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AsiaIntervention

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10th INDIA LIVE 2019 MUMBAI

Official Journal of the Asian Pacific Society of Interventional Cardiology (APSIC) and the Interventional Cardiology Foundation of India (ICFI)

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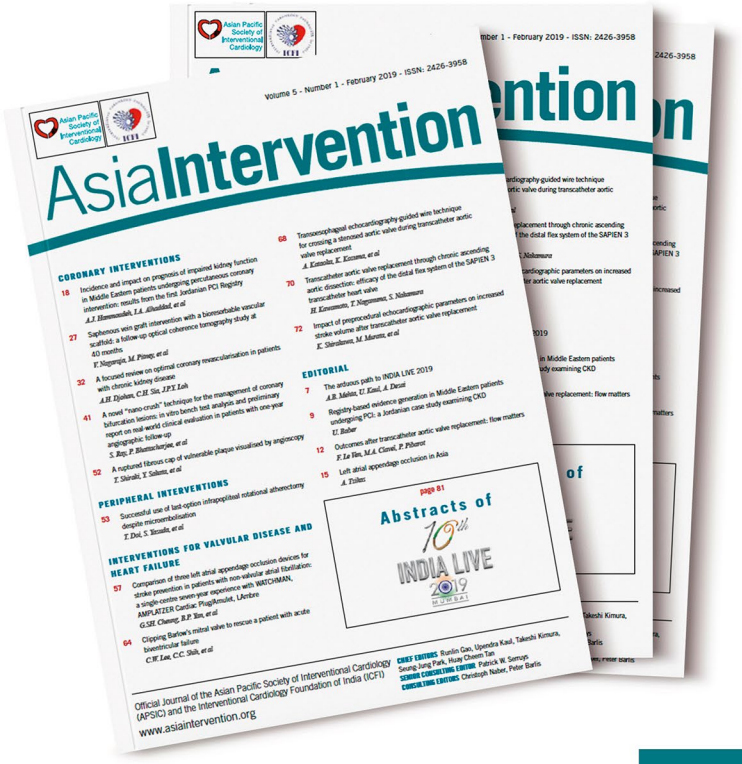

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Incidence and impact on prognosis of impaired kidney function in Middle Eastern patients undergoing percutaneous coronary intervention: results from the first Jordanian PCI Registry

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Patients who had undergone percutaneous coronary intervention (N=2,426) were divided into three groups according to the estimated glomerular filtration rate (eGFR): those with normal renal function (eGFR ≥90 ml/min/1.73 m^2), mild renal impairment (RI) (eGFR 60-89 ml/min/1.73 m^2), or moderate to severe RI (eGFR <60 ml/min/1.73 m^2). At one year, patients with moderate to severe RI (14.2% of all patients) had a higher incidence of cardiac mortality compared with patients who had mild or no RI (3.78% vs. 1.77% vs. 1.49%; respectively, p=0.03). In multivariate analysis, patients who had moderate to severe RI were about four times more likely to die at one year compared with patients who had mild or no RI (odds ratio=3.7; 95% CI: 2.8-5.0, p=0.001).

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This case report illustrates the findings of optical coherence tomography (OCT) imaging of a BVS in a vein graft at 40 months post implantation. It is unique given that it is the longest follow-up period to date of such an intervention with an Absorb scaffold in a saphenous vein graft conduit. In this particular case the scaffold demonstrated excellent late angiographic patency confirmed on invasive OCT imaging.

Comparison of three left atrial appendage occlusion devices for stroke prevention in patients with non-valvular atrial fibrillation: a single-centre seven-year experience with WATCHMAN, AMPLATZER Cardiac Plug/Amulet, LAmbre

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This study demonstrated similar procedural and long-term outcomes among three different left atrial appendage occlusion devices (WATCHMAN, AMPLATZER Cardiac Plug/Amulet, and LAmbre) for stroke prevention in patients with non-valvular atrial fibrillation.

Impact of preprocedural echocardiographic parameters on increased stroke volume after transcatheter aortic valve replacement

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A novel "nano-crush" technique for the management of coronary bifurcation lesions: in vitro bench test analysis and preliminary report on real-world clinical evaluation in patients with one-year angiographic follow-up

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The provisional stenting technique with a single drug-eluting stent cannot be applied to all bifurcation lesions. We hereby propose a novel technique which is easy to perform and suitable for all bifurcation angles. After confirming the feasibility of the two-stent "nano-crush" technique in an *in vitro* bench test and intravascular ultrasound (IVUS) study, 42 patients with *de novo* coronary bifurcation stenosis were treated by this novel procedure. Procedural success was achieved in all patients. Total number of MACE at one-year follow-up was three (7.14%), with one death at nine months post procedure. Initial experience with the nano-crush technique demonstrates that it is associated with acceptable clinical outcomes.

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ABSTRACTS

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Aims and scope

AsiaIntervention Journal is an international, English language, peer-reviewed journal whose aim is to create a forum of high quality research and education in the field of percutaneous and surgical cardiovascular interventions.
It is released twice a year, in paper and electronic formats. AsiaIntervention has applied for indexation in Science Citation Index® (ISI), SciVerse Scopus, MEDLINE®/PubMed®.
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AsiaIntervention 2019;5:7-8

The arduous path to INDIA LIVE 2019

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India Live was started in 2010 with the idea of passing on the knowledge of interventional cardiology to the next generation. The Interventional Cardiology Foundation of India was established. This flagship organisation is now a decade old.

The toughest challenge for the organisers of the 10th India Live conference was to maintain the high standard set by the preceding conferences, by simplifying interventional cardiology for young interventionists while simultaneously having sessions of advanced intervention for shaping interventionists into masters of their trade.

The India Live 2019 scientific programme starts with the Fellows Course where our primary focus is on young and upcoming interventional cardiologists. The basic concepts of interventional cardiology will be discussed throughout the day with lectures from prominent international and national speakers. The next three days focus on interventions in complex subsets such as left main diseases, bifurcation lesions, CTOs, calcified lesions, graft interventions, and peripheral interventions, and also on structural interventions such as TAVR, mitral valve interventions, LAA closures, etc. There are also 35-40 live cases from national and international centres, live-in-box sessions, where there will be stimulating, detailed discussion on the selected topic. Every session in the programme is followed by additional time for discussion with our esteemed panellists and chairpersons in order to encourage maximum participation from the audience. The quality of this tailormade programme is sure to impress all the delegates.

The theme of India Live 2019 is "An Era of Emerging Technology". The scientific programme will showcase several technologies and innovations such as robotic interventions, orbital atherectomy, Impella, transcatheter interventions of the aortic, mitral and pulmonary valve, and the importance of coronary flow measurement during procedures as well as that of intravascular imaging. These innovations and tools will be showcased in the live cases and discussed in detail by experts in the academic sessions.

The feather in the cap of India Live 2019 is the India Live faculty which comprises the leading experienced interventional cardiologists from India as well as from abroad, who are global leaders in their field, sharing their expertise. India Live 2019 will also have a "Training Village" where delegates can get hands-on experience and training of the novel hardware and technology, showcased by our industry partners. Additionally, we plan to have candid, one-to-one interaction with masters in the field, for a behind the scenes look into the challenges faced by cardiologists and to unravel their "secrets of success" in the India Live Studio.

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This year, it is the privilege of India Live to bestow lifetime achievement awards on three legendary interventional cardiologists – Drs Antonio Colombo, Bernhard Meier and Patrick W. Serruys. Each of these stalwarts has been a pioneer of cardiology. They have revolutionised the field of cardiology through their innovations.

Prof. Antonio Colombo is one of the premier developers of the concept of coronary stent placement. His observations were pivotal in allowing the utilisation of stenting with only antiplatelet therapy, liberating this procedure from oral anticoagulation and minimising the risk of stent thrombosis. Prof. Colombo's contribution has been pivotal for the utilisation of coronary stents in the treatment of complex coronary artery disease, formulating the concept of focal treatment and also of stenting very long lesions. Subsequently, Prof. Colombo developed various procedures for the treatment of structural heart disease such as transcatheter aortic valve implantation, correction of mitral and tricuspid regurgitation and the treatment of a number of congenital heart diseases presenting at adult age. He was Director of Research in Angioplasty at Lenox Hill Hospital, New York, USA from 1996 to 2004. For the past 15 years, Prof. Colombo has been the Director of Interventional Cardiology at San Raffaele Scientific Institute and is Professor of Cardiology at Vita-Salute University, Milan, Italy. He is a member of both European and U.S. professional societies. Prof. Colombo is connected as a board member to 10 organisations across 13 different industries. Prof. Colombo has published over 1,000 papers in peer review journals, several books in the field of coronary intervention and has contributed several chapters in important interventional cardiology books.

Prof. Bernhard Meier was actively involved with Dr Andreas Gruentzig, who performed the first human coronary angioplasty on 16th September 1977. Prof. Meier dedicated his professional life to refining and simplifying PCI and other interventional procedures derived from it. More recently, he expanded that technique to allow transaortic valve implantation without the need for a temporary pacemaker by pacing the left ventricle by the guidewire used for valve implantation. He also introduced the intracoronary ECG and coronary occlusion pressure measurements to demonstrate and quantify coronary collateralisation. Prof. Meier was an early pioneer fostering recanalisation of chronic total occlusions, introducing the ball-tipped Magnum wire in the early 1980s. In 1992, Prof. Meier was appointed Chairman of Cardiology at the University Hospital of Bern, Switzerland. On 10th September 1997, in Switzerland, he implanted the world's first dedicated PFO device together with Kurt Amplatz. In 2002 he also implanted the world's first left atrial appendage closure device in an awake patient without echocardiographic guidance. Prof. Meier has been a dedicated practical teacher in the catheterisation laboratory to the present date, promoting a frugal approach using minimal material. He is known to think out of the box and to preserve a sober opinion of what coronary angioplasty can do.

Prof. Patrick W. Serruys has been an interventional cardiologist since 1977, Chief of Interventional Research since 1988, the Chief of Interventional Cardiology at the Thoraxcenter from 1997-2012, and Professor of Medicine until 1st April 2014 at the Erasmus MC, Rotterdam, the Netherlands. He is known for his contribution in setting up Cardialysis, a well-known research organisation in Europe. Currently, he is Professor of Cardiology in the Cardiovascular Science Division of the National Heart and Lung Institute (NHLI) of Imperial College London, London, United Kingdom. Prof. Serruys conducted the first randomised trial with coronary stenting that led to the approval of the technique in Europe. Prof. Serruys and Eduardo Sousa in Brazil introduced the use of drug-eluting stents for the first time in the world in 1999. In 2006 Prof. Serruys introduced worldwide the use of fully biodegradable drug-eluting scaffolds that eliminated the presence of a permanent metallic foreign body in the coronary circulation. He is the author of over 1,800 publications in cardiology and interventional cardiology.

The organising committee of India Live has worked tirelessly for the last 12 months to put together this academic feast. We welcome all the delegates and faculty attending the sessions and hope that they will enjoy the conference to the fullest.

With all these achievements it is only fitting that India Live is associated with AsiaIntervention. AsiaIntervention is dedicated to providing the highest level of medical content from cutting-edge research to the latest techniques and technologies. Our ongoing aim is to continue to enhance the work of our colleagues, both regionally and internationally. In order to do this, each issue features key articles on those topics of critical interest to interventional cardiologists throughout the Asia-Pacific region and globally.

In this issue alone, along with editorials by leading experts throughout the region, you will find special reports, expert reviews and a focus on innovations as well as clinical research articles. Under coronary interventions, there is an interesting paper by A.J. Hammoudeh et al (Jordan) on impaired renal function and PCI outcome, and one from S. Ray et al (India) concerning the latest research on the nano-crush technique for bifurcation lesions. In the field of interventions for valvular disease and heart failure, we have a fascinating piece by G. SH. Cheung et al (Hong Kong) comparing three left atrial appendage occlusion (LAAO) devices for stroke prevention. Additionally, K. Shirakawa et al (Japan) look at the impact of preprocedural echocardiographic predictors of increased stroke volume (SV), a prognosticator of severe aortic stenosis (AS), after TAVR.

We are confident that as you peruse the following pages you will agree that AsiaIntervention is a valued reference for interventional medicine in our region and internationally.

AsiaIntervention 2019;5:9-11

Registry-based evidence generation in Middle Eastern patients undergoing PCI: a Jordanian case study examining CKD

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Leveraging "real-world" data via administrative claims, registries or other curated sources is increasingly utilised to inform clinical practice, characterise disease epidemiology and guide public policy. The digitisation of medical records, coupled with rapid advances in computational speed and sophistication, has enabled this electronic transition. Resources such as the United States Center for Disease Control (CDC) National Health and Nutrition Examination Survey (NHANES) provide ongoing and representative estimates of various health, nutrition and fitness metrics for the US adult population. In contrast, dedicated registries focused on disease or procedural domains provide temporal trends on healthcare resource utilisation, variation in practice patterns and consequences of policy or guideline implementation **(Table 1)**. In certain instances, registries are increasingly utilised to facilitate the conduct of pragmatic clinical trials that increase study efficiency, and reduce costs and time to trial completion[1]. These data also enable the evaluation of aetiologic associations between various exposures and disease epidemiology, which may be discerned more reliably from real-world as opposed to clinical trial cohorts[2]. One illustration of this concept was the seminal paper by Go et al demonstrating the prevalence and impact of renal impairment on cardiovascular outcomes using administrative claims data from a million healthcare plan participants[3]. Subsequent reports have confirmed these earlier observations in both primary and secondary prevention settings, and chronic kidney disease (CKD) is now included as a risk-enhancing feature that warrants a more aggressive approach towards risk factor modification and control of blood lipids[4]. Nevertheless, the evidence base for CKD and related prognosis is primarily derived from Western European and North American populations comprised of European or African ancestry. Indeed, validated equations that provide estimates of glomerular filtration rate (eGFR) include terms for self-described African or non-African race[5,6]. Analogous data evaluating similar associations among individuals in lower middle-income countries in the Middle East or other non-Western regions remain limited.

To address this gap, Hammoudeh et al examined the prevalence, clinical profile and impact of CKD using data from the first, national all-comer Jordanian PCI registry (n=2,426)[7].

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Despite a relatively young mean age of only 56 years, the prevalence of reduced eGFR (<90 ml/min) was 60%, with

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Table 1. Selected national PCI registries.

Registry	Country	Inception	Details
CathPCI	USA	1998	Voluntary participation; in-hospital outcomes
SWEDEHEART*	Sweden	1989	National coverage; longitudinal outcomes via unique identifiers
BCIS-CCAD	United Kingdom	1994	Captures over 90% of all PCI procedures performed in UK
K-PCI	Korea	2014	Voluntary participation; in-hospital outcomes

*SWEDEHEART is a merger of multiple registries with the PCI component starting in 1989. BCIS-CCAD: British Cardiovascular Intervention Society Central Cardiac Audit Database; K-PCI: Korea PCI registry; PCI: percutaneous coronary intervention; SWEDEHEART: Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies

approximately 14% of patients presenting with at least moderate to severely reduced kidney function (eGFR <60 ml/min). Not surprisingly, patients with more advanced CKD were characterised by older age and more comorbidities including hypertension, diabetes mellitus and prior revascularisation. Discharge pharmacotherapy, including use of beta-blockers and statins, did not vary substantially in relation to renal function. With respect to outcomes, in-hospital bleeding was relatively uncommon yet higher among those with the most severe renal impairment, a finding entirely consistent with the well-known association between CKD and bleeding risk[8]. Similar numerical patterns were observed at 30 days and one year, albeit not statistically significant due to limited power. With regard to ischaemic events, CKD emerged as an independent correlate of cardiovascular death, while differences in rehospitalisation for acute coronary syndrome (ACS) and revascularisation did not vary by renal function.

An intriguing result from the present report is the excess risk for cardiovascular death observed among those with CKD in the absence of a concordant rise in ACS hospitalisation, which may serve as a crude surrogate for non-fatal myocardial infarction (MI). Indeed, this finding is consistent with the transition in cardiovascular epidemiology that occurs as renal function worsens. Specifically, while atherosclerosis-mediated mechanisms modulate cardiac risk in mild CKD, vascular calcification, myocardial fibrosis and electrical instability emerge as contributors at more advanced levels of renal impairment[9,10]. The numerical trend suggesting more frequent heart failure hospitalisation with worsening CKD in the current study is also consistent with this paradigm. Hence, treatments that target the unique vascular phenotype present in moderate to advanced CKD[11] may provide greater benefit than established therapies commonly used to treat atherosclerosis in the absence of renal dysfunction.

The authors contend that PCI is safe and effective among those with CKD and that an invasive strategy should be considered more frequently in such patients. While this may be true, inferential claims based upon observational data should be interpreted cautiously. In addition, the relatively low rate of adverse events may have introduced a type II error when comparing across different levels of renal function. In contrast, stent thrombosis occurred relatively frequently (~1.5-2%), a substantially higher rate in comparison to other contemporary registries[12]. This is a concerning result, and more details on stent type and one-year adherence would be insightful, along with the type of $P2Y_{12}$ inhibitor prescribed at discharge. More granularity for these data elements would certainly be welcome in future reports from this registry.

Notwithstanding these limitations, the authors and investigators leading JoPCR1 should be commended for these efforts. In addition to evaluating outcomes in a broad population of Jordanian patients undergoing PCI, this resource will provide opportunities for data sharing, academic collaboration and identification of risk factors and treatment approaches unique to the Middle East versus other regions. As with any registry-based product it will be important to implement processes, such as periodic auditing, to ensure that data are valid, reproducible and high-quality. Representing the latest entry into the global market of outcome-oriented PCI registries, additional insights from JoPCR1 are eagerly awaited.

Conflict of interest statement

The author has received speaker's fees from AstraZeneca and Boston Scientific.

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AsiaIntervention 2019;5:12-14

Outcomes after transcatheter aortic valve replacement: flow matters

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Recent studies have reported that low flow (LF), defined by a stroke volume index (SVi) <35 ml/m², is highly prevalent in patients with severe aortic stenosis (AS), and is associated with reduced survival[1-5]. This LF condition may occur in the context of either a reduced (i.e., classic LF) or preserved (i.e., paradoxical LF) left ventricular (LV) ejection fraction (LVEF), and is often associated with a low transvalvular pressure gradient[6]. Indeed, the pressure gradient is highly flow dependent and an LF state may thus be associated with a low gradient despite the presence of a severe AS. In patients undergoing transcatheter aortic valve replacement (TAVR), the presence of LF was one of the most powerful echocardiographic predictors of mortality and its impact was independent of LVEF or gradient[7]. Furthermore, the presence of LF early after the procedure was associated with a significant increase in subsequent mortality[7].

In this issue of AsiaIntervention, Shirakawa et al[8] present an elegant study in which they evaluated the preprocedural echocardiographic parameters that were associated with improved LV outflow following TAVR.

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The authors showed that an increase in SVi following TAVR led to better one-year cardiac outcome (cardiac death and heart failure readmission). They also found that right ventricle fraction area change (RVFAC) and aortic regurgitation (AR) grade were associated with an increase in SVi after TAVR in multivariable analysis.

Prognostic impact of improvement in flow post TAVR

When compared to preprocedural flow, four situations may occur after TAVR: i) LF is present prior to and after the procedure (i.e., maintained LF); ii) LF is present prior to the procedure but flow (SVi) is normal after the procedure (i.e., normalised flow); iii) flow is normal prior to the procedure but low after the procedure (i.e., new-onset LF); and iv) flow is normal both before and after the procedure (i.e., maintained normal flow [NF]). Patients with persistent or new-onset LF seem to have an increased risk of mortality following TAVR compared with patients with normalised flow or maintained NF[7,9]. Persistent LF may reflect the presence of an advanced myocardial impairment with focal fibrosis, which is probably irreversible despite correction of the

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severe AS[10], while new-onset LF may be related to periprocedural complications, such as myocardial injury (caused by the transapical approach for example) or atrial fibrillation[7,11]. Conversely, a normalised flow may happen in patients with diffuse myocardial fibrosis and/or very severe AS. The correction of the afterload excess by the TAVR procedure in those patients is generally beneficial and translates into improved survival. In the long term, the increase in SVi appears to be mainly related to an improvement in LVEF, regression of LV mass and concentric remodelling (which may, in turn, lead to improvement in LV diastolic function) **(Figure 1)**. In their study, Shirakawa et al[8] also found that increased SV, defined by the ratio of post-procedural SV/preprocedural SV >1, was associated with fewer cardiovascular events one year after TAVR. In addition, they found that, globally, SVi improves after TAVR, which corroborates the findings of previous studies[7,12]. Interestingly, the transapical approach did not appear to impact negatively on the improvement in SVi.

Predictors of SV improvement

In previous studies, the predictors of early post-procedural LF were lower preprocedural flow, the presence of atrial fibrillation, the use of the transapical approach, a lower post-procedural mean gradient and a lower baseline LVEF **(Figure 1)**[7,9]. Interestingly, Shirakawa et al found that patients harbouring a reduction in AR severity actually had an improvement in SVi. The underlying mechanism of this finding is unclear. Indeed, AR is typically associated with an increase in stroke volume. Accordingly, a previous study reported that moderate to severe AR on discharge echocardiography was associated with an increase in postoperative SVi[9]. However, the increase in flow related to AR is mainly observed in patients with chronic native AR with preserved LV systolic function. In the context of the TAVR population, there is a large proportion of patients with LV systolic dysfunction. The AR severity changes acutely with TAVR and is also associated with a concomitant reduction in the major LV afterload excess associated with severe AS. In this context, it is not necessarily surprising that an acute decrease in AR severity with TAVR is associated with improvement in LV outflow.

Right ventricular dysfunction is associated with lower right and LV outflow and has been identified as an independent predictor of adverse outcomes in TAVR[13] **(Figure 1)**. In the present study, improvement in RVFAC was associated with an increase in SV following TAVR. We can hypothesise that, in addition to multiple complex factors such as LV/RV interrelations, a decrease in pulmonary artery pressure following a major reduction in LV afterload improvement may make a significant contribution to the improvement in LV outflow.

Clinical implications and future perspectives

This study by Shirakawa et al further demonstrates and emphasises that flow, as defined by SVi, is an important Doppler-echocardiographic parameter which should be assessed before as well as after intervention to evaluate early haemodynamic benefit and enhance long-term prognostication. LV outflow is an important overall surrogate marker of cardiac performance and prognosis **(Figure 1)**. It thus appears logical and important to measure this parameter systematically in patients with AS. Despite its retrospective and observational design, this study also generates new hypotheses regarding the relationship between RV dysfunction, LF state and worse prognosis in patients with AS.

Conflict of interest statement

P. Pibarot has received funding from Edwards Lifesciences and Medtronic for echo core lab services in the field of TAVR with no personal compensation. The other authors have no conflicts of interest to declare.

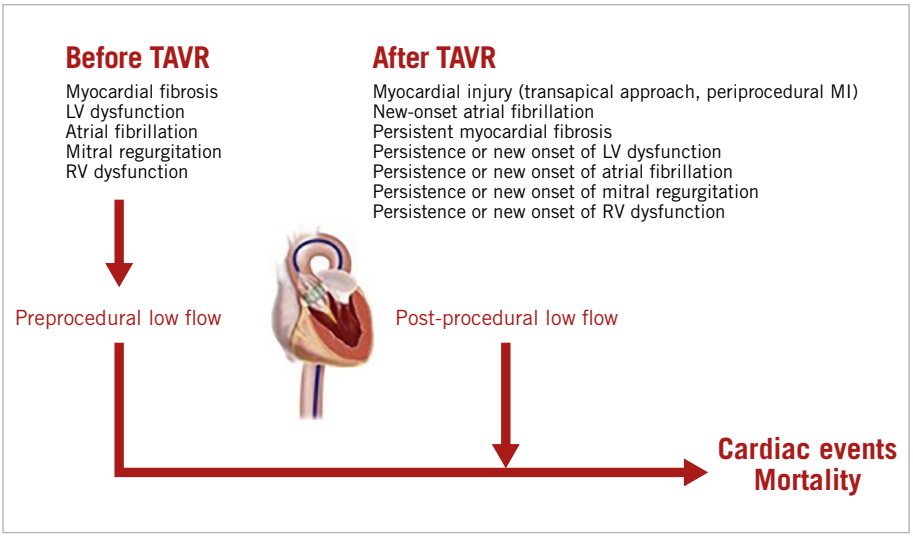

Figure 1. *Predictors and impact on outcomes of low flow state prior to and after TAVR. MI: myocardial infarction*

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Left atrial appendage occlusion in Asia

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Stroke and peripheral thromboembolism related to atrial fibrillation (AF) represent a major medical and socio-economic problem worldwide. The left atrial appendage (LAA) is considered the main reservoir for thrombus formation in patients with AF and therefore eliminating it has been attempted for more than 50 years[1]. The first-in-human percutaneous occlusion of the LAA with a dedicated device was performed in August 2001 by Horst Sievert in Frankfurt, Germany, using the (now discontinued) PLAATO device[2,3]. The most widely used devices since then have been the WATCHMAN™ device (Boston Scientific, Marlborough, MA, USA), the AMPLATZER™ Cardiac Plug (ACP) and its successor, the AMPLATZER Amulet™ device (both by Abbott Vascular, Santa Clara, CA, USA), and more recently the LAmbre™ device (Lifetech Scientific Co, Ltd, Shenzhen, China)[4]. In this issue of AsiaIntervention, Cheung et al present a series of Chinese patients who were treated (in Hong Kong) with the WATCHMAN, ACP, Amulet or LAmbre device[5].

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This is an observational non-randomised study so direct device comparisons cannot be made. However, it is a valuable report of real-world LAAO therapy with four different devices that includes the learning curve effects and technical and procedural evolutionary steps in the field. Moreover, it is one of the few studies performed in a Chinese population, which makes it extremely valuable for the development of LAAO therapy in Asia.

The original quote of Hippocrates regarding the role of a physician «ἀσκεῖν περὶ τὰ νοσήματα δύο, ὠφελεῖν ἢ μὴ βλάπτειν» or "Primum non nocere" in Latin or "First do no harm" in English (首先不要做成傷害 in Chinese) applies perfectly to AF-related stroke prevention therapies. Finding the fine balance between medication/intervention efficacy and safety, i.e., stroke prevention versus bleeding for oral anticoagulation (OAC) therapy, and stroke prevention versus procedure-related complications for LAAO, is surely the path to success[6]. The current gold standard OAC therapy is limited by a number of factors such as bleeding, poor patient compliance, cost, etc. The driving force for the development of percutaneous LAAO is the patient's need for a minimally invasive, safe, "local" therapy for reducing their risk of AF-related thromboembolism, without suffering from major or minor bleeding problems. Therefore, there is a need for LAAO; the question is how to respond to it and how to become skilled in doing so.

The biggest technical challenges of percutaneous LAAO therapy are the highly variable LAA anatomy, the fact that the LAA tissue is very fragile, and (for less experienced operators) the need for

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transseptal access. Preprocedural imaging with good quality transoesophageal echocardiography and/or cardiac computed tomography (CT) (or 3D printing) has been recognised as an important factor for procedural success, in an analogy of transcatheter aortic and mitral valve procedures. Advances in and technical improvement of the LAAO technique *per se* are also highly important. For example, the use of a pigtail catheter to access the LAA has decreased the pericardial bleeding events with the WATCHMAN device, whereas the use of the "ball" and "triangle" shape techniques has led to optimised and safer LAA implants with the ACP or the Amulet device **(Figure 1)**[7].

Another important challenge of LAAO therapy that is often not adequately discussed is the patient's actual needs and characteristics. For example, the most common indication for LAAO in the study of Cheung et al is poor compliance to OAC therapy, whereas in the vast majority of European or American studies the principal indication is previous major bleeding and high bleeding risk[6]. A patient with poor compliance may not have a high bleeding risk at all so procedural and post-procedure antithrombotic therapy may be very different compared to a patient who had a major bleeding and/or a stroke with documented LAA thrombus related to it. Knowing the patient is, therefore, crucial.

Before proceeding to decide which parts of LAAO therapies need further improvement, it is necessary to define all LAAO-related clinical and technical endpoints. The "Munich consensus document on definitions, endpoints, and data collection requirements for clinical studies" which was published in EuroIntervention in 2016 is a good tool for this purpose[8]. The relation between the presence and the degree of peri-device leaks and stroke is not yet fully understood. The rate of device thrombosis is fairly low and not clinically relevant in most studies; however, it is difficult to explain to a patient that a device that was implanted to prevent thromboembolism has developed a thrombus[9]. In any case, device design improvement, implant optimisation techniques, and structured operator teaching programmes are expected to tackle most of these issues in the near future.

In Asia, and particularly in China, LAAO therapy development needs to address a couple of different matters. As compared to Western countries, there is less compliance to OAC therapy due to lower patient education, increased medication cost, living in remote areas, etc.[5,10]. In addition, the reimbursement and cost of the LAAO procedure is different, with many patients having to pay out of their own pocket to get treated. In China, many of the LAAO procedures are combined with AF catheter ablation, in a "one stop shop" concept that may be clinically appealing but not yet fully investigated[11]. Finally, operator training and dissemination of technical expertise is another important challenge.

The number of centres engaging in LAAO therapy in Asia, and especially in China, is growing fast. Several very skilled operators perform a lot of procedures with optimal outcomes. Yet, the

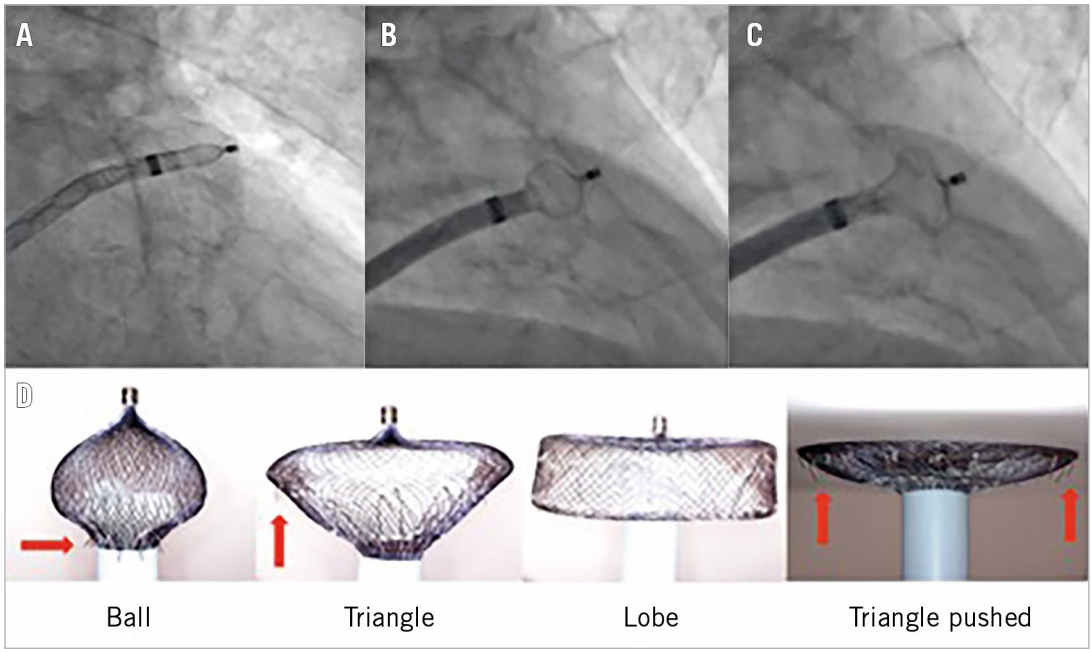

Figure 1. *Evolutionary steps in safer deployment of the AMPLATZER Cardiac Plug and the AMPLATZER Amulet device. "Unsheathing" in the left atrial appendage (A) to form a "ball" to enter (B) to create a "triangle" for harmless device pushing in shallow anatomies (C). Gradual and controlled pushing of the delivery wire forms the Amulet lobe in different ways and shapes (D). The "ball" shape is used for initial engagement and rotation/orientation of the sheath as the stabilising wires (red arrows) are close to the sheath and cannot damage the LAA wall, whereas the "triangle" shape is used to push against the LAA wall as the distal lobe pin is retracted inside the lobe, but without rotating the device as the stabilising wires are now exposed (red arrows).*

published data in the field are scarce. Hopefully, researchers will be encouraged by the efforts of Dr Cheung, the Prince of Wales physicians and their mentor and pioneer on LAAO, Yat Yin Lam, to publish more about LAAO in AsiaIntervention or another medical journal.

Conflict of interest statement

A. Tzikas is a clinical proctor for Abbott.

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Incidence and impact on prognosis of impaired kidney function in Middle Eastern patients undergoing percutaneous coronary intervention: results from the first Jordanian PCI Registry

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KEYWORDS

- ACS/NSTE-ACS
- NSTEMI
- stable angina
- STEMI

Abstract

Aims: The aim of this study was to evaluate the impact on prognosis of renal impairment (RI) in Middle Eastern patients after percutaneous coronary intervention (PCI).

Methods and results: PCI patients (N=2,426) were divided into three groups according to the estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2): normal renal function (eGFR ≥90), mild RI (eGFR 60-89), or moderate to severe RI (eGFR <60). Mean age of participants was 56±11 years. Normal renal function was present in 41.6%, mild RI in 44.2%, and moderate to severe RI in 14.2%. Patients with moderate to severe RI were older and had higher prevalence of hypertension and diabetes mellitus compared with other patients (p≤0.002). At one year, patients with moderate to severe RI had a higher incidence of cardiac mortality (3.78%) compared with patients with mild (1.77%) or no RI (1.49%), p=0.03. In multivariate analysis, moderate to severe RI was associated with higher one-year cardiac mortality compared to mild or no RI (odds ratio=3.7; 95% CI: 2.8-5.0, p=0.001).

Conclusions: Impaired renal function was present in about six out of 10 Middle Eastern patients undergoing PCI. Moderate to severe RI carries a higher risk of cardiac mortality at one year compared with mild or no RI.

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Abbreviations

ACS	acute coronary syndrome
BMI	body mass index
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CI	confidence interval
CVD	cardiovascular disease
DM	diabetes mellitus
eGFR	estimated glomerular filtration rate
Hct	haematocrit
JoPCR1	first Jordanian percutaneous coronary intervention registry
MDRD	Modification of Diet in Renal Disease equation
NSTE-ACS	non-ST-segment elevation acute coronary syndrome
NSTEMI	non-ST-segment elevation myocardial infarction
OR	odds ratio
PCI	percutaneous coronary intervention
RBC	red blood cell
RI	renal impairment
SD	standard deviation
STEMI	ST-segment elevation myocardial infarction
UA	unstable angina

Introduction

Cardiovascular disease (CVD) is the leading cause of death in the Middle East[1,2]. The number of patients who undergo percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS) and stable coronary disease in this region is increasing[3,4]. Impaired renal function is a known risk factor for CVD, has a significant prevalence among patients who are admitted with ACS[5,6], and is associated with an increased risk of cardiovascular events including death and major bleeding during the index hospitalisation and long-term follow-up[7,8]. Furthermore, patients who have renal impairment (RI) are frequently excluded from cardiovascular outcome trials[9].

The incidence of impaired renal function and its impact on short- and long-term outcome have not been evaluated in an exclusive PCI population in the Middle East. Only a few large regional registries have addressed cardiovascular outcome among patients admitted with ACS in relation to the severity of RI[10,11]. Of those studies, two evaluated the incidence of renal dysfunction and its impact on the in-hospital outcome in patients admitted with ACS and ST-segment elevation myocardial infarction (STEMI)[12,13]. Major limitations of these studies include the low rate of utilisation of coronary angiography and PCI, the heterogeneous groups of enrolled patients (native citizens and South Asian workers) and the lack of evaluation of long-term outcome.

We utilised data from the prospective, multicentre first Jordanian PCI Registry (JoPCR1)[14] to study in detail the prevalence of RI and its impact on the short- and long-term outcome after PCI in a Middle Eastern country. The study was designed to address cardiovascular outcome in an increasing number of patients who undergo PCI on an emergency or elective basis in this region. We aimed to evaluate the incidence of various degrees of RI in a PCI population, clinical and coronary angiographic features of patients who have RI, and the impact of RI on major adverse events during the index hospitalisation and up to one year of follow-up.

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Methods

JoPCR1 is a prospective, observational, multicentre registry of consecutive patients who underwent PCI at 12 tertiary care centres in Jordan between January 2013 and February 2014. Data were recorded prospectively at hospital admission and discharge, and at one, six and 12 months after the discharge. Data were collected during out-patient clinic visits or by phone calls to patients, household relatives or primary care physicians. Baseline data included clinical, laboratory, electrocardiographic, echocardiographic, and coronary angiographic features. Severity of coronary artery disease (CAD) was categorised as single CAD (≥70% luminal narrowing of one epicardial coronary artery, except the left main, on coronary angiography), or multivessel CAD (≥70% luminal narrowing of at least two epicardial coronary arteries or ≥50% of the left main coronary artery). Single-vessel PCI refers to percutaneous intervention in one epicardial coronary artery, except the left main, regardless of the number of stents used. Multivessel PCI refers to percutaneous intervention in two or more coronary arteries regardless of the number of stents used.

Baseline serum creatinine values were measured for all patients at admission, and renal function was assessed online by the estimated glomerular filtration rate (eGFR) using the abbreviated Modification of Diet in Renal Disease (MDRD) equation[15]. Stages of RI were defined according to Chronic Kidney Disease Working Group guidelines and categorised according to the eGFR into three groups: normal renal function (≥90 mL/min/1.73 m^2), mild RI (60-89 mL/min/1.73 m^2), and moderate to severe RI (<60 mL/min/1.73 m^2)[16]. Clinical, electrocardiographic, and coronary angiographic profiles, and in-hospital and one-year major adverse cardiovascular events were evaluated in the three groups of patients.

All PCI procedures were performed according to current standard guidelines. Details of the PCI procedures and complications were also prospectively recorded during hospitalisation and up to one year of follow-up. The arterial access site, type and number of stents, and the use of oral and intravenous antiplatelet agents were left to the operator's discretion. PCI was indicated for either ACS or stable coronary disease. ACS was classified as STEMI or non-ST-segment elevation ACS (NSTE-ACS) that included NSTEMI and unstable angina (UA). Stable coronary disease was defined as either chronic stable angina or silent ischaemia.

The studied adverse cardiovascular events were cardiac mortality, stent thrombosis, major bleeding events, stroke, coronary revascularisation and readmission for heart failure or ACS in the three groups.

Cardiac mortality was defined as any death not attributed to a clear non-cardiac cause. Definite or probable stent thrombosis was defined according to the Academic Research Consortium

definition[17]. Major bleeding events were defined according to the CRUSADE study classification and included intracranial haemorrhage, retroperitoneal bleeding, haematocrit (Hct) drop ≥12% from baseline, any red blood cell (RBC) transfusion when baseline Hct was ≥28%, or any RBC transfusion when baseline Hct was <28% with witnessed bleeding[18]. The study was approved by the Institutional Review Board of each participating hospital.

STATISTICAL ANALYSIS

Collected data were analysed using the SPSS statistical package, Version 22 (IBM Corp., Armonk, NY, USA). Descriptive statistics were compiled using means and standard deviation (SD) to describe the continuous variables. Frequencies and percentages were used to describe the categorical variables. The differences between the means of the normally distributed variables were examined using multivariate tests of the general linear model in the three groups of patients with different degrees of RI. Correlations of RI with age, gender, diabetes mellitus (DM), past history of CVD, ST-segment deviation, elevated cardiac biomarkers, multivessel CAD, and heart failure were analysed using Pearson's two-tailed correlation for numeric variables. Frequencies and percentages for each stratum according to the participants' eGFR were calculated and compared using the Mantel-Haenszel chi-square (χ^2) and Fisher's exact tests. A multivariable binary logistic regression analysis was performed to examine collectively the association between the cardiac deaths at one year and the significant risk factors identified from the chi-square univariate and multivariate analyses. The final multivariable logistic regression model for cardiac deaths at one year was constructed using manual stepwise forward logistic regression analysis. All reported p-values were two-tailed, and $p \leq 0.05$ was considered to be statistically significant.

Results

The baseline features of the consecutive patients who had PCI (N=2,426) are shown in **Table 1** in three groups according to the renal function. Normal renal function was present in 1,009 (41.6%), mild RI in 1,073 (44.2%), and moderate to severe RI in 344 (14.2%) of all patients. Among patients in the latter group, 308 (12.7%) had moderate RI (eGFR 30-59 ml/min/1.73 m^2), 17 (0.7%) had severe RI (eGFR 15-29 ml/min/1.73 m^2), and 19 (0.8%) had very severe RI (eGFR <15 ml/min/1.73 m^2). There were 26 (1.1%) haemodialysis-dependent patients. Patients who had severe or very severe RI (N=36, 1.5%) were grouped with those who had moderate RI because the validity of statistical analysis of such a small sample might be compromised.

Patients with moderate to severe RI were older, more likely to be female, to have hypertension and DM, and tended to be more overweight than patients with normal renal function or mild RI. Compared with patients who had mild or no RI, those with moderate to severe RI had more stable coronary disease as an indication for PCI (27% vs. 24% vs. 20%, respectively, p=0.03), and less STEMI as an indication for PCI (23% vs. 29% vs. 34%, respectively, p=0.001) **(Figure 1)**.

Table 1. Baseline features in three groups of patients stratified by the estimated glomerular filtration rate.

Clinical feature	Moderate to severe renal impairment (N=344)	Mild renal impairment (N=1,073)	Normal renal function (N=1,009)	MANOVA *p*-value
Age (years), mean±SD	66.2±9.1	59.2±10.6	54.8±10.2	0.001
Women, n (%)	173 (50.3)	193 (18.0)	134 (13.3)	0.001
Hypertension, n (%)	285 (82.8)	674 (62.8)	552 (54.7)	0.001
Diabetes mellitus, n (%)	224 (65.1)	568 (52.9)	508 (50.3)	0.002
Hypercholesterolaemia, n (%)	177 (51.5)	522 (48.6)	485 (48.1)	0.55
Current cigarette smoking, n (%)	67 (19.5)	438 (40.8)	550 (54.5)	0.001
BMI (kg/m^2), mean±SD	28.5±5.1	25.7±4.5	27.9±4.3	0.06
History of MI, n (%)	116 (33.7)	407 (37.9)	434 (43)	0.004
Prior PCI, n (%)	101 (29.4)	258 (24.0)	230 (22.8)	0.01
Prior CABG, n (%)	16 (4.7)	39 (3.6)	29 (2.9)	0.31
Past history of heart failure, n (%)	34 (9.9)	86 (8.0)	74 (7.3)	0.32
ST-segment deviation, n (%)	162 (47.1)	503 (46.9)	516 (51.1)	0.13
Elevated cardiac enzymes, n (%)	120 (34.9)	410 (38.2)	440 (43.6)	0.005
Serum creatinine (mg/dl), mean±SD	1.8±1.7	1.0±0.13	0.8±0.13	0.001
eGFR (ml/min/1.73 m^2), mean±SD	47.5±13.5	77.6±8.2	116.4±24.4	0.001
LVEF <45%, n (%)	54 (15.7)	141 (13.1)	107 (10.6)	0.27

BMI: body mass index; CABG: coronary artery bypass graft surgery; CAD: coronary artery disease; eGFR: estimated glomerular filtration rate; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention

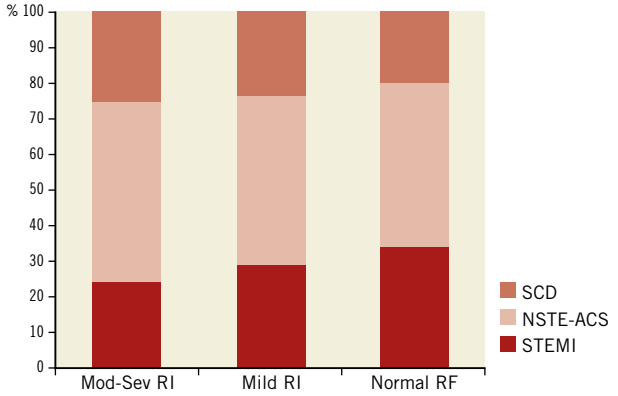

Figure 1. *Indications for PCI in 2,426 PCI patients according to the degree of renal impairment. Mod-Sev RI: moderate to severe renal impairment; NSTE-ACS: non-ST-segment elevation acute coronary syndrome; RF: renal function; SCD: stable coronary disease; STEMI: ST-segment elevation myocardial infarction*

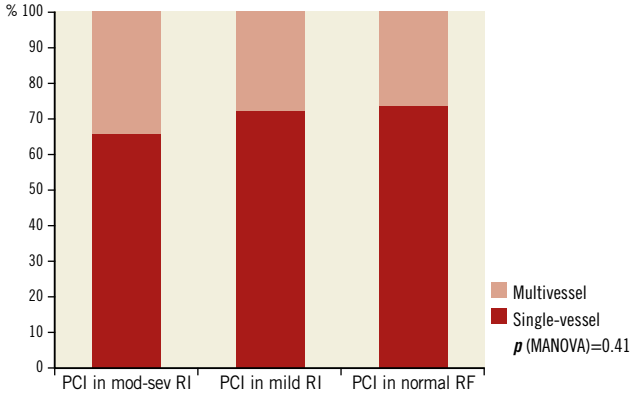

Figure 2. *Single-vessel and multivessel PCI in 2,426 patients according to the degree of renal impairment. mod-sev RI: moderate to severe renal impairment; PCI: percutaneous coronary intervention; RF: renal function*

Patients with moderate to severe RI also had higher prevalence of multivessel CAD than the other two groups (47% vs. 42% vs. 39%, respectively, p=0.03). However, the differences in the rates of PCI for multivessel CAD in the three groups were not significant (34% vs. 28% vs. 27%, respectively, p=0.41) **(Figure 2)**. Most of the coronary stents used (N=3,038) were drug-eluting (90%). Bare metal stents and bioresorbable scaffolds comprised 9% and 1% of all stents, respectively.

Table 2 depicts in-hospital complications and use of medications in the three groups of patients. Of seven major in-hospital complications, major bleeding was the only event that occurred in a significantly higher proportion of patients with moderate to severe RI compared with patients with normal renal function (2.0% vs. 0.6%, p=0.02). The incidence rates of other events, heart failure, cardiogenic shock, ventricular tachyarrhythmias, and emergency coronary bypass surgery were not statistically different among the three groups.

There were no differences among the three groups of patients in the rates of in-hospital use of the four classes of recommended cardiovascular medications (dual antiplatelet agents, statins, beta-blockers and renin-angiotensin blockers). Similarly, at one

Table 2. In-hospital complications and medications.

Clinical features		Moderate to severe renal impairment (N=344)	Mild renal impairment (N=1,073)	Normal renal function (N=1,009)	MANOVA *p*-value
In-hospital complications, n (%)	Ventricular tachyarrhythmia	1 (0.3)	13 (1.2)	7 (0.7)	0.15
	Heart failure	34 (9.9)	86 (8.0)	74 (7.3)	0.31
	Cardiogenic shock	1 (0.3)	7 (0.7)	6 (0.6)	0.74
	Emergency CABG	0 (0)	1 (0.1)	2 (0.2)	0.62
	Stent thrombosis	0 (0)	5 (0.47)	4 (0.40)	0.46
	Major bleeding events	7 (2.0)	10 (0.93)	6 (0.59)	0.01
	Cardiac mortality	2 (0.58)	11 (1.03)	6 (0.59)	0.49
In-hospital medications, n (%)	Aspirin	339 (98.5)	1,063 (99.1)	1,002 (99.3)	0.85
	$P2Y_{12}$ inhibitor	344 (100)	1,067 (99.4)	1,004 (99.5)	0.02
	Heparin	341 (99.1)	1,054 (98.2)	967 (95.8)	0.001
	Thrombolytic agents	8 (2.3)	39 (3.6)	34 (3.4)	0.55
	Glycoprotein IIb/IIIa inhibitors	21 (6.1)	129 (12.0)	177 (17.5)	0.001
	Beta-blockers	265 (77.0)	785 (73.2)	762 (75.5)	0.19
	Renin-angiotensin blockers	189 (54.9)	638 (59.5)	557 (55.2)	0.09
	Statins	328 (95.3)	1,018 (94.9)	961 (95.2)	0.88

CABG: coronary artery bypass grafting

year, the rates of use of these four classes of medications were not different among the three groups of patients. Dual antiplatelet agents and statins were used in about nine out of 10 patients in each of the three groups, beta-blockers in about seven out of 10, and renin-angiotensin blockers in about six out of 10, with no statistically significant differences among the three groups of patients.

Cardiovascular events at one month and one year after the index hospitalisation are shown in **Table 3**. Patients with moderate to severe RI were at higher risk of cardiac death at one month and at one year.

As for the incidence of major bleeding events at one month and one year, patients with moderate to severe RI did not have excess events compared with patients with mild RI (2.3% vs. 1.1%, p=0.1 at one month, and 2.3% vs. 1.3%, p=0.2 at one year). However, these patients had significantly higher incidence of major bleeding compared with those with normal renal function at one month (2.3% vs. 0.7%, p=0.01), and at one year (2.3% vs. 0.8%, p=0.02).

The impact of nine variables on cardiac mortality at one year was determined using the multivariate logistic regression model **(Table 4)**. Renal impairment was a strong predictor of cardiac mortality at one year (odds ratio [OR] 3.7, 95% CI: 2.8-5.0, p=0.001). Other predictors included heart failure (OR 7.5, 95% CI: 4.0-13.9, p=0.001), elevated cardiac enzymes (OR 2.2, 95% CI: 1.1-4.2, p=0.02), age ≥60 years (OR 1.9, 95% CI: 1.0-3.6, p=0.04), and prior CVD (OR 1.3, 95% CI: 1.0-1.6, p=0.03).

Table 4. Multivariate logistic regression model for one-year cardiac mortality.

Variable	*p*-value	OR	95% CI for OR	
			Lower	Upper
Age ≥60 years	0.04	1.9	1.02	3.58
Female gender	0.16	1.6	0.83	3.11
Diabetes mellitus	0.53	1.1	0.77	1.66
Prior CVD	0.03	1.3	1.03	1.62
ST-segment deviation	0.68	1.1	0.81	1.39
Elevated cardiac enzymes	0.02	2.2	1.13	4.15
Multivessel CAD	0.07	1.4	0.98	1.96
Renal impairment	0.001	3.7	2.8	5.00
Heart failure	0.001	7.5	4.00	13.89

Hosmer and Lemeshow test: χ^2=4.616; df=8; *p*-value=0.798.
p-value <0.05 is statistically significant. CAD: coronary artery disease; CI: confidence interval; CVD: cardiovascular disease; OR: odds ratio

Discussion

The major findings of this study are that (1) in a contemporary cohort of Middle Eastern patients who underwent PCI, less than half (44%) had mild RI and 14% had moderate to severe RI, (2) patients with moderate to severe RI were older, more likely to be female and to have hypertension and DM compared with those with mild or no RI, (3) patients with moderate to severe RI had higher prevalence of multivessel CAD and more PCI for stable coronary disease than patients with mild or no RI, and (4) moderate to severe RI was an independent predictor of cardiac mortality. These findings are the first from this region to address specifically the impact of RI on cardiovascular outcomes, and will thus serve as assuring evidence for the practising cardiologists that PCI for patients with RI is both safe and feasible. The misconception that PCI is better avoided or delayed in this high-risk population is not

Table 3. Adverse cardiovascular events one month and one year after hospital discharge.

Event		Moderate to severe renal impairment (N=344)	Mild renal impairment (N=1,073)	Normal renal function (N=1,009)	MANOVA *p*-value
Cardiac mortality, n (%)	One month	8 (2.33)	14 (1.30)	7 (0.69)	0.05
	One year	13 (3.78)	19 (1.77)	15 (1.49)	0.03
Stent thrombosis, n (%)	One month	2 (0.58)	15 (1.40)	16 (1.59)	0.38
	One year	5 (1.45)	22 (2.05)	20 (1.98)	0.78
Major bleeding events, n (%)	One month	8 (2.33)	12 (1.12)	7 (0.69)	0.05
	One year	8 (2.33)	14 (1.30)	8 (0.79)	0.08
Stroke, n (%)	One month	1 (0.29)	2 (0.19)	3 (0.30)	0.87
	One year	4 (1.16)	4 (0.37)	4 (0.40)	0.16
Heart failure, n (%)	One month	37 (10.76)	90 (8.39)	80 (7.93)	0.26
	One year	42 (12.21)	98 (9.13)	83 (8.23)	0.09
Readmission for ACS, n (%)	One month	5 (1.45)	12 (1.12)	15 (1.49)	0.74
	One year	15 (4.36)	52 (4.85)	46 (4.56)	0.92
Coronary revascularisation, n (%)	One month	3 (0.87)	12 (1.12)	15 (1.49)	0.60
	One year	6 (1.74)	32 (3.0)	35 (3.47)	0.27

ACS: acute coronary syndrome

supported by clinical trials. The current study will be the first to dissipate this misconception.

Impaired renal function, an important risk factor for CVD and a strong predictor of adverse events after ACS, has not been extensively studied in the Middle East despite the high prevalence of CVD and the increasing number of patients admitted with ACS[3,4,10-13]. Previous studies have indicated that, among ACS patients, 8 and 6 out of 10 undergo diagnostic coronary angiography or coronary intervention, respectively[4], reflecting a high degree of adherence to guidelines that recommend an invasive strategy in these patients. The prevalence of moderate to severe RI reported in the current study (14%) is lower than the prevalence rates of 30-40% reported by investigators from other regions[19,20], possibly due to the relatively younger age of the enrolled patients in this region.

Renal function in this study was assessed by the eGFR using the abbreviated MDRD[15], which is the recommended method for estimation of the GFR in adult patients with CVD and is also a validated tool for the estimation of GFR in a typical office setting[21]. The online equation calculator is simpler and produces essentially similar results to the original equation[22]. Several other validated estimation equations for GFR that use easily obtained clinical data and laboratory test results are readily available, including the Cockcroft-Gault[23] and Chronic Kidney Disease Epidemiology Collaboration[24] formulas. These equations are more practical than the more accurate formal GFR measurement using iothalamate or a similar marker, but they are time-consuming, expensive, generally unsuitable for clinical practice, available in only a few centres, and certainly not cost-effective for kidney disease screening[22]. Regardless of the method used, it is advisable to estimate the GFR for patients admitted with ACS or those who are planned to undergo PCI to facilitate risk stratification according to the degree of RI[25], and for identification of high-risk patients in whom close monitoring and vigilance could lower the incidence of adverse events.

Patients who are admitted with ACS and found to have RI are less frequently referred for invasive coronary diagnostic and revascularisation procedures, and less commonly treated with guideline-based cardiovascular medications compared with patients who have normal renal function[9]. These patients also experience higher rates of adverse cardiovascular events regardless of the conservative or invasive therapeutic strategies adopted[9,20,26]. RI doubles the mortality rates in ACS patients compared with patients who have normal renal function[27]. Moreover, PCI in patients who have RI is associated with an increased risk of major adverse cardiovascular events during and after the procedure including death, major bleeding events, heart failure, cardiogenic shock and target vessel revascularisation[28,29]. Several pathophysiological factors that explain the excess cardiovascular adverse events in patients with RI include the coexistence of comorbidities and cardiovascular risk factors (old age, female gender, DM, and hypertension), elevated state of inflammatory and oxidative stress, high levels of matrix metalloproteinase that are implicated in destabilisation of the coronary plaque fibrous cap, heavy and complex CAD burden, and accelerated MI expansion[30-32]. Despite the high-risk clinical and angiographic profiles of patients who have RI and physicians' reluctance to manage them aggressively, there is strong evidence of significant symptomatic benefits, reduction of short- and long-term adverse events, and improved prognosis when such patients are referred to an invasive strategy to treat ACS regardless of the degree of RI[33].

The relatively younger age, high prevalence of single-vessel CAD in more than half of all the patients, enrolling only patients who underwent PCI, the high rate of utilisation of medications shown to be associated with improved outcome including dual antiplatelet agents, renin-angiotensin system antagonists and statins, and the almost exclusive use of drug-eluting stents in the current study might be potential explanations for the absence of excess non-fatal in-hospital events in patients with RI[32-34]. It is very reassuring that the incidence of significant complications during the index hospitalisation was generally low and less than 1% in patients with moderate to severe RI for each single complication, except for heart failure (9.9%) and major bleeding events (2.0%). Furthermore, this study has clearly demonstrated that, among patients with variable degrees of RI, PCI is generally safe and effective in the long run with a one-year event rate comparable to or better than those observed by other investigators from other regions. This should encourage cardiologists in this region to refer this high-risk group of ACS patients to an invasive strategy in this contemporary era of interventional practice.

Management of ACS in the vulnerable patient group with severe RI and end-stage kidney disease requiring haemodialysis is challenging due to the high cardiovascular morbidity and mortality even after surgical or percutaneous coronary revascularisation[34]. In this study, only a minority of patients (0.8% and 1.1%) had very severe RI or end-stage renal disease requiring haemodialysis, respectively; thus, their impact on the overall incidence of adverse events is limited.

In agreement with other studies, PCI patients in this study who had moderate to severe RI had a higher rate of major bleeding events from the index hospital admission to one year of follow-up[32,35]. The bleeding risk is related to the prolonged bleeding time, abnormal platelet aggregation and adhesion, and the exaggerated response to and use of inappropriate doses of antiplatelet and fibrinolytic agents[32,35].

The in-hospital cardiac mortality rates observed in this study among the patients with RI (≤1%) were lower than those reported by other regional registries that ranged between 12% and 40% in STEMI patients and from 0.8% to 13% in ACS patients depending on the degree of RI[10-12]. Cardiac mortality at one year in this study was significantly higher in patients with moderate to severe RI compared with those who had mild or no RI, in concordance with the findings of other investigators[34-36]. Older age, female gender and excess bleeding events could all contribute to the high cardiac mortality rate. However,

after correction for other factors associated with mortality risk, moderate to severe RI was an independent predictor of one-year mortality.

Limitations

The current study has a few limitations. Data were collected from an observational study and might be subject to potential bias. ACS was defined according to current guidelines. However, the method of case identification may not have been completely specific, because patients with RI are more likely to have elevated levels of cardiac markers. The GFR estimated at admission reflected the renal function before any intervention during the index hospitalisation. The renal function was not re-evaluated pre-discharge or during follow-up and thus worsening or improvement of renal function could not be ruled out. Larger studies are needed to define better the impact on renal dysfunction, especially in those with severe RI and/or on haemodialysis, in all ACS patients, whether they are treated conservatively or by an invasive strategy, and also to re-evaluate renal function during the study course.

Conclusions

In this Middle Eastern patient population who had PCI, the presence of moderate to severe RI was an independent predictor for in-hospital and one-year cardiac mortality and major bleeding events. Estimating the GFR in such a population is strongly recommended in order to define better high-risk groups among these patients such that vigilance can be exercised for adverse cardiovascular events.

Impact on daily practice

The relatively low incidence rate of adverse cardiovascular events in a PCI-exclusive group should encourage healthcare professionals to refer ACS patients with RI to an invasive strategy.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Saphenous vein graft intervention with a bioresorbable vascular scaffold: a follow-up optical coherence tomography study at 40 months

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This paper also includes supplementary data published online at: www.asiaintervention.org

Introduction

Bioresorbable vascular scaffolds (BVS)[1-3] were designed to be an effective substitute to conventional metallic stents and overcome limitations including positive vessel remodelling, stent fracture, neoatherosclerosis, being a perpetual nidus for stent thrombosis and inhibition of physiological vasodilation[4,5]. The most widely studied polymeric devices comprise poly-L-lactide (PLLA) struts coated with poly-D, L-lactide (PDLLA) and an antiproliferative agent[4,5]. Although late outcomes with the Absorb™ bioresorbable vascular scaffold (Abbott Vascular, Santa Clara, CA, USA) are disappointing[6], this only confirms the need to gain a better understanding of the late behaviour of these scaffolds. The literature so far suggests that there is some evidence supporting their use in venous grafts[7-10]. This case description illustrates the unique findings of optical coherence tomography (OCT) imaging of a BVS in a vein graft at 40 months post implantation.

Methods

A 77-year-old lady had previously undergone two bypass operations, the latter following recurrent restenoses of conventional metallic stents. Approximately seven years post second bypass (April 2013), she had symptoms (angina) with inducible ischaemia on a stress echocardiogram. Angiography found high-grade proximal disease in a saphenous venous graft to the left anterior descending artery. The lesion was adequately prepared using a 3.0 mm predilatation balloon (Tazuna® [Terumo Corp., Tokyo, Japan] – a semi-compliant percutaneous transluminal coronary angioplasty [PTCA] balloon catheter). A 3.5×28 mm Absorb BVS was deployed at 14 atmospheres and post-dilation was performed with a 3.75 mm non-compliant balloon (Hiryu® [Terumo Corp.] – a non-compliant PTCA balloon catheter) to 21 atmospheres. A distal protection device was utilised (3.0 mm SpiderFX™ [Medtronic, Minneapolis, MN, USA] embolic protection device) and the patient was placed on dual antiplatelet therapy for six months (aspirin 100 mg daily and clopidogrel 75 mg daily).

Results

Approximately 40 months post implant, she again developed symptoms (angina); an exercise test was abnormal and repeat coronary angiography was performed. This demonstrated new flow-limiting disease in a small to medium-sized native marginal circumflex artery, successfully treated with plain balloon

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angioplasty using a 2.0 mm predilatation balloon (Tazuna). Given concerns as to whether the diseased circumflex artery explained her presentation and the fact that the proximal segment of the vein graft to the left anterior descending artery appeared to have reduced volume **(Figure 1)**, an OCT study **(Moving image 1, Figure 2)** was performed to assess the BVS in the vein graft to the left anterior descending artery. This demonstrated good apposition of the scaffold, tissue coverage with a neointimal depth of 0.48 mm and five uncovered struts. There were several struts manifesting various stages of PLLA degradation ranging from early cellular infiltration of dissolving struts (very high peak intensity at the core with low median intensity) to late degradation of the strut (moderately high peak intensity with a high median intensity). No intervention was performed on the vein graft. Post procedure, she was placed on dual antiplatelet therapy for six months (aspirin 100 mg daily and clopidogrel 75 mg daily) and has remained well since.

Discussion

In September 2017, Abbott Vascular ceased supplying BVS, citing low demand but more likely due to disappointing clinical results. They also signalled their intention to release a newer improved device for future clinical trials. Accepting that initial poor implantation technique and inappropriate vessel selection played a role, the four-year ABSORB II data[6] showed a statistically higher rate of target lesion failure (TLF) (11.1% vs. 5.6%). There were no cases of stent/scaffold thrombosis between three and four years and some see this as the potential start of scaffold benefit. Data do support a "learning curve": the three-year data of ABSORB III[11] showed only a trend towards a higher rate of TLF in the ABSORB arm (13.4% vs. 10.4%) but with a persistently higher rate of device thrombosis (2.3% vs. 0.7%), whilst the 30-day ABSORB IV (using an optimal implantation technique) reported reduced early events (30-day scaffold thrombosis reduced from 1.1% in ABSORB III to 0.4% in ABSORB IV at 30 days) to the extent that ABSORB IV shows non-inferiority at 30 days. Given that a "learning curve" probably exists, cases such as this and any knowledge gained remain clinically relevant.

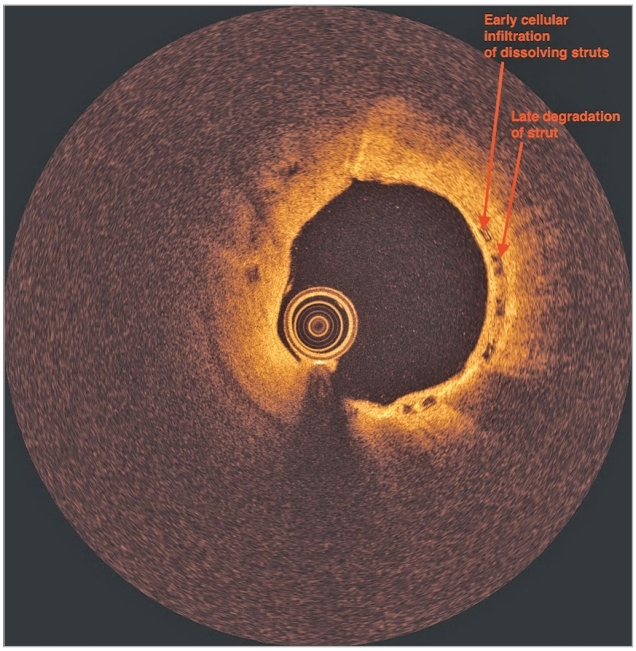

Figure 2. *Optical coherence tomography image of the BVS.*

The development of a "vascular restoration" strategy in the form of BVS has been considered by many as the "fourth revolution" in the percutaneous management of coronary artery disease[12,13]. So far, seven trials have been published comparing everolimus-eluting bioresorbable scaffolds and everolimus-eluting metallic stents[14,15]. The benefit of bioresorbable stents is thought to pay off in the long term: at around twelve months there is a loss of mechanical support that allows conditioning of tissue to enhance healing[16], and at three years[1] full reabsorption is noted, that assists in physiological

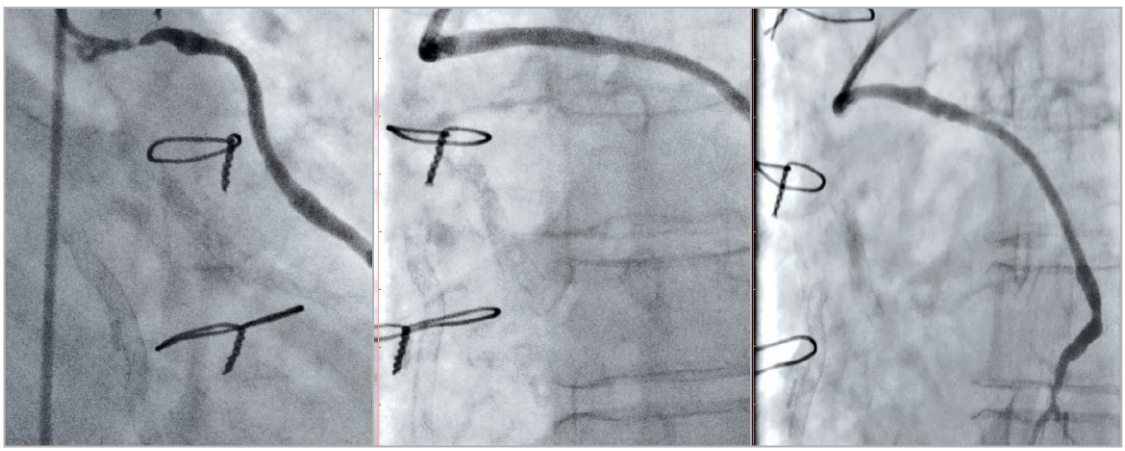

Figure 1. *Saphenous vein graft to the left anterior descending artery pre implantation, immediately post implantation of the BVS and at 40 months post implantation of the BVS. BVS: bioresorbable vascular scaffold*

function and neo-media formation in coronary arteries. Based on trial evidence at 60 months[17], the BVS struts disappear completely.

Recently, Nakatani and colleagues[18] performed an intravascular ultrasound echogenicity analysis and light intensity analysis on OCT in a porcine model with a follow-up duration of 48 months. There was good correlation observed for the strut depolymerisation process and integration process post comprehensive bioresorption. In addition, late luminal enlargement was observed at three to four years and was associated with strut integration.

Some bioresorbable stents are still commercially available; however, we are still awaiting the results of ABSORB IV, due for release in the next few years. Newer-generation stents such as the Magmaris™ (Biotronik, Bülach, Switzerland) are showing promising results after publication of BIOSOLVE II and III[19], in which improved stent and study design adds strength to the argument that BVS may still play a role in future percutaneous interventions.

Limitations

Little is known about the role of bioresorbable vascular scaffolds in venous grafts. The publications[7-10,20] so far in this genre are summarised in **Table 1**. Indications for use in venous grafts are beyond the scope of this report, and the stent inserted was done so prior to release of ABSORB II and III. Our rationale for implantation in this high-risk patient was that she had incessant restenosis of metallic stents and was willing to allow sequential non-invasive imaging with computed tomography.

Conclusion

This report is unique given that it is the longest follow-up period to date of such an intervention with an Absorb scaffold in a saphenous vein graft. In an era when the use of BVS has been questioned, in this particular case the scaffold demonstrated excellent late angiographic patency confirmed on invasive OCT imaging. Meticulous attention to Absorb scaffold implantation technique is critical to providing good short-term as well as long-term clinical results[21,22]. Despite the Absorb BVS being recalled due to an increased incidence of target vessel myocardial infarctions[11], there is still potential for benefit after scaffold resorption, and newer-generation BVS devices remain a viable option. Published data are still lacking to debunk its use entirely[6] .

Impact on daily practice

Our findings suggest that late OCT images of the scaffold treatment site are consistent with the existing chronology of events in intracoronary imaging of Absorb scaffolds in native coronary arteries. Further research and ideally a robust randomised trial comparing Absorb bioresorbable vascular scaffolds to conventional stenting are needed to clarify their role in this cohort.

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Table 1. Summary of bioresorbable vascular scaffolds in saphenous venous grafts.

Author	Country	Cohort	Gender	Age	Size	Dilatation	Imaging	Comments
Ong[7]	Singapore	1	M	52 years	3.0×18 mm	Pre	CTCA 3 months post insertion	Presentation with NSTEMI and patent stent at 3 months on CTCA
Roleder[9]	Poland	1	M	83 years	2.5×15 mm	N/A	Repeat angiography 2 weeks post insertion	Re-presentation with unstable angina and patent stent at 2 weeks on conventional angiography
Roleder[10]	Poland	6	M ×4 F ×2	Median 73 years (57-83)	Median RLD 3.13 mm (2.25-3.45). Median MLD 1.12 (0.52-1.86 mm)	Pre (100%) Post (100%)	Post-procedure OCT, surveillance OCT at 6 months and 18 months	Only one with 18-month and the rest 6-month follow-up with optical coherence imaging, with the majority showing neointimal formation.
Yew[8]	Malaysia	1	M	53 years	3.0×28 mm	Pre + Post	Repeat PCI 4 weeks post angiogram	Presentation with ACS followed up with conventional angiography 4 weeks later
Wojakowski*	Poland	1	M	54 years	3.5×12 mm	Pre	Post-procedure OCT 3 months following insertion	54-year-old man with stable angina. Optical coherence imaging at 3 months showed complete apposition
Picard[20]	Canada	10	M ×9 F ×1	Median 75 years (64-81)	Median diameter 3.5 mm (3-3.5). Median length 18 mm (18-28)	Pre (84%) Post (77%)	N/A	Target vessel revascularisation similar to conventional stents (13 lesions)

* TCT 2014 C-167; ACS: acute coronary syndrome; CTCA: computed tomography coronary angiography; F: female; M: male; MLD: minimal lumen diameter; mm: millimetres; N/A: not available; NSTEMI: non-ST elevation myocardial infarction; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; Post: post-dilation; Pre: predilation; RLD: reference lumen diameter

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Moving image 1. Optical coherence tomography study of the saphenous vein graft bioresorbable vascular scaffold.

The supplementary data are published online at: www.asiaintervention.org

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A focused review on optimal coronary revascularisation in patients with chronic kidney disease

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KEYWORDS

- atherectomy
- bare metal stent
- drug-eluting stent
- renal insufficiency
- stent thrombosis

Abstract

Concomitant chronic kidney disease (CKD) and coronary artery disease (CAD) is known to have poor outcomes. With a thorough literature review, we discuss the pathophysiological basis behind accelerated atherosclerosis in CKD, and the role of percutaneous coronary intervention (PCI) in these patients, focusing on drug-eluting stents, coronary artery bypass grafting, and adverse outcomes. We discuss factors contributing to poor outcomes in these patients, and the need for more work in this subgroup.

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Abbreviations

BMS	bare metal stent(s)
CABG	coronary artery bypass grafting
CAC	coronary artery calcification
CAD	coronary artery disease
CHF	congestive heart failure
CKD	chronic kidney disease
DAPT	dual antiplatelet therapy
DES	drug-eluting stent(s)
EES	everolimus-eluting stent(s)
eGFR	estimated glomerular filtration rate
ESRD	end-stage renal disease
LVD	left ventricular dysfunction
MI	myocardial infarction
OAS	orbital atherectomy system
PCI	percutaneous coronary intervention
RA	rotational atherectomy
SES	sirolimus-eluting stent(s)
ST	stent thrombosis
TLR	target lesion revascularisation
TVF	target vessel failure
TVR	target vessel revascularisation

Introduction

Chronic kidney disease (CKD) is defined as the presence of kidney damage or reduced kidney function (eGFR <60 mL/min/1.73 m^2) for ≥3 months[1]. Most studies concluded that an eGFR <60 mL/min/1.73 m^2 is associated with increased risk of restenosis, recurrent myocardial infarction (MI), congestive heart failure (CHF) and mortality[2].

The current recommendation for DES use in end-stage renal disease (ESRD) patients is deduced from extrapolation of information from patients with normal renal function[3]. Furthermore, CKD is sub-classified into stages 1-5[1], each associated with different mortality and revascularisation events with best pharmacological therapy, PCI, and coronary artery bypass grafting (CABG).

Unique vascular pathobiology in CKD

Inflammation drives atherosclerosis[4]. CKD patients have co-existing traditional cardiovascular risk factors propagating inflammation. Among non-traditional risk factors, contributors to inflammation include advanced glycated end products (AGEs), uraemia, peritoneal dialysis and haemodialysis[5].

Retention of AGEs secondary to decreased renal function causes oxidative damage, recruitment of mononuclear cells and an inflammation, which is intensified by fluid retention via bacterial or endotoxin translocation from bowel oedema, producing pro-inflammatory cytokines (interleukin-6 [IL-6], high-sensitivity CRP [hsCRP]) **(Figure 1)**. These are not adequately cleared secondary to uraemia. This is of clinical importance as IL-6 and hsCRP are independent predictors of mortality in CKD[6].

Reduced renal function is associated with disruption of the balance between endothelin and nitric oxide, functional platelet abnormalities and coagulopathy[7], predisposing to atherosclerosis.

Efficacy and safety of DES compared to BMS/CABG

The bare metal stent (BMS) superseded balloon angioplasty as the treatment of choice following improved angiographic and clinical outcomes. However, BMS-related adverse events such as in-stent restenosis with rates of 20-30%[8] led to the development of the drug-eluting stent (DES) which shares the same complications but at a delayed interval.

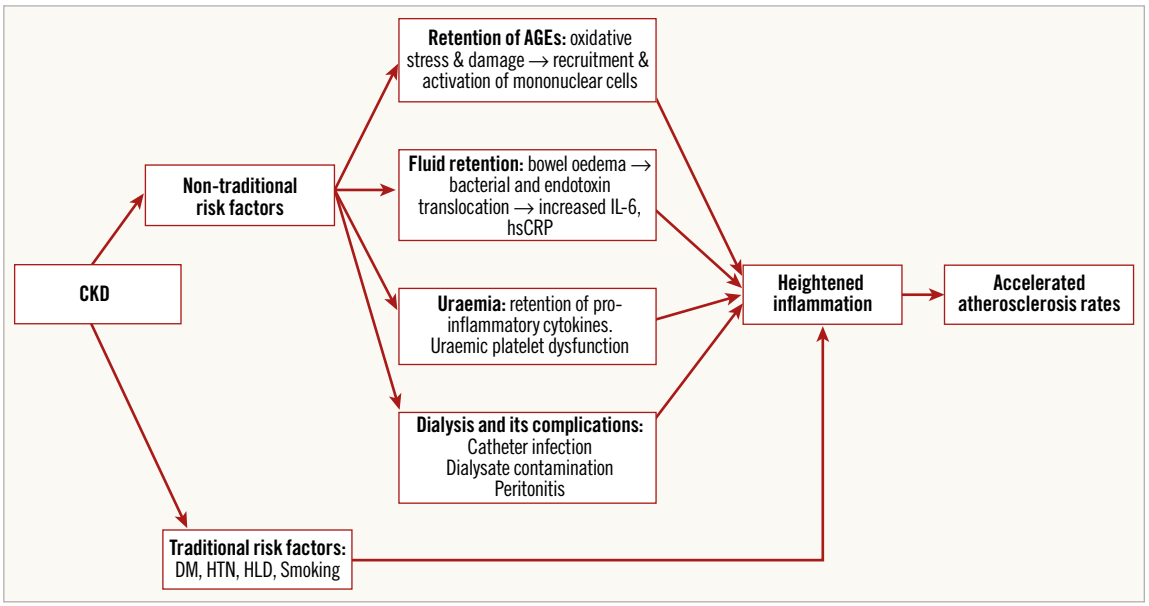

Figure 1. *Pathophysiology of accelerated atherosclerosis in CKD. AGEs: advanced glycated end products; CKD: chronic kidney disease; DM: diabetes mellitus; HLD: hyperlipidaemia; hsCRP: high-sensitivity C-reactive protein; HTN: hypertension; IL-6: interleukin-6*

New-generation DES with a reduced load of antiproliferative drugs, thinner metallic struts and improved biocompatibility of stent polymer are the new standard of care[9]. The NORSTENT trial[10] failed to demonstrate benefits in mortality and non-fatal MI with the use of DES over BMS but revealed benefits in stent thrombosis and repeat revascularisation. Furthermore, NORSTENT did not target patients with CKD where the improved designs of new-generation DES might be less thrombogenic. Also, a recent meta-analysis comparing DES and BMS use in CKD patients concluded with observed benefits seen across mortality, MI, stent thrombosis (ST) and target vessel revascularisation (TVR). No difference was observed between first- and second-generation DES[11].

A meta-analysis comparing second-generation DES (everolimus-eluting stent [EES]) with CABG reported increased rates of MI and repeat revascularisation in patients receiving EES, despite comparable mortality rates[12]. Hence, there might be a role for consideration of CABG in patients who are surgically fit to improve their quality of life.

Comparative outcomes of DES versus BMS in CKD

Mortality rates are inversely related to the degree of renal dysfunction, with tripling of mortality rates in patients with both CAD and severe CKD compared to patients with normal renal function[13].

MORTALITY

Tsai et al[14] **(Table 1)** reported benefits in all-cause mortality with DES compared to BMS both in patients with normal renal function and in those with CKD. This was echoed by similar findings in a *post hoc* analysis of the PRODIGY trial[15] and in a study by Jeong et al[16]. However, Lemos et al[17] reported insignificant differences in mortality despite improvements in clinical restenosis.

The benefits of second- over first-generation DES in the CKD population are unclear, with a retrospective analysis failing to demonstrate mortality benefits with the use of second-generation DES[18], probably due to systemic factors which are recognised to worsen oxidative stress and systemic inflammation independently[19]. Other contributing factors include left ventricular dysfunction (LVD) which is associated with adverse outcomes post PCI[20].

STENT THROMBOSIS

An increased risk of stent thrombosis secondary to abnormal vascular pathobiology in CKD was demonstrated by a study which found that rates of ST were significantly raised in CKD compared to normal renal function at one-year follow-up post DES implantation[7].

In PRODIGY, the number needed to treat to prevent one definite or probable ST at two-year follow-up was 20 in CKD patients versus 50 in patients with normal renal function, reinforcing the significant benefits of DES[15].

The higher incidence of ST in CKD is related to increased severity of systemic atherosclerosis, and diffuse and calcified coronary artery disease which increases the risk of stent malapposition and underexpansion[7]. Restenosis rates following PCI range from 60-81% when assessed via repeat coronary angiography. In contrast to patients with normal kidneys, clinical restenosis is not raised in patients with CKD, suggesting silent progression of cardiac ischaemia, hence a high risk of adverse cardiac events[21].

TARGET VESSEL/LESION REVASCULARISATION

The benefits of DES over BMS in relation to TVR/target lesion revascularisation (TLR) are unclear. While several studies have demonstrated a reduced incidence of repeat revascularisation with DES compared to BMS[15,22], Tsai et al's[14] work on DES implantation demonstrated a significant reduction in repeat revascularisation only in patients with normal renal function. Besides inflammation, alternative explanations include antiplatelet resistance observed in chronic renal failure[23,24]. Nevertheless, a lack of guideline-directed antiplatelet therapy in the CKD population might be contributory[2,25,26], which needs to be explored further.

NON-FATAL MI

The incidence of higher MI rates post PCI is universally increased in CKD patients compared to those with normal renal function[7,27]. Despite an overall raised incidence of post-PCI MI in CKD patients, the use of DES over BMS is associated with reduced MI rates[14]. Increased MI rates in CKD patients despite DES use indicate that systemic inflammation and/or metabolic derangement have a greater impact on endpoints. This is insufficiently addressed by the local effects of antiproliferatives in current DES[27].

In summary, the current evidence suggests that CKD is an independent predictor of mortality, MI and stent thrombosis. Also, DES are superior to BMS in the CKD population, with the caveat that the requirement for dual antiplatelet therapy (DAPT) is unlikely to disrupt subsequent non-cardiac treatment.

Revascularisation in ESRD/haemodialysis

DES VS. BMS

In line with contemporary guidelines advocating the use of DES in ESRD patients on dialysis[28], a meta-analysis has demonstrated mortality and adverse cardiac event benefits in ESRD patients who are treated with DES[3].

Despite a lack of benefit at one-year follow-up, Ishii et al[29] **(Table 2)** reported reduced revascularisation rates in haemodialysis patients treated with DES over BMS on longer follow-up[29,30]. This suggests the need for adequate endothelialisation of the deployed stent in the uraemic state, hence the need for extended follow-up.

FIRST- VS. SECOND-GENERATION DES

Despite a paucity of data on outcomes of second-generation DES in patients on maintenance haemodialysis, ESRD and haemodialysis are recognised as major predictors of adverse outcome following first-generation DES implantation, with approximately double the incidence of target vessel failure (TVF) in patients who received sirolimus-eluting stents (SES) compared to non-haemodialysis patients[31].

Table 1. Summary of studies comparing coronary revascularisation approaches in CKD (including ESRD).

	Study design	Study size	CKD (eGFR <60 ml/min/1.73 m²)	Comparison/ intervention	DES stent use	Primary outcome	Secondary outcomes	All-cause mortality	Stent thrombosis	Repeat revascularisation	Non-fatal MI	Follow-up period	Inclusion period
Crimi et al[15]	Multicentre RCT	1,981	373 (18.8%)	BMS vs. DES (PES/EES/ZES)	1,484 (75%)	Definite/probable ST	Composite of MI, stroke, death, and all-cause mortality	Within CKD population: lowest in ZES (10.6%) compared to EES (14.9%), PES (25.5%), BMS (18.1%), p=0.040.	Within CKD population: lower in EES and ZES compared to BMS (HR 0.288 and 0.394; p=0.014 and 0.037, respectively)	Non-significant	Non-significant	2 years	2006-2008
Miao et al[7]	Single-centre prospective	2,862	445 (15.5%)	DES-related ST in CKD vs. normal renal function	2,862 (100%)	Definite/probable ST	Composite of all-cause mortality, non-fatal MI, TVR	CKD (10.6%) vs. normal renal function (4.1%); p<0.001.	Definite/probable ST: CKD (1.8%) vs. normal renal function (0.6%); p=0.014.	Non-significant	CKD (7.4%) vs. non-CKD (4.3%); p=0.005	1 year	2008-2009
Tsai et al[14]	Multicentre prospective	283,593	121,446 (42.8%)	DES vs. BMS	218,540 (77.1%)	All-cause mortality, MI, repeat revascularisation, bleeding	NA	Lower in DES-treated patients regardless of renal function.	NA	Lower in DES-treated patients with normal renal function only.	Lower in DES-treated patients regardless of renal function, excluding haemodialysis patients.	2.5 years	2004-2007
Roberts et al[55]	Single-centre prospective	4,687	1,543 (33%)	CABG vs. MM CABG vs. BMS CABG vs. DES	1,278 (27%)	All-cause mortality	Composite of death, MI, revascularisation	CABG vs. MM: superior in CKD, excluding ESRD. CABG vs. BMS: superior in severe CKD CABG vs. DES: no significant differences. ESRD: no significant differences in CABG/BMS/PCI/MM	NA	Secondary endpoint lower with CABG vs. BMS/DES/MM except in dialysis patients.	Secondary endpoint lower with CABG vs. BMS/DES/medical management except in dialysis patients.	5.1 years	2003-2010
Lemos et al[17]	Retrospective	1,080	186 (17.2%)	DES vs. BMS	537 (49.7%)	All-cause mortality	Repeat revascularisation	All-cause mortality higher in CKD vs. normal renal function regardless of DES or BMS use. DES did not provide additional mortality benefit over BMS in CKD states.	NA	Reduced with SES in both CKD and normal renal function.	NA	1 year	2001-2002
Wanha et al[18]	Retrospective	1,908	331 (17.3%)	DES-I (PES, SES) vs. DES-II (EES, ZES, BES)	1,908 (100%)	DES efficacy: MACCE (MI, TVR, death, stroke) DES safety: ST	NA	No improvement with DES-II over DES-I irrespective of renal function.	No difference between CKD vs. normal renal function.	No improvement with DES-II	No improvement with DES-II	1 year	2009-2010
Cooper et al[35]	Retrospective	483,914	379,034 (78.3%)	CABG	NA	All-cause mortality (within 30 days of CABG)	Stroke, repeat CABG	Operative mortality rose inversely with decline in renal function.	NA	Repeat CABG rose inversely with decline in renal function	NA	NA	2000-2003

BES: biolimus-eluting stent; BMS: bare metal stent; CABG: coronary artery bypass grafting; CKD: chronic kidney disease; DES: drug-eluting stent; DES-I: first-generation DES; DES-II: second-generation DES; EES: everolimus-eluting stent; eGFR: estimated glomerular filtration rate; ESRD: end-stage renal disease; HR: hazard ratio; MACCE: major adverse cardiac and cerebral events; MI: myocardial infarction; MM: medical management; NA: not applicable; PES: paclitaxel-eluting stent; RCT: randomised controlled trial; SES: sirolimus-eluting stent; ST: stent thrombosis; TVR: target vessel revascularisation; ZES: zotarolimus-eluting stent

Table 2. Summary of studies comparing coronary revascularisation approaches in ESRD (dialysis-dependent).

	Study design	Study size	ESRD	Comparison/ intervention	DES stent use	Primary outcome	Secondary outcomes	All-cause mortality	Stent thrombosis	Repeat revascularisation	Non-fatal MI	Additional comments	Follow-up period	Inclusion period
Li et al[3]	Meta-analysis	62,250	62,250 (100%)	DES vs. BMS	NR	All-cause mortality MI MACE TVR/TLR	NA	Favours DES	NR	Favours DES	Non-significant difference	NA	NR	2006-2016
Ishii et al[29]	Retrospective	505	505	DES vs. BMS	SES, PES	TLR	Composite of cardiovascular death, non-fatal MI, ST, TLR	Non-significant difference	Non-significant difference	Favours DES (beyond 1 year)	Non-significant difference	NA	42 months	1999-2009
Sakakibara et al[32]	Single-centre prospective	100	100	DES-I vs. DES-II	SES (50%), EES (50%)	Restenosis at 8-month follow-up	MACE (all-cause death, non-fatal MI, TLR)	Non-significant difference	Non-significant difference	Non-significant difference	Non-significant difference	EES reduced restenosis rates compared to SES	8 months	2010
Nevis et al[38]	Systematic review	32,388	32,388 (100%)	CABG vs. PCI	NR	Short-term (30 days) or long-term (>1 year) mortality	NA	Short-term: favours PCI Long-term: favours CABG	NA	Favours CABG	Favours CABG	NA	PCI: 28 months CABG: 31 months	1991-2007

BMS: bare metal stent; CABG: coronary artery bypass grafting; CKD: chronic kidney disease; DES: drug-eluting stent; DES-I: first-generation DES; DES-II: second-generation DES; EES: everolimus-eluting stent; ESRD: end-stage renal disease; MACE: major adverse cardiac events; MI: myocardial infarction; NA: not applicable; NR: not recorded; PCI: percutaneous coronary intervention; SES: sirolimus-eluting stent; ST: stent thrombosis; TLR: target lesion revascularisation; TVF: target vessel failure; TVR: target vessel revascularisation

When implemented on maintenance haemodialysis patients, EES significantly reduced the incidence of restenosis compared to SES with an equal safety profile[32], with consistent results in improvements in diameter stenosis on follow-up compared with the OUCH-PRO registry[31]. Mechanisms for reduction in restenosis rates include reduced arterial injury and inflammation secondary to thinner struts and polymer of second-generation DES, respectively[32,33].

PCI VS. CABG

Despite increased early post-CABG mortality in ESRD[34,35], Zheng et al[30] demonstrated significant long-term benefits in mortality, MI, and repeat revascularisation compared to PCI. Supporting this is a systematic review reporting benefits in repeat revascularisation and major adverse cardiac events (MACE) with CABG, despite a higher early mortality risk[36]. The proposed pathophysiology includes significant medial calcification in haemodialysis patients, predisposing to stent underexpansion, reduced efficacy of eluted drugs and suboptimal endothelialisation of stent struts, culminating in restenosis and stent thrombosis[37].

Nevertheless, there is an elevated baseline risk of long-term mortality in haemodialysis patients regardless of the choice of revascularisation technique[38].

Rotational atherectomy (RA) for the treatment of coronary artery calcification (CAC)

Severely calcified coronary lesions have lower PCI success rates, higher complication rates, and suboptimal long-term results. Contemporary PCI guidelines recommend RA as an option for heavily calcified lesions that might not be adequately traversed or dilated prior to stent implantation[39].

The ROTAXUS trial, comparing RA followed by stenting or stenting alone in complex native CAD, demonstrated higher success with use of RA and higher acute lumen gain post PCI. However, in-stent late lumen loss was significantly higher in the RA group compared to DES alone[40], indicating that rotablation alone failed to increase the efficacy of DES.

The Diamondback 360® coronary orbital atherectomy system (OAS; Cardiovascular Systems, Inc., St. Paul, MN, USA) presents an alternative in revascularisation of CACs. ORBIT I demonstrated 98% device success (≤50% residual stenosis post-OAS treatment) while ORBIT II exceeded primary safety (freedom from MACE at 30 days) and efficacy (residual stenosis <50% post stent without in-hospital major cardiac events) endpoints, highlighting its suitability for implementation in CACs. Furthermore, subgroup analysis of DES use revealed a lower rate of TLR compared to BMS[41,42].

Besides technique, the approach to complex CACs should include accurate lesion assessment and characterisation which is poorly delineated by angiography alone[41,43]. Optical coherence tomography might be the supplemental imaging modality of choice for the assessment of intraluminal calcium thickness[41]. Accurate assessment will facilitate optimal stent placement, reduce stent underexpansion, malapposition, damage to the DES polymer coating and subsequent drug delivery[42]. Compared to bail-out atherectomy, planned atherectomy is associated with a reduced procedural time, less use of contrast and reduced rates of complications[44].

Overall, our review suggests that, while results regarding mortality benefit are mixed when DES are compared with BMS in both CKD and ESRD, DES are shown to improve rates of MI and repeat revascularisation[3,14,15,29]. There is no significant benefit of second- over first-generation DES[18]. The benefits of rotational atherectomy warrant consideration for planned instead of bail-out use in appropriate lesions[44].

Choice and duration of DAPT in CKD

DAPT use post PCI is critical to minimise the rate of adverse cardiovascular events[25]. Contemporary European and US guidelines recommend a DAPT duration of six to 12 months post DES deployment, followed by lifelong aspirin[9,39]. However, no consensus for DAPT drugs and duration in patients with CKD/ESRD exists, owing to the lack of clinical trials[25]. Though not targeted at CKD patients, the DAPT trial demonstrated that prolonged DAPT (30 months) significantly decreased rates of ST and the composite outcome of death, MI and stroke, at the expense of bleeding[45]. However, the extrapolation of findings from a non-CKD/ESRD population into this high-risk population is probably inappropriate, due to an increased incidence of cardiovascular events or bleeding complications after PCI in haemodialysis patients[46,47].

Both CKD and prolonged DAPT independently predict elevated bleeding complications. However, it is uncertain whether prolonged DAPT worsens bleeding risk in CKD patients[48].

A pooled analysis comparing the safety and efficacy of short-term (three to six months) versus long-term (≥12 months) DAPT post DES implantation in CKD patients found that the presence and degree of CKD have no effect on the rates of coronary thrombotic events, regardless of the duration of DAPT[25], which is in sync with a study by Baber et al[48], where severity of CKD has no effect on cardiovascular risk post DAPT cessation. Further, Chen et al's analysis[49] in the haemodialysis subgroup reported a six-month DAPT duration cut-off that reduces post-PCI death or MI, but shows no difference in long-term outcomes when compared to longer duration of DAPT (>6 months). However, these studies used clopidogrel instead of more potent $P2Y_{12}$ inhibitors such as prasugrel or ticagrelor, which may have had an impact on overall study outcome.

In summary, CKD and DAPT independently predict bleeding risk, while CKD contributes to an increased risk of ST. A lack of consensus regarding antiplatelet therapy in CKD/ESRD leads to a reduced use due to a perceived lack of benefit, coupled with fear of coagulopathy and antiplatelet resistance[7,23,24]. Also, our review suggests that thrombotic complications post cessation of DAPT are independent of the severity of CKD. Future studies concerning DAPT and bleeding complications ought to have a uniform use of antiplatelets and duration to minimise possible confounding effects on stent choice and CKD severity.

Role of CABG in CKD

The 2014 European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS) Guidelines[50] on myocardial revascularisation recommend CABG over PCI in patients with moderate to severe CKD and multivessel CAD, considering acceptable surgical risks and life expectancy beyond one year.

Given complex coronary lesions in CKD, findings from ASCERT reporting long-term mortality benefits with CABG over PCI in multivessel CAD could be applied. Though patients with CKD often have more complex coronary lesions with multivessel disease, increased coronary calcification, and the presence of thrombus in culprit coronary lesions, their SYNTAX score is comparable to patients with normal kidneys[18]. CABG should be considered since extensive coronary calcifications reduce PCI success rates and is also associated with significant improvements in symptoms and mortality[51].

The FREEDOM trial[52] comparing coronary revascularisation techniques in CKD concluded that CKD is an independent risk factor for adverse events regardless of revascularisation strategy, where there is no evidence of additional benefit in outcomes according to CKD severity. Being an independent risk factor for stent thrombosis, coronary revascularisation in CKD has shifted in favour of CABG especially on long-term follow-up[52,53]. Nevertheless, CABG is superior to PCI with regard to reductions in rates of MI and repeat revascularisation regardless of renal function provided patients do not present with acute coronary syndrome[52,54].

Comparing rates of adverse events in CABG against BMS in CKD/ESRD, CABG is associated with reduced mortality rates though there was statistical significance only in severe CKD (eGFR <30 mL/min/1.73 m^2)[55]. A subsequent analysis comparing CABG against DES observed a trend towards mortality reduction for CABG without statistical significance. No mortality difference was observed in patients on dialysis, regardless of revascularisation strategy[55].

However, a five-year follow-up on the SYNTAX trial demonstrated that a statistically significant long-term benefit in mortality, MI and stroke is associated with revascularisation with CABG over DES. Differences in event rates were attributed to the higher rates of all-cause death and repeat revascularisation in the CKD population who received DES, secondary to diffuse atherosclerosis and reduced prevalence of guideline-directed antiplatelet therapy[26,52].

In conclusion, CKD and ESRD are independent risk factors for adverse events regardless of revascularisation strategy[17,35]. CABG is associated with long-term benefits in both mortality and adverse cardiac events both in patients with CKD and in those with ESRD[38,55]. However, physicians and patients ought to consider and accept higher risks of early complications such as mortality and stroke[53], stressing the importance of patient selection.

Conclusions

Despite an increasing prevalence of patients with CKD and CAD, there remain limited studies evaluating the optimum method of coronary revascularisation, and DAPT duration in this subgroup.

Our review highlights the following. 1) CKD is an independent predictor of mortality, MI and stent thrombosis. 2) DES is superior to BMS in a CKD population. 3) CKD and DAPT are independent predictors of bleeding complications post PCI, though the severity

of CKD seems not to affect the rates of coronary thrombotic events. 4) CABG is the revascularisation modality of choice **(Table 3)** in CKD patients who are surgically fit due to mortality and symptomatic benefits, and the reduced need for repeat revascularisation compared to PCI. 5) It is also imperative for a consensus on DAPT choice and duration to be validated to maximise the benefits of high-risk, invasive procedures in this fragile subset of patients.

Table 3. Summary of findings and clinical implications.

What is already known	Patients with CKD have an increased risk of post-PCI adverse events compared to the general population. DES is generally associated with improved outcomes compared to BMS in both the general population and CKD patients. DES implantation in the ESRD population on regular dialysis shows a reduced rate of revascularisation over longer follow-up (>1 year).
What this review adds	No study focusing on DAPT duration post PCI in CKD/ESRD patients has yet been done. Results from available trials highlight that adverse events are higher in the CKD population. Among the CKD population, there is no observable benefit in extending DAPT duration beyond 12 months. In non-dialysis-dependent CKD patients, CABG improves mortality, repeat revascularisation and MI compared to PCI. There is no mortality difference when comparing first- and second-generation DES, while comparison of DES with BMS yields mixed results. In ESRD on regular haemodialysis, CABG provides long-term benefit despite short-term increased risk of adverse events. There is no significant mortality difference when first- and second-generation DES are compared, though there is a reduced repeat revascularisation rate with second-generation DES. Finally, DES provides mortality benefit over BMS.
Clinical implications & future directions	CABG is still the intervention of choice for CKD/ESRD patients requiring coronary revascularisation, provided fitness for surgery. CKD/ESRD patients will greatly benefit from RCTs/prospective studies focusing on DAPT choice and duration, especially in the advent of novel $P2Y_{12}$ inhibitors and second-generation DES.

BMS: bare metal stent; CABG: coronary artery bypass grafting; CKD: chronic kidney disease; DAPT: dual antiplatelet therapy; DES: drug-eluting stent; ESRD: end-stage renal disease; PCI: percutaneous coronary intervention; RCT: randomised controlled trial; ST: stent thrombosis

Conflict of interest statement

The authors have no conflicts of interest to declare.

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A novel "nano-crush" technique for the management of coronary bifurcation lesions: in vitro bench test analysis and preliminary report on real-world clinical evaluation in patients with one-year angiographic follow-up

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KEYWORDS

- bifurcation
- drug-eluting stent
- stable angina

Abstract

Aims: Although provisional stenting with a single drug-eluting stent has proven clinical efficacy in the treatment of bifurcation stenosis, some patients may require two stents. We propose a novel technique, called "nano-crush", which is easy to perform and can be used in all bifurcation angles.

Methods and results: The feasibility of the nano-crush technique was confirmed in an *in vitro* bench test and intravascular ultrasound (IVUS) study. Subsequently, 42 patients with *de novo* coronary bifurcation stenosis were treated by this novel procedure using drug-eluting stents at our centre between January 2008 and December 2015. We experienced procedural success in all (100%) patients without any complications. The primary efficacy endpoint of the one-year incidence of major adverse cardiac events (MACE) was noted in three (7.14%) patients, comprising one case of cardiac death at nine months post procedure and two cases of repeat revascularisation due to in-stent restenosis. There were no cases of periprocedural myocardial infarction or stent thrombosis. Angiographic follow-up at one year indicated intact stent patency in the remaining patients.

Conclusions: Initial experience with the nano-crush technique demonstrates that it can be performed easily without any procedural complications. Further, the angiographic and clinical follow-up indicates that the nano-crush technique is associated with acceptable clinical outcomes in a real-world scenario.

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Abbreviations

ACC	American College of Cardiology
AHA	American Heart Association
ARC	Academic Research Consortium
CRF	chronic renal failure
DK	double-kissing
IVUS	intravascular ultrasound
LAD	left anterior descending artery
LCL	lower confidence limit
LCx	left circumflex artery
LMCA	left main coronary artery
MACE	major adverse cardiac events
NC	non-compliant
OCT	optical coherence tomography
POT	proximal optimisation technique
TIMI	Thrombolysis In Myocardial Infarction
UCL	upper confidence limit

Introduction

In unselected coronary bifurcation lesions, the provisional stenting technique with a single drug-eluting stent in the main branch has proven clinical efficacy[1-3]. However, some patients will still require two stents for the proper treatment of their bifurcation stenosis. Various elective double-stenting techniques are available; some of these double-stenting strategies have undergone various modifications in order to make them simpler and to optimise clinical outcomes. The "culotte" technique is one such long-standing strategy for the management of bifurcation lesions. Its efficacy has been documented in various trials (NORDIC I and BBC ONE)[4,5], but has been questioned for distal left main bifurcation treatment[6,7]. Similarly, the "crush" technique has evolved over time after its first description by Colombo et al[8]. Although the short-term outcomes with the crush technique were encouraging, the midterm or long-term outcomes remain not fully satisfactory due to the high risk of periprocedural stent thrombosis and subsequent restenosis. To overcome these drawbacks, the "double-kissing (DK) crush" technique[9], and "mini-crush" technique[10] were developed. Their clinical performance has been appraised in studies. Further modifications of the crush technique have also been documented[11].

In general, experts believe that an ideal crush technique should: (a) have a limited length of crushed segment in the main branch; (b) use an NC balloon in the main branch to crush the side branch stent; (c) push away the first layer of stent struts from the side branch orifice by performing a first kissing balloon inflation after stent crush to appose the struts fully on the carina side, thus increasing the success of final kissing balloon inflation[8]. Against this background, we have developed a novel technique considering all three points which are necessary for an optimum outcome in an elective double-stent technique for the treatment of bifurcation lesions. The proposed technique is easy to perform and can be used in almost all bifurcation angles. We have called our technique "nano-crush". A detailed description of the technique and clinical experience is reported here.

Methods

STUDY POPULATION

A retrospective observational single-centre study was conducted at our centre. Patients with *de novo* coronary bifurcation lesions, who were treated with the nano-crush stenting technique between January 2008 and December 2015, were analysed. Here, patients were treated with the nano-crush technique if they had symptomatic *de novo* coronary bifurcation lesion stenosis with (a) diameter narrowing ≥50% in both main branch and side branch, (b) Medina class 1,1,1, and (c) vessel size ≥2.75 mm in the main branch and ≥2.5 mm in the side branch by visual estimation on coronary angiography. Exclusion criteria were: (a) contraindications to prolonged use of dual antiplatelet drugs; (b) life expectancy <1 year; (c) left ventricular ejection fraction <30%; and (d) acute myocardial infarction and acute coronary syndrome patients before stabilisation. All patients provided informed consent for the procedure and subsequent data collection and analysis for research purposes.

NANO-CRUSH TECHNIQUE

For significant coronary bifurcation lesions **(Figure 1A)**, the nano-crush stenting technique can be performed with a 6 Fr guide catheter, but a 7 Fr guide catheter is preferable. Proper dilatation of both the branches, main branch and side branch, is performed. In calcified vessels, plaque modification may be needed with a scoring balloon, cutting balloon or rotational atherectomy. After vessel preparation, a stent is placed in the side branch according to the distal diameter and a non-compliant balloon (one size smaller than the distal diameter of the artery, e.g., 2.5 mm balloon in 3.5 mm artery) is placed in the main branch **(Figure 1B)**. Then, the main branch balloon is inflated at nominal pressure and the side branch stent is pulled to the inflated balloon (so that some part of the side branch stent enters into the main branch) and the side branch stent is deployed at nominal pressure. Both balloons are deflated and the side branch balloon is pulled into the main branch so that 50% of it remains inside the side branch stent and is dilated at high pressure to open the ostium of the side branch nicely. Subsequently, the side branch balloon is deflated and the main branch balloon is inflated at a high pressure (≥20 atm) to crush the edge of the side branch stent in the main branch **(Figure 1C)**. First kissing balloon inflation with the side branch stent balloon (pulled inside the main branch) and the main branch balloon is carried out at 14-16 atm **(Figure 1D)**. The side branch balloon and the wire along with the main branch balloon are removed. Then, the main branch stent is chosen according to the distal diameter of the vessel and the stent is placed and deployed at nominal pressure **(Figure 1E)**. The proximal optimisation technique (POT) is carried out with a 0.5 mm larger NC balloon in the proximal part of the main branch stent and the side branch is accessed trans-strut through the middle struts of the main branch stent overhanging the side branch ostium by a second wire **(Figure 1F)**. The final kissing balloon inflation is performed with appropriately sized non-compliant balloons at a moderate 14-16 atm **(Figure 1G)**. Post-procedural check angiography is performed to evaluate the final result **(Figure 1H)**.

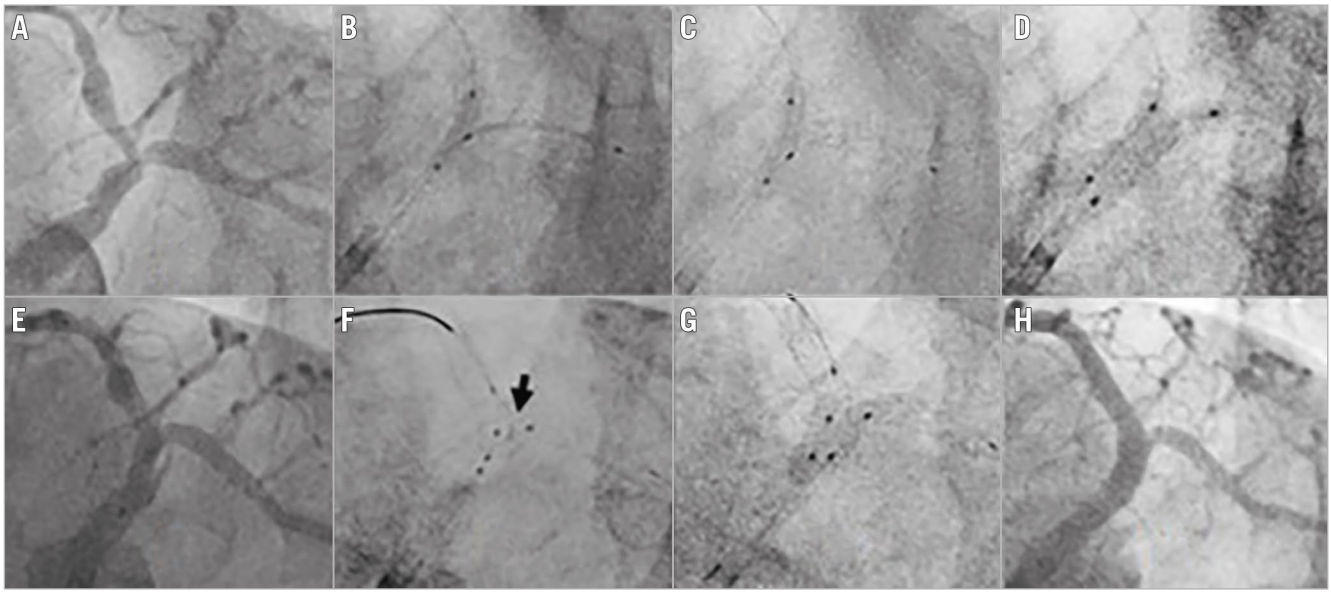


Figure 1. *Angiography showing the steps of the nano-crush technique. A) Vessel anatomy showing bifurcation lesion in the distal LM and the ostio-proximal LAD and LCx. B) Side branch stent positioning with an inflated NC balloon in the main branch. C) Balloon crushing of the side branch stent. D) First kissing balloon inflation with the stent balloon and an NC balloon. E) Positioning of the main branch stent after removing the balloon and stent from the side branch. F) Positioning NC balloons in the main branch and side branch after re-crossing the side branch. Arrow shows minimally crushed stent at the carina. G) Final kissing balloon inflation. H) Final result.*

IN VITRO BENCH TESTING AND IVUS STUDIES

Prior to evaluation in real-world patients, the feasibility of this novel procedure was evaluated using an *in vitro* bench test and IVUS study. The *in vitro* bench test was conducted using a bifurcation model by fusing 3.0 mm and 2.5 mm thermoplastic tubes in Y fashion according to Finet's model based on fractal arguments. The deployment of stents was carried out in the model in a water bath with all steps such as side branch wire access, stent deployment in the side branch **(Figure 2A)**, crushing and first kissing balloon inflation **(Figure 2B)**, stent deployment in the main branch **(Figure 2C)**, final kissing balloon **(Figure 2D)**, and final result **(Figure 2E)**, and were viewed live and recorded fluoroscopically. Intravascular ultrasound (Atlantis™ SR Pro; Boston Scientific, Marlborough, MA, USA) was also performed in this model along with *in vitro* IVUS studies.

INTERVENTIONAL PROCEDURE IN REAL-WORLD PATIENTS

We used the femoral access in all cases. All patients were treated with dual antiplatelet therapy (DAPT) before the procedure, according to ACC/AHA guidelines[12] (e.g., aspirin and either clopidogrel, prasugrel or ticagrelor after a proper loading dose). During the intervention, heparin was given intra-arterially as anticoagulant to maintain an activated coagulation time >250 seconds. The nano-crush technique was performed as detailed above. IVUS was used in cases with a significant bifurcation lesion in the left main coronary artery **(Figure 3A, Figure 3B)** and in cases which required rotational atherectomy. After the procedure, all patients were advised to maintain DAPT (i.e., aspirin and clopidogrel or prasugrel or ticagrelor) for at least 12 months.

DATA COLLECTION AND PATIENT FOLLOW-UP

Demographic data including age, gender, cardiovascular risk factors, medical history, and clinical presentation were collected from hospital records. Details of the affected lesions and implanted stents were obtained from angiography and angioplasty reports. Adverse events were monitored during hospital stay. Subsequently, patients were called into the out-patient department after 1 month, 3 months, 6 months and 12 months for clinical evaluation. A mandatory coronary angiogram was planned after one year in all cases.

STUDY ENDPOINTS

The procedural success rate was considered to be the performance endpoint. The primary efficacy endpoint was the one-year incidence of major adverse cardiac events (MACE). Events of Academic Research Consortium (ARC)-defined stent thrombosis were also considered to be an additional safety endpoint[12].

DEFINITIONS AND CLINICAL ENDPOINTS

Procedural success was defined as successful delivery and deployment of the coronary stents at the intended coronary bifurcation lesions and successful withdrawal of the stent delivery systems with achievement of a final diameter stenosis of <30% and TIMI grade 3 flow in both the main branch and side branch vessels, without the occurrence of death, MI, and repeat revascularisation of the treated lesions in the index hospitalisation. MACE was defined as a composite of cardiac death, myocardial infarction, and any repeat revascularisation in the target vessel. All deaths were considered cardiac in origin unless otherwise documented.

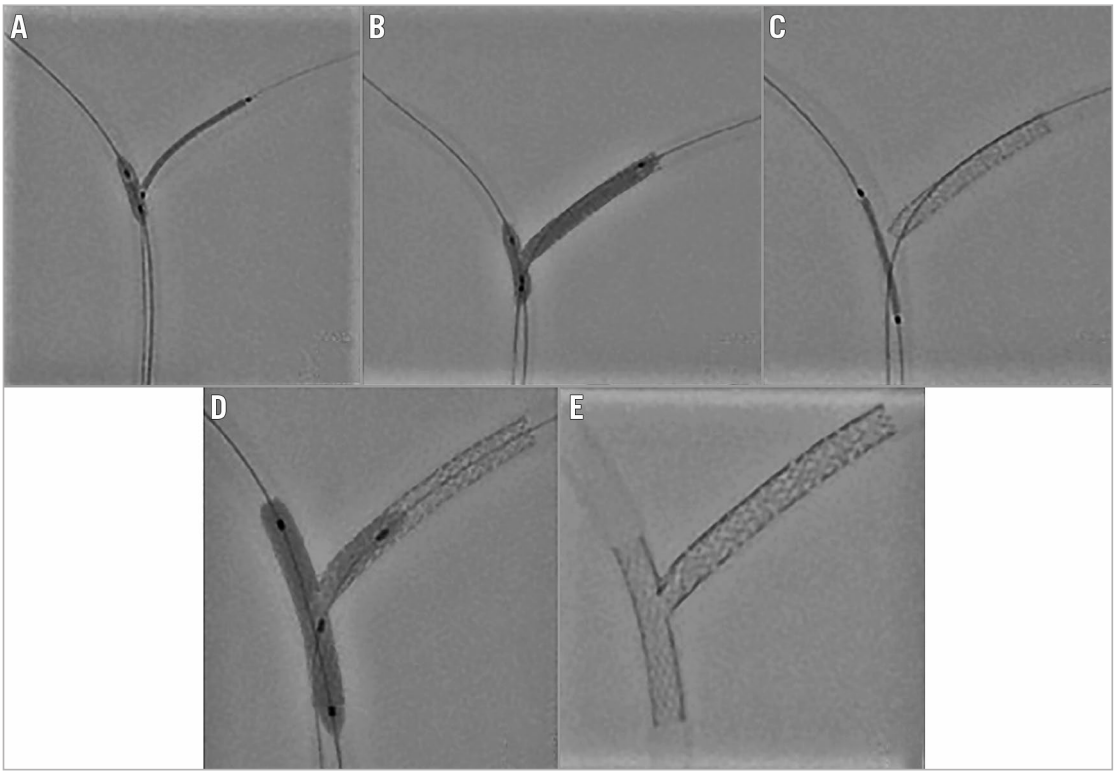


Figure 2. *Nano-crush bench test. A) The main branch balloon is inflated at nominal pressure and the side branch stent is pulled to the inflated balloon. B) First kissing balloon inflation with the side branch stent balloon (pulled inside the main branch) and main branch balloon carried out at 14-16 atm. C) The main branch stent is placed and deployed at nominal pressure. D) Final kissing balloon inflation is performed. E) Final result showing minimally crushed stent.*

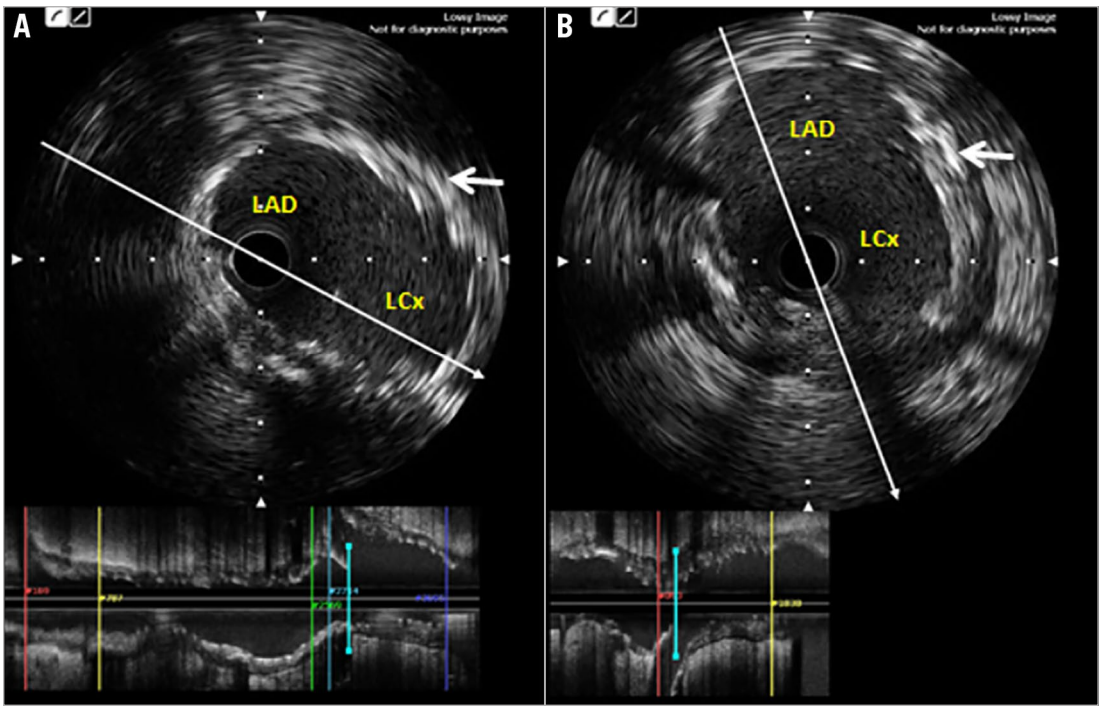


Figure 3. *IVUS images of a patient with LMCA bifurcation stenting using the nano-crush technique. A) LAD to LMCA pullback showing full coverage of the LCx ostium by the stent strut. B) LCx to LMCA pullback. White arrow indicates minimally crushed stent segment in panels A and B.*

Myocardial infarction was defined as either development of new ischaemic ST-T changes or pathological Q-waves in at least two contiguous leads of the electrocardiogram or elevation of cardiac troponin >5 times the normal[13]. Target vessel revascularisation was defined as any repeat revascularisation (either percutaneous or surgical) procedure in the target vessel. Renal failure was defined as an estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2. Stent thrombosis was defined using the Academic Research Consortium (ARC) definitions[14]. The stent thrombosis was considered as "definite" when it was detected angiographically, "probable" if the patient had a target vessel-related myocardial infarction or died of a coronary event within the first 30 days, and "possible" if any unexplained death occurred from 30 days after the index procedure until the final follow-up.

STATISTICAL ANALYSIS

All categorical variables were expressed as counts (percentage, %) with number of patients (n=42) as denominator; continuous variables were expressed as mean±standard deviation (SD). Cox regression analysis was used to find the hazard ratio and identify predictors for the occurrence of MACE. The time-dependent occurrence of MACE was obtained using the Kaplan-Meier method with log-rank comparison. All tests were two-sided and a p-value less than 0.05 was considered statistically significant. Statistical software R was used for analysis (with the package "survival"), and the R statistical function used coxph and survfit (R Foundation for Statistical Computing, Vienna, Austria).

Results

IN VITRO BENCH TESTING

The *in vitro* bench test and *in vitro* IVUS studies showed proper covering of the carina and circular opening of the side branch stent, without any major distortion of the side branch stent at the ostium **(Figure 4)**.

BASELINE DEMOGRAPHICS

Baseline clinical characteristics for the 42 patients analysed in the study are shown in **Table 1**. In brief, the mean age of the study population was 63.05±8.65 years; 38 (90.48%) were male. Hypertension was present in 39 (92.86%) patients, while type 2 diabetes mellitus was present in 33 (78.57%) patients. Four (9.52%) patients had chronic renal failure (CRF) and were maintained on haemodialysis. In addition, 17 (40.48%) patients had left main coronary artery (LMCA) bifurcation disease. Eight (19.05%) patients with calcified arteries required rotational atherectomy for plaque modification. Four (9.52%) patients with an LMCA bifurcation required rotational atherectomy.

Table 1. Population characteristics (n=42).

Population characteristics	42 patients
Age (years)	63.05±8.65
Male	38 (90.48%)
Female	4 (9.52%)
Comorbidities	
Hypertension	39 (92.86%)
Diabetes mellitus	33 (78.57%)
Smoking	17 (40.48%)
Chronic renal failure	4 (9.52%)
Angiographic characteristics	
Distal LMCA	17 (40.48%)
LAD–diagonal	11 (26.19%)
LCx–obtuse marginal	11 (26.19%)
Distal RCA	3 (7.14%)
Calcified lesions	8 (19.05%)

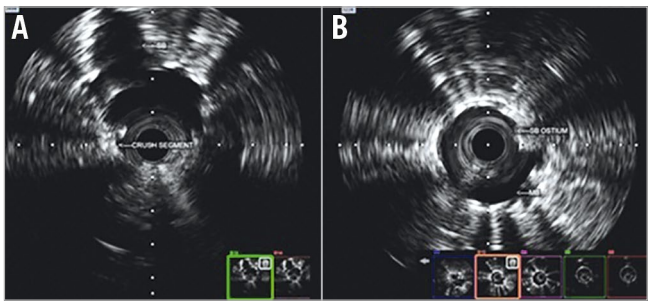


Figure 4. *IVUS pullback. A) Main branch. B) Side branch to main branch.*

CLINICAL OUTCOMES

The procedural success rate was 100% with no cases of periprocedural myocardial infarction or other complications. All patients were followed up for one year and underwent follow-up angiography. The median follow-up period was 24 months (IQR: 16-53 months). Subsequently, the primary endpoint of cumulative MACE at one-year follow-up was noted in three (7.14%; 95% confidence interval [CI]: 0-14.93) patients, which included one case of cardiac death due to left ventricular failure nine months after the index procedure and two cases of repeat revascularisation due to diffuse in-stent restenosis after nine months. Angiographic follow-up in the remaining patients indicated intact stent patency at one year **(Figure 5)**. There was no stent thrombosis event in any patient up to one-year follow-up. The detailed study outcomes are shown in **Table 2**. The Kaplan-Meier MACE-free survival curve for the overall patient population is illustrated in **Figure 6A**.

PREDICTORS OF ADVERSE EVENTS AFTER THE NANO-CRUSH TECHNIQUE

The Cox regression analysis findings for the predictors of adverse events after the nano-crush technique are given in **Table 3**. No significant difference was reported in the occurrence of MACE with respect to gender (male vs. female), age (≤60 years vs. >60 years), type 2 diabetes mellitus, hypertension, and calcified lesion. However, a significant difference in MACE was noted with respect to LMCA lesions (17.65% vs. 0.0%,

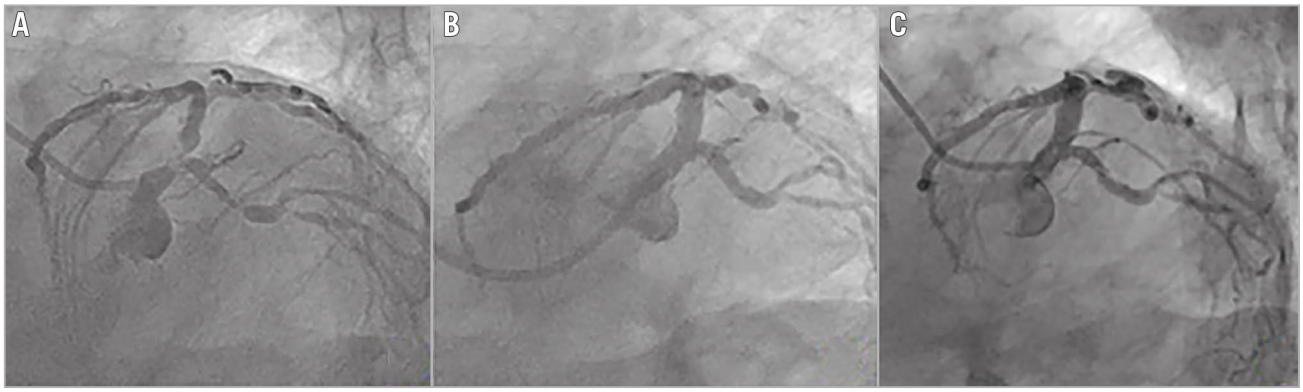
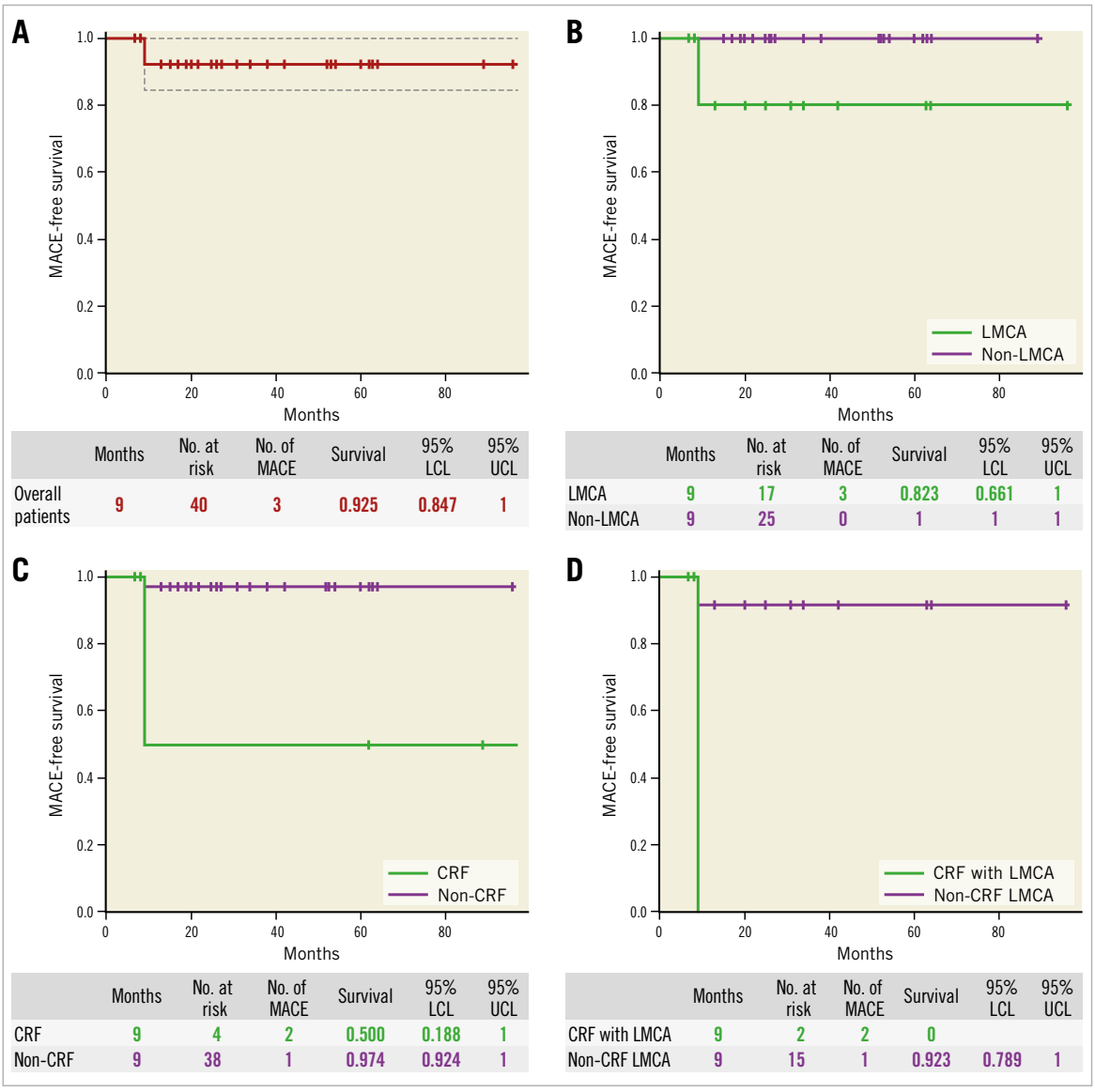


Figure 5. *Coronary angiography of a patient showing significant bifurcation lesion at baseline (A), good coronary flow after stenting with the nano-crush technique (B), and stent patency at one-year follow-up (C).*



	Months	No. at risk	No. of MACE	Survival	95% LCL	95% UCL
Overall patients	9	40	3	0.925	0.847	1

	Months	No. at risk	No. of MACE	Survival	95% LCL	95% UCL
LMCA	9	17	3	0.823	0.661	1
Non-LMCA	9	25	0	1	1	1

	Months	No. at risk	No. of MACE	Survival	95% LCL	95% UCL
CRF	9	4	2	0.500	0.188	1
Non-CRF	9	38	1	0.974	0.924	1

	Months	No. at risk	No. of MACE	Survival	95% LCL	95% UCL
CRF with LMCA	9	2	2	0		
Non-CRF LMCA	9	15	1	0.923	0.789	1

Figure 6. *Kaplan-Meier MACE-free survival curve. A) Overall patient population. B) Patients with an LMCA bifurcation lesion vs. patients with non-LMCA bifurcation lesions. C) Patients with CRF vs. patients without CRF. D) Patients with an LMCA bifurcation lesion with CRF vs. patients with LMCA bifurcation lesions without CRF.*

Table 2. Clinical outcomes at 1-year follow-up (n=42).

Outcomes	At 1-year follow-up (n=42)
Major adverse cardiac events	3 (7.14%)
Cardiac death	1 (2.38%)
Myocardial infarction	0
Target vessel revascularisation	2 (4.76%)
Overall stent thrombosis*	0
Definite stent thrombosis	0
Probable stent thrombosis	0
Possible stent thrombosis	0
*According to the Academic Research Consortium (ARC) criteria.	

p=0.0205) **(Figure 6B)** and with respect to chronic renal failure (50.00% vs. 2.63%; HR 21.8, p=0.0003) **(Figure 6C)**. Further, a significant difference in the number of MACE was also noted for patients having LMCA lesions and CRF vs. patients having LMCA lesions and no CRF (100% vs. 7.69%; HR 21.5, p=0.0006) **(Figure 6D)**.

Table 3. Evaluation of predictors of MACE after nano-crush technique.

Characteristics	MACE	HR	95% CI	*p*-value
Female (n=4)	1 (25.00%)	0.207	0.019-2.29	0.155
Male (n=38)	2 (5.26%)			
Age >60 years (n=24)	3 (12.50%)			0.109
Age ≤60 years (n=18)	0 (0.00%)			
Hypertension (n=39)	3 (7.69%)			0.617
Non-hypertension (n=3)	0 (0.00%)			
Diabetes (n=33)	3 (9.09%)			0.343
No diabetes (n=9)	0 (0.00%)			
Calcified lesion (n=8)	1 (12.50%)	2.04	0.185-22.5	0.551
Non-calcified lesion (n=34)	2 (5.88%)			
Diabetes mellitus and calcified lesion (n=6)	1 (16.67%)	2.15	0.195-23.7	0.522
Diabetes mellitus and non-calcified lesion (n=27)	2 (7.41%)			
LMCA bifurcation lesion (n=17)	3 (17.65%)			0.0205
Non-LMCA bifurcation lesion (n=25)	0 (0.00%)			
Calcified LMCA bifurcation lesion (n=4)	1 (25.00%)	1.41	0.128-15.6	0.778
Non-calcified LMCA bifurcation lesion (n=13)	2 (15.38%)			
Diabetic LMCA bifurcation lesion (n=14)	3 (21.43%)			0.364
Non-diabetic LMCA bifurcation lesion (n=3)	0 (0.00%)			
Chronic renal failure (CRF) (n=4)	2 (50.00%)	21.8	1.96-242	0.0003
Non-CRF (n=38)	1 (2.63%)			
LMCA bifurcation lesion with CRF (n=2)	2 (100%)	21.5	1.86-250	0.0006
LMCA bifurcation lesion without CRF (n=15)	1 (6.67%)			

Discussion

Bifurcations vary not only in terms of anatomy (plaque burden, location of the plaque, angle between the branches, diameter of the branches, and bifurcation site), but also in relation to dynamic changes in the anatomy during treatment (plaque shift, dissection). As a result, no two bifurcations are identical and no single strategy exists that can be applied to every bifurcation[15].

A provisional single-stent strategy is currently regarded as the default strategy for the treatment of bifurcation lesions. However, this approach cannot be applied broadly across all bifurcation lesions because of the likelihood of side branch compromise in the presence of high-risk features (e.g., significant side branch ostial disease), or because the side branch has significant disease beyond its ostium requiring treatment. In such circumstances, a two-stent strategy is required in a bid to maintain optimal vessel patency and blood flow in both the main and side branches[15].

An ideal two-stent strategy should offer: (a) optimal coverage of the side branch ostium, with no gaps between the main branch and the side branch stents; (b) minimal distortion of the side branch stent at the ostium; (c) minimal overlap between the main branch stent and the side branch stent; (d) short procedural time; (e) minimal requirement of additional guidewires and balloons; (f) the ability to maintain control of both the main branch and the side branch, so that there is little risk of compromised blood flow in either branch; (g) an easy to perform, reproducible, and predictable method[16-19]. Considering these, a number of different two-stent techniques have been described in an attempt to optimise the immediate and long-term results of the side branch following treatment. To date, no single approach is able to deliver all the desired attributes as described and each of these strategies has its own limitations, including stent distortion, inadequate ostial coverage and multiple stent layers that contribute to restenosis[20,21].

The main disadvantage of T-stenting is the risk of missing the side branch ostium. Burzotta et al described modified T-stenting by intentionally protruding the side branch stent within the main branch stent[22]. Though this technique ensures that the side branch ostium is not missed, there is a risk of the side branch stent inadvertently protruding too much inside the main branch. In addition, access to the main branch stent struts with balloons and stents could be difficult in some cases such as a tortuous side branch and a long side branch stent.

The crush technique was the first of the elective double stenting techniques introduced to ensure ostial side branch coverage, which was one of the limitations in the classic "T-stent" technique[8]. Though the crush technique yielded comparatively better clinical outcomes than the T-stent technique[23], there were several concerns about the original crush technique. One such concern involves the 3-4 mm of drug-eluting stent overlap at the bifurcation. A study on long-term (nine months) follow-up with the crush technique for coronary bifurcation lesions has demonstrated a stent thrombosis rate of up to 4.3%, while the restenosis rate, mostly at the side branch ostium, was as high as 25.3%[24].

Later, the importance of appropriate final kissing balloon inflation with this technique was established[25]. The use of mandatory high-pressure dilatation of the side branch and kissing balloon inflation during the crush technique displayed a reduced restenosis rate of 8.6% in a more recent multicentre registry. However, the rate of stent thrombosis with this technique remained unchanged at 3.3% despite the kissing inflation[23]. The subsequently developed mini-crush technique (with step balloon crushing)[26], which calls for a reduced stent overlap of 1-2 mm, demonstrated improved final kissing inflation rates, low MACE rates, and a very low restenosis rate of 2.0% at the side branch ostium in a small patient cohort[10].

Although the DK crush technique satisfies many of the ideal features for a two-stent strategy, it is complex and needs crossing of a crushed segment through the proximal struts, which is time-consuming, requires more than one balloon, and is often difficult[19]. It should also be noted that the DK crush technique is essentially a "mini double-kissing crush" technique, where the side branch is stented with a 1-2 mm protrusion inside the main branch. In acute side branch angles (Y-shaped), the side branch ostium is longer, and oval-shaped. Such an anatomic configuration implies the need for wider protrusion of the side branch stent inside the main, resulting in a longer neocarina[19,27]. Further, the bifurcation angle (>50 degrees) has been noted to be an independent predictor of MACE after crush stenting[24]. This may be due to inadequate expansion of the side branch stent ostium, even after kissing inflation. Considering these, striving to limit protrusion while implanting the side branch stent becomes vital[19].

At our centre, extensive experience of treating bifurcation stenosis with "crush" stenting helped us make some refinements to it. These include: (a) limiting the length of the crushed stent segment (mini/micro/nano) during stent implantation in the side branch; (b) use of a balloon in the main branch to crush the side branch stent (step crush) in place of a stent as in classic crush techniques; and (c) performing first kissing balloon inflation after crush in order to push away the first layer of stent struts from the side branch orifice and to appose the stents fully on the carina side (securing wire re-crossing towards the side branch), thus increasing the rate and success of final kissing balloon inflation (DK crush).

The nano-crush technique proposed by us is much simpler and easy to perform. The technique is compatible with a 6 Fr guide catheter. In addition, the wire in the side branch is never lost before adequate deployment and crushing, and further optimises opening and apposition by the first kissing balloon inflation. Our method also overcomes the limitations of the DK crush technique as the one size smaller balloon in the main branch is inflated at nominal pressure (i.e., 3.0 mm balloon in a 3.5 mm vessel), which ensures some amount of stent strut protrusion into the main branch, and prevents the side branch stent protruding into the main branch excessively, while covering the ostium of the side branch completely. In high-angled (≥70°) bifurcation lesions, the edges, medial and lateral parts of the side branch stent struts will protrude into the main branch. On the other hand, in patients with a narrow angle bifurcation (≤70°), the operator should be careful to ensure that there is minimal entry of the side branch stent into the main branch before deployment.

Unlike the modified T-stenting technique, there will be definite crush in this technique, though minimal, and that is why we call this technique nano-crush. The guidewire re-crosses easily through the expanded side branch ostium due to a lesser metal load and the first kissing balloon inflation. Further, the minimal amount of metal which may remain in the medial wall of the side branch may form a metallic neocarina after the final kissing balloon, indicating that the side branch ostium is not fully covered by the crushed segment and the retained stent balloon comes out without much difficulty. The same observation was confirmed in the bench test and *in vitro* IVUS studies before performing the technique in real-world patients. We did not experience any difficulty in removing the side branch balloon after crushing with the main branch balloon in any of our cases. Here, the trick is to ensure minimal protrusion of the side branch stent by selecting the correct size of main branch balloon. Our initial experience of managing patients with bifurcation lesions with the nano-crush technique suggested good immediate and long-term clinical results. Further, the technique is easy to perform and can be used in all bifurcation angles.

One of the anticipated pitfalls of this technique is a short proximal segment before bifurcation. In that case it would be difficult to wire the side branch after the stent placement in the main branch. Hence, it is advisable to choose stents with minimal or no balloon overhang for accurate positioning of the side branch stent. It should also be noted that, if the operator re-crosses the guidewire in the expanded side branch stent ostium and not in the crushed lateral cell, the stenting would be only a modification of the modified T-stenting technique. During the first kissing balloon inflation, the side branch stent strut near the carina may open towards the distal main branch or towards the side branch ostium, depending upon the angle of bifurcation. If it opens towards the distal main branch, the wire will re-cross through the middle strut of the main branch stent. If, due to a narrow angle, the side branch stent protrudes more inside the main branch near the carina, the struts are more likely to be displaced towards the side branch ostium during the first kissing balloon inflation. Due to the relatively lower metal load compared to the classic crush, re-entry will be relatively easy through the middle strut. Nevertheless, rewiring of the side branch through the distal strut should be avoided. Subsequently, high-pressure final kissing balloon inflation is recommended in all cases. IVUS could be helpful in identifying suboptimal opening of the stent struts at the side branch ostium.

In our study, we observed significantly higher MACE rates in patients with bifurcation lesions in the LMCA as compared to patients with bifurcation lesions in other vessels. The COBIS II registry demonstrated similar outcomes, i.e., that two-stent bifurcation techniques in LMCA bifurcation lesions are associated with more target vessel failure as compared to non-LMCA

bifurcation lesions[28]. In our study, we also observed significantly higher MACE rates in CRF patients with bifurcation lesions as compared to non-CRF patients with bifurcation lesions. Further, the coexistence of CRF with an LMCA bifurcation lesion was also associated with significantly higher MACE rates. In line with these findings, a recent study by Cho et al also demonstrated that CRF is an independent predictor of MACE in LMCA bifurcation stenting[29].

Overall, our study shows that the nano-crush is an optimum elective double stent technique for bifurcation lesions which is safe and can be performed easily, does not require complex wiring and ballooning, can be performed with less hardware and is 6 Fr guide catheter-compatible. The bench test and *in vitro* IVUS examination did not show any major distortion of the side branch stent at the ostium and this is reflected in the actual clinical outcome. This operator-friendly and safe technique can be adopted as a two-stent bifurcation strategy in a real-world scenario.

Study limitations

The major limitations of our study include its retrospective observational study design and the small number of patients. The lack of comparison of clinical and angiographic outcomes with the nano-crush technique vs. other strategies could also be considered a limitation of the study. In addition, although angiographic follow-up was mandatory in all patients at one-year follow-up, we did not perform IVUS, or optical coherence tomography (OCT) imaging in all patients. In addition, acute myocardial infarction and thrombotic lesions were excluded from the study.

Conclusions

These results demonstrate that the nano-crush technique is associated with acceptable clinical outcomes with no episodes of definite or probable stent thrombosis. Further studies should compare the nano-crush technique with other double-stent strategies in the management of bifurcation lesions.

Impact on daily practice

Management of coronary bifurcation lesions with a dedicated two-stent technique is technically challenging. We propose a novel technique, called nano-crush, which can be performed easily and can be used in all bifurcation angles. In this technique, minimal protrusion of the proximal part of the side branch stent was controlled by main branch dilation with a small size balloon. This novel technique has the following advantages: (a) minimal metal overlap; (b) less metallic carina formation compared to other crush stenting techniques; and (c) less geographic miss in the side branch ostium compared to T-stenting. The feasibility of this technique has been confirmed in bench testing. In addition, an acceptably lower MACE (7.14%) rate at long-term follow-up was observed in our initial experience in a real-world setting in patients with true bifurcation lesions with large side branches (>2.5 mm).

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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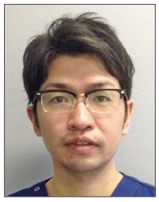
AsiaIntervention 2019;5:52

A ruptured fibrous cap of vulnerable plaque visualised by angioscopy



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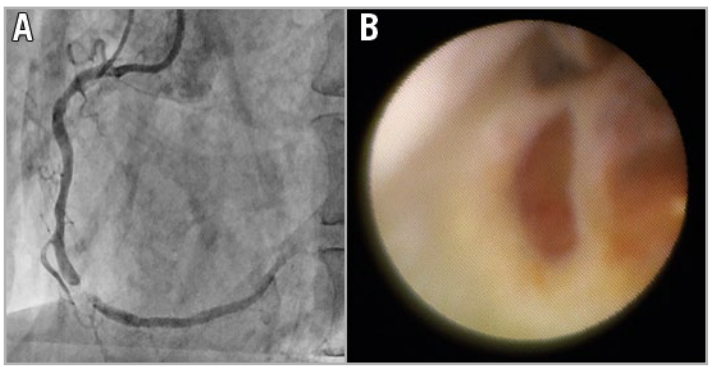
This paper also includes supplementary data published online at: www.asiaintervention.org



An 82-year-old male patient presented with a 99% stenosis in the middle part of the right coronary artery **(Panel A)**. Percutaneous coronary intervention was performed with the latest angioscope (Forwardlooking®; Taisho Biomed Instruments Co., Ltd., Osaka, Japan). The angioscope is of the non-occlusion type, consisting of a probe catheter which has a monorail wire lumen and a fibre catheter and has a resolution of 9,000 pixels with full colour. After the culprit lesion was crossed with a 0.014-inch wire, the angioscopy catheter was advanced to the lesion with the Guide Plus™ guide extension catheter (NIPRO, Osaka, Japan) as delivery catheter and 10% dextran was continuously flushed through the delivery catheter for the displacement of blood at a rate of 4 mL/second for a total of 40 mL by a power injector. Then, all sequences were recorded using a digital recording system to observe the angioscopic movie. The lack of a fibrous cap and the exposed lipid core of the plaque were clearly recognised on angioscopy **(Panel B, Moving image 1)**. The surface of the ruptured fibrous cap was yellow and some gloss findings were suggestive of the presence of cholesterol crystals. Based on this finding, distal protection was initiated and, subsequently, the stent was implanted. Although coronary slow-flow phenomenon had occurred, the coronary flow was immediately improved after removal of the distal protection catheter. Attenuated plaque by intravascular ultrasound and thin-cap fibroatheroma by optical coherence tomography have been reported as the cause of no-reflow phenomenon. As in this case, the ruptured fibrous cap seen on angioscopy may also be related to no-reflow phenomenon.

Conflict of interest statement

The authors have no conflicts of interest to declare.

Supplementary data

Moving image 1. The lack of a fibrous cap and the exposed lipid core of the plaque were clearly recognisable on angioscopy.

The supplementary data are published online at: www.asiaintervention.org

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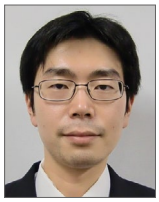
Successful use of last-option infrapopliteal rotational atherectomy despite microembolisation



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KEYWORDS

- atherectomy
- calcification
- critical limb ischaemia
- infrapopliteal artery disease
- infrapopliteal intervention
- peripheral artery disease

Abstract

Calcified lesions pose a technical challenge even in contemporary endovascular intervention. A 71-year-old man who had been receiving haemodialysis required infrapopliteal revascularisation for the treatment of ischaemic infectious gangrene of the right toes. Baseline angiography suggested that the multiple stenotic lesions in the anterior tibial artery were amenable to endovascular therapy for the purpose of establishing one straight-line flow to the foot. However, even a 1.25×15 mm semi-compliant balloon catheter failed to cross and dilate the focal lesion because of the underlying severe calcification in the mid segment of the anterior tibial artery. We adjunctively used high-speed rotational atherectomy with the ROTABLATOR device (1.5 mm burr) to ablate the focal calcified lesion while paying attention to minimise the ablation length and the ablation time. Subsequent balloon angioplasty with a 2.0×40 mm balloon catheter was successful. The skin perfusion pressure in the right foot increased from 32 to 48 mmHg, suggesting a high probability of wound healing. Pathological examination of the right toe amputated on schedule found non-clinically relevant microembolisation involving a couple of cholesterol crystals (20-30 µm) located in the arterioles and capillaries of the necrotic tissue. As an adjunctive device, the ROTABLATOR could provide a last resort for limb salvage, albeit that microembolisation can occur.

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Introduction

Given the growing global burden of peripheral artery disease patients with diabetes mellitus and renal failure, calcified lesions pose a technical challenge, even in contemporary endovascular interventions[1]. In the field of coronary intervention, high-speed rotational atherectomy using the ROTABLATOR™ (Boston Scientific, Marlborough, MA, USA) device has been used adjunctively for the treatment of calcified lesions for some considerable time. Now might be the prime time to embark on ROTABLATOR use in peripheral interventions in cases of balloon failure, such as unsuccessful crossing or dilatation of a balloon catheter due to underlying severely calcified lesions.

Methods

A 71-year-old man who had been receiving haemodialysis for 16 years due to chronic nephritis required infrapopliteal revascularisation for the treatment of ischaemic infectious gangrene of the right toes. Skin perfusion pressure (SPP) in the right foot was 32 mmHg, even after stenting of the iliac and femoropopliteal artery and surgical endarterectomy of the common femoral artery, suggesting insufficient improvement of the foot circulation for wound healing. Baseline infrapopliteal angiography revealed infrapopliteal artery disease, including multiple stenotic lesions in the anterior tibial artery as well as the affected plantar artery **(Figure 1)**. Based on our interpretation of the baseline angiogram, stenotic lesions in the anterior tibial artery were amenable to endovascular therapy for the purpose of establishing one straight-line flow to the foot. However, following a successful balloon angioplasty in the proximal segment lesions of the anterior tibial artery, even a 1.25×15 mm semi-compliant balloon catheter supported by a 4 Fr-long sheath inserted via the ipsilateral common femoral artery failed to cross and dilate the focal stenotic lesion in the mid segment of the anterior tibial artery because of the underlying severe calcification **(Figure 2)**.

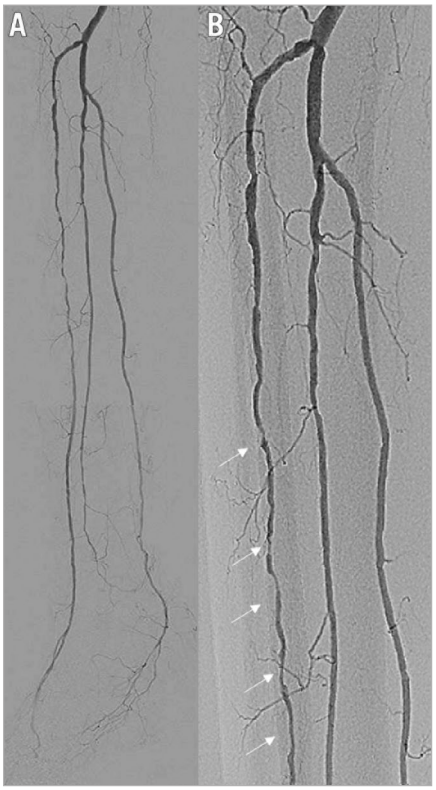

Figure 1. *Pre intervention. A) Baseline angiography showing multiple severe stenotic lesions in the anterior tibial artery as well as plantar artery disease. B) Magnified image of multiple severe stenotic lesions in the anterior tibial artery (arrows).*

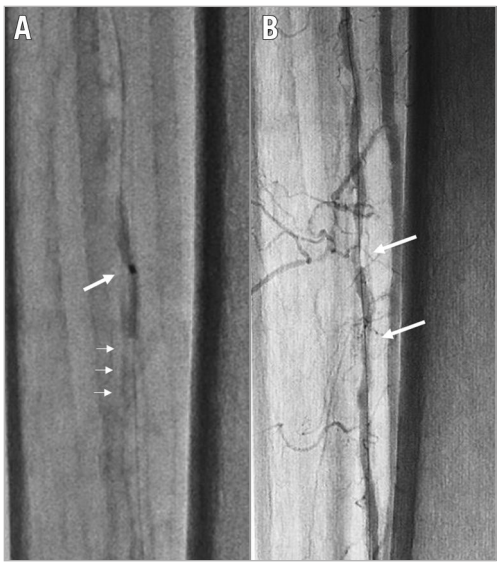

Figure 2. *Balloon failure due to underlying calcification in the mid segment of the anterior tibial artery. A) Even a 1.25×15 mm semi-compliant balloon was stuck just before the calcified lesion (small arrows), and the balloon waist remained due to calcification (large arrow). B) Angiography showing the remaining severe stenosis in the mid segment of the anterior tibial artery (arrows).*

We decided to use the ROTABLATOR adjunctively, to facilitate balloon angioplasty. After exchanging the 0.014-inch guidewire for a ROTAWire™ Floppy (Boston Scientific) using a microcatheter, we focally ablated the calcified lesion using a 1.5 mm burr while being careful to minimise the ablation length and the ablation time. Subsequent balloon angioplasty with a 2.0×40 mm balloon catheter was performed successfully **(Figure 3)**.

Results

Final angiography demonstrated the establishment of one straight-line flow to the pedal arch **(Figure 4)**. The SPP of the right foot increased to 48 mmHg, suggesting a high likelihood of wound healing[1]. Thus, scheduled minor amputation of the right toes was performed to facilitate wound healing and avoid major amputation. Pathological examination of the amputated right toe found non-clinically relevant microembolisation involving a couple of cholesterol crystals (20-30 μm) located in the arterioles and capillaries of the necrotic tissue **(Figure 5)**.

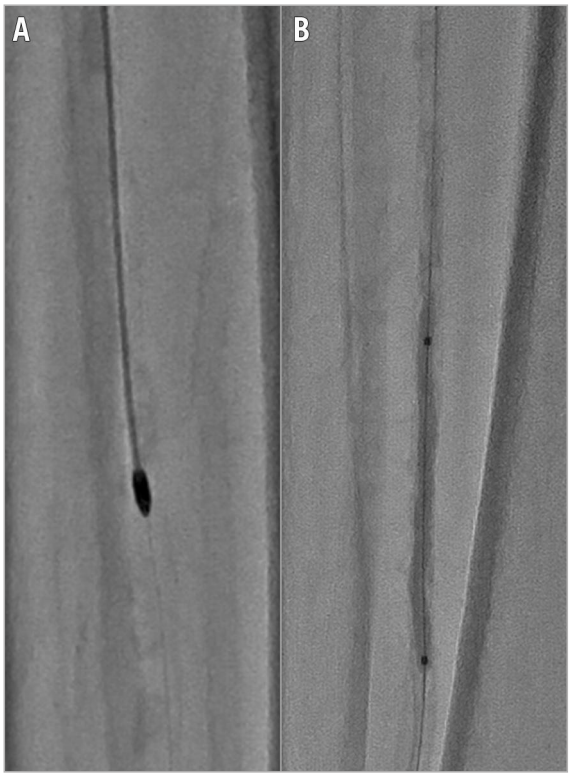

Figure 3. *Use of the ROTABLATOR for balloon failure. A) ROTABLATOR with a 1.5 mm burr was employed to ablate the calcified lesion focally. B) Subsequent balloon angioplasty with a 2.0×40 mm balloon catheter was successfully performed.*

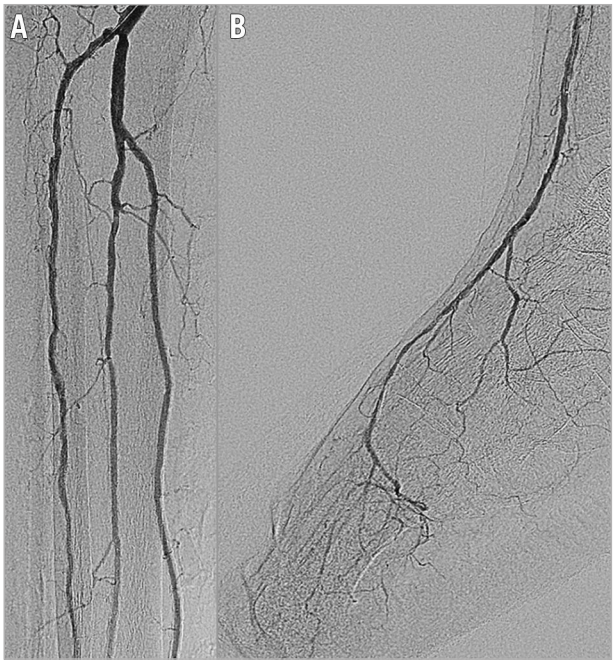

Figure 4. *Post intervention. A) Final angiography showing excellent revascularisation. B) The establishment of one straight-line flow to the pedal arch was achieved. Note the absence of angiographically relevant distal embolisation, even in the below-the-ankle segment.*

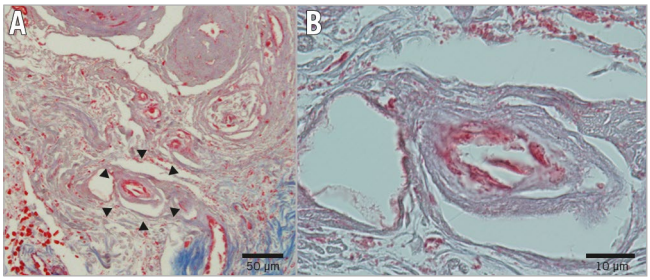

Figure 5. *Pathological findings of the amputated right toe. A) 20 µm-long cholesterol crystal in the capillaries (arrows). B) Magnified image of the crystal.*

Discussion and limitations

In the coronary vasculature, the ROTABLATOR has been used as an indispensable adjunctive device to treat severely calcified lesions for over 20 years. However, the role of the ROTABLATOR in the peripheral vasculature has been underappreciated.

According to a multicentre study on peripheral ROTABLATOR use over two decades ago[2], the angiographic success (residual stenosis <25%) rate of ROTABLATOR use as a standalone procedure in lower limb interventions was approximately 80% with a variety of complications including haemoglobinuria (13%), embolisation (10%), dissection (6%), perforation (4%), haematoma (5%), infection (1%), thrombosis (11%), and device-related amputation (2.5%). In conjunction with an unacceptably high restenosis rate, enthusiasm for peripheral use of the ROTABLATOR waned. However, recently, there has been increasing interest in using the ROTABLATOR adjunctively in order to facilitate subsequent balloon angioplasty in cases where balloon catheters cannot cross or dilate below-the-knee lesions, because no device can take its place. In a study by Dormal et al[3], the ROTABLATOR was used in approximately 10% (18/183) of procedures, mainly for the treatment of calcified infrapopliteal artery disease that was not suitable for balloon angioplasty alone. The technical success rate of ROTABLATOR use was 100% (61% of the cases underwent subsequent balloon angioplasty); the only complication was a case of haemoglobinuria. Despite significant comorbidity (89% of cases with critical limb ischaemia, 89% with very poor run-off, 72% with diabetes, and 22% of patients on dialysis), the limb salvage rate was 89% at 13-month follow-up. Indeed, as shown in our case, the adjunctive use of the ROTABLATOR device could provide an additional endovascular solution for limb salvage in the clinical setting.

According to a previous experimental investigation[4], pulverised atherosclerotic particles generated by the use of a ROTABLATOR could theoretically pass harmlessly through the distal microcirculation. However, it is widely recognised that no/slow flow can potentially occur following coronary use of the ROTABLATOR. There has even been a report of a fatal adverse event due to embolisation following the use of a ROTABLATOR in coronary intervention, with a post-mortem autopsy revealing many atherosclerotic fragments in the small arteries, arterioles and capillaries in the territory of the treated coronary artery[5].

As with coronary interventions, the potential risk of ROTABLATOR-induced distal embolisation might exist in the setting of critically ischaemic limbs with diminished vascular beds. In our case, we used the ROTABLATOR very focally to minimise the ablation length and the ablation time. Even so, although clinical outcomes were satisfactory, pathological examination found microemboli in the amputated toes. Therefore, when using the ROTABLATOR in the clinical setting, there seems to be a trade-off between blood flow restoration following opening the artery and blood flow disturbance due to microembolisation, even in the affected foot. With this in mind, if the ROTABLATOR is used focally, it should be an indispensable tool even when severely calcified infrapopliteal artery disease does not allow advancement or dilatation of a balloon catheter.

Conclusion

Adjunctive use of the ROTABLATOR in infrapopliteal revascularisation could provide a last resort for limb salvage in case of balloon failure due to the underlying calcified lesions, albeit that procedure-related microembolisation may occur.

Impact on daily practice

The ROTABLATOR can be considered as an adjunctive option in cases of balloon failure for the treatment of infrapopliteal artery disease with severely calcified lesions, though the potential of procedure-related microembolisation should always be kept in mind.

Conflict of interest statement

O. Kawarada reports receiving honoraria for lectures and advisory board fees from Boston Scientific Corporation, and honoraria for lectures and research grants from Terumo. The other authors have no conflicts of interest to declare.

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Comparison of three left atrial appendage occlusion devices for stroke prevention in patients with non-valvular atrial fibrillation: a single-centre seven-year experience with WATCHMAN, AMPLATZER Cardiac Plug/Amulet, LAmbre

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KEYWORDS

- atrial fibrillation
- bleeding
- death
- specific closure device/technique
- stroke

Abstract

Aims: We aimed to compare long-term "real-world" outcomes of three left atrial appendage occlusion (LAAO) devices for stroke prevention in a Chinese population with non-valvular atrial fibrillation (NVAF).

Methods and results: Consecutive patients who underwent LAAO from June 2009 to October 2016 at a university-affiliated hospital were retrospectively analysed. In-hospital and major adverse events (MAE) including mortality, stroke and major bleeding rates were compared by LAAO device. One hundred and sixty-one (161) patients (mean age 71.4±8.2 years; 67.7% male) with mean CHA_2DS_2-VASc score of 4.1±1.6 and HAS-BLED score of 2.9±1.1 underwent 162 LAAO procedures, of which 47.5% (n=77), 41.4% (n=67) and 11.1% (n=18) were AMPLATZER Cardiac Plug (ACP)/Amulet, WATCHMAN and LAmbre, respectively. The procedural success rate was 97.5% (158/162). The in-hospital adverse event rate was 7.4% (12/162) and comparable among devices (p=NS). Mean follow-up duration was 28.3±24.4 months (373 patient-years). There were no significant differences in long-term MAE rates among devices (p=NS). Observed annual ischaemic stroke (1.1% vs. 5.1%, p<0.001) and major bleeding rates (2.7% vs. 4.5%, p=NS) were lower compared with the predicted rates, respectively.

Conclusions: The WATCHMAN, ACP/Amulet and LAmbre LAAO devices demonstrated similar long-term safety and efficacy in prevention of ischaemic stroke and major bleeding in patients with NVAF.

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Abbreviations

ACP	AMPLATZER Cardiac Plug
NVAF	non-valvular atrial fibrillation
CHA_2DS_2-VASc score	congestive heart failure, hypertension, age, diabetes mellitus, previous stroke/transient ischaemic attack, female sex, and vascular disease score
HAS-BLED score	hypertension, abnormal renal/liver function, stroke, bleeding history or predisposition, labile INR, elderly, drugs/alcohol concomitantly score
INR	international normalised ratio
LAAO	left atrial appendage occlusion
MAE	major adverse events
NOAC	non-vitamin K oral anticoagulants
NVAF	non-valvular atrial fibrillation
OAC	oral anticoagulation
RRR	relative risk reduction
TEE	transoesophageal echocardiography
TIA	transient ischaemic attack
TTR	time in therapeutic range

Introduction

The risk of ischaemic stroke in non-valvular atrial fibrillation (NVAF) patients is fivefold higher compared to the general population, accounting for about 15% of all strokes[1]. Oral anticoagulation (OAC) therapy with either warfarin or non-vitamin K oral anticoagulants (NOAC) is the standard treatment for stroke prevention in patients with NVAF at increased risk of stroke. Although effective in preventing stroke, OAC is associated with risk of bleeding and poor long-term drug compliance[2]. In a recent study of 1,461 Chinese patients with NVAF, 44.4% of patients discontinued warfarin within one year and 57.6% by two years after initiation of therapy[3]. In another study, 83.7% of Chinese patients on warfarin therapy failed to achieve >65% time in therapeutic range (TTR)[4].

Among patients who do not tolerate OAC, percutaneous left atrial appendage occlusion (LAAO) has emerged as an alternative treatment option for stroke prevention. The main advantages of LAAO over OAC include lower risk of major bleeding[5] and issues with blood monitoring and drug compliance. Currently, the WATCHMAN™ (Boston Scientific, Marlborough, MA, USA) and the AMPLATZER™ Cardiac Plug (ACP) or later Amulet (St. Jude Medical, St. Paul, MN, USA) are the most commonly used commercially available LAAO devices. The LAmbre (Lifetech Scientific, Shenzhen, China) is a relatively new device which has recently received CE mark approval[6].

In most published data on percutaneous LAAO, Asian patients consisted of <1% of cases[7,8]. In this study, we aimed to evaluate the safety and efficacy of different LAAO devices in Chinese NVAF patients for stroke prevention.

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Methods

Consecutive NVAF patients who underwent LAAO at the Prince of Wales Hospital in Hong Kong were enrolled between June 2009 and October 2016. Data including baseline clinical and procedural characteristics, CHA_2DS_2-VASc and HAS-BLED scores, indication for LAAO, and follow-up clinical and transoesophageal echocardiography (TEE) results were recorded. The study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee.

Indications for LAAO included NVAF (permanent, persistent, or paroxysmal) with a CHA_2DS_2-VASc score ≥2 and one of the following: (i) history of bleeding; (ii) high risk of bleeding defined by HAS-BLED score ≥3; (iii) labile international normalised ratio (INR) on warfarin; (iv) non-compliance with OAC therapy; and (v) allergy or side effects from OAC therapy.

DEVICE AND IMPLANTING PROCEDURE

Four LAAO devices were used in our institution. The WATCHMAN device has been available since October 2009, while the ACP was available from June 2009 and then the Amulet device from February 2015 onwards. The LAmbre device has been used since April 2014. The choice of device was at the discretion of the operator.

TEE was performed prior to LAAO procedure to rule out LAA thrombus and to measure LAA dimensions. After transseptal puncture, patients were heparinised to achieve an activated clotting time of 250-300 seconds throughout the procedure. A selective LAA angiogram was performed using a pigtail catheter. The device size was selected based on both angiographic and TEE measurements. Device stability, positioning, compression, and peri-device leaks were thoroughly assessed on TEE and angiography before final release of the device.

Chest radiography and transthoracic echocardiography were performed before discharge. Follow-up TEE was mandatory for all patients on day 45±7 after the procedure. Lifelong aspirin (80 mg daily) was prescribed for all patients. Clopidogrel (75 mg) was prescribed for six months for the ACP/Amulet and LAmbre devices. For the WATCHMAN device, warfarin was administered for at least 45 days until mandatory follow-up TEE, and warfarin was discontinued if peri-device flow was <5 mm on TEE and replaced with clopidogrel until six months after implant.

DEFINITIONS

Technical success was defined as successful implantation of the LAAO device without significant residual leak on TEE at the end of the procedure (i.e., ≤5 mm for all devices)[9].

In-hospital adverse events were defined according to the Valve Academic Research Consortium-2 (VARC-2) criteria[10] as any adverse events occurring post procedure and prior to discharge, including death, stroke, transient ischaemic attack (TIA), systemic embolisation, device embolisation, significant pericardial effusion or cardiac tamponade, myocardial infarction, major bleeding (requiring intervention or transfusion), and major vascular complications (requiring percutaneous or surgical intervention). Peri-device leak was considered significant if the colour Doppler jet width was >5 mm for all devices on TEE[9]. Follow-up major

adverse events (MAE), a composite of death, ischaemic or haemorrhagic stroke and TIA, or major bleeding, were recorded.

The actual event rates of stroke and bleeding at follow-up were compared with the predicted event rates by CHA_2DS_2-VASc and HAS-BLED scores, respectively. The average annual risks of stroke and bleeding for the study cohort were calculated. The actual % event rate was the total number of events divided by the total number of patient-years of follow-up and then multiplied by 100. Risk reduction was calculated using the formula: (estimated % event rate - actual % event rate)/ estimated % event rate[11].

STATISTICAL ANALYSIS

Numerical results were presented as mean±SD or median (interquartile range [IQR]). One-way ANOVA and Kruskal-Wallis tests were performed to compare means and medians among groups. Categorical results were presented as percentages and compared using the chi-square test or Fisher's exact test. Kaplan-Meier event-free survival curves were estimated, and differences were compared using the log-rank test. All statistical analyses were performed using SPSS statistical software, Version 22.0 (IBM Corp., Armonk, NY, USA). All analyses were two-tailed and p-values <0.05 were considered statistically significant.

Results

A total of 161 patients underwent 162 procedures. Baseline characteristics are summarised in **Table 1**. Mean patient age was 71.4±8.2 years, 67.7% were male and more than one third had a history of stroke (38.5%). The mean CHA_2DS_2-VASc score was 4.1±1.6 and HAS-BLED score 2.9±1.1. There were no significant differences in baseline characteristics among patients receiving different LAAO devices (all p=NS). The most common indication for LAAO was non-compliance to OAC therapy (34.2%) followed by history of bleeding (31.7%), high risk of bleeding (14.9%) and labile INR on warfarin therapy (12.4%). Non-compliance to OAC therapy included patients with poor drug compliance or refusal to continue OAC lifelong.

PROCEDURE

One patient underwent two LAAO procedures on different dates, resulting in 162 procedures. Of 162 procedures, 47.5% (n=77), 41.4% (n=67) and 11.1% (n=18) were ACP/Amulet, WATCHMAN and LAmbre, respectively. Procedural findings are summarised in **Table 1**. Mean procedural time using the WATCHMAN, ACP/Amulet and LAmbre devices was 91.6±23.4 minutes, 102.9±31.2 minutes, and 89.1±23.3 minutes, respectively (p=0.03). The median fluoroscopy time was 11 minutes (IQR 8-17.0) for WATCHMAN, 17 minutes (IQR 12-22) for ACP/Amulet, and 12 minutes (IQR 9-14.5) for the LAmbre device (p=<0.001).

The overall technical success rate was 97.5% (158/162). One patient failed the initial procedure due to ACP device embolisation, which was successfully retrieved with a snare. He subsequently underwent a successful second LAAO procedure with the WATCHMAN device. Three (two WATCHMAN and one ACP) procedures failed the stability test despite upsizing to the largest respective devices.

IN-HOSPITAL EVENTS

In-hospital adverse events occurred in 7.4% (12/162) of cases **(Table 2)**. There was a non-procedure-related death due to peritoneal dialysis peritonitis on day 15. Cardiac tamponade occurred in five patients (3.1%); in four cases this required open surgical repair. There were three cases (1.9%) of major bleeding from oesophageal laceration by the TEE probe. In one case the patient developed chest pain with acute ST elevation during the procedure; immediate coronary angiography revealed a critical stenosis of the left anterior descending artery which was successfully treated by angioplasty and stented without an associated rise in cardiac enzymes. There was one case (0.6%) of a major femoral access-site complication which required endovascular intervention. The 30-day MAE rates were the same as the in-hospital MAE rates.

TEE FOLLOW-UP

Post-procedural TEE was performed in 94.3% of successful cases (149/158) **(Table 3)**. Eight patients refused and one died before scheduled TEE. Significant peri-device leak was observed in 1.4% (1/71) of ACP/Amulet cases, but none with LAmbre or WATCHMAN devices. OAC therapy cessation at 45 days in the WATCHMAN group was 93.8% (61/65). Device thrombus was detected in five (3.4%) patients by TEE (four WATCHMAN and one ACP). Clopidogrel was changed to OAC therapy in the patient with ACP device thrombus, and OAC therapy was extended for three months in the WATCHMAN patients. Follow-up TEE after three months showed complete resolution of thrombus in three cases (two WATCHMAN and one ACP) and persistent thrombus on two WATCHMAN devices. Long-term OAC therapy was continued for these two WATCHMAN patients.

LONG-TERM FOLLOW-UP

The mean follow-up duration was 28.3±24.4 months and a total of 373 patient-years **(Table 2)**. There were 14 deaths (8.9%); however, none was related to the LAAO procedure (causes and time of death are shown in **Table 4**). Six strokes, including four ischaemic and two haemorrhagic strokes, occurred during follow-up.

The estimated annual risk of ischaemic stroke based on CHA_2DS_2-VASc score was 5.1% compared to the observed rate of 1.1% (four events/373 patient-years). This translated to a 79.2% relative risk reduction (RRR) in ischaemic stroke (p<0.001) **(Figure 1)**. There were seven cases of major bleeding events during post-discharge follow-up. All bleeding events in the WATCHMAN group occurred during the period after stopping OAC. The observed annual major bleeding rate was 2.7% (10 events/373 patient-years) compared to a 4.5% predicted rate of annual major bleeding based on HAS-BLED score. This translated to a 39.9% RRR in major bleeding but was not statistically significant (p=0.10) **(Figure 1)**. There were no significant differences in MAE-free survival rates among devices during follow-up (log-rank p=0.89).

Table 1. Patient characteristics and procedural findings.

Patient characteristics		WATCHMAN (n=66)	ACP/Amulet (n=77)	LAmbre (n=18)	Total (n=161)	*p*-value
Age (years)		72.6±7.9	71±8.6	68.7±7	71.4±8.2	0.16
Male		45 (68.2)	50 (64.9)	14 (77.8)	109 (67.7)	0.57
Weight (kg)		65±10.3	65.2±11.8	69.1±11.1	65.5±11.1	0.35
Body mass index (kg/m^2)		25.2±2.9	24.9±3.9	25.7±3.8	25.1±3.5	0.70
Medical history						
Prior heart failure		9 (13.6)	15 (19.5)	7 (38.9)	31 (19.3)	0.05
Hypertension		52 (78.8)	59 (76.6)	12 (66.7)	123 (76.4)	0.56
Diabetes mellitus		31 (47.0)	31 (40.3)	10 (55.6)	72 (44.7)	0.45
Previous stroke/TIA		28 (42.4)	26 (33.8)	8 (44.4)	62 (38.5)	0.49
Cardiovascular disease/peripheral arterial disease		8 (12.1)	12 (15.6)	2 (11.1)	22 (13.7)	0.79
Prior myocardial infarction		12 (18.2)	13 (16.9)	2 (11.1)	27 (16.8)	0.78
Prior percutaneous coronary intervention/coronary artery bypass grafting		13 (19.7)	22 (28.6)	3 (16.7)	38 (23.6)	0.35
Pacemaker implanted		8 (12.1)	18 (23.4)	2 (11.1)	28 (17.4)	0.16
History of bleeding		26 (39.4)	31 (40.3)	6 (33.3)	63 (39.1)	0.86
CHA_2DS_2-VASc score (continuous)		4.3±1.4	3.9±1.7	3.8±1.4	4.1±1.6	0.37
CHA_2DS_2-VASc score (categorical)	0	0 (0)	0 (0)	0 (0)	0 (0)	0.45
	1	1 (1.5)	6 (7.8)	0 (0)	7 (4.3)	
	2	7 (10.6)	13 (16.9)	4 (22.2)	24 (14.9)	
	3	10 (15.2)	11 (14.3)	3 (16.7)	24 (14.9)	
	4	21 (31.8)	17 (22.1)	7 (38.9)	45 (28.0)	
	5	16 (24.2)	13 (16.9)	2 (11.1)	31 (19.3)	
	6	6 (9.1)	14 (18.2)	1 (5.6)	21 (13.0)	
	7	4 (6.1)	2 (2.6)	1 (5.6)	7 (4.3)	
	8	1 (1.5)	1 (1.3)	0 (0)	2 (1.2)	
	9	0 (0)	0 (0)	0 (0)	0 (0)	
HAS-BLED score (continuous)		3.1±1	2.7±1.1	2.8±0.9	2.9±1.1	0.12
HAS-BLED score (categorical)	0	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.29
	1	3 (4.5)	10 (13)	2 (11.1)	15 (9.3)	
	2	10 (15.2)	24 (31.2)	3 (16.7)	37 (23.0)	
	3	33 (50.0)	24 (31.2)	9 (50.0)	66 (41.0)	
	4	14 (21.2)	16 (20.8)	4 (22.2)	34 (21.1)	
	5	4 (6.1)	2 (2.6)	0 (0)	6 (3.7)	
	6	1 (1.5)	1 (1.3)	0 (0)	2 (1.2)	
	≥7	0 (0)	0 (0)	0 (0)	0 (0)	
Atrial fibrillation	Paroxysmal	19 (28.8)	23 (29.9)	5 (27.8)	47 (29.2)	0.98
	Permanent	47 (71.2)	54 (70.1)	13 (72.2)	114 (70.8)	
Indications for left atrial appendage occlusion	Non-compliance to OAC/NOAC	21 (31.8)	28 (36.4)	6 (33.3)	55 (34.2)	0.21
	Prior bleeding including previous intracranial bleeding	20 (30.3)	26 (33.8)	5 (27.8)	51 (31.7)	
	High risk of bleeding	14 (21.2)	8 (10.4)	2 (11.1)	24 (14.9)	
	Labile INR	9 (13.6)	8 (10.4)	3 (16.7)	20 (12.4)	
	Allergic, or side effect after OAC/NOAC	0 (0)	7 (9.1)	1 (5.6)	8 (5.0)	
	Stroke on OAC/NOAC	2 (3)	0 (0)	1 (5.6)	3 (1.9)	
Procedural findings		**WATCHMAN (n=67)**	**ACP/Amulet (n=77)**	**LAmbre (n=18)**	**Total (n=162)**	***p*-value**
Anaesthesia	General anaesthesia	23 (34.3)	31 (40.3)	0 (0)	54 (33.3)	<0.001
	Local anaesthesia	0 (0)	3 (3.9)	17 (94.4)	20 (12.3)	
	Monitored anaesthetic care	44 (65.7)	43 (55.8)	1 (5.6)	88 (54.3)	
Procedural time, minutes		91.6±23.4	102.9±31.2	89.1±23.3	96.6±27.8	0.03
Fluoroscopy time, minutes		11 (8-17)	17 (12-22)	12 (9-14.5)	14 (10-19)	<0.001
Length of stay, days		3 (2-4)	3 (2-4)	2 (2-2.3)	3 (2-4)	0.08
Procedural success		65 (97.0)	75 (97.4)	18 (100)	158 (97.5)	0.77

Values are expressed as mean±SD, median (IQR) or n (%). ACP: AMPLATZER Cardiac Plug; INR: international normalised ratio; NOAC: non-vitamin K oral anticoagulants; OAC: oral anticoagulants; TIA: transient ischaemic attack

Table 2. In-hospital events of patients undergoing LAAO and long-term follow-up outcomes of successfully implanted patients.

	WATCH-MAN (n=67)	ACP/ Amulet (n=77)	LAmbre (n=18)	Total (n=162)	*p*-value[a]
In-hospital events					
Death	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.47
Cardiac death	0 (0)	0 (0)	0 (0)	0 (0)	NA
Non-cardiac death	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.47
Stroke/TIA	0 (0)	0 (0)	0 (0)	0 (0)	NA
Device embolisation	0 (0)	1 (1.3)	0 (0)	1 (0.6)	1.00
Systemic embolism	0 (0)	0 (0)	0 (0)	0 (0)	NA
Cardiac tamponade	2 (3)	3 (3.9)	0 (0)	5 (3.1)	1.00
Major bleeding	0 (0)	3 (3.9)	0 (0)	3 (1.9)	0.25
Myocardial infarction	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.47
Major vascular complications (requiring endovascular intervention)	0 (0)	1 (1.3)	0 (0)	1 (0.6)	1.00
Total	4 (6.0)	8 (10.4)	0 (0)	12 (7.4)	0.34
Long-term follow-up (FU)	**WATCH-MAN (n=65)**	**ACP/ Amulet (n=75)**	**LAmbre (n=18)**	**Total (n=158)**	***p*-value[b]**
FU months	27.5±24.2	30.1±27	23.5±8.3	28.3±24.4	0.55
FU, total patient-years	149	189	35	373	NA
Risk scores					
CHA_2DS_2-VASc score	4.2±1.5	4.0±1.7	3.8±1.4	4.1±1.6	0.52
Estimated annual risk of stroke, based on CHA_2DS_2-VASc score, %	5.25±2.64	5.22±3.02	4.40±2.32	5.14±2.79	0.50
HAS-BLED score	3.1±1	2.7±1.1	2.8±0.9	2.9±1.1	0.15
Estimated annual risk of major bleeding, based on HAS-BLED score, %	4.91±3.15	4.12±3.07	4.23±2.65	4.46±3.06	0.31
Death					
In-hospital	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.49
Cardiac death	0 (0)	0 (0)	0 (0)	0 (0)	NA
Non-cardiac death	1 (1.5)	0 (0)	0 (0)	1 (0.6)	0.49
Post-discharge	4 (6.2)	7 (9.3)	3 (16.7)	14 (8.9)	0.37
Cardiac death	1 (1.5)	1 (1.3)	1 (5.6)	3 (1.9)	0.48
Non-cardiac death	3 (4.6)	6 (8.0)	2 (11.1)	12 (7.6)	0.56
Total	5 (7.7)	7 (9.3)	3 (16.7)	15 (9.5)	0.51
Stroke/TIA					
In-hospital	0 (0)	0 (0)	0 (0)	0 (0)	NA
Ischaemic	0 (0)	0 (0)	0 (0)	0 (0)	NA
Haemorrhagic	0 (0)	0 (0)	0 (0)	0 (0)	NA
Post-discharge	2 (3.1)	3 (4.0)	1 (5.6)	6 (3.8)	0.88
Ischaemic	1 (1.5)	3 (4.0)	0 (0)	4 (2.5)	0.50
Haemorrhagic	1 (1.5)	0 (0)	1 (5.6)	2 (1.3)	0.16
Total	2 (3.1)	3 (4.0)	1 (5.6)	6 (3.8)	0.95
Observed annual risk of stroke, %	0.67 (1/149) *100	1.59 (3/189) *100	0 (0/35) *100	1.07 (4/373) *100	0.75
Stroke reduction, %	87.2 ([5.25-0.67]/5.25) *100	69.5 ([5.22-1.59]/5.22) *100	100.0 ([4.40-0]/4.40) *100	79.2 ([5.14-1.07]/5.14) *100	<0.001
NNT	22	28	23	25	
Major bleeding					
In-hospital	0 (0)	3 (4.0)	0 (0)	3 (1.9)	0.18
Post-discharge	4 (6.2)	2 (2.7)	1 (5.6)	7 (4.4)	0.59
Total	4 (6.2)	5 (6.7)	1 (5.6)	10 (6.3)	0.95
Observed annual risk of major bleeding, %	2.68 (4/149) *100	2.65 (5/189) *100	2.86 (1/35) *100	2.68 (10/373) *100	1.00
Major bleeding reduction, %	45.4 ([4.91-2.68]/4.91) *100	35.7 ([4.12-2.65]/4.12) *100	32.4 ([4.23-2.86]/4.23) *100	39.9 ([4.46-2.68]/4.46) *100	0.16
NNT	45	68	73	57	
Major adverse events (MAE)[c]					
In-hospital	1 (1.5)	3 (4.0)	0 (0)	4 (2.5)	0.50
Post-discharge	9 (13.8)	10 (13.3)	4 (22.2)	23 (14.6)	0.62
Total	10 (15.4)	13 (17.3)	4 (22.2)	27 (17.1)	0.89

Values are expressed as mean±SD or n (%). [a]Statistical tests were performed for comparison between WATCHMAN and ACP/Amulet devices. [b]Statistical tests were performed for comparison between WATCHMAN, ACP/Amulet and LAmbre devices. [c]A major adverse event (MAE) is defined as a composite of death, ischaemic or haemorrhagic stroke and TIA, or major bleeding. ACP: AMPLATZER Cardiac Plug; NNT: number needed to treat; TIA: transient ischaemic attack

Discussion

The main finding of this study was that different LAAO devices comprising the WATCHMAN, ACP/Amulet and LAmbre were comparable in terms of long-term efficacy in reducing ischaemic stroke and avoiding major bleeding events in Chinese NVAF patients. To the best of our knowledge, this is the largest reported cohort of LAAO with the longest follow-up in a Chinese population and the first clinical experience with the LAmbre device.

Our procedural success rate (97.5%) was comparable with other LAAO studies, with reported success rates from 90.9% to 98.5%[7,8,11,12]. The safety profile of LAAO in our cohort also compared favourably with these studies. Our in-hospital MAE rate was driven by the occurrence of cardiac tamponade (n=5/12 MAE), which occurred during the early phase of our LAAO programme. A similar learning curve has been reported with the WATCHMAN device where rates of cardiac tamponade decreased over time with increasing operator experience from 4% in PROTECT AF[7] to 1.9% in PREVAIL[8] and 0.2% in EWOLUTION[12]. Furthermore, after two cases of guidewire perforation using the Amplatz Super Stiff™ guidewire (Boston Scientific), our procedural protocol was revised and placement of the Super Stiff guidewire within the LAA was no longer allowed. No guidewire-related perforation or cardiac tamponade occurred after this change.

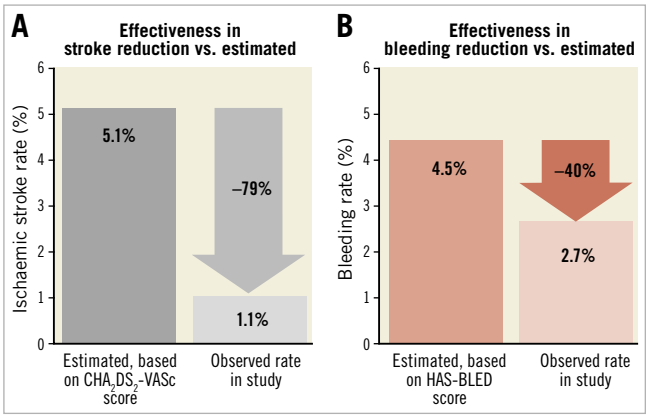

Figure 1. *Effectiveness of LAAO in reduction of (A) ischaemic stroke rate and (B) major bleeding rate compared with estimated annual rates from CHA_2DS_2-VASc score and HAS-BLED score, respectively.*

When LAAO devices are recaptured and repositioned repeatedly, the reverse-facing stabilising hooks can cause damage and perforation to the LAA wall. Accurate preoperative device sizing is crucial to prevent this complication. Traditionally, device sizing is guided by TEE and fluoroscopy. Recently, we have incorporated 3D printed modelling of the LAA from CT images for preprocedural planning and device size selection[13] to reduce inappropriate sizing and device manipulation during implantation.

Long-term compliance with warfarin treatment for stroke prevention is a major problem in Chinese patients with NVAF[3]. In our cohort of Chinese patients, non-compliance to OAC therapy (34.2%) was the most common indication for LAAO, whereas previous bleeding and high bleeding risk were the major indications for LAAO in Caucasian populations[11,12]. LAAO obviates the need for long-term anticoagulation (except in a small number of patients with persistent device-related thrombus) and hence the risk of bleeding and also stroke from subtherapeutic INR. Although there are no direct comparisons between LAAO and NOAC, our group recently published a study using the Markov decision analytic model to compare the cost-effectiveness of LAAO with seven pharmacological strategies including aspirin alone, clopidogrel plus aspirin, warfarin, dabigatran (110 mg and 150 mg), apixaban and rivaroxaban from a Hong Kong healthcare provider perspective[14]. We found that LAAO was considered cost-effective compared to warfarin, with an incremental cost-effectiveness ratio (ICER) of USD 6,298 per quality-adjusted life years (QALY) gained; LAAO was considered dominant (i.e., less costly and more effective) compared to all three NOAC. Sensitivity analysis demonstrated that ICERs of LAAO remained favourable against NOAC in various

Table 3. Transoesophageal echocardiography (TEE) follow-up findings.

	WATCHMAN (n=61)	ACP/Amulet (n=71)	LAmbre (n=17)	Total (n=149)	*p*-value
Thrombus detection over device	4 (6.6)	1 (1.4)	0 (0)	5 (3.4)	0.19
Leak at TEE follow-up 45 days	20 (32.8)	13 (18.3)	8 (47.1)	41 (27.5)	0.03
Significant peri-device leak[a]	0 (0)	1 (1.4)	0 (0)	1 (0.7)	0.58

Values are expressed as n (%). [a]Peri-device leak was considered significant if the colour Doppler jet width was >5 mm for all devices. ACP: AMPLATZER Cardiac Plug; TEE: transoesophageal echocardiography

Table 4. Characteristics of deceased patients.

Patient	Age (years)	Sex	CHA_2DS_2-VASc score	HAS-BLED score	Device	Cause of death	Time between procedure and death (months)
1	62	M	1	1	ACP	Brain tumour	20
2	69	M	3	3	ACP	Ischaemic stroke on warfarin	76
3	48	M	5	2	ACP	Type A aortic dissection	65
4	81	M	4	2	WATCHMAN	Acute renal failure	84
5	63	M	3	2	ACP	Liver tumour	39
6	66	M	5	3	WATCHMAN	Sudden collapse	22
7	83	F	8	4	WATCHMAN	End-stage renal failure	17
8	65	M	6	4	ACP	Pneumonia	24
9	76	M	4	4	WATCHMAN	Necrotising fasciitis	16
10	68	M	5	4	LAmbre	Pneumonia	4
11	80	M	5	3	LAmbre	Haemorrhagic stroke	18
12	65	M	3	2	LAmbre	Unknown cause	6
13	80	F	5	3	ACP	Malignant duodenal obstruction	6
14	83	F	7	6	WATCHMAN	Peritoneal dialysis peritonitis	1
15	84	M	5	4	Amulet	Pneumonia	7

ACP: AMPLATZER Cardiac Plug

$CHADS_2$ scores, HAS-BLED scores, time horizons and LAAO costs. Therefore, LAAO could be considered a cost-effective option for stroke prophylaxis in Chinese patients with NVAF.

Limitations

The limitations of the study included a small sample size and being from a single centre. Nonetheless, this is the largest reported cohort of LAAO with the longest follow-up in Chinese patients with NVAF.

Conclusions

Percutaneous LAAO was a safe and effective treatment option for stroke prophylaxis in Chinese patients with NVAF. The WATCHMAN, ACP/Amulet and LAmbre LAAO devices were comparable in long-term safety and efficacy in stroke reduction and avoidance of major bleeding.

Impact on daily practice

The majority of published data concerning left atrial appendage occlusion (LAAO) have come from Western populations. This article provides "real-world" long-term data of LAAO in a Chinese population. We demonstrated that LAAO with three different devices is a safe and effective treatment strategy for stroke prophylaxis in Chinese patients with non-valvular atrial fibrillation who are not candidates for oral anticoagulation therapy.

Conflict of interest statement

G. Cheung is a clinical proctor for WATCHMAN and Amulet LAAO to Boston Scientific and St. Jude Medical, respectively. Y-y. Lam is a clinical proctor for LAmbre and Amulet LAAO to Lifetech and St. Jude Medical, respectively. The other authors have no conflicts of interest to declare.

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Clipping Barlow's mitral valve to rescue a patient with acute biventricular failure

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KEYWORDS

- mitral regurgitation
- mitral valve repair
- transoesophageal echocardiogram

Abstract

Percutaneous edge-to-edge mitral repair with the MitraClip device is an alternative therapy for patients with severe mitral regurgitation. Given that Barlow's disease is characterised by multiple prolapsed segments and multiple regurgitant jets, the MitraClip is not recommended. Herein, we present the case of a 42-year-old gentleman who suffered acute biventricular failure due to a primary chordae rupture of Barlow's mitral valve. Because of prohibitive surgical risk, he was successfully rescued using transcatheter edge-to-edge mitral repair. Our critical case may demonstrate the feasibility of MitraClip use as a rescue therapy for patients with acute severe mitral regurgitation.

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Abbreviations

LAD	left anterior descending artery
MR	mitral regurgitation
MVA	mitral valve area
PEEP	positive end-expiratory pressure
TEE	transoesophageal echocardiography

Introduction

Clinical trials have demonstrated the efficacy and safety of transcatheter edge-to-edge mitral valve repair, using the MitraClip® device (Abbott Vascular, Santa Clara, CA, USA), as an alternative therapy for severe mitral regurgitation (MR). However, anatomical eligibility for this procedure is critically important. Barlow's disease is characterised by an abnormal matrix structure and multiple leaflet scallops prolapsing into the left atrium. The major limitation of the MitraClip procedure in treating multiple flail segments is the residual mitral valve area (MVA) after the repair. As a result, patients with Barlow's disease are considered inappropriate for the MitraClip procedure[1]. On the other hand, open heart surgery may sometimes not be feasible for patients with acute severe MR and prohibitive risks. The case here presented with inoperable Barlow's disease was finally successfully rescued using the MitraClip procedure.

Methods

A 42-year-old gentleman with Marfan's syndrome, who had undergone Bentall's operation at the age of 32, presented to the emergency department with acute pulmonary oedema and was soon intubated due to respiratory failure. Transoesophageal echocardiography (TEE) elucidated multiple MR jets, arising from both the flail A3 leaflet and the prolapsed P1 leaflet **(Figure 1A-Figure 1C)**. The mitral regurgitant volume was 195 ml by the flow convergence method. Otherwise, the billowing bileaflets and marked dilatation of the mitral annulus were typical presentations of Barlow's mitral valve disease. The transthoracic echocardiogram showed a left ventricular ejection fraction (LVEF) of 45% and a right ventricular fractional area change (FAC) of 25%. In addition, the blood tests disclosed marked elevations of aspartate aminotransferase (2,228 u/l), N-terminal prohormone brain natriuretic peptide (4,350 pg/ml) and serum lactate level (48.5 mg/dl), indicating acute biventricular failure and cardiogenic shock. He was

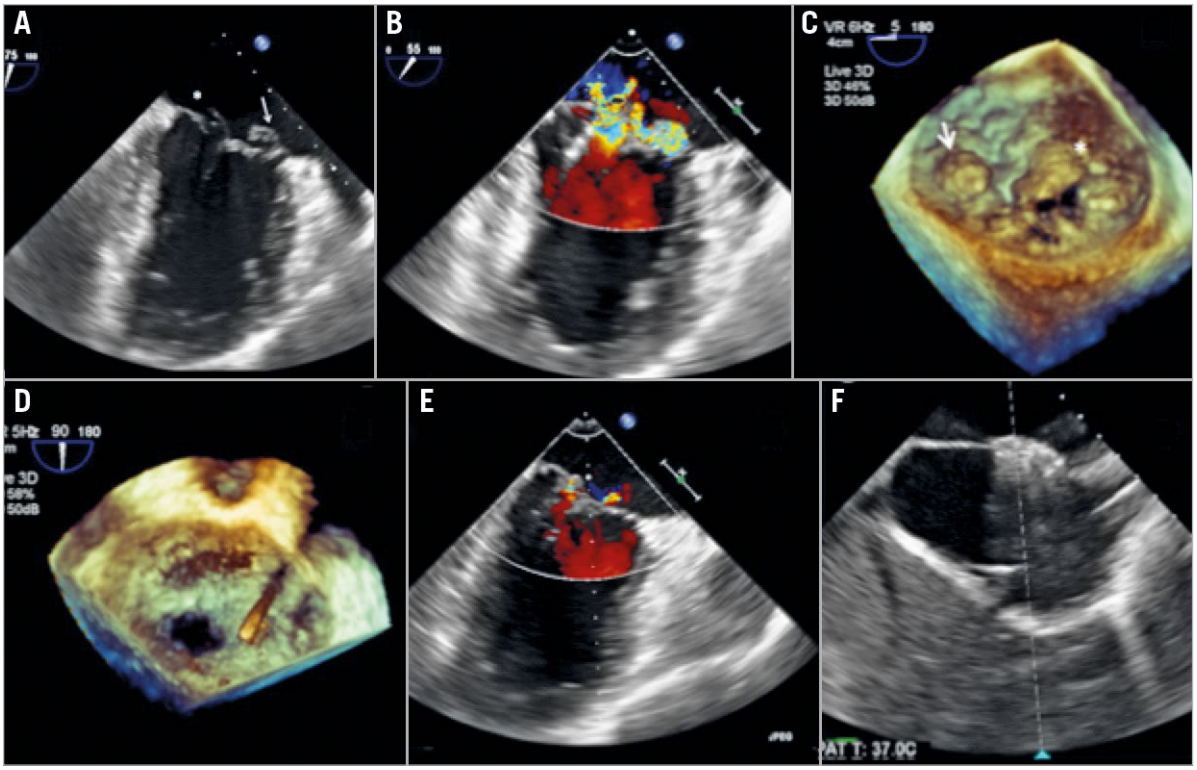

Figure 1. *Transoesophageal echocardiography images during the MitraClip procedure. A) Bi-commissural view of the transoesophageal echocardiogram demonstrating the complexity of the Barlow's mitral valve. Arrow marks the medial A3 flail segment and the asterisk marks the P1 prolapse segment of the mitral valve. B) Bi-commissural view with colour Doppler demonstrating the significant mitral regurgitation arising from both the lateral and the medial site of the mitral valve. C) Three-dimensional en face view elucidating the complexity of the Barlow's mitral valve. Arrow marks the medial A3 flail segment and the asterisk marks the P1 prolapse segment of the mitral valve. D) Three-dimensional en face view demonstrating a total of three clips successfully implanted. E) Bi-commissural view of the transoesophageal echocardiogram showing only trivial mitral regurgitation after the procedure. F) The iatrogenic atrial septal defect was closed by an AMPLATZER atrial septal defect occluder.*

put on high-dose dopamine of 10 mcg/kg/min. Right heart catheterisation demonstrated a mean pulmonary artery wedge pressure of 26 mmHg, a giant V-wave pressure of 33 mmHg, mean pulmonary artery pressure of 39 mmHg, and right atrial pressure of 18 mmHg. The coronary angiogram disclosed a critical stenosis at the proximal portion of the left anterior descending artery (LAD). Given that the calculated EuroSCORE II risk was 60% for surgery, transcatheter intervention was the preferred rescue option through the shared decision-making process. Since the patient did not improve after percutaneous coronary intervention to the LAD, a MitraClip procedure was conducted 48 hours later.

The procedure was conducted using the standard approach with a classic MitraClip device. Due to the higher coaptation point from the prolapse/flail and medial location, we aimed at a higher puncture site of the interatrial septum. The transseptal height from the annulus was 4.4 cm. Continuous left atrial pressure monitoring with a pigtail catheter in the left upper pulmonary vein was performed to assess the immediate haemodynamic response throughout the procedure[2]. We failed to grasp directly at the largest gap of the flail A3 leaflet and therefore applied the anchoring strategy from the medial commissure. With the increasing of positive end-expiratory pressure (PEEP) to 10 cm H_2O, the first clip was applied at the medial site of the A3-P3, followed by additional clips at the lateral site of the A3-P3 and a third clip over the P1 prolapse segment **(Figure 1D, Figure 1E)**. Only trivial to mild residual MR and a transmitral mean pressure gradient of 3 mmHg remained. Before withdrawal of the steerable guide to the left atrium, a right to left shunt from the iatrogenic septal defect was observed by TEE **(Moving image 1)**. Arterial blood gas analysis showed a significant drop of the oxygenation after removal of the steerable guide. The PaO_2/FiO_2 ratio significantly reduced to 49% as compared with the start of the procedure (372 preoperatively and 184 after removal of the guide). We therefore closed the septal defect with a 12 mm AMPLATZER™ atrial septal defect occluder (St. Jude Medical, St. Paul, MN, USA) **(Figure 1F)**. The vascular access was closed with a "figure-of-eight" suture.

Results

The patient recovered well, and was extubated on the next day and then discharged in a week. At the three-month visit he was asymptomatic, and the transthoracic echocardiogram showed mild MR and normally functioning ventricles.

Discussion

To the best of our knowledge, this is the first report of a MitraClip procedure as the rescue therapy for a Marfan's patient with Barlow's mitral valve disease. Barlow's disease is the most complex form of degenerative mitral valve disease due to the extensive leaflet thickening, multiple segment prolapsing, elongated and ruptured chordae tendineae, and annular dilatation. It is challenging to conduct a MitraClip procedure for Barlow's disease because the anatomical eligibility is more rigorous than for a central flail leaflet. The huge volume of prolapsing leaflet and poor chordae support make the clipping process more difficult and even warrant multiple clips to stabilise the coaptation. The two most useful techniques to complete this procedure are the anchoring clip strategy[2] and applying PEEP to improve coaptation[3]. With growing experience and newer-generation devices, i.e., MitraClip NT or XTR, mitral cleft[4], large flail gap[5], or even papillary muscle rupture[6] can also be treated by the transcatheter procedure, only if the residual MVA is sufficient. Furthermore, Asians have smaller hearts than Westerners, which makes the MitraClip procedure more challenging in respect of adequate residual MVA[7]. The presented case had a native MVA of 5.6 cm^2 and a residual MVA of 3.2 cm^2 after three clips. Even though multiple clips are usually required in Barlow's disease, the risk of small residual MVA is counterbalanced by the dilated annulus. However, surgical correction of Barlow's mitral insufficiency should be the first-line therapy since its long-term efficacy has been well documented[8].

Limitations

Although over 50% of the patients who have undergone MitraClip implantation have a persistent septal defect for more than six months[9], it was not usual to develop an interatrial right-to-left shunt after clipping. The right-to-left or bidirectional shunt may cause systemic hypoxaemia and warrant immediate closure[10,11]. The presence of the interatrial right-to-left shunt was related to the elevated right atrial pressure. In addition, a 12 mm AMPLATZER atrial septal defect occluder is usually suggested for the closure of an iatrogenic defect[12].

Conclusions

While surgical mitral repair is the default treatment for severe MR in patients with Barlow's disease, MitraClip implantation can be a viable alternative if patients are at prohibitive surgical risk.

Impact on daily practice

Patients with Barlow's mitral valve disease are considered unfavourable candidates for MitraClip procedures. Surgical correction of the complex anatomy is the gold standard in patients with Barlow's mitral insufficiency. However, MitraClip implantation can serve as a rescue therapy in critical Barlow's patients who carry a prohibitive surgical risk.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Moving image 1. Transoesophageal echocardiographic image of Barlow's mitral valve with severe mitral regurgitation.

The supplementary data are published online at: www.asiaintervention.org

AsiaIntervention 2019;5:68-69

Transoesophageal echocardiography-guided wire technique for crossing a stenosed aortic valve during transcatheter aortic valve replacement

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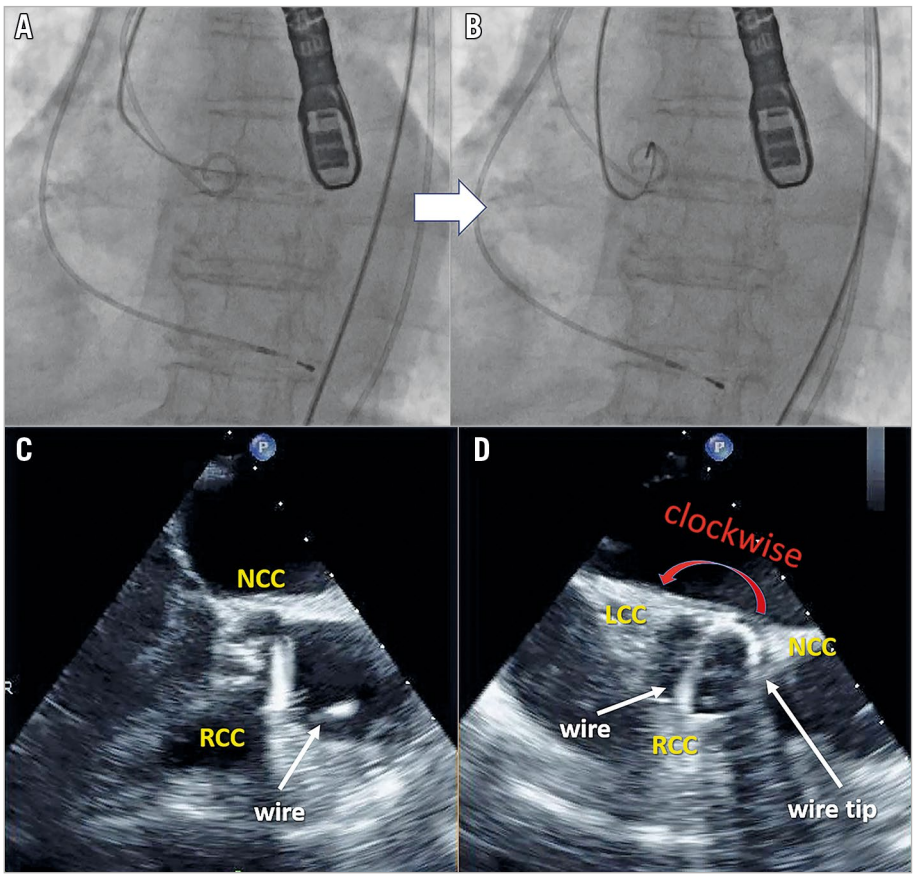
This paper also includes supplementary data published online at: www.asiaintervention.org



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A 90-year-old woman, with severe calcific aortic stenosis (maximum velocity 4.9 m/sec, mean pressure gradient 58 mmHg, and aortic valve area 0.43 cm^2), underwent transfemoral transcatheter aortic valve replacement (TAVR) using general anaesthesia and transoesophageal echocardiography (TOE), IE-33 (Philips Medical Systems, Andover, MA, USA) with an X7-2t matrix transducer, which can visualise the aortic valve (AV) simultaneously in the long and short axes[1]. We encountered difficulty crossing the stenosed AV with the tip of the catheter, which was slightly close to the AV **(Panel A, Panel B, Moving image 1**). The live X-plane mode of the TOE showed that the tip of the wire was located and trapped on the non-coronary cusp **(Panel C, Panel D, Moving image 2)**. Based on the echocardiologist's suggestion, the interventionist moved the wire clockwise and pulled the Judkins right catheter slightly, so that it could be relocated between the non-coronary and left coronary cusps, resulting in crossing of the wire.

This case shows the crossing of a TOE-guided wire in a stenosed AV during TAVR. We achieved crossing by running the wire between the non-coronary cusp and the left coronary cusp. Obtaining detailed assessment of wire location and direction is difficult using a fluoroscope only; frequent wire adjustment increases the risk of cerebral embolism substantially[2]. This simple and easy technique can decrease risk in patients, decrease radiation exposure and save time.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Moving image 1. Failure of wire crossing to the aortic valve under a fluoroscope.

Moving image 2. Failure of wire crossing to the aortic valve in live X-plane transoesophageal echocardiography mode.

The supplementary data are published online at: www.asiaintervention.org

AsiaIntervention 2019;5:70-71

Transcatheter aortic valve replacement through chronic ascending aortic dissection: efficacy of the distal flex system of the SAPIEN 3 transcatheter heart valve

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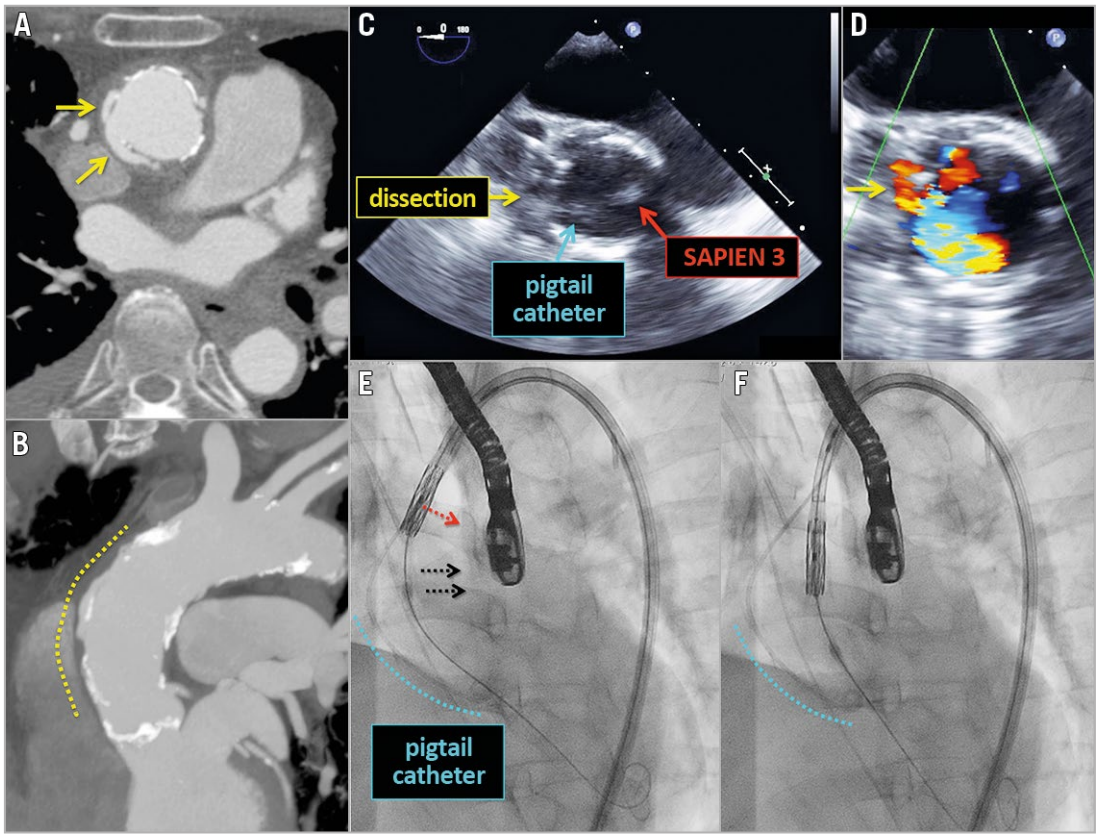
This paper also includes supplementary data published online at: www.asiaintervention.org



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An 80-year-old male with severe aortic stenosis was admitted in a state of congestive heart failure. The patient's medical history comprised myocardial infarction with a reduced left ventricular ejection fraction (EF 30%). Furthermore, computed tomography revealed a chronic aortic dissection (yellow arrows and dotted line) localised along the greater curvature of the ascending aorta **(Panel A-Panel D, Moving image 1)**.

We planned transfemoral transcatheter aortic valve replacement (TAVR) with a balloon-expandable bioprosthesis (SAPIEN 3; Edwards Lifesciences, Irvine, CA, USA) under general anaesthesia. We placed a pigtail catheter along the greater curvature of the ascending aorta as a guide to the chronic aortic dissection (blue arrows and dotted lines) **(Panel C, Panel E, Panel F)**. Next, we successfully crossed the valve system without touching the aortic dissection using the distal flex system of the valve (dotted red arrow) and tension of the stiff wire (dotted black arrows) **(Panel C-Panel F, Moving image 2-Moving image 4)**. While advancing the valve system, transoesophageal echocardiography facilitated monitoring of the position of the valve system and confirmed no extension of the chronic aortic dissection in the ascending aorta.

In this case, active distal flexion of the valve delivery system offered a unique advantage and allowed controlled tracking of the valve while avoiding contact with the dissection plane. Furthermore, this case highlights the benefit of transoesophageal echocardiography even in the era of the minimally invasive TAVR procedure.

Conflict of interest statement

T. Naganuma is a proctor for Edwards Lifesciences and Medtronic. The other authors have no conflicts of interest to declare.

Supplementary data

Moving image 1. Axial view of baseline computed tomography.

Moving image 2. Doppler transoesophageal echocardiography showing aortic dissection in the ascending aorta.

Moving image 3. Crossing the valve system through the chronic aortic dissection.

Moving image 4. Deploying the valve.

The supplementary data are published online at: www.asiaintervention.org

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Impact of preprocedural echocardiographic parameters on increased stroke volume after transcatheter aortic valve replacement

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KEYWORDS

- aortic stenosis
- TAVI
- transthoracic echocardiogram

Abstract

Aims: Increased stroke volume (SV) is a prognosticator of severe aortic stenosis (AS) after transcatheter aortic valve replacement (TAVR). This study aimed to investigate preprocedural echocardiographic predictors of increased SV after TAVR.

Methods and results: Clinical and echocardiographic data were retrospectively analysed in 129 patients with severe AS who underwent TAVR (2013-2015). We compared the echocardiographic data and cardiac events between the decreased SV group (n=28) and the increased SV group (n=101). Univariate and multivariate analyses were used to assess the predictors of increasing SV. AS severity significantly diminished, left and right ventricular function improved, and SV index (SVi) increased after TAVR: aortic valve area index (0.46±0.13 vs. 1.18±0.33 cm^2, p<0.001); aortic regurgitation (AR) grade (1.85±0.55 vs. 1.60±0.54, p<0.001); left ventricular ejection fraction (59.9±12.7 vs. 64.1±12.0%, p<0.001); right ventricular fractional area change (RVFAC) (48.8±11.9 vs. 53.3±14.0%, p<0.001); SV index (SVi) (46.7±11.0 vs. 52.8±12.0 ml/m^2, p<0.001). Kaplan-Meier survival estimates suggested that the SVi increase was associated with the decreased cardiovascular events one year after TAVR (hazard ratio 4.08, 95% confidence interval [CI]: 1.32-12.7, p=0.02). On multivariate analysis, preprocedural AR grade (odds ratio [OR] 7.00, 95% CI: 2.76-17.8, p<0.001) and preprocedural RVFAC (OR 1.05, 95% CI: 1.01-1.10, p=0.011) correlated with the SV increase.

Conclusions: Preprocedurally, greater AR and higher RVFAC could predict an increased SVi and thus the occurrence of fewer cardiac events. Preserved preprocedural RV systolic function is crucial for an increased SV after TAVR.

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Abbreviations

3D	three-dimensional
3D-RVEF	three-dimensional right ventricular ejection fraction
AR	aortic regurgitation
AS	aortic stenosis
CI	confidence interval
LVEDV	left ventricular end-diastolic volume
LVEF	left ventricular ejection fraction
LVESV	left ventricular end-systolic volume
LVOT	left ventricular outflow tract
MR	mitral regurgitation
OR	odds ratio
PVL	paravalvular leak
RVEDA	right ventricular end-diastolic area
RVESA	right ventricular end-systolic area
RVFAC	right ventricular fractional area change
RV S′	right ventricular S′
S'	pulsed Doppler peak velocity at the annulus
SV	stroke volume
TAVR	transcatheter aortic valve replacement
TR	tricuspid regurgitation
TTE	transthoracic echocardiography

Introduction

Cardiac output is strongly related to the symptoms and prognosis of patients with severe aortic stenosis (AS)[1]. Recently, several studies have shown the impact of stroke volume (SV) on the prognosis of AS patients following transcatheter aortic valve replacement (TAVR)[2,3]. Herrmann et al demonstrated that preprocedural low flow independently predicted mortality and was a more powerful predictor of outcome than left ventricular ejection fraction (LVEF) or the mean transaortic pressure gradient of patients following TAVR[4]. Anjan et al demonstrated that severe low flow at discharge was associated with an increased risk of mortality[2], and Le Ven et al showed that increased SV following TAVR resulted in better long-term outcomes among patients with preprocedural low-flow AS[3]. These studies suggest that increased SV is a prognostic predictor in patients following TAVR.

There are several possible mechanisms for increased SV following TAVR, including improved left and right heart function and less severe valvular regurgitation. However, there have been few investigations of the haemodynamic parameters related to increased SV following TAVR. We therefore investigated predictors of increased SV following TAVR, evaluating the preprocedural echocardiographic parameters.

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Methods

STUDY POPULATION

We retrospectively reviewed 140 consecutive patients who underwent TAVR from October 2013 to September 2015 in our institution. Among those patients, three did not have follow-up transthoracic echocardiography (TTE) records because they died during the acute phase after TAVR, and there was insufficient image quality for assessing right ventricular fractional area change (RVFAC) in eight, leaving 129 patients who were evaluated. The one-year (336.8±6.8 days) assessment after TAVR revealed that heart failure, ischaemic heart disease, arrhythmia requiring admission, and cardiac death comprised the cardiac events that had occurred during this period. Patient selection for TAVR conformed to a standard process that comprised clinical evaluation, multidetector computed tomography scanning, and echocardiography prior to when decisions about treatment were made by our multidisciplinary Heart Team. All patients received an Edwards SAPIEN XT valve (Edwards Lifesciences, Irvine, CA, USA). Data were retrieved from our computerised database, and clinical information was obtained retrospectively for all patients. The institutional review board of our institution approved the study.

COMPREHENSIVE TRANSTHORACIC ECHOCARDIOGRAPHY

Comprehensive TTE studies were performed at baseline (42.2±2.8 days before TAVR) and after TAVR (2.1±0.2 days). All TTE studies were obtained using a Philips iE33 ultrasonography system (Philips Medical Systems, Best, the Netherlands) and Vivid E9 or Vivid 7 ultrasonography system (GE Healthcare, Chicago, IL, USA). They were evaluated according to the guidelines of the American Society of Echocardiography[5].

Left ventricular end-diastolic volume (LVEDV) and left ventricular end-systolic volume (LVESV) were measured using the method of discs (modified Simpson's rule), and the LVEF was calculated. The stroke volume (SV) was calculated according to the guideline using pulsed-wave Doppler recording at the left ventricular outflow tract (LVOT)[5]. The aortic valve area was calculated using the continuity equation. The area of the right ventricle was measured by outlining the endocardial borders at end-diastole and end-systole in the apical four-chamber view. The RVFAC was calculated as follows:

$$[\text{RVEDA} - \text{RVESA}]/\text{RVEDA}$$

where RVEDA is the right ventricular end-diastolic area, and RVESA is the right ventricular end-systolic area. Mitral regurgitation (MR) severity was graded as none-to-mild, moderate, moderate-to-severe, or severe, based primarily on the jet area and vena contracta width of the MR jet[5]. Preprocedural aortic regurgitation (AR) severity was graded according to the same guideline based primarily on the jet width and vena contracta[5]. The post-procedural AR severity was graded according to the American Society of Echocardiography guideline[6] or other recommendations[7], based primarily on the circumferential extent of paravalvular regurgitation (PVL) and jet area evaluated on multiple TTE planes.

DEFINITION OF INCREASED/DECREASED SV AND CARDIOVASCULAR EVENTS ONE YEAR AFTER TAVR

The increase in SV was defined as the post-procedural SV/preprocedural SV >1. Otherwise, the SV was considered to have worsened. Cardiovascular events were assessed at the one-year follow-up visit following TAVR. Primary cardiovascular events were heart failure, ischaemic heart disease, or arrhythmia requiring admission, and cardiac death.

STATISTICAL ANALYSIS

Data are presented as numbers with percentages for categorical variables or as means±standard deviations (SD) for continuous variables. Categorical variables were compared with a χ^2 test or Fisher's exact test, as appropriate. Differences between groups were analysed by a paired or unpaired t-test in case of normal distribution or by the Wilcoxon or the Mann-Whitney U test, as appropriate, in case of non-normal distribution. Cumulative event rates were calculated using the Kaplan-Meier estimates for the increases and decreases in SV after TAVR. The log-rank test for time-to-event data at one year for cardiac events was used for statistical comparison. Multiple logistic regressions were used to identify factors associated with increased SV after TAVR. Variables with probability values <0.20 in individual analyses were included in the multivariate analysis. We analysed intra-observer and inter-observer reproducibility for preprocedural and post-procedural LVEF, RVFAC, and SV from TTE data in 15 randomly selected patients and expressed them using the Bland-Altman analysis. A two-sided value of $p<0.05$ was considered to indicate statistical significance. Statistical analyses were performed using SPSS, Version 21.0 software (IBM Corp., Armonk, NY, USA).

Results

BASELINE CHARACTERISTICS AND PREPROCEDURAL AND POST-PROCEDURAL ECHOCARDIOGRAPHIC MEASUREMENTS

The baseline data for the 129 patients are shown in **Table 1**. SAPIEN XT valve diameters during the study period were 20, 23, 26, and 29 mm. The echocardiographic changes are shown in **Table 2**. Despite no significant difference in the LVEDV and RVEDA, the LVESV and RVESA decreased following TAVR. As a result, the LVEF and RVFAC had improved postoperatively. AS severity, assessed by mean transaortic pressure gradient and aortic valve area index, diminished following TAVR. The AR grade improved in 46 patients (35.6%), did not change in 67 patients (51.9%), and worsened in 16 patients (12.4%). There were also three patients whose AR severity was moderate or greater after TAVR (2.3%). The MR and tricuspid regurgitation (TR) grades did not change significantly following TAVR **(Figure 1)**. Stroke volume index (SVi) increased significantly after TAVR.

BASELINE CHARACTERISTICS AND CARDIAC EVENTS OF INCREASED OR DECREASED SV PATIENTS AFTER TAVR

Overall, 12 patients had cardiac events (one cardiac death and 10 admissions for heart failure, one for sick sinus syndrome) during the observational period (336.8±6.8 days). There was no significant difference in the history of coronary artery disease (42.9% vs. 39.6%, p=0.76) or in the percentage of the transapical approach (10.7% vs. 11.9%, p=0.58) between patients with increased or decreased SV after TAVR. Kaplan-Meier survival estimates suggested that increased SV was associated with fewer cardiovascular events one year after TAVR (hazard ratio [HR] 4.08, 95% CI: 1.32-12.7, p=0.02) **(Figure 2)**.

PREPROCEDURAL AND POST-PROCEDURAL ECHOCARDIOGRAPHIC MEASUREMENTS

Table 3 shows preprocedural and post-procedural echocardiographic measurements. Patients with increased SV had greater RVFAC and AR severity than those with decreased SV before

Table 1. Baseline and procedural characteristics.

		All patients (n=129)
Age, years		84.4±4.6
Female gender, n (%)		91 (70.5)
Body surface area, m^2		1.41±0.17
Atrial fibrillation, n (%)		17 (13.2)
Coronary artery disease, n (%)		52 (40.3)
Hypertension, n (%)		90 (69.7)
Chronic renal failure, n (%)		68 (52.7)
Diabetes, n (%)		28 (21.7)
Chronic lung disease, n (%)		18 (14.0)
Pacemaker implantation, n (%)		7 (5.4)
Prior open surgery, n (%)		13 (10.0)
Transapical approach, n (%)		15 (11.6)
Prosthesis size	20 mm, n (%)	3 (2.3)
	23 mm, n (%)	91 (70.5)
	26 mm, n (%)	32 (24.8)
	29 mm, n (%)	3 (2.3)
Values are n (%) or mean±SD.		

Table 2. Preprocedural and post-procedural echocardiographic parameters of all patients undergoing TAVR (n=129).

		Pre	Post	*p*-value
LV	Ejection fraction, %	59.9±12.7	64.1±12.0	<0.001
	End-diastolic volume, mL	78.4±31.9	77.9±28.7	0.58
	End-systolic volume, mL	34.0±25.3	30.1±22.3	<0.001
RV	Fraction area change, %	48.8±11.9	53.3±14.0	<0.001
	End-diastolic area, cm^2	13.6±4.0	13.5±3.7	0.98
	End-systolic area, cm^2	7.1±3.2	6.4±3.0	0.01
Stroke volume index, mL/m^2		46.7±11.0	52.8±12.0	<0.001
Mean transaortic gradient, mmHg		48.1±16.3	10.4±5.3	<0.001
Aortic valve area index, cm^2/m^2		0.46±0.13	1.18±0.33	<0.001
Peak E velocity (cm/s)		82.2±35.7	96.8±3.6	<0.001
Deceleration time (cm/s)		284.7±110.8	261.3±7.9	0.01
E/e'		17.7±10.1	18.1±8.8	0.41
PA pressure (mmHg)		33.2±11.5	29.7±16.4	0.12
Values are n (%) or mean±SD. LV: left ventricle; PA: pulmonary artery; RV: right ventricle				

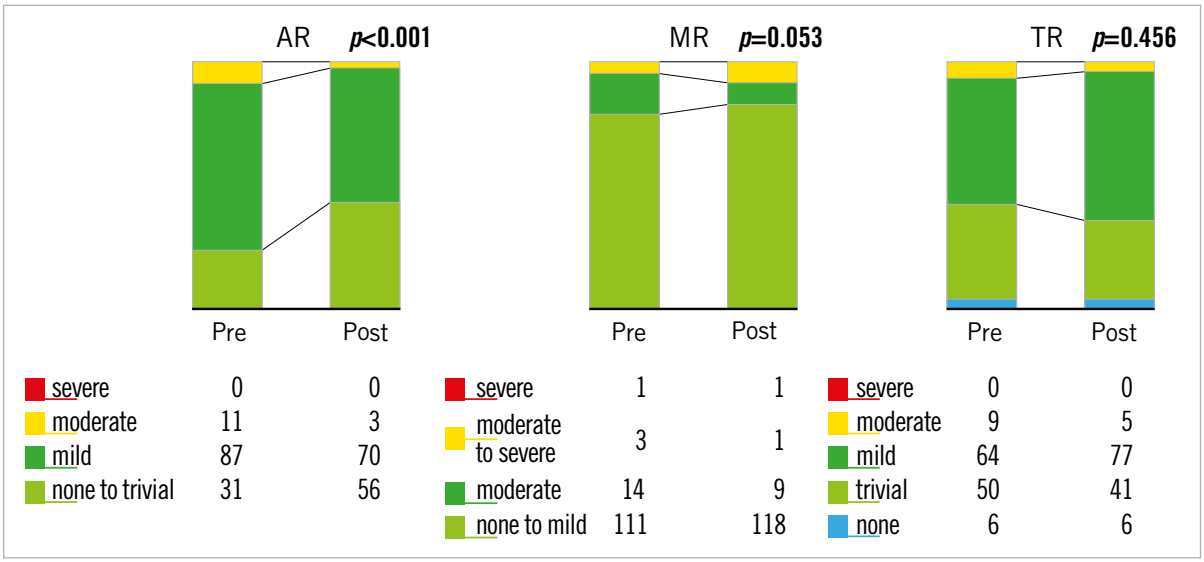

Figure 1. *Changes in valvular regurgitation following TAVR.*

TAVR. There was no significant difference in LVEF or the severity of MR or TR. The mean transaortic gradient decreased significantly after TAVR in both groups, whereas increased LVEF and RVFAC and less severe AR and MR were observed in patients with increased SV.

PREDICTORS OF IMPROVED SV AFTER TAVR

Results of univariate and multivariate analyses of preprocedural parameters of the severity of valvular diseases and LV or RV function on increased SV are shown in **Table 4**. In the univariate analysis, we selected a value of p<0.2 to indicate significance for the mean aortic pressure gradient (OR 1.02, 95% CI: 1.00-1.05, p=0.099), RVFAC (OR 1.04, 95% CI: 1.00-1.08, p=0.030), and AR grade (OR 5.868, 95% CI: 2.46-14.0, p<0.001). In the multivariate analysis, RVFAC (OR 1.05, 95% CI: 1.01-1.10, p=0.011) and AR grade (OR 7.00, 95% CI: 2.76-17.8, p<0.001) were found to be independent predictors of increased SV after TAVR.

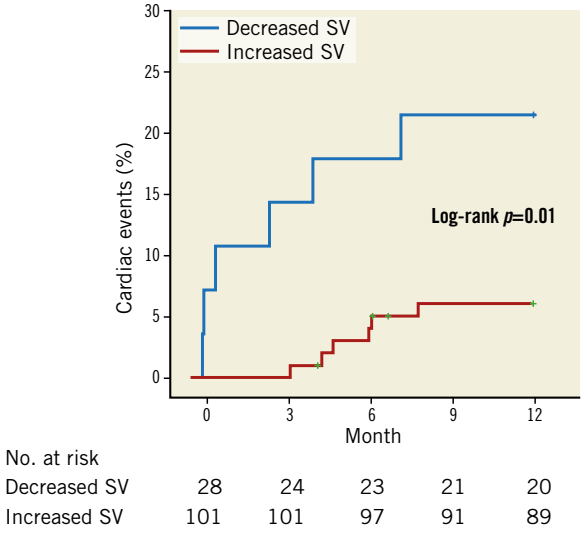

Figure 2. *Kaplan-Meier plots for cardiac events between decreased and increased SV. Increased SV was associated with decreased cardiovascular events one year after TAVI (HR 4.08; 95% CI: 1.32-12.7, p=0.02).*

INTRA-OBSERVER AND INTER-OBSERVER VARIABILITY

The intra-observer variability for the TTE measurements, which was demonstrated by the 95% CI of the Bland-Altman method, was as follows: preprocedural LVEF −2.6 to 1.9%, RVFAC −3.4 to 4.3%, SV −4.8 to 3.8 mL, and post-procedural LVEF −2.7 to 1.4%, RVFAC −2.8 to 1.7%, SV −5.6 to 4.3 mL. The inter-observer variability differences were as follows: preprocedural LVEF −2.8 to 1.9%, RVFAC −5.0 to 5.0%, SV −2.5 to 3.9 mL, and post-procedural LVEF −3.0 to 2.2%, RVFAC −2.5 to 3.4%, SV −3.0 to 3.6 mL.

Discussion

We showed that the increased SV afforded by TAVR led to a significant decrease in cardiac events, including cardiac death and readmission due to heart failure within one year. TAVR influenced haemodynamic parameters as follows: 1) the LVEF and RVFAC increased after TAVR due to the decrease in LVESV and the systolic RV area, and 2) the severity of AR, but not of MR, was significantly diminished following TAVR. In addition, the greater severity of AR and higher RVFAC before TAVR were correlated with the increased SV following TAVR.

Table 3. Preprocedural and post-procedural echocardiographic parameters of patients with decreased SV or increased SV following TAVR.

			Decreased SV (n=28)			Increased SV (n=101)			Pre-parameters comparison
			Pre	Post	*p*-value	Pre	Post	*p*-value	*p*-value*
LV	Ejection fraction, %		62.0±10.2	64.2±8.1	0.126	59.3±13.3	64.0±12.9	<0.001	0.54
	End-diastolic volume, mL		77.3±24.2	79.4±21.1	0.168	78.7±33.8	77.6±30.5	0.173	0.7
	End-systolic volume, mL		30.2±14.8	29.1±12.9	0.28	35.0±27.5	30.4±24.3	<0.001	0.95
RV	Fraction area change, %		44.4±12.0	44.3±13.9	0.924	50.0±11.6	55.8±13.0	<0.001	0.013
	End-diastolic area, cm^2		14.6±4.3	14.6±3.5	0.846	13.3±3.8	13.2±3.7	0.756	0.172
	End-systolic area, cm^2		8.2±3.4	8.2±3.0	1	6.8±3.0	6.0±2.8	0.001	0.008
Severity of valvular disease	Mean transaortic gradient, mmHg		43.5±16.0	9.4±2.9	<0.001	49.3±16.2	10.7±5.8	<0.001	0.06
	Aortic valve area index, cm^2/m^2		0.50±0.03	1.1±0.3	<0.001	0.45±0.12	1.2±0.3	<0.001	0.19
	Aortic regurgitation grade (average)	none to trivial, n (%)	16 (57.1)	5 (17.9)	0.05	15 (14.9)	61 (60.4)	<0.001	<0.001
		mild, n (%)	11 (39.2)	20 (71.4)		76 (75.2)	50 (49.5)		
		moderate, n (%)	1 (3.6)	3 (10.7)		10 (9.9)	0 (0)		
		severe, n (%)	0 (0)	0 (0)		0 (0)	0 (0)		
	Mitral regurgitation grade (average)	none to mild, n (%)	24 (85.7)	23 (82.1)	0.257	87 (86.1)	95 (94.1)	0.001	0.68
		moderate, n (%)	4 (14.3)	4 (14.3)		10 (9.9)	6 (5.9)		
		moderate to severe, n (%)	0 (0)	0 (0)		3 (3.0)	0 (0)		
		severe, n (%)	0 (0)	1 (3.6)		1 (1.0)	0 (0)		
	Tricuspid regurgitation grade (average)	none, n (%)	2 (7.1)	0 (0)	0.248	4 (4.0)	6 (5.9)	0.862	0.62
		trivial, n (%)	13 (46.4)	12 (42.9)		37 (36.6)	29 (28.7)		
		mild, n (%)	11 (39.3)	15 (53.6)		53 (52.4)	62 (61.4)		
		moderate, n (%)	2 (7.1)	1 (3.6)		7 (6.9)	4 (4.0)		
		severe, n (%)	0 (0)	0		0 (0)	0 (0)		
Stroke volume index, mL/m^2			50.5±11.9	45.9±10.4	0.001	45.6±10.5	54.6±11.8	<0.001	0.04
Peak E velocity (cm/s)			89.5±32.2	89.5±32.2	0.428	81.3±37.5	98.8±43.0	<0.001	0.3
Deceleration time (cm/s)			287.6±109.6	249.2±88.1	0.143	283.9±111.7	264.7±89.8	0.043	0.88
E/e'			17.2±8.7	14.2±5.8	0.068	17.9±10.5	19.1±9.2	0.095	0.94
PA pressure (mmHg)			31.0±9.4	29.6±16.7	0.971	33.8±11.9	29.8±16.4	0.083	0.67

Values are n (%) or mean±SD. *Comparison of pre-parameters between decreased SV group and increased SV group. LV: left ventricle; PA: pulmonary artery; RV: right ventricle

CLINICAL IMPLICATION OF THE INCREASED SV

As Anjan et al previously reported, not only preprocedural but also post-procedural low flow were predictors of a poor prognosis following TAVR[2]. Le Ven et al showed that six-month and one-year all-cause mortality of patients with normalised flow following TAVR was lower than that in those with persistent low flow regardless of their preprocedural SV[3]. These findings suggested that increased SV was the important beneficial effect of TAVR. SV tends to be calculated higher by the Doppler method at the LVOT compared with the Simpson method in the previous validation study[8]; our data were consistent with that report. We adopted SV calculated by the Doppler method as previously reported and demonstrated that patients with decreased SV had a higher risk of cardiac events than those with increased SV at the one-year follow-up after TAVR[2,3]. These results are consistent with previous studies **(Figure 2)**.

INFLUENCE OF THE SEVERITY OF VALVULAR DISEASE ON SV

Several studies have reported that paravalvular leak (PVL) has a negative impact on midterm and long-term prognosis following TAVR[9,10]. Consequently, preventing PVL is an important requirement for TAVR. We showed herein that the severity of AR was significantly reduced following TAVR in patients with

Table 4. Univariate and multivariate logistic regression analyses for estimating increasing SV (n=129).

	Univariate	Multivariate	
	p-value	OR [95% CI]	*p*-value
Mean aortic pressure gradient, mmHg	0.099	–	0.287
LV ejection fraction, %	0.322	–	–
RV fraction area change, %	0.03	1.05 [1.01-1.10]	0.011
Aortic regurgitation grade	<0.001	7.00 [2.76-17.8]	<0.001
Mitral regurgitation grade	0.665	–	–
Tricuspid regurgitation grade	0.278	–	–
E/e'	0.756	–	–

CI: confidence interval; OR: odds ratio; SV: stroke volume

increased SV but not in those with decreased SV **(Table 3)**. Furthermore, the improved AR grade correlated with the increase in SV in all patients. The multivariate analysis showed that more severe AR before TAVR was an independent predictor of the subsequent increase in SV, which is consistent with the results of a previous study[2]. Because the severity of post-TAVR AR was rated almost always "mild or less" (126/129) in our study, patients with significant AR prior to TAVR could have had a greater reduction of AR volume following TAVR, resulting in the significantly increased SV. These results suggest that the reduced AR volume, even if it was from mild to trivial, is an important therapeutic effect of TAVR in addition to expansion of a narrowed aortic valve area. Thus, sophisticated techniques designed to leave no PVL are required. We need more data to clarify the mechanism by which the reduced AR improved the SV index after TAVR.

Previous studies have reported that preprocedural significant MR predicted a poor prognosis after TAVR, and that following TAVR 38.0-77.7% of patients exhibited significantly diminished MR severity[11-14]. In the present study, however, the severity of MR did not change significantly and was not correlated with the improved SV after TAVR in any patients **(Figure 1, Table 4)**. These results indicate that the improved AR may have greater impact on the increase in SV than MR following TAVR.

INFLUENCE OF LEFT AND RIGHT VENTRICULAR FUNCTION ON SV

Several studies, including the PARTNER trial (Placement of Aortic Transcatheter Valves), showed that a preprocedural low ejection fraction was an independent predictor of a poor prognosis[9,15,16], whereas others reported that it was not[17-19]. Thus, the results of previous studies are controversial.

In our study, the reduction in LVESV led to increased LVEF after TAVR, and increased LVEF was observed in patients with increased SV. Preprocedural LVEF, however, was not an independent predictor of the increased SV following TAVR. The LVEF reflects the contractility of the left ventricle. It does not, however, accurately reflect the forward flow itself because of the influence of other haemodynamic factors. For instance, because aortic or mitral regurgitation (which fluctuates dynamically following TAVR) interferes with LVEF, preprocedural LVEF might not have independently predicted the increase in SV in the present study.

Several reports on RV function in patients following TAVR have described using parameters such as tricuspid annular plane systolic excursion, three-dimensional right ventricular (3D-RV) volume, RVFAC, right ventricular S′ (RV S′), TR severity, and pulmonary arterial systolic pressure. The effect of RV function on prognosis after TAVR, however, is not widely recognised[20,21]. The 3D right ventricular ejection fraction (3D-RVEF), measured by 3D transoesophageal echocardiography (3D-TEE) or magnetic resonance imaging, is a reliable parameter with respect to RV systolic function[22-24]. Lindsay et al reported that low 3D-RVEF was a predictor of poor prognosis in patients undergoing TAVR, but LVEF was not[21]. We adopted RVFAC – a conventional, accurate parameter of RV contraction in patients undergoing TAVR – to evaluate RV function[25,26]. RVFAC was significantly increased after TAVR in patients with increased SV but not in those with decreased SV. In addition, preprocedural RVFAC was significantly higher in patients with increased SV than in those with decreased SV, and the multivariate analysis showed that preprocedural RVFAC was an independent predictor of increased SV following TAVR. There were no significant differences in the other parameters that influence RVFAC, such as preprocedural LVEF, TR severity, and morbidity associated with chronic obstructive pulmonary disease between the two groups. Actually, preprocedural RVFAC independently predicted increasing SV; however, the odds ratio was low. The reason may be that RVFAC reflected forward flow less accurately compared with 3D-RVEF. Because RV function is composed of various factors – not only RVFAC but also RV strain, 3D-RVEF, RV S′, and RV myocardial performance index (MPI) – we need more analyses of these parameters in the future. Our results suggest that preserved preprocedural RV systolic function is important in TAVR patients because it affects their SV after TAVR.

Limitations

The study has limitations. The analyses were retrospective and observational. We were unable to measure all RV parameters, including the tricuspid annular plane systolic excursion or RV S′ in every patient. Of note, 3D-RVEF may be a more accurate parameter than RVFAC. In the present retrospective study, however, we could not accumulate an adequate number of cases with

3D-RVEF data. Therefore, we adopted RVFAC as the indicator of RV systolic function based on previous studies[24]. Because RV function is affected by LV function in general[11], LV dysfunction might have resulted in low RVFAC in our study. Therefore, additional analyses focused on the LV-RV interaction in patients undergoing TAVR are now ongoing. Moreover, although the results of 28 patients with decreased SV suggested that the decreased preprocedural RVFAC was a predictor of decreased SV after TAVR, this finding should be investigated further in a larger group of patients.

Conclusions

Increased SV is an important therapeutic effect of TAVR associated with fewer cardiovascular events. Preprocedural higher AR grade and RVFAC could predict an increased SV. According to these results, the reduced AR volume by sophisticated techniques designed to leave no PVL and preserved preprocedural RV systolic function are crucial for increased SV after TAVR.

Impact on daily practice

An increased stroke volume index improves the outcomes of aortic stenosis patients following transcatheter aortic valve replacement (TAVR), as shown in previous studies. The present study revealed that preprocedural aortic regurgitation and right ventricular function are correlated with the increase in stroke volume after TAVR.

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Conflict of interest statement

K. Shimizu and K. Hayashida are clinical proctors for Edwards Lifesciences. The other authors have no conflicts of interest to declare.

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Abstracts of

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ATHEROSCLEROSIS

CALCIFIED CORONARIES

CAROTID INTERVENTION

CONGENITAL HEART DISEASE

CHRONIC TOTAL OCCLUSION

DRUG-ELUTING BALLOON

ELECTROPHYSIOLOGY

IMAGING PHYSIOLOGY

IN-STENT RESTENOSIS

LEFT MAIN

MISCELLANEOUS

STENTS

STRUCTURAL

ATHEROSCLEROSIS

Coronary artery disease in HIV-infected patients – a study of clinical profile, presentation, angiographic characteristics and outcome

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Aims: as an increasing proportion of HIV-infected patients have access to antiretroviral therapy and achieve virologic suppression, the focus of clinical care is shifting from treating the infectious complications of advanced immunodeficiency to managing and preventing chronic diseases and non-infectious complication.

Methods and results: the present study is a single-center, retrospective study. All HIV positive patients who underwent coronary angiography and percutaneous coronary intervention between 1 Jan 2015- 31 Dec 2017. Patients were followed for a period of 11 months to 46 months (36 males and 4 female patients). 21 were first time diagnosed with HIV during admission. CD4+ count ranged from 192-1002 per cmm (mean- 421). Risk factor profile-chronic smoker-17 (including current and past), hypertensive – 8, chronic alcoholic – 8, diabetes – 5, dyslipidaemia- 19 patients. 24 patients presented with STEMI (14- AWMI and 10 IWMI), 10 patients with UA/NSTEMI, 6 with stable angina. 20 patients had Single vessel disease, 14 had double vessel disease and six had triple vessel disease. SYNTAX score: 33 patients had SS< 22, 7 had SS >22 (mean - 8 ±4). In all except 3 patients, standard PCI hardware which included workhorse PCI wire/balloon/Drug-eluting stent were required. In 98.4% of PCI procedures, TIMI III flow was achieved. No patient required re-intervention in a previously treated artery during the same hospital stay. No deaths and readmissions in any of the 40 patients during follow up.

Conclusions: HIV+ patients had, overall, a less amount of multi-vessel disease with mild CAD burden, and their lesions were, for the most part, non/mild calcified, of moderate length and mildly obstructive. HIV+ lesions were characterized by a lower degree of diameter stenosis, localized in more proximal coronary segments. Proximal LAD is the most common lesion site. Despite their observed low-risk angiographic lesion profile, HIV+ patients were more likely to present with STEMI.

ATHEROSCLEROSIS

Retroviral positive patients (HIV) presenting with acute coronary syndrome – dilemma for coronary interventions: to do or not to do

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Aims: the current spectrum of HIV infections has dramatically shifted after the advent of effective antiretroviral therapy. Cardiovascular disease is an increasing cause of morbidity and mortality in HIV patients in the post-antiretroviral therapy era. The aim of our study was to study the clinical profile, angiographic profile of HIV infected patients presenting with ACS.

Methods and results: prospective observational study conducted from January 2013 to September 2018 with 109 consecutive patients infected with HIV and presenting with ACS. The baseline clinical characteristics, response to fibrinolytic therapy, angiographic findings, and results of PCI and in hospital outcome were studied. Mean age of patients was 46 years which is lower than HIV uninfected patients. Most patients presented with AWMI (n=98, 89%). Thrombolysis was successful in 96 (78.33%) and failed in 13 (21.67%) patients. Four patients underwent rescue angioplasty and primary PCI was done in 3 patients. CAG was done in all the patients revealing significant residual stenosis in 51 patients. Three-vessel coronary artery diseases were seen in 4 patients (3.7%), Two vessels coronary artery disease was seen in 16 patients (14.7%). 69 patients (81.6%) had significant single vessel lesion. All patients with significant residual lesions (n=51) underwent PCI with DES.

Conclusions: HIV-associated atherosclerosis and its complications are a significant human health burden for which the pathogenesis remains elusive. HIV infected patients hospitalized for an ACS is relatively younger. Anterior wall STEMI is the most common presentation hence LAD is the most common culprit vessel.

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ATHEROSCLEROSIS

Major adverse cardiovascular events comparison between accepted versus denied invasive coronary evaluation in NSTEMI patients

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Aims: review of importance of early coronary angiography with revascularization of significant coronary artery disease to reduce major cardiovascular adverse events (MACE).

Methods and results: N=4772 divided in groups. The early group received angiography within 3 hours (Group-A) 28%, a delayed group received angiography 12 to 48 hours (Group-B) 36% and third group was denied for angiography (Group-C) 34% due to different reasons after NSTEMI. Primary endpoint at 30 days and at 6 months. All groups had similar baseline characteristics, such as history of MI, Hypertension, Diabetes, and aspirin and P2Y12-ADP use. Angiography was done within 1.5 hour in the early group and at 19.5 hours in the delayed group. PCI was performed on 57% of the study population, 10 % underwent CABG and 33 % received medical therapy. The MACE rate was 3.6% in the early group, 12.8% in the delayed and 29.3% in the denied group. Rates of recurrent ischemic events were 3.2% for the early group, 11.5% for the delayed group and 19.4 % for the denied group during hospitalization, and 5.0%, 17.4% & 28,6% at 30 days and 5.0%, 17.4% & 28,6% at 6 months. Rates of cardiovascular death were 0.8% for the early group, 1.5% for the delayed group and 7.2 % for the denied group during hospitalization, and 1.5%, 3.4% & 13.6% at 30 days and 3.0%, 7.1% & 21.4% at 6 months.

Conclusions: study revealed fourfold lower rate of MACE in the early group compared to delayed group and tenfold lower rate of MACE compared to denied group. The positive effect of early revascularisation in early diagnosed patients was beneficial to reduce rate of recurrent ischemia and death.

ATHEROSCLEROSIS

Awareness on Risk Factors of Cardiovascular Disease among Patients with Diabetes Mellitus Attending Diabetic Clinic of BP Koirala Institute of Health Sciences

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Aims: to assess the awareness on risk factors of CVD among patients with diabetes mellitus attending diabetic clinic of BPKIHS and to find the association between awareness with their selected socio demographic variables.

Methods and results: a descriptive cross sectional study was conducted among 112 patients with diabetes in diabetic clinic of BPKIHS. Convenient sampling technique was used for data collection over duration of one month using interview schedule by HDFQ II tool. Data were analysed by using descriptive and inferential statistics. The mean age of respondents was 55.4±12.13 years. That mean HDFQ score was 14.31± 5.08. Only 33% of the respondents had adequate level of awareness whereas majority of the respondents (67%) had inadequate level of awareness. Majority of respondent (83.9%) were aware about smoking, (78.6%) physical activity, (75%) increasing age, (75.9%) high blood pressure, (71.4%) overweight respectively. Whereas most of the respondents were not aware about high cholesterol, fatty diet, preventive strategies and association of diabetes with CVD. Awareness was statistically significant with (p=0.043) educational status, (p=0.025) monthly income, (p=0.05) residence, (p=0.006) CVD information received and (p=0.022) co morbid condition as a heart disease.

Conclusions: most of the respondents had inadequate level of awareness on risk factors of CVD. So effective education and appropriate preventive strategies of CVD are indeed important to reduce CVD burden in diabetes patients.

ATHEROSCLEROSIS

Clinical outcome of women with Coronary Artery Disease (CAD) requiring revascularisation at Tertiary Care Hospital in South India

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Aims: CAD remains the leading cause of death in women. There is no consensus or guidelines specific to management of CAD in women. Real world data regarding clinical outcomes in women among different treatment strategies is lacking.

Methods and results: retrospective and prospective observational study. A total of 202 female patients requiring revascularisation (>70% stenosis on CAG) underwent PCI or CABG or opted for medical management were included. All patients were evaluated in terms of MI, death, TVR, Stroke and MACE for a min. period of 2 years extending up to 5 years. The mean age of study population is 63.73±9.31 years with mean follow up of 32.25 months. In High SYNTAX score, the mean event free survival is 9.5 months in medical management, 11.6 months in PCI group and 11.742 months in CABG group at end of 1 year. There is lower event free survival in medical management group compared to PCI and CABG in High Syntax score at 1 year and it is statistically significant (p-value −0.002). In High SYNTAX score, the mean event free survival is 14.803 months in medical management, 21.20 months in PCI group and 20.294 months in CABG group at end of 2 year. There is lower event free survival in medical management group compared to PCI and CABG group in High Syntax score at 2 year and it is statistically significant (p-value −0.001). There is significantly higher MACE in medical management group compared to PCI and CABG in high syntax score at 1 and 2 years.

Conclusions: the mean event free survival is less in medical treatment arm compared to PCI vs CABG group in High Syntax score at 1 and 2 years. In low syntax score the mean event free survival was lower in CABG group but the number of patients in CABG group was small. Patients with high syntax score on medical management have higher mortality and MACE. We also conclude patients with ACS managed medically had higher mortality compared to revascularisation group.

CALCIFIED CORONARIES

A Single-centre study evaluating the real-life usage of Excimer laser-facilitated angioplasty in complex coronary lesions: procedural success and medium-term outcome

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Aims: ELCA has been recently used for the treatment of complex coronary lesions. The aim of this study was to evaluate the indications and outcome of this approach on patients with complex coronary lesions at a single centre.

Methods and results: we evaluated the indications and clinical outcome of patients who were treated with ELCA at University Hospital of Wales, Cardiff, between May 2011 and August 2018. A total of 62 patients were treated with ELCA catheter 0.9 – 2.0 mm in diameter, with a maximum fluence of 80 mJ/mm^2 and a maximum repetition rate of 80 Hz. The mean age was 68.8±11.1 years. Fifty-four (87%) were male. Of the 62 patients, 27 (43.5%) were treated for compliance modification, 13 (20.9%) for ISR, 14 (22.5%) for thrombus vaporization, 5 (8.0%) for plaque debulking, 1 (1.6%) for under-deployed stent and 2 (3.2%) for treating stent recoil. A 0.9 and 1.7 mm-diameter ELCA catheters were used most frequently (33.8%), followed by 1.4 mm-diameter catheter (24.1%). RCA (37.0%) and LAD (35.4%) were the most frequently treated vessels, followed by SVG (17.7%), LCx (8.0%) and intermediate (1.6%). The technical success was achieved in 87.0%, procedural success in 82.2%. Mean follow-up was 543.6±720.3 and median 195 days.

Conclusions: this study suggests that laser-facilitated coronary angioplasty is a safe and effective device for the management of complex coronary lesions associated with good technical and procedural success.

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CAROTID INTERVENTION

Carotid Artery Stenting – Single-centre experience, results and long-term follow-up

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Aims: be it symptomatic or asymptomatic patients the role of CAS for carotid artery disease is well established. Indian data on the outcomes of these procedures is limited.

Methods and results: 116 patients underwent CAS from 2000 to 2017. Stenosis quantification was done using North American Symptomatic Carotid Endarterectomy Trial (NASCET) method. The mean follow-up period for the patients is 4.5 years. Out of 116 patients, 36 were asymptomatic, 50 had motor weakness, 8 had LOC, 9 had Amaurosis, 6 giddiness, 5 dysarthria and 2 had headache. Embolic protection device (EPD) were used in 41 (35.3%) patients and no significant difference was found when compared to those without EPD (p=0.535). In 1st 30 days patient had 1 death (0.86%) and 2 major strokes. Long term follow-up (with 55% follow-up) revealed 14 deaths with 4 major strokes.

Conclusions: CAS is an effective treatment modality of symptomatic/asymptomatic carotid artery disease, but should be done carefully in high risk groups with cardiovascular disease (those planned for elective CABG).

CONGENITAL HEART DISEASE

Use of Atrial Septal Defect Occluders – Nine years follow-up

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Aims: this study presents the results of endovascular treatment of patients with ASD or PFO, in a cardiovascular unit of Paraná, Brazil.

Methods and results: 50 patients were analysed, in a prospective study, between May 2009 and December 2018. Patients with no atrial rim or from the National Health Service, were excluded. Mean age was 42.12±18.23 years, 27 (54%) were female, 31 had PFO (62%) and 19 ASD (38%). Occlusion (PFO group), was indicated on those who had transient ischemic attacks, unknown cause migraines and positive transoperative bobble test. Procedures were performed under general anaesthesia or sedation, with transoesophageal echocardiographic monitoring. Immediate results showed no intercurrences, no signs of embolism or neurological deficits. No deaths occurred and all maintained NYHA class I. Mean times were: hospitalization 2.00±1.44 (2-10), preoperative 0.56±0.62 days and postoperative was 2.00±1.15 days. Patients had double antiplatelet therapy with clopidogrel 75mg/day, for six months, and aspirin 100mg/day indefinitely. Patients continue to be monitored annually with a control echocardiogram, with a mean of 2.87±2.49 years of total follow-up, the longest follow-up being nine and a half years and the shortest of four and a half months.

Conclusions: in selected patients, the use of the percutaneous technique for occlusion of ASD and PFO presents low rate of complications, less trauma and shorter post-procedure recovery time, with results similar to surgical results, with a good cost-benefit ratio.

CONGENITAL HEART DISEASE

Clinical profile of patients of atrial septal defect device closure with special reference to short & intermediate term complications

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Aims: to study the clinical profile of patients with ostium secundum ASD undergoing trans-catheter device closure and complications related to ASD device closure procedure with special reference to short and intermediate term outcomes.

Methods and results: prospective observational study of 184 patients with ostium secundum ASD undergoing device closure and followed up till end of study or death whichever occurred first. All the patients were discharge and had follow up at 15-30 days (short) and 3 to 12 months (intermediate). Amplatzer (ASO) was used in majority of patient (90.7%) followed by Life Tech cera (9.3%). The most common device (waist) size was 22mm in Amplatzer and 28mm in Life tech cera. Out of 184 patients who underwent procedure, there were four procedure failures (2.17%) and 180 procedure success (97.83%). Out of 184 patients, 167 (90.76%) underwent uncomplicated procedures, 11 (5.97%) had major complications, one patient had post-procedure death (0.54%) whereas 5 (2.7%) patients had minor complications (including vascular access site complications). On regular short and intermediate-term follow-up, symptoms of 69 patients (38.12%) resolved at short term, while that of 92 (50.82%) patients resolved at intermediate term. However, symptoms persisted in 20 patients (10.9%) at the end of 1-year follow-up. At end of 1 year, all patients having pre-procedure abnormal ECG and CXR findings in subsets with moderate and multiple defects showed normal ECG and CXR. Also, 21% of patients with large defects had persistent ECG abnormalities and 16% of patients with large defects had persistent CXR abnormalities at 1 year. In present study residual shunt was noted in 34% patients, which resolved in 100% at the end of 6 months. Post procedure persistent PAH was noted in 21 (11.48%) patients while PAH regressed in nearly 15 (8%) patients.

Conclusions: transcatheter ASD closure is highly successful not only in small children but in patients of all age groups despite associated morbidities as patients of all ages experience reduction in PA pressure and an improvement in functional capacity after transcatheter device closure of ASD and these improvements appear to be greater if the defect is closed earlier. Given the low rate of complications and virtual lack of mortality, isolated secundum ASDs which are larger than 5 mm should be considered for percutaneous device closure regardless of symptoms or patient age. Amplatzer device appears to be best available option at the present time.

CONGENITAL HEART DISEASE

Successful percutaneous balloon dilatation of supravalvular aortic membrane in a 10-year-old male

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Aims: supravalvular aortic stenosis is the least common type of left ventricular outflow tract obstruction. Three anatomical types have been described – hourglass, hypoplastic, and membranous obstruction. Of these, the hourglass is the most common and membranous the rarest.

Methods and results: 10-year-old male admitted with effort intolerance since 3 years. A harsh, loud V/VI grade systolic murmur was heard in right first and second intercostal space radiating to right carotid more than left carotid artery. Transthoracic echocardiography showed left ventricular hypertrophy, a membrane was noted at the sinotubular junction. Peak gradient was 106 mmHg. Cardiac catheterization showed systolic left ventricular pressure of 236 mmHg. The aortic systolic pressure was 106 mmHg. Gradient across the membrane was 130 mmHg. The position of the membrane was confirmed on Left ventriculogram. TYSHAK 16 mm×40 mm balloon was used based on the measurement of aortic annulus. After inflation, LV systolic pressure reduced to 130 mmHg and systolic aortic pressure was 116 mmHg with gradient reduced to 14 mmHg from 130 mmHg. The procedure was uneventful. The patient was discharged after 2 days. Patient is asymptomatic on subsequent follow-ups.

Conclusions: balloon dilatation may be an alternative to surgery in selected patients with supravalvular stenosis. Excellent results are obtained in the membranous type of supravalvular stenosis, possibly related to the tearing of the membrane by the balloon. It provides good immediate results. Follow-up of successfully dilated patients shows sustained relief of stenosis.

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CONGENITAL HEART DISEASE

Transcatheter device closure of patients with Outlet Ventricular Septal Defects – Defining the anatomy and feasibility of closure based on intermediate follow-up

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Aims: to report midterm follow up of transcatheter device closure in outlet VSDs in a tertiary cardiac centre from September 2011 to February 2018, thus defining the anatomy and methodology of closure of these difficult VSDs

Methods and results: a retrospective observational cohort study was conducted which included all children with outlet VSDs who underwent device closure between September 2011 to February 2018. Outlet VSDs were categorized into three subgroups: subarterial, outlet muscular [intracristal] and subpulmonary. Patients underwent device closure using ADO/ADO II based on the size of defect and type of outlet VSDs. All patients underwent follow up at predefined time intervals. 29 patients were enrolled into the study cohort. This included 14 subarterial, 12 outlet muscular VSDs [intracristal] and 3 subpulmonary. Median age was 8 years (7m-30years) and median weight was 19.5 kg (6.5kg -81kg). ADO II device was used in 26 (90%) of these patients and ADO I was used for 3 (10%) of them. One child developed device embolization (3%) which required surgical intervention whereas two patients developed mild AR (6%) which got resolved for one patient on follow-up and one patient had ventricular bigeminy which was controlled medically. Procedure success rate was 27/29 (93%) as per prior defined criteria for success and follow up was obtained for all except one patient. Four patients (14%) had trivial shunt on follow up. 9 patients (31%) had trivial AR pre-procedure which did not worsen on follow up. New onset trivial AR was seen in one child with subarterial VSD (3%).

Conclusions: transcatheter device closure of outlet VSDs is difficult but possible procedure with reasonably good success rate. The ADO I/ADO II device can be used as per size and location of the VSD with few peri and post procedural complications. Further studies with larger populations are needed to establish device closure option for outlet VSDs as a reliable one.

CHRONIC TOTAL OCCLUSION

Percutaneous Coronary Intervention Provided Better Results Than Optimal Medical Therapy in Patients with Chronic Total Occlusion: Meta-analysis of Published Data

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Aims: this study aims to conduct a meta-analysis of published data of observational as well as randomized studies comparing long term outcomes of PCI+OMT versus OMT alone.

Methods and results: the present protocol is registered in PROSPERO. PubMed, Embase and Cochrane databases were systematically reviewed. Fourteen studies meeting criteria were included in the meta-analysis. The Cochrane Risk of Bias scale was used to appraise the overall quality of the studies. Revman 5.3 software was used to analyse the data and random-effects model with inverse variance method was undertaken. Baseline parameters of both the groups were comparable. Major adverse cardiovascular events (MACE) which comprises of cardiac death, myocardial infarction, stroke, unplanned revascularization and heart failure [Figure 1] were significantly lower in the PCI+OMT group. (OR:0.74; 95% CI:0.55 to 0.98; p=0.03; I^2=84%). All-cause mortality and cardiac death [Figure 2, 3 respectively] were significantly lower in the PCI+OMT group (p<0.00001 in both). Myocardial infarction (p=0.25) and stroke rates (p=0.15) were lower in the PCI+OMT group, however they did not reach statistical significance. Unplanned revascularization (of any vessel) showed a higher trend in the PCI+OMT group, without reaching statistical significance (p=0.46, I^2=88%).

Conclusions: PCI of CTO is rewarded with better long term outcome, in terms of MACE and all-cause mortality but limited to greater unplanned revascularisation.

CHRONIC TOTAL OCCLUSION

Complex CTO interventions in retroviral positive patients: challenges and dilemmas

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Aims: to assess clinical profile and risk factors associated with coronary chronic total occlusions in retro viral positive patients.

Methods and results: prospective and observational study of total of 6 consecutive patients who were reported as having retroviral positive with CTO between august 2014 and June 2018 were evaluated. Detailed clinical profile and coronary angiography of all patients were evaluated. All 6 patients underwent revascularisation with percutaneous coronary intervention. Mean age of the patients are 42.667 years, mean duration of HIV was 3.433 years. Mean duration of angina was 7.833 months, 4 patients had 100% LAD occlusion, and 2 patients were 100% RCA occlusion. Out of 6 patients, 2 had PCI to LAD, 2 had PCI to RCA, and 1 patient each had PCI to LMCA to LAD, LCX and LMCA to LAD. Average size of the stent was 3x32mm. Procedural success rate was achieved in 100% of cases.

Conclusions: risk of coronary CTO lesions is high in HIV infected patients and is seen to occur at much younger age compared to general population and seems to occur during the initial phase of the natural course of HIV infection. PCI is an adequate and safe treatment strategy of coronary revascularisation in HIV patients with CTO.

CHRONIC TOTAL OCCLUSION

Balloon-assisted guidewire crossing technique in Coronary total occlusion – Safe and cost-effective technique

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Aims: crossing guidewire in patients with coronary total occlusion is confronted with number of challenges. We describe an innovative yet cost-effective method for crossing the totally occluded artery.

Methods and results: twenty symptomatic patients (chronic stable angina and ACS) having total occlusion of >1 month duration (majority) were included in the study. Initially the totally occluded lesion was chased with multiple CTO guidewires but when failed to cross, uninflated, semi-compliant, low profile balloon were used as a support to cross the totally occluded segment. Mean age of the patients were 51.1 years. Two third of patients were males, 5 patients had diabetes, 8 were hypertensive. Majority(n=14) of patients had SVD and 3 patients had TVD. Ten patients had LAD lesion, RCA in 7 patients, LCx in 2 patients. One patient had occlusion of both LCx and RCA. Balloon assisted guidewire crossing technique was successful in majority (14 out of 20 patients). 13 out of 20 patients had totally occluded segment for more than one month and one patient had duration more than seven month. Mean fluoroscopy time required to cross the lesion was < five minutes. There were no periprocedural dissections/perforations.

Conclusions: balloon assisted technique is safe and cost-effective method for crossing the totally occluded coronary lesions with significantly less fluoroscopic time and peri-procedural events.

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CHRONIC TOTAL OCCLUSION

Percutaneous intervention for chronic total occlusion in resource limited settings

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Aims: we report here overall procedural results and clinical outcome of 199 consecutive CTO intervention performed since June 2014 till December 2017.

Methods and results: we performed retrospective analysis of the data collected for all 199 CTO interventions performed at our centre. The interventions were performed with significant financial limitations. Mean age of 199 patients undergoing CTO intervention was 59±10 years. CTO was present in left anterior descending (LAD) artery in 89 (44%), left circumflex (Lcx) in 27 (14%) and right coronary artery (RCA) in 83 (42%). Overall the J-CTO score of the lesion was 0 in 43 (20.4%), 1 in 81 (38.4%), 2 in 56 (26.5%) and 3 in 19 (9%). Overall success in antegrade crossing, balloon dilation and stenting the CTO segment was achieved in 157 (78.9%) of lesions. Success rate differed significantly (p= 0.00) between the different J-CTO scores of lesion (95.2% with score 0, 91.3% with score 1, 58.2% with score 2, and 44.4% with score 3). The success rate did not differ significantly (p=0.58) between CTO intervention of the three arteries. Significant rise in ejection fraction by 4% (p=0.01) after successful CTO intervention, limited to patients having successful outcome in LAD artery. The average number of guide wire and balloon used were 2.26±0.63 and 2.27±0.86 respectively. With an average length of CTO segment to be 21.4±8.6 mm, average length of stent used was 46±20 mm. Average number of stents used per lesion were 1.3±0.7. To determine the clinical outcome, these patients were followed up over a mean duration of 16±11 months. TLR and TVR rate at 1 year was 8% and 11% respectively. Overall survival at 1 year was 78%. Major procedural adverse events (pericardial effusion, cardiac tamponade, femoral hematoma, ventricular tachycardia, precipitation of angina) occurred in 12 (6%) of patients and one patient died during the procedure because of cardiac tamponade.

Conclusions: we describe here a fair success rate and good clinical outcome in patients undergoing intervention for CTO even in significant resource constraints.

INDIA LIVE 2019 MUMBAI

DRUG-ELUTING BALLOON

Safety and Efficacy of Sirolimus Coated Balloon in Treatment of Small Vessel Disease

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Aims: stenting of small coronary vessels with reference diameter of ≤ 2.75 mm is always complex. Drug coated balloon is one of the alternative to treat the small vessels. We evaluated the safety and efficacy of MagicTouch (Concept Medical) – Sirolimus coated balloon in *de novo* small vessels sub population.

Methods and results: NANOLUTE is a prospective, all comers, real world population registry which enrolled 450 patients. Out of 450 patients, 197 patients had small vessel disease. The main endpoint of this registry was MACE rate which includes Cardiac death, TV- MI, and TLR/TVR at 1 year. 2 year clinical outcome was assessed to evaluate the performance of MagicTouch for the longer duration. 205 lesions were treated in 197 patients and more than 80% patients among them were male. 30.2% lesions were present in left anterior descending followed by 21.0% in diagonal. 93.4% patients were treated with DCB only while 6.6% patients required additional therapy. At 1 year, 100% clinical follow-up was achieved and MACE rate was recorded as 3.5% with 2.5% TLR/TVR and 0.5% cardiac death. No TV-MI was reported at 1 year. 89.3% patients completed the clinical follow-up at 2 years and clinical follow-up is still ongoing for the remaining patients. MACE rate was found to be 3.9% with 2.8% TLR/TVR and 1.1% cardiac death.

Conclusions: long term clinical follow-up shows low MACE rates hence reflecting the safety and efficacy of MagicTouch SCB in complex small vessel disease.

DRUG-ELUTING BALLOON

Safety and Efficacy of Sirolimus-Eluting Stent in Diabetic Patients compared to Non-Diabetic Patients: Data from en-ABL e-registry

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Aims: the aim of this registry is to assess the long term outcome of ABLUMINUS Sirolimus eluting stent (Envision Scientific) in patient with diabetes. ABLUMINUS DES has unique fusion coating which addresses the complexity of the lesion in diabetic patients.

Methods and results: en-ABL e-registry was all comers, real world population study. Total 2,500 patients. Primary endpoint was MACE rate which comprises of Cardiac Death, TV-MI and TLR at 1 year. Secondary endpoint was total ST and MACE rate up to 2 years. Out of 2,500 patients, 859 patients were diabetics. Demographic characteristics were almost same for both diabetic and non-diabetic cohorts. At 1 year, 96.5% and 96.6% patients in diabetic and non-diabetic cohorts completed the follow-up respectively and incidence of MACE was 2.9% in DM group versus 2.0% in non-DM group (p=0.152). Total ST was 0.8% vs 0.4% (p=0.260) at 1 year respectively. At 2 years, MACE rate for DM and non-DM cohorts was 3.5% vs. 2.3% (p=0.119) respectively and ST was 1.0% vs 0.5% (p=0.263) respectively. There was no significant difference observed between DM and non-DM cohorts and follow-up of remaining patients is still on-going.

Conclusions: in diabetic real world population, ABLUMINUS DES was associated with lower MACE rate and low ST hence proves similar safety and effectiveness in diabetic patients compared to non-diabetics.

DRUG-ELUTING BALLOON

Long-Term Performance of Novel Sirolimus Drug-Eluting Stent in Real-World Population

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Aims: the objective of this study is to capture the long term clinical outcome of ABLUMINUS DES which has unique fusion coating which coats stent as well as exposed part of the balloon to assess its safety and efficacy in complex real world population.

Methods and results: en-ABL e-registry was multicentre, all comers, real world registry. Total, 2,500 patients. Primary endpoint was major adverse cardiac events at 1 year [MACE: cardiac death, TV-MI, and TLR/TVR]. Secondary end-point were the Stent Thrombosis (ST) & MACE rate up to 2 years. Mean age of the population was 57.0 ± 12.6 years and 78.9% were men. 78.6% patients had cardiovascular risk factors (34.3% diabetes mellitus, 42.2% hypertension and 2.0% renal failure). 2,969 lesions were treated with 3,287 number of devices. 14.8% patients had 2-vessel disease while 1.9% and 0.4% patients had 3-vessel and 4-vessel disease respectively. Clinical follow-up of 96.6% and 81.3% patients at 1 year and 2 years was achieved respectively. Follow-up for the remaining patients is still on-going. Analysis have revealed a MACE rate of 2.3% and 2.8% at 1 year and 2 years respectively while ST rates were 0.6% and 0.7% respectively.

Conclusions: this result suggest a well maintained safety and efficacy profile of ABLUMINUS DES when used in routine clinical practice.

DRUG-ELUTING BALLOON

Long-Term Safety and Efficacy of Sirolimus Coated Balloon in Real-World Population from NANOLUTE Registry

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Aims: Magictouch – Sirolimus coated balloon (Concept Medical) is a novel approach to treat atherosclerotic plaques. We evaluated the safety and effectiveness of this device in real world complex population.

Methods and results: NANOLUTE is a prospective, multicentre registry with a total of 450 patients. The main endpoint was MACE rate which includes Cardiac death, TV-MI, TLR/TVR at 1 year. MACE rate at 2 and 3 years was also calculated to assess the performance of the device in longer duration. Mean age of the population was (60.08 ± 10.08 years) with more than 80% were men. 211 patients had in-stent restenosis out of which, 169 patients had drug eluting stent restenosis. 197 patients had *de novo* small vessel disease with vessel diameter ≤ 2.75 mm. 448 (99.6%) patients had completed the clinical follow-up at 1 year. The observed MACE rate was 3.8% constituting 0.4% Cardiac Death, 0.2% TV-MI, and 3.1% TLR/TVR. At 2 and 3 years, clinical follow-up of 396 (88.0%) patients and 337 (74.9%) patients were achieved respectively and the incidences of MACE were 4.5% and 5.3% respectively. MACE rate in ISR subgroup at 1 year was recorded as 4.8% while MACE rate in *de novo* small vessel disease was 3.6%. Clinical follow-up of remaining patients is still on going.

Conclusions: lower MACE rate in overall population as well as in subgroups shows that MagicTouch SCB is promising alternative to treat the coronary disease.

ELECTROPHYSIOLOGY

Early experience in use of point of care basic ultrasound for emergency temporary pacemaker insertion

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Aims: in haemodynamically unstable patients with bradycardia it is proven that a prompt insertion of TPM is lifesaving until the definitive treatment is available. We propose a modified technique of insertion which is ultrasound guided and avoids the inherent complexities of the blind techniques.

Methods and results: 10 consecutive patients with haemodynamically unstable bradyarrhythmia recruited. Right femoral vein access ensured with 6FR sheath. Length of TPM lead from inguinal canal to umbilicus and then to angle of Louis marked. TPM inserted with curve facing upwards. Flat ultrasound probe of portable ECHO utilised to follow the TPM lead in inferior vena cava up to right atrium. Clockwise turn and a push used to place it at right ventricle. Confirmation can be achieved with an ECHO probe. RV ectopics will be an indirect clue. All 10 cases were successfully completed utilising the above technique. Subsequent fluoroscopy confirmed 8 leads to be in right ventricle and 5/8 to be exactly in RV apex. 2 cases were paced at right atrium. Procedure time on average was 7minutes and no perforation/complications noted.

Conclusions: as the skills set of using abdominal quick scan is prevalent in most of medical centres due to frequent assessment in dengue patients we believe IVC scan guided TPM insertion can be achieved in most of the critical care centres. It would be a more scientific and trustworthy way of TPM insertion.

ELECTROPHYSIOLOGY

Incidence of venous thrombosis in post pacemaker implantation

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Aims: to evaluate incidence of venous thrombosis in patients with post pacemaker implantation

Methods and results: all consecutive adult patient's scheduled for an implantation of their first pacemaker PM or ICD and without contraindication for venography were eligible for study. Total 50 patients were enrolled Intravenous contrast venography was performed at baseline (i.e. at the time of discharge, then 1 month & at the end of 1 year) on all 50 patients in order to access patency after PM implantation. Mean age was 66.8 (+/- 12.3) years, males (60.7 %). Mean procedure duration was 1 hour and 13 minutes. Longer procedures in patients implanted with a biventricular PM compared to other device types (mean 183 vs. 66 minutes, p<0.001), and longer in patients receiving multiple as opposed to a single lead (mean 81 vs. 59 minutes, p=0.003). Majority (42, 84 %) of the devices were implanted on the left side. Intravenous contrast venography was abnormal in 5 patients among them 2 patients have total venous occlusion. During the first 4 weeks, significant acute complications of PM implantation developed in a total of 8 (3.7 %) of the 50 patients. These included 1 case (0.5%) of atrial lead dislodgement, 1 case (0.5 %) of pericardial effusion, 1 case (0.5 %) of pneumothorax, 3 (1.2 %) wound infection, and 2 (1%) hematoma treated conservatively.

Conclusions: this study shows that venous thrombosis is relatively common after maintenance as asymptomatic PM insertion, although chronically benign. Early detection of subclinical venous thrombosis in asymptomatic patient leads to early treatment and improve outcome in future. Totally occluded veins may hamper future upgrading or replacement of pacing system. Venous complication seems difficult to prognosticate as firm predictors were not identified from wide range of parameter analysed. Decrease number of leads and decrease in size of leads will reduce chances of removal thrombosis.

ELECTROPHYSIOLOGY

Innovative techniques to stabilise LV lead in difficult coronary sinus anatomy – a single-centre experience

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Aims: to depict the various techniques deviced by the implanters to stabilize the LV lead while implanting in a difficult CS and its tributaries anatomy.

Methods and results: retrospective analysis of 132 CRT-P/CRT-D implanted at a single centre. A total of 17 procedure required innovative techniques. In 11 patients LV lead was stabilized by retaining the guidewire over which the LV lead was placed at the desired location. 2 patients require balloon dilation of the veins for placement of LV lead because of stenosis in the posterolateral or lateral vein. 2 patients required placement of stent into the posterolateral vein, through which the LV lead was negotiated. For 2 patients we had to place the stent besides the LV lead to stabilize the lead between the stent and the wall of vein. The measured LV threshold at the time of implantation was 1.1±0.7 V. The average impedance at the time of implantation was 840±240Ω. At an average follow-up of 24±11 months the average threshold have remained 1.6±1.0 V and the impedance to be 980±360Ω. 1 patient had macro dislodgement of LV lead 6 months after the initial procedure, completed with permanent stylet technique. He required re-implantation of LV lead by the right side as the left subclavian vein developed stenosis after the initial procedure. Another patient started developing alarm of high impedance after 1 year of implantation. He was found to have fracture of LV lead confirmed on fluoroscopy. He has been managed on medical management as the patient remained class I despite stopping of biventricular pacing.

Conclusions: in patients with difficult CS anatomy and unstable LV lead position we may have to use different innovative techniques to stabilize the LV lead. However, in some of these patients despite using these technique micro or macro dislodgement or lead fracture may be seen.

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ELECTROPHYSIOLOGY

Knowledge regarding Care of Patient with Pacemaker among Nurses Working at Selected Wards of BP Koirala Institute of Health Sciences

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Aims: the objectives of this study were to assess the knowledge regarding care of patient with pacemaker among the nurses working at selected wards of BPKIHS.

Methods and results: descriptive cross-sectional study design was used to conduct the study among the Nurses working at selected wards of BPKIHS. Total 69 subjects meeting the eligibility criteria were included in the study using total enumerative sampling technique. Data were collected using the questionnaire. The knowledge score of majority of the nurses were about natural pacemaker of heart (97%), function of pacemaker is to regulate heart rhythm (91%), pacemaker works as fast emergency treatment (82%), care of patient with pacemaker (77.53%), indication of pacemaker is complete heart block (69%) & dual chamber pacemaker (61.20%), evidence of infection and failure of pacemaker implantation (50.72%), discharge teaching of patient (70.53%). The mean score for the overall knowledge of the nurses was 67.6%. The knowledge with age & area of service of the nurses was associated significantly at 5% significance ($p<0.05$) i.e. nurses of >25 years of age & working in critical care unit had adequate knowledge ($p=0.001$) respectively.

Conclusions: the study concluded that nearly one fourth of the nurses had satisfactory knowledge regarding care of patients with pacemaker among nurses working at selected wards of BPKIHS. The socio demographic characteristics: age and working ward was only associated with the knowledge regarding care of patients with pacemaker among nurses working at selected wards of BPKIHS.

IMAGING PHYSIOLOGY

Utility of fractional flow reserve in moderate in-stent restenosis and jailed side branches and comparison of fractional flow reserve with SPECT-MPI in native coronary artery stenosis

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Aims: FFR demonstrated discrepancy between angiographic and functional significance of jailed side branches (JSB) as well as moderate In-stent restenosis, with only minority of such lesions having functional significance. An attempt was made to study utility of FFR in such scenarios and comparison of FFR with SPECT-MPI in native coronary artery stenosis.

Methods and results: total 101 lesions from 79 patients with stable ischemic coronary artery disease were subjected to FFR and SPCT-MPI including Native, ISR and Jailed side branches. Clinical follow up was performed for CCS class of angina and MACE events. Data was analysed using SSPS for significance. 101 lesions were studied [LAD 54/101(53.5%), LCx 22/101(21.8%), and RCA 25/101(24.7%)]. Native 78/101(77.2%), 11/101 (10.9%) ISR and 12/101(11.9%) were JSB. There was statistically significant negative correlation between summed difference score (SPECT- MPI) with FFR values. There was no statistically significant difference between FFR groups and MACE.

Conclusions: QCA/Operator visual interpretation is an inappropriate tool for assessing functional significance in native coronary stenosis as well as In-stent restenosis and Jailed side branches. FFR value of <0.75 or less can safely be considered for revascularization in such scenario. Although summed difference score in SPECT-MPI, which denotes myocardial reversibility extent correlates well with FFR, SPECT- MPI often tends to underestimates severity and extent of ischemia especially in multivessel CAD.

IMAGING PHYSIOLOGY

Impact of plaque burden and composition on coronary slow flow in ST-segment elevation myocardial infarction patients undergoing percutaneous coronary intervention: Intravascular ultrasound and virtual histology analysis

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Aims: coronary slow flow is an important complication of PCI with poor prognosis. The aim was to assess gray-scale IVUS and VH-IVUS features of culprit lesion in STEMI.

Methods and results: a total of 252 consecutive patients with STEMI underwent coronary angiogram and IVUS. Following PCI, divided into 2 groups; slow flow (TIMI flow ≤ 2, n = 61) and normal flow (TIMI flow > 2, n = 191). Coronary plaque and composition in relation to slow flow evaluated. On IVUS, plaque area (14.30 ± 9.80 mm^2 vs. 12.92±9.11 mm^2, p=0.047), plaque volume (121.38±41.28 mm^3 vs. 102.94±30.70 mm^3, p=0.001), lesion external elastic membrane cross-sectional area (15.77±4.70 mm^2 vs. 14.28±3.25 mm^2, p=0.038) and remodelling index (1.38±0.36 vs. 1.27±0.32 mm^2, p=0.035) were significantly higher in slow flow group. On VH- IVUS, absolute fibrous volume (52.48±21.55 mm^3 vs. 43.48±15.74 mm^3, p=0.002), necrotic core volume (12.42±6.50 mm^3 vs. 6.75±4.79 mm^3, p<0.001), dense calcium volume (1.94±2.46 mm^3 vs. 1.26±1.71 mm^3, p=0.016) and thin cap fibroatheroma single (31.10% vs. 16.80%, p=0.015) or multiple (4.90% vs. 0.5%, p=0.045) were higher in slow flow arm. In multivariable analysis absolute necrotic core volume (odds ratio=1.184; 95% CI 1.087 -1.288, p<0.001) was the only independent predictor of slow flow.

Conclusions: VH-IVUS derived absolute NC volume is closely associated with the coronary slow flow phenomenon in patients with STEMI after PCI.

IMAGING PHYSIOLOGY

Clinical Outcomes of patients with coronary artery disease who underwent FFR evaluation of intermediate coronary lesions – COFFRS study – 5-year follow-up

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Aims: we undertook this study to validate the impact of FFR guided coronary interventions among Indian patients on long term.

Methods and results: 282 patients with intermediate stenosis in their coronary arteries, who underwent FFR to assess the functional severity of the lesion. Divided into 3 groups: Group 1-FFR > 0.8- kept on medical follow up; Group 2–FFR ≤ 0.8 - underwent revascularisation and Group 3–FFR ≤ 0.8- refused for revascularisation. 277 (98.22%) patients had regular follow-up. Primary end point was MACE defined as composite of cardiovascular death, ACS and target vessel revascularisation.

Mean follow-up was 5.68 years, 230 were males. Mean age was 57 years (28–78). 84 patients were in Group 1, 176 in group 2 (PCI in 144 & CABG in 32) and 17 in group 3. 16 patients (19.04%) in Group 1; 19 patients (10.79%) in Group 2 and 5 patients (29.41%) in Group 3 had MACE. There was no difference in MACE in patients with FFR > 0.8 kept under medical therapy when compared with FFR ≤ 0.8 who underwent revascularisation (p=0.17). There was much higher rate of MACE in patients with FFR ≤ 0.8 and did not undergo revascularisation compared to those who underwent revascularisation (p<0.001).

Conclusions: FFR based revascularisation decision appears to be a safe strategy in Indian patients. However, it warrants revascularisation if FFR ≤ 0.8. This is the first Indian study to assess the impact of FFR based revascularisation on long term.

IMAGING PHYSIOLOGY

Comparison of Intravascular Ultrasound Virtual Histology parameters in Diabetes versus non-Diabetes with Acute Coronary Syndrome

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Aims: the progression and the pattern of coronary atherosclerosis in Diabetes Mellitus is different from non-DM, leading to higher rate of vascular complications in DM. This study aims to assess and compare the plaque characteristics in the culprit artery of DM and non-DM patients with ACS using VH-IVUS.

Methods and results: this was a prospective single-centre study carried out in a tertiary care institute in North India. A total of 158 patients of ACS were included, out of which 63 were known to have DM on the basis of ADA guidelines. IVUS analysis was done in the culprit vessel, for which percutaneous intervention was planned. The mean age of the study population was 52.4±11.6 years. No significant difference was observed in quantitative IVUS parameters like lesion length, luminal and vessel volume and plaque area. However, there was significant difference in VH-IVUS parameters like higher necrotic core and dense calcium in DM as compared to non-DM patients ($p<0.01$). Thin-cap fibroatheroma in the culprit vessel was significantly higher in DM group as compared to the non-DM group (63.5% vs. 5.2%; $p<0.01$). Positive remodelling was noted in both groups ($p=0.74$).

Conclusions: the DM patients had plaque composition features like higher necrotic core and calcium which are the markers of plaque vulnerability. Thus, aggressive medical therapy targeting vascular inflammation using high dose statins and angiotensin converting enzyme (ACE) inhibitors would help in stabilisation of unstable plaque morphology and decrease in major cardiovascular events.

IN-STENT RESTENOSIS

Safety and Efficacy of Sirolimus Coated Balloon in Coronary In-Stent Restenosis: Insights from NANOLUTE Registry

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Aims: in-stent restenosis (ISR) is one of the major risk associated with DES as well as in BMS. We investigated the safety and efficacy of MagicTouch (Concept Medicals) – Sirolimus coated balloon in patients with in-stent restenosis in coronary arteries.

Methods and results: NANOLUTE is a prospective, all comers, real world population registry. Total 450 patients were enrolled in the registry out of which, 211 patients had ISR. The main endpoint of this registry was MACE rate which includes Cardiac death, TV-MI, and TLR/TVR at 1 year. We also assessed MACE rate at 2 years and 3 years to investigate the device in longer duration. Average age of the population was 60.60 ± 9.58 years with 80.1% were male. 54.0% patients had diabetes and 51.7% patients had hypertension. 53.8% had focal ISR followed by 21.8% diffuse intra-stent ISR out of 225 lesions. Most of the patients had Drug eluting stent associated in-stent restenosis (80.1%). At 1 year, 99.1% (209/211) clinical follow-up was available and MACE rate was 4.8% with 4.3% TLR/TVR and 0.5% TV-MI. No cardiac death was reported at 1 year. MACE rate at 2 years was 6.1% with 5.0% TLR/TVR and 0.6% TV-MI in 85.8% patients. Only one cardiac death was reported at 2-years. At 3 years, 74.4% clinical follow-up was completed and MACE rate was 7.0% with 5.7% TLR/TVR.

Conclusions: lower MACE rates in longer duration proves the long term promising performance of Magictouch device in patients with coronary ISR.

IN-STENT RESTENOSIS

Determinants of DES-ISR and generation of a predictive model for in-stent restenosis following DES implantation. First model from Indian subcontinent

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Aims: despite major advances in coronary hardware, particularly the newer generation DES, in-stent restenosis (ISR) following stent implantation is considered the Achilles' heel in PCI treatment of CAD. We sought to study demographics and clinical outcomes of stent restenosis following PCI from our Institute.

Methods and results: patients who underwent PCI with DES between January 1 2009 and December 31, 2017 and returned with symptoms suggesting ISR were evaluated as per demographic parameters, functional status, comorbidities, and echocardiographic parameters, including LVEF, angiographic, and angioplasty details including type of stent and instituted medical therapy were collected at baseline, and at 9th month follow-up, and till last available. When patient returned for a second suspected ISR, they were similarly reevaluated. Using a split-sample validation technique (100 for Derivation cohort and 111 as Validation cohort), predictors of TLR due to ISR development were identified from approximately one-half of the subjects (derivation cohort) using multiple logistic regression. Integer point values were created for each predictor based on the OR of each variable, and the summed risk score (range, 0 to 20) was applied to the remaining sample (validation cohort). At 18 months, TLR occurred in 3.2% of patients, and after excluding stent thrombosis and early mechanical complications, the incidence of late TLR (most likely representing restenosis-related TLR) was taken into account.

Conclusions: a simple risk model incorporating readily available clinical and angiographic variables helps identify individuals at extremely low (< 1.5%) to markedly increased (> 9%) risk of TLR after DES implantation up to 1.5 years in a linear interestingly, controlling for the above factors, the type of DES (G1 DES V/S G2 DES) did not make a significant impact on future ISR probability. DES ISR presented as a new ACS in almost 3 5% of patients. Also, no relation of second ISR was seen with the use of same or hetero-DES after the first ISR episode.

IN-STENT RESTENOSIS

Long-Term Clinical Follow-up of Sirolimus Coated Balloon in Treatment of In-Stent Restenosis in Drug-Eluting Stent

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Aims: ISR remains a major problem in drug eluting stents. The aim of this registry is to evaluate the safety and efficacy of MagicTouch (Concept Medical) – Sirolimus coated balloon in patients with DES associated ISR.

Methods and results: NANOLUTE is a prospective, all comers and real world population registry - 450 patients. Out of 450 patients,169 patients with DES-ISR were analysed. The endpoint was MACE rate which comprised of CD, TV-MI and TLR/TVR at 1 year. MACE rate for 2 years was also compiled to assess the long term efficacy and safety of the device. Average age of the population was 59.8 ± 9.2 years with 77.5% were male. 53.8% were diabetics while 52.5% had hypertension. 46.2% lesions were present in left anterior descending followed by 28.0% in right coronary artery and 23.6% in left circumflex. 61.5% ISR were focal while 37.9% were of diffused pattern lesions. At 1 year, 98.8% patients completed the clinical follow-up and MACE rate was recorded as 4.8% with 4.2% TLR/TVR and 0.6% TV-MI. No cardiac death was reported at 1 year. 83.4% patients completed the clinical follow-up at 2 years with MACE rate of 6.4% [Cardiac death: 0.7%, TV-MI: 0.7% and TLR/TVR: 5.0%]. Clinical follow-up of the patients is still ongoing.

Conclusions: the clinical outcomes in the present study were very promising. Overall, the present data shows the beneficial effect and safety of Magictouch Sirolimus coated balloon in patients with DES-ISR.

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LEFT MAIN

Safety of unprotected Left main PCI: An observational analysis from large single-centre experience

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Aims: in patients with coronary artery disease, approximately 3-5 % have LM disease. Although trials have shown efficacy of unprotected left main percutaneous coronary intervention (uLMPCI), data from Indian subcontinent are lacking. Hence, we planned this observational analysis of single-centre uLMPCI data of last 3 years in tertiary care institute.

Methods and results: Retrospective observational study of clinical, risk factor, angiographic profile and long-term outcome after uLMPCI. 52 consecutive patients of uLMPCI between May 2015 and May 2018 were retrieved from a computerised database wherein detailed records were maintained. Clinical history, Risk factors, examinations findings and angiographic images were analysed. Data of patient of LM disease was categorized into LM alone (ostial, mid part, distal) and LM with single/multivessel disease. Patient counselling done and treatment options were explained in details as CABG, a standard treatment of choice. Written informed consent was taken. IVUS study was performed in 30 (58%) patients to confirm the lesion of LM before stenting. DES was used of revascularisation. Post stent IVUS study was done to check for residual lesion, dissection, flap and LCX ostium pinch. Mean age of the patients was 58 years. Men comprised 35 (67%) and females constituted 17 (33%) of the total. A total of 25 (48%) patients were diabetics. HTN was present in 23 (44%) and 18 (34.6%) were current smokers. The most common clinical presentation was stable angina in27 (52%), followed by unstable angina (USA) in 16 (30.7%). Non-ST elevation myocardial infarction (NSTEMI) was diagnosed in 7 (13.4%) at admission and 3 (5.7%) presented with ST elevation myocardial infarction (STEMI). mean hospital stay was 4.1 days. Out of 52 patient 1 (1.9%) patient died with cardiogenic shock post LM PTCA.

Conclusions: Unprotected left main percutaneous coronary intervention (uLMPCI) is safe and effective alternative to CABG for LM alone and LM plus single/multivessel disease.

MISCELLANEOUS

Spontaneous Coronary Artery Dissection In Women With Different Clinical Presentation, Risk Scenario And Coronary Angiographic Evaluation: Multicentric Analysis

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Aims: Analysed all myocardial infarction patients in Asia and collected data of SCAD through multi centric randomised observational study (From 2012 to 2017) with assessment of risk scenario and clinical presentation. We accessed invasive coronary evaluation with support of Intravascular ultrasound or OCT.

Methods and results: 181 cases of SCAD (1.8% of 9863 patients) were registered for SCAD Registry, mostly women n=146 (80.6%). 146 female patients of SCAD from different cardiac centres Age- 33 to 54 years, mean weight was 61+/-17.5 kg. We found STEMI patients 61% and NSTEMI (39%) with different symptoms like; chest pain 65%, palpitation 26%, shortness of breath 24%, sweating 19%, tiredness 16%, nausea 14%, dizziness 11%, syncope 6%. We categorized risk scenario of SCAD like; pregnancy (n=9) 6.1%, during delivery (n=8) 5.5%, post-delivery (n=7) 4.8%, menstrual periods 4.8%, fibromuscular dysplasia (n=14) 9.6%, accelerated hypertension (n=5) 3.4%, heavy exercise 6.1%, severe emotional stress 5.5%, tobacco (n=3) 2.05%, %, cocaine abuse 2.05%, cannabis (n=2) 1.36% , systemic lupus erythematosus 2.05%, Marfan syndrome 2.05%, Ehlers denlos syndrome 1.36%, polyarteritis nodosa 1.36%, ulcerative colitis 1.36%,Crohn's disease 1.36%, poly cystic kidney (n=1) 0.68%, endometriosis 0.68%, uterine fibroid 0.68% and hormonal therapy /contraceptives / Treatment for infertility (n=10)6.8 %. CAG revealed single vessel were often like: Left Main (n=16), LAD (n=77)-simple (n=59) & bifurcation (n=18), LCX (n=34)-simple (n=28) & bifurcation (n=6), RCA (n=19)-simple (n=17)-& bifurcation (n=2).

Conclusions: High rates of recurrent SCAD; its association with female sex, pregnancy, stress triggers; and concurrent systemic arteriopathies, particularly fibromuscular dysplasia. Research has increased awareness improved diagnostic capabilities and findings led to changes in approaches to initial and long-term management.

MISCELLANEOUS

Risk scoring system to predict contrast-induced nephropathy after PCI in Indian population – Validation

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Aims: we aimed to externally validate the new Risk scoring system to predict contrast induced nephropathy after PCI.

Methods and results: prospective, multi-centre study that consists of 1850 consecutive patients who underwent PCI from 2016 to 2018. CIN was defined as an increase of 25% and/or 0.5 mg/dl in serum creatinine at 48 hours after PCI when compared to baseline value. Patients with renal failure on regular dialysis, acute renal failure before PCI, cardiogenic shock, patients who were exposed to contrast media within 14 days, patients requiring IABP support and patients who developed PCI related complications were excluded from the study. The risk scoring system was then assessed in the study group. Patient's outcomes and need for renal replacement therapy were noted meticulously. Data were collected and analysed using SAS, 9.2 version. Discriminatory power was analysed by calculating the value of the area under the ROC curve. Calibration of the model was evaluated using the Hosmer-Lemeshow goodness of fit test. The mean (±SD) age was 55.3 (±10.2) years. 84% were males. Diabetes and hypertension were prevalent at 56% & 58%. The total incidence of CIN was 9.8% (n=181). The total risk of renal replacement therapy in the study group is 1.1% (n=21). Mortality is 0.5% (n=9). The risk score system had sensitivity of 92.3%, specificity was 82.1% and demonstrated excellent discriminative power (c – statistic = 0.91) in the study group. The Hosmer-Lemeshow 'p' value for the calibration of the score was significant at 0.001.

Conclusions: a simple risk scoring equation can be employed to predict the probability of CIN following PCI, applying it to each individual. More vigilant preventive measures can be applied to the high risk candidates.

STENTS

Short- and intermediate-term outcome of percutaneous coronary intervention in octogenarians

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Aims: the aim of the present study was to assess clinical characteristics, procedural details, and intermediate term outcomes in the patients older than 80 under-going PCI.

Methods and results: Single centre, randomised prospective study. Patients equal to or above the age of 80 years (Octogenarians) both male and female presented with symptoms and signs of ACS or chronic stable angina, and planned for PCI were included in the study. Parameters were assessed at baseline, pre-discharge and at 6 months post-procedure. MACE (Cardiac death, non-fatal MI, CVA, stent thrombosis, bleeding and target vessel revascularization) was taken as primary composite end point. Patients (n= 50) were divided into 2 groups: Group I (80–85 years, n=35, 70%) and Group II (≥85 years, n= 15, 30%). At baseline, overall presentation with STEMI, cardiogenic shock and heart failure were significantly more in Group II compared to Group I {53.33% GpII vs 31.42% GpI ($p<0.001$), 26.67% GpII vs 8.57% GpI ($p<0.001$), 80% GpII vs 45.71% GpI ($p<0.001$), respectively}. Incidence of double and triple vessel disease were more in Group II than in Group I {93.33% GpII vs 82.85% GpI ($p<0.001$)}. Procedural success was significantly decreased in Group II {94.28% GpI vs 86.67% in GpII ($p<0.001$)}. Bleeding complications significantly increased in Group II {46.67% GpII vs 20% GpI ($p<0.001$)}. On 6 monthly follow-up, the overall (n= 50) all-cause mortality was 24%, MI incidence 8% and TVR 6%. MACE were significantly increased in Group II {46.67% GpII vs 17.14% GpI ($p<0.001$)}.

Conclusions: PCI and stenting can be done in elderly patients (>80 years) with reasonably high success and acceptable complication rates. Within the group, the more elderly (>85 years) have higher risk profile, lesser success and higher complications and MACE.

STENTS

One-year clinical outcomes of ultrathin strut everolimus-eluting coronary stent system (50 µm) for treatment of patient with de novo coronary artery lesions

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Aims: Previous generation of DES had thicker struts and were associated with increase rate of stent thrombosis. Hence newer generation biodegradable DES with thinner strut are developed. The Evermine 50 EES-KLES study was designed to evaluate clinical safety and performance of Evermine 50 EES in "real-world" patients with *de novo* coronary artery lesions.

Methods and results: Retrospective, single-arm and observational study – 171 patients. The safety endpoint was the occurrence of MACE, a composite of cardiac death, any MI and ID-TLR 12 month follow-up. The performance endpoint was ID-TVR at 12 months follow-up. Among 171 patients (average age 57.85 ± 10.05 years), hypertension and diabetes mellitus were found in 69 (40.35%) and 70 (40.94%) patients, respectively. A total of 246 Evermine 50 EES were implanted to treat 258 *de novo* coronary lesions. DVD and TVD reported in 55(32.16%) and 16 (9.36%) patients. According to ACC/AHA lesion classification majority lesions were B1 (41.87%) and B2 (47.97%) followed by 14 (5.69%) C type. The cumulative MACE rate was observed 0.58% at 6-month and 1.81% at 12-month follow-up. Occurrence of ID-TLR was reported in one case. No MI and ST were identified at 6 and 12 months. No ID-TVR reported at 12-month follow-up.

Conclusions: The study revealed favourable clinical safety and performance of Evermine 50 as for treatment of *de novo* coronary artery lesions evident by lower MACE rate at 12-month follow-up.

STRUCTURAL

The Initial Experience of Transcutaneous Aortic Valve Implantation (TAVI) in a Brazilian Centre

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Aims: the present study presents the immediate and medium results of the initial experience in the treatment of high-risk patients with severe aortic valve stenosis.

Methods and results: prospective study, from December 2014/18, of 22 patients, with severe aortic stenosis referred for endovascular treatment, 16 submitted to PCI, 4 died before the procedure, and are in the waiting list. Mean age was 79±9.27 years, being 10 patients female (62.5%). One patient was in New York Heart Association (NYHA) functional class II (6.25%), 3 in III (18.75%) and 12 in IV (75.00%). Mean preoperative gradient was 71.16±17.72 mmHg and the mean logistic EuroScore was 17.98±12.15. 13 patients had a normal postoperative evolution (81.25%), in 2 cases a definitive pacemaker was implanted (12.5%), due to AVblock, and in one cardiac tamponade occurred (6.25%), that was drained. Mean postoperative hospitalization was 10 ± 15.97 days. 2 hospital deaths occurred (12.5%), on the 4th day due to metabolic disorder, and on the 64th day to pneumopathy. Mean postoperative gradient was 22,35±9,93. All patients were, NYHA class I, after 70 days. After 180 days, 9 were class I (81.82%) and 3 class II (18.18%).

Conclusions: patients with high surgical risk and/or with important comorbidities, TAVI is a viable option with an acceptable risk. The procedure should be performed before symptoms increase in an elective way.

STRUCTURAL

Balloon pulmonary angioplasty in chronic distal pulmonary thromboembolic disease and pulmonary hypertension

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Aims: this is the first study conducted in Indian patients, for evaluating the impact of BPA in patients with distal CTEPH.

Methods and results: total 11 CTEPH patients who underwent BPA and met our inclusion and exclusion criteria. Detail case record from containing information on demographics, clinical features and necessary blood and imaging investigations, V/Q scan, CT pulmonary angiogram, right heart catheterization study, pulmonary angiogram, BPA procedure details obtained for all our participants before BPA. Patients than assessed after, 8 weeks of last BPA session and evaluated for improvement in 6 minutes' walk distance (6mwd), RV function (TAPSE), PASP. Mean age of presentation: 39.81±12 years. Pulmonary angiography in all our patients revealed segmental and sub-segmental disease. 30 BPA sessions performed. Minimum BPA session underwent was 1 and maximum BPA sessions underwent by 1 patient was 5. 45% of patients underwent 2 BPA sessions. Total number of segmental arteries dilated was 104.segmental vessels dilated per each session was 3.46. 2 patients had developed mild breathing difficulty associated with blood streaky sputum during procedure but stabilised by non-invasive ventilation. There was statistically significant improvement in 6mwd after BPA. 6mwd increased from 299m to 421m (p value <0.001). This improvement in functional capacity is strongly associated with the improvement in RV function (TAPSE from 15.3mm to 18.9 mm) and with the reduction in PASP (from 92 mmHg to 60 mmHg).

Conclusions: in patients with CTEPH who undergo BPA there was statistically significant improvement in 6mwd. These changes correspond to a treatment induced reduction in pulmonary artery pressure and lend support to use of BPA in Indian patients with distal CTEPH 6mwd can be used for evaluating BPA efficacy and monitoring of disease progression.

STRUCTURAL

Immediate results, safety and efficacy of percutaneous transmitral commissurotomy (PTMC) in juvenile mitral stenosis

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Aims: although PTMC has become an established method of treatment for mitral stenosis (MS) in adults, reports of this technique in the younger age group are scarce. The study presents the tertiary care experience regarding PTMC in juvenile MS (JMS).

Methods and results: single centre retrospective observational study (January 2008 to January 2018). Pre and post procedure clinical, echocardiographic and intra procedural data was systematically analysed. Procedure was considered successful when post procedural mitral valve area increased by more than 50% and mean TMG fell by more than 50%. Total number of patients: 305. 79% patients were in NYHA class II and 20% patients were in class III and 1% was in class IV. All patients were in sinus rhythm except 7 of which 2 spontaneously reverted to SR after procedure. Mean pre PTMC mitral valve area by planimetry was 0.7 cm^2 and post PTMC area was 1.39 cm^2. Mean pre PTMC TMG was 25.13 and mean post PTMC was 5.26. Procedure was successful in most of the patients with procedural success rate of 99.39%. The most common complication was commissural MR. Total 7 patient developed post PTMC severe MR, of which 4 required immediate MVR and rest were managed medically. One patient developed severe pericardial effusion amounting to cardiac tamponade which was relieved with tapping & PTMC was performed successfully as staged procedure.

Conclusions: PTMC in JMS is efficacious and safe and should be considered as first line of treatment.

STRUCTURAL

Immediate maternal and foetal outcome of percutaneous balloon mitral valvuloplasty during pregnancy

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Aims: we studied immediate maternal and foetal outcomes of women undergoing balloon mitral valvuloplasty (BMV) during pregnancy.

Methods and results: retrospective single centre observational study of ten years duration. 163 pregnant patients with severe rheumatic mitral stenosis or restenosis underwent BMV using Inoue technique at tertiary care hospital in western India. Mean age of patients was 26.7 years + 5 years (range 19-45 years) with mean gestational age by USG scan was 26 weeks (range is 6 weeks to 38 weeks). Gestational age during intervention was: less than 20 weeks- 27 patients (16.8%), between 20-28 weeks -96 patients (59.6%) and >28 weeks- 38 patients (23.6%). NYHA status of the patient: class IV - 16 patients, Class III – 49 patients and class II-96 patients. Mean Wilkins score was 8.5 (range from 7 to 11). Inoue balloon size used during procedure was: 24 number in 27 patients, 26 number in 130 patient, 28 number in 6 patients. A detailed echocardiographic evaluation was performed before and after the procedure. Special shield was used during the procedure to limit radiation to the foetus. Obstetric Ultrasonography (USG) for foetal viability was done in all case before and after procedure. Immediate clinical, hemodynamic and echocardiography improvement was seen in 97.5% patients after valvuloplasty. The BMV procedure was successful in 151 patients (93.78%), partly successful in 6 patients (3.8%) and unsuccessful in 4 patients (2.4%). Mitral valve area increased from 0.8 cm^2 ±0.19 cm^2 to 1.4 cm^2 ± 0.23 cm^2 and transmitral peak gradient decreased from 27.33 mmHg + 9.9 to 14.13 + 5 and mean gradient decreased from 17.8 mmHg ± 7.8 to 7.9 mmHg + 3.5. Four patients (2.5%) developed significant commissural MR and managed conservatively, two patients (1.2%) complicated with rupture of anterior mitral leaflet and was sent for emergency mitral valve replacement. There was no immediate adverse foetal outcomes in the form of foetal distress, foetal hematoma or foetal death documented on obstetric USG.

Conclusions: BMV by the Inoue technique is feasible, safe, and effective during pregnancy. BMV provides good immediate results without significant maternal risk or foetal morbidity or mortality.

STRUCTURAL

Diagnostic accuracy of a novel “winking coronary angiographic sign” in patients presenting with ventricular septal rupture complicating acute myocardial infarction

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Aims: ventricular septal rupture (VSR) is an uncommon but potentially lethal complication of acute myocardial infarction (MI). Its prompt recognition is essential to permit timely institution of corrective measures. The present study was undertaken to assess the diagnostic accuracy of a novel and unique angiographic sign, the “winking coronary sign (WCS)”, for recognizing post-MI VSR. The WCS is defined as partial transient occlusion of the infarct-related culprit artery overlying the site of VSR during ventricular systole with near normal filling in the diastole.

Methods and results: a total of 56 patients with post-MI VSR (mean age 60.9 ± 9.9 years, 75% male) were compared with 73 age- and sex-matched acute MI patients without VSR. The extent of coronary artery disease was not different between the two groups, but higher number of patients in the VSR group had thrombolysis in MI grade 3 flow (57.1% vs 34.5%, p 0.01). The WCS was observed in 67.9% of the patients with VSR but in none of the patients without VSR ($p<0.0001$), yielding a sensitivity of 67.9% and specificity of 100% for this sign for diagnosing underlying VSR.

Conclusions: this demonstrates the potential utility of the WCS for diagnosing VSR in patients in whom the VSR has developed in the time frame between the echocardiography and angiography or has been missed during the initial clinical and/or echocardiographic evaluation.

STRUCTURAL

TAVR using the Hydra self-expanding bioprosthesis – A single-centre experience

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Aims: TAVR using Hydra self-expanding bioprosthesis.

Methods and results: 8 cases of TAVI with Hydra self-expandable valve from April 2017 to August 2018. 4 Females. Mean age: 77.1 years. Age range: 72-84 years. NYHA II (6), NYHA III (2). Pre TAVI PCI: 2. Previous BAV: 1. Mild CKD: 2 Dialysis dependent: Nil. COPD: 7, Neb dependent: 4, O2. Dependent: 0. Atrial fibrillation: 1. LV Dysfunction: 1 (30% > 45%). All cases were transfemoral, right side. GA with online TEE: 6. Conscious sedation with Preclose Proglide technique: 3. Temporary pacemaker: All patients RCFA (valve), LFA & LFV access. Standard heparinization after sheath insertion. 18 F Long (Cook) sheath. Predilated in 7 cases. Direct valve implantation in 2 cases. At 30 days: all were transfemoral, in calcific tricuspid aortic valves. Valve deployment was successful in all patients in first attempt (Hydra valve: 9). All were post dilated. CHB: 1; Transient for 3 hours; Recovered and doing well till date. PPI: Nil. New onset LBBB: 3, Maximum QRSD was 150 msec. Static on Holter follow up. Doing fine so far. Significant PVL: Nil. LV function normalized: 1. Mortality: 1.

Conclusions: TAVR is a unique procedure. Despite it is minimally invasive, it has high risk patient subset and hence, minimal reserve for errors.

STRUCTURAL

Thrombolysis is an Effective and Safe therapy In Stuck Mitral Valves with Delayed Presentation As Well As Haemodynamically Unstable patients – single-centre study in India

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Aims: study conducted in tertiary care cardiology unit to evaluate the effectiveness and safety of thrombolytic therapy in stuck mitral bi leaflet heart valves.

Methods and results: prospective observational study, fluoroscopy was the mainstay in diagnosis of stuck mitral valve. Gradient across the valve is used to monitor the therapy every 6 hourly. Fall of mean gradient more than 50% considered as successful thrombolysis. And final results were again checked by fluoroscopy with documentation of improved leaflet movement. Patients (34 total) receiving thrombolytic therapy with streptokinase achieved an overall 82.7% freedom from a repeat operation or major complications, a large subcutaneous hematoma occurred in one (2.9%), reoperation required in two (5.9%), allergic reaction in one (2.9%), one patient developed transient neurologic dysfunction (2.9%) and one patient died during therapy (2.9%). All patients including those with delayed presentation (>14 days) and hemodynamically unstable patients had good results similar to those who presented within 14 days and hemodynamically stable patients. Mortality is higher in unstable patients and reoperation higher with delayed presentation.

Conclusions: by comparing data from the main reports on thrombolytic therapy in stuck bileaflet mitral valves, it is evident that the outcome in this study ranks among the best reported in the current literature. In patients with stuck bileaflet mitral valves without large clots, thrombolysis offers a valid alternative to surgery with a high success rate and minimal complications. This therapy may be implemented in a wide variety of patients, regardless of symptom duration or severity, especially in centres where round the clock cardiothoracic surgery back up not available. Since recurrent episodes may be subclinical, frequent follow-up echocardiograms are advocated after a successful thrombolysis, and fluoroscopy should be liberally instituted to evaluate leaflet motion. Further studies are required to substantiate the encouraging results of our study and to establish the best thrombolytic regimens.

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STRUCTURAL

A comparative study of oversizing with underdilation vs. undersizing with full dilation using Accura-Balloon in BMV

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Aims: to compare oversizing with under dilation vs undersizing with full dilation using Accura-Balloon in BMV.

Methods and results: 178 patients, who underwent BMV from Jan 2012 to Jan 2018 were selected in non-randomised manner into 2 groups of Group A (n=107) (undersizing with full dilation) & Group B (n=71) (oversizing with under dilation). Reference size (RS) for balloon calculated using Hung's formula. Oversizing defined as use of balloon 1-2 mm larger than RS, similarly undersizing defined as 1-2 mm smaller than RS. Immediate and Intermediate outcomes of the two groups compared & results interpreted. The mean balloon size in Grp A was 25.3 ± 1.1 mm vs 26.4 ± 1.4 mm in Grp B and mean intraballoon pressure in Grp A was 276 ± 24 kpa vs 249 ± 19 kpa in Grp B (p=0.02). Post procedure change in MVA in Grp A (1.06 ± 0.14 cm^2) vs (0.87 ± 0.11 cm^2) in Grp B (p=0.04). MR worsening Grade II in Grp A vs Grp B (7.5% vs 15.5%) (p=0.014). Two patient in each group developed mitral restenosis (1.9% vs 2.8%).

Conclusions: We conclude that undersizing with full dilatation gave adequate mitral valve area without increasing incidence of significant mitral regurgitation.

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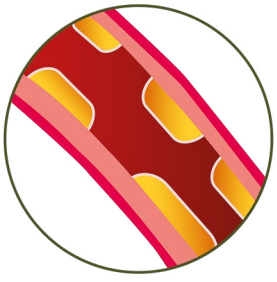

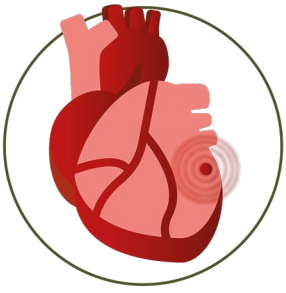

859 REAL-WORLD DIABETIC PATIENTS

2.9%	0.8%
MACE	ST

999 REAL-WORLD AMI PATIENTS

2.1%	1.1%
MACE	ST

829 (96.5%) & 944 (94.5%) no. of patients completed clinical follow-up till November 2018 in Diabetic and AMI sub-groups respectively.
The present study is still on-going hence follow-ups of rest of the patients are yet to come.

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