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EDITORIAL COMMENT

The Prognostic Value of Cardiac CT After Coronary Artery Bypass Surgery

As Easy as 1, 2, 3?*

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Over the past decade, coronary computed tomographic angiography (CTA) has emerged as a useful noninvasive test to evaluate selected low-to-intermediate risk patients with suspected coronary artery disease (CAD). In this population, the absence of coronary stenoses on CTA can exclude the presence of obstructive disease with a negative predictive value that exceeds 90%. Coronary CTA

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can also detect nonobstructive plaque, which signifies the presence of subclinical disease and often leads to intensification of medical therapy for primary prevention (1). However, in higher risk populations, the potential advantages of CTA can be offset by the fact that the functional significance of a moderate to severe stenosis (i.e., >50%) is often unknown (2). A physiological assessment of lesion severity is often required, especially in patients for whom coronary revascularization is being considered.

The evaluation and management of symptomatic patients after coronary artery bypass graft (CABG) surgery represents a challenging area for clinicians. Notably, these patients—who are rarely included in clinical trials—have increased morbidity and mortality rates when undergoing repeat revascularization, whether percutaneous or surgical. The cause of ischemic symptoms in this population may be due to disease involving either or both of the native coronary arteries and bypass conduits. At 10 years after CABG surgery, approximately 50% of vein grafts and 10% of internal mammary arterial grafts are occluded (3); long-term patency rates with radial grafts are less well established. Consequently, when assessing the prognosis of patients after CABG surgery, it is essential to integrate data on the integrity of both the native coronary and bypass graft circulations (4). Other important variables include left ventricular systolic function, arrhythmic substrate, mitral regurgitation, diabetes, and the scope and intensity of medical therapy.

The noninvasive evaluation of symptomatic patients after CABG surgery has traditionally relied on the assessment of myocardial perfusion and function. More recently, it has been shown that coronary CTA can accurately identify the presence of stenosis in both venous and arterial bypass grafts (5). However, the diagnostic accuracy of CTA to evaluate the native coronary arteries in patients with previous CABG is limited by extensive vessel wall calcification frequently observed in those with chronic CAD. In addition, the evaluation of bypass grafts with CTA is vulnerable to artifacts from metal clips. Such artifacts can be particularly problematic if they occur at the site of the distal graft anastomosis, a location that demands careful evaluation.

In this issue of the *iJACC*, Chow et al. (6) report the first study evaluating the prognostic value of coronary CTA in patients with previous CABG surgery. They followed 250 patients who had previous CABG surgery over a mean of 20.8 ± 10.0 months using a composite hard endpoint of cardiac death and nonfatal myocardial infarction.

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To capture anatomic information regarding both native coronary arteries and bypass grafts, patients were categorized according to the number (i.e., 0, 1, 2, or 3) of unprotected coronary territories (UCTs). An unprotected territory was defined by: 1) significant obstructive CAD in a native, ungrafted vessel; 2) significant obstructive CAD in a native vessel distal to the site of graft anastomosis; and 3) significant obstructive disease involving both the native artery and its bypass graft. Using this index, the observed annual event rate (cardiac death, nonfatal myocardial infarction) was 2.4%, 5.8%, 11.1%, and 21.7% for patients with 0, 1, 2, or 3 UCTs, respectively. Thus, the number of UCTs enabled the identification of patient subgroups with progressively worse outcomes. Furthermore, the authors suggest that number of UCTs may provide prognostic information incremental to that which is available from routine clinical variables.

This investigation advances our knowledge regarding the application of coronary CTA to CABG patients and supports the biologically plausible hypothesis that the prognosis of these patients depends on the integrity of both the native coronary arteries and bypass grafts. However, the findings of this study must be interpreted with caution. First, to identify the incremental value of any imaging study, it is important to consider all the nonimaging risk markers that are typically available to clinicians. In this study, the authors chose to incorporate clinical variables and scoring systems targeted traditionally to patients considered at risk of CAD. Their applicability to a population of patients with established CAD is limited. It is not surprising that the clinical model used in this study had a poor ability to discriminate between patients with and without events (*c*-statistic: 0.61). Although the addition of the UCT index improved the c-statistic, it may not have done so to this extent if the clinical model had been more robust, with inclusion of other variables such as left ventricular ejection fraction, time since revascularization, type of conduits used, intensity of medical therapy, and smoking status.

A second limitation of the study is that, by definition, the categorization of the number of UCTs also relies heavily on the ability to evaluate small-caliber distal vessels. However, as discussed previously, the majority of patients with a previous CABG have significant degrees of native vessel calcification that render many segments nonassessable. In the study by Chow et al. (6), readers were forced to provide "their best educated guess" for nonassessable segments (patients were only excluded if there were >5 nonassessable segments, a criterion that only applied to 10 patients). Although specific data regarding the number of nonassessable segments are not provided, it is almost certain that there were far more nonassessable segments involving native coronary arteries than bypass grafts.

A useful statistic used in this study is the net reclassification index (NRI). The NRI is a proportion that represents the *net* number of individuals in whom events develop who are appropriately up-classified to a higher risk category *plus* the number of patients in whom events do not develop who are appropriately down-classified to a lower risk category (7). The authors report an NRI of 27%, suggesting that that the proportion of patients who were appropriately up-classified or down-classified minus the proportion of patients who were inappropriately up-classified or down-classified was approximately one-fourth. Although this is a sizable proportion, the NRI provided in this paper is difficult to interpret because the NRI depends on the categories of risk chosen. These categories must be clinically meaningful (i.e., patients in different categories will be treated differently) because a benefit could only occur if reclassification would lead to differences in patient management. As noted, the categories of risk chosen in this study (<10%, 10% to 20%, >20%) are less applicable to the management of patients with established CAD after CABG surgery, particularly because most are, by definition, high risk.

If we calculate the components of the NRI in this study, we observe that among the 23 patients who experienced events, the NRI was approximately −4% (4 were up-classified, whereas 5 were inappropriately down-classified). Among the 227 patients who experienced no events, the NRI was approximately 32% (80 were down-classified, whereas 7 were inappropriately up-classified). This suggests that the benefit captured by the NRI statistic was entirely driven by the ability of the UCT index to appropriately down-classify patients in whom events did not occur. Although 94% (80 of the 85) of patients who were down-classified experienced no events, only 4 of 11 patients who were up-classified experienced events (it is unknown whether any of them were revascularized). These findings are consistent with the known high negative predictive value of coronary CTA and suggest that its positive predictive value for identifying patients who experienced adverse events is more limited.

How can the information provided by this study be used to improve patient outcomes? Intuitively,

we would want to treat higher risk patients more aggressively. However, most such patients should already be on evidence-based secondary prevention therapy with aspirin, statins, beta-blockers, and angiotensin-converting enzyme inhibitors when indicated. The next most relevant question is whether patients with increased UCT indices would benefit from repeat coronary revascularization. Given that both symptoms and the physiological significance of a lesion are important predictors of the benefit of coronary revascularization, future studies should examine the incremental value of combining the anatomic data obtained with coronary CTA with functional data derived from myocardial perfusion imaging.

Although the number of UCTs is a useful marker, which integrates data on clinically relevant obstructive disease, it may not maximize the potential information that can be obtained with cardiac computed tomography. Future studies should incorporate data regarding: 1) the presence and extent of nonobstructive plaque in both native vessel and bypass grafts; 2) type of grafts used; 3) the presence and extent of previous myocardial infarction; and 4) global and regional left ventricular function. Such studies will require a large, ideally multicenter cohort with longer term follow-up.

In conclusion, the study by Chow et al. (6) provides important evidence that the anatomic information provided by coronary CTA is prognostically important and can identify patients with a high rate of cardiovascular death or myocardial infarction. So is an initial evaluation of coronary and bypass graft anatomy as easy as 1, 2, 3, a good starting point from which to separate low- from high-risk patients? The answer likely depends on the patient population studied. In the study by Chow et al. (6), 51% of patients had no abnormal territories (UCTs = 0), whereas <20% had ≥2 UCTs. Will this distribution of disease be observed in other centers? Can we identify better pre-imaging risk models that can help identify which patients should first be evaluated with coronary CTA versus those who may benefit from perfusion and functional imaging? Will patient management, and ultimately outcomes, be influenced by our imaging studies? If only it were *that* easy . . .

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