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EDITOR'S PAGE

Quantitative Myocardial Perfusion CMR

Is the Game Worth the Candle?

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First-pass contrast-enhanced magnetic resonance myocardial perfusion imaging has evolved into an established technique over the past 2 decades, and appropriate clinical indications in ischemic heart disease have been identified (1). Qualitative analysis suggested superior accuracy compared with single-photon emission computed tomography in 1 large single-center study (2) and was equivalent in terms of predicting events at 1 year to x-ray angiography with measurement of fractional flow reserve in a multicenter study of 918 patients that was presented preliminarily at the 2017 meeting of the American College of Cardiology (3).

In theory, semiquantitative or fully quantitative analysis of perfusion data could improve on visual analysis, as there are artifacts that can contribute to misdiagnosis with the latter. Quantitative pixelwise approaches have been carefully validated (4). One study from our group suggested that although overall accuracy was similar, quantitative analysis identified the extent of coronary artery disease (CAD) more accurately, especially in patients with multivessel disease (5). Compared with positron emission tomography, the ratio of stress to rest myocardial perfusion or myocardial perfusion reserve are quite comparable, although there are significant differences in absolute values of rest and stress flow between techniques (6). A meta-analysis suggested good performance of semiquantitative and quantitative cardiac magnetic resonance (CMR) perfusion analysis, with areas under the receiver-operating characteristic curve of 0.86 against x-ray angiography and 0.88 against functional gold standards including fractional flow reserve (7).

It is against this backdrop that 2 studies using quantitative analysis techniques are reported in this month's issue of *iJACC* (8,9). Hsu et al. (8) took their previously published pixelwise approach mentioned earlier (4) and performed automated analysis of the data, which removed some potential human error in the quantitative analysis. They studied 80 patients with known or suspected CAD and 17 healthy volunteers using 70% stenosis by quantitative coronary angiography as the gold standard. They showed areas under the curve of 0.86 to 0.92 on a per patient basis and 0.84 to 0.86 on a per vessel basis, with good sensitivities and specificities. One wonders if the accuracy would have been even higher if a functional gold standard such as invasive fractional flow reserve had been used rather than the anatomic gold standard. Certainly this study validates the use of their automated analysis techniques, which would make quantification of flows much easier to integrate into clinical work flows. A similar automated approach performed well against positron emission tomography as a gold standard in a relatively small study of 21 patients (10).

Interestingly, Hsu et al. (8) demonstrated reduced stress flow in remote regions in patients with CAD. This is likely due to underlying microvascular disease, which in turn is likely driven by inflammation and underlying cardiac risk factors such as hypertension, diabetes mellitus, and hyperlipidemia, which were highly prevalent in this population.

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A recent study from our group demonstrated reduced myocardial perfusion reserve measured quantitatively in 46 patients with chest pain and no obstructive CAD, due primarily to reduced stress flow, compared with 20 healthy control subjects (11). The Oxford group showed similar findings but with external validation by index of microcirculatory resistance measures in the catheterization laboratory (12). Thus, differentiating obstructive CAD from microvascular disease with quantitation may be problematic because of overlap in quantitative myocardial perfusion reserve measures. This is where a visual analysis may actually help, and unfortunately Hsu et al. (8) do not present the results of such a qualitative visual analysis in this particular paper. Certainly, they show that quantitative analysis performs well at identifying obstructive disease, but we are left wondering if it performs better than qualitative analysis.

Sammut et al. (9) present data on 395 patients who underwent quantitative and qualitative analysis of stress CMR studies over a 6-year period at 1 institution. They were then followed for 2 years for events, including death, myocardial infarction, aborted sudden cardiac death, and late (>90 days) revascularization. Fifty-two patients had events, 39 of which were late revascularizations. Both visual and quantitative analysis predicted events with similar areas under the curve (0.84 and 0.85, respectively). However, they also examined thresholds of ischemia (>2 segments and >10% of the myocardium) and found that this threshold performed better than visual assessment when added to a baseline model of age, sex, and scar as identified by late gadolinium enhancement, which was seen in approximately one-third of patients. This finding suggests that quantitative analysis of stress CMR images can assess cardiac prognosis based on ischemic burden in a fashion similar to that seen in the nuclear substudy of the COURAGE trial (13). However, in this study, most of the events were late revascularizations. Larger multicenter studies with longer follow-up are needed to fully validate these findings with regard to extent of ischemia. It may be that the ISCHEMIA trial offers answers about the relative values of different modalities for identifying ischemia and ischemic burden (14).

The questions remain: Is the game worth the candle? Is quantitation really superior to the more straightforward qualitative analysis? Multicenter studies are needed with automated analyses of quantitative data with comparison to core laboratory qualitative analysis to definitively answer this question. Quantitation by CMR must become as quick and automated as the polar plots used for computer-aided diagnosis by single-photon emission computed tomography (15). It may be that deep-learning approaches are applicable here and speed up the quantitation, although applications to date have been in chamber segmentation and quantitation from cine images (16). In general, the speed of image acquisition and quantitation of all CMR data, not just perfusion imaging, needs to be improved through a combination of deep learning and magnetic resonance fingerprinting. A 15- to 20-min examination with post-processing completed by the time the patient is pulled out of the scanner is where the field should be aiming at this point. However, we first need to definitively demonstrate that quantitation of perfusion is worth the effort.

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