Before the emergence of noninvasive coronary angiography, we were able to gather detailed information on coronary arterial anatomy only in selected, high-risk patients undergoing cardiac catheterization. Multidetector computed tomography (CT) angiography opened the door to assessing a wide array of coronary arterial characteristics, in some ways surpassing the information available by invasive angiography, which can now be obtained in all patients with suspected coronary artery disease.\(^1\) Indeed, the information on coronary anatomic details from CT coronary angiography has been overwhelming. The past several years saw numerous clinical studies on coronary arterial stenosis assessment, atherosclerotic plaque characteristics, remodeling status, and local as well as total disease burden. At the same time, discussions arose over what information is most critical for guiding the management of patients with suspected or known coronary artery disease. The Fractional Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study suggested that hemodynamically significant coronary artery disease is most important for determining the need of percutaneous coronary intervention in patients with stable symptoms.\(^2\) These results triggered numerous efforts to noninvasively determine hemodynamic significance of coronary artery disease. Notable outcomes from these efforts include CT-derived fractional flow reserve assessment, lumen density gradient analysis, and CT myocardial perfusion imaging. Unfortunately, the FAME study was misinterpreted with regards to the significance of nonflow limiting coronary artery disease for risk of myocardial infarction and death.\(^3\) Indeed, the FAME2 study revealed similar rates of myocardial infarction and death among patients with and without hemodynamically significant coronary artery disease.\(^4\) Total coronary atherosclerotic disease burden is a more consistent predictor of myocardial infarction and cardiac death than provokable atherosclerotic disease for risk of myocardial infarction found \(\geq 50\%\) diameter stenosis\(^8\) but it is conceivable that organized thrombus, which is frequently found in culprit lesions, is not being considered in these situations. There is some evidence that lumen obstruction accelerates in the days before an infarction which may lead to greater culprit lesion stenosis at the time of event.\(^7\) Autopsy studies found culprit lesion diameter stenosis to be on average 49\% in patients dying suddenly.\(^10\) Thus, it is clear that a substantial number of patients experience acute myocardial infarction and death because of coronary lesions that are not obstructive. However, event rates of myocardial infarction and death are typically higher in patients with obstructive versus nonobstructive disease.\(^11\) This apparent paradox may be explained by the fact that patients with obstructive coronary artery disease generally have a greater atherosclerotic disease burden when compared with patients with nonobstructive stenoses, with the disease burden being the actual driver for events.

**See Article by Mushtaq et al**

In this context, the study by Mushtaq et al\(^12\) in this issue of *Circulation: Cardiovascular Imaging* adds interesting new data. The authors analyzed CT angiograms in 1304 registry patients for the presence and extent of atherosclerotic disease using the segment involvement score (SIS) and segment stenosis score (SSS) in comparison with a CT-adapted Leaman score, which integrates information on disease burden, stenosis severity and location, as well as plaque composition, for predicting cardiac death and myocardial infarction. The authors found overall similar performances of the 3 scores for predicting events using area under the curve analysis (0.81–0.82). Hazard ratio for myocardial infarction or death was highest for the CT-adapted Leaman score but confidence intervals largely overlap suggesting no significant differences among the scores. Risk models in this study did not include all 3 scores for assessing independent (comparing scores) hazard prediction. The authors found the CT-adapted Leaman score to be superior to the other 2 methods for reclassifying patients from higher to lower risk categories. The 3 scores predicted high risk with similar accuracy. Several study strengths are noted. The sample size and number of events are solid and suitable for the performed analysis. The authors ought to be particularly lauded for using hard events as their outcome measure as opposed to including revascularization procedures, which are driven...
by study results. However, it has to be acknowledged that the selected categories for SSS and SIS are rather arbitrary and one wonders how different categorization would have affected the results of reclassification, particularly, given the similar area under the curve results for discrimination among the 3 scores. Of particular importance for clinical management is information that identifies patients at exceedingly low risk who are unlikely to benefit from further testing or interventions. In this context, it is noteworthy that no events occurred in the low-risk categories of SSS and SIS, whereas 4 events did occur in the low-risk category of the CT-adapted Leaman score. Finally, it remains to be seen if the advantage of reclassifying patients is associated with clinically meaningful benefit, as acknowledged by the authors.

The larger and more exciting question is which of the assessed anatomic features is most critical for determining the risk of myocardial infarction and cardiac death? The SSS purely looks at the presence of atherosclerotic disease in a given artery segment, whereas the SIS additionally considers the extent of lumen obstruction. The CT-adapted Leaman score considers both, presence of disease and obstruction, but also integrates information on plaque location and tissue characteristics (calculated versus noncalculated or mixed). Because the 3 scores performed similarly for predicting events, it seems that the number of segments with evidence of atherosclerotic disease (as the smallest common denominator) is most relevant for performance, supporting the concept of atherosclerotic disease burden as the most critical factor for determining events. A key question remains: what is the contribution of stenosis severity, location, and plaque characterization for risk prediction? Using the authors’ risk scores, it is difficult to disentangle their respective, individual performances. The trend of greater hazard ratios with the SSS and CT-adapted Leaman scores, which consider additional information to mere disease presence as provided with the SIS, may suggest incremental risk prediction. However, a fundamental limitation of all 3 scores is that they are insensitive to the total plaque volume in a given segment. For example, one can envision a coronary segment with diffuse, yet nonobstructive disease and one with a single, small plaque. Both would receive the same score by each method, respectively, whereas the associated risks are likely different based on extensive data documenting poorer patient outcome with greater atherosclerotic disease burden. Thus, coronary atherosclerotic plaque volume is not fully considered in any of these scores, leaving uncertainty with regards to its comparative performance.

The study by Mushtaq et al brings us exactly to the key question for imaging patients with suspected or known coronary artery disease: what information, among the many available options, is most relevant for patient management? The authors’ results are in line with several recent reports suggesting that the risk of adverse events in patients with nonobstructive disease may equal that of high-risk patients, that is, those with obstructive disease, if the nonobstructive disease affects a greater number of artery segments. Thus, the authors are correct in postulating more refined methods to distinguish patients who have nonobstructive coronary artery disease and are truly at low risk from those who have conventional coronary artery disease risk equivalence. The authors’ results confirm that atherosclerotic disease burden is a critical factor for determining risk but it remains unclear whether other anatomic features are of additional value.

These are truly exciting times for noninvasive imaging in patients with suspected or known coronary artery disease as we have many options for imaging tools and targets. The upcoming years will bring clarity which tool(s) and which target(s) are most effective for guiding patient management. The study by Mushtaq et al demonstrates that cardiac CT is well positioned to accept this challenge.

Disclosures

None.

References


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What Imaging Characteristics Determine Risk of Myocardial Infarction and Cardiac Death?
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