Coronary CT as a first-line investigation in chronic coronary syndromes: pros and cons

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Introduction

Coronary computed tomography angiography (CCTA) has been increasingly used in recent years, and currently represents an important diagnostic tool for patients presenting with chronic coronary syndrome. The advantages of CCTA are more apparent with latest-generation scanners, which use lower doses of radiation to generate the high-quality images that are responsible for the high diagnostic accuracy of this tool. However, CCTA also has limitations, particularly in patients with an irregular heart rate or a high burden of coronary calcium; in addition, although software for physiological assessment has been developed and validated, functional testing can still be preferable in certain contexts. Based on these considerations, the role of CCTA as a first-line investigation in unselected chronic coronary syndrome patients is still uncertain.

Pros

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Coronary computed tomography angiography is a non-invasive, safe and lower-cost alternative to invasive coronary angiography (ICA) that provides excellent images with a high diagnostic accuracy and negative predictive value (NPV). Moreover, it can identify atherosclerotic plaque components and high-risk features,

which may lead to plaque rupture or erosion and subsequent acute coronary syndrome (ACS). Of note, with the latest generation of computed tomography (CT) scanners, radiation dose, contrast amount and patient turnaround time have decreased substantially, while image quality has improved. Several clinical trials have demonstrated that CCTA is a powerful imaging modality for the initial evaluation of patients with suspected coronary artery disease (CAD). This led the European Society of Cardiology (ESC) Clinical Practice Guidelines on chronic coronary syndromes to acknowledge its role as a "first line tool for evaluation of chronic coronary syndromes for low-to-intermediate risk patients, with a class I, Level of Evidence B recommendation"[1]. More recently, in the updated 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guidelines for chest pain evaluation and diagnosis, CCTA received a class I, level of evidence A recommendation as a first-line test for stable chest pain evaluation in intermediate- to high-risk patients with suspected CAD[2]. Compared to functional tests, the major strengths of CCTA as an initial diagnostic strategy for low-risk patients are both its ability to effectively rule out obstructive CAD and to determine the atherosclerosis burden. The latter information plays a pivotal role in improving risk stratification and guiding risk-based patient management, such as early initiation of preventive therapy versus revascularisation. In this regard, the SCOT-HEART Trial demonstrated at 5-year follow-up

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a significant reduction of death from CAD and non-fatal myocardial infarction (MI) in patients who underwent CCTA in addition to standard care versus standard care alone (hazard ratio [HR] 0.59, 95% confidence interval [CI]: 0.41-0.84; p=0.004)[3]. The alleged mechanism for these benefits is the initiation of evidence-based preventive therapy in patients with non-obstructive disease (i.e., atherosclerosis that does not cause ischaemia) that is not detectable with stress testing. Indeed, patients in the CCTA arm were more likely to be started on lipid-lowering, antihypertensive, antiplatelet, and antianginal drugs (14.7% vs 19.4%, HR 1.40, 95% CI: 1.19-1.65). Additionally, the CCTA anatomical assessment may be complemented by CT-derived fractional flow reserve (FFR_{CT}) technology that provides haemodynamic significance data characterising lesion-specific physiology and that has demonstrated a role in clinical decision-making, procedural planning and complex revascularisation guidance[2]. In CAD patients with prior surgical revascularisation, CCTA is also a viable alternative to ICA, allowing assessment not only of bypass grafts but also of non-grafted and distal postanastomotic native vessels. Compared to the small and tortuous coronary arteries, bypass conduits have larger luminal diameters, less calcification and remain relatively stationary during the cardiac cycle, enabling a more accurate CCTA evaluation. The largest meta-analysis (31 studies: 1,975 patients and 5,364 grafts) compared the diagnostic performance of 64-slice CCTA to ICA and reported a 96% sensitivity (95% CI: 94-97%) and a 96% specificity (95% CI: 95-97%) for graft stenosis or occlusion detection[4]. Although evaluation of coronary stents remains challenging because of metal alloy artefacts, which are more relevant in smaller diameter and thicker-strut devices, tremendous advances in CT technology have significantly improved its diagnostic performance. A new wide-array scanner with better spatial resolution, an iterative reconstruction algorithm and an intra-cycle motion-correction algorithm showed encouraging results in 100 patients (192 stents) representing a real-world CAD population (13% atrial fibrillation, 26% heart rate >65 bpm, and 37% <3 mm stents)[5]. Indeed, 97% of large diameter stents and 92% of small diameter stents were evaluable, while sensitivity, specificity, positive predictive value, and negative predictive value for in-stent restenosis detection were 92%, 96%, 75%, and 99% and 90%, 80%, 48%, and 98%, respectively. Currently, according to the Society for Cardiovascular Computed Tomography (SCCT) 2021 Expert Consensus Document, it is appropriate to perform CCTA in symptomatic patients with prior coronary artery bypass grafting or intracoronary stents with a diameter >3.0 mm[6].

Conflict of interest statement

The authors have no conflicts of interest to declare.

Cons

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The current treatment paradigm of chronic coronary syndromes (CCS) consists of restoring epicardial coronary blood flow of angiographically severe or ischaemia-producing obstructive coronary lesions using percutaneous or surgical revascularisation[1]. Among patients presenting with CCS, detection of myocardial ischaemia using functional testing is currently the most commonly used method to diagnose obstructive CAD. In the most recent European Society of Cardiology Guidelines for the management of CCS, both non-invasive functional imaging for myocardial ischaemia and CCTA are recommended as the initial test to diagnose obstructive CAD[1]. While the evidence supporting the use of CCTA as a first-line approach to manage CCS has been evolving over the last decade, it still remains inconclusive. In the PROMISE Trial, among 10,003 patients with symptoms suggestive of CAD, an upfront anatomical-based testing strategy using CCTA did not result in improved clinical outcomes at ~2 years and was associated with more frequent referral for ICA and greater radiation exposure compared with a functional-based testing strategy using exercise electrocardiography (ECG), exercise or pharmacological nuclear stress testing, and stress echocardiography[7].

However, CCTA has important advantages that could be seen as complementary to functional testing. CCTA could be considered the preferred test in patients with a low likelihood of CAD, no previous diagnosis of CAD and who are less likely to have a CCTA study of suboptimal quality. In particular, CCTA can be helpful in detecting the presence of atherosclerosis in low-risk patients, which can guide an intensification of pharmacological preventative therapies. For example, in the SCOT-HEART Trial, among 4,146 patients with stable chest pain randomised to a strategy of CCTA plus standard of care versus standard-of-care assessment alone, patients who underwent CCTA were more likely to be initiated on preventive pharmacological therapies and had a lower incidence of cardiovascular death or MI at 5 years of follow-up[3]. However, a major limitation of this trial is that only ~9% of patients in the standard-of-care group underwent stress imaging[3]. CCTA may be also preferred in situations where non-atherosclerotic causes of cardiac chest pain are suspected (e.g., myocardial bridge, anomalous coronary arteries, or spontaneous coronary dissections). Conversely, non-invasive functional tests aimed at detecting the presence of ischaemia have better sensitivity than CCTA and have been associated with fewer referrals for downstream ICA compared with an anatomical imaging-based strategy[2]. In addition, before a decision can be made on revascularisation, demonstration of the evidence of ischaemia (either with a non-invasive or invasive assessment) remains necessary[1]. Therefore, a functional non-invasive test remains the standard modality in patients with a high likelihood of obstructive CAD or if they are likely to require coronary revascularisation.

Another substantial advantage of functional testing over an anatomical imaging-based strategy is the characterisation of the patient's functional status with dynamic exercise testing combined

with an imaging modality to detect ischaemia. Data points, such as reproduction of symptoms at peak exercise, exercise tolerance, onset of arrhythmias, or heart rate and blood pressure response to exercise, provide important diagnostic and prognostic information which cannot be obtained with a CCTA-only approach[1].

CCTA has only modest specificity for the detection of intermediate coronary stenosis found to be physiologically significant by abnormal invasive fractional flow reserve. FFR_{CT}, which implements proprietary computational fluid dynamic modelling to estimate the functional significance of stenosis observed on CCTA, has been shown to improve the specificity of CCTA for the prediction of invasive FFR values when used for the assessment of lesions of intermediate severity[4]. However, this technique has multiple limitations, including (i) the accuracy of FFR_{CT} depends on the CCTA quality and is influenced by CCTA-related artefacts (such as motion, misalignment or blooming); (ii) abnormal FFR_{CT} values can sometimes be seen in mild stenosis, in particular, gradually decreasing or abnormally low FFR_{CT} values can be seen at the distal vessel level; and (iii) FFR_{CT} is currently a proprietary technology which requires offsite analysis and is not widely available. Finally, FFR_{CT} has not been evaluated in patients with known CAD, such as those with prior stents, prior bypass graft surgery or prior MI[8].

Another important factor to consider which goes against a strategy of CCTA-first as a diagnostic modality is the likelihood of obtaining an optimal imaging study. The presence of an irregular heart rate, obesity, extensive coronary calcifications or the inability to cooperate with breath-hold commands are associated with an increased likelihood of non-diagnostic image quality[1,8]. Finally, even assuming that a CCTA-based approach could be the preferred first-line test for obstructive CAD, there are a number of logistical and economical barriers for its widespread adoption, including (i) the well-established availability of nuclear medicine cameras and stress echocardiography laboratories; (ii) lack of widespread medical and technical expertise required to produce high-quality CCTA imaging and interpretation; (iii) reimbursement disparities between CCTA and other cardiac imaging tests; and (iv) multiple generations of cardiologists have been trained and currently practise with a functional testing-first approach to detect CAD. Shifting to a CCTA-first approach on a global scale would therefore require significant efforts in developing consistent high-quality CCTA facilities, revising cardiovascular training programs to provide consistent, adequate training in CCTA, and revising the structures of reimbursement for CCTA.

In conclusion, CCTA is a valuable imaging modality to evaluate patients with CCS. However, due to the lack of extensive clinical evidence, logistical and health care economics issues, CCTA should only be considered as an alternative to functional imaging in selected patients.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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