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Editorial

Small Coronary Vessel Size: A Great Need for a Standardized Definition

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"The beginning of wisdom is a definition of terms."

-Socrates

In this issue of *JSCAI*, Sanz-Sánchez et al[1] propose that a reference vessel diameter (RVD) of <2.5 mm measured with intracoronary imaging (ICI) should be adopted as the standardized definition of small vessel coronary artery disease (CAD). They correctly note that there is currently no standardized definition for small vessel CAD and suggest that adopting this definition may be useful to guide both clinical decision-making and future clinical trials.

The authors should be applauded for their commitment to addressing this important issue and for performing a comprehensive systematic review of the literature on this topic. The adoption of a standardized definition for small vessel CAD could be clinically useful for several reasons. For example, smaller coronary arteries may be more vulnerable to the impact of stent malapposition and, therefore, may be best treated differently than larger vessels (ie, balloon-based modalities may be more beneficial in smaller vessels). Although we agree with the authors that there is a clear need to adopt a standardized definition for small vessel CAD, there are some points that should be considered when evaluating their proposal.

Despite the fact that the authors performed a comprehensive systematic review, they also reported that the high degree of heterogeneity among the trials prevented them from performing a pooled comparison according to vessel size. The sources of this heterogeneity included both the use of different methods to assess the RVD and the use of implanted stent size to define vessel size in some studies. The authors are correct to suggest that implanted stent size cannot be reliably taken as indicative of the true vessel size. Stents may be over- or undersized relative to the vessel, and there is a recognized association between stent undersizing and an increased risk of recurrent major adverse coronary events, which would be an important potential confounder of the reported results.[2] Another potentially important point in considering vessel size is that reference vessel size is not uniform along the length of a coronary vessel. A previous angiographic study of normal coronary arteries reported that the average proximal left anterior descending coronary artery diameter was 3.7 ± 0.4 mm, whereas the distal left anterior descending coronary artery diameter was 1.9 ± 0.4 mm.[3] Indeed, the coronary tree has been shown to observe a fractal geometric pattern as the various vessels bifurcate and give rise to daughter vessels.[4] As such, it may be more accurate and meaningful to refer to the size of a vessel segment rather than of the entire vessel.

Given that the authors were unable to perform a pooled comparison of the identified studies, they primarily reference an analysis of the DUrable Polymer-based STent CHallenge of Promus Element Versus ReSolute Integrity (DUTCH PEERS) trial to support their proposed definition for small vessel CAD.[5,6] In this study, outcomes were evaluated for patients treated for lesions in at least 1 small coronary vessel (<2.50 mm) and compared with those in patients with target lesions in larger-sized vessels (≥2.50 mm). The authors appear to have based their proposed definition of small vessel CAD on a threshold that maximizes the difference in risk of adverse outcomes[5]; however, the interpretation of observational data of this nature may be challenging for several reasons. First, the baseline characteristics of the small vessel and larger-sized vessel groups were markedly different, with an increased prevalence of diabetes mellitus, previous myocardial infarction, and stable angina pectoris in the small vessel group.[5] Multivessel treatment, chronic total occlusions, and bifurcation lesions were all also more frequently encountered in the small vessel group. Moreover, the total stented length was longer in the small vessel group, with a greater number of stents implanted. Therefore, the increased incidence of major adverse cardiac events in the small vessel group may have been influenced by these differences in baseline patient, lesion, and procedural characteristics. Although propensity score analysis was used to adjust for potential confounders, it is recognized that there are limitations to the use of this statistical technique in some settings.[7] This can relate to the presence of unmeasured confounders that are not incorporated into the propensity score, and propensity score matching may, in some circumstances, actually increase imbalances between the 2 groups.[7] As such, we should, at the very least, be circumspect when interpreting the findings of this analysis.[5]

Another important point to consider when discussing small vessel CAD is that the capacity for small vessels to induce ischemia and benefit from percutaneous coronary intervention (PCI) may be reduced

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compared with larger vessels because the benefit of myocardial revascularization is related not only to the degree of coronary stenosis but also to the volume of subtended myocardium.[8] As such, the risk-benefit ratio of PCI may be different for small vessels compared with larger vessels and this will also be an important consideration for physicians, in particular for PCI in the setting of chronic coronary syndromes. Drug-coated balloons have been proposed as a valuable therapeutic alternative to stents in this patient population, and although early results have shown some promise, further data are required.[9-12] A relevant point in this regard is that the definition of small vessel disease in these studies has varied, highlighting the need for standardization.

The authors conclude by proposing that an RVD of <2.50 mm measured with ICI should be used as the cutoff value for classifying small coronary vessels. Indeed, although the authors are correct in stating that it could be useful to adopt a "standardized definition" for small vessel CAD, the requirement for ICI to define this may be challenging given the relatively low use of ICI in real world clinical practice.[13] It may be overly optimistic to think that the assessment of small vessel CAD would represent an indication that would result in a sufficiently increased frequency of ICI use on a day-to-day basis in the cardiac catheterization laboratory, particularly given the technical challenges that may be associated with performing ICI in smaller vessels with a more distal arterial location. Therefore, from a practical perspective, this would suggest that angiographic assessment will be the only viable method for consistently defining small vessel CAD in clinical practice; however, as the authors correctly note in their limitations, angiographic assessment of vessel size remains limited, particularly in the setting of diffuse CAD.

On a final note, although it remains to be seen whether their proposed definition will be adopted in clinical practice, the authors are to be congratulated for addressing this important issue in their study, which will offer valuable guidance to future dedicated randomized controlled trials with the objective of assessing different therapeutic strategies in patients with lesions in smaller caliber coronary arteries.

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