Editorial

Editorial to 1-year outcomes of FFR_{CT}-guided care in patients with suspected coronary disease

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Stable chest pain is a common clinical presentation that often requires further investigation using non-invasive or invasive testing (1). Diagnostic testing is performed to clarify the diagnosis, document the presence or absence of coronary artery disease (CAD), and direct subsequent care, which includes revascularization, intensified medical treatment, or both (1).

Noninvasive stress testing, often combined with myocardial perfusion imaging or echocardiography, is currently recommended for stable patients with new onset of symptoms who have an intermediate pretest probability of CAD (2). Invasive coronary angiography is recommended as an initial test for patients with a high pretest probability of CAD (2). However, invasive angiography does not assess the functional significance of visualized lesions, and is more costly and carries greater risk than noninvasive testing. Noninvasive coronary computed tomography angiography (CTA) is very sensitive in detecting obstructive CAD (3,4). The recently completed PROMIS (Prospective Multicenter Imaging Study for Evaluation of Chest trial Pain) (5) and SCOT-HEART (Scottish Computed Tomography of the HEART) Trial (6) trials suggest that an initial evaluation using CTA increases diagnostic certainty, improves efficiency of triage to invasive catheterization, and may reduce radiation exposure when compared with functional stress testing, with similar rates of cardiac events.

Although CTA can adequately characterize the anatomic severity of CAD, it cannot determine the hemodynamic significance of a stenosis and it has high false positive rate in contrast to a hemodynamic index, such as fractional flow reserve (FFR) (7). FFR is defined as the ratio of maximal blood flow achievable in a stenosis artery to the theoretical maximal flow in the same vessel when stenosis is absent (8). Because FFR can identify the hemodynamic significance of coronary stenosis (9,10), and is used to identify those stenosis that can most likely benefit from percutaneous coronary intervention (PCI). Measurement of the FFR during invasive coronary angiography is the accepted "gold standard" for assessing the functional significance of coronary artery stenosis by characterizing blood flow proximal and distal to a coronary stenosis during pharmacologically-mediated microvascular hyperemia (11). FFR now has a class IA indication from the European Society of Cardiology for identifying hemodynamically significant coronary lesions when non-invasive evidence of myocardial ischemia is unavailable (12). FFR is the only diagnostic method available to date for ischemia detection that has been demonstrated to improve event-free survival (13). Several prospective randomized trials have demonstrated that FFR-guided PCI can optimize benefits of revascularization and improve long-term outcomes compared with angiographic data alone (14-17). FFR measured during invasive coronary angiography identified patients for whom performing PCI was cost-effective compared with medical therapy in a randomized trial of patients who had an FFR <0.80 (18). FFR can now be

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estimated noninvasively from standardly acquired computed tomography data (FFR_{CT}), based on computational fluid dynamics (19). FFR_{CT} was recently cleared for clinical use by the U.S. Food and Drug Administration, and in 2011 received a CE mark in Europe.

The clinical effectiveness of a strategy of using FFR_{CT} to guide management, compared with conventional testing, has been demonstrated in PLATFORM (Prospective Longitudinal Trial of FFR_{CT}: Outcomes and Resource Impacts) (20). The PLATFORM study showed that, in patients with planned invasive coronary angiography, compared with usual care, FFR_{CT} led to cancellation of 60% of planned invasive coronary angiography, and reducing the rate of finding no obstructive CAD at invasive coronary angiography (from 73% to 12%) (20), with significantly lower costs of care over next 90 days in patients with a planned invasive coronary angiography (21). In patients with planned non-invasive testing, there was no difference between use of CTA/FFR_{CT} and usual care. While PLATFORM has much strength, it is important to note that the sample size and follow-up duration were insufficient to detect an impact on clinical outcomes (20).

A recent study assessed the quality of life (QOL) and economic outcomes of diagnostic strategies that use FFR_{CT}, based on data collected prospectively in the PLATFORM study. The investigators have shown that a strategy of using CT angiography with FFR_{CT} to evaluate patients with suspected CAD was more cost effective than a strategy of invasive coronary angiography. The strategy was also associated with improved QOL compared with a strategy of using other noninvasive tests. The number of patients in the study was too small to evaluate any effect on occurrence of major cardiac events.

The current multicenter, prospective study highlights these problems and sought to determine the 1-year clinical, economic, and QOL outcomes of using FFR_{CT}-guided management instead of usual care. The investigators found that in stable, symptomatic patients with suspected CAD, an evaluation strategy based on use of CTA selectively augmented by FFR_{CT} was associated with a high rate of cancellation of planned invasive catheterization; a significantly lower rate of invasive coronary angiography showing no obstructive CAD; improved information available to guide revascularization; and equivalent clinical outcomes, QOL, and radiation exposure compared with a usual care strategy of invasive coronary angiography. Furthermore, the FFR_{CT}-guided strategy was associated with significantly lower resource utilization and cost in patients with planned invasive evaluation. The investigators suggested that the combination of anatomic and functional data provided by the FFR_{CT}-guided diagnostic strategy may safely reduce use of invasive catheterization and costs of care incurred over 1 year in selected patients undergoing evaluation for suspected CAD.

Furthermore, the investigators demonstrated an improvement in QOL from baseline to 1 year of follow-up in the entire PLATFORM study population after 1 year. Although there was a greater magnitude of improvement found in the noninvasive group at 90 days, the degree of improvement was not significantly different between the FFR_{CT}-guided and usual care groups at 1 year. Presumably the symptoms and QOL generally tend to equalize over time in actively managed patient populations as clinicians respond to patient-reported outcomes and seek to control their symptoms. In most coronary revascularization studies, the initial differences between strategies in QOL scores early after randomization also appeared to equalize over longer-term follow-up (22).

Although the PLATFORM study has much strength, the authors acknowledge the limitations of the study, including a small sample size and relatively short follow-up duration that may be insufficient to detect an impact on clinical outcomes in this low- to intermediate-risk population. The study was not randomized and did not evaluate the performance of CTA alone. The authors concluded that when used as an alternative diagnostic strategy to guide care in patients with planned invasive catheterization, CTA plus selective FFR_{CT} was associated with a significantly lower rate of angiography showing no obstructive CAD, low rates of adverse clinical outcomes, similar QOL, and significant cost savings. When used in those with planned noninvasive testing, clinical events were rare, and there were few differences in resource use or QOL, although the small sample size in this group precluded any definitive conclusions. The CT-FFR technique has some limitations, including high cost, low tolerance for sub-optimal image quality and the need to transmit large image files to a supercomputer for off-line analysis which often takes several hours (3 to 6 hours). Given these drawbacks, the inability to compare a CTA only strategy against the CT-FFR strategy is also a significant limitation of the PLATFORM study.

As acknowledged, further testing in larger randomized settings groups is warranted to fully understand the impact of FFR_{CT}-guided care in patients being evaluated for

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suspected CAD. The period of observation should be much longer in order to supplement conclusions of studies already mentioned and additional consequences of using other diagnostic and treatment modalities. This article highlights important problems faced in diagnosis and treatment of patients with CAD.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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