Tullio Palmerini, MD

Dr. Palmerini discusses outcome prediction tools, revascularization strategies, and his ongoing research on optimal DES use and antiproliferative drugs.

Is there hesitance among the interventional cardiology community to adopt drug-eluting stents (DES) as a primary approach to coronary intervention? What level of evidence might it take to convince naysayers?

Although first-generation DES have significantly improved the outcomes of patients undergoing percutaneous coronary revascularization by significantly reducing the risk of ischemia-induced target vessel revascularization, concern has been raised over their ongoing propensity for the risk of very late stent thrombosis. This concern had a significant impact on daily clinical practice, with the use of DES in the United States decreasing from rates of almost 90% before 2006 to a nadir of 60% in the following years.

Second-generation DES have therefore been developed to overcome the flaws of first-generation DES by using different stent platforms, alternative drugs, and more importantly, either bioabsorbable or more biocompatible durable polymers. Several studies have consistently shown a better safety profile for second-generation DES compared to first-generation DES, and therefore safety concerns about these new devices do not appear to be further justified.

During the past 18 months, you've published network meta-analyses of randomized clinical trials (one on stent thrombosis, one on STEMI patients) comparing bare-metal stents (BMS) and DES. What prompted you to conduct these analyses, and what finding was the most surprising to you?

In most trials investigating the use of cobalt-chromium everolimus-eluting stents (Co-Cr EES), a signal appeared suggesting that these devices could be associated with lower rates of stent thrombosis compared to other DES. However, most of these trials had a noninferiority design and therefore were insufficiently powered to detect significant differences in the risk of stent thrombosis. To investigate whether this signal was real or just the play of chance, we performed several meta-analyses, which confirmed the better safety profile of Co-Cr EES compared to the other first- and second-generation DES.

The most important and unexpected result of the network meta-analysis was that Co-Cr EES was associated with lower rates of stent thrombosis, not only compared to other DES, but even lower than BMS, which were considered the gold standard in terms of safety at that time. The network meta-analysis therefore suggested a paradigm shift from the contention that DES are associated with higher rates of stent thrombosis than BMS to the converse.

What do you think is driving this difference in performance?

DES are made of three components: the platform, the polymer, and the eluted antiproliferative drug. All these components interact with the vessel wall and the blood, characterizing the safety and efficacy profile of the device. In the case of Co-Cr EES, the thin-strut structure of the stent platform, the thromboresistant properties of the fluoropolymer, and the reduced polymer and drug load may contribute to the low rate of stent thrombosis associated with this device. In particular, fluorinated polymers have been shown to generate less thrombin activation and platelet aggregation compared to other types of polymers, and an in vitro study of stent perfusion suggested that Co-Cr EES was associated with lower platelet adhesion compared to its BMS counterpart. As the only difference between these two devices is the polymer, the results of that study are likely due to the thromboresistant properties of fluorinated polymers.

In your research on the predictors of potential negative outcomes, is there one predictor that stands out as deserving much more attention during preprocedural evaluation?

A major breakthrough of the SYNTAX trial was the demonstration that the complexity of the coronary anatomy, measured with the SYNTAX score, has a significant impact on the outcomes of patients treated with percutaneous coronary intervention (PCI) but not on those treated with coronary artery bypass surgery (CABG). The SYNTAX score is therefore a potent stratification tool that should guide physicians in selecting the

(Continued on page 73)

(Continued from page 74)
optimal strategy of revascularization between CABG and PCI in patients with multivessel coronary artery disease. The SYNTAX score has been validated in several clinical contexts, and it has been further refined in subsequent studies, improving its prognostication ability.

In studying strategy selection and risk assessment for revascularization of unprotected left main coronary artery disease, PCI had a higher risk of target vessel revascularization than CABG, but they were comparable otherwise. How do these findings affect your patient selection for PCI versus CABG?

The observation that PCI has similar rates of death and myocardial infarction, but higher rates of target vessel revascularization, compared to CABG comes mainly from observational studies or subgroup analyses of randomized trials, and therefore, it should be considered hypothesis generating. Current American and European guidelines endorse CABG as the treatment of choice for patients with unprotected left main coronary artery disease. However, there are several settings in which PCI of left main coronary artery disease has been shown to be safe and probably as effective as CABG, such as ostial and mid-shaft lesions, simple bifurcated lesions that can be treated with one stent, or in patients with left main coronary artery disease associated with a low to intermediate SYNTAX score (≤ 32).

I believe that the optimal strategy of revascularization for patients with left main coronary artery disease should be decided by the heart team, including an interventional cardiologist, surgeon, and anesthesiologist. The ongoing, multicenter, prospective, randomized EXCEL trial will better define the role of PCI relative to CABG in patients with unprotected left main coronary artery disease and SYNTAX score ≤ 32.

Although the stroke rate post-CABG has been consistently higher than with PCI, the extent of coronary artery disease does not seem to play a role (at 30 days and 1 year). What might account for these findings?

In a recent meta-analysis including randomized trials comparing CABG versus PCI for the treatment of coronary artery disease, surgical therapy was associated with higher rates of stroke than PCI, with no apparent interaction between the extent of coronary artery disease and the risk of stroke. However, the interaction analysis may have been underpowered, and a trend was apparent suggesting a greater difference in the risk of stroke between CABG and PCI in patients with left main disease, intermediate in patients with multivessel disease, and lower in patients with single-vessel disease. Therefore, further studies should investigate whether the higher risk of stroke with CABG than PCI is independent from the extent of coronary artery disease.

I believe that the optimal strategy of revascularization for patients with left main coronary artery disease should be decided by the heart team, including an interventional cardiologist, surgeon, and anesthesiologist.

What do you believe is the proper role of balloon aortic valvuloplasty in high-risk patients who are not suitable for surgery or transcatheter aortic valve replacement (TAVR)?

Balloon aortic valvuloplasty has very limited clinical indications including: (1) bridge to aortic valve replacement or TAVR in hemodynamically unstable patients, (2) treatment of patients with severe aortic valve stenosis who require urgent major noncardiac surgery, and (3) palliation for patients who are not eligible for surgery or TAVR. In this last category of patients, balloon aortic valvuloplasty can significantly improve symptoms and quality of life, but the prognosis of these patients remain poor.

Can you tell us about your experience with the CRF Scholars Program?

It is a fantastic experience and a unique opportunity to share ideas and research projects with outstanding physicians and scientists who are truly opinion leaders in the world.

What are your future areas of investigation?

We are currently following several lines of investigations including coronary thrombosis, biology of stent thrombosis, and antiplatelet and anticoagulant therapy, to mention only some of the ongoing projects. ■

Tullio Palmerini, MD, is with Dipartimento Cardiovascolare, Policlinico S. Orsola, University of Bologna in Bologna, Italy. He disclosed that he has received a lecture fee from and is on the advisory board for Abbott Vascular. Dr. Palmerini may be reached at +39 051 6364522; tulliopalmerini@hotmail.com.