

or intravascular imaging endpoints. The recent PICCOLETO II (Drug Eluting Balloon Efficacy for Small Coronary Vessel Disease Treatment) trial (1) was a randomized comparison of a drug-coated balloon with an everolimus-eluting stent in patients with de novo lesions in small coronary vessels. The primary endpoint, late lumen loss (LLL) at 6-month angiographic follow-up, was reduced in patients treated with drug-coated balloons compared with drug-eluting stents.

LLL is an inappropriate primary endpoint for coronary interventional trials that compares stenting with balloon treatment. In the first randomized stent trials, Benestent (2) and Stress (3), LLL was greater with bare-metal stents than after balloon angioplasty, but stents were beneficial because the immediate post-procedural gain was much greater, which more than offset the LLL. At 6-month angiography, the mean minimum luminal diameter was greater, the mean percentage diameter stenosis was less, and the proportion of patients with >50% diameter stenosis was reduced in stented patients.

In the PICCOLETO II trial, acute gain was approximately 50% greater in the drug-eluting stent than the drug-eluting balloon group, so it is unsurprising that there was more LLL in stented patients. What is important is the size of the lumen at follow-up, not how much of the initial gain was lost. Either mean percentage stenosis or mean minimum luminal diameter (which did not differ between treatment groups) would have been a more appropriate primary endpoint. Only 7 of 214 (3%) patients followed to 12 months died or had myocardial infarction; a much larger trial is needed to assess the relative safety of the 2 strategies.

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## REPLY: Seeking an Appropriate Primary Endpoint for Trials Comparing DCB and DES



*“The owl of Minerva spreads its wings only with the falling of the dusk.”*

—G.W.F. Hegel, *Philosophy of Right* (1821) (1)

We appreciate the letters from Dr. Byrne and colleagues and Dr. Ormiston and colleagues regarding our publication of the PICCOLETO II (Drug Eluting Balloon Efficacy for Small Coronary Vessel Disease Treatment) study (2), which tested new-generation drug-coated balloons (DCB) with drug-eluting stents (DES). However, we would also like to make some considered comments. Late lumen loss (LLL), we fully agree, is not a perfect measurement for assessing the difference between stent-based or a drug-coated balloon-based technology, providing some advantages to the latter (3). We should also keep in mind that the mechanisms of these 2 strategies to reduce recurrences are truly different: DES block acute vessel recoil and suppress neointimal hyperplasia, whereas DCB prevent tissue proliferation without sharing the metal-mediated more aggressive neointimal hyperplasia induced by stents due to larger and persistent vessel wall injury (larger acute gain leading to larger late loss) (3). However, we still wonder whether there is an “impartial” measurement for the matter, knowing also that other endpoints, such as percent diameter stenosis, may yield several drawbacks in terms of reliability. We also fully agree that other already used modalities, including minimal lumen diameter at follow-up, may be more impartial arbiters, but this comes at the expense of experiences that were not yet available back in 2014 (see Hegel citation [1]). However, LLL is particularly important in small vessels: some previous studies in the same setting (4,5) selected LLL as the primary endpoint, providing an interesting framework as reference.

Indeed, our study conclusions remain correct and scientifically sound because we considered also those depicted angiographic endpoints: the “PICCOLETO II trial for the first time shows the angiographic superiority in terms of LLL, and the equivalence in terms of [minimal lumen diameter] and percent diameter stenosis” (2).

The real problem here is that we would like to know whether a patient fares better with one treatment instead of the other in terms of hard clinical endpoints, whereas all of these angiographic endpoints are just surrogates. Besides, minimal lumen diameter is far from being a perfect endpoint. In a given segment, what is important is to know how many stenoses are there, not just the narrowest one, because the impact on distal flow and its turbulence is determined by all of them. In this regard, recent developments suggest using different endpoints to have more reliable substitutes of clinical endpoints: 1) intravascular imaging to depict more detailed and comprehensive anatomic information and to inform on the best treatment strategy; and 2) physiology-derived data, including new noninvasive tools such as quantitative flow ratio, to provide more reliable information (functional significance) on the vessel flow distal to the lesion(s).

In the end, we believe that dogmas in interventional cardiology should not exist: any endpoint is the son of its period, and the endpoint of tomorrow is always a better one.

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## TO THE EDITOR

# Transcatheter Pulmonary Valve Replacement With 32-mm Balloon-Expandable Prosthesis



## Another Strategy in Mildly Dilated RVOT

Congenital and acquired pulmonary valve disease has been shown to be suitable for transcatheter pulmonary valve replacement. However, right ventricular outflow tract (RVOT) morphology and dimension may limit implantation of currently available devices. Kamioka et al. (1) recently showed how downsizing the RVOT using commercially available endografts could allow implantation of a 29-mm Sapien-3 valve (Edwards Lifesciences, Irvine, California) even in severely dilated RVOT. We would like to suggest another possibility to treat mildly dilated RVOT: oversizing of a large balloon-expandable prosthesis.

A patient recently presented with severe pulmonary regurgitation, severe right ventricle overload, and effort dyspnea 41 years after surgical Fallot correction. Computed tomography revealed an RVOT landing zone diameter of 27.8 mm (area 604 mm<sup>2</sup>). Without landing zone calcification (Figure 1), a 20% area oversizing was considered necessary for balloon-expandable prosthesis anchoring, thus achieving an area of 725 mm<sup>2</sup>. A 29-mm balloon expandable valve was deemed too small to fit in this anatomy.

Myval (Meril Life Sciences, Gujarat, India) is a balloon-expandable prosthesis that recently gained CE approval for larger sizes (30.5 mm and 32 mm) in the aortic position. The 32-mm Myval fits virtual basal ring ranging from 700 to 840 mm<sup>2</sup> and was deemed suitable for this RVOT anatomy. A Lunderquist wire (Cook Medical, Bloomington, Indiana) was advanced over a multipurpose catheter in the right pulmonary artery. The prosthesis was then implanted easily in the RVOT landing zone, achieving ideal anchoring with no paravalvular leak (Figure 1). Post-procedural course was uneventful. Follow-up echocardiography showed normal transprosthetic gradient (mean gradient 8 mm Hg) and no paravalvular leak.

This case highlights how significant oversizing (up to 20%) of balloon-expandable prosthesis may be a valuable option for transcatheter pulmonary valve replacement with mildly dilated RVOT, thus avoiding endograft implantation.