A selection of live cases were presented on Thursday afternoon at JIM, with Eberhard Grube, Georg Nickenig and Nikos Werner (University Hospital Bonn, Germany) joined by guest operators Paul Hsien-Li Kao (National Taiwan University Hospital, Taipei, Taiwan) and Marco Wainstein (Hospital de Clínicas de Porto Alegre, Brazil).

Retrograde PCI of LAD CTO
Dr Grube presented the session’s first case of a retrograde PCI of chronic total occlusion (CTO) of the left anterior descending (LAD) artery, in 51-year-old male patient with risk factors including arterial hypertension, hypercholeserolemia and smoking. Past medical history included previous two-vessel coronary artery disease (08/2017, primary PCI RCA (STEMI); 01/2018, retrograde PCI LAD CTO attempt)), ventricular fibrillation (09/2017, ICD implantation) and atrial fibrillation. The patient was presently admitted to hospital with angina pectoris CCS III, with J-CTO score of 3.

Angiography identified two-vessel coronary artery disease (CAD), consisting in LAD occlusion from the ostium on, with patent right coronary (RCA) after PCI last year, mildly impaired left ventricular function (ejection fraction 53%). Nuclear scan after physical exercise was positive.

The team decided on a procedural strategy of retrograde PCI of the LAD CTO. A bifemoral approach was adopted with 8 F guides going into the RCA and LCA. A 20-25 mm CTO was noted by Dr Kao, as well as disease presence distal to the CTO cap. The presence and viability of several septals was noted, although sepal passage was unsuccessful during previous retrograde PCI attempt.

A 150 cm FineCross micro catheter (Terumo, Japan) with Sion guidewire (Asahi Intecc, Japan) was positioned within a candidate septal vessel. The wire was advanced in the LAD, although the FineCross could not be advanced and so was replaced with a 135 cm Corsair pro (Asahi Intecc). Hence the septal channel was dilated sufficiently to then manoeuvre the FineCross across.

“You were using a FineCross at the beginning, so why not just use a Corsair Longline to do that rather than switching several times?” Panel member Dr Yeung asked.

“We had a discussion about this,” acknowledged Dr Kao. “Actually the pushability of a 150-cm Corsair is much worse than a 135-cm. If you were to use a 150-cm, maybe you would not pass. Turnpike [Vascular Solutions, MN, USA] is also a good choice. But FineCross is also cheaper in Taiwan!”

“There are going to be new and interesting microcatheters being developed,” added Dr Leon. “Boston Scientific [USA] has the Mamba, which people are starting to get some experience with. I think we are going to see major changes in micro-

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catheters over the next one to two years.

Back to the procedure at hand, Dr Kao discussed crossing approach: “For this kind of lesion wire crossing, either retrograde or antegrade, is very unlikely. So we are prepared to do a reverse-CART if we have to. Then we will focus on achieving regular wire crossing.”

From the JIM floor, session chair Martin B Leon commented: “Not every hospital has these expert CTO operators. This, I think, would have been a good case for LIMA [left internal mammary artery] to LAD. This would be an option if you didn’t have the ability to do it like this.”

On the retrograde active wire, a Gaia II (Asahi Intecc), Dr Leon commented: “This has become very popular for CTO operators as part of the armamentarium. It certainly began as an antegrade crossing wire but is now being used more and more retrogradely.”

Delegates took a short break to watch a segment from a different live case. Dr Kao then returned to describe highlights of the procedural strategy adopted in this case. The CTO’s proximal cap was hard, he said, demanding control of wire direction to prevent deflection into subintimal space. “This is why we wanted to use the Gaia II, which is more directional,” he said. “Even when we end up in the subintimal space, we can still correct its position.”

After wire penetration was achieved, and the retrograde system was removed, IVUS was carried out to assess procedural results: “I would always do IVUS for these ostial LADs just to see if you were true-to-true,” said Dr Leon.

“We want to know first of all our wire position,” added Dr Kao. “We want to know the distal landing zone. We want to know whether the LAD ostium has been touched or not.”

Describing the stenting procedure and sizing, Dr Kao said: “These days I just look at cross-sectional area. Drug-eluting stents are so good at inhibiting neointimal hyperplasia that you don’t really have to go for external elastic membrane (EM) to EM – that would be too stressful for the vessels.”

Dr Leon added: “That was a good choice. In
terms of sizing, everybody has their own tricks. And the reason why I think you need to use IVUS in these cases is that this is an LAD ostium of a 51-year-old. You have to have a result which is as good as a surgeon putting a mammary artery in. You have to be meticulous to make sure that the sizing and the location of the stent are correct. So I applaud your use of the IVUS.”

Transfemoral mitral VIV

Drs Nickenig and Werner presented a transfemoral mitral valve-in-valve (VIV) implantation in a 75-year-old male patient with past medical history including three-vessel CAD (now stable), paroxysmal atrial fibrillation (CHADS-VASc score of 3) and chronic kidney disease (eGFR 56 ml/min). Surgical history included surgical mitral valve replacement in 2010 (with 29-mm Carpentier-Edwards SAV bioprosthetic valve (Edwards Lifesciences, USA) of inner diameter 28 mm), and additional CABG surgery. The patient presented with dyspnea NYHA III.

The present procedure was carried out due to degeneration of the previously implanted mitral valve. The patient arrived with normal LVEF, but with severe mitral regurgitation due to a flail leaflet of bioprosthetic mitral valve. Coronary angiography indicated patent graft vessels. CT workup allowed measurement of valve dimensions and simulation of implantation, landing zone and left ventricular outflow tract (LVOT) obstruction risk. Importantly, neo-LVOT estimation suggesting that correct implantation should not significantly impair outflow.

The team opted for a transseptal transfemo-ral mitral VIV using a 29-mm Sapien 3 (Edwards Lifesciences). While 26 mm was an option, in this particular patient the team prioritised a maximised neo-LVOT area.

Dr Leon commented: “This is a very exciting case, with relatively early bioprosthesis dysfunction. This is a perfect case for a balloon-expandable transapical VIV. We have got more and more experience with these. We used to do them transapically, but we think the transseptal approach is better.”

Commenting in general on procedural planning in transseptal VIV, panel member Alan Yeung asked: “There is a question about all the angles – each patient is quite different because of issues like enlarged left atrium. We usually try to do a 3D print of the heart to help guide us as to where to do the transseptal puncture. Some cases go very smoothly, and in some cases you struggle and struggle because of the angles. Do you do any additional preparation to understand the anatomy between the septum and the mitral valve in the transseptal approach?”

Dr Nickenig replied: “It is extremely crucial if you don’t have a visible ring, for example, in implanting a valve-in-ring. Then you have to do a really extreme workup upfront with CT scans and so on. If you have a visible stent frame you can go with fluoroscopy, you have to have a plain view of the valve, and you have to have transoesophageal echo (TOE) guidance at the same time.

“Back to the angle, you don’t have the freedom to choose your angle. Sometimes the problem is that you cannot get superior enough because you are still in the muscular part of the atrial septum. That was also the case here.”

On the team’s wire and catheter choice, he continued: “You could use, for example, an IMA catheter. You could also use a steerable sheath, but this is usually not necessary. Right now we have a Confida [CoreValve, Medtronic, USA] wire sitting in the left ventricle.”

During valve placement, Dr Leon commented: “As you see it almost never is truly coaxial. As balloon expands it will begin to right itself. I don’t want to say ‘you have to guess’, but you have to be aware of valve shortening issues, so you have to be careful where you place it because of this. How much it is going to foreshorten is hard to say. These valves shorten from bottom to top.”

Following deployment, the team concluded by confirming positioning and haemodynamics with TOE and angiography. Dr Leon noted: “You can see that the Sapien 29 is a little bit indented, and that is because there is enough in the way of tissue that you don’t get full expansion. You actually look for indentation, which gives you reassurance that it is secure in its location.”

Dr Nickenig added: “If we didn’t have any indentation, I would be worried that it would embolise later on.”

Georg Nickenig
ACURATE and Lotus: A tale of two valves

Thursday’s TAVI 1 session welcomed a range of cutting-edge reports from invited experts, with a number of key technologies placed under the spotlight.

Lars Søndergaard (Righospitalet, Copenhagen, Denmark) stepped up to the podium to discuss the Lotus and ACURATE family of transcatheter aortic valves (Boston Scientific, USA), touching on their place in contemporary TAVI.

Speaking to JIM Today prior to his talk, Professor Søndergaard outlined the potential of both technologies.

How important is it to tailor a particular TAVI valve to patient, and what specific challenges is the Lotus valve hoping to address?

In a subset of patients undergoing TAVI, specific transcatheter heart valves may be related to better outcomes. One example is bicuspid aortic valves, which are often a challenge. Due to the anchoring on the leaflets, rather than annulus – as well as severe calcification – a high rate of paravalvular leakage, valve embolisation and conduction abnormalities are common.

However, the experience at many TAVI centres is that this can be overcome with the Lotus valve. Due to the controlled deployment, possibility for re-capturing the fully deployed valve prosthesis, and its adaptive sealing, Lotus valves have very similar procedural outcomes in bicuspid as in tricuspid aortic valves.

How does the newer Lotus Edge valve build on the technology?

The Lotus Edge adds several features to the previous Lotus platform. Firstly, the introducer sheath will be expandable with a profile of 14 or 15 F, which will allow more patients to undergo a transfemoral procedure. This is important, firstly because it has been shown that the transfemoral approach is related to better outcomes for the patient, as well as a shorter hospital stay. Secondly, the shaft of the delivery system is smaller, which makes the system more flexible, with improved safety when used in tortuous vessels.

Thirdly, the mechanical features of the valve deployment have been modified, and now include the Depth Guard. This means that the valve frame will extend less into the left ventricle outflow tract during deployment, and therefore potentially reduce the risk of conduction abnormalities and the need for permanent pacemaker. Fourthly, adding radiopaque markers to the locking system makes it easier to check for complete locking of the frame during deployment. Finally, two new valve sizes (21 mm and 29 mm) will be added to the portfolio, which will now cover all aortic annulus sizes.

Lotus Mantra takes this a step further, with a shorter design that should reduce pacemaker use?

That is correct. The current height of the Lotus valve frame will be reduced. This means that it will be possible to implant the prosthesis in a higher position without jeopardising the access to the coronary arteries. And since high-position prosthesis implantation is the key in reducing conduction disturbance, this new valve design may potential reduce pacemaker rate.

The ACURATE valve has now been incorporated into the Boston Scientific valvular family. What unique aspects or benefits does the technology bring to the fore?

The ACURATE valve is a different concept than Lotus. It is a self-expanding technology with supra-annular position of the leaflets. Furthermore, it is a simple two-step deployment and therefore an attractive valve prosthesis for many interventionalists.

What trials, either ongoing or upcoming, are important for Lotus (e.g. REPRISE III)?

REPRISE III is a global, prospective, multicentre, randomised controlled trial to compare safety and effectiveness with the Lotus valve (N=607) versus a self-expanding CoreValve (N=305; Medtronic) in patients at extreme or high surgical risk. The trial shows that Lotus is non-inferior to CoreValve with the 30-day primary composite safety endpoint of all-cause mortality, stroke, life-threatening/major bleeding, stage 2/3 AKI and major vascular complications.

Furthermore, Lotus is superior to CoreValve for the primary combined effectiveness endpoint of all-cause mortality, disabling stroke and moderate or greater paravalvular leak. So, REPRISE III confirms that Lotus is an attractive alternative to the ‘established’ TAVI systems on the market.

Similarly, what can you tell us about the ACURATE data?

The SAVI TF registry included 1,000 patients with severe aortic stenosis treated with ACURATE. Despite a mean age of 81 years and STS score of 6.0%, the 30-day mortality was only 1.4%, and disabling stroke rate 1.2%. Furthermore, the reported pacemaker rate of 8.3% and more than mild paravalvular leakage in 4.1% of the patients is among the best in class.

In your opinion, do you think the two valves will indeed build a new and promising chapter in TAVI?

I believe the Lotus and ACURATE platforms offer an attractive solution for most patients with aortic stenosis. This will be even better with the next generation devices such as Lotus Mantra and ACURATE with advanced sealing.

“I believe the Lotus and ACURATE platforms offer an attractive solution for most patients with aortic stenosis. This will be even better with the next generation devices.”

Lars Søndergaard
In defense of GPIs in high risk ACS

Alberto Menozzi (University of Parma, Italy) joined others to discuss the crossroads on antithrombotic therapy for patients treated with PCI yesterday at JIM 2018. Dr Menozzi argued that, in contrast to current guidelines, there remains a justification for the use of intravenous glycoprotein IIb/IIIa inhibitors (GPIs) in high thrombotic risk patients with acute coronary syndrome (ACS) despite the availability of potent oral antiplatelet agents and direct thrombin inhibitors.

GPIs were a key drug during the development of primary PCI in general during the 1990s. They confer a powerful antithrombotic effect, which is partially hampered by an increase in bleeding risk. Within the last decade, increasing concern for patients’ bleeding risk, coupled with increasing availability of new oral antiplatelet drugs targeting thrombosis pathways (e.g. ticagrelor and prasugrel), have led to a drop in the use of GPIs.

“We have progressively seen a reduction in the use of GPIs, and a rapid downgrade of the indication by guidelines,” said Dr Menozzi in conversation with JIM Today. “In the latest ST-elevated myocardial infarction (STEMI) guidelines of 2017, they have a class 2A indication only in cases of bailout – so in cases of no flow or thrombotic complications.”

However, despite the progressive downgrade by guidelines, the use of GPIs remain quite common in clinical practice in the setting of primary PCI, as shown in registry data.

“My position is different on this topic,” continued Dr Menozzi. “I only partially agree with the view of guidelines. I believe that in high thrombotic-risk patients with ACS, particularly in the setting of STEMI, the need for intravenous antiplatelet agents is still present. I believe that, if GPIs are used in a modern manner, which means strongly limiting the bleeding risk associated with these drugs, not in the manner of 10 to 15 years ago, GPIs can guarantee better clinical outcomes for the patients at high thrombotic risk.”

Picking apart the current recommendation of GPI use in PCI bailout, Dr Menozzi highlighted that the value of GPIs is lowered after the complication has occurred, compared to its value as prophylaxis. “I am convinced you should still use GPIs in a provisional manner, not for every patient but for selected patients,” he said. “In those selected patients, you have to use these drugs very early in the procedure, to prevent thrombotic complications.

“You read in guidelines that GPIs should be considered for bailout, but there is no specific study about bailout. So, the use of GPIs in bail-out situations is just common sense – when you have a disaster, you try to recover it.”

A 2013 review by Ianetta et al. highlights the evidence supporting a positive role of GPIs in a certain patients subset, stating that “guidelines try in general to address routes on the basis of ‘one concept fits all’ which is definitely quite impossible in clinical conditions such as acute myocardial infarction, as STEMI or NSTEMI, represent a spectrum of clinical situations rather than a clear-cut pathology.” Commenting on the state of evidence regarding GPIs use in this area, Dr Menozzi said: “The evidence on GPIs is weak because we have no trials from the present era. On the other hand, data against the use of intravenous drugs are non-existent. Many authors hypothesise that oral antiplatelet drugs we use at present substitute the intravenous ones. But this is not demonstrated.”

And recent evidence is not entirely lacking, argued Dr Menozzi. A 2015 study of the National Cardiovascular Data Registry investigated the effects of GPIs on outcomes after percutaneous coronary intervention, finding that in unselected acute coronary syndrome patients undergoing, PCI, GPIs use was associated with reduced in-hospital mortality and increased bleeding.

“The focus is to identify the patients who can derive the best benefit with the lowest harm risk,” summarised Dr Menozzi. “This is possible, because we know the characteristics of the patients, and we know definite characteristics of the drug now.

“In 2018, the use of GPIs should be driven by a very correct patient selection, selecting for example a patient with very large myocardial infarction, younger in age, early presenters, patients with symptoms occurring just within one or two hours such that the thrombus is very fresh and can be very easily dissolved by GPI, patients with very large thrombus burden on angiogram, patients with multivessel disease or cardiogenic shock: in summary, patients with a very high ischaemic risk.”

He went on to stress that, to optimise the use of GPIs, it is very important to also manage haemorrhagic risk. “This is done by carefully selecting the patient, using radial access to minimise bleeding at access site, being very careful in not overdosing heparin, using reversal agents, and administering a short duration infusion, sometimes also only tirofiban bolus,” he said.

The possibility to use reversal agents is another prominent difference in contemporaneous GPI use. In addition, short infusion duration can improve safety, reducing bleeding risk without affecting efficacy, noted Dr Menozzi, adding that the intravenously administered GPIs can be employed to prevent complications during the procedure, after which an oral agent can be given.

Asked whether he foresees new study being carried out to build a clearer picture of where GPIs are most appropriate, Dr Menozzi was doubtful: “There will be no new study on the use of GPIs in the present era, although it would be very welcome.

“And it would be very interesting to see a trial comparing, in the setting of high risk STEMI, a strategy of GPIs versus no GPIs. Continued on page 6
Taking it all into consideration: antithrombotic therapy in patients with AF undergoing PCI

The management of patients with atrial fibrillation (AF) undergoing PCI remains problematic, with uncertainty on how to best manage patients requiring both oral anticoagulation therapy (OAC) and dual antiplatelet therapy (DAPT). Speaking to JIM Today ahead of the meeting, Ghada Mikhail (Imperial College Healthcare NHS Trust, London, UK) discussed how clinical decisions can be made in light of this, with a look at the latest guidance and data on the topic.

A recent review by Vidula et al presents the latest understanding of the balance that must be struck between ischaemic risk and bleeding risk, in terms of duration of dual antiplatelet therapy for patients undergoing PCI. Both ischaemic and bleeding events increase the risk of mortality, the authors report, citing a study that placed cumulative incidence of death at 0.5% after an ischaemic event and 0.3% after a bleeding event, in reported outcomes at 12 and 33 months after PCI.

While stressing that determining the best course of action for individual patients requires an assessment of bleeding and ischaemic risk, the authors note that a changing landscape of newer generation stents, coupled with the bleeding risks associated with long-term DAPT, mean that shorter-term DAPT has been addressed in recent studies.

AF patients undergoing PCI present a further clinical problem, namely that of determining the duration of DAPT given that they also need OAC therapy. In the same work, Vidula et al review studies investigating alternatives to triple therapy (OAC + P2Y12 inhibitor + aspirin) that may provide equal efficacy while reducing relative bleeding risk.

“You need to take a number of points into consideration,” said Dr Mikhail, summarising the best course of action for stented patients undergoing OAC: “The thrust from all the studies is that we should be using direct oral anticoagulants (DOAC) rather than warfarin. We should be using low dose rather than full dose DOACs, and clopidogrel rather than aspirin combined with anticoagulation therapy.”

Describing the data available to date, Dr Mikhail cited the WOEST trial, (What is the Optimal antiplatelet and anticoagulant therapy in patients with oral anticoagulation and coronary StenTing trial), which randomised patients on OAC undergoing PCI to either double therapy (clopidogrel + OAC) or triple therapy (clopidogrel + aspirin + OAC). Whilst patients on double therapy were at lower risk of bleeding, the study was not powered to detect differences in thrombotic complications.

More recently, DOACs have been investigated in this context. PIONEER AF was an open-label, randomised, controlled, multicentre study exploring two treatment strategies of rivaroxaban, and a dose-adjusted oral vitamin K antagonist treatment strategy in sub-

References
3. Iannetta et al. Is There Still a Role for Glycoprotein IIb/IIIa Antago-

“My personal point of view is that, in my clinical practice … the patients who can be managed safely only with oral drugs are the minority.”

Alberto Menozzi

Crossroads on optimal antithrombotic therapy in patients treated with PCI Parini Friday 12:45

In defense of GPIs in high risk ACS

Continued from page 5

On the other hand, a possible competitor is cangrelor (which is the topic of the presentation following mine, by Dominick Angiolillo), which is an intravenous antiplatelet agent and an ADP blocker. This drug is probably less powerful as an antithrombotic, but it is still a very efficacious antiplatelet drug, and probably with a profile that is maybe a compromise for some patients.

“...the patients who can be managed safely only with oral drugs are the minority.”

Alberto Menozzi
jects with atrial fibrillation undergoing percutaneous coronary intervention. It demonstrated reduced bleeding risk with 15 mg rivaroxaban + P2Y12 inhibitor alone for one year, or 2.5 mg twice daily rivaroxaban + DAPT (for 1, 6, or 12 months), as compared to vitamin K antagonist + DAPT (for 1, 6, or 12 months). Rates of stroke, MI, or CV death were not statistically significant between groups.4

Dr Mikhail also noted the REDU-AL PCI trial (randomised evaluation of dual antithrombotic therapy with dabigatran versus triple therapy with warfarin in patients with nonvalvular atrial fibrillation undergoing percutaneous coronary intervention), wherein patients were randomised to either warfarin + aspirin + clopidogrel/ticagrelor, or dabigatran (110 mg or 150 mg twice daily) + P2Y12 inhibitor. Bleeding risk was significantly lower at mean follow-up of 14 months in the dabigatran + P2Y12 inhibitor group, with no difference found in rate of stroke, systemic embolism, MI, unplanned revascularisation, or death.5 Choice of stent can also affect DAPT duration, explained Dr Mikhail. “More studies are needed, but as an example, the BioFreedom (Biosensors International, Singapore) and zotarolimus-eluting Endeavor (Medtronic, USA) stents, can be used with shorter duration of DAPT.”

ZEUS (Zotarolimus-eluting Endeavor sprint stent in uncertain DES candidates) and LEADERS FREE (prospective randomised comparison of the BioFreedom Biolimus A9 drug-coated stent versus the Gazelle bare-metal stent in patients at high bleeding risk), assessed the use of one month of DAPT in patients at high risk of bleeding. These studies found that patients implanted with drug-coated stent fared better at one year in terms of MI, target vessel revascularisation, or death (in ZEUS), and in terms of MI, stent thrombosis, and death (in LEADERS FREE), relative to bare metal stenting.6,7

Concluding with a reflection on current ESC guidelines for patients on OACs undergoing PCI, Dr Mikhail stated: “We don’t know the exact answer and more studies are needed. But the length of triple therapy should be kept as short as possible because of the risk of bleeding. We should be considering the use of DOACs rather than warfarin, clopidogrel rather than prasugrel or ticagrelor. We should also consider a lower dose of DOAC as well as the use of dedicated new-generation stents to lower the duration of DAPT.8,9

“Patients with a high risk of ischaemia and low bleeding risk, we should be using triple therapy for up to six months followed by OAC and a single antiplatelet agent. For patients with a high bleeding risk, we should be using one month of triple therapy followed by dual therapy. After 12 months we should then consider using OAC alone.”

References
Intravascular lithotripsy: Hopes of improving vessel compliance without vessel injury

Intravascular lithotripsy (IVL; Shockwave Medical, USA) is a technology that delivers pulsatile sonic pressure waves that fracture intravascular calcium that commonly hampers vessel compliance hindering stent delivery, expansion and apposition. Todd Brinton (Stanford University, CA, USA), the physician co-founder of Shockwave Medical, spoke at JIM 2018 yesterday, delivering the latest on IVL trial data as well as discussing future developments.

In conversation with JIM Today, Dr Brinton described the technology’s nascent years: “We first developed a peripheral product for the SFA. Over the last couple of years we have been working on coronary calcification – this was originally my primary insight.”

The technique is similar to that of urological lithotripsy. However, the Shockwave IVL system was developed specifically for intravascular use. The IVL system consists of an IV-pole mountable generator, connection cable, along with a catheter that houses an array of emitters within an integrated balloon. The IVL catheter is advanced to the lesion in standard fashion on the physician’s choice of guidewire, and a 3kV generator powers the IVL catheter. When the emitters discharge it has the effect of vaporising the saline/contrast mixture within the integrated balloon, causing high-amplitude sonic output. The technique is similar to that of urological lithotripsy. However, the Shockwave IVL system was developed specifically for intravascular use. The IVL system consists of an IV-pole mountable generator, connection cable, along with a catheter that houses an array of emitters within an integrated balloon. The IVL catheter is advanced to the lesion in standard fashion on the physician’s choice of guidewire, and a 3kV generator powers the IVL catheter. When the emitters discharge it has the effect of vaporising the saline/contrast mixture within the integrated balloon, causing high-amplitude sonic pressure waves that exceed 50 atm to disrupt adjacent calcium, both at its surface and in its media due to the field effect of the pressure wave. Each catheter emits a total of 80 pulses at a rate of one pulse per second.

“We’ve studied many different types of pressure wave frequencies and found this optimal window for patients,” explained Dr Brinton. “It provides the most significant large-amplitude pulses, which with a recovery time minimises the impact of heat. In contrast, this is the ‘opposite’ of ultrasound, in the sense that IVL is high amplitude, low frequency, rather than low amplitude, high frequency. This is pure mechanical energy being converted to disrupt and fracture the calcium. “One of the common problems we have in the coronaries with placing stents is that we have hard pieces of calcium that don’t allow the stent to expand. IVL allows us to truly alter vessel compliance and maximise acute gain.”

The DISRUPT CAD 1, which completed last year, trialled 60 patients with heavily calcified coronary lesions using IVL. A 31-patient sub-study of this trial also investigated the mechanism of IVL, demonstrating its effects on stenting and its optimal deployment using OCT. DISRUPT CAD 2 is just beginning enrolment of a further 120 patients in 15 centres from nine countries in Europe. In addition, DISRUPT CAD 3, a global US IDE study, is in its final planning stages.

The European DISRUPT CAD II trial will include de novo lesion lengths of up to 32 mm, and excludes CTO. Unlike CAD I, the follow-on study will include patients undergoing dialysis, which, Dr Brinton noted, was a significant addition. The study’s aim is to assess the procedural efficacy and safety of IVL, and includes angiographic core-lab as well as an independent clinical events committee adjudication in order to evaluate procedure-related MACE and issues such as slow flow, no reflow, and the potential for perforation. “We know that other technologies used for calcification certainly have some challenges in this regard,” said Dr Brinton. “For more complex problems we tend to use more complex tools, and the safety profile is not as favourable as traditional PCI tools.”

“Because IVL is encased in an integrated balloon, it is used like a balloon, which is optimal for safety. Rotational and orbital atherectomy are great tools for very calcified, high-grade, difficult to cross lesions. If you can’t get traditional tools across then rotational atherectomy is excellent. However, it doesn’t address how to get optimal radial acute gain. Often, most people will use these tools to allow them to then use higher pressure balloons and stents. Instead, the idea of IVL is to allow for optimal stent implantation.”

“Because IVL is encased in an integrated balloon, it is used like a balloon, which is optimal for safety. Rotational and orbital atherectomy are great tools for very calcified, high-grade, difficult to cross lesions. If you can’t get traditional tools across then rotational atherectomy is excellent. However, it doesn’t address how to get optimal radial acute gain. Often, most people will use these tools to allow them to then use higher pressure balloons and stents. Instead, the idea of IVL is to allow for optimal stent implantation.”

Dr Brinton concluded with a look to further applications of the lithotripsy principle: “We have done our work in DISRUPT CAD I and are starting enrolment in DISRUPT CAD II. A second-generation device will be available in Europe mid-year. This device is further optimised for deliverability with a 10 percent reduction in profile and greater flexibility, without compromising sonic output.

“We are in the midst of developing an embodiment of the core technology for use in treatment of calcified aortic valves. Its use is for transvalvular aortic lithotripsy. We have demonstrated clinical feasibility and are in the development of a truly percutaneous transfemoral system. This approach uses sonic pressure waves to fracture calcium on the aortic leaflets and improve aortic leaflet mobility. That is a piece of the company’s vision, growing the technology for other clinical applications.”

“One of the common problems we have in the coronaries with placing stents is that we have hard pieces of calcium that don’t allow the stent to expand.”

Todd Brinton

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Calcific lesion preparation: the role of imaging

Intracoronary imaging was laid bare on Thursday at JIM, during a session that included discussion of imaging in calcific lesions, vulnerable patients, and stent optimisation. Opening the session was Carlo Di Mario (Careggi University Hospital, Florence, Italy), who focussed on the two main modalities widely available in modern day cath labs: IVUS and OCT.

Speaking to JIM Today, Dr Di Mario noted the fundamental differences in the way IVUS and OCT assess calcium: “When calcium is treated with Rotablator [Boston Scientific, USA] or cutting/scoring balloons, OCT is able to detect the small cracks and fractures much better than IVUS, and assess the distance of struts to the wall in the frequent case of stent malapposition along the irregular non-circular lumen surrounded by protruding calcium. But having stated these advantages of OCT, let me clarify that both IVUS and OCT can provide the essential information on the circular and longitudinal extent of calcification, and in fact IVUS is more reliable in case of deep calcium that can be missed with OCT due to its limited penetration.”

Calcified lesions are frequent in atherosclerosis but become truly prevalent in older patients, and in those with diabetes or renal insufficiency. Severely calcified lesions are a risk factor for stent failure, even in the drug-eluting stent era. What imaging has brought to the understanding of the impact of this pathophysiological process, explained Dr Di Mario, is an improved appreciation of the significance of under-expansion below the dangerous absolute threshold of 5.0-5.5 mm², and poor stent apposition (with struts very far from the wall, situated in the elliptical irregular lumens present when a large calcific plaque remains protruded).

Dr Di Mario also spoke of optimal lesion preparation: “It is an exciting time for operators that are challenging heavily calcified lesions,” he commented. “In the past Rotablator – or, in the United States, orbital atherectomy – were used to deal with uncrossable/undilatable lesions. Some operators, after these initial passes, were using cutting or scoring balloons, concentrating the force of the balloon on the blade/wire in contact with the wall.

“The majority of cases were treated just with brutal force, increasing the diameter and pressure of the balloon until the wall was giving up, and sometimes too much, leading to perforation. The presence of calcium at angiography/fluoroscopy is not enough for an informed decision on the need to use dedicated calcium ablation systems, nor the selection of type of device. Results were often suboptimal, despite the use of these cumbersome techniques guided by intracoronary imaging.”

He continued: “We now have a novel method to crack calcium inside the wall, with no risk of microembolisation and slow flow, as easy as the insertion of a normal balloon. Lithotripsy has the potential to revolutionise and simplify our approach to treatment of calcific lesions.”

Asked what evidence currently supports the use of imaging in the accurate assessment of accumulation and distribution of calcium, and the effect this has on procedural outcomes, Dr Di Mario responded: “We do not have convincing evidence in general that imaging modalities truly make a difference in outcome after PCI.

“For calcified lesions, we can certainly help in selecting the most appropriate size or type of device, but we are not always able to ensure full expansion.”

Imaging is very good at showing the problem, he went on, but it does not mean that one is necessarily able to solve it. “With lithotripsy everything may change,” he said. “It will be worthwhile to use imaging to ensure we apply these expensive balloons only when we truly need them, and select balloons large enough to be in contact with the wall, and to transmit the shockwaves – a prerequisite for effective calcium fragmentation.

“The rest should come easier, but it is reassuring to see calcium fractures more often, and see a more circular larger lumen with better strut apposition.”
EVOLUTion of a TAVI family

Thursday’s programme featured an exploration of an evolving transcatheter aortic valve family, with Anna Sonia Petronio (University Hospital, Pisa, Italy) walking the audience through the past, present and future of the technology.

The self-expandable valve family was first introduced with the CoreValve (Medtronic, USA) – a tri-leaflet porcine pericardial tissue valve with a nitinol frame. Early data with the device was positive, with all-cause mortality and stroke rate showing significant reduction when using the CoreValve versus surgical aortic valve replacement (SAVR). However, the valve – as with other first generation technologies – had several limitations, including bulkiness and a need for large diameter catheters (18-24 F), vascular complications, permanent pacemaker requirement, and paravalvular leak (PVL).

Dr Petronio stressed that PVL was under-emphasised in the early years of TAVI, but its impact became more and more apparent as time went on.

In the next iteration of the self-expanding CoreValve family, the EVOLUT R, PVL was tackled head on, as well as resolution of several other limitations present in the first-generation devices. By reducing the overall height of the prosthesis – all the while preserving the height of the pericardial skirt – the device allowed superior sealing to reduce PVL.

In addition, the EVOLUT R can be captured and repositioned during deployment, thus hoping to improve final placement. “When you have a valve that is repositionable, you have the chance of positioning the valve the best you can,” said Dr Petronio. “If you are not satisfied you can just close it back and reposition it.”

The system also benefits from a smaller, 14 F delivery system, opening up the possibility to use the EVOLUT R, we have already demonstrated a step forward for the repositionable valve.”

Anna Sonia Petronio
EVOLUTion of a TAVI family

Continued from page 11

EVOLUT R in smaller vessels. “With EVOLUT R, we have already demonstrated a step forward for the repositionable valve, as well as a reduction in diameter, which has enabled us to treat patients with small femoral arteries,” said Dr Petronio.

Compared to the first-generation CoreValve, initial data using EVOLUT R unveiled significant reduction in PVL when using the new device, as well significant reductions in vascular complications, bleeding events and permanent pacemaker need.1

The latest-generation device, the EVOLUT PRO, builds on the previous EVOLUT R platform, but incorporates an external pericardial wrap, designed to increase surface contact with the native anatomy, and adds overall tissue volume to reduce gaps between anatomy and valve.1 Importantly, Dr Petronio noted that this makes the EVOLUT PRO more conformable to eccentric and calcified anatomicies, including left ventricular outflow tract (LVOT) calcification. “In these cases, paravalvular leak can be a problem, and of course the PRO allows you to treat with a higher chance of reducing or even avoiding paravalvular leak,” she said.

The EVOLUT PRO comes with a 16 F delivery system – i.e. moderately larger than the EVOLUT R’s 14 F, but still smaller than the first-generation CoreValve. In addition, Dr Petronio relayed that it is possible to work without the in-line sheath, which makes for a very reduced diameter puncture compared to the first generation. Furthermore, she shared that there are plans to reduce the PRO’s delivery to a 14 F system in the near future.1

In terms of the data, early work with the EVOLUT PRO has shown further reductions in permanent pacemaker implantation rates when compared to previous-generation CoreValves. In terms of PVL, one report demonstrated “none to trace” PVL in 72.4% of patients, with mild PVL present in the remaining 27.6%.1

“The EVOLUT PRO arrived just before Autumn 2017, so I think we will definitely have more patients later this year [to discuss],” said Dr Petronio.

She went on to note that valve-in-valve patients could also benefit from the valves, because they have good sealing, first of all, and secondly they are positioned suprannularly. “If you have an intrannular position, then you have to cope with the dimensions of the old valve: you can’t change it,” she said.

“EVOLUT valves allow you to treat the sorts of patients which, with other valves, could be more difficult,” Dr Petronio said in closing.

References
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Cerebral protection with Emblok

On Friday at JIM, preliminary feasibility and safety results were presented for the Emblok device (Innovative Cardiovascular Solutions [ICS], USA) – the first embolic protection system to provide full circumferential aortic coverage.1

Introducing the device, and its associated data, was Azeem Latib (San Raffaele Hospital, Milan), who undertook the first clinical cases using Emblok. In conversation with JIM Today, Dr Latib delved deeper into the ins and outs of the technology.

Can you please introduce the Emblok device and its novel design?
The ICS Emblok system is a cerebral embolic protection device that provides full coverage of all three aortic arch branches. The device consists of a nitinol frame and porous laser drilled urethane membrane delivered through an 11 F delivery system, with an integrated custom 4 F pigtail catheter. The frame geometry can be adjusted to accommodate aortic vessel diameter ranges of ~30-35 mm. The pigtail has marker bands along the distal section, which allow the catheter to denote the annulus, thereby saving contrast usage.

How easy is it to use?
The greatest strength of the system is its ease of use. Positioning the device proximal to the brachiocephalic take-off takes less than one minute. Deploying the system and optimising apposition can take as little as 10 seconds using the two slider buttons. Retrieval is also safe and simple: using the sliders, it takes minimal time and force.

You were involved in the first clinical cases using Emblok. How were patients selected, and what lessons were learned?
Finding patients for the first cases was fairly straightforward, as the system takes on virtually all patient anatomies, with just an aortic length and diameter requirement; anatomies such as bovine arch do not have any significance for patient selection with this device. The learning curve was very quick, given the simplicity of the system and its ease of use. We did see some minor limitations using the system. [We thought it would benefit from] improved visibility of the tapered tip, a widening of the range of aortic diameters treatable, and the ability to keep the filter open during the entire procedure. Feedback of the system was taken into consideration by the company in working toward the development of the next iteration.

What’s the status of the feasibility and safety study/studies?
As of the 12th of February, we have treated 20 patients in two Italian centres for the CE-Mark study. Plans for a concurrent US IDE study will be conducted later this year, and data from both US and EU studies are needed to support the safety and performance of this device.

The company has been busy working on the next-generation Emblok system; hopefully this will be rolled out for the ongoing CE-Mark study.

Should Emblok find its way into...
common practice do you think?

Yes: I think by now we have all realised the benefit that CEP brings to patients. The future will be CEP that is used in everyday practice for TAVI, and other left-sided heart procedures. The Emblok system’s strengths are its applicability to a wide range of anatomies, and its ease of use. It definitely has a place in CEP to advance protection, retrieval, and ease of use. The next generation device could potentially become a routinely used device.

As we move to low-risk patients, the bar ensuring good TAVI outcomes will be set much higher. CEP could potentially become standard of care if:

- We accept, as a community, that silent brain infarction has a negative impact on long-term outcomes, and that prevention of these silent embolic events is as important as preventing stroke
- CEP devices are easy to use, safe, give full protection during the procedure, and can be rapidly implanted without adding significant time to the procedure, or interfering with valve positioning or deployment
- Specific reimbursement for CEP during TAVI becomes available and/or the costs of devices decreases significantly

References

1. The Emblok™ Embolic Protection System. Available at: www.emblok.com

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Pay a visit to the wine corner at JIM for a refreshing chance to try delicious wines from the Colombo vineyard!
Faculty 2018. Continued

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