Editorial

Clues to Discordance and Dissimilarity Between Coronary Stenosis and Lesion-Specific Ischemia

Leslee J. Shaw, PhD; James K. Min, MD

Traditional diagnostic accuracy statistics have defined discordance between a stenosis and preserved coronary blood flow as a false-positive finding. With expanded use of invasive and noninvasive fractional flow reserve (FFR), as well as positron emission tomography measures of coronary flow reserve, our knowledge base has grown substantially, providing greater insight into the underlying rationale for discordant findings. We now understand that the presence of an obstructive stenosis is but one parameter which may elicit reductions in blood flow and prompt ischemic symptoms. Vessel size, collateral flow, and the length of the diseased segment are a few of the factors influencing coronary blood flow.[1] Thus, for any given patient with an obstructive stenosis, reductions in coronary blood flow may or may not be present. Throughout the prior reported series,[2,3] limited evidence is available with regards to coronary stenosis severity and location, as well as clinical patient subgroups, where the disconnect between stenosis severity and lesion-specific ischemia with FFR may be greatest.

See Article by Adjedj et al

In this issue of *Circulation: Cardiovascular Imaging*, Adjedj et al[4] examined the diagnostic accuracy of coronary angiography by visual estimate and quantitative measurement with invasive FFR. This report includes a robust patient sample with over 1000 patients undergoing invasive coronary angiography with FFR measurements. Findings from this report detail the challenges in over- and underestimation of stenosis based on visual estimation of percent stenosis when compared with quantitative measurements, which has dramatic implications for therapeutic effectiveness of revascularization strategies and clinical outcomes. Imprecision is commonplace in medicine but the cumulative impact of challenges in symptom presentation and stress ischemia interpretation coupled with angiographic assessment has an unknown but likely impact on the quality of patient care.

Moreover, this variability of visual estimation of coronary stenosis further contributed to an observed weak correlation with FFR (r=−0.42). Interestingly, results from the receiver operating characteristics curve analysis revealed that the visually estimated stenosis was more accurate in estimating FFR when compared with the quantitative measurement. In this report, the angiographer overestimated nonobstructive stenosis but underestimated a high-grade stenosis when compared with quantitative measurements. It is likely that the patient's presenting symptoms and stress ischemia severity impacted the visual estimation of stenosis, thus, strengthening the concordance with lesion-specific ischemia by FFR.

Perhaps, the most intriguing findings from this article is detailed in the gradient decline in accuracy of invasive angiography in estimating FFR across patient subgroups. The authors examined the accuracy of anatomic measures of coronary stenosis to estimate FFR among patients with 0 to 4 cardiac risk factors. There was a graded loss in accuracy, in terms of decrease in the area under the receiver operating characteristic curve, for patients with multiple cardiac risk factors. In fact, the area under the receiver operating characteristic curve was reduced to 0.63 for patients with ≥4 cardiac risk factors and was as low as 0.52 for a small subgroup of 97 diabetic patients, as compared with 0.78 for those with 0 to 1 risk factor. These analyses may illustrate the commonly discussed influence or, perhaps, melding of clinical data into an imprecise estimate of coronary anatomy. Alternatively, the authors propose that coronary microvascular dysfunction (in the absence of obstructive coronary artery disease) may be operational and would be more prevalent among hypertensive, dyslipidemia, and diabetic patients.[5] Thus, discordance would occur with physiological abnormalities or ischemia without a high-grade stenosis along with stenosis without ischemia, as previously described by Ahmadi et al.[3] Data from positron emission tomography imaging support the independent prognostic significance of reduced coronary flow reserve even among patients with nonobstructive coronary artery disease.[6] Although there are differences between positron emission tomography and invasive physiological measures, these data underscore the complexity of clinical care and the limitations of management based on anatomic data alone.

Of course, compositional changes within the plaque, diffusivity, eccentricity, as well as shear stress and other factors may belie much of the confusion and provide insightful clues as to patterns of discordant physiological and anatomic parameters. It remains likely that a given plaque burden (absent of a critical stenosis) may elicit reductions in FFR. These and other answers to questions remain ill-defined but prove to be fruitful areas of ongoing research exploration. It is clear that more data, such as the report by Adjedj et al,[4] are needed and provide important clues to the anatomy–physiology disconnect. Moreover, these data remain fundamental to patient care and impact a large proportion of patients and, thus, are informative. Future strategies can no longer be guided solely by simplicity but must endeavor

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.

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to explore the complexities of anatomic and physiological variants and how they relate to differing strategies of medical and revascularization therapy and future ischemic event risk.

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