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Letter to the Editor

On location, territory, and significance

Intracoronary pressure measurement under maximally hyperemic conditions (FFR) has become the gold standard in assessing the functional significance of intermediate coronary artery stenoses. In this issue, Barbin et al. assess the potential importance of lesion location in predicting the functional significance of coronary stenoses.

In their study, 618 patients had one or more coronary vessels interrogated to determine the functional significance of angiographically intermediate stenoses. FFR was determined to be "positive" – (distal to proximal pressure ratio <0.8 under maximal hyperemia) twice as frequently in LAD lesions compared to those in other native coronary vessels (33% vs 16.5% $p < .001$). Lesions length tended to be greater in the LAD (22 mm vs 18 mm), though this was not statistically significant [1].

Is this simply chance, or are there potential differences in the left anterior descending artery that do in fact predict this outcome? Leone and colleagues assessed multiple clinical, plaque, and arterial characteristics of coronary lesions in an attempt to predict FFR positivity. In their study, FFR was also more frequently positive in the LAD compared with the other coronary arteries (39% vs 9% $p < .05$). Proximal LAD stenoses were more frequently positive than mid and distal LAD lesions (52% vs 32%), despite similar plaque characteristics. In their multivariate model, Myocardial Jeopardy Index, an indicator of the amount of myocardium at risk from the assessed stenosis, was the strongest predictor of a positive FFR [2].

Others have also shown that interrogation of intermediate stenoses in the LAD is more likely to be positive. In separate studies, Kang et al. and Härle et al. reported higher median values of FFR in LAD compared to non-LAD stenoses [3,4]. And, again, in the study by Kang et al., LAD lesion location was found to be an independent predictor of a positive FFR (<0.80) [3]. Nakamura and colleagues found "reverse angiographic mismatch" (visually estimated angiographs stenosis <75% with FFR <0.08) to be more common in LAD stenoses, whereas the inverse was more common in non-LAD stenoses [5].

What explains this repeated finding of greater FFR "positivity" in the LAD? As we noted earlier, FFR is inversely correlated with myocardial jeopardy index, as larger areas of subtended myocardium require higher flow, and, potentially, a higher pressure gradient during maximal hyperemia [2]. Additionally, Härle and colleagues analyzed 70 CT angiograms, largely from patients being assessed for TAVR, and found that, in the supine position (in which FFR is also assessed) the LAD generally "flows uphill", with its lowest point at the left main bifurcation, and highest at the apex. The Left Circumflex, in contrast, generally takes a "downhill" course, with the course of the RCA somewhat variable. Perhaps this invokes differences in hydrostatic pressure, particularly under conditions of maximal hyperemia, in the higher frequency of positive FFR findings in the LAD. In this study which included intra-arterial pressure measurements, this effect was particularly pronounced when aortic pressure was low [6].

Barbin et al. confirm what had been previously noted – that FFR measurement is more likely to be positive in LAD stenoses than in non-LAD lesions, despite similar stenosis severity and plaque characteristics. A larger arear of myocardium supplied and even, perhaps, an "uphill course" may be potential explanations. But the validity and utility of FFR endures, regardless of the vessel studied [7].

Scott W. Shurmur
Texas Tech University Health Sciences Center, Lubbock, TX, United States of America
Division of Cardiology, Texas Tech University Health Sciences Center, 3601 4th Street, MS 9410, Lubbock, TX 79430, United States of America.
E-mail address: Scott.shurmur@ttuhsc.edu.

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