EDITORIAL COMMENT

The Synergy Between Percutaneous Therapies and Noninvasive Diagnostic Imaging*

James K. Min, MD
New York, New York

The whole is greater than the sum of its parts. (1)
—Aristotle

In only the past few years, we have witnessed innovations in percutaneous coronary intervention and noninvasive imaging that promise to “disrupt” the treatment and diagnosis of coronary artery disease (CAD). At first glance, these technologies appear disconnected from one another, with little overlap for clinical use. Yet, as Onuma et al. (2) describe in an elegant study published in this issue of JACC: Cardiovascular Interventions, these technologies, when combined, hold the potential to encourage a new clinical paradigm that may enhance the treatment and follow-up of patients with CAD in a safe, clinically effective, and economically efficient manner.

As the fourth in the generation of percutaneous coronary stents, bioabsorbable drug-eluting vascular scaffolds (BVS) have emerged as an effective platform that rivals, if not exceeds, prior drug-eluting stents for safety and efficacy. As 1 example, the fully resorbable everolimus-eluting Absorb BVS, the particular stent evaluated in the present study, couples an antiproliferative kinase inhibitor with a scaffold composed of poly-l-lactide (PLLA) and poly-D,L-lactide (PDLLA), both of which are naturally metabolized by the body via the Krebs cycle to water and carbon dioxide (3). The rationale behind this type of stent is obvious, and early studies have substantiated the safety of BVS stents, with no observed stent thromboses and with major adverse cardiovascular event rates that are comparable to those seen with latest generation drug-eluting stents (4). In the study by Onuma et al. (2), long-term ischemia-driven major adverse cardiovascular events after Absorb BVS implantation were evaluated and occurred at an incidence of 3.4% at 5 years, which was unchanged from the 1-year and 2-year follow-up studies. Given the bioabsorbable design, these scaffolds demonstrate lucency by both invasive (angiography and optical coherence tomography) and noninvasive (coronary computed tomographic angiography [CCTA]) imaging.

The latter of these techniques has also witnessed numerous technological advancements. Since the introduction of 64-detector row CCTA in 2005, several multicenter trials have established the high diagnostic performance of CCTA, which, when compared with a quantitative angiographic reference standard, exhibits an ability to identify and exclude anatomic-ally obstructive CAD in a manner superior to that of other noninvasive tests (5). Importantly, for patients without known CAD, the negative predictive value to exclude obstructive CAD in native coronary arteries approaches 100%.

Despite this, for patients with known CAD, particularly for those with prior metallic stent implantation, the diagnostic performance of CCTA is generally poor, with a high rate of nonevaluable stents. The primary diagnostic challenge of CCTA for stents, particularly smaller stents, is related to partial volume effects, a phenomenon that relates to the limited spatial resolution of current-generation CCTA. Because of these limitations, aside from evaluation of left main stents $\geq 3$ mm in diameter, the most current American College of Cardiology appropriate use criteria consider the use of CCTA for the evaluation of metallic stents as inappropriate (6). This contrasts starkly with 35 clinical indications for which CCTA for native coronary arteries is considered appropriate.

Yet even with improved resolution, CCTA alone does not provide physiologic information such as that enabled by invasive fractional flow reserve (FFR), thus precluding its ability to identify stenoses that reduce coronary flow and pressure. Recently, however, FFR derived from CCTA (FFRCT) has emerged an adjunctive test to CCTA for the diagnosis of hemodynamically significant coronary stenoses. In 2 prospective multicenter studies, FFRCT compared favorably with invasive FFR (7,8). Advantageously, FFRCT can be performed on any typically acquired CCTA, thus negating the need for additional imaging, administration of medications, or added radiation dose. In addition, given the entire patient-specific arterial geometry provided by CCTA segmentation, an FFR value can be calculated at any point in the coronary vascular bed, thus delivering a comprehensive “3-vessel” FFR from a single noninvasive test.

The study by Onuma et al. (2) combines these seemingly disparate therapeutic and diagnostic technologies to evaluate the feasibility of a new clinical paradigm: implantation of a BVS stent with follow-up evaluation by CCTA and FFRCT. Given the lucency enabled by resorption of PLLA and PDLLA in the Absorb BVS stents, initial images from
CCTA of BVS appear strikingly similar to those of native coronary arteries. In the present study, CCTA was evaluable in 18 of 18 patients, with quantitative measures of minimal luminal area, and FFR_{CT} was feasible in 13 of 18 patients who underwent CCTA. These are important findings and have potentially large ramifications, given the common occurrence of patients’ presenting with symptoms after stent placement and the frequent need for invasive and costly testing.

In this regard, the study by Onuma et al. (2) raises 2 important noninvasive possibilities. First, aside from radiopaque platinum markers at the ends of the Absorb BVS stent, the stented coronary artery segments appear indistinguishable from native coronary artery segments, thus raising the possibility that CCTA may rule out in-stent restenosis in these segments with the near 100% accuracy that is observed for native coronary arteries. Second, even among those identified with in-stent restenosis, the concomitant use of FFR_{CT} raises the opportunity to evaluate the physiologic significance of any identified lesion.

Given the small study sample of the present investigation, these goals could not be fully evaluated but rather are presented as a “proof-of-principle” study. This feasibility study allowed the performance of CCTA at sites to be dictated by local site practices rather than by guideline-based methods but did required pre-study site certification to demonstrate the quality of CCTA. Furthermore, blinded independent core laboratories provided interpretation of both CCTA as well as FFR_{CT}, thus rendering this a diagnostic efficacy rather than effectiveness study.

Thus, although exciting as a novel clinical paradigm for the treatment of patients receiving Absorb BVS stents with follow-up by CCTA and FFR_{CT}, numerous questions beyond those already raised remain that require answers before this approach can be widely adopted. Perhaps most important, this study evaluated only single stents ≥3 mm in diameter for simple anatomic lesions, and the feasibility of CCTA for Absorb BVS stents <3 mm remains in need of further investigation. Also, although each of the patients in this small study could be evaluated by CCTA, more than one-fourth could not be evaluated by FFR_{CT}. Future larger studies determining the rate of well-performed CCTA than can be evaluated by FFR_{CT} in this population appear needed. A prospective multicenter European FFR_{CT} trial is ongoing, and with enrollment completed, these study results may inform this question. Furthermore, although the present study examined the long-term appearance of the Absorb BVS stent, the use of CCTA in the near-term period after implantation is still in question. PLLA and PDLLA fully absorb by 9 and 36 months, respectively, and clinical data regarding the appearance on CCTA of the Absorb BVS over time are not yet fully available. In addition, although the initial appearance of the Absorb BVS on CCTA appears to replicate that of native coronary arteries, whether the diagnostic performance of CCTA for BVS stents is superior to traditional metallic stents remains unknown. Head-to-head comparison studies are now needed. Finally, the use of Absorb BVS followed by use of noninvasive testing for the evaluation of patients with suspected in-stent restenosis seems is intuitively safer and more economically efficient, but cost-effectiveness studies are now indicated.

In sum, Onuma et al. (2) should be commended for combining the use of seemingly disparate invasive and noninvasive technologies into a single common clinical paradigm. Although only a feasibility investigation, their study results raise hope for a safer method of treatment and follow-up for patients with CAD who require percutaneous interventions. By uniting these different methods into a single clinical pathway, they have taken the first step toward substantiating Aristotle’s claim that the whole is greater than the sum of its parts.

Reprint requests and correspondence: Dr. James K. Min, Departments of Radiology and Medicine, Weill Cornell Medical College and the New York-Presbyterian Hospital, 520 East 70th Street, Starr Pavilion 8A19, New York, New York 10021. E-mail: jkm2001@med.cornell.edu.

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