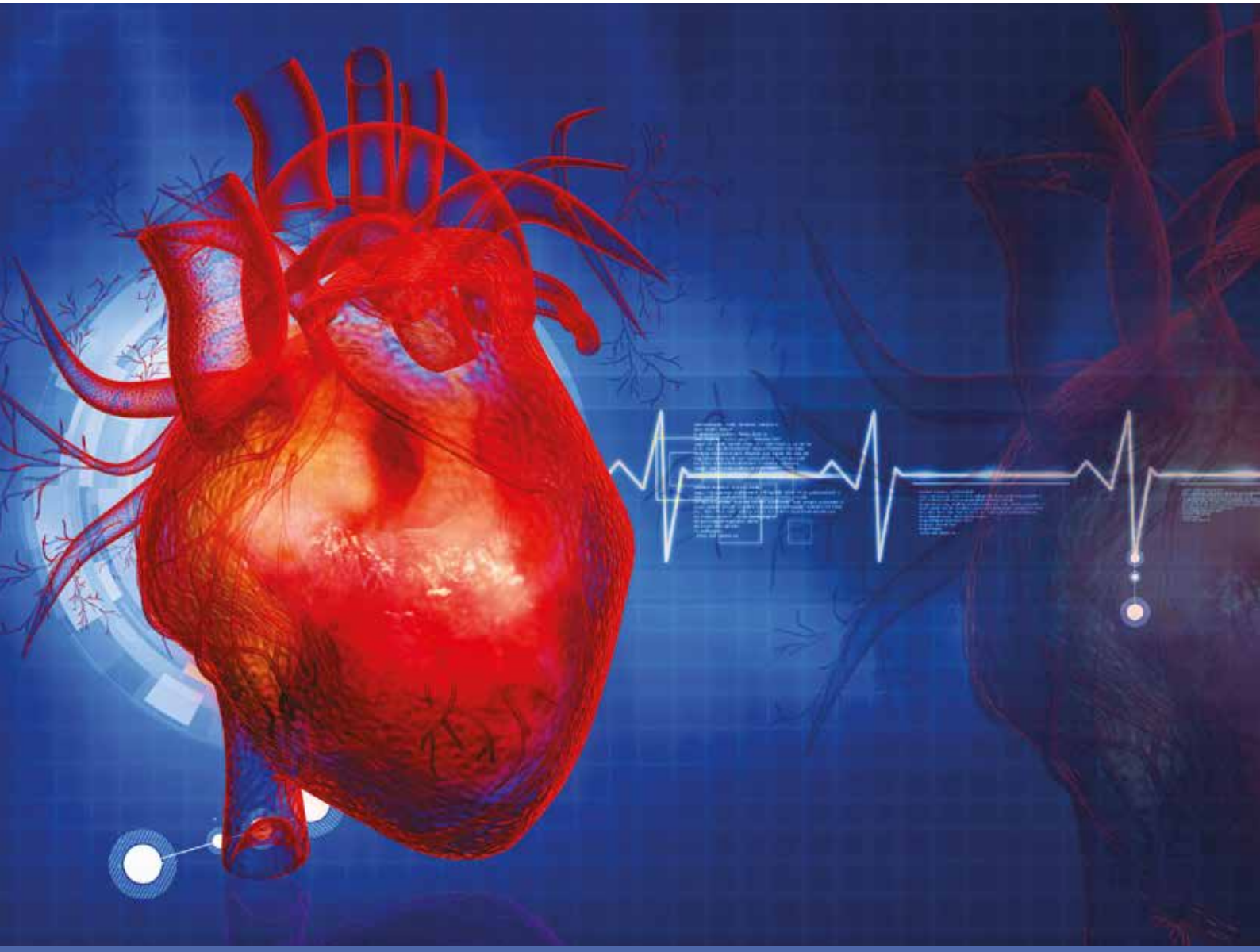
February 2015

Cardiovascular News

EDUCATIONAL SUPPLEMENT



Current issues in PCI

The Stenting in Complex PCI meeting was supported by an unrestricted educational grant from Boston Scientific. Boston Scientific has also provided an educational grant for the production of this supplement but has had no input into the final editorial content

Contents

Introduction

Current issues discussed at complex PCI meeting

The Stenting in Complex PCI meeting (2 December 2014, Milan, Italy) reviewed some of the most important issues in percutaneous coronary intervention (PCI) today. This included how PCI has developed since the SYNTAX (Synergy between PCI with Taxus and cardiac surgery) trial[1] showed that the intervention was associated with a significantly higher rate of major adverse cardiac or cerebrovascular events than coronary artery bypass grafting (CABG) at one year in patients with three-vessel or left main disease.

According to Javier Escaned (Interventional Cardiology, Hospital Clinico San Carlos, Madrid, Spain), there is a "great expectation" that the ongoing SYNTAX II study, which is investigating the effectiveness of contemporary PCI techniques—including the use of an everolimus-eluting stent with a biodegradable polymer (Synergy, Boston Scientific)—in patients with *de novo* three-vessel disease, will indicate better outcomes with PCI than those observed with PCI in the original study.

Another topic discussed at the meeting was the need to tailor duration of dual antiplatelet therapy (DAPT) to the individual patient, balancing the risks of stent thrombosis with the device being used in the procedure against the patient's risk of bleeding. Thomas Cuisset (Interventional Cardiology Unit, University Hospital, La Timone, Marseille, France) said: "We know that in specific populations, balancing the risk of stent thrombosis vs. the risk of bleeding is more difficult. For example, the window between the risk of stent thrombosis and the risk of bleeding is even smaller in older patients. So, that is one population that could potentially receive great benefit from a new drug-eluting stent that allows a shorter duration of DAPT."

Robert Byrne (Deutsches Herzzentrum, Technische Universität, Munich, Germany) explained why he felt that drug-eluting stent technology was still "very much a work in progress" and reviewed the emerging evidence for drug-eluting stents with biodegradable polymers. Exploring the topic of biodegradable polymers further, Patrizia Presbitero (Department of Invasive Cardiology, Humanitas Mirasole Clinic, Rozzano, Milan, Italy) reviewed the data from the EVOLVE II study, which was presented at the 2014 American Heart Association Scientific Sessions (15–19 November, Chicago, USA). This study found that Synergy was non-inferior to an everolimus-eluting stent with a permanent polymer (Promus Element Plus, Boston Scientific).

The meeting, the course director of which was Antonio Colombo (San Raffaele Scientific Institute, Milan, Italy), also explored different aspects of complex PCI through live cases and cases studies. Robert-Jan Van Geuns (Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands) reviewed stenting in left main disease, Colm Hanratty (Department of Cardiology, Belfast Health and Social Care Trust, Belfast, Northern Ireland) looked at bifurcation stenting, and Simon Walsh (Department of Cardiology, Belfast Health and Social Care Trust, Belfast, Northern Ireland) and Jonathan Hill (King's College Hospital, London, UK) discussed chronic total occlusions. Also, Stephane Cook (Swiss Cardiovascular Centers in Bern & Fribourg, Switzerland) gave a talk on imaging optimisation and Gennaro Sardella (Department of Cardiovascular, Sapienza University of Rome, Rome, Italy) gave the presentation "Complex lesion modification—tips and tricks from the frontline."

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SYNTAX II trial

PCI technologies have evolved since the SYNTAX trial

The SYNTAX (Synergy between PCI with Taxus and cardiac surgery) study,[1] which failed to show that percutaneous coronary intervention (PCI) was non-inferior to coronary artery bypass grafting (CABG) in patients with three-vessel or left main disease, and other studies led to recommendations, such as those from the European Society of Cardiology (ESC),[2] that CABG should be used in preference to PCI for the management of patients with the highest tercile SYNTAX score. However, there have been many new developments in PCI strategies, eg. next-generation drug-eluting stents and new imaging modalities, since the study was published in 2009. This article reviews the potential of these developments to improve PCI outcomes in patients with complex disease.

The investigators of the SYNTAX trial, Patrick Serruys (Erasmus University Medical Center, Rotterdam, The Netherlands) and others, assessed patient eligibility for the study (patients had to be suitable for revascularisation with either CABG or PCI) using the SYNTAX score. According to the results, patients with high SYNTAX scores (≥33) undergoing PCI had a significantly higher risk of major adverse cardiac or cerebrovascular events than patients with high SYNTAX scores undergoing CABG. But, there was no significant difference in this risk between PCI and CABG among patients with low or intermediate SYNTAX scores.[1]

Revised SYNTAX score

However, speaking at a conference on stenting in complex PCI, Javier Escaned (Interventional Cardiology, Hospital Clinico San Carlos, Madrid, Spain) reported that the SYNTAX score has limitations because it assesses risk on the basis of angiographic characteristics, leaving out clinically relevant patient characteristics. Vasim Farooq (Thoraxcenter, Erasmus Medical Center, Rotterdam, The Netherlands) and others[3] report in *The Lancet* that this limitation led some researchers to "suggest that the SYNTAX score and other category-based scores that label patients as low risk, intermediate risk, or high risk might be concealing higher risk patients in lower risk groups or vice versa." Therefore, the authors revised the SYNTAX score to incorporate additional patient characteristics (eg. age) and found that long-term mortality in patients with complex coronary artery disease "can be well predicted" by the combination of anatomical and clinical factors in the SYNTAX score II. An important added value of the SYNTAX II score, which is based on the long-term outcome of both the PCI and CABG arms in the SYNTAX study, is that it calculates the expected outcome for both revascularisation techniques. Escaned commented that he believed that this new score not only provides "better risk stratification of patients" than the original SYNTAX score, but also facilitates the decision-making process by allowing comparisons between expected long-term outcomes with PCI and CABG.

Javier Escaned

FFR/iFR

Another development since the SYNTAX study has been the introduction of ischaemia-driven revascularisation. For example, the FAME (Fractional flow reserve versus angiography) study[4] found that the use of fractional flow reserve (FFR) to guide PCI in patients with multivessel coronary artery disease was associated with a significant reduction (by about 30%) in the rate of major adverse cardiac events at one year compared with standard angiography-guided PCI. Furthermore, the ADVISE (Adenosine vasodilator independent stenosis evaluation) study[5] (of which Escaned was a principal investigator) and the most recent ADVISE II study, which was reported at TCT 2013, found that instantaneous wave-free ratio (iFR) had "excellent diagnostic efficacy" in identifying stenoses with an FFR of <0.80 (which indicates treatment for a stenosis can be deferred) and could be used for "intracoronary functional assessment when administration of adenosine is not desirable [a possible limitation of FFR]".

Escaned told delegates at the conference that the use of ischaemia-driven revascularisation, with the combination of iFR/FFR applied in the ADVISE II study, may facilitate the treatment of patients with multivessel disease. He explained: "Firstly, you treat only what you need to treat [and defer treatment in some patients]. Secondly, by reclassifying the number of vessels requiring revascularisation on the grounds of iFR/FFR, PCI can be considered in a significant number of patients in which CABG was indicated on anatomical grounds."

IVUS

As well as developments in pre-procedural assessment, there have also been developments in optimising stent deployment. A meta-analysis[6] found that stent deployment guided by intravascular ultrasound (IVUS) was associated with significantly lower rates of adverse clinical events compared with angiography guidance.

While, according to the meta-analysis, further study is needed to clarify which subgroups of patients would benefit most from IVUS-guided stent deployment, Escaned stated that IVUS "is generally accepted as an important tool in contemporary complex PCI."

He added that the involvement of expert chronic total occlusion operators, and the use of IVUS and new tools (such as exten-

SYNTAX II trial

PCI technologies have evolved since the SYNTAX trial

sion catheters), has meant that the success rate of treating chronic total occlusions with PCI has "dramatically increased" since the SYNTAX study. In this study, chronic total occlusions were the strongest predictor of incomplete revascularisation in the PCI arm.

Second-generation drug-eluting stents

For Escaned, one of the "biggest changes" in technology since the SYNTAX study has been the type of stents that are used in PCI. In the trial, patients underwent PCI with a paclitaxel-eluting stent with a permanent polymer (Taxus, Boston Scientific). Compared with bare metal stents, paclitaxel-eluting stent and other "first-generation" drug-eluting stents reduce the rate of restenosis. However, they are also associated with an ongoing risk of stent thrombosis and require prolonged use of dual antiplatelet therapy to mitigate this risk. Therefore, next-generation drug-eluting stents were developed to improve safety and efficacy.

According to the results of the SPIR-IT IV study,[7] an everolimus-eluting stent (Xience, Abbott Vascular) significantly reduced the rate of target lesion failure at one year in all patients except those with diabetes compared with a paclitaxel-eluting stent (Taxus Express, Boston Scientific). It also significantly reduced the rate of stent thrombosis at one year (0.17% vs. 0.85% for the paclitaxel-eluting stent; p=0.004). The safety and efficacy of these second-generation stents (which as well as Xience include Resolute Integrity, Medtronic, and Promus Premier, Boston Scientific) means that they are now considered to be the gold standard devices for PCI.

Biodegradable polymers

To further improve outcomes, third-generation stents have been developed. These stents are either completely bioresorbable or they have a metallic stent with a biodegradable polymer. The EVOLVE II study, which was presented by Dean Kereiakes (The Lindner Research Center, The Christ Hospital Heart and Vascular Center, Cincinnati, USA) at the American Heart Association Scientific Sessions (15–19 November, Chicago, USA),[8] found that an everolimus-eluting stent with a biodegradable polymer (Synergy, Boston Scientific) was non-inferior to an everolimus-eluting stent with a permanent polymer (Promus Element Plus, Boston Scientific) in terms of target lesion failure at one year. The study, which investigated more complex patients (eg. 31% had diabetes) than previous IDE trials of second-generation stents, also found that the rate of stent thrombosis was 0.4% in the Synergy arm (non-inferior to the Promus arm) and that there were no reported incidences of definite stent thrombosis after 24 hours. About the Synergy stent, Escaned commented: "Its strut is nearly half the thickness of the paclitaxel stent and the amount of polymer is truly small—it is a very thin layer."

Polaris IVUS system

According to Escaned, "we are fortunate" because we are now able to "combine these different strengths of PCI" in the form of contemporary PCI. He added that a new study, the SYNTAX II trial (Clinical trials identifier NCT02015832 PCI), is exploring the role of contemporary PCI in patients with *de novo* three-vessel disease. "The SYNTAX II trial aims to recruit 450 patients across 25 centres. Basically, we are comparing the results with the new PCI strategies with the historical PCI cohort of the SYNTAX study," Escaned, who is a principal investigator of the study, reported.

He noted that there is also an exploratory endpoint that will look at how the results with contemporary PCI compare with contemporary CABG.

SYNTAX II trial

Escaned and colleagues will use the SYNTAX II score to assess eligibility for patient enrolment. All patients recruited to the study will undergo iFR/FFR assessment at the index procedure to identify which vessels need treatment, and they will receive a Synergy stent in the vessels that require revascularisation. Furthermore, IVUS-guided stent deployment is mandatory. Escaned commented that the use of Synergy and other new PCI techniques in the study "provides a great expectation" that the outcomes with contemporary PCI in patients with three-vessel disease will be "much better" than those of the PCI arm of the original study. "The study is building up and, hopefully, we will have results soon," he stated.

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Dual antiplatelet therapy

No definite answers about DAPT duration after PCI

Thomas Cuisset (Interventional Cardiology Unit, University Hospital, La Timone, Marseille, France) told delegates at the Stenting in Complex PCI conference that the DAPT (Dual antiplatelet therapy) study has not provided any firm conclusions about the optimum duration of dual antiplatelet therapy (DAPT) in patients who undergo percutaneous coronary intervention (PCI). Therefore, he argued, DAPT duration should be based on the patient's risk of bleeding vs. the risk of stent thrombosis of the device being used in the procedure.

In the DAPT study,[1] patients undergoing PCI for acute coronary syndromes—with either a first- or second-generation drug-eluting stent—were randomised to receive dual antiplatelet therapy for 12 months or for 30 months (prolonged DAPT). Cuisset reported that there was a significant 71% reduction in stent thrombosis ($p<0.001$) in the prolonged DAPT group. Prolonged DAPT was also associated with a significantly reduced rate of major adverse cardiac or cerebrovascular events (4.3% vs. 5.9% for 12-month DAPT; $p<0.001$) and a significantly reduced rate of myocardial infarction (2.1% vs. 4.1%, respectively; $p<0.001$). However, the rate of moderate or severe bleeding was significantly higher with prolonged DAPT (2.5% vs. 1.6% for 12-month DAPT; $p<0.001$) and the rate of all-cause mortality was also significantly higher (2% vs. 1.5% for 12-month DAPT; $p=0.05$). Cuisset commented that this higher rate of all-cause mortality "might be due to the bleeding complications in this arm". On the basis of these results, Cuisset noted, the DAPT study does not provide a "definite answer" about DAPT duration.

Implications of DAPT study

In an accompanying commentary[2] to the study in *The New England Journal of Medicine*, Antonio Colombo and Alaide Chieffo (both Interventional Cardiology Unit, San Raffaele Scientific Institute, Milan, Italy) write that the need for DAPT can be separated into a mandatory phase and a "possible beneficial phase", explaining: "The mandatory period is defined as the interval during which premature discontinuation of DAPT would lead to unacceptably high levels of stent thrombosis whereas the possible beneficial period is the subsequent interval during which the benefit versus the risk of continued uninterrupted therapy is more a matter of debate. The DAPT study addresses the possible beneficial period rather than the mandatory period." They add that prolonged DAPT is "most likely" to be of benefit in patients who are at high risk for stent thrombosis but are at relatively low risk for bleeding. However, the DAPT study excluded patients who had a major adverse cardiovascular or cerebrovascular event in the 12 months preceding the study, which resulted in (along with other criteria) 23% of patients who had been initially enrolled in the study being excluded. Colombo and Chieffo state that these excluded patients may be "the very patients" who would benefit from prolonged DAPT. They also report that the DAPT study indicates that patients receiving a paclitaxel-eluting stent would gain the most from prolonged DAPT and those receiving an everolimus-eluting stent would gain the least, noting: "This suggests that the potential benefit of prolonged DAPT may depend on the type of stent that is implanted."

Other studies

Cuisset commented that a meta-analysis indicated that DAPT could be interrupted before three months in patients receiving an everolimus-eluting stent (Xience, Abbott Vascular) without an increase in stent thrombosis, which led to a change in the CE mark for the device. However, he added that the mean DAPT duration in the study was "much longer than three months" and that "the change in CE mark and the meta-analysis does not mean you can stop DAPT after three months. It showed it can be done in selected cases." According to Cuissset, there is the potential for shorter DAPT duration with the latest generation of stents because they have been designed to lower the risk of stent thrombosis. He said: "They have thinner struts with abluminal polymers that are biodegradable. However, this is not the case with the bioresorbable vascular scaffold (Absorb, Abbott Vascular). Its struts are two times thicker than next-generation drug-eluting stents." For example, he explained, it has a strut thickness of 150µm whereas the Synergy stent (an everolimus-eluting stent with a biodegradable polymer, Boston Scientific) has a strut thickness of 74µm. Cuisset added that at present, if using the bioresorbable scaffold, he uses 12-month DAPT for stable coronary artery disease, ST-segment elevation myocardial infarction (STEMI), and NSTEMI. He stated that he is a co-principal investigator of the ongoing SENIOR study, which is comparing the rate of major adverse cardiovascular or cerebrovascular events in patients undergoing PCI with the Synergy stent compared with those undergoing PCI with a bare metal stent (Omega/Rebel, Boston Scientific). For all patients, DAPT will be given for one month if they have stable angina/silent ischaemia or for six months if they have an acute coronary syndrome.

Thomas Cuisset

Dual antiplatelet therapy

No definite answers about DAPT duration after PCI

Individualised DAPT

In the absence of a definite answer from clinical trials, Cuisset stated, the duration of DAPT should be based on the patient's individual risk of bleeding vs. the risk of stent thrombosis. He reported, therefore, he would consider shorter DAPT duration for patients who were older, at high risk of bleeding, already taking oral anticoagulation, had undergone single PCI with single vessel disease, not diabetic, or who had received a new-generation drug-eluting stent. However, he would consider longer DAPT duration for younger patients, those at low bleeding risk, had multivessel disease, had undergone complex PCI, had experienced prior stent thrombosis, had a STEMI, were diabetic, or who were receiving a first-generation drug-eluting stent.

Cuisset noted that another issue with DAPT duration is that the risk of stent thrombosis may reduce over the first month to the extent that the risk of bleeding becomes the greater risk. "Maybe we could change therapy according to the evolving risk of the patient. We know that in specific populations, balancing the risk of stent thrombosis vs. the risk of bleeding is more difficult. For example, the window between the risk of stent thrombosis and the risk of bleeding is even smaller in older patients. So, that is one population that could potentially receive great benefit from a new drug-eluting stent that allows a shorter duration of DAPT."

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Stent developments

Drug-eluting stents are a "work in progress"

Compared with first-generation drug-eluting stents, second-generation drug-eluting stents significantly reduce both target lesion failure and stent thrombosis. They, therefore, have become the gold standard devices for percutaneous coronary intervention (PCI). However, studies suggest that improvements in safety and efficacy with drug-eluting stents may still be needed.

Speaking at the Stenting in Complex PCI conference, Robert Byrne (Deutsches Herzzentrum, Technische Universität, Munich, Germany) reported that drug-eluting stent technology was still "very much a work in progress". He explained that a review[1] of 204 lesions in 149 autopsy cases (with duration of implantation between >30 days and ≤3 years) found that an everolimus-eluting stent was associated with significantly lower rates of late and very late stent thrombosis compared with paclitaxel- or sirolimus-eluting stents. However, he added that the review also found that rates of neoatherosclerosis and fracture-related adverse pathological events were comparable among devices.

Limitations of current devices

Byrne also noted that second-generation stents have "not done away with the problem of late catch-up". He explained that results from ISAR-TEST 4[2] showed that there were no significant differences in the rate of the primary endpoint (a composite of cardiac death, target vessel-related myocardial infarction or target lesion revascularisation) at three years between a sirolimus-eluting stent and an everolimus-eluting stent: 22.3% vs. 19.6% (p=0.26). Furthermore, according to Byrne, both first- (eg. the Cypher sirolimus-eluting stent, Cordis) and second-generation (eg. the everolimus-eluting Xience stent, Abbott Vascular and the zotarolimus-eluting Resolute stent, Medtronic) contain a methacrylate polymer (eg. PBMA). He stated: "PMBA degrades to the monomer methacrylic acid, which has proven cellular toxic effects."

Robert Byrne

Possible solutions

To overcome these limitations, drug-eluting stents with biodegradable polymers have been developed. Bryne explained that for these stents to become the gold standard rather than second-generation stents, they need to pass a "proof-of-concept" chain of investigation—including preclinical studies, human imaging studies, randomised controlled trials with early follow-up (to show non-inferiority), and randomised controlled trials with late follow-up (to show superiority). At present, randomised controlled data have indicated that drug-eluting stents with biodegradable polymers have comparable stent coverage at

six to eight months[3] and have also shown that they have comparable outcomes[4] at one year to permanent polymer stents (including everolimus-eluting stents).

However, a network meta-analysis[5] has indicated that drug-eluting stents with biodegradable polymers may increase the risk of stent thrombosis compared with everolimus-eluting stents with permanent polymers. For Byrne, these data (as with all data from network meta-analsyses) need to be "interpreted with caution," commenting that the authors of this particular meta-analysis (Palmerini *et al*) only looked at one drug-eluting stent with a biodegradable polymer (Biolimus A9, Biosensors) and that "not all drug-eluting stents with biodegradable polymers are equal". He added that another study[6] found that a sirolimus-eluting stent with a biodegradable polymer had comparable outcomes to an everolimus-eluting stent with a permanent polymer at five years.

"A stent is composed of many components, including a stent backbone and coating, the drug coating and the drug load—all of these may play a role. We have certainly realised over the last four to six years that strut thickness is important as far as thrombotic risk is concerned," Byrne noted. He reported that, in an animal model, Kolandaivelu *et al*[7] found that "optimal stent geometries and surfaces, as demonstrated with thin stent struts, help reduce the potential for thrombosis despite complex stent configurations and variability in deployment".

Byrne commented: "New generation drug-eluting stents with bioresorbable polymers with improved backbones and thinner struts promise to further improve patient outcomes over the medium to long term." He added that, in his view, he thought such stents may become the "workhorse" drug-eluting stent of the next five to 10 years, commenting: "Outcomes for drug-eluting stents with biodegradable polymers beyond five years remain unclear but all other things being equal, I would prefer a stent without a polymer."

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New data

EVOLVE II continues to show promise of Synergy stent

The EVOLVE II study, which was presented by Dean Kereiakes (The Christ Hospital Heart and Vascular Center/The Linder Research Center, Cincinnati, USA) at the American Heart Association Scientific Sessions (15–19 November, Chicago, USA), showed that an everolimus-eluting stent with a biodegradable polymer (Synergy, Boston Scientific) was non-inferior to an everolimus-eluting stent with a permanent polymer (Promus Element Plus, Boston Scientific). It is one of several studies to suggest that the device may be a useful addition to the interventional cardiologist's armamentarium.

Patrizia Presbitero (Department of Invasive Cardiology, Humanitas Mirasole Clinic, Rozzano, Milan, Italy) noted, at the Stenting for Complex PCI meeting, that a polymer on a drug-eluting stent "had no function after drug release is complete". She added that permanent polymers potentially increase the risk of late or very late stent thrombosis and that patients who receive a stent with permanent polymer, because of this possible risk of late or very late stent thrombosis, may require long-term dual antiplatelet therapy. Therefore, a stent with a biodegradable polymer may have advantages over a stent with permanent polymer.

The Synergy stent is one of the latest stents with a biodegradable polymer to be developed. It has a thin strut platinum chromium platform (74µm), a PGLA polymer coating (4µm thick), and eluts everolimus (100µg/cm2). Presbitero said: "The drug disappears from the stent in the first three months and the polymer disappears one month later—so by four months, it is like a bare metal stent. Compared with other biodegradable polymer stents, the absorption is quite quick". She noted that the polymers of the Nobori (Terumo) and Biomatrix (Biosensors) stents took more than nine months to absorb, the polymer of the Orsiro (Biotronik) took more than 12 months, and the Absorb (Abbott Vascular) bioresorbable vascular scaffold took more than two years to absorb (the complete scaffold disappears).

EVOLVE I and EVOLVE II

Data from the first human trial of the Synergy stent, EVOLVE I,[1] has already shown that the device is non-inferior to an everolimus-eluting stent (Promus Element, Boston Scientific) at one year for the management of *de novo* coronary lesions. Stefan Verheye (Antwerp Cardiovascular Institute, Antwerp, Belgium), who presented the data at the 2012

Patrizia Presbitero

EuroPCR meeting, said at the time: "The six-month intravascular ultrasound data suggest antirestenotic activity is maintained with the Synergy stent, even after four months, when the drug and polymer coating are designed to be absorbed. Importantly, the Synergy stent has shown equivalent clinical and safety and effectiveness in the EVOLVE data compared to the Promus Element stent."

The aim of the EVOLVE II study was to provide support for FDA approval for the Synergy stent (which was awarded the CE mark on the basis of the EVOLVE data). If the stent is approved on the basis of the study, it will be the first drug-eluting stent

New data

EVOLVE II continues to show promise of Synergy stent

with a biodegradable polymer to be approved in the USA. In the study, 1,684 patients (in 19 countries across 150 centres) with ≤3 *de novo* coronary lesions in ≤2 major epicardial vessels (average lesion length ≤34mm) were randomised to undergo percutaneous coronary intervention (PCI) with the Synergy stent (842 patients) or the Promus Element Plus stent (842). Presbitero commented: "I want to highlight that the average age of patients was quite high (63.5±10.4 for Synergy and 63.9±10.5 for Promus Element Plus). The percentage of patients with diabetes was also relatively high—31.1% of patients in the Synergy arm and 30.8% of patients in the Promus Element Plus stent arm. Furthermore, I would like to underline that patients with non-ST-segment elevation myocardial infarction [NSTEMI] were enrolled. Therefore, the study population is quite complex and similar to one that we see in our cath labs." Additionally, in both arms, just under a quarter of patients had small vessels (reference vessel diameter of <2.25mm) and nearly 20% had a lesion length of >20mm.

The primary endpoint of the study was the rate of target lesion failure (a composite of cardiac death, target vessel related myocardial infarction, or target lesion revascularisation) at 12 months with follow-up through to five years. Additional endpoints included the individual components of target lesion failure, stent thrombosis, technical success, clinical procedural success, and longitudinal stent formation. All patients were given dual antiplatelet therapy for six months or longer if tolerated (the protocol mandated DAPT for at least six months). Presbitero noted: "If the p value from the one-sided Farrington-Manning test was <0.025, Synergy was seen as being non-inferior to Promus Element Plus."

Results

According to Presbitero, the Synergy stent was associated with significantly better technical success—98.3% vs. 96.9% for Promus Element Plus (p=0.04). She said this difference was probably due to the "extreme flexibility" of the Synergy stent. There were no other significant differences in the procedural characteristics, but Presbitero noted that a case of longitudinal stent deformation that was reported in Synergy arm (the rate was 0.1% in each arm) actually occurred with the Promus Element Plus device that was used in a patient in the Synergy arm; therefore, no cases of longitudinal stent deformation actually occurred with Synergy stent implantation.

At 12 months, there were no significant differences between groups in the rate of the primary endpoint in either the intention-to-treat population (6.5% for Promus Element Plus vs. 6.7% for Synergy; p=0.005 for non-inferiority) or the per protocol population (6.4% for both arms; p=0.0003 for non-inferiority). There were also no significant differences in any of the components of the primary endpoint. There were five cases of stent thrombosis (two definite and three probable) with Promus Element Plus and three cases (two definite and one probable) with Synergy—a non-significant difference (p=0.5). Presbitero commented: "If you look more deeply at the cases of the stent thrombosis with Synergy, the two cases of definite stent thrombosis occurred within the first 24 hours. Therefore, they were very much related to the implanting of the stent. The one case of probable stent thrombosis occurred in the first week—there were no cases of probable or definite stent thrombosis after six days." The cases of definite/probable stent thrombosis with the Promus Element Plus stent all occurred within the subacute phase (two to 30 days post procedure).

She concluded: "In this pivotal, non-inferiority trial designed to support approval of the first drug-eluting stent with a biodegradable polymer in the USA, the Synergy stent proved non-inferior to the Promus Element Plus stent for target lesion failure at one year. Procedural angiographic and clinical outcomes were comparable between stents in a 'more comers' population." Presbitero added: "The longer term relative efficacy and safety of the Synergy stent is currently under evaluation."

Synergy trials

EVOLVE II is one of several trials that form part of Boston Scientific's trial programme for the Synergy stent. As well as the aforementioned EVOLVE I, there is also EVOLVE II QCA, EVOLVE China, and EVOLVE DAPT. EVOLVE II QCA is a registry study that has enrolled 100 patients, across 10–15 sites, to evaluate late lumen loss (with quantitative coronary angiography) at nine months in patients who have received the Synergy stent. EVOLVE China is also looking at late lumen loss at nine months, but is a randomised controlled trial rather than a registry. Its aim is to provide support for regulatory approval of the Synergy stent in China and is currently enrolling up to 400 patients (across 15 sites) to compare late lumen loss with the Synergy stent with that of the Promus Element Plus stent. EVOLVE DAPT, which has yet to start enrolling patients (4,000 patients is the goal), has been designed to compare three-month dual antiplatelet therapy (DAPT) with 12-month DAPT in patients who undergo PCI with the Synergy stent. The primary endpoint is cardiac death or myocardial infarction.

Further to the trials in the Boston Scientific trial programme, there are also several investigator-sponsored studies of Synergy. For example, there is the real-world, the all-comers SORT OUT VIII study (comparing Synergy with Biosensors' BioMatrix NeoFlex), TRANSFORM OCT (comparing Synergy with Resolute Integrity) study, and the aforementioned SYNTAX II study. Overall, there are more than 20 studies involving more than 20,000 patients being treated with the Synergy stent. A high proportion of these studies are investigator led.

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