JACC: CARDIOVASCULAR IMAGING VOL. 11, NO. 5, 2018

PUBLISHED BY ELSEVIER

EDITORIAL COMMENT

Is Qualitative Cardiac Perfusion MRI "Good Enough"?*

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Noninvasive regional cardiac perfusion assessment is clinically valuable, particularly for patients with angina or decreased cardiac function, who may benefit from invasive cardiac catheterization and possible revascularization. However, conventional radionuclide perfusion imaging has limitations, including the use of ionizing radiation, limited spatial resolution, and susceptibility to some artifacts. Thus, alternative cardiac perfusion imaging methods, particularly magnetic resonance imaging (MRI)-based approaches, are attractive to investigate.

Imaging approaches to cardiac perfusion have primarily involved the imaging of tracers that are delivered to the heart through the blood. In particular, MRI methods have primarily focused on the rapid T1-weighted imaging of the transit of a bolus of contrast agent through the myocardium. The arrival of the contrast agent produces a transient increase in the local signal of the blood and the tissue; regional differences in the timing and amount of the contrast enhancement reflect corresponding differences in the underlying delivery and distribution of the contrast agent. Thus, simple qualitative visual assessment of the dynamic contrast enhancement images can reveal regional delays and decreases in the enhancement that can reflect underlying regional ischemia. Subendocardial ischemia can also be detected, which can be missed with lower resolution radionuclide imaging. Multiple image locations can be monitored during the first-pass enhancement, although there is an associated tradeoff between number of locations imaged and spatial and temporal resolution of the images. Imaging is usually performed at rest and under stress, to look for reductions in perfusion reserve. However, such visual analysis is subjective, and cannot be easily combined with other imaging results; "balanced" multivessel disease may potentially lead to underestimation of the presence of disease. Quantitative analysis of the first-pass contrast enhancement dynamics usually relies on classical indicator-dilution analysis methods; these can provide estimates of myocardial blood flow (MBF) and other related variables of potential interest, such as the volumes of the plasma and extracellular spaces, and the permeability-surface area product of the capillaries. Comparing flow at rest and under stress allows calculation of myocardial perfusion reserve (MPR).

However, turning a series of T1-weighted images into a corresponding estimate of the underlying changes in the concentration of contrast agent, as is needed for such quantitative analysis, requires dealing with many technical issues that can affect the results. Imaging-related issues that can affect quantitative analysis include signal calibration (conventional MRI uses arbitrary intensity units and has regional intensity variations; signal changes are nonlinearly related to concentration changes), the need to compensate for regionally varying contrast agent input functions (both normally and in the potential presence of collateral or shunt supply; transit through the coronaries affects input functions measured upstream), respiratory motion or arrhythmias during the acquisition, "dark rim artifact" that may decrease the apparent intensity of the subendocardium, and limited spatial resolution of the imaging. Other analysis issues include exchange of contrast agent with the extravascular space during its transit, hematocrit differences in the microcirculation, and potentially limited tissue water interaction with the contrast agent. The patient also may not be in a baseline state during the "rest" imaging. Prior studies of quantitative cardiac perfusion MRI have dealt to varying degrees with these issues, but have typically not included all of them in any given study. Although many of these issues can also affect qualitative analysis, it is uncertain if the additional information to be gained from quantitative analysis of MRI

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

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ISSN 1936-878X/$36.00 https://doi.org/10.1016/j.jcmg.2017.11.038

JACC: CARDIOVASCULAR IMAGING, VOL. 11, NO. 5, 2018
MAY 2018:719–21

first-pass contrast enhancement is worth the associated cost in additional imaging and analysis time.

A growing number of studies of myocardial perfusion MRI, including the CE-MARC (Clinical Evaluation of Magnetic Resonance Imaging in Coronary Heart Disease) study (1), have found excellent agreement of perfusion MRI (primarily qualitative) with other assessment methods, including radionuclide imaging and cardiac catheterization, in the setting of coronary artery disease. The paper by Biglands et al. (2) in this issue of *iJACC* sought to compare both qualitative and quantitative perfusion MRI findings with quantitative coronary x-ray angiogram stenosis, in a 128-patient subset of the CE-MARC study population, using receiver-operating characteristic analysis. The authors concluded that using quantitative analysis of MBF and MPR did not significantly improve performance over simple qualitative visual analysis of the perfusion MRI.

SEE PAGE 711

In evaluating this conclusion, we need to consider the strengths and potential limitations of the study, and its practical implications. The study was carefully done, and included one of the largest patient groups to date for quantitative analysis. Both the qualitative and quantitative analysis results compared well with the quantitative coronary x-ray angiogram. However, there are several potential issues with how the study was performed. First, the qualitative and quantitative perfusion assessments were not handled in quite the same way. Segmental scores for visual ischemia (0 for normal to 3 for transmural) were summed for 16 segments, so even patients with relatively few affected segments would likely show up as "abnormal." However, only the lowest segmental MBF or MPR value was used for the quantitative analysis assessment; this approach may effectively increase sensitivity to "outliers," and could thus potentially diminish the apparent relative utility. Second, although the subendocardium is most commonly affected by ischemia, possible transmural differences in perfusion were not considered in the calculations (because of signal-to-noise ratio considerations), which may dilute and obscure local changes in the quantitative analysis; subendocardial ischemia was explicitly looked for in the visual analysis, which would tend to boost its relative apparent performance. In the case of "balanced" lesions, transmural differences in perfusion may produce visually apparent changes, which may be partially obscured by segmentally averaging the numbers in the quantitative analysis.

Third, the validation method used was just coronary artery "stenosis," without consideration of its actual hemodynamic significance (e.g., as assessed with fractional flow reserve). This could affect the apparent accuracy of both the qualitative and quantitative analyses, as noted in the paper. Fourth, the quantitative analysis methods used here were relatively limited (e.g., not accounting for the nonlinear relationship between signal changes and contrast agent concentration), and thus may not provide a fair assessment of the potential performance of more complete analysis methods. Fifth, infarction can be associated with quite variable degrees of perfusion alteration, depending on the stage of the healing process. Thus, the presence of late gadolinium enhancement in many patients could have introduced additional variability in the results.

Sixth, it was noted that ~70% of the minimum perfusion segments mapped to the "correct" coronary artery territory; it would be interesting to know how the visual analysis performed in this regard. Finally, as alluded to in the paper, it is likely that one would use different considerations in seeking to optimize the imaging methods for qualitative and quantitative analysis; the specific imaging methods used here may have somewhat biased the results, as noted in the paper. Thus, although this study did not find any significant additional benefit from the use of quantitative perfusion analysis, this may in part just reflect some of the limitations of the way the study was done, and should not be taken as an indication to abandon further research in this promising area.

Although the particular quantitative analysis methods used in this study were not able to improve on the simple visual analysis of the images, for identification of patients with significant coronary artery stenosis, ongoing developments in both imaging and analysis methods offer the potential of additional utility of quantitative cardiac perfusion MRI. Higher performance MRI methods are continuing to be developed, offering the potential for increased spatial and temporal resolution and more extensive coverage of the ventricle, which would benefit qualitative and quantitative perfusion imaging. Better quantitative analysis methods would include accounting for the effects of more of the various factors mentioned previously that can affect the calculated MBF and MPR values, which could lead to better absolute accuracy and decreased scatter in the numbers. Although most quantitative cardiac perfusion MRI studies have focused on the calculation of MBF and MPR from first-pass contrast enhancement dynamics, one can potentially also use the additional fitting results from indicator-dilution

analysis to better characterize other aspects of the tissue, such as changes related to inflammation. Similarly, although most cardiac perfusion MRI studies have focused on atherosclerosis, there are many other diseases where perfusion and related variables may be significantly altered, and where quantitative perfusion analysis may also be valuable. Producing regional maps of perfusion and related variables offers the possibility of creating multidimensional displays of the heart, with spatial registration of the perfusion-related variables with regional function and other tissue characterization variables (e.g., late gadolinium enhancement). This would facilitate better assessment of the functional significance and likely response to treatment of coronary artery disease.

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KEY WORDS cardiovascular magnetic resonance, diagnostic accuracy, myocardial ischemia, quantitative myocardial perfusion