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EDITORIAL COMMENT

FFR_{CT} Versus SPECT to Diagnose Coronary Artery Disease

Toward a Tailored Approach*

Paul Knaapen, MD, PhD

The yield of invasive coronary angiography (ICA) to detect obstructive coronary artery disease (CAD) is low (1). In an effort to reduce the rate of negative ICA, noninvasive imaging is extensively utilized to act as a gatekeeper to the catheterization laboratory. Basically, these tests acquire information on coronary anatomy *or* physiology. Coronary computed tomography angiography (CTA) has been widely adopted to serve as an alternative to its invasive counterpart whereas myocardial perfusion imaging (MPI) with single-photon emission computed tomography (SPECT) has been the workhorse for over decades to detect the physiological consequences of CAD. It is important to realize that both modalities provide fundamentally different insight into the disease process of CAD and neither give information on anatomy *and* physiology (2). European Society of Cardiology guidelines therefore suggest that coronary CTA should be the initial test of choice, especially in low-intermediate likelihood patients, and could be followed by SPECT MPI in case of an abnormal coronary CTA (3). In more recent years, however, computational fluid dynamics have been applied to coronary CTA images to derive functional information and now allow to fairly accurately estimate fractional flow reserve (FFR) values throughout the coronary tree (4). The addition of coronary CTA-derived FFR (FFR_{CT}) to coronary CTA alone has proven to improve the diagnostic accuracy to detect CAD (5). An important potential advantage of $\mathbf{FFR_{CT}}$ is that functional information is readily available from the coronary CTA images alone without the need of an additional test. Nonetheless, it remains unclear which strategy after an equivocal coronary CTA provides the best diagnostic information: FFR_{CT} or SPECT MPI?

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In this issue of *iJACC*, Sand et al. (6) report the results of the ReASSESS (PRospEctive Comparison of FFR Derived From Coronary CT Angiography With SPECT PerfuSion Imaging in Stable Coronary ArtEry DiSeaSe) study to further clarify this diagnostic dilemma. A total number of 143 patients without a prior history of CAD and an abnormal coronary CTA with at least 1 coronary lesion (diameter stenosis 40% to 90%) were referred for ICA and FFR interrogation where appropriate. All patients also underwent vasodilator SPECT MPI and the initial coronary CTAs were subjected to $\mathbf{FFR_{CT}}$ analysis, results of which were blinded to the invasive operator in the catheterization laboratory. Diagnostic accuracy did not significantly differ between FFR_{CT} and SPECT (70% vs. 68%; p = NS). However, FFR_{CT} demonstrated a markedly higher sensitivity than SPECT did (91% vs. 41%; $p < 0.001$), with an opposite pattern for specificity (55% vs. 86%; $p < 0.001$). These differences resulted in overestimation of the prevalence of disease by FFR_{CT} (63%) and underestimation by SPECT (23%), as 41% were ultimately diagnosed with obstructive CAD at ICA or FFR. These intriguing results highlight that the subsequent choice of a non-invasive test after an equivocal coronary CTA impacts downstream clinical decision making that affect the use of medical therapy, referral for ICA, and coronary revascularization procedures.

Several observations of this study warrant debate. First, the notably low sensitivity of SPECT MPI when taking FFR as a reference. Contemporary similar investigations such as the PACIFIC (Prospective Comparison of Cardiac PET/CT, SPECT/CT

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From the Department of Cardiology, VU University Medical Center, Amsterdam, the Netherlands. Dr. Knaapen has reported that he has no relationships relevant to the contents of this paper to disclose.

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Perfusion Imaging and CT Coronary Angiography With Invasive Coronary Angiography) trial have shown comparable data (7). One of the potential explanations for this phenomenon might be the threshold of current-day FFR (0.80) to diagnose ischemia. It is conceivable that many patients with a grey zone FFR between ~0.70 and 0.80 or so do not have actually severely flow-limiting lesions that become apparent with SPECT MPI. Particularly as it is well documented that in a not inconsequential number of patients there is discordancy between pressure and flow and preserved perfusion can occur even when FFR is low (8). It is therefore questionable to assume that a borderline decreased FFR value in the presence of a normal SPECT MPI should always be considered to be a false negative perfusion study. It also does not change the fact that a normal SPECT MPI is associated with an excellent prognosis (9). It is therefore still a viable strategy to withhold ICA in a patient with a normal SPECT MPI after an equivocal coronary CTA, especially if the patient responds well to medical therapy, as this group constitutes a low risk for future events. The second interesting observation is the low specificity of FFR_{CT}. Since the introduction of coronary CTA, its Achilles heel has always been overestimation of lesion severity resulting in a low specificity and positive predictive value. For this reason, coronary CTA has been deemed a rule-out rather than rule-in technique. It is well documented that specificity of coronary CTA can be raised by implementing FFR_{CT} but apparently still leaves some room for improvement in the computational fluid dynamic calculation, as in the current study specificity was only 55%. A recently presented substudy of the PACIFIC trial revealed similar results with a specificity for FFR_{CT} of 63% on a per-patient basis, yet a higher C-statistic for FFR_{CT} than SPECT on diagnostic accuracy (0.92 vs. 0.75; $p < 0.001$) (10). Third, the acceptance rate of coronary CTA for FFR_{CT} (97%) was much higher than previously observed in other studies in which rejection rate was at least in the double-digit range (5,10). The investigators should be lauded for their experience and expertise in driving image quality of coronary CTA to such high levels that inability to compute FFR_{CT} was rare in this cohort. We should be aware, however, that these results may not be generalizable for less advanced CT hardware and less experienced sites.

So, what can we conclude from these results and to what extent can they alter our practice? Since the introduction of FFR_{CT} and subsequent software iterations of its computation, there is now accumulating evidence that it is mature enough to utilize in clinical practice and can compete with traditional imaging modalities such as SPECT MPI. As with any imaging technique, we should try to get the maximal diagnostic information out of a single exam. The fact that FFR_{CT} comes without additional burden for the patient after coronary CTA is of considerable benefit. On the other hand, there are several shortcomings that should be acknowledged. Obviously, the individual patient must be suitable to undergo coronary CTA. These are typically symptomatic patients suspected of but without a prior history CAD, a low and stable heart rate and without contraindications to the administration of contrast media. A large percentage of patients who are eligible for noninvasive evaluation of CAD or ischemia do not fulfill these criteria and are better assessed with SPECT MPI than with coronary CTA. In addition, as opposed to coronary CTA, SPECT allows for physical exercise protocols that can monitor the effect of medical therapy or revascularization in an effort to reduce ischemic burden and provides additional important parameters such as ejection fraction.

The ReASSESS study has provided more scientific insight to reassess the diagnostic choices we can make to optimize our patient care. Coronary CTA and its evaluation by FFR_{CT} have many strengths and weaknesses, as does SPECT MPI. Knowledge of these characteristics allows us to tailor our approach to the individual patient at hand.

ADDRESS FOR CORRESPONDENCE: Dr. Paul Knaapen, VU University Medical Center, Department of Cardiology, De Boelelaan 1117, 1081 HV Amsterdam, the Netherlands. E-mail: p.knaapen@vumc.nl.

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