined 53 randomized trials (n = 8,185) and 9 observational studies (n = 1,479) and found no significant impact on mortality, myocardial infarction, stroke, or MACE versus a control when using the longest duration of follow-up[11].

Stents

There are several so called "dedicated" stents, designed for specific lesion categories such as bifurcations or vein grafts, which are on the market. None of them has showed clinical benefit as compared to the standard technique[12]. Covered stent are of real utility in case of coronary artery perforation such as the Grafmaster® RX, Abott, and mPK Papyrus, Biotronik, Switzerland - a more flexible stent. Specially designed drug eluting stents capable to accommodate multiple drugs in a special reservoirs incited a great hope at the beginning. The example is the NEVO® Cordis, USA, coronary stent but it was retrieved from the market after Johnson & Johnson Company announced halt of their research activities in interventional cardiology. The MGuard (Inspire MD, Boston USA) stent utilizes MicroNet™ technology, which is a circular knitted mesh that wraps around the stent to protect patients from plaque debris flowing downstream upon deployment (during acute myocardial infarction). Bioresorbable vascular scaffolds (BVS) are very promising devices and will certainly expand in the future[13].

CTO

Recanalization of Chronic total coronary occlusions (CTO) has been for years and is still now a real battlefield for use of adjunctive devices (Figure 2). A recent meta-analysis[14] study including 18,061 patients showed an angiographic success rate of 77% with following complications: contrast nephropathy 3.8%, coronary perforation 2.9%, myocardial infarction 2.5%, death 0.2%, emergent coronary surgery 0.1%, tamponade 0.3% and stroke 0.01%.

The concept of mechanical recanalization with consequent angioplasty is still applied with different possibilities such as sub intimal tracking, re-entry technique or retrograde approach. Micro catheters represent a real

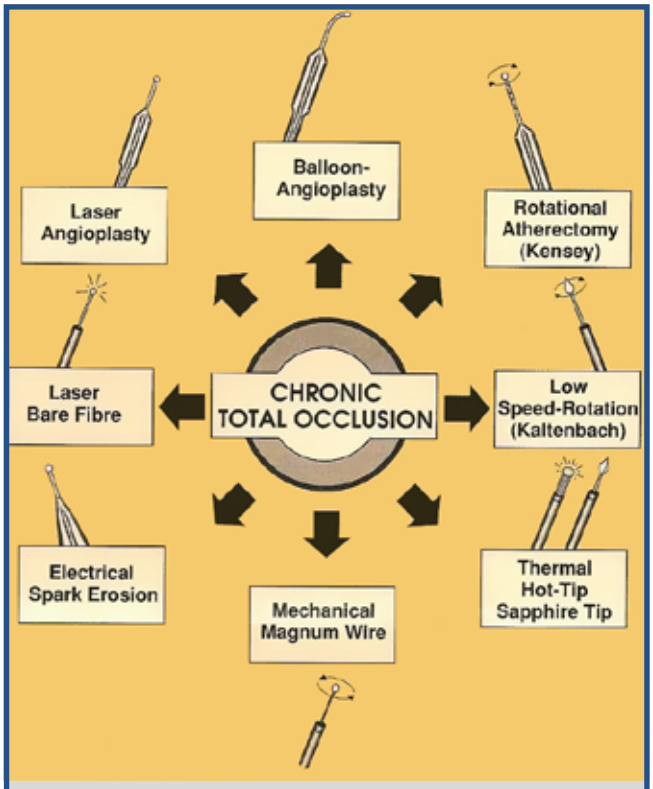


Figure 2. Adjunctive devices for CTO as proposed in the year 1990

advancement, the most known are Transit® (Cordis, Miami, United States), Finecross®, Pro Great® (Terumo, Japan). They have the advantage of large lumen and trackability for selective injection and tortuosity, whereas Corsair® (Asahi Intecc, Aichi, Japan) has more support, even beyond a calcified or tortuous segment. The Tornus device (Asahi) is a catheter made of 8 stainless steel strands woven together to enhance flexibility and strength in exchanging wires, delivering balloons and providing support for CTO procedures. The Frontrunner (LuMend, Cordis, USA) device is designed to create intraluminal blunt micro dissection to facilitate penetration of the fibrous cap. Two other recent systems for lesion crossing and lumen re-entry technologies include CrossBoss catheter (BridgePoint Medical, Plymouth, Minnesota), a metal micro catheter with a rounded tip that can advance through a CTO eventually into the sub intimal space. Then Stingray balloon and Stingray guide wire systems (BridgePoint Medical) which are employed to penetrate the distal true lumen for re-entry. In a catheterization laboratory that performs these interventions, other adjunctive safety devices are necessary like: covered stents, thrombectomy devices, snares, embolization coils and delivery systems to manage possible complications. With the advancement of medical technology, adjunctive devices will play more important role in the future, especially for recanalization of chronic total occlusion and for patients with acute coronary syndrome undergoing percutaneous coronary intervention.

References

1. Laslett LJ, Alagona P Jr, Clark BA, Drozda JP Jr, Saldivar F, Wilson SR, Poe C, Hart M. The worldwide environment of cardiovascular disease: prevalence, diagnosis, therapy, and policy issues: a report from the American College of Cardiology. J Am Coll Cardiol. 2012; 60(25 Suppl):S 1-49.
2. http://www.escardio.org/congresses/esc-2015/call-science/Pages/welcome.aspx.
3. Michael SL, Varinder S, Thomas JN, James RW. Review: cutting balloon angioplasty. J Invasive Cardiol. 2002;14 (9). http://www.medscape.com/viewarticle/442312.
4. Piccolo R, Galasso G, Piscione F, Esposito G, Trimarco B, Dangas GD, Mehran R. Meta-analysis of randomized trials comparing the effectiveness of different strategies for the treatment of drug-eluting stent restenosis. Am J Cardiol. 2014;114(9):1339-46.
5. Colombo A, Panoulas VF. After 3 decades, at long last, a new device to deal with calcific lesions. JACC Cardiovasc Interv. 2014;7(5):519-20.
6. Chambers JW, Feldman RL, Himmelstein SI, Bhatheja R, Villa AE, Strickman NE Shlofmitz RA, Dulas DD, Arab D, Khanna PK, Lee AC, Ghali MG, Shah RR, Davis TP, Kim CY, Tai Z, Patel KC, Puma JA, Makam P, Bertolet BD, Nseir GY. Pivotal trial to evaluate the safety and efficacy of the orbital atherectomy system in treating de novo, severely calcified coronary lesions (ORBIT II). JACC Cardiovasc Interv. 2014;7(5):510-8.
7. Abdel-Wahab M, Richardt G, Joachim Büttner H, Toelg R, Geist V, Meinertz T, Schofer J, King L, Neumann FJ, Khattab AA. High-speed rotational atherectomy before paclitaxel-eluting stent implantation in complex calcified coronary lesions: the randomized ROTAXUS (Rotational Atherectomy Prior to Taxus Stent Treatment for Complex Native Coronary Artery Disease) trial. JACC Cardiovasc Interv. 2013;6(1):10-9.
8. Sinclair A., Dendukuri N. Excimer laser atherectomy for uncrossable coronary lesions and improperly deployed coronary stents. Montreal (Canada): Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC) 2014; Report no. 75. 28 p. Available at http://www.mcgill.ca/tau/files/tau/muhc_tau_2014_75_excimer_b.pdf.
9. Lu YG, Chen YM, Li L, Zhao RZ, Fu CH, Yan H. Drug-eluting stents versus intracoronary brachytherapy for in-stent restenosis: a meta-analysis. Clin Cardiol. 2011 ; 34(6):344-51.
10. Costopoulos C, Gorog DA, Di Mario C, Kukreja N. Use of thrombectomy devices in primary percutaneous coronary intervention: a systematic review and Meta-analysis. Int J Cardiol. 2013 Mar 10;163(3):229-41.
11. Sobieraj DM, White CM, Kluger J, et al. Adjunctive devices for patients with acute coronary syndrome undergoing percutaneous coronary intervention. Comparative effectiveness review No. 42 Rockville, MD: Agency for Healthcare Research and Quality 2011; AHRQ Publication No. 11(12)-EHC089-EF. Available at www.effectivehealthcare.ahrq.gov/thrombusacs.cfm.
12. Généreux P, Kumsars I, Lesiak M, Kini A, Fontos G, Slagboom T, Ungi I, Metzger DC, Wykrzykowska JJ, Stella PR, Bartorelli AL, Fearon WF, Lefèvre T, Feldman RL, LaSalle L, Francese DP, Onuma Y, Grundeken MJ, Garcia-Garcia HM, Laak LL, Cutlip DE, Kaplan AV, Serruys PW, Leon MB. A randomized trial of a dedicated bifurcation stent versus provisional stenting in the treatment of coronary bifurcation lesions. J Am Coll Cardiol. 2015; 65(6):533-43.
13. Di Mario C, Caiazzo G. Biodegradable stents: the golden future of angioplasty? Lancet 2015; II vol 384:10-12.
14. Patel VG, Brayton KM, Tamayo A, Mogabgad O, Michael T, Lo N, Alomar M, Shorrock D, Cipher D, Abdullah S, Banerjee S, Brilakis E. Angiographic Success and Procedural Complications in Patients Undergoing Percutaneous Coronary Chronic Total Occlusion Interventions: A Weighted Meta-Analysis of 18,061 Patients From 65 Studies. J Am Coll Cardiol Intv. 2013;6(2):128-136.

Srce i krvni sudovi 2015; 34(1):9-13

Originalan rad

"Tip-In" method: a novel, wire randez-vous method in need of retrograde CTO PCI

Masahisa Yamane

Vice President of Saitama Sekishinkai Hospital, Saitama, Japan

Background

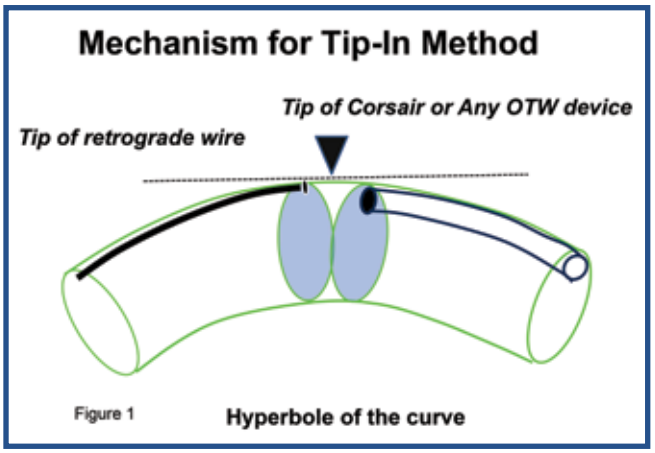
With an introduction of the Corsair microcatheter (Asahi Intecc, Japan), more epicardial collateral channels (CC) have become available in retrograde approach, increasing the chances for successful revascularization in CTO PCI. Once a retrograde wire crosses a CTO using reverse CART technique, advance the retrograde wire into the antegrade guide catheter, so that the wire is trapped inside the Guide to advance the retrograde Corsair or the microcatheter into the guide. When the tip of the microcatheter enters the guide, the retrograde wire can be replaced by a long "externalization" wire (either a Viper wire of 335 cm (Vascular Solution, USA) or a RG3 of 330 cm (Asahi Intecc, Japan) to thread through the Y connector of the antegrade guide. Subsequent procedure will be performed over the wire in an antegrade manner[1]. Alternatively, one can advance the Corsair or other microcatheter over the retrograde wire until it reaches the antegrade guide in the aortic arch. Deliver the antegrade microcatheter to the retrograde microcatheter similar to the kissing technique. Wiring can be completed by threading an antegrade wire through the retrograde microcatheter and crossing the CTO (Rendezvous Method)[2].

There are, however, some limitations using either Externalization or Rendezvous Method. Most notably, both techniques require a retrograde microcatheter to reach the antegrade guide through CC and CTO.

This report represents 4 cases in which the retrograde guide wire entered the antegrade guide by reverse CART, but the Corsair could not cross through CC and/or CTO over the guide wire. A novel, but simple technique is to place an antegrade microcatheter at the aortic arch and deliver the retrograde wire into it. The antegrade microcatheter over the retrograde wire is advanced to cross the CTO and a softer floppy wire is placed once the Corsair or the micro catheter has reached a distal non-CTO segment. This is a modification of Rendezvous Method, in which one can switch retrograde wiring to antegrade microcatheter crossing without losing guide wire position. This new technique overcomes shortcomings of the contemporary retrograde recanalisation in need of "bail-out" situation.

Principle and application of the Method

This is a technique to deliver retrograde wire into the antegrade Corsair or the microcatheter in the curved segment of the antegrade guide after retrograde wire successfully entered the guide. One can confirm whether the retrograde wire is successfully introduced into the antegrade Corsair by advancing another wire through the Corsair and having both guide wires contact inside. Rotate the Corsair to advance over the retrograde wire antegrade, which then crosses the CTO and go beyond. After withdrawing the retrograde wire and delivering a soft workforce wire into the distal vessel, Corsair could be removed by a balloon trapping. The procedure can then finish as of any other current PCI. We name this technique "Tip-In" method.



Case 1

A 44-year-old male, who had been treated with two Cypher stents (Johnson and Johnson, Cordis) implantation of left anterior descending artery (LAD) (3.0mm x 28mm and 2.5mm x 23mm), was referred for Right coronary artery (RCA) CTO treatment. Final coronary angiography revealed Rentrop grade II collaterals from LAD and left circumflex artery (LCX). 6 month later, an attempt was made to recanalise CTO/RCA. Coronary angiography showed Rentrop grade II CC from right ventricular branch (RVB) to posterior descending artery (PD) of RCA (Figure 1-A, B). A Fielder XT guide wire (Asahi In-

Corresponding author: Masahisa Yamane, MD, FACC, e-mail: masahisa-yamane@sayamahp.org

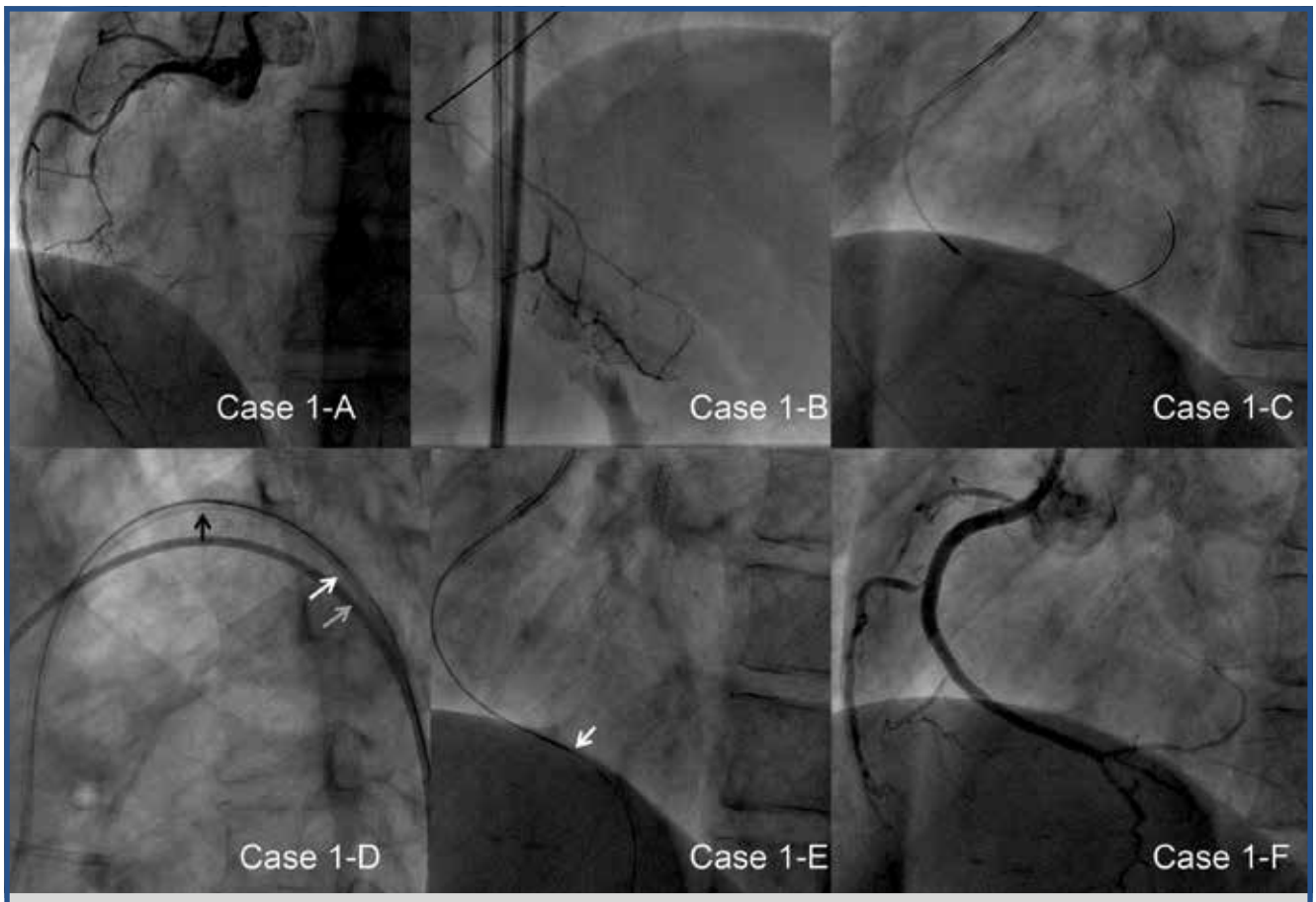


Figure 1. Once the retrograde wire into the antegrade guide, an antegrade mirocatheter is advanced to the aortic arch (top of the curve) closer to the retrograde wire. The mechanical properties of wires or micro catheters tend to track the outer side of large curve inside the guide, where both can easily face each other in a straight line. Torque control of the wire allows the tip to enter the central lumen of the micro catheter (Figure1).

tecc, Japan) and a Corsair were delivered to the distal RCA by antegrade, but the guide wire never reached the true lumen in the PDA. Retrograde approach from the RCA CC was then undertaken by Suoh wire (Asahi Intecc, Japan) over a Finecross microcatheter (Terumo, Japan). Eventually, a Fielder FC wire (Asahi Intecc, Japan) could cross the CC, but the Corsair failed to cross the CC due to its acute angle and tortuosity. Fortunately the Fielder FC guide wire successfully crossed the CTO into proximal true lumen by Reverse CART technique (Figure 1-C). Another Corsair was placed at the aortic arch and the retrograde Fielder FC was successfully introduced into it (Figure 1-D). The Corsair crossed the CTO over the retrograde wire (Figure 1-E) and a new soft floppy wire of Route (Asahi Intecc, Japan) was delivered into the Corsair and placed in the distal RCA after removal of the retrograde wire. The Corsair was then removed from the artery by a 2.5 mm balloon trapping method. Following the small-sized balloon dilation throughout the CTO, four Xience V stents (Abbott Vascular, USA) of a 2.5mm x 28mm, a 3.0 mm x 28mm, a 3.5mm x 28mm, and a 3.5mmX18mm were delivered and deployed. Angiography confirmed an excellent final result (Figure 1-F).

Case 2

A 63-year-old male was admitted to the hospital with ACS. Coronary angiography showed a 75-90% segmental disease of LAD, involving the proximal LAD diagonal branch and the total occlusion at the mid LAD. Rentrop grade III CC was noted from RCA via apical epicardial CC. Two Endeavor stents (Medtronic, USA) were delivered and deployed successfully without any complications, a 2.5mm x 24mm for the mid LAD to the diagonal branch as jailed for the CTO ostium and another 3.0mm x 18mm for the proximal LAD. 5 month later, CTO-PCI was attempted using epicardial CC from the PD of the RCA (Figure 2-A). A Fielder FC was advanced over a Corsair, which succeeded in crossing the CC to the distal LAD. Then a Confianza Pro 12 (Asahi Intecc, Japan) penetrated the previous stent struts at the mid LAD under IVUS-guidance (Figure 2-B). The retrograde wire was successfully introduced into the antegrade guide, where the retrograde Corsair couldn't cross because of possible stent-struts jail. Therefore, a guide wire externalization was not possible (Figure 2-C). Another Corsair was advanced to the aortic arch, where the retrograde wire succeeded in entering the Corsair (Figure 2-D), which crossed the CTO antegrade over the retrograde wire by simple back and forth rotation (Figure 2-E). After the CTO segment was dilated by balloon catheter, two DESs (a Xience V of 3.0mm×28mm at the distal of CTO and another

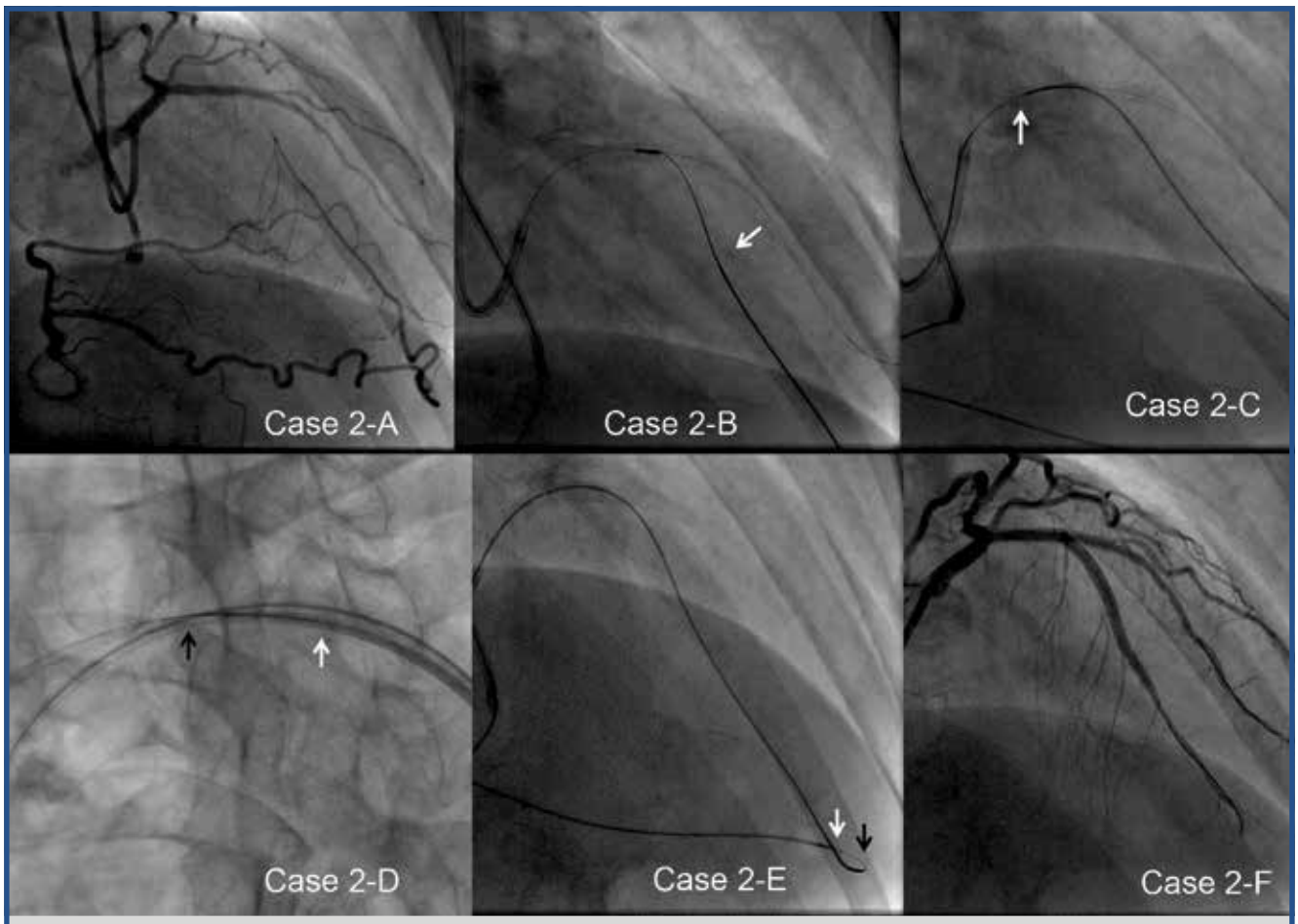


Figure 2.

3.0mmx18mm at the CTO) were implanted by culotte stenting, followed by KBT at 16 atm (Figure 2-F).

An excellent angiographic result was obtained.

Case 3

An 80-year-old male presented with low threshold angina and CAG disclosed a triple-vessel disease, including a CTO of the mid RCA (Figure 3-A). Rentrop grade II CCs were visualized from the septal branch near the LAD apex and ipsilateral bridging collaterals from the middle to the distal RCA (Figure 3-B, C). PCI was attempted after patient's decline to surgical option for treating CAD. After balloon dilatation of the LAD and LCX lesions, which were treated by V-stenting of the DES simultaneously, followed by KBT of a 3.5 mm and a 3.0 mm NC balloons. The RCA was engaged with a 7F SAL 1.0 SH (Launcher, USA). Since there was a poor target vessel beyond the CTO, an attempt to cross the CC was made from the LAD septal to the RCA, and a Fielder FC successfully crossed to the distal PDA (Figure 4-C). After a Corsair (150cm) advancement (Figure 3-D), a retrograde wire was successfully advanced to the antegrade guide by reverse CART (Figure 3-E, F). However, the Corsair could not cross the CC because of the strong resistance over the long CC, so another Corsair was advanced in the aortic arch in the guide and was able to receive a retrograde Fielder FC (Figure 3-G). The Corsair was then advanced over the wire and crossed the CTO (Figure 3-H). When it reached the distal RCA, the retrograde wire was removed, an antegrade soft wire was placed over the Corsair, and, the Corsair removed by a 2.5 mm balloon trapping. After 1.5mm and 2.0 mm balloon dilation, 3 DESs were deployed (a 2.5mm×28mm, a 3.0mm×28mm, and a 3.5mm×28mm, respectively) and the procedure successfully terminated (Figure 3-I).

Modification of the technique inside a native coronary artery

Case 4

The case is a 57 year-old male with effort angina, and CAG demonstrated a high-grade calcified CTO in the proximal LAD with CC via the septal through the PDA/RCA and the epicardial cc through the LAD Diagonal (Figure 4-A,B). PCI attempt for the first time had failed due to inability to advance any device after successful wire crossing to the distal LAD.

The Second PCI attempt was made using an antegrade approach with a Gaia 1 wire (Asahi Intecc, Japan), which entered the distal true lumen without trouble (Figure 4-C). However, any device could not go through the CTO (those are a Corsair, a Finecross (Figure 4-D), and a Tornus Pro (2.1F) penetration microcatheter (Asahi Intecc, Japan) (Figure 4-E).

Also, neither a 1.0mm nor a 1.25mm balloon could go beyond the occlusion (Figure 4-F). A Sion black wire (Asahi Intecc, Japan) was tried through an epicardial CC between the intermediate and the LAD (Figure 4-G),

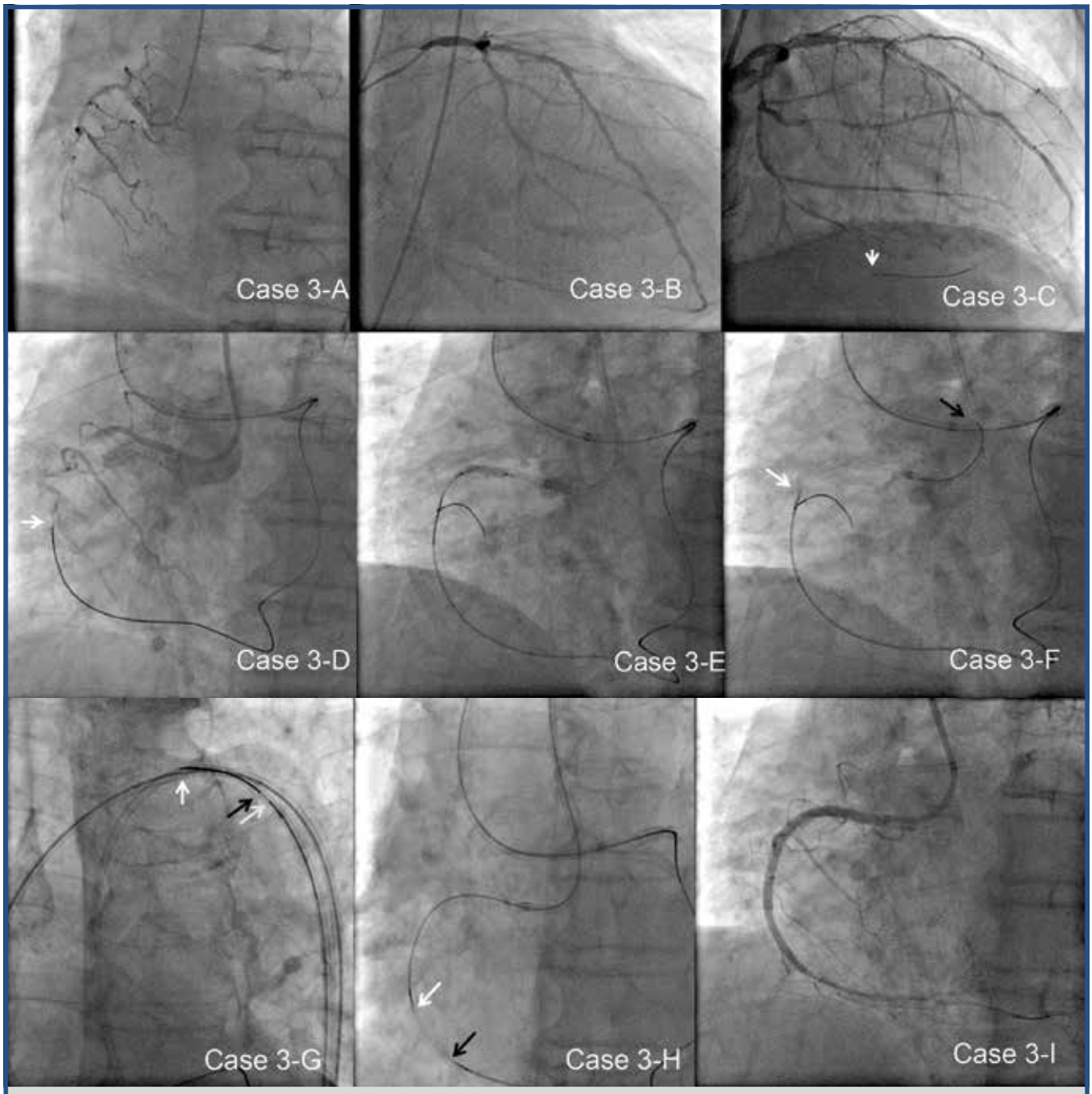


Figure 3.

which successfully crossed the CC and the CTO (Figure 11), and entered the antegrade guide (Figure 4-H, I). Of note, in this ipsilateral CC crossing, two 7F Guides (a 7F EBU3.5 SH, and a 7F SL3.5F SH,) were used to avoid confusion of the antegrade and the retrograde gears.

Even with a trapping by 2.5 mm balloon over the retrograde wire inside the guide, the retrograde Corsair could not enter the antegrade guide, so the wire alone was further advanced to the level of aortic arch (Figure 4-J). A Tornus 88Flex (2.6F) was placed in the aortic arch with an intension of "tip-in" method, which succeeded. Despite over the retrograde wire support, the Tornus could not go through the lesion (Figure 4-K). The retrograde Corsair was replaced by a 150cm Finecross, which successfully crossed the CTO, but was caught in the proximal calcified segment. An antegrade wire was exchanged to a "Rota floppy wire (Boston Scientific, Minneapolis, MN)" aiming at the Finecross lumen, using modified " tip-in" method inside of the curved segment of LAD (Figure 4-L). Rotablation was performed with a 1.25 mm burr (Figure 4-M), resulting in successful crossing, when bradycardia and hypotension (BP= 70 mmHg systolic) developed. Angiography demonstrated no flow over the entire left system with marked ST segment elevation in the precordial monitor leads (Figure 4-N).

Prompt 2.0 mm balloon inflation restored the flow toward the LCX and the intermediate branch, but ST-segment elevation persisted. A new 1.5 mm balloon successfully crossed the LAD lesion, followed by 2.0 mm balloon inflation (Figure 4-O). The DES of 2.25 mm x28 mm and of 3.0mm x 24 mm was deployed in the proximal segment at 18 atm (Figure 4-P). An excellent angiographic result was restored with marked resolution of ST elevation (Figure 4-Q).

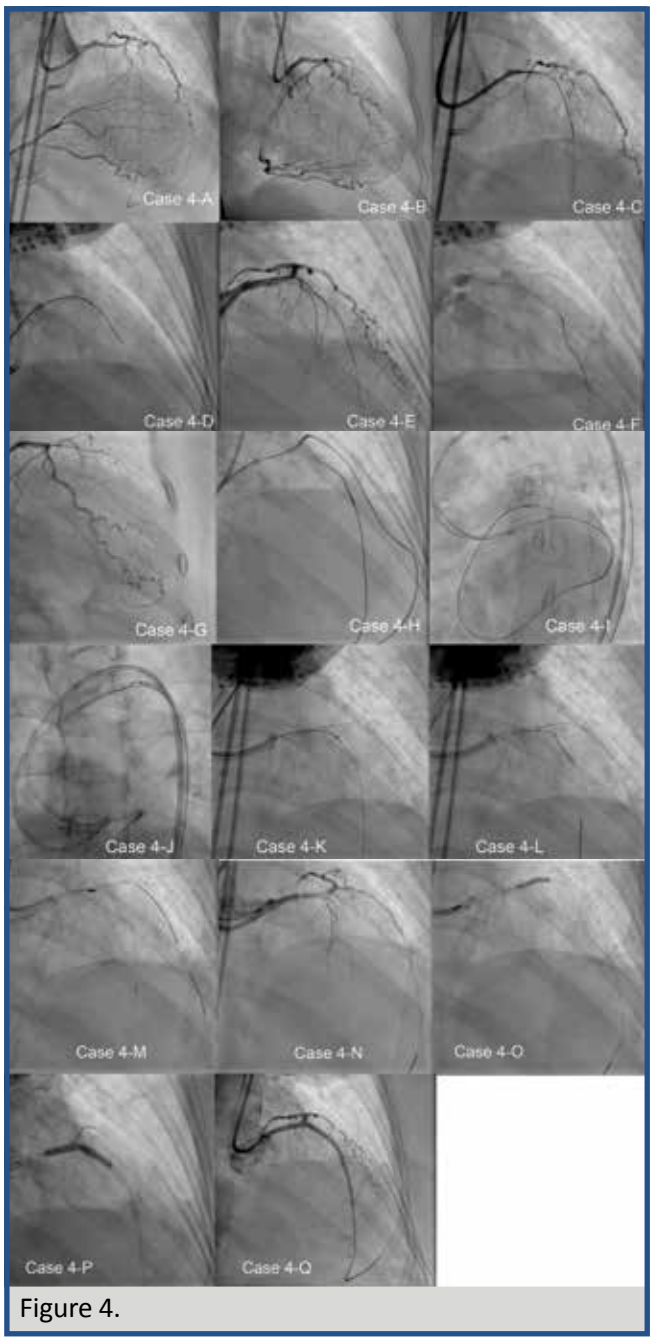


Figure 4.

Discussion

In retrograde CTO-PCI after successful CC wire crossing, wire externalization, using a long dedicated wire (>300cm) becomes almost default setting, once the retrograde microcatheter has engaged into the antegrade guide. Over the externalized long wire, excellent back-up support is obtained in delivering the long stent(s) beyond the tortuous, sometimes calcified, diseased segments. However, there are occasional difficulties in microcatheter crossing over the CC or CTO, due to the resistance or a shortage of the microcatheter. Excessive rotation and aggressive push of a microcatheter will increase the risk of vessel injury, dissection and rupture, in the worst case. One of the precautionary measures to overcome a shortage includes cutting a guide short by putting a piece of one size smaller sheath as a connecting tube, when the length of the retrograde guide permits[3].

Tip-in method can provide rapid solution from problems associated with retrograde wire based PCI, once the retrograde wire has crossed to the proximal vascular lumen. Accordingly, the method cannot provide the strong support in delivering a balloon or a stent as externalization method can, due to inherent nature of the antegrade system.

Conclusion

Since retrograde CTO-PCI occasionally develops with an unexpected wire crossing over the least possible long epicardial CC, or with an unexpected resistance of CC and/or CTO, “tip-in” method could provide a simple, quick, but effective countermeasure for bailing-out of stagnation mode to a successful recanalization.

References

1. Joyal D, Thompson CA, Grantham JA, Buller CE, Rinfret S: The retrograde technique for recanalization of chronic total occlusions: a step-by-step approach, JACC Cardiovasc Interv. 2012 :P1-11.
2. Kim MH1, Yu LH, Mitsudo. A new retrograde wiring technique for chronic total occlusion: Catheter Cardiovasc Interv 2010;p117-9.
3. Brilakis, Emmanouil:Manual of Coronary Chronic Total Occlusion Interventions: A Step-by-Step Approach, Academic Press,2013.

Srce i krvni sudovi 2015; 34(1):14-17

Prikaz pacijenta

Percutaneous repair of mitral regurgitation with the Mitraclip system: clinical indications and first Slovenian experience

Jana Ambrožič [1], Matjaž Bunc[1,2]

[1]Department of Cardiology, University Medical Centre Ljubljana, Ljubljana, Slovenia
[2]Institut for Pathophysiology, School of Medicine, University Ljubljana, Slovenia

Abstract The MitraClip is the first percutaneous therapy for mitral regurgitation. It can be used in both etiologies: primary (degenerative) and secondary (functional) mitral regurgitation. The technique mimics surgical suture-based approach by implanting a clip that grasps free edges of both leaflets and creates dual mitral valve orifice. After Conformité Européenne (CE) mark in 2008, the MitraClip system is increasingly used in Europe for both types of mitral regurgitation. The Food and Drug Administration (FDA) so far has approved the Mitraclip only for patients with severe primary mitral regurgitation who are at high surgical risk. The decision for the MitraClip therapy should be accepted within the heart team. Transesophageal echocardiography plays a key role in selection of the patients, procedural guidance and follow-up and is essential to the Mitraclip success. First Mitraclip implantation performed in Slovenia is presented.

Key words: mitral regurgitation, MitraClip, first experience

Introduction

Percutaneous transcatheter mitral valve repair using the MitraClip system (MClip, Abbott Vascular, Abbott Park, Illinois, USA) is a relatively novel method for treatment of mitral regurgitation. The technique is based on the creation of a double mitral orifice, similar to surgical Alfieri's stitch, by connecting ideally the middle scallops of the anterior and the posterior leaflet of a regurgitant mitral valve[1]. The MClip is currently the only percutaneous procedure available in clinical practice. According to the latest European and American guidelines it is considered as an alternative treatment for selected high-risk inoperable patients with primary mitral regurgitation[2,3]. The European guidelines have included MClip as a potential option also for patients with secondary mitral regurgitation due to ischemic or non-ischemic dilated cardiomyopathy who remain symptomatic despite optimal medical therapy and cardiac resynchronization when indicated[2] (Table 1). Namely, surgical correction of secondary MR is controversial, because the primary pathology is left ventricular dysfunction and not the diseased mitral valve, the results of surgery are not favorable and operative mortality is much higher compared to primary mitral disease[4,5]. The initial data of the EVEREST trials (Endovascular Valve Edge-to-Edge Repair Study), including predominately patients with degenerative mitral regurgitation demonstrated feasibility and safety of the MClip procedure. Compared to surgery percutaneous repair was less effective at reducing mitral regurgitation[6,7]. Subsequent studies and registries have confirmed MClip feasibility and low procedural risk and shown promising results in terms of reducing mitral regurgitation grade, improvement of functional status and quality of life[8-11]. In real-life practice there has been a shift in the indications for MClip toward secondary mitral regurgitation, which presents currently about 80% of MClip implantations in Europe.

Patient selection for the MClip therapy depends on clinical factors as well as specific anatomical criteria that need to be fulfilled. Echocardiography has an essential role in patient selection and evaluation of the final results after clip implantation. Moreover, it is the central imaging modality for guiding the procedure[12]. The first step in the patients selection is to assess the severity of mitral regurgitation, then to determine the morphology of the mitral valve and abnormalities in left ventricular function. According to the EVEREST studies mitral regurgitation needs to be moderate to severe or severe (grade 3+ or 4+, respectively, when classifying regurgitation into four grades). The mitral valve morphology and the etiology of mitral regurgitation should be assessed in detail by transoesophageal echocardiography (TEE), as suitable morphology is essential to a successful Mitraclip procedure. For patients with secondary mitral regurgitation, the co-

Corresponding author: Jana Ambrožič, Zaloška 7, 1000 Ljubljana, Slovenia, e-mail: jana.ambrozic@gmail.com

Table 1. Indications for percutaneous mitral valve repair using the Mitraclip system according to the latest European and American guidelines.

	ESC	AHA/ACC
	Class of recommendation/ level of evidence	**Class of recommendation/ level of evidence**
Percutaneous mitral valve repair may be considered in patients with symptomatic severe **primary** MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a heart team and have life expectancy greater than 1 year	**IIb C**	**IIb B**
Percutaneous mitral valve repair may be considered in patients with symptomatic severe **secondary** MR despite optimal medical therapy (including CRT if indicated) who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a heart team and have life expectancy greater than 1 year	**IIb C**	

ESC=European Society of Cardiology guidelines on the management of valvular heart
Disease, AHA/ACC=American Heart Association/American College of Cardiology guidelines on the management of valvular heart disease, MR=mitral regurgitation, CRT=cardiac resynchronization therapy.

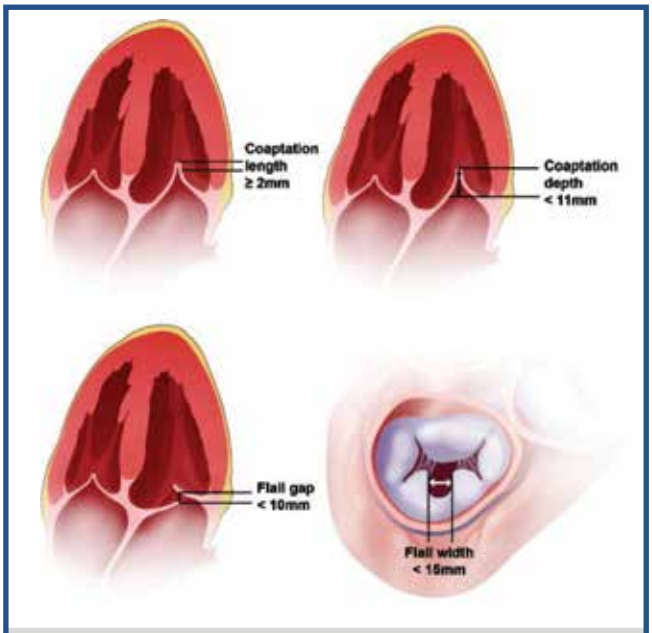


Figure 1. Anatomic eligibility criteria for MitraClip (EVEREST trial). In secondary MR the coaptation length must be at least 2 mm and coaptation depth <11 mm, so that there is some tissue for grasping with the clip. In primary MR with prolapse and/or flail, flail depth must be <10 mm and flail width <15 mm. EVEREST=Endovascular valve edge-to-edge repair study, MR=mitral regurgitation.

aptation length must be at least 2 mm, and the coaptation depth < 11 mm. For patients with primary mitral regurgitation due to prolapse or flail leaflet, the gap of the prolapsed or flailed segment must be <10 mm and its width <15 mm (Figure 1). MClip is not applicable to patients not fulfilling above echocardiographic criteria, those with rheumatic mitral disease or with calcifications of the grasping area. The mitral valve area should not be less than 4 cm² in order to avoid creating mitral stenosis after the procedure[6,7].

We present the first Slovenian MClip procedure in a patient with secondary mitral regurgitation due to ischemic cardiomyopathy.

Case report

A 75-year old man with a long history of diabetes type 2 on insulin, arterial hypertension, hypercholesterolemia and chronic renal disease (creatinine of 150 µmol/L) had been admitted to our department for heart failure. He had a history of surgical coronary revascularization 2 years ago (LIMA to LAD and vein grafts to RCA and OM1). In 2014 he was admitted to our hospital with heart failure and angina. Coronary angiogram had shown occlusion of all grafts and percutaneous coronary recanalization of LAD, LCX and RCA was undertaken. 6 months later he was admitted again due to heart failure. He was in sinus rhythm, with narrow QRS complex. Transthoracic echocardiography demonstrated mild enlargement of the left ventricle with moderately reduced ejection fraction (45%), akinesia of the apical segments and hypokinesia of inferior and inferolateral wall. Significant functional mitral regurgitation was present that was graded as severe regarding the ischemic etiology (effective regurgitant orifice area of 0.26 cm², regurgitant volume of 30 ml). Right ventricle function was preserved and estimated systolic pulmonary pressure was 55 mmHg. According to nuclear imaging the antero-apical myocardial wall was non-viable. TEE confirmed normal morphology of the mitral valve and reviled the mechanism of regurgitation: left ventricular remodeling with symmetric tenting and malcoaptation of the mitral valve leaflets. Echocardiographic anatomical criteria were suitable for Mitraclip implantation (Figure 2). The patient's coronary situation was the same as 6 months before; there were no additional revascularization options. He was already on optimal medical therapy and not a candidate for cardiac resynchronization. His therapeutic options were discussed at our hospital heart team which agreed that he was suitable for a Mitraclip procedure.

The procedure was done under general anaesthesia, with a venous femoral access. The interatrial septum was punctured in postero-superior aspect under TEE guidance, using short axis, bicaval and four chamber views (Figure 3). The 24F Mitraclip catheter was introduced into the left atrium. According to the wide mitral

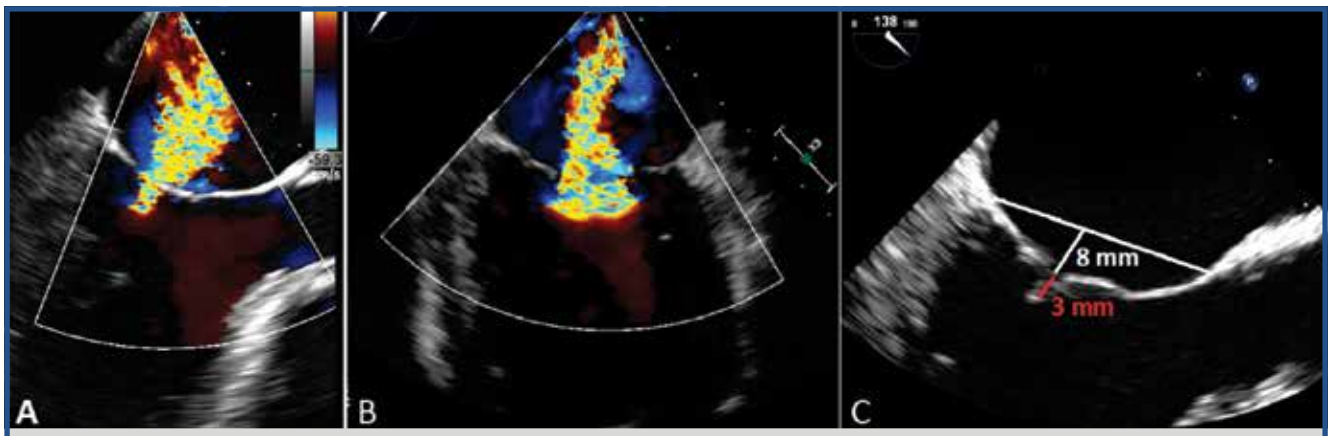


Figure 2. 2-dimensional TEE at mid-esophageal long axis (A) and inter-commissural view (B) showing the regurgitant mitral jet which is smaller in the long axis, but much wider in inter-commissural view, pointing ellipsoid shape of the regurgitant area, typical for secondary mitral regurgitation. C illustrates tenting of the mitral valve leaflets. Remaining degree of coaptation is enough for grasping (3 mm) and the coaptation length is not too long (8 mm).

regurgitation jet we assumed two clips would be needed. The first clip was positioned more to the medial part of the regurgitant jet with the aid of 2- and 3-dimensional TEE (Figure 4). The clip was then introduced into the left ventricle where the two leaflets were grasped and clipped. Mean gradient across the mitral valve was 4 mmHg (what is acceptable) and residual mitral regurgitation at the lateral aspect of the valve. According to the initial decision the second clip was introduced and aligned laterally to the first clip under TEE guidance. After grasping and clipping the leaflets with the second clip the mean gradient and residual regurgitation was assessed. The result was satisfactory with considerable reduction in regurgitation and without significant mitral obstruction (Figure 4). After the system was pulled out through the interatrial septum we noticed small and hemodynamically non significant iatrogenic atrium septum defect. There were no complications after the procedure. The patient was discharged on a 5th day with dual antiplatelet therapy for 3 months.

Conclusion

We presented first Slovenian experience with the MClip procedure. The MClip represents an exciting advancement in the field of percutaneous structural heart interventions. As for aortic valve disease with great expansion of transcatheter aortic valve implantations, the MClip system has been developed to enable mitral valve repair in patients with severe mitral regurgitation. To date more than 15.000 MClip procedures were performed worldwide. It should be offered to carefully selected patients who fulfill echocardiographic anatomical criteria and are discussed within a heart team comprising of cardiac surgeon, interventional cardiologist, referring cardiologist, imaging specialist and cardiac anesthesiologist. There is growing tendency for MClip therapy in heart failure patients with secondary mitral regurgitation, as an adjunctive treatment when optimal medical therapy fails to provide clinical improvement. There are currently ongoing prospective, randomized, comparative studies (MITRA-FR, COAPT), which will assess the MClip device efficacy in this population of patients, already on optimal medical therapy [13].

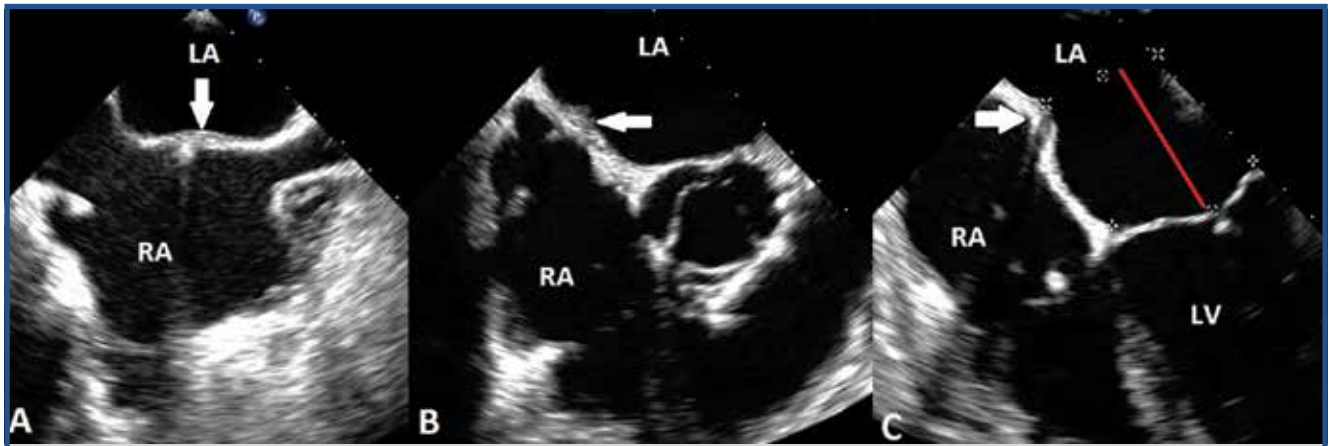


Figure 3. Puncture of the interatrial septum. Determination of the puncture site is shown in a bicaval view (A) and short axis view at the base (B). The tenting of the needle is demonstrated (white arrows). In four chamber view the measurement of the height above the mitral valve annulus is done (C).
LA=left atrium, RA=right atrium, LV=left ventricle.

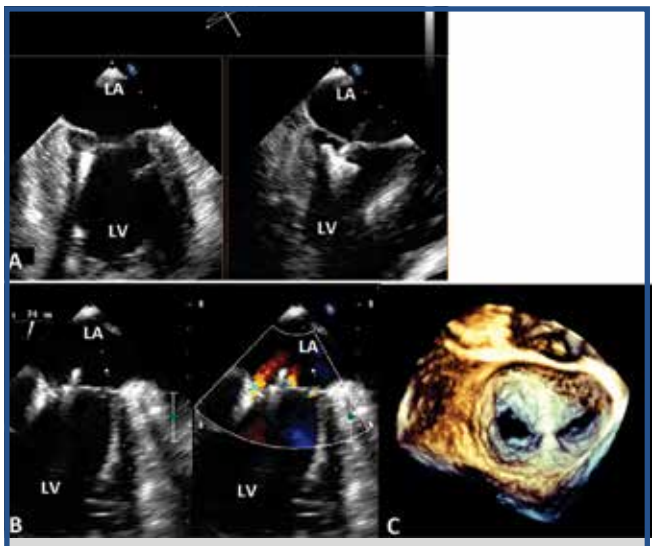


Figure 4. A: simultaneous biplane imaging at intercommissural and long axis view demonstrates positioning of the Mitraclip. Once the proper position is set, the opened Mitraclip is advanced into the left ventricle. B: mild residual regurgitant jets after the second clip deployment. C: 3-dimensional TEE imaging using enface surgical view from the left atrium showing the final result-newly created double mitral valve orifice.
LA=left atrium, LV=left ventricle.

References

1. Fucci C, Sandrelli L, Pardini A, Torracca L, Ferrari M, Alfieri O. Improved results with mitral valve repair using new surgical techniques. Eur J Cardiothorac Surg 1995; 9: 621-6, discuss 626-7.
2. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC); European Association for Cardio-Thoracic Surgery (EACTS). Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J 2012; 33: 2451-96.
3. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, et al. ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: a Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2014; 129: e521-643.
4. Glower DD, Tuttle RH, Shaw LK, Orozco RE, Rankin JS. Patient survival characteristics after routine mitral valve repair for ischemic mitral regurgitation. J Thorac Cardiovasc Surg 2005; 129: 860-8.
5. Mihaljevic T, Lam BK, Rajeswaran J, Takagaki M, Lauer MS, Gillinov AM, et al. Impact of mitral valve annuloplasty combined with revascularization in patients with functional ischemic mitral regurgitation. J Am Coll Cardiol 2007; 49: 2191-201.
6. Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, et al.; EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011; 364: 1395-40.
7. Mauri L, Foster E, Glower DD, Apruzzese P, Massaro JM, Herrmann HC, et al.; EVEREST II Investigators. 4-year results of a randomized controlled trial of percutaneous repair versus surgery for mitral regurgitation. J Am Coll Cardiol 2013; 62: 317-28.
8. Nickenig G, Estevez-Loureiro R, Franzen O, Tamburino C, Vanderheyden M, Lüscher TF, et al. Transcatheter valve treatment sentinel registry investigators of the EURObservational Research Programme of the European Society of Cardiology. Percutaneous mitral valve edge-to-edge repair: in-hospital results and 1-year follow-up of 628 patients of the 2011-2012 Pilot European Sentinel Registry. J Am Coll Cardiol 2014; 64: 875-84.
9. Maisano F, Franzen O, Baldus S, Schäfer U, Hausleiter J, Butter C, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU, a prospective, multicenter, nonrandomized post-approval study of the MitraClip therapy in Europe. J Am Coll Cardiol 2013; 62: 1052-61.
10. Franzen O, Baldus S, Rudolph V, Meyer S, Knap M, Koschyk D, et al. Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: emphasis on adverse valve morphology and severe left ventricular dysfunction. Eur Heart J 2010; 31: 1373-81.
11. Tamburino C, Ussia GP, Maisano F, Capodanno D, La Canna G, Scandura S, et al. Percutaneous mitral valve repair with the MitraClip system: acute results from a real world setting. Eur Heart J 2010; 31: 1382-9.
12. Wunderlich NC , Siegel RJ. Peri-interventional echo assessment for the MitraClip procedure. Eur Heart J Cardiovasc Imaging 2013; 14: 935-49.
13. Obadia JF, Armoiry X, Iung B, Lefèvre T, Mewton N, Messika-Zeitoun D, et al. The MITRA-FR study: design and rationale of a randomised study of percutaneous mitral valve repair compared with optimal medical management alone for severe secondary mitral regurgitation. EuroIntervention 2015; 10: 1354-60.

Srce i krvni sudovi 2015; 34(1):18-23

Originalni rad

Most relevant complications of transcatheter aortic valve implantation related to the site of implantation: results of Slovenian national registry

Polonca Kogoj[1], Tjaša Furlan[1], Nikola Lakič[3], Špela Mušič[2], Bojan Kontestabile[2], Jana Ambrožič[1], Darko Zorman[1], Bunc Matjaž[1]

[1]Clinical Department for Cardiology, UKC Ljubljana, Slovenia
[2]Clinical Department for Anesthesiology, UKC Ljubljana, Slovenia
[3]Clinical Department for Cardiovascular Surgery, UKC Ljubljana, Slovenia

Abstract

Background: Transfemoral valve implantation is the most widely used approach for transcatheter aortic valve implantation (TAVI) and transapical approach is considered to be associated with increased morbidity and mortality. The aim of our study was to compare TAVI related complications in trasfemoral and transapical approach and to compare the long-term outcome in these two groups.

Methods and results: We enrolled 171 patients who underwent transfemoral or transapical TAVI between October 2009 and January 2015 (143 transfemoral approach, 28 transapical approach). Patients with transapical approach were more often men and more of them had coronary artery disease and carotid stenosis. The most common complications were related to vascular damage that resulted in minor bleeding and were more common in transfemoral approach. There were no other significant differences in periprocedural complications between transfemoral and transapical site of implantation. We observed no statistical difference in 30 days survival between transfemoral and transapical approach, but long-term survival was better with the transfemoral approach (log Rank = 0.025).

Conclusions: We observed comparable results with transfemoral and transapical TAVI approach. The long-term survival, which was better in transfemoral group, could be improved with valve and access route individualization to each patient's anatomy and general condition.

Key words: aged, aortic valve stenosis, aortic valve replacement, transcatheter, postoperative complications/mortality

Introduction

Surgical aortic valve replacement (SAVR) is the primary treatment for severe symptomatic aortic stenosis (AS)[1,2]. Transcatheter aortic valve implantation (TAVI) has emerged as a viable alternative in selected high-risk patients, who are not surgical candidates due to comorbidities and age[3]. The percutaneous valve can be implanted using many access routes including an anterograde (transapical) and retrograde (transfemoral, transsubclavian and transaortic) approach[4-7]. The transfemoral approach has been the most widely used and is commonly the first choice for access. The limitations of this approach are atherosclerotic and calcific lesions of femoro-iliac vascular segments, thoracic and abdominal aorta. Because of large delivery systems, carefully evaluation of these vessels is necessary before the procedure and in case of severe atherosclerotic plaques and calcifications transapical approach is preferred.

In Slovenia, TAVI was introduced in late 2009 and has been performed only at University medical centre Ljubljana, so far. The present study reports the results of the prospective, non-randomized single-centre Slovenian national registry. The aim of our study was to compare TAVI related complications in trasfemoral and transapical site of implantation and to compare the long-term outcome in these two groups.

Materials and methods

Patient population and selection

From October 2009 to January 2015, 171 consecutive patients underwent TAVI via transapical or transfemoral approach for symptomatic severe AS and were enrolled in our study. We divide the enrolled patients into two groups based on the site of implantation (transfemoral or transapical). Between the groups, we retrospectively analyzed the baseline characteristics, echocardiographic

Corresponding author: prof. Matjaž Bunc, MD PhD, Zaloška c. 002, Slovenia e-mail: mbuncek@yahoo.com

parameters, periprocedural complications and long-term outcome.

Criteria for TAVI included:

- severe, symptomatic aortic stenosis confirmed by transthoracic echocardiography with aortic valve area < 1 cm2 (< 0.6 cm2/m2),
- high surgical risk determinated by logistic EuroSCORE (European System of Cadiac Operative Risk Evalutation) > 15 % or STS score > 8.5 %
- contraindication to surgery because of concomitant comorbid conditions assessed and agreed by both an independent cardiologist and a cardiovascular surgeon.

The final decision to perform TAVI was made by a multidisciplinary team consisting of interventional cardiologist, cardiovascular surgeon, anesthesiologist and echo specialist.

Echocardiographic data

With transthoracic echocardiography before TAVI we determined the severity of aortic stenosis (aortic valve area and gradients through the valve), left ventricular ejection fraction and pulmonary artery systolic pressure[8].

CT scan evaluation and delivery rout selection

Multidetector computer tomography (CT) with angiography was performed in all patients with the aim to select the prosthesis size and type and the site of implantation[9]. Based on the measurement of the aortic annulus and the aortic valve sizing charts provided by the manufacturer, the size and the type of the device were selected[10, 11]. The degree of aortic and ilio-femoral arterial atherosclerosis and calcification were evaluated and the vessels diameters were measured. In the presence of significant vascular aneurysmal dilatation, extent atherosclerotic plaques and small ilio-femoral vessels diameters, the transapical approach was preferred to transfemoral[12].

TAVR procedure

The procedures were performed in our cardiac catheterization laboratory or hybrid operating room. All the procedures were performed by only one operator. In most of the cases we used either balloon-expandable Edwards Sapien valve (Edwards, Lifescience, Irvine, CA, USA) either self-expandable CoreValve (Medtronic Inc, Mineapolis, MN, USA)[13-15]. In six cases we implanted Acurate TF (Symetis, CH) valve. The transfemoral delivery system was 18-F through 20-F catheters. The self-expandable valve was positioned in a controlled manner either without pacing or under slow-rapid pacing with allowance for limited repositioning. The balloon-expandable valve was deployed under rapid pacing without cardiopulmonary support. Predilatation of native aortic valve was used in 55% of cases.

The procedure was mainly performed under analgosedation (without endotracheal intubation) using fluoroscopic guidance and in selected cases using transesophageal echocardiographic guidance as appropriate. General anesthesia was used in 35% of procedures, especially in the early phase of the TAVR program introduction.

Data collection and follow-up

Baseline clinical data were retrospectively collected by chart review. Logistic EuroSCORE was calculated for all patients. All clinically relevant baseline and follow-up variables as well as periprocedural complication were prospectively entered into a dedicated database. Major periprocedural adverse events were defined as periprocedural death from any cause, myocardial infarction, severe aortic regurgitation, stroke, cardiac tamponade, cardiogenic shock, aortic dissection, major vascular complications, urgent conversion to surgery and permanent pacemaker implantation. In-hospital follow-up consisted of vital parameters, complete blood count, monitoring of renal function, puncture site assessment and transthoracic echocardiography within few days after TAVI. Acute renal impairment, myocardial infarction, stroke, vascular complications and major bleeding were defined according to the Valve Academic Research Consortium proposed criteria (VARC)[16]. Clinical and echocardiographic follow-up was planned at 3 to 6 months after TAVI, and data were obtained by chart review.

Statistical analysis

Qualitative variables were expressed as percentages and quantitative variables as mean ± standard deviation. Continuous variables were compared using the Student's paired t-test. The $\chi 2$ test was used to compare qualitative variables. Survival rates were presented as Kaplan-Meier curves, and the log-rank test was used for comparison. Differences were considered statistically significant at $P < 0.05$. All data were processed using the Statistical Package for Social Sciences, version 17.0 (SPSS, Inc., Chicago, Illinois).

Results

Baseline characteristics

We enrolled 171 consecutive patients who underwent TAVI via transfemoral (n = 143,83.6%) or via transapical approach (n = 28,16.4%). All patients had symptomatic severe aortic stenosis, with high risk for SAVR (mean logistic EUROSCORE 13±9.8%). The common comorbidities, echocardiographic parameters and baseline characteristics of the enrolled patients as well as the comparison of the baseline parameters between the different sites of the valve implantation are displayed in Table 1. In the group where TAVI was performed via transapical approach more patients were male, they have more often coronary artery disease and carotid stenosis. The rest of the observed baseline parameters were similar in the two groups.

Table 1. Baseline characteristics of the enrolled TAVI population and the comparison of the baseline parameters between the transfemoral and transapical site of valve implantation.

Variables	Overall TAVI (n = 171)	Transfemoral (n = 143)	Transapical (n = 28)	P (TF vs. TA)
Age, y, mean (± SD)	82.8 (6.1)	83.1 (5.7)	81.5 (7.8)	0.350
Men, n (%)	61 (36)	46 (32)	15 (54)	0.031
Logistic EuroSCORE, %, mean (± SD)	13.0 (9.8)	13.0 (9.7)	13.3 (10.7)	0.874
Coronary artery disease, n (%)	57 (33)	41 (29)	16 (57)	0.003
Prior myocardial infarction, n (%)	13 (8)	11 (8)	2 (7)	0.920
Carotid artery stenosis > 50 %, n (%)	25 (15)	15 (10)	10 (36)	0.001
Atrial fibrillation, n (%)	62 (36)	54 (38)	8 (29)	0.355
Prior CVI/TIA, n (%)	9 (5)	8 (6)	1 (4)	0.661
Diabetes mellitus, n (%)	39 (23)	32 (22)	7 (25)	0.762
COPD, n (%)	26 (15)	24 (17)	2 (7)	0.194
Previous pacemaker, n (%)	11 (6)	7 (5)	4 (14)	0.064
Prior CABG, n (%)	16 (9)	11 (8)	5 (18)	0.091
Prior MVR, n (%)	6 (4)	4 (3)	2 (7)	0.253
Mean aortic gradient, mm Hg, mean (± SD)	46.1 (15.8)	46.8 (16.2)	42.6 (13.2)	0.167
Baseline AVA, cm2, mean (± SD)	0.63 (0.16)	0.62 (0.17)	0.65 (0.14)	0.365
LVEF, %, mean (± SD)	58.2 (11.1)	59.0 (10.2)	54.0 (14.3)	0.102
SPAP, mmHg, mean (± SD)	46.9 (12.7)	47.6 (13.1)	43.3 (9.7)	0.081

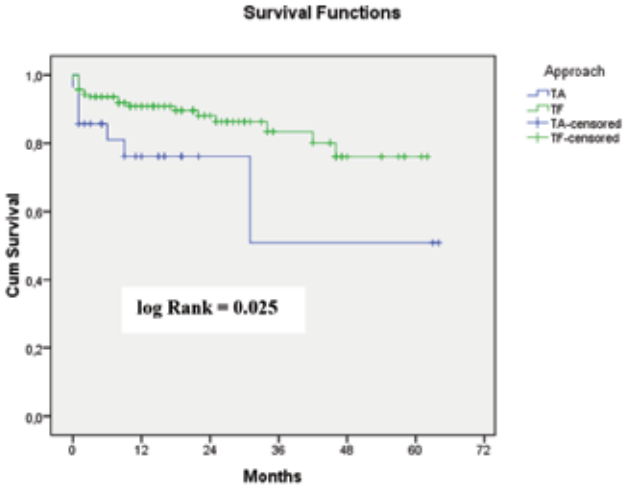
Abbreviations: *CVI/TIA*, cerebrovascular insult/ transient ischemic attack; *COPD,* chronic obstructive pulmonary disease; *CABG,* coronary artery bypass graft; MVR, mitral valve replacement; *AVA,* aortic valve area; *LVEF,* left ventricular ejection fraction; *TAVI,* transcatheter aortic valve replacement; SPAP, Systolic pulmonary artery pressure

Periprocedural complications

Periprocedural complications are summarized in Table 2. Procedural related death (30 days) occurred in 8 patients (5 %) because of annulus rupture during the procedure (n = 1), hemorrhagic shock due to vascular perforation (n = 1) and retroperitoneal bleeding (n = 1), aortic rupture (n = 2), myocardial infarction (n = 1) and sepsis of pulmonary and urologic origo (n = 2).

In our series we observed 14 (8%) surgical complications, mostly involving the access site (1 arteriovenous fistula, 9 pseudoaneurysm requiring surgical treatment), 2 cases involved vascular injury (1 internal iliac artery dissection, 1 femoral artery rupture) and 2 cases of cardiac tamponade (1 because of left ventricular perforation). All surgical interventions were successful.

The most common complications were related to vascular damage that resulted in minor bleeding and were more common in transfemoral approach. There were no other significant differences in periprocedural complications between transfemoral and transapical site of implantation.



Pt at risk

Transfemoral	143	88	50	25	10	4
Transapical	28	13	3	2	2	2

Figure 1. 5-year outcome after transcatheter aortic valve implantation. Kaplan Meier analysis between transfemoral (TF) and transapical (TA) site of percutaneous valve implantation.

Table 2. Periprocedural complications in overall TAVI, transfemoral and transapical population and comparison between transfemoral and transpical site of valve implantation.

Periprocedural complications	Overall TAVI (n = 171)	Tranfemoral (n = 143)	Transapical (n = 28)	P (TF vs. TA)
LBBB, n (%)	12 (7)	12 (8)	0	0.112
RBBB, n (%)	1 (0.6)	1 (0.7)	0	0.657
AV grade I., n (%)	5 (3)	5 (3)	0	0.315
PM, n (%)	14 (8)	13 (9)	1 (4)	0.330
Moderate PVL, n (%)	17 (10)	17 (12)	0	0.055
Moderate-severe PVL, n (%)	0	0	0	
Severe PVL, n (%)	0	0	0	
Surgical complication, n (%)	14 (8)	14 (10)	0	0.084
CVI, n (%)	3 (2)	3 (2)	0	0.439
AMI, n (%)	10 (6)	1 (0.7)	0	0.657
Life threatening bleeding, n (%)	8 (5)	7 (5)	1 (4)	0.762
Major bleeding, n (%)	7 (4)	6 (4)	1 (4)	0.879
Minor bleeding, n (%)	23 (13)	23 (16)	0	0.023
Major vascular complication, n (%)	5 (3)	4 (3)	1 (4)	0.824
Minor vascular complication, n (%)	11 (6)	11 (8)	0	0.129
Acute kidney failure, n (%)	2 (1)	1 (0.7)	1 (4)	0.196
Death in 30 days, n (%)	8 (5)	5 (3)	3 (11)	0.098

Abbreviations: LBBB, left bundle branch block; RBBB, right bundle branch block; AV, atrioventricular; PM, pacemaker, PVL, paravalvular leak; CVI, cerebrovascular insult; AMI, acute myocardial infarct.

Follow up and mortality

Long-term follow-up was evaluated using Kaplan Meier analysis. We did observe a statistically significant survival benefit in the group where TAVI was implanted via transfemoral compared to transapical approach. (Log Rank = 0.025) (Figure 1).

Discussion

Procedural related complications

Percutaneous techniques are less invasive treatment options designed to relief symptoms and improve prognosis in comorbid, high-risk patients who are not surgical candidates. Despite being less invasive, TAVI carries potential procedural related risks that differ from those associated to SAVR and might be related to the site of percutaneous valve implantation. TAVI related complications include valve malpositioning, valve migration or embolization, conversion to open surgery, renal failure, need for pacemaker implantation, stroke, myocardial infarction, major or life threatening bleeding and other major complications.

In our series of 171 TAVI patients, we compared the complication rate between transfemoral and transapical approach**.**

Patient selection

Transfemoral approach is preferred and always selected, when the diameter of pelvic arteries is suitable. Our second selection is transaortic approach. Just in case of ascending aorta calcifications at the excess site we select transapical approach. Transapical approach was performed under general anesthesia with direct access to the left ventricle apex through an intercostal mini-thoracotomy or mini sternothomy in case of direct aortic approach. No cardiopulmonary bypass was needed. The analysis of baseline patient's characteristics in our TAVI group had shown that the patients selected for transapical approach suffered more often for generalized atherosclerosis that was demonstrated with higher incidence of coronary artery disease and carotid stenosis, similar to observations in other studies[17].

Stroke

The most frequent etiology of procedural stroke is likely to be atheroembolism from the ascending aorta or the aortic arch. Other potential causes include calcific embolism from the aortic valve, thromboembolism from catheters, prolonged hypotension, and dissection of arch vessels[18]. The incidence of stroke varies and rate ranges from 0% to 10% in the published reports as the consequence of the learning curve, the evolution in technique, and equipment but also the completeness of neurologic assessment[6, 19-22]. Some authors have suggested that stroke risk might be lower with transapical access due to less manipulation within the aortic arch, but this has not been a universal finding[6, 21]. In our series of transapical patients, we did not observe any stoke comparing to 3 cases (2 %) in the transfemoral group. Because of a small number of patients in the transapical group, the difference was not statistically significant.

Paravalvular aortic regurgitation

In the literature, some studies report higher paravalvular aortic regurgitation rates after transfemoral approach[23-25] and other studies no difference between the techniques[17]. In our study, it appears that the paravalvular regurgitaion is less common after transapical approach but the finding is not statistically significant. The degree of paravalvular leak in all cases was not severe and should not influence the long-term outcome. We observed the reduction of paravalvular leaks rate in case of direct valve implantation. The rate of post dilatation of the valves was less than 30%.

New pacemaker

In our study there were no significant differences in the requirement for a pacemaker between the transfemoral and transapical techniques, what has been also confirmed in the literature. It has been shown that the type of implanted valve is correlated with a pacemaker implantation rate[26]. In our registry, pacemaker implantation rate was 5% and 18% for Edwards and CoreValve, respectively. The pacemaker implantation rate might be explaint by TAVI devices structure, implantation technic and characteristics of natural anatomy and calcification distribution.

Renal failure

Acute kidney injury is one of the most serious complications following TAVI due to its strong impact on short- and long-term mortality. Renal failure requiring dialysis appears to be more frequent with the transapical than with transfemoral approach[17]. In our study, we did not notice a statistically significant difference in acute kidney failure between the two procedures.

Vascular complications

We confirmed that transfemoral approach is associated with higher vascular complications compared to transapical approach as reported in most of the published series[33-36]. Most of the complications were resolved with blood transfusions or vascular surgery. There is a trend toward reduction of the vascular complications in the last performed TAVI procedures due to the improvement of delivery system with reduction of the sheath size and development of arterial closure devices[37]. Better patient selection by using preoperative imaging[37] may also contribute to reduction of the complications rate. In the last 54 transfemoral cases we used percutaneous closure device (ProStar, Abbott, USA) in 85% of cases with a success rate of 91%.

Long-term follow-up

We did observe a statistically significant survival benefit in the group where TAVI was implanted via transfemoral compared to transapical approach. One of the studies in the literature confirmed our flinging [33], the other did not observe any difference in long-term survival comparing the two sites of implantation[17]. In our case, the population of the patients for different approaches was not the same. Usually the patients, which are not suitable for transfemoral approach, have general atherosclerosis and therefore higher operative and mortality risk.

Conclusion

TAVI is a feasible alternative to SAVR in selected, high-risk patients with severe, symptomatic aortic stenosis. Knowing the benefits and the risks of this developing procedure, will likely improve the selection of the proper candidates based also on the preexisting morbidities. On the other hand, knowing the possible procedure-related complications is crucial for the development of better devices and improving the implantation procedure. Future clinical studies need to focus on individualizing each specific valve and access route to each patient's anatomy and general condition.

References

1. Vahanian A, Alfieri O, Andreotti F, et.al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Cardiothorac Surg 2012; 42(4): 1-44.
2. Nishimura RA, Otto CM, Bonow RO, et.al.; ACC/AHA Task Force Members. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.Circulation 2014; 129(23): 2440-92.
3. Smith CR, Leon MB, Mack MJ, et.al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011; 364(23): 2187-98.
4. Kempfert J, Rastan A, Holzhey D, et al. Transapical aortic valve implantation: analysis of risk factors and learning experience in 299 patients. Circulation 2011; 124(11): 124-9.
5. Rodes-Cabau J. Transcatheter aortic valve implantation: current and future approaches. Nature Reviews Cardiology 2012; 9(1): 15-29.
6. Webb JG, Altwegg L, Boone RH, et al. Transcatheter aortic valve implantation: impact on clinical and valve-related outcomes. Circulation 2009; 119(23): 3009-16.
7. Bande M, Michev I, A. Sharp SP, et al. Percutaneous transcatheter aortic valve implantation: past accomplishments, present achievements and applications, future perspectives. Cardiology in Review 2010; 18(3): 111-24.
8. Baumgartner H, Hung J, Bermejo J, et.al; EAE/ASE. Echocardiographic assessment of valve stenosis: EAE/ASE racommendations for clinical practice. Eur J Echocardiogr 2009; 10(1): 1-25.
9. Delgado V, Ewe SH, Ng AC et al. Multimodality imaging in transcatheter aortic valve implantation: key steps to assess procedural feasibility. EuroIntervention 2010; 6: 643–652.
10. Schoenhagen P, Numburi U, Halliburton SS et al. Three-dimensional imaging in the context of minimally invasive and transcatheter cardiovascular interventions using multi-detector computed tomography: from pre-operative planning to intra-operative guidance. Eur Heart J 2010; 31: 2727–40.
11. Schultz CJ, Moelker A, Piazza N et al. Three dimensional evaluation of the aortic annulus using multislice computer tomography: are manufacturer's guidelines for sizing for percutaneous aortic valve replacement helpful? Eur Heart J 2010; 31: 849–856.
12. Kaleschke G, Seifarth H, Kerckhoff G et al. Imaging decision-making for transfemoral or transapical approach of transcatheter aortic valve implantation. EuroIntervention 2010; 6: G20–G27.
13. Ye J, Cheung A, Lichtenstein SV, et al. Transapical aortic valve implantation in humans. J Thorac Cardiovasc Surg 2006; 131: 1194–6.

14. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006; 113: 842–50.
15. Grube E, Laborde JC, Gerckens U, et al. Percutaneous implantation of the CoreValve self-expanding valve prosthesis in high-risk patients with aortic valve disease: the Siegburg First-In-Man study. Circulation 2006; 114: 1616 –24.
16. Leon MB, Piazza N, Nikolsky E, et.al. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the Valve Academic Research Consortium. Eur Heart J 2011; 32(2): 205-17).
17. Schymik G, Würth A, Bramlage P et al. Long-term results of transapical versus transfemoral TAVI in a real world population of 1000 patients with severe symptomatic aortic stenosis. Circ Cardiovasc Interv 2014 Dec 31;8(1).
18. Berry C, Cartier R, Bonan R. Fatal ischemic stroke related to non permissive peripheral artery access for percutaneous aortic valve replacement. Catheter Cardiovasc Interv 2007; 69: 56–63.
19. Walther T, Falk V, Kempfert J, et al. Transapical minimally invasive aortic valve implantation; the initial 50 patients. Eur J Cardiothorac Surg 2008; 33: 983– 8.
20. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. J Am Coll Cardiol 2007; 50: 69 –76.
21. Walther T, Simon P, Dewey T, et al. Transapical minimally invasive aortic valve implantation: multicenter experience. Circulation 2007; 116: I240 –5.
22. Cribier A, Eltchaninoff H, Tron C, et al. Treatment of calcific aortic stenosis with the percutaneous heart valve: mid-term follow-up from the initial feasibility studies: the French experience. J Am Coll Cardiol 2006; 47: 1214 –23.
23. Ewe SH, Delgado V, Ng AC, et al. Outcomes after transcatheter aortic valve implantation: transfemoral versus transapical approach. Ann Thorac Surg 2011; 92: 1244-51.
24. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis. J Am Coll Cardiol 2011; 58: 2130-8.
25. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic-valve implantation in high risk patients. N Engl J Med 2012; 366: 1705-15.
26. Thomas M, Schymik G, Walther T, et al. Thirty-day results of the SAPIEN aortic Bioprothesis European Outcome (SOURCE) Registry: A European registry of transcatheter aortic valve implantation using the Edwards SAPIEN valve. Circulation 2010;122:62-9.
27. Lefèvre T, Kappetein AP, Wolner E, et al. One year followup of the multi-center European PARTNER transcatheter heart valve study. Eur Heart J 2011; 32:148-57.
28. Moat NE, Ludman P, de Belder MA, et al. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis. J Am Coll Cardiol 2011; 58:2130-8.
29. Gilard M, Eltchaninoff H, Iung B, et al. Registry of transcatheter aortic-valve implantation in high risk patients. N Engl J Med 2012; 366:1705-15.
30. Svensson LG, Dewey T, Kapadia S, et al. United States feasibility study of transcatheter insertion of a stented aortic valve by the left ventricular apex. Ann Thorac Surg 2008; 86:46 –55.
31. Walther T, Falk V, Kempfert J, et al. Transapical minimally invasive aortic valve implantation; the initial 50 patients. Eur J Cardiothorac Surg 2008; 33:983– 8.
32. M. Johansson, S. Nozohoor, P. O. Kimblad, J. Harnek, G. K. Olivecrona, and J. Sjgren. Transapical versus transfemoral aortic valve implantation: a comparison of survival and safety. Ann Thorac Surg. 2011; 91(1):57-63.
33. M. Z. Khawaja, M. Sohal, H. Valli et al. Standalone balloon aortic valvuloplasty: indications and outcomes from the UK in the transcatheter valve era. Catheter Cardiovasc Interv. 2013;81(2):366-73.
34. K. Hayashida, T. Lef` evre, B. Chevalier et al. True percutaneous approach for transfemoral aortic valve implantation using the Prostar XL device: impact of learning curve on vascular complications. JACC Cardiovasc Interv. 2012; 5(2):207-14.
35. Ben-Dor, A. D. Pichard, L. F. Satler et al. Complications and outcome of balloon aortic valvuloplasty in high-risk or inoperable patients. JACC Cardiovasc Interv. 2010; 3(11):1150-6.
36. H. Eltchaninoff, A. Prat, M. Gilard et al. Transcatheter aortic valve implantation: early results of the FRANCE (FRench Aortic National CoreValve and Edwards) registry. Eur Heart J. 2011; 32(2):191-7.
37. V.Stratiev,P.Guyon,E.Teiger,andJ.P.Collet. Reducingthe risk of vascular complications during percutaneous aortic valve replacement. Ann Cardiol Angeiol (Paris). 2012; 61(4):281-6.

Srce i krvni sudovi 2015; 34(1):24-28

Originalni rad

Endovascular treatment of severe aortic stenosis in high and intermediate surgical risks patients

Kochkina KV[1], Shtark AA[2], Protopopov AV[3]

Regional State Clinical Hospital; Krasnoyarsk Medical University by the name of prof. V.F. Voino-Yasenetckiy, Krasnoyarsk, Russia

[1]Kochkina KV, Invasive Cardiology Department, Krasnoyarsk State Clinical Hospital

[2]Shtark AA, Cardiac surgery department, Krasnoyarsk State Clinical Hospital

[3]Protopopov AV, PhD, Head of the Invasive Cardiology department, State Clinical Hospital, professor of Radiology faculty of postdoc education of Krasnoyarsk Medical University by the name of prof. V.F. Voino-Yasenetcki

Abstract

Aims. To evaluate the safety and efficacy of transcatheter aortic valve replacement with CoreValve bioprothesis in patients with severe aortic stenosis in high and intermediate surgical risk.

Methods and results. Data was prospectively collected from 81 patients with severe aortic stenosis, who underwent CoreValve implantation in one centre. After risk stratification 38 patients (46.9%) were at high risk (STS score >8%). In 43 cases (53.1%) patients were at intermediate STS score (STS score >3 and <8%), but due to different coexisting characteristics patients were not candidates for surgery. Technical success was achieved in all cases. All-cause hospital mortality was 6.2% (5 cases) generally, without statistical difference between two groups (10.5% in high risk group, 4 patients; 2.3% in intermediate group, 1 patient). In two patients post-operation period was complicated by stroke (1 minor stroke, 1 major stroke; 2.5±1.7% of cases); in one case acute myocardial infarction developed 6 hours post CoreValve implantation (1.2%); in one case acute renal failure developed, leading to death of the patient. No significant differences in cerebrovascular accidents and myocardial infarction between the different risk groups were observed throughout hospital period. During three years 56 patients (72±5,0%) were available for follow up. Two patients died during follow-up: one patient died due to cancer progression (23 months after the implantation), one due to progression of chronic kidney insufficiency (18 months after implantation). No cerebrovascular or cardiac accidents were observed during follow up period.

Conclusion. In selected patients with intermediate surgical risk TAVR procedure with the use of CoreValve system have good clinical outcomes in hospitalisation period and long-term follow-up.

Key words Severe aortic stenosis, self-expanding valve, STS score risk evaluation.

Abbreviations

BMI = body mass index;
CT = computer tomography;
PCI = percutaneous coronary intervention;
STS = Society of Thoracic Surgeons;
TAVR = transcatheter aortic valve replacement;
TEE = transesophageal echocardiography

Introduction

Aortic stenosis is the most common valvular heart disease, which affects 2-4% of individuals older 65 years in USA and performs 43% of all valvular heart diseases in Europe[1]. Aortic stenosis increase in incidence with age, so one in eight people over the age of 75 have moderate to severe aortic valve disease[2]. Regarding the population aging, this condition becomes a serious public health problem. Medical management of severe aortic stenosis is a suboptimal strategy, may provide temporary symptom relief but is not effective long term[3]. Surgical aortic valve replacement is a gold standard recommended treatment, but patients with severe symptoms have been found to have a significantly higher operative mortality than those with no or only mild symptoms[4]. The use of a bioprosthetic valves can be an opportunity in treatment of elderly patients with severe stenosis (<0.6 cm^2) or severe left ventricular dysfunction[5-6]. Approximately 30% of the patients with severe symptoms and coexisting conditions are not candidates for surgery[7-9]. Endovascular treatment of severe aortic stenosis - transcatheter aortic valve replacement (TAVR) proved to be

Address for correspondence: Protopopov AV, PhD, Head of the Invasive Cardiology department, State Clinical Hospital, professor of Radiology faculty of postdoc education of Krasnoyarsk Medical University by the name of prof. V.F. Voino-Yasenetckiy. 660022, Krasnoyarsk, P. Zheleznyaka street, 3A. aprotopopov@yandex.ru +73912201577

effective and safe treatment in a group of inoperable and high-risk for surgery operation patients[10-12] since 2002, when the procedure was first performed[13-14]. Patients, undergoing TAVR procedure usually in advanced age, with serious comorbidity conditions (Logistic EuroSCORE> 20%), and with contra indications to open surgery[15-18]. 30-days mortality rate is reported on 5-20% level; myocardial infarction observed in 2-11% of cases, stroke in 3-9%, other vascular complications in 10-15% and AV-block in 4-30% of the patients. Mild to moderate paravalvular aortic valve regurgitation is present almost in half of the patients. The survival rate for 1 year with the use of transfemoral approach is 80-90%[19-20].

Bioprosthesys CoreValve (Medtronic, USA) is a representative of third generation of artificial aortic valves for endovascular implantation. It is manufactured by suturing 3 valve leaflets and a skirt, made from a single layer of porcine pericardium, onto a self-expanding, multi-level, radiopaque frame made of Nitinol. It can be implanted from femoral, left subclavian, axillar approach. TAVR procedure with CoreValve system is performed in cathlab or hybrid room, by physicians who have received Medtronic CoreValve™ training, under TEE guidance and under general anesthesia.

The aim of the study is clinical-functional analysis of immediate and long-term results of TAVR with the use of CoreValve transcatheter aortic valve in patients with severe aortic stenosis at high and intermediate surgical risk as defined by a Society of Thoracic Surgeons (STS) risk score[21].

Methods

Data was prospectively collected in the period 2011-2014 from 81 TAVR cases on the base of cardio-vascular center of Regional Clinical Hospital. Patients had severe aortic stenosis and cardiac symptoms for whom conventional surgery to replace the aortic valve was associated with high risk, or low risk in combination with contraindications for surgery. Two patients (2.5%) had additional severe aortic regurgitation. In four cases combined valve disease was present: severe aortic stenosis and mild mitral stenosis. Two patients had relative contra indication for TAVR procedure – bicuspid aortic valve. All patients underwent precise evaluation for TAVR procedure with the use of CT angiography, echocardiography (transesophageal echo was used, if visualization on transthoracic echo was not appropriate), aortography in selected cases. Risk for surgical procedure was evaluated using STS risk score. Decision to a transcatheter or surgical strategy was made by heart team, that includes interventional cardiologist, cardiac surgeon, anesthesiologist and additional specialists in the case of pertinent comorbidities (nephrologist, endocrinologist). Written informed consent was obtained in all cases prior to the procedures.

In our center all TAVR cases are performed under general anesthesia, under TEE guidance during all the procedure.

All procedures were performed with transfemoral access. Four patients underwent access site closure with the Perclose device (Abbott Vascular Devices, Santa Clara, CA, USA) using pre-closure technique. In 77 cases standard arterial surgical cut-down was used, due to calcification (48 patients) and obesity (28 patients with BMI>30). According to the standard recommendations at the time of the procedure, patients were treated with 100 mg of acetylsalicylic acid, a 600 mg loading dose of clopidogrel, and unfractionated heparin 70-100 U/kg.

After TAVR procedure patients were followed up at 1, 6, 12 months and once a year after 12th months by means of a clinical visit or a standardized telephone interview. In the case of necessity additional hospital visit was administrated. Control TTE was performed every 6 months after the CoreValve implantation to assess valve function, peri-device flow and general echo parameters.

Results

All 81 patients were available for follow-up. Technical success was achieved in all cases. After risk stratification 38 patients (46.9%) were at high risk (STS score >8%). In 43 cases (53.1%) patients were at intermediate STS score (STS score ≥3 and ≤8%), but due to different coexisting characteristics patients were not candidates for surgery (Table 1).

Table 1. Patients, refused for surgery with low and intermediate STS score.

Coexisting condition	Value
Patients, refused for surgery, n (%)	43 (53.1)
Porcelain aorta, n (%)	27 (62.8)
Chest-wall irradiation, n (%)	11 (25.6)
Chest-wall deformation, n (%)	2 (4.7)
Frailty, n (%)	2 (4.7)
Mental health features, n (%)	1 (2.3)

Patients in high risk group were significantly older, with lower body mass index, but in both groups prevalence of arterial hypertension was very high (>95%) (Table 2). Significant symptoms of heart failure (NYHA III-IV) were prevalent in high risk group (76.3% vs. 34.9%, p=0.03). Chronic obstructive pulmonary disease and renal failure were also more prevalent in high risk patients. In past medical history there was no difference in frequency of myocardial infarction, coronary arteries interventions between two groups, but high risk patients had more previous strokes (31.6% vs. 4.7%, p=0.006). Left ventricular ejection fraction was higher among intermediate risk patients (58±2.16 vs. 49.8±13.3, p<0.001). No difference in echocardiographic variables were find between two groups, mean aortic valve gradient was 45.2±14.7 mmHg in high risk patients and 44.7±13.9 mmHg in intermediate risk group (p=0.04); aortic valve area was 0.6±0.3 cm^2 in high risk patients and 0.6±0.2 cm^2 in intermediate patients (p=0.7).

Significant coronary arteries disease was diagnosed in 57.9% in high risk group and in 41.9% in intermediate group (p=0.26, 40 patients in both groups). The decision about the time of the revascularisation (simultaneous or

Table 2. Clinical characteristics, echo findings.

Characteristic	High risk group (38 patients)	Intermediate risk group (43 patients)	p
Age, years	82.6±6.6	74.8±8.4	p<0.001
Male, n (%)	18 (47.4)	23 (53.5)	p=0,19
BMI (kg/m^2)	23.9±5.4	29.2±5.8	p<0.001
STS score	10.2±2.1	4.1±1.8	p<0,001
Diabetes Mellitus	13 (34.2)	8 (18.6)	p=0,16
Arterial hypertension	37 (97.4)	41 (95.3)	p=0,53
Hypercholesterolemia	25 (65.8)	24 (60.1)	P=0,39
Heart Failure (NYHA III – IV), n (%)	29 (76.3)	15 (34.9)	p=0,03
Coronary arteries disease	22 (57.9)	18 (41.9)	p=0,26
Prev. Myocardial infarction	4 (10.5)	5 (11.6)	
Coronary arteries interventions – total number (%) CABG PCI	 1 (2.6) 21 (55.3)	 0 18 (41.9)	 p=0,47 p=0,3
Peripheral Vascular disease, n (%)	13 (34.2)	10 (23.3)	p=0,28
COPD (any)	15 (39.5)	5 (11.6)	p=0,02
Chronical kidney disease	17 (44.7)	3 (6.9)	p=0,001
Cancer	5 (13.2)	12 (27.9)	p=0,04
Atrial fibrillation	10 (26.3)	11 (25.5)	p=0,57
Permanent pacemaker	4 (10.5)	3 (7.0)	p=0,44
Previous stroke	12 (31.6)	2 (4.7)	p=0,006
Echocardiography characteristics: Mean aortic-valve gradient, mm Hg Aortic-valve area, (cm^2) Pulmonary hypertension, n(%) Mitral regurgitation (moderate to severe)	 45.2±14.7 0.6±0.3 14 (36.8) 8 (21.1)	 44.7±13.9 0.6±0.2 13 (30.2) 9 (20.9)	 p=0,4 p=0,7 p=0,41 p=0,6
EF, % ±SD	49.8±13.3	58±2.16	p<0,001

staged procedure) was made individually in every patient, considering the significance of lesion and clinical condition. In 82.5% (33 patients) – PCI was performed at the time of diagnostic (ad-hock procedure) or before 1 month-2 weeks before planned TAVR, and in 17.5% of cases (7 patients) simultaneous PCI and TAVR was performed.

Post TAVR—need for permanent pacemaker was at the same for both groups – in 9 patients in high risk group (23.7%), in 10 patients in intermediate group (23.3%, p=0.58).

All-cause hospital mortality was 6.2% (5 cases) generally, without statistical difference between two groups, probably due to the small amount of patients (10.5% in high risk group, 4 patients; 2.3% in intermediate group, 1 patient). In two patients post-operation period was complicated by stroke (1 minor stroke, 1 major stroke; 2.5±1.7% of cases); in one case acute myocardial infarction developed 6 hours post CoreValve implantation (1.2%); in one case acute renal failure developed, leading to death of the patient. No significant differences in cerebrovascular accidents and myocardial infarction between the different risk groups were observed throughout hospital period. During three years 56 patients (72±5,0%) were available for follow up. Two patients died during follow-up: one patient died due to cancer progression (23 months after the implantation), one due to progression of chronic kidney insufficiency (18 months after implantation). No cerebrovascular or cardiac accidents were observed during follow up period.

Discussion

The performed analysis is based on a single-centre experience with patients undergoing TAVR in high and intermediate surgical risks, with the use of CoreValve self-expanding system. All patients, included in analysis, were precisely discussed by heart team of our multidisciplinary hospital. The risk for surgical aortic valve replacement was counted with the use of STS score, as the most exact predictor of outcome, as it was recognised, that the logistic EuroSCORE overestimates the risk for adverse clinical outcomes[22]. In big randomized trials, such as SURTAVI, STS score was chosen for risk evaluation of the patients[23]. Several conditions, such as porcelain aorta, chest wall irradiation or deformation, frailty making intermediate and low surgical patients contra-indicated for surgery. These factors are always discussed by a heart team, for choosing the appropriate treatment strategy. According to contemporary practice in Europe[24], intermediate risk patients were included to our analysis. In several single-centre and multi-centre studies patients in low surgical risks were also included[24-25].

All cause death in our centre was 6.2% for all patients, which is similar to analysis, performed by Wenaweser et. al.[26], where all cause death was 6.4%. But in these study, patients were divided in three

Table 3. Clinical outcomes at 30 days

Hospitalization period	All patients (81 patients)	High risk group (38 patients)	Intermediate risk group (43 patients)	p
All cause death, n (%)	5 (6.2)	4 (10.5)	1 (2.3)	0.16
Minor stroke, n (%)	1 (1.2)	1 (2.6)	0 (0)	0.47
Major stroke, n (%)	1 (1.2)	0 (0)	1 (2.3)	0.53
Myocardial infarction, n (%)	1 (1.2)	0 (0)	1 (2.3)	0.53
Acute renal failure, n (%)	1 (1.2)	1 (2.6)	0 (0)	0.47
Access cite complications, n (0)	0 (0)	0 (0)	0 (0)	

groups: low, intermediate and high risk patients. All cause mortality rate was lower in low risk patients and intermediate risk patients compared with high risk group. In our experience, statistically significant difference between intermediate and high risk patients was not achieved (p=0.16), probably because of small amount of patients. All-cause death during hospitalisation was observed on a rate 2.3%, what can be considered as a good result of implantation. Long-term results in intermediate group were not worse, compare with high risk group. We consider, that selected patients with intermediate surgical risk will have good clinical outcomes in hospitalisation period and long-term follow-up. Randomized trials, PARTNER II and SURTAVI should be completed, to prove, that TAVR procedure can be preferred for patients with intermediate surgical risk.

References

1. Singh IM, Shishehbor MH, Christofferson RD, Tuzcu EM, Kapadia SR. Percutaneous treatment of aortic valve stenosis. Clevel Clin J Med 2008 (11):805-812.
2. Nkomo VT, Gardin JM, Skelton TN, et al. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005-1011.
3. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G, Baumgartner H, et al. Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J 2012;33(19):2451-2496.
4. Society of Thoracic Surgeons. STS national database: STS U.S. cardiac surgery database: 1997, Aortic valve replacement patients: preoperative risk variables. Chicago: Society of Thoracic Surgeons, 2000. http://www.ctsnet.org/doc/3031.
5. Bonow RO, Carabello BA, Kanu C, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing committee to revise the 1998 Guidelines for the Management of Patients With Valvular Heart Disease): developed in collaboration with the Society of Cardiovascular Anesthesiologists: endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. Circulation 2006;114:e84-231.
6. Vahanian A, Baumgartner H, Bax, et al. Guidelines on the management of valvular heart disease: the Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology. Eur Heart J 2007;28:230-68.
7. Iung B, Cachier A, Baron G, et al. Decision-making in elderly patients with severe aortic stenosis: why are so many denied surgery? Eur Heart J 2005;26:2714-2720.
8. Varadarajan P, Kapoor N, Bansal RC, Pai RG. Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis. Ann Thorac Surg 2006;82:2111-2115.
9. Bach DS, Siao D, Girard SE, Duvernoy C, McCallister BD Jr, Gualano SK. Evaluation of patients with severe symptomatic aortic stenosis who do not undergo aortic valve replacement. Circ Cardiovasc Qual Outcomes 2009;2:533-539.
10. Tom Kai Ming Wang, Janarthanan Sathananthan,Nicholas Chieng, et al. Aortic valve replacement in over 70- and over 80-year olds: 5-year cohort study. Asian Cardiovascular & Thoracic Annals 2014; 22(5) 526–533.
11. Thomas Pilgrim, Lars Englberger, Martina Rothenbühler, et al. Long-term outcome of elderly patients with severe aortic stenosis as a function of treatment modality. Heart 2014; 56:1-7.
12. Josep Rodés-Cabau, MD; John G. Webb, MD; Anson Cheung, MD, et al. Transcatheter Aortic Valve Implantation for the Treatment of Severe Symptomatic Aortic Stenosis in Patients at Very High or Prohibitive Surgical RiskAcute and Late Outcomes of the Multicenter Canadian Experience. J Am Coll Cardiol 2010;55(11):1080-1090.
13. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006-3008.
14. Cribier A, Eltchaninoff H, Tron C, et al. Early experience with percutaneous transcatheter implantation of heart valve prosthesis for the treatment of end-stage inoperable patients with calcific aortic stenosis. J Am Coll Cardiol 2004;43:698-703.
15. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. J Am Coll Cardiol 2007;50:69-76.
16. Lichtenstein SV, Cheung A, Ye J, et al. Transapical transcatheter aortic valve implantation in humans: initial clinical experience. Circulation 2006;114:591-596.
17. Ye J, Cheung A, Lichtenstein SV, et al. Six-month outcome of transapical transcatheter aortic valve implantation in the initial seven patients. Eur J Cardiothorac Surg 2007;31:16-21.
18. Walther T, Falk V, Kempfert J, et al. Transapical minimally invasive aortic valve implantation; the initial 50 patients. Eur J Cardiothorac Surg 2008;33:983-8.
19. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. Circulation 2006;113:842-50.
20. Grube E, Schuler G, Buellesfeld L, et al. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patients using the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. J Am Coll Cardiol 2007;50:69-76.
21. Shroyer AL, Coombs LP, Peterson ED, et al. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. Ann Thorac Surg 2003;75:1856-1864.
22. Piazza N, Wenaweser P, van Gameren M, Pilgrim T, Tzikas A, Otten A, Nuis R, Onuma Y, Cheng JM, Kappetein AP, Boersma E, Juni P, de Jaegere P, Windecker S, Serruys PW. Relationship between the logistic EuroSCORE and the Society of Thoracic Surgeons Predicted Risk of Mortality score in patients implanted with the CoreValve ReValving system—a Bern-Rotterdam Study. Am Heart J 2010;159:323-329.
23. van Mieghem NM, Head SJ, van der Boon RM, Piazza N, de Jaegere PP, Carrel T, Kappetein AP, Lange R, Walther T, Windecker S,

van Es GA, Serruys PW. The SURTAVI model: proposal for a pragmatic risk stratification for patients with severe aortic stenosis. EuroIntervention 2012;8:258-266.
24. Lange R, Bleiziffer S, Mazzitelli D, Elhmidi Y, Opitz A, Krane M, Deutsch MA, Ruge H, Brockmann G, Voss B, Schreiber C, Tassani P, Piazza N. Improvements in transcatheter aortic valve implantation outcomes in lower surgical risk patients: a glimpse into the future. J Am Coll Cardiol 2012;59:280- 287.
25. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, Thomas M, Kovac J, Spyt T, MacCarthy PA, Wendler O, Hildick-Smith D, Davies SW, Trivedi U, Blackman DJ, Levy RD, Brecker SJ, Baumbach A, Daniel T, Gray H, Mullen MJ. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. J Am Coll Cardiol 2011;58:2130–2138.
26. Clinical outcomes of patients with estimated low or intermediate surgical risk undergoing transcatheter aortic valve implantation.Wenaweser P, Stortecky S, Schwander S, Heg D, Huber C, Pilgrim T, Gloekler S, O'Sullivan CJ, Meier B, Jüni P, Carrel T, Windecker S. Eur Heart J 2013;34(25):1894-905.

Srce i krvni sudovi 2015; 34(1):29-32

Originalni rad

Prevention of adverse ischemic events with Watchman device in non-valvular patients with atrial fibrillation and contraindications for long-term anticoagulation therapy

Kochkina KV[1], Protopopov AV[2]

Regional State Clinical Hospital, Medical University by the name of prof. V.F. Voyno-Yasenetckiy, Krasnoyarsk, Russian Federation

[1]Kochkina KV, Invasive Cardiology Department, Krasnoyarsk State Clinical Hospital, 660022, Krasnoyarsk

[2]Protopopov AV, PhD, Krasnoyarsk Medical University by the name of prof. V.F. Voyno-Yasenetckiy 660022, Krasnoyarsk, P. Zheleznyaka street, 3A. aprotopopov@yandex.ru

Abstract

Aims. To evaluate efficacy and safety of endovascular occlusion of left atrial appendage (LAA) with Watchman device in patients, contraindicated for long-term anticoagulant therapy

Methods and Results. Watchman device implantation performed in 37 patients with non-valvular AF, CHA2DS2VASc score >2 (mean 4.73±1.15), HAS-BLED>3 (mean 3.84±0.76), with contraindications for long-term anticoagulation therapy, with > 6 months follow-up period. Technical success was achieved in 94.6% (35 patients). Periprocedural complications were device embolization in 1 patient and pericardial effusion, requiring treatment. During 14.8±6.7 months follow-up neither haemorrhagic/ischemic stokes or TIA were observed.

Conclusion. The LAA occlusion with Watchman device can be safely performed in selected patients with contraindications to oral anticoagulation (OAC).

Key words: Atrial fibrillation, Left atrial appendage closure, Watchman device.

Abbreviations

AF = atrial fibrillation;
LAA = left atrial appendage;
TEE = transesophageal echocardiography;
OAC = oral anticoagulation;
PCI = percutaneous coronary intervention

Introduction

Atrial Fibrillation (AF) is the most common rhythm disorder with clinical symptoms and the number of affected patients enlarges every year[1]. Ischemic events are the most dangerous complications of AF, neurological disorders and deficits are more severe than those outcoming from non-AF stroke[2], and ischemic stroke associated with AF are nearly twice as likely to be fatal as non-AF stroke[3].

Anticoagulation therapy is recommended to all AF patients with high individual risk of ischemic complications, also in the case of successful cardioversion. Major bleeding is a serious complication in patients undergoing anticoagulant therapy, more frequent for elderly people[4]. 10% of AF patients have contraindications for anticoagulation therapy because of the high risk of bleeding[5] and optimal therapeutic range of the anticoagulant therapy is achieved only in 50% of the patients[6]. Endovascular occlusion of LAA, as the main place of life threatening thrombus formation during non-valvular AF, is an alternative, save and effective method of thromboembolic events prophylactic in patients, contraindicated for anticoagulation therapy.

In the article we present our experience in LAA occlusion with Watchman device for the patients with non-valvular AF and contraindications for life-long anticoagulation therapy.

Methods

In Krasnoyarsk Regional Clinical hospital 59 patients with AF and with high individual risk of stroke (CHA2DS2VASc>2) and high risk of bleeding complications (HAS-BLED>3) were examined as a candidates for LAA occlusion with Watchman device. All patients had contraindications for long-term anticoagulant therapy. TEE echo was performed in all cases to exclude LA or LAA thrombus, to evaluate LAA and intraatrial septum anatomy. In 1 patient there was a need for computed tomography, for precise evaluation of LAA anatomy. In 5 cases implantation of Watchman device was not possible due to anatomical characteristics. 2 patients had LAA consisted from 2 big lobes, in 1 patient LAA ostium

Address for correspondence: Protopopov AV, PhD, Head of the Invasive Cardiology department, State Clinical Hospital, professor of Radiology faculty of postdoc education of Krasnoyarsk Medical University by the name of prof. V.F. Voyno-Yasenetckiy 660022, Krasnoyarsk, P. Zheleznyaka street, 3A. aprotopopov@yandex.ru

was 32 mm and in 1 patient maximal LAA diameter was 15 mm. For available Watchman modification LAA should have a diameter from 16 to 32 mm, with an appropriate depth.

Implantation was not possible in 1 female patient hypersthenic type (BMI 31), because of absence of visualisation in supine position, although in standard TEE LAA was visualized in 0^0, 90^0 and 135^0.

Eventually 54 patients were scheduled for the LAA closure procedure. We perform the analysis of 37 patients, with >6 months follow-up period.

In our clinic we perform the procedure under general anaesthesia, with TEE and fluoroscopic control. In the case of presence persistent foramen ovale or atrial septal defect it was used for septal crossing, without septal puncture. Implantation was considered successful, if Watchman device was implanted to LAA with total exclusion of LAA from blood circulation and absence of significant residual flow around device. All adverse events during procedure, hospitalisation and follow-up period were registered.

If the patient was on warfarin before the procedure, it was cancelled 4 days before the implantation with transmission on LMH. If the patient was on clopidogrel, it was not cancelled. In the case of absence of anticoagulant or antithrombotic treatment, loading dose of clopidogrel was administered on the day of procedure, after implantation and control TTE in the evening time, with transmission to 75 mg of clopidogrel next day. On the day of procedure heparin was administered intravenously in a weight dose 100 U/kg after transseptal puncture or crossing to LA, to achieve recommended activated clotted time (ACT) 200-300 seconds. Every 30 minutes ACT control was performed, if it was less then 200 seconds additional boluses of intravenous heparin were administrated. Further anticoagulation regime was administrated individually for each patient, according to recommended protocols, eligibility or contraindications for treatment, possibility of INR checking. TTE was performed 6-12 hours after the procedure and before patient's discharge.

After device implantation, patients were followed up at 3, 6, 12 months and once a year after 12th months by phone call. In the case of necessity hospital visit was administrated. Control TEE was performed at 6-8 weeks after the implantation, 6 months and in selected cases 12 months after the procedure to assess device position, residual peri-device flow and device-related thrombus. After total endothelisation, absence of thrombus and peri-device flow warfarin/clopidogrel was cancelled, while aspirin treatment stayed life-long.

Results

The mean age of patients was 65.0±7 years, 20 from 37 (54%) were females (Table 1). Attempt to implant Watchman device was performed in 37 patients. In 35 cases procedure was successful (Table 2). In one case Watchman device was not implanted due to anatomical characteristics (multi lobes anatomy, not possible to precise evaluation by TEE). One case of device embolization occurred. Mean CHA_2DS_2VASc score was 4.73±1.15, so the risk of stroke in analysed group was very high. 70.3% of patients had stroke previously; 18.9% had TIA; 5,4% had systemic thromboembolism (thromboembolism of brachial artery, with surgical intervention). More than half of these patients with adverse thromboembolic events took warfarin, with adequate INR level 2-3 with 60-80% therapeutic range.

Serious device and procedure related events occurred in 2 cases (5.4%). In one case device embolization was observed, after device releasing from delivery system, in spite of satisfactory compression on TEE, and tug-test both on TEE and angiogram. Watchman device migrated to LV, where it fixed in posterior mitral leaflet chords. Patient was send to surgery. Device was retrieved and MACE procedure was performed. 2 weeks after patient was discharged from hospital in sinus rhythm with low dose of antiarrhythmic drugs. In a second case, LA perforation with delivery system hap-

Table 1. Clinical characteristics, stroke and bleeding risks.

Characteristic	Value
Age, years + SD	65.0±7
Female, n (%)	20 (54)
BMI (kg/m2)	26 (23-29)
AF type: Paroxysmal AF, n (%) Persistent AF, n (%)	 12 (32.4) 25 (67.6)
Arterial hypertension, n (%)	37 (100)
Diabetes mellitus, n (%)	3 (8.1)
Thromboembolic event, n (%): Stroke TIA Peripheral thromboembolism	 26 (70.3) 7 (18.9) 2 (5.4)
Coronary arteries disease, n (%)	12 (32.4)
Vascular disease, n (%)	5 (13.5)
Heart Failure (NYHA III – IV), n (%)	5 (13.5)
Bleeding events, n (%)	2 (5.4)
Labile INR, n (%)	18 (48.5)
CHA2DS2VASc score, ±SD CHA2DS2VASc score, n (%) 2 3 4 5 6 7 8 9	4.73±1.15 1 (2.7) 4 (10.8) 16 (43.2) 5 (13.5) 7 (18.9) 3 (8.1) 0 1 (2.7)
HAS-BLED score, ±SD	3.84±0.76
Antithrombotic/anticoagulant drugs, n (%) none aspirin aspirin+clopidogrel warfarin NOAC	 4 (10.8) 9 (24.3) 3 (8.1) 17 (45.9) 4 (10.8)
EF, % ±SD	58±2.16

Table 2. Procedure characteristics, device-related adverse events and outcomes.

Characteristic	Value
Time of the procedure, ±SD, min	51±26
Technical success, n (%)	35 (94.6)
Implant failure, n (%)	1 (2.7)
Air embolization, n (%)	0
Device embolization, n (%)	1 (2.7)
Pericardial effusion, n (%)	1 (2.7)
Stroke/TIA, n (%)	0
All cause death	0
Femoral hematoma/bleeding	0
Femoral pseudoaneurism	0

pened, operator made a decision to finish implantation of 33 mm Watchman occluder. Pericardial centesis was performed, 400 cc of blood was evacuated. Two days after patient was transferred from ICU to cardiology department, discharged 7 days after without complains.

All patients, that underwent implantation procedure where available for follow up. TEE was performed 6-8 weeks after the procedure and in 6 months. In 1 case residual flow (3 mm) persisted after 7 weeks from implantation, 6 months later residual flow was not observed (Figure 1). No cases of device embolization or thrombosis in post-operative period were observed.

Annual ischemic stroke rate was expected to be 6.1%, based on CHA_2DS_2VASc score between patients in

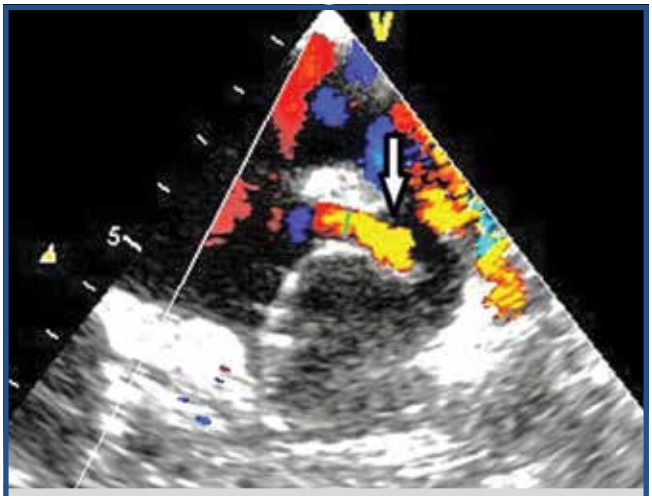


Figure 1. Persistent residual flow around Watchman device, 3 mm.

analyzed group. During 14.8±6.7 months follow-up period none of haemorrhagic/ischemic stokes or TIA were observed. During long-term follow up period 5 patients overcame open surgery, 2 patients now get combined treatment of oncological process (laringeal cancer, gastric cancer) The procedure of LAA closure, performed timely, dramatically decreased possible adverse thromboembolic events between these patients.

Discussion

In a group of the patients with non valvular AF, life-threating thrombus, causing stroke/TIA or systemic thromboembolism are formed in LAA in 90% of the cases[7]. Anticoagulant treatment is necessary for ischemic events prophylactic, but bleeding complications reduce frequency of admission of these treatment. Endovascular methods of LAA occlusion, as the main place of thrombus formation, got their fast development as a prophylactic method, with potentially lower risk of bleedings development.

Several devices for LAA occlusion are aloud to use in clinical practice. In Krasnoyarsk Regional Hospital we implant "Watchman LAA occlusion device" (Boston Scientific, USA), as the most examined, with efficacy, proved in several big randomised studies.

PROTECT-AF study, the only available randomized study, proved the efficacy of Watchman device, by demonstrating the noninferiority of the device-based prophylactic against standard anticoagulant therapy with warfarin. In additional safety end-points more adverse events were fixed in patients, undergoing device implantation – 5.5%[8]. In our clinical practice device-related safety events were observed in the same level – 5.4% (one device embolization with a need for surgical operation and one pericardial effusion due to LAA perforation). Significant decline in device/procedure related events with operator's experience was shown in CAP Registry (nonrandomized registry of patients undergoing Watchman implantation[9].

In an ESC Guidelines for the management of atrial fibrillation 2012, LAA percutaneous closure in patients with high stroke risk and contraindications for long-term oral anticoagulation has IIb class of recommendations and B level of evidence[10]. In ESC/EACTS Guidelines on myocardial revascularization 2014 percutaneous LAA closure and antiplatelet therapy is also recommended as a possible strategy in the patients with AF undergoing PCI in a case of high stroke risk and contraindications for long-term combined antiplatelet and anticoagulation therapy (Class IIb, Level of Evidence B)[11]. (Figure 2 a,b,c). In AHA/ASA Guidelines for the Primary Prevention of Stroke 2014 for the same group of patients it is recommended to perform LAA occlusion in a centre with low rates of periprocedual complications, and added that patient should tolerate the risk of at least 45 days of postprocedual anticoagulation (Class IIb; Level of Evidence B)[12].

Data of 4-year follow-up of the PROTECT-AF study have demonstrated statistically significant all-cause death reduction in the Watchman group compared to the control group due to reduction of the haemorrhagic strokes (0.4% vs 2.9% in a patients on warfarin, $p<0.001$)[13].

Based on this results, in October 2014 the Food and Drug Administration Circulatory System Devices Panel of the Medical Devices Advisory Committee voted in favor of the Device. By a vote of 6 to 5 (with 1 abstention) the Panel concluded that the benefits of the WATCHMAN Device outweigh the potential risks and that there is reasonable assurance that the Device is safe (12 Yes to 0 No). But on the question of reasonable assurance

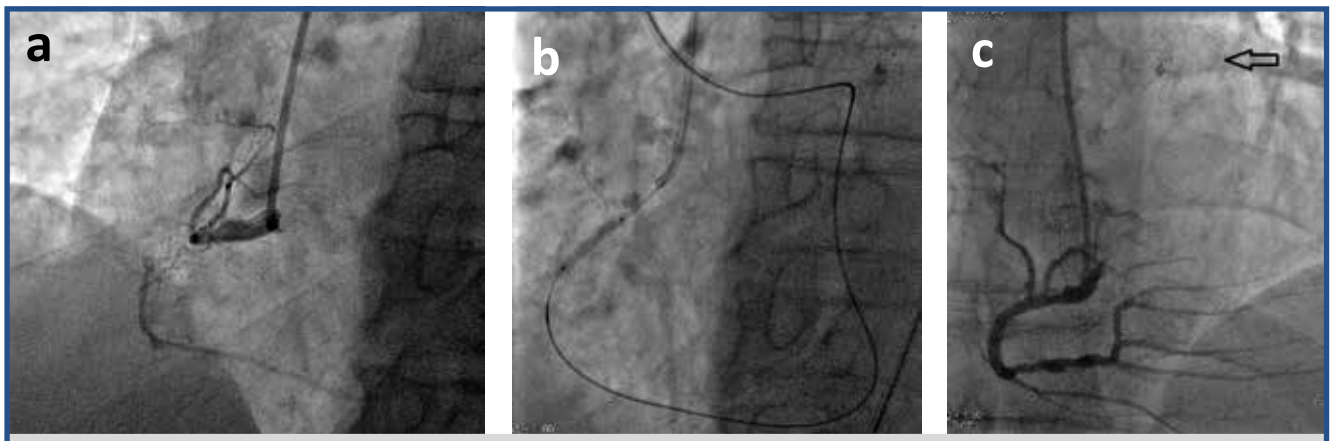


Figure 2. (a,b,c). Implanted Watchman device in patient with CTO of RCA, with retrograde recanalisation.
a – CTO of RCA in mid/3; b – balloon angioplasty after retrograde recanalisation; c – recanalised RCA+Watchman 24 mm device.

of effectiveness, the Panel vote was unfavorable (6 Yes to 7 No). It should be mentioned, that the vote was about using the device for the group of the patients, without contraindications for anticoagulant warfarin therapy. Probably, if a patients with contraindications for anticoagulant therapy and high risk of bleeding complications were discussed, the results of the vote could be different.

Finally, the WATCHMAN Device received U.S. Food and Drug Administration (FDA) approval on Friday, March 13, 2015. Now in the USA the WATCHMAN™ LAA Closure Technology is indicated to reduce the risk of thromboembolism from the left atrial appendage in patients with non-valvular atrial fibrillation who: are at increased risk for stroke and systemic embolism based on $CHADS_2$ or CHA_2DS_2-VASc scores and are recommended for anticoagulation therapy; are deemed by their physicians to be suitable for warfarin; and have an appropriate rationale to seek a non-pharmacologic alternative to warfarin, taking into account the safety and effectiveness of the device compared to warfarin.

The decision about method of ischemic events prophylactic for the patients with non-valvular AF should be taken individually for each patient, after precise analysis of potential risks of medicament strategies and innovative endovascular technologies, basing on available data and guidelines.

References

1. Fuster V, Rydén LE, Wann LS, et al. 2011 ACCF/AHA/HRS focused updates incorporated into the ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011;57:e101–e198.
2. Anderson DC, Kappelle LJ, Eliasziw M, et al. Occurrence of hemispheric and retinal ischemia in atrial fibrillation compared with carotid stenosis. Stroke 2002; 33:1963.
3. Lin HJ, et al. Stroke severity in atrial fibrillation: the Framingham study. Stroke 1996;27:1760-4.
4. Hylek EM, Evans-Molina C, Shea C, Henault LE, Regan S. Major hemorrhage and tolerability of warfarin in the first year of therapy among elderly patients with atrial fibrillation. Circulation. 2007;115:2689-96.
5. Wysowski DK, Nourjah P, Swartz L. Bleeding complications with warfarin use: a prevalent adverse effect resulting in regulatory action. Arch Intern Med 2007;167:1414–9.
6. Glader EL, Sjolander M, Eriksson M, Lundberg M. Persistent use of secondary preventive drugs declines rapidly during the first 2 years after stroke. Stroke. 2010;41:397-401.
7. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg. 1996;61:755-9.
8. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sievert H, Buchbinder M, Mullin CM, Sick P; PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009;374:534-42.
9. Reddy VY, Holmes D, Kar S, et al. Safety of percutaneous left atrial appendage closure: results from the WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients with AF (PROTECT AF) clinical trial and the Continued Access Registry. Circulation 2011;123:417–424.
10. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation. European Heart Journal (2012) 33, 2719–2747.
11. 2014 ESC/EACTS Guidelines on myocardial revascularization. European Journal of Cardio-Thoracic Surgery 46 (2014) 517–592.
12. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, Council on Functional Genomics and Translational Biology, and Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association [published online ahead of print October 29, 2014.
13. Alli O, Doshi S, Kar S, Reddy V, Sievert H, Mullin C, Swarup V, Whisenant B, Holmes D Jr. Quality of life assessment in the randomized PROTECT AF (Percutaneous Closure of the Left Atrial Appendage Versus Warfarin Therapy for Prevention of Stroke in Patients With Atrial Fibrillation) trial of patients at risk for stroke with nonvalvular atrial fibrillation. J Am Coll Cardiol. 2013;61:1790-8.

MitraClip

Percutaneous Mitral Valve Repair

Patient Referral

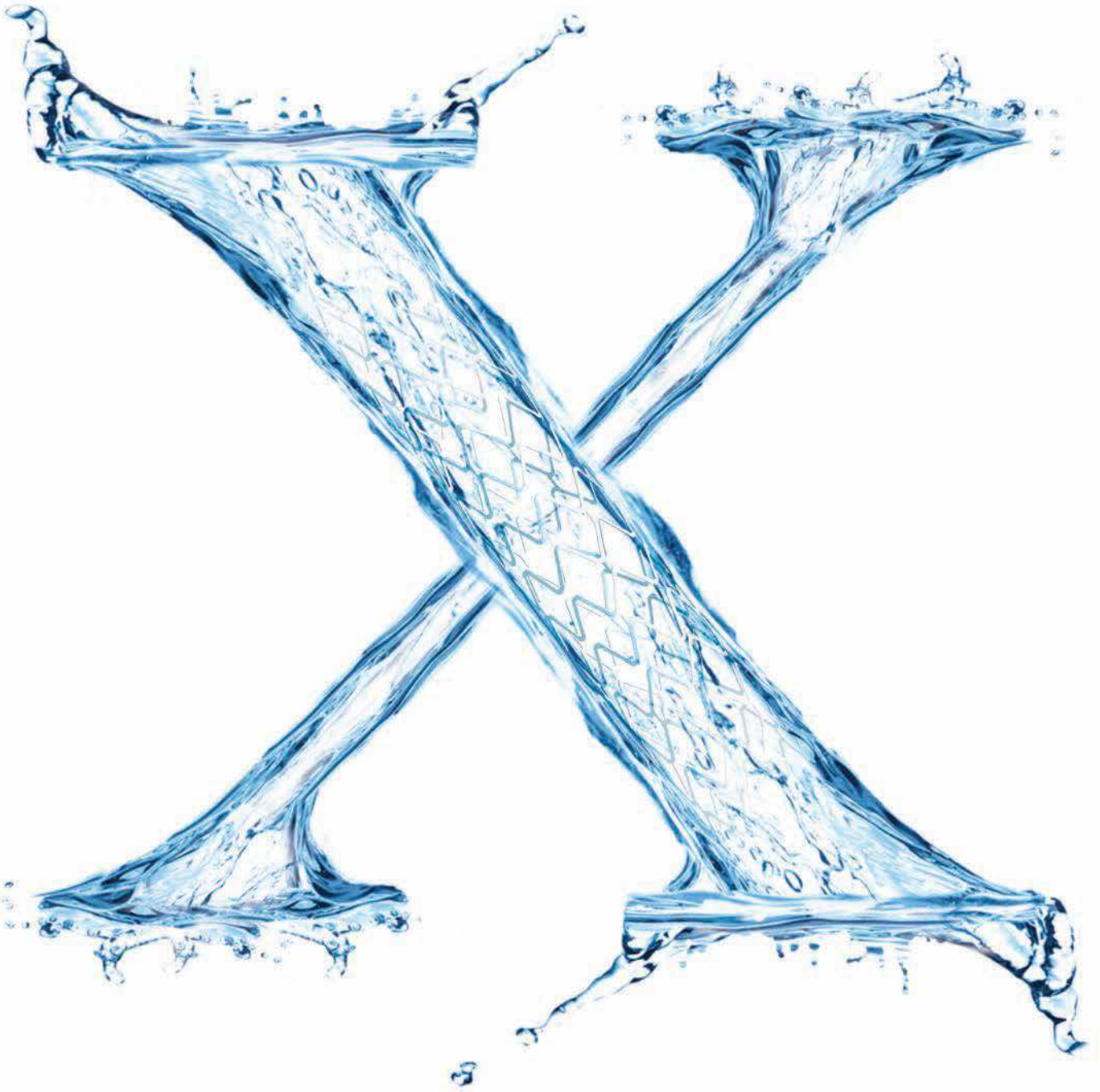
Expanding Your Treatment Options for Patients with Mitral Regurgitation

Abbott
A Promise for Life

DESolve®

NOVOLIMUS ELUTING BIORESORBABLE CORONARY SCAFFOLD SYSTEM

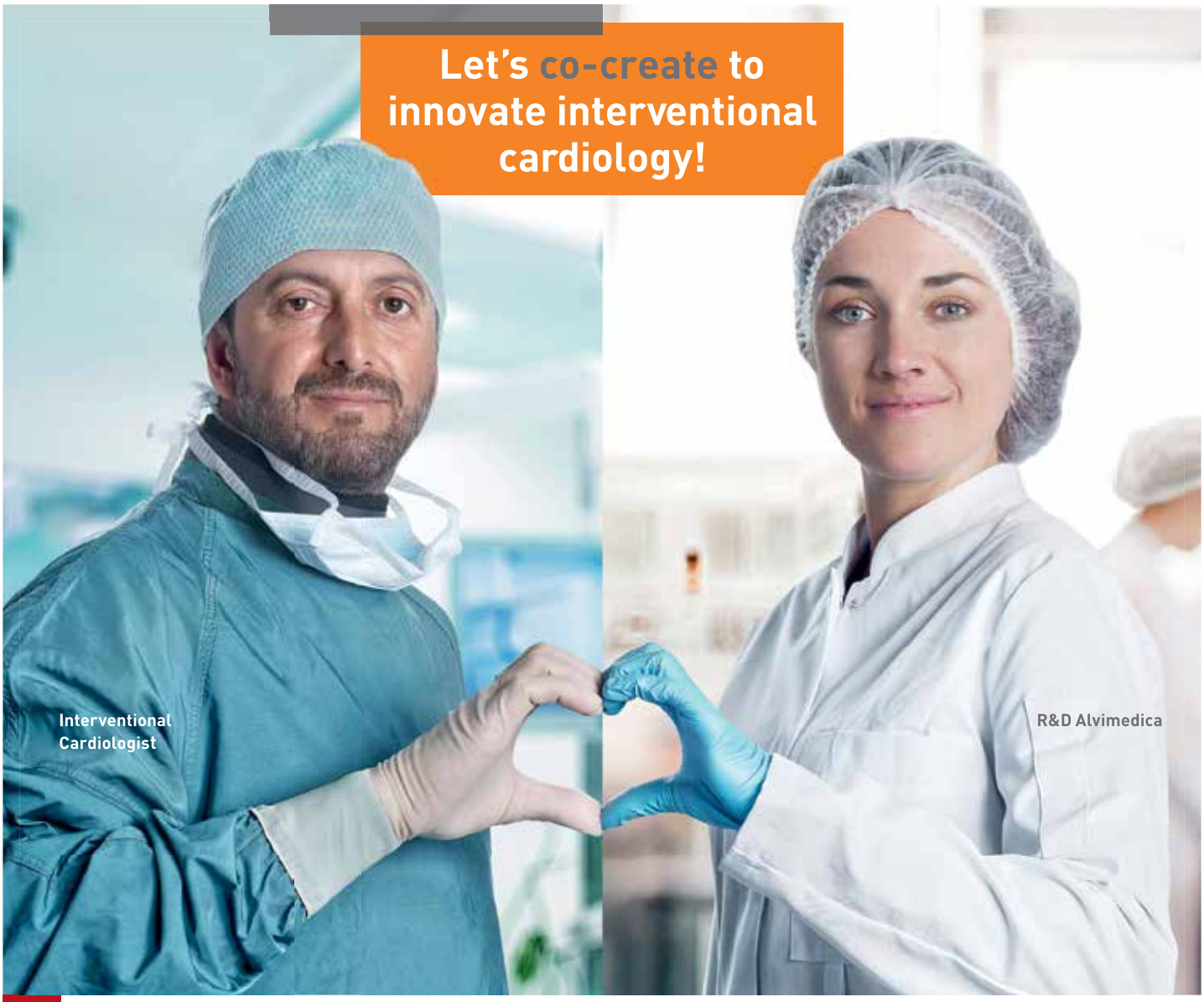
PRECISION IN TECHNOLOGY
PRECISION IN THERAPY



Elixir®
MEDICAL CORPORATION

INNOVATION FOR LIFE®

Let's co-create to innovate interventional cardiology!

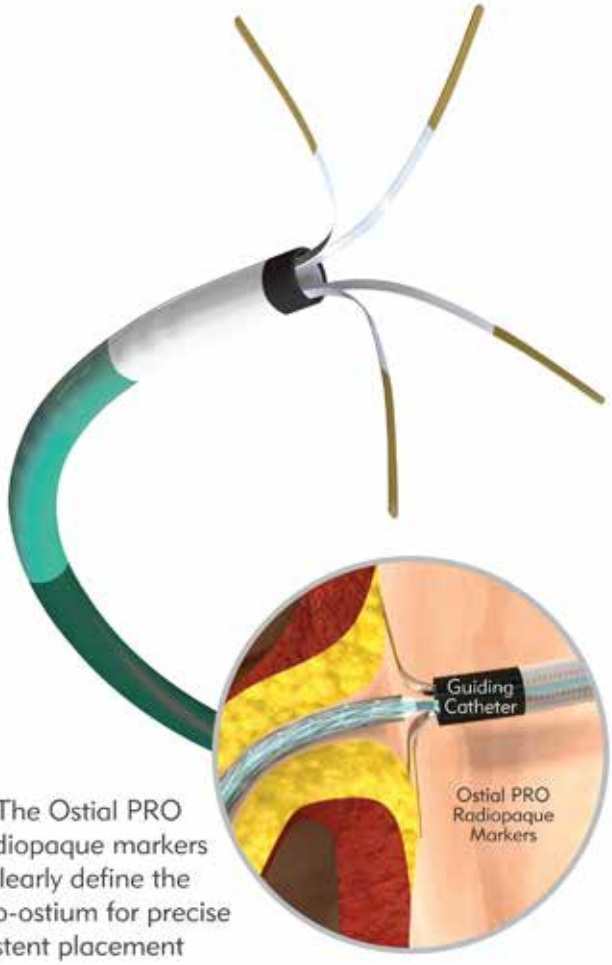


INTERVENTIONAL **CARDIOLOGY**

Alvimedica is a young, agile company devoted to developing minimally-invasive medical technologies in close cooperation with medical professionals such as yourself: physicians looking for next-level innovations in the operating room. Our 'co-creation approach' results in a range of products aiming to meet needs so far unmet in interventional cardiology.

Certainly we can offer you worldclass DES, BMS, guidewires and diagnostic, guiding and balloon catheters. But Alvimedica also brings you the exclusive polymer-free, balloon expandable DES stent: Cre8™! Our commitment to improving surgical procedures through innovation is driven by our sincere care for patients' quality of life and our goal to positively impact clinical outcomes. As our motto says: we want to help physicians bring their patients **'Back to Life!'** as soon as possible, and based on safe medical practices.

MERIT MEDICAL™



The Ostial PRO radiopaque markers clearly define the aorto-ostium for precise stent placement

ASAHI INTECC

Your dreams. Woven together.

ASAHI SION

PTCA GUIDE WIRE

The Right Wire for Any Case

BRILIQUE®
tikagrelor

AstraZeneca

Izvedeno iz materijala odobrenog od strane ALIMS-a.
Broj rešenja: 515-00-00719-2012-3-005 od 9.10.2012.
Lek se izdaje samo uz lekarski recept.
Samo za stručnu javnost.
Detaljne informacije dostupne na zahtev.

Broj dozvole za Brilique 56x90mg: 515-01-1105-11-001; od 08.05.2012.

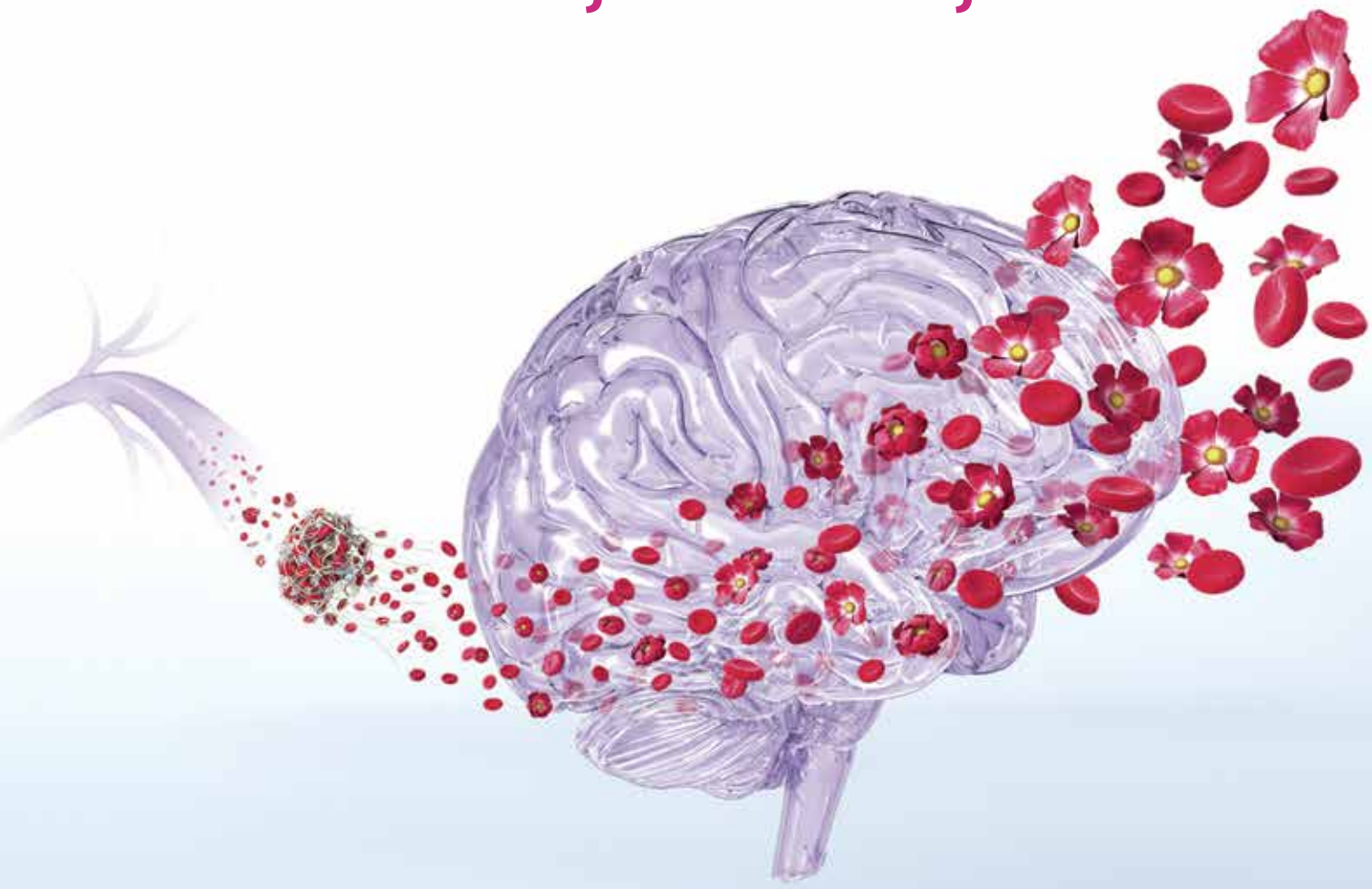
Predstavništvo AstraZeneca UK Ltd.
Bul. Vojvode Mišića 15
11000 Beograd, Srbija
T: +381 11 3336 900
F: +381 11 3690 083

Bayer HealthCare

Xarelto®: efikasna zaštita

1 x DNEVNO

U prevenciji moždanog udara kod atrijalne fibrilacije



Xarelto®
rivaroxaban

Samo za stručnu javnost

Način izdavanja leka: lek se može izdavati samo uz lekarski recept.
Broj i datum dozvole: Xarelto®, film tablete, 14x(15mg): 515-01-8741-11-001 od 18.04.2013.,Xarelto®, film tablete, 14x(20mg): 515-01-8742-11-001 od 18.04.2013., Xarelto®, film tablete, 28x(15mg): 515-01-3983-12-001 od 18.04.2013., Xarelto®, film tablete, 28x(20mg): 515-01-3985-12-001 od 18.04.2013. Xarelto®, film tablete, 42x(15mg): 515-01-3984-12-001 od 18.04.2013.
Nosilac dozvole: Bayer d.o.o. Omladinskih brigada 88b, 11070 Beograd

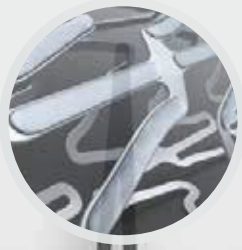
Increased Safety and Comfort for Clinicians

The growing number and complexity of fluoroscopic procedures performed each year has increased workload for interventionists, resulting in cumulative radiation doses and orthopedic strain that can limit careers or even cut them short. [1]

The Zero-Gravity radiation protection system is designed to increase the level of radiation protection and at the same time reduce the weight burden for the operator.

www.terumo-europe.com

Your Partner in AMI Management



❸ Intervention
Ultimaster™
Nobori®
Drug Eluting Stents

❶ Puncture
Radifocus® Introducer II
Introducer Kit

❺ Closure
TR Band™
Compression device

❷ Aspiration
Eliminate™
Aspiration Catheter

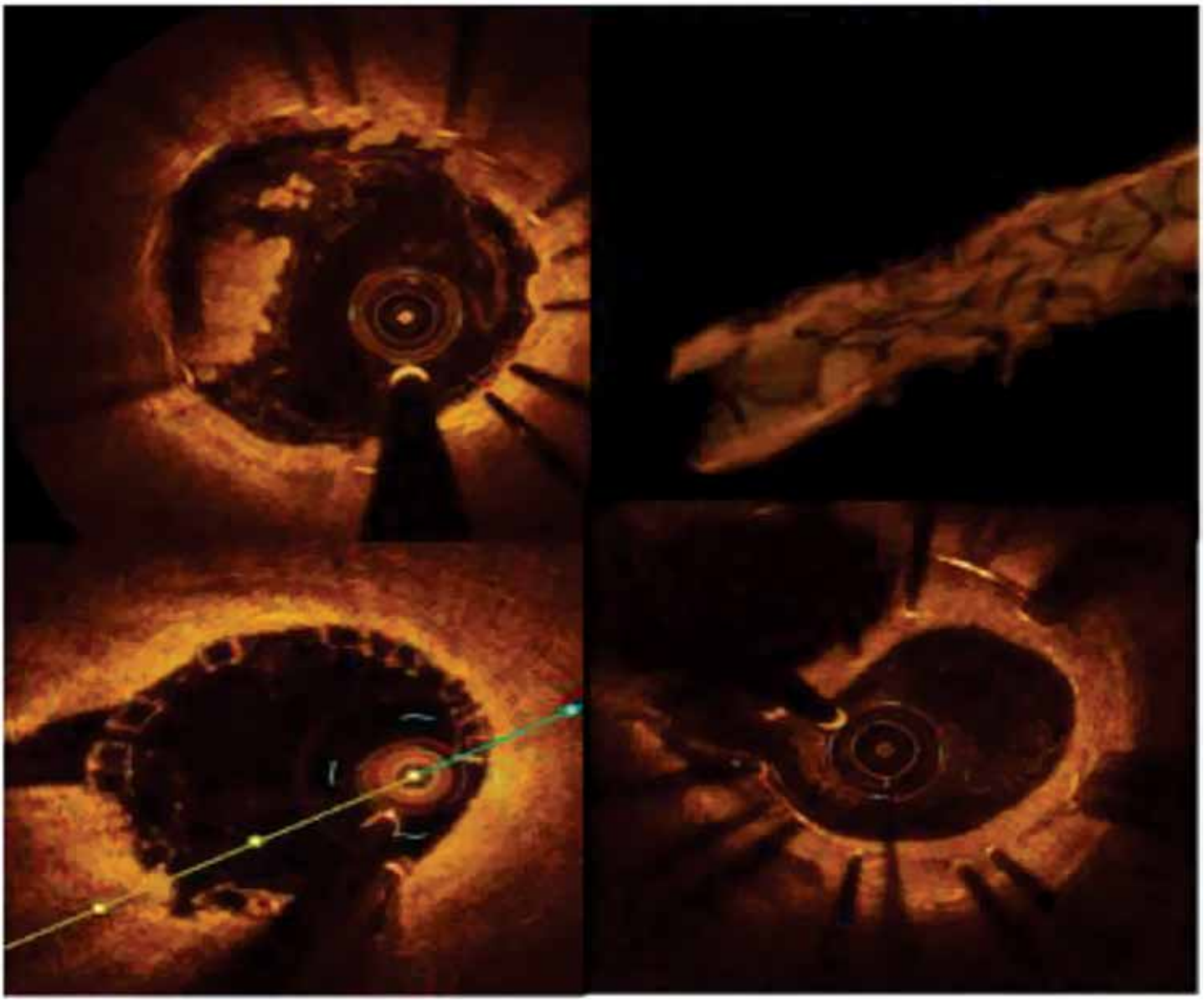
❹ Imaging
Lunawave®
Optical Frequency Domain Imaging

SOLUTIONS FOR AMI
ACUTE MYOCARDIAL INFARCTION

IS461GB0414MDI

TERUMO®

POWER OF RESOLUTION



ST. JUDE MEDICAL™

RUBICON
TRAVEL

LONDON
ESC Evropski kongres
29.08. - 02.09.2015

MEXICO CITY
WHF Svetski kongres
04.07. - 07.07.2015

Puna organizaciona podrška za sva individualna i grupna kongresna putovanja

RUBICON TRAVEL
Vojvode Stepe 146, Beograd
+381 11 3981 411
kongresi@rubicontravel.rs
www.kongresi.rs
www.rubicontravel.rs

الإتحاد

ETIHAD

AIRWAYS

ABU DHABI

BelgrAde Summit of Interventional CardiologistS

9th +

Belgrade, April 22-25 2015.

ORGANIZED BY

Working Group on Interventional Cardiology Cardiology Society of Serbia

1955 UKS CSS Cardiology Society of Serbia

Medtronic

CoreValve System

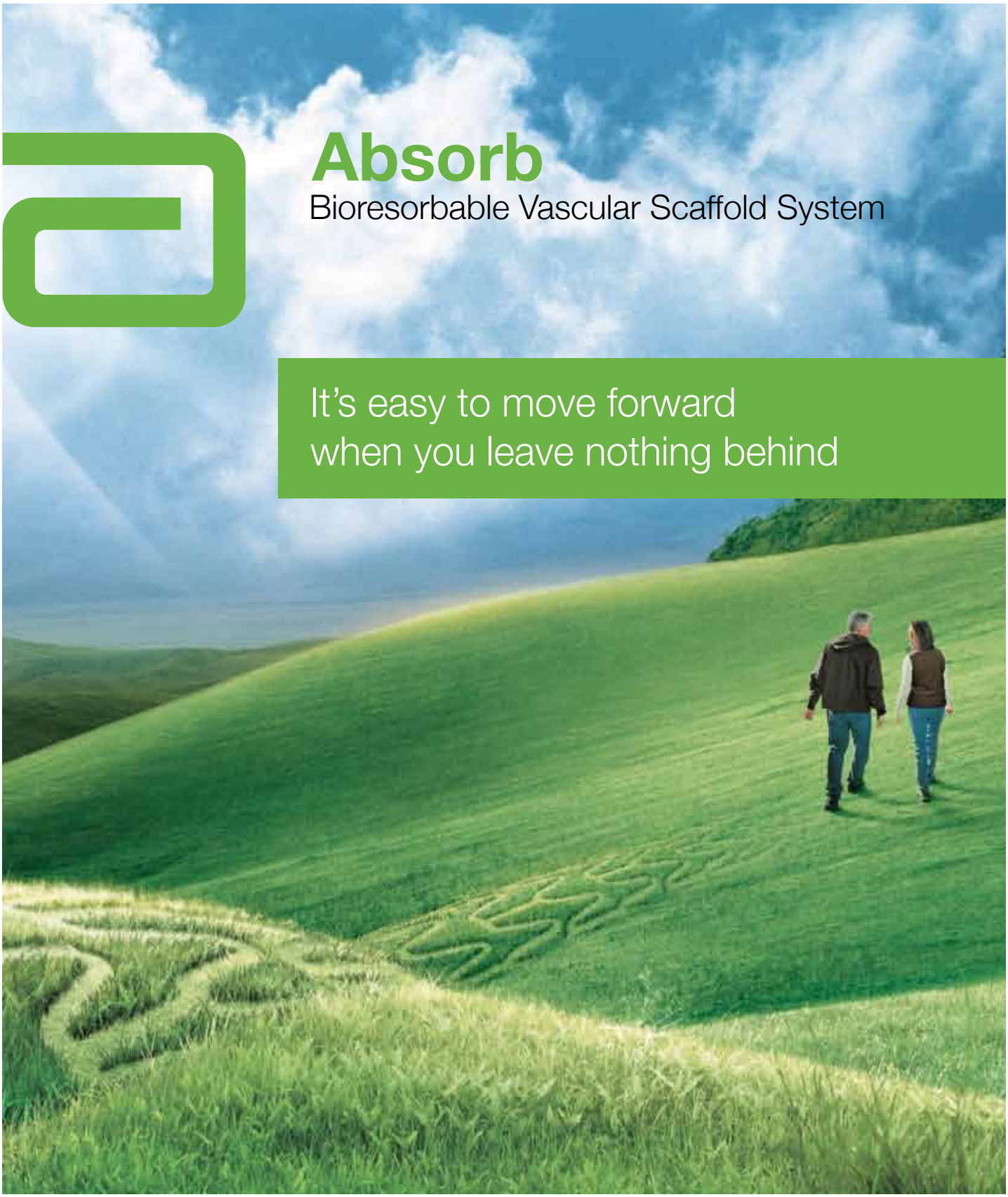
TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI) SYSTEM

Simpli
Adaptable.

Absorb

Bioresorbable Vascular Scaffold System

It's easy to move forward
when you leave nothing behind



Restore Freedom

Abbott
A Promise for Life