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iVIEW

EDITOR'S PAGE

Noninvasive FFR_{CT} After STEMI

Looking for the Guilty Bystander

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In patients presenting with ST-segment elevation myocardial infarction (STEMI), coronary revascularization of the non-infarct-related artery (N-IRA) is often performed. This is performed primarily as a staged procedure rather than at the time of primary percutaneous cutaneous intervention (PCI), a protocol in keeping with the most recent American College of Cardiology and American Heart Association guidelines for patients with STEMI (1). This guidance document lists coronary revascularization of the N-IRA as a class IIb recommendation, wherein the utility of such an approach is as yet fully unresolved. Nevertheless, nonstaged PCI with the goal of complete revascularization in the same setting is becoming increasingly more common, on the basis of a limited number of randomized open-label trials reporting outcomes benefit for N-IRA revascularization.

The trials supporting N-IRA intervention in the acute setting include the CvLPRIT (Complete Versus Lesion-Only Primary PCI Trial), PRAMI (Preventive Angioplasty in Acute Myocardial Infarction), and DANAMI-3 (Third Danish Study of Optimal Acute Treatment of Patients With STEMI) trials. CvLPRIT randomized 296 patients to complete revascularization versus IRA-only revascularization at the time of STEMI with subsequent revascularization of coronary lesions exhibiting >70% diameter stenosis; a 65% reduction of death, myocardial infarction (MI), heart failure, and ischemia-driven revascularization was reported in the complete revascularization arm (2). In the PRAMI trial of 465 patients with STEMI with multivessel coronary artery disease (CAD; defined by anatomic luminal narrowing of >50% diameter in a major epicardial artery), a 65% reduction in adverse events rates at 23 months was observed in the preventive PCI group; the trial was stopped early, but the benefit was driven largely by a lower incidence of refractory angina and nonfatal MI (3). More recently, in the DANAMI-3-PRIMULTI (Primary PCI in Multivessel Disease) trial, 627 patients with STEMI were randomized to fractional flow reserve (FFR)-guided revascularization of the N-IRA versus deferral of revascularization in lieu of medical therapy alone. Similar to the previous 2 trials, a 44% reduction in a primary composite endpoint was observed, driven largely by reduction in ischemia-guided revascularization rather than death or nonfatal MI (4). This stepwise evaluation of N-IRA-related ischemia evaluation by stress testing in the past, and more recently on the basis of upon stenosis alone or FFR-verified hemodynamic significance, emphasizes the evolving strategies toward greater precision of intervention-worthy coronary stenoses in a lesion-specific manner.

In the past 5 years, FFR calculated from coronary computed tomographic angiography (CTA), or FFR_{CT}, has emerged as a powerful noninvasive tool for the identification and exclusion of ischemic coronary artery lesions (5). In several prospective multicenter trials, FFR_{CT} has demonstrated high accuracy and discriminatory power compared with the invasive FFR reference standard (6-8). However, these studies restricted evaluation primarily to patients in stable condition with suspected CAD, and the diagnostic performance of FFR_{CT} in patients with known CAD has as yet been unreported. In this issue of *iJACC*, Gaur et al. (9) report their evaluation of coronary lesions in patients who had recently presented with STEMI, prior to staged invasive coronary angiography

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(ICA) for intended revascularization of the N-IRA, in which they assessed the performance of FFR_{CT} in patients with known CAD. In this study, 66 patients underwent repeat ICA at 38 days after primary PCI and CTA within 1 day of the repeat ICA; the diagnostic accuracy of FFR_{CT} (72%) proved superior to stenosis assessment alone by CTA (64%) for ischemia judged by invasive FFR and was similar to stenosis assessment by ICA (72%). A comparison of FFR_{CT} and ICA stenosis revealed higher sensitivity for FFR_{CT} over ICA (83% vs. 76%) at the cost of specificity (66% vs. 76%), with no difference in the discriminatory power as judged by the area under the receiver-operating characteristic curve.

Compared with higher diagnostic accuracy for FFR_{CT} of 86% for patients in stable condition without known CAD (demonstrated in the most recent NXT [Analysis of Coronary Blood Flow Using CT Angiography: Next Steps] trial), the reasons for the lower diagnostic performance of FFR_{CT} in the recent STEMI population remain unclear. There are a number of possible explanations for these differences. Given their recent history of STEMI as well as the presence of a >50% stenosis in a N-IRA, patients in the present study represented significantly greater extent and severity of CAD than those in the NXT study, and it is possible that FFR_{CT} might play a greater role in evaluation of patients with a lower burden of high-grade coronary stenoses (8). More likely, given the more advanced forms of CAD in the present population, the presence of severe coronary calcification and blooming artifacts from partial volume effects may have confounded the accuracy of FFR_{CT}. Coronary artery calcium scores were available for some of the patients, but their influence on FFR_{CT} accuracy was not reported. The presence of relatively large necrotic cores may further compound the relationship between the luminal stenosis and its hemodynamic consequence (10,11). Evaluation of atherosclerotic plaque characteristics in the post-STEMI population might offer more information regarding this possibility, as has been reported by this investigative group for patients in stable condition with suspected CAD. It is worthy to note that the comprehensive evaluation of the coronary arterial tree, wherein FFR_{CT} can pinpoint every point in all 3 major epicardial territories, entails higher order modeling by computational fluid dynamics. Thus, inaccuracies in coronary artery evaluation in any given coronary artery may potentially influence the accuracies of FFR_{CT} in other arteries. Although reduced-order computational fluid dynamics models have recently been reported to have generally high diagnostic performance, these approaches limit evaluation to single arteries, have also been restricted to evaluations in patients in stable condition without known CAD, and do not involve the totality of form-function relationships required for 3-vessel FFR_{CT}.

The form-function relationships embedded in the calculation of FFR_{CT} include the relationship of coronary artery vessel volume to left ventricular mass, a metric also evaluated by Gaur et al. (9) in this study. This measure offers a simple anatomic assessment over the more complex physiological information offered by FFR_{CT} and is represented by the ratio of the 3-dimensional size of coronary arteries to the left ventricular mass that they subtend. The hypothesis proposed entailed that larger arteries subtending more myocardial mass were less well evaluated for ischemia by FFR_{CT} than larger arteries subtending smaller myocardial mass. Furthermore, the former may represent patients in whom FFR_{CT} may be more accurate. Intuitively, this makes sense, and the findings of the present study support this. The diagnostic accuracy of FFR_{CT} was higher for patients in the highest tertile volume-to-mass ratio of >65 mm^3/g versus those in the lower tertile of <49 mm^3/g (83% vs. 56%). In this regard, the study investigators may have identified a population of patients who may be suitable for CTA to evaluate the need for FFR_{CT} prior to ICA of the N-IRA, although it should be noted that this represented only 41 patients of the study group and that this information can be identified only after performance of CTA before post-primary PCI ICA. It would be interesting to know whether the higher accuracy of FFR_{CT} for higher volume-to-mass ratio is simply related to a higher coronary volume from better vasodilation at the time of coronary CTA, but this information was not available.

Other pathophysiologic processes should also be considered for the coronary volume-to-mass ratio in this select population of patients post-STEMI. Given the infarcted myocardial with associated decrement in left ventricular mass, it may be that this regional mismatch may influence the diagnostic accuracy of this metric compared with a group of patients in whom the relationship of mass to coronary volume is preserved. Understanding the relationship of severity of STEMI, perhaps as represented by a troponin biomarker surrogate to volume-to-mass ratios, would be helpful, but such biomarkers were not routinely available for analysis in this study. Importantly, it has been demonstrated that coronary arteries adapt in size, wherein they may become smaller when less myocardial mass is present. Given the short inter-test interval of 38 days between STEMI presentation and CTA, whether this adaptive process had a sufficient period to occur remains unknown and hence,

whether CTA performed further downstream of STEMI would proffer different study findings than those reported here.

Overall, these investigators should be commended for undertaking this study, which was likely difficult considering that enrollment required consent in the peri-MI period. Given the generally small study size at a single institution without core laboratory confirmation of study findings, no definitive conclusions can be drawn from the present study findings. Yet these study results represent several important first-step attempts to decipher not only the diagnostic accuracy of FFR_{CT} in a patient population with recent STEMI but also consideration of a novel anatomic metric that may offer incremental information to identify patient- or vessel-level coronary ischemia. Whether the latter measure can add incremental information regarding the physiological significance of a coronary artery lesion in a manner incremental to FFR_{CT}, better select patients who may benefit most from FFR_{CT}, or N-IRA that may benefit from staged intervention remains unknown but is certainly worthy of future investigation.

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REFERENCES

1. Levine GN, Bates ER, Blankenship JC, et al. 2015 ACC/AHA/SCAI focused update on primary percutaneous coronary intervention for patients with ST-elevation myocardial infarction: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention and the 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. J Am Coll Cardiol 2016;67:1235–50.

2. Gershlick AH, Khan JN, Kelly DJ, et al. Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial. J Am Coll Cardiol 2015;65:963–72.

3. Wald DS, Morris JK, Wald NJ, et al. Randomized trial of preventive angioplasty in myocardial infarction. N Engl J Med 2013;369:1115–23.

4. Hofsten DE, Kelbaek H, Helqvist S, et al. The Third Danish Study of Optimal Acute Treatment of Patients with ST-Segment Elevation Myocardial Infarction: ischemic postconditioning or deferred stent implantation versus conventional primary angioplasty and complete revascularization versus treatment of culprit lesion only: rationale and design of the DANAMI 3 trial program. Am Heart J 2015;169:613–21.

5. Min JK, Taylor CA, Achenbach S, et al. Noninvasive fractional flow reserve derived from coronary CT angiography: clinical data and scientific principles. J Am Coll Cardiol Img 2015;8:1209–22.

6. Koo BK, Erglis A, Doh JH, et al. Diagnosis of ischemia-causing coronary stenoses by noninvasive fractional flow reserve computed from coronary computed tomographic angiograms. Results from the prospective multicenter DISCOVER-FLOW (Diagnosis of Ischemia-Causing Stenoses Obtained via Noninvasive Fractional Flow Reserve) study. J Am Coll Cardiol 2011;58:1989–97.

7. Min JK, Leipsic J, Pencina MJ, et al. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. JAMA 2012;308:1237–45.

8. Norgaard BL, Leipsic J, Gaur S, et al. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial (Analysis of Coronary Blood Flow Using CT Angiography: Next Steps). J Am Coll Cardiol 2014;63:1145–55.

9. Gaur S, Taylor CA, Jensen JM, et al. FFR derived from coronary CT angiography in nonculprit lesions of patients with recent STEMI. J Am Coll Cardiol Img 2017;10:424–33.

10. Ahmadi A, Stone GW, Leipsic J, et al. Association of coronary stenosis and plaque morphology with fractional flow reserve and outcomes. JAMA Cardiol 2016;1:350–7.

11. Ahmadi A, Stone GW, Leipsic J, et al. Prognostic determinants of coronary atherosclerosis in stable ischemic heart disease: anatomy, physiology, or morphology? Circ Res 2016;119:317–29.