Heart, Lung and Circulation (2023) **32**, 297–306
1443-9506/22/$36.00
https://doi.org/10.1016/j.hlc.2022.12.003

DISCUSSION PAPER

Contemporary Chest Pain Evaluation: The Australian Case for Cardiac CT

Abdul Rahman Ihdayhid, MBBS, PhD [a,b,*], Nick S. R. Lan, MBBS, MClinRes [a,c], Gemma A. Figtree, MBBS, DPhil [d,e], Sanjay Patel, MBBS, PhD [f], Clare Arnott, MBBS, PhD [f,g], Christian Hamilton-Craig, MBBS, PhD [h], Peter J. Psaltis, MBBS, PhD [i], Jonathon Leipsic, MD [j], Timothy Fairbairn, MBChB, PhD [k], Sudhir Wahi, MBBS, MD [l], Graham S. Hillis, MBBS, PhD [m], James M. Rankin, MBBS [a], Girish Dwivedi, MD, PhD [a,c], Stephen J. Nicholls, MBBS, PhD [n]

[a]Department of Cardiology, Fiona Stanley Hospital, Perth, WA, Australia
[b]Harry Perkins Institute of Medical Research, Curtin University, Perth, WA, Australia
[c]Harry Perkins Institute of Medical Research, University of Western Australia, Perth, WA, Australia
[d]Faculty of Medicine and Health, University of Sydney, Sydney, NSW, Australia
[e]Kolling Institute of Medical Research, Royal North Shore Hospital, Sydney, NSW, Australia
[f]Department of Cardiology, Royal Prince Alfred Hospital, Sydney, NSW, Australia
[g]Cardiovascular Division, The George Institute for Global Health, Sydney, NSW, Australia
[h]The Centre for Advanced Imaging, The University of Queensland, Brisbane, Qld, Australia
[i]Department of Cardiology, Royal Adelaide Hospital, Central Adelaide Local Health Network, Adelaide, SA, Australia
[j]University of British Columbia, St Paul's Hospital, Vancouver, Canada
[k]Liverpool Heart and Chest Hospital, Liverpool, UK
[l]Princess Alexandra Hospital, University of Queensland, Brisbane, Qld, Australia
[m]Department of Cardiology and University of Western Australia, Royal Perth Hospital, Perth, WA, Australia
[n]Monash Cardiovascular Research Centre, Victorian Heart Institute, Monash University, Melbourne, Vic, Australia

Received 13 June 2022; received in revised form 7 October 2022; accepted 6 December 2022; online published-ahead-of-print 5 January 2023

Computed tomography coronary angiography (CTCA) is a non-invasive diagnostic modality that provides a comprehensive anatomical assessment of the coronary arteries and coronary atherosclerosis, including plaque burden, composition and morphology. The past decade has witnessed an increase in the role of CTCA for evaluating patients with both stable and acute chest pain, and recent international guidelines have provided increasing support for a first line CTCA diagnostic strategy in select patients. CTCA offers some advantages over current functional tests in the detection of obstructive and non-obstructive coronary artery disease, as well as for ruling out obstructive coronary artery disease. Recent randomised trials have also shown that CTCA improves prognostication and guides the use of guideline-directed preventive therapies, leading to improved clinical outcomes. CTCA technology advances such as fractional flow reserve, plaque quantification and perivascular fat inflammation potentially allow for more personalised risk assessment and targeted therapies. Further studies evaluating demand, supply, and cost-effectiveness of CTCA for evaluating chest pain are required in Australia. This discussion paper revisits the evidence supporting the use of CTCA, provides an overview of its implications and limitations, and considers its potential role for chest pain evaluation pathways in Australia.

Keywords Chest pain • Tomography • X-ray computed • Cardiovascular diseases • Coronary artery disease

*Corresponding author at: Harry Perkins Institute of Medical Research, Fiona Stanley Hospital, 11 Robin Warren Drive, Murdoch, WA 6150, Australia; Email: abdul.ihdayhid@perkins.org.au

Introduction

Chest pain is one of the most common reasons for emergency department presentations in adults [1]. Although the cause of chest pain is often not life-threatening, patients presenting with chest pain remain a diagnostic challenge, and serious causes such as coronary artery disease (CAD), need to be rapidly ruled out [1]. Atherosclerotic CAD, of which chest pain is a common symptom, is a leading cause of death in Australia [2]. Traditionally, chest pain diagnostic algorithms have relied on pre-test probability scores for obstructive CAD, risk scores for early adverse outcomes, and the use of functional stress testing [3]. The past decade has witnessed an increase in the role of computed tomography coronary angiography (CTCA) for evaluating patients with both stable and acute chest pain. In 2016, the National Institute for Health and Care Excellence (NICE) recommended CTCA as the first line investigation in stable chest pain, followed by a similar recommendation in the 2019 European Society of Cardiology (ESC) guidelines [4,5]. More recently, the American Heart Association (AHA) and American College of Cardiology (ACC) published their updated chest pain guidelines, which similarly provided support for a first line (class 1, level A) CTCA diagnostic strategy in select patients [6]. Taken together, there is now increasing consensus for the central role of CTCA in the diagnosis and management of patients with chest pain presentations. The aim of this paper is to revisit the evidence supporting the use of CTCA, provide an overview of its implications and limitations, and briefly consider its potential role in chest pain evaluation pathways in Australia.

CTCA or Functional Test First?

Invasive coronary angiography (ICA) is generally considered the gold standard for diagnosing obstructive CAD in the setting of an acute coronary syndrome. However, the risk of major complications, radiation exposure and high health care costs associated with ICA highlight the importance of non-invasive risk-stratification as a gatekeeper for appropriate referrals for ICA and revascularisation procedures in the setting of stable symptoms [7]. There are a multitude of non-invasive diagnostic tests for CAD, with the choice of test dependent on patient characteristics, local availability, cost and expertise of imaging centres [8]. CTCA is a well-established non-invasive diagnostic modality that provides a three-dimensional assessment of the coronary anatomy, assessment of luminal stenosis, and can also evaluate the vessel wall for the presence and composition of coronary atherosclerosis [9] (Figure 1A). It is important to emphasise that coronary artery calcium scoring (CACS), which is frequently used in Australian clinical practice, differs from CTCA and only provides non-contrast assessment of the degree of calcific coronary atherosclerosis. The use of CACS is generally reserved for risk-stratification and guiding primary prevention in asymptomatic individuals, not for the investigation of chest pain [10]. This is because a calcium score of zero does not rule out the presence of CAD secondary to non-calcified plaques, which are responsible for the majority of myocardial infarcts [11].

The addition of contrast allows more comprehensive assessment of the coronary arteries and CTCA has been shown to have very high sensitivity (>95%) for detecting the

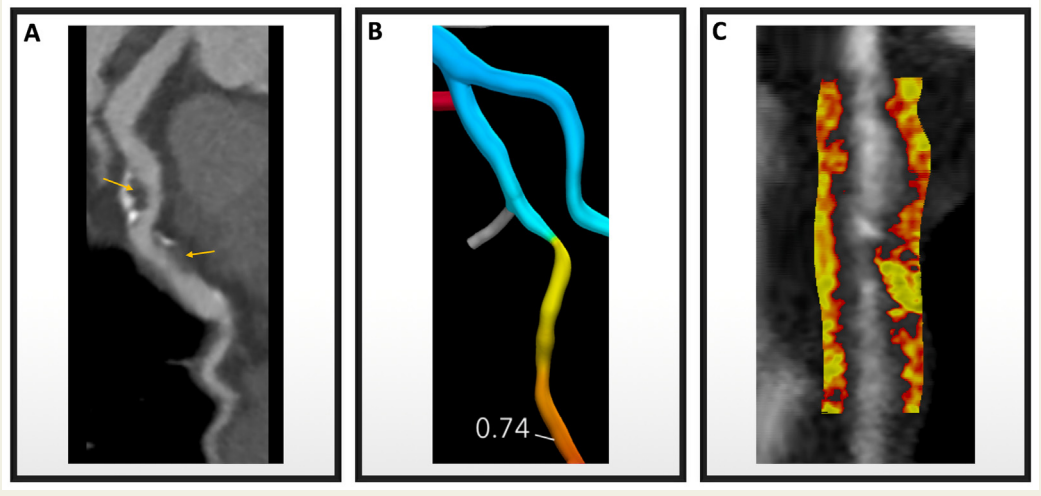

Figure 1 Emerging CTCA Technology.
A) CTCA of the LAD with moderate stenosis. High risk plaque features with large burden of low-attenuation non-calcified plaque and positive remodelling. B) CT-FFR of LAD showing a haemodynamically significant stenosis with a value of 0.74. C) Representation of CT-derived perivascular fat attenuation.
Abbreviations: CTCA, computed tomography coronary angiography; LAD, left anterior descending; CT-FFR, CT-derived fractional flow reserve; CT, computed tomography.

presence of coronary stenosis with ICA as the comparator [12,13]. Due to its very high negative predictive value (>95%) at both a patient and vessel level, clinicians can also confidently rule out CAD when the scan demonstrates normal coronary arteries, and thus the need for functional testing or ICA can be safely avoided [14–16]. CTCA is also helpful for ruling out malignant anomalous origin of coronary arteries as a cause of chest pain and can comprehensively evaluate the ostium, course and termination of anomalous arteries if present [17]. Reports from studies such as the PROspective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE) trial have shown that in the presence of CAD, CTCA-based strategies for investigating low-intermediate risk chest pain might increase the rate of ICA and coronary revascularisation procedures compared to functional testing [18–20]. However, the proportion of patients with normal ICA was lower in those investigated with initial CTCA compared with functional testing, reflecting a higher yield of identifying obstructive CAD at ICA following CTCA [18,21].

The main role of functional testing is to either exclude or identify ischaemia, suggestive of obstructive CAD. However, non-obstructive CAD, the presence of which may alter patient management, is not detected by functional tests. For example, a patient with a negative functional test but who has diffuse non-obstructive CAD may be falsely reassured, thus impacting initiation or adherence to preventive medication. Furthermore, studies have demonstrated that stress echocardiography and single photon emission computed tomography (SPECT) are less sensitive and specific for identifying anatomically significant disease on ICA, defined as >50% stenosis, as compared to anatomical assessment with CTCA [22–24]. Positive functional test results can also occur in the setting of microvascular dysfunction rather than obstructive CAD, an observation more prevalent in women and can result in unnecessary referral for ICA [25,26].

In defence of functional testing, anatomical measures of lesion severity (i.e., stenosis) are a poor measure of functional significance when assessed by invasive fractional flow reserve (FFR), a measure of coronary blood flow and inducible ischaemia [27]. However, with invasive FFR as the reference standard, CTCA is more sensitive but less specific for ischaemia as compared to non-invasive functional testing [28,29]. Therefore, in the presence of moderate stenosis (i.e. 50%–69%) on CTCA and ongoing symptoms, patients are typically further investigated with functional testing in an attempt to determine haemodynamic significance before deciding if ICA is indicated. Revascularisation in stable CAD has been shown to provide symptom benefit but has limited prognostic value in addition to medical therapy, which suggests that further functional testing may add unnecessary costs [30]. Real-world studies have also highlighted that patients with moderate stenosis on CTCA who are referred for ICA do not often undergo revascularisation [31]. Based on this, the need for additional testing after CTCA in stable CAD should be rationalised, with consideration for a stronger emphasis on a trial of medical therapy first, and further testing reserved for those with ongoing symptoms suggestive of angina.

The ACC and ESC guideline recommendations for the choice of initial diagnostic test in the setting of new onset chest pain (see Table 1) are influenced by the pre-test probability of obstructive CAD [5,6]. Functional testing to evaluate ischaemia is favoured over CTCA by the recent ACC guidelines in patients who are ≥65 years of age, or when more obstructive CAD, myocardial scar or microvascular dysfunction are suspected [6]. The presumed rationale for this approach is that in patients with low–intermediate risk of obstructive CAD, the diagnostic priority is to *rule out* disease, and therefore CTCA with its excellent sensitivity receives a strong recommendation. In contrast, in those with high probability, or who have known obstructive CAD, the diagnostic question is to establish whether the patients' symptoms are related to myocardial ischaemia, hence the recommendation for functional testing. A limitation to this approach is that pre-test probability models can over-estimate risk in the contemporary era, where many patients undergoing investigation of chest pain are typically low–intermediate risk and therefore it would be reasonable to consider the first line use of CTCA in the majority of patients [32].

Management and Prognostic Impact of CTCA

The ideal first line imaging modality for investigating chest pain should have excellent sensitivity, such that most patients can be reassured that their symptoms are not cardiac. In addition, the modality should risk-stratify the remaining patients to enhance decision-making regarding medical therapy and the need for further investigations. The presence of CAD, even if non-obstructive, is associated with significantly greater risks of cardiovascular events and mortality, and thus the ability to identify CAD is essential [33,34]. In addition, myocardial infarction from plaque rupture can occur in patients with non-obstructive CAD (which is undetected by functional testing), and overall plaque burden rather than stenosis may be the main driver for future events [35]. Compared with functional testing, CTCA better identifies patients with non-obstructive, as well as obstructive CAD, thereby providing information across all stages of CAD and the opportunity to commence or intensify risk-reducing preventive therapies [36,37]. Although the presence and degree of ischaemia on non-invasive functional testing associates with worse outcomes, an ischaemia-driven approach to revascularisation did not reduce the rate of death or cardiovascular events compared with medical therapy in trials of stable CAD [38–40].

Several large-scale randomised trials have compared the prognostic value of non-invasive functional testing with CTCA. The PROMISE trial, which randomised 10,003 low-risk symptomatic patients with suspected CAD to outpatient CTCA or functional testing did not show any difference

Table 1 Summary of guideline recommendations for CTCA and functional testing in evaluating chest pain.

Guideline	CTCA	Functional Testing
NICE (updated 2016)	• First-line test for below regardless of pre-test probability • Consider CTCA if clinical assessment indicates typical or atypical stable angina • Consider CTCA if clinical assessment indicates non-anginal chest pain, but resting ECG indicates ST-T changes or Q waves	• Consider functional testing when there is uncertainty about whether chest pain is caused by myocardial ischaemia in patients with CAD • Consider functional testing if CTCA has shown CAD of uncertain functional significance or is non-diagnostic
ESC 2019	• CTCA or functional testing are initial tests to diagnose CAD in symptomatic patients when obstructive CAD cannot be excluded by clinical assessment (*class I, level B*) • CTCA may be an alternative to ICA if another non-invasive test is equivocal or non-diagnostic (*class IIa, level C*)	• CTCA or functional testing are initial tests to diagnose CAD in symptomatic patients when obstructive CAD cannot be excluded by clinical assessment (*class I, level B*) • Consider functional test if CTCA has shown CAD of uncertain functional significance or is non-diagnostic (*class I, level B*) • Imaging functional test is preferred over exercise stress ECG
	• Preferentially consider CTCA if: o Low clinical likelihood of CAD o Patient characteristics suggest high image quality is likely o Information on atherosclerosis desired o No history of CAD • CTCA not recommended (*class III, level C*) when there is: o Extensive coronary calcification o Irregular heart rate o Significant obesity o Inability to cooperate with breath-holding o Or any other conditions that make obtaining good image quality unlikely	• Preferentially consider functional testing if: o High clinical likelihood of CAD o Revascularisation likely o Viability assessment also required o Information on heart rate response and exercise tolerance desired
AHA/ACC 2021	• CTCA can be used in intermediate-risk patients with acute chest pain and: o No known CAD (*class I, level A*), to exclude CAD o Previous (≤1 year) mildly abnormal functional test (*class 2a, level C*), to diagnose obstructive CAD o Inconclusive stress test (*class 2a, level C*), to exclude CAD o Known non-obstructive CAD (*class 2a, level B*), to evaluate burden and progression	• Functional testing can be used to diagnose ischaemia in intermediate-risk patients with acute chest pain and: o No known CAD (*class I, level B*) o Inconclusive CTCA and no known CAD (*class 2a, level C*) o Known CAD (*class 2a, level B*)
	• CTCA can be used in intermediate-high risk patients with stable chest pain and: o No known CAD (*class I, level A*), to diagnose/exclude CAD o Inconclusive/abnormal functional test and no known CAD (*class 2a, level B*) o Known non-obstructive CAD (*class 2a, level B*), to evaluate burden and progression o High suspicion of CAD despite negative functional test (*class 2b, level C*)	• Functional testing can be used to diagnose ischaemia in intermediate-high risk patients with stable chest pain and: o No known CAD (*class I, level B*) o Inconclusive CTCA and no known CAD (*class 2a, level B*) o Known non-obstructive CAD (*class 2a, level C*) o Known obstructive CAD (*class I, level B*)
	• CT-FFR can diagnose vessel-specific ischaemia and guide revascularisation when stenosis of 40%–90% is present on CTCA in proximal or middle segment (*class 2a, level B*)	• In patients with prior CABG surgery, functional testing can be used to evaluate for ischaemia or CTCA for graft stenosis/occlusion in acute chest pain (*class I, level C*) or stable chest pain (*class 2a, level C*)

Table 1. (continued).

Guideline	CTCA	Functional Testing
	• CTCA favoured when: o Goal is to rule out obstructive CAD or detect non-obstructive CAD o High-quality imaging and expert interpretation is routinely available o Lower likelihood of CAD (age <65 yrs) o Prior functional test is inconclusive o Assessment of anomalous coronary arteries, aorta or pulmonary arteries is also desired	• Functional testing favoured when: o Management is guided by ischaemia o High-quality imaging and expert interpretation is routinely available o Higher likelihood of CAD (age ≥65 yrs) o Prior CTCA is inconclusive o Myocardial scar or coronary microvascular dysfunction is suspected

Abbreviations: ACC, American College of Cardiology; AHA, American Heart Association; CTCA, computed tomography coronary angiography; CABG, coronary artery bypass graft; CAD, coronary artery disease; ECG, electrocardiogram; ESC, European Society of Cardiology; ICA, invasive coronary angiography; NICE, The National Institute for Health and Care Excellence; CT-FFR, computed tomography fractional flow reserve.

in death, myocardial infarction, hospitalisation for unstable angina, or major procedural complications over a median follow-up of 25 months, although findings on CTCA was a superior predictor of subsequent events [18,36]. There are several postulated reasons for the findings of the PROMISE trial, the most pertinent being the trial was likely underpowered to detect differences in the primary outcome, as follow-up was reduced from the planned 2 years to a minimum 1 year, leading to lower than anticipated event rates [41]. Interestingly, compared to functional testing, CTCA was better able to predict subsequent cardiovascular events. The more recent Scottish Computed Tomography of the Heart (SCOT-HEART) trial, which randomised 4,146 patients referred to cardiology clinics with stable chest pain to standard care plus CTCA or standard care alone (mostly exercise stress testing), demonstrated that CTCA increased diagnostic certainty by two-fold and significantly reduced the 5-year risk of death from coronary heart disease and non-fatal myocardial infarction on extended follow-up beyond the primary focus of the trial [42]. Although rates of ICA were greater in the CTCA group in the first few months, no significant increase in rates of ICA or coronary revascularisation was seen at 5-year follow-up, suggesting that patients with obstructive CAD were referred earlier for the procedure [42]. In contrast to PROMISE, the SCOT-HEART investigators actively prompted attending clinicians to review their treatment decisions in light of the CTCA results and encouraged medical therapy for non-obstructive CAD. Therefore, the addition of CTCA led to a 30% increase in the use of preventive medications such as aspirin and statins, across all degrees of disease (obstructive and non-obstructive) highlighting an important advantage over functional testing [42]. The results are particularly impressive as despite only a modest increase in the use of preventive medical therapies, the trial demonstrated significant event reductions and the benefits were seen despite relatively low event rates [42]. The prognostic benefit of CTCA was similar for both men and women and, in particular, led to reduced medication use in women due to detection of normal coronary arteries [43].

The management of stable CAD continues to be debated following the International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA) trial [44]. The decision to undergo coronary revascularisation has traditionally been based on the presence and extent of myocardial ischaemia. The ISCHEMIA trial randomised 5,179 patients and demonstrated that in patients with stable CAD and moderate or severe ischaemia on functional testing, an initial invasive strategy did not reduce cardiovascular events compared with an initial conservative strategy of medical therapy alone over a median follow-up of 3.2 years [44]. Arguably, these results favour medical therapy and potentially CTCA as a first-line approach in the evaluation of patients with stable CAD without unprotected left main CAD and with normal left ventricular function (or strictly speaking, any other ISCHEMIA trial exclusion criteria), as any degree of ischaemia could potentially be managed medically in the first instance [45]. The use of CTCA in this context would have utility in ruling out left main CAD which may require an invasive strategy, for quantifying the burden of plaque and in guiding medical therapy. However, it must be noted that the ISCHEMIA trial was not evaluating the use of CTCA in the management of patients with ischaemia or guiding revascularisation decisions.

Recent Advances Strengthen the Role of CTCA

Advances in computational fluid dynamics now permit the derivation of CT-derived fractional flow reserve (CT-FFR) to provide a non-invasive assessment of lesion-specific ischaemia from a standard CTCA acquisition, without additional radiation exposure (Figure 1B). CT-FFR has demonstrated superior diagnostic performance when compared with stenosis severity on CTCA, with the main benefit being its improved specificity and positive predictive value for detecting haemodynamically significant CAD

[46]. In addition, compared to other non-invasive functional tests for CAD, CT-FFR has greater accuracy for diagnosing vessel-specific ischaemia [47]. In clinical practice, the value of CT-FFR is in reclassifying anatomically significant coronary stenosis on CTCA as being functionally non-significant, thereby avoiding the need for further downstream stress testing and unnecessary ICA [48]. In the presence of CAD, CT-FFR is also a strong predictor of clinical outcomes and the application of CT-FFR guided virtual stenting techniques can potentially be used to non-invasively plan and predict the effect of revascularisation procedures [49–51]. CT-FFR is now recommended by the ACC guidelines for diagnosing vessel-specific ischaemia and to guide revascularisation when stenoses of 40%–90% are present in proximal or middle segments of a coronary artery [6]. As yet, CT-FFR is not available in Australia and with a cost of approximately AUD$1,000 per case, further research is needed to evaluate its utility and cost-effectiveness in the Australian context.

Another advance in the application of CTCA is the ability to non-invasively assess plaque composition and morphology, which provides a personalised risk assessment and also prognostic information over and above stenosis severity [52] (Figure 1A). Adverse characteristics which identify "vulnerable" or "high-risk" plaque, such as low-attenuation plaque, positive remodelling, spotty calcification or the "napkin ring" sign, and overall calcified plaque burden, are associated with a higher risk of future acute coronary syndrome and this is further supported by subsequent analyses of the PROMISE and SCOT-HEART trials [53–55]. In addition, perivascular fat attenuation index, an emerging biomarker of coronary artery inflammation and atherosclerosis on CTCA, predicts adverse outcomes and can identify vulnerable plaques as well as the "vulnerable patient" [56,57] (Figure 1C). Emerging software applications and the integration of validated artificial intelligence algorithms promises to optimise image acquisition and analysis, improve diagnostic accuracy, and enhance clinical workflow efficiency and performance by reducing human workload and increasing analysis speeds [58,59]. Artificial intelligence could also help to rapidly identify high-risk features on CTCA, further providing prognostic information. Additionally, newer hardware technologies, such as photon counting detectors, could allow further advanced plaque characterisation [60]. Future studies should evaluate management implications and outcomes following identification of high-risk CTCA features and perivascular inflammation, as currently the mainstay of management remains intensive risk factor control, including lipid-lowering.

Limitations of CTCA

Advantages and limitations of CTCA are presented in Table 2. Due to technological advances, introduction of 64-slice (and higher) scanners, prospective electrocardiogram-gating and strict requirements for optimal image acquisition, the temporal and spatial resolution of CTCA has improved and the scan can be performed with radiation doses <5 mSv [61,62]. Despite low radiation dose from contemporary CTCA scanners, select functional tests with no radiation exposure may be favoured in younger women, due to radiation-sensitive tissue.

The accuracy of CTCA for diagnosing obstructive CAD is significantly affected by image quality and increasing burden of calcific CAD. For example, CTCA may overestimate the severity of lesions when there is heavy calcification, motion artefacts or different reference points for lumen size in plaques with positive remodelling, thus potentially resulting in

Table 2 Strengths and limitations of CTCA in the assessment of chest pain.

Strengths	• Can include coronary artery calcium scores
	• Able to effectively rule out CAD, detect non-obstructive CAD and quantify burden of CAD
	• Guides use of preventative medical therapy and adds prognostic value
	• An efficient, safe, and potentially cost-effective tool for emergency department chest pain assessment pathways
	• Can identify and characterise high-risk plaque features and perivascular inflammation, predictors of coronary events
	• Incorporating CT fractional flow reserve or CT perfusion can guide revascularisation
	• Increasing potential for artificial intelligence, automation, and commercial software for optimising assessment
	• Detects congenital anomalous coronary arteries
Limitations	• Exposure to ionising radiation, although now at low doses due to advancements in technology and image acquisition
	• Contraindicated in severe contrast allergies or renal impairment due to need for iodinated contrast
	• Image quality reduced if heart rate cannot be controlled, irregular heart rhythm, dense calcification, significant obesity or multiple or small-diameter (<3 mm) stents are present
	• May increase downstream invasive coronary angiography in the short-term, likely due to better patient selection
	• Increased resources, education and highly trained readers are needed to facilitate more widespread use
	• Further trials are needed to evaluate emerging technologies

Abbreviations: CAD, coronary artery disease; CTCA, computed tomography coronary angiography; CT, computed tomography.

referral for ICA [63]. The image quality of CTCA is optimised by administering rate-slowing medications, typically beta blockers to reduce the heart rate to <60 bpm at the time of acquisition. Furthermore, sublingual glyceryl-trinitrate is given to vasodilate the coronary arteries and allow for more accurate evaluation of luminal stenosis, which is particularly relevant in the presence of calcific disease. Recognising this, guidelines for investigating chest pain typically advise against CTCA when the heart rate cannot be adequately controlled, such as patients with atrial fibrillation and rapid ventricular response, and in patients in whom glyceryl-trinitrate is a relative contraindication, such as severe aortic stenosis. Given the need to administer radiocontrast, CTCA is not advised in those with severe contrast allergy or renal dysfunction (estimated glomerular filtration rate ≤30 mL/min/1.73 m^2). CTCA has generally not been recommended in patients with coronary stents due to blooming artefact from metallic stent struts which may reduce diagnostic accuracy, although with improvements in image reconstruction, a recent meta-analysis highlighted that large calibre (≥3 mm) thin-strut (<100 μm) stents permit acceptable diagnostic accuracy for assessing instent-restenosis [64].

Implications for Australian Chest Pain Pathways

Overall, the majority of patients undergoing investigation of chest pain in real-world settings have pre-test probabilities of obstructive CAD that are low–intermediate, and which are substantially lower than what is predicted by previous scoring models across nearly all strata of age, sex and presenting symptoms [65–68]. Furthermore, large real-world registries have consistently demonstrated that most patients undergoing functional testing prior to ICA are found to have non-obstructive CAD [7,24]. Although the NICE guideline has moved away from assessment of pre-test probabilities, both the ESC and ACC guidelines have provided contemporary pre-test probability charts using age, sex and symptoms [4–6]. Recognising that these risk models are derived from older data and depend on the population studied, there is a need for updated models in the Australian population to better define risk [32].

Overseas, first line use of CTCA in the evaluation of chest pain and suspected CAD has been shown to be safe and cost-effective in low–intermediate risk patients [8,69]. Studies implementing CTCA-based strategies for chest pain evaluation in the emergency department have shown that it results in more rapid and cost-efficient diagnoses [70–73]. Overall diagnostic costs can be reduced due to avoidance of ICA and other subsequent tests in those who have obstructive CAD ruled out by CTCA [74,75]. However, few studies in Australia have evaluated the utility of CTCA in chest pain evaluation pathways and the impact on downstream testing, costs and safety [76,77]. Such pathways will need to be designed according to patient needs, available resources and local service delivery. An example of a contemporary chest pain pathway utilising CTCA as a first line outpatient diagnostic modality for stable troponin negative chest pain in intermediate risk patients that is being evaluated in a West Australian tertiary hospital is illustrated in Figure 2.

The Cardiac Society of Australia and New Zealand guidelines for appropriate use of non-invasive coronary imaging were published in 2011 and updated guidelines are needed [78]. There is evidence that use of CTCA has steadily increased in Australia, which may have future implications for adequate resourcing and workforce planning [79]. In the United Kingdom, studies have highlighted that the limited number of CTCA scanners, trained personnel and variation in health care between regions were major barriers to expanding the use of CTCA for evaluating chest pain [80]. These studies are dependent on local availability, expertise, economic factors and disease prevalence, therefore research evaluating demand, supply and cost-effectiveness needs to be conducted in the Australian context. The opportunity for implementing CTCA in rural and remote areas also needs consideration given the challenges of delivering accessible health care [81,82]. Significant investment in CTCA technology, training, accreditation, and research may be needed to implement guideline recommendations and maintain efficient and effective care throughout Australia. With a potential increase in demand for CTCA, changes to Medicare funding may be needed to provide greater access to the technology. Currently, Medicare reimbursement for CTCA is only available via specialist referral in low–intermediate risk patients with symptoms consistent with coronary ischaemia, however, given the ability of primary care physicians to order functional tests, a similar mandate for CTCA may be reasonable to consider in the future.

Conclusion

CTCA is a robust non-invasive imaging modality that is becoming increasingly accepted as a first line test for the evaluation of chest pain in patients at low–intermediate risk. It offers advantages over functional testing in the detection of obstructive and non-obstructive CAD, as well as for confidently ruling out CAD. The ability to accurately quantify the anatomical burden and location of coronary artery plaque improves prognostication and promotes the use of guideline-directed preventive therapies, thereby improving patient outcomes. With its excellent negative predictive value, CTCA serves as an ideal "gatekeeper" to ICA in low–intermediate risk patients. In addition, recent advances in CTCA technology have better positioned the modality as a comprehensive diagnostic test for chest pain. Although the use of innovative tools such as CT-FFR and identification of high-risk plaque characteristics by CTCA are not widely used in Australia, they have the potential to allow for more personalised risk assessment and may inform patient management if incorporated into future clinical practice. Given the evolving evidence and recommendations from several international guidelines, there should be strong consideration

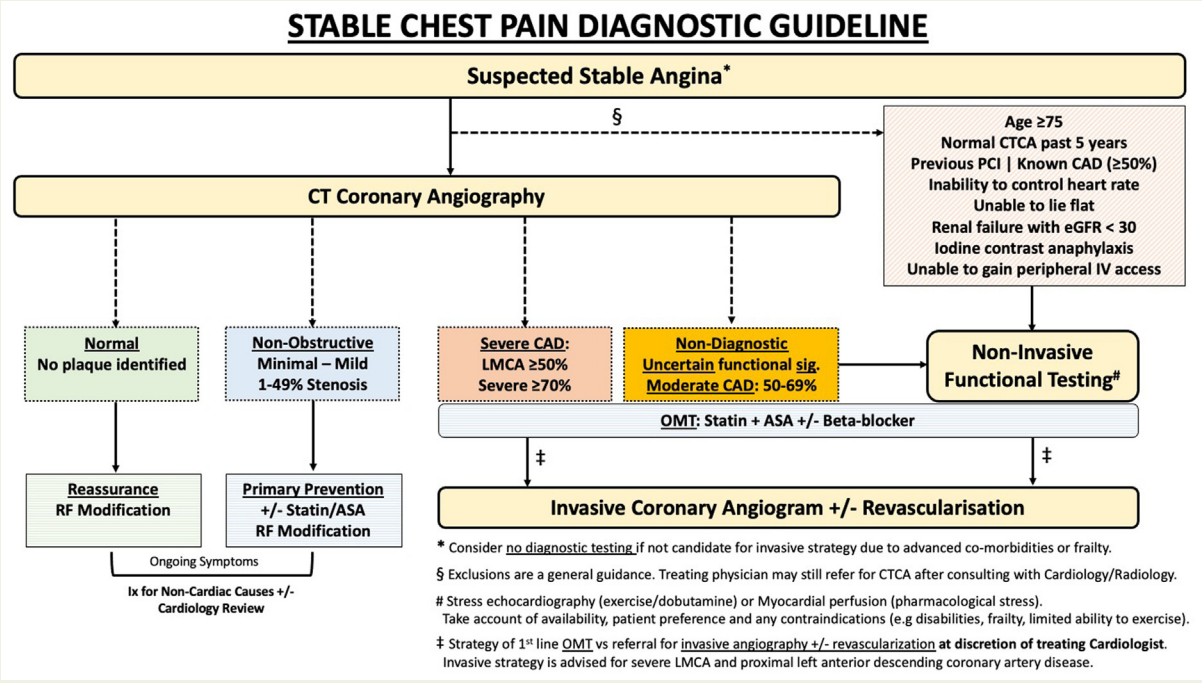

Figure 2 Example chest pain pathway utilising first line CTCA strategy.
Abbreviations: CTCA, CT coronary angiography; CT, computed tomography; PCI, percutaneous coronary intervention; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; IV, intravenous; LMCA, left main coronary artery; OMT, optimal medical therapy; ASA, aspirin; RF, risk factor.

for incorporating CTCA into chest pain evaluation pathways in Australia. Future research in Australia should define the demand for CTCA, assess clinical pathways incorporating CTCA, and evaluate its impact on downstream testing, clinical outcomes and cost-effectiveness.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosures

ARI is a consultant for Abbott Medical, Boston Scientific and Artrya Ltd (including equity interest). NSR Lan has received research funding and speaker honoraria from Sanofi and conference support from Boehringer Ingelheim and Amgen. GF is a consultant for CSL. JL is a consultant and hold stock options in HeartFlow and Circle CVI. GD is a consultant and has equity interest in Artrya Ltd. SJN is a consultant for Amgen, Akcea, AstraZeneca, Amarin, Boehringer Ingelheim, CSL Behring, Eli Lilly, Esperion, Kowa, Merck, Takeda, Pfizer, Sanofi-Regeneron, and Novo Nordisk.

References

[1] Hsia RY, Hale Z, Tabas JA. A national study of the prevalence of life-threatening diagnoses in patients with chest pain. JAMA Intern Med. 2016;176:1029–32.
[2] Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi S, AlKatheeri R, et al. Global epidemiology of ischemic heart disease: results from the Global Burden of Disease Study. Cureus. 2020;12:e9349.
[3] Wright RS, Anderson JL, Adams CD, Bridges CR, Casey DE Jr, Ettinger SM, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Academy of Family Physicians, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2011;57:e215–367.
[4] Moss AJ, Williams MC, Newby DE, Nicol ED. The updated NICE guidelines: cardiac CT as the first-line test for coronary artery disease. Curr Cardiovasc Imaging Rep. 2017;10:15.
[5] Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J. 2020;41:407–77.
[6] Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the evaluation and diagnosis of chest pain: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021: Cir0000000000001030.
[7] Patel MR, Peterson ED, Dai D, Brennan JM, Redberg RF, Anderson HV, et al. Low diagnostic yield of elective coronary angiography. N Engl J Med. 2010;362:886–95.
[8] Genders TS, Petersen SE, Pugliese F, Dastidar AG, Fleischmann KE, Nieman K, et al. The optimal imaging strategy for patients with stable chest pain: a cost-effectiveness analysis. Ann Intern Med. 2015;162:474–84.
[9] Abdelrahman KM, Chen MY, Dey AK, Virmani R, Finn AV, Khamis RY, et al. Coronary computed tomography angiography from clinical uses to emerging technologies: JACC state-of-the-art review. J Am Coll Cardiol. 2020;76:1226–43.
[10] Jennings GL, Audehm R, Bishop W, Chow CK, Liaw ST, Liew D, et al. National Heart Foundation of Australia: position statement on coronary

artery calcium scoring for the primary prevention of cardiovascular disease in Australia. Med J Aust. 2021;214:434–9.
[11] Mortensen MB, Gaur S, Frimmer A, Bøtker HE, Sørensen HT, Kragholm KH, et al. Association of age with the diagnostic value of coronary artery calcium score for ruling out coronary stenosis in symptomatic patients. JAMA Cardiol. 2022;7:36–44.
[12] Mowatt G, Cook JA, Hillis GS, Walker S, Fraser C, Jia X, et al. 64-Slice computed tomography angiography in the diagnosis and assessment of coronary artery disease: systematic review and meta-analysis. Heart. 2008;94:1386–93.
[13] von Ballmoos MW, Haring B, Juillerat P, Alkadhi H. Meta-analysis: diagnostic performance of low-radiation-dose coronary computed tomography angiography. Ann Intern Med. 2011;154:413–20.
[14] Hulten EA, Carbonaro S, Petrillo SP, Mitchell JD, Villines TC. Prognostic value of cardiac computed tomography angiography: a systematic review and meta-analysis. J Am Coll Cardiol. 2011;57:1237–47.
[15] Andreini D, Pontone G, Mushtaq S, Bartorelli AL, Bertella E, Antonioli L, et al. A long-term prognostic value of coronary CT angiography in suspected coronary artery disease. JACC Cardiovasc Imaging. 2012;5:690–701.
[16] Budoff MJ, Dowe D, Jollis JG, Gitter M, Sutherland J, Halamert E, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. J Am Coll Cardiol. 2008;52:1724–32.
[17] Gentile F, Castiglione V, De Caterina R. Coronary artery anomalies. Circulation. 2021;144:983–96.
[18] Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, et al. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372:1291–300.
[19] Gongora CA, Bavishi C, Uretsky S, Argulian E. Acute chest pain evaluation using coronary computed tomography angiography compared with standard of care: a meta-analysis of randomised clinical trials. Heart. 2018;104:215–21.
[20] Siontis GC, Mavridis D, Greenwood JP, Coles B, Nikolakopoulou A, Jüni P, et al. Outcomes of non-invasive diagnostic modalities for the detection of coronary artery disease: network meta-analysis of diagnostic randomised controlled trials. BMJ. 2018;360:k504.
[21] Williams MC, Hunter A, Shah ASV, Assi V, Lewis S, Smith J, et al. Use of coronary computed tomographic angiography to guide management of patients with coronary disease. J Am Coll Cardiol. 2016;67:1759–68.
[22] Nielsen LH, Ortner N, Nørgaard BL, Achenbach S, Leipsic J, Abdulla J. The diagnostic accuracy and outcomes after coronary computed tomography angiography vs. conventional functional testing in patients with stable angina pectoris: a systematic review and meta-analysis. Eur Heart J Cardiovasc Imaging. 2014;15:961–71.
[23] Arbab-Zadeh A, Di Carli MF, Cerci R, George RT, Chen MY, Dewey M, et al. Accuracy of computed tomographic angiography and single-photon emission computed tomography-acquired myocardial perfusion imaging for the diagnosis of coronary artery disease. Circ Cardiovasc Imaging. 2015;8:e003533.
[24] Patel MR, Dai D, Hernandez AF, Douglas PS, Messenger J, Garratt KN, et al. Prevalence and predictors of nonobstructive coronary artery disease identified with coronary angiography in contemporary clinical practice. Am Heart J. 2014;167:846–852.e2.
[25] Masi S, Rizzoni D, Taddei S, Widmer RJ, Montezano AC, Lüscher TF, et al. Assessment and pathophysiology of microvascular disease: recent progress and clinical implications. Eur Heart J. 2021;42:2590–604.
[26] Jones E, Eteiba W, Merz NB. Cardiac syndrome X and microvascular coronary dysfunction. Trends Cardiovasc Med. 2012;22:161–8.
[27] Tonino PA, De Bruyne B, Pijls NH, Siebert U, Ikeno F, van' t Veer M, et al. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. N Engl J Med. 2009;360:213–24.
[28] Danad I, Szymonifka J, Twisk JWR, Norgaard BL, Zarins CK, Knaapen P, et al. Diagnostic performance of cardiac imaging methods to diagnose ischaemia-causing coronary artery disease when directly compared with fractional flow reserve as a reference standard: a meta-analysis. Eur Heart J. 2017;38:991–8.
[29] Danad I, Raijmakers PG, Driessen RS, Leipsic J, Raju R, Naoum C, et al. Comparison of coronary CT angiography, SPECT, PET, and hybrid imaging for diagnosis of ischemic heart disease determined by fractional flow reserve. JAMA Cardiol. 2017;2:1100–7.
[30] Bangalore S, Maron DJ, Stone GW, Hochman JS. Routine revascularization versus initial medical therapy for stable ischemic heart disease: a systematic review and meta-analysis of randomized trials. Circulation. 2020;142:841–57.
[31] Morgan-Hughes G, Williams MC, Loudon M, Roobottom CA, Veitch A, Van Lingen R, et al. Downstream testing after CT coronary angiography: time for a rethink? Open Heart. 2021;8.
[32] Foldyna B, Udelson JE, Karády J, Banerji D, Lu MT, Mayrhofer T, et al. Pretest probability for patients with suspected obstructive coronary artery disease: re-evaluating Diamond-Forrester for the contemporary era and clinical implications: insights from the PROMISE trial. Eur Heart J Cardiovasc Imaging. 2019;20:574–81.
[33] Maddox TM, Stanislawski MA, Grunwald GK, Bradley SM, Ho PM, Tsai TT, et al. Nonobstructive coronary artery disease and risk of myocardial infarction. JAMA. 2014;312:1754–63.
[34] Hadamitzky M, Achenbach S, Al-Mallah M, Berman D, Budoff M, Cademartiri F, et al. Optimized prognostic score for coronary computed tomographic angiography: results from the CONFIRM registry (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter Registry). J Am Coll Cardiol. 2013;62:468–76.
[35] Mortensen MB, Dzaye O, Steffensen FH, Bøtker HE, Jensen JM, Rønnow Sand NP, et al. Impact of plaque burden versus stenosis on ischemic events in patients with coronary atherosclerosis. J Am Coll Cardiol. 2020;76:2803–13.
[36] Hoffmann U, Ferencik M, Udelson JE, Picard MH, Truong QA, Patel MR, et al. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: insights from the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain). Circulation. 2017;135:2320–32.
[37] Neglia D, Rovai D, Caselli C, Pietila M, Teresinska A, Aguadé-Bruix S, et al. Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. Circ Cardiovasc Imaging. 2015;8.
[38] Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, et al. Optimal medical therapy with or without PCI for stable coronary disease. N Engl J Med. 2007;356:1503–16.
[39] Frye RL, August P, Brooks MM, Hardison RM, Kelsey SF, MacGregor JM, et al. A randomized trial of therapies for type 2 diabetes and coronary artery disease. N Engl J Med. 2009;360:2503–15.
[40] Stergiopoulos K, Boden WE, Hartigan P, Möbius-Winkler S, Hambrecht R, Hueb W, et al. Percutaneous coronary intervention outcomes in patients with stable obstructive coronary artery disease and myocardial ischemia: a collaborative meta-analysis of contemporary randomized clinical trials. JAMA Intern Med. 2014;174:232–40.
[41] Budoff MJ. What does the PROMISE trial mean for cardiac CT? Outcome of coronary CT angiography vs functional testing in suspected coronary artery disease. J Cardiovasc Comput Tomogr. 2015;9:250–1.
[42] Newby DE, Adamson PD, Berry C, Boon NA, Dweck MR, Flather M, et al. Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med. 2018;379:924–33.
[43] Mangion K, Adamson PD, Williams MC, Hunter A, Pawade T, Shah ASV, et al. Sex associations and computed tomography coronary angiography-guided management in patients with stable chest pain. Eur Heart J. 2020;41:1337–45.
[44] Maron DJ, Hochman JS, Reynolds HR, Bangalore S, O'Brien SM, Boden WE, et al. Initial invasive or conservative strategy for stable coronary disease. N Engl J Med. 2020;382:1395–407.
[45] Hanson CA, Patel TR, Villines TC. The new role of cardiac imaging following the ISCHEMIA trial. Curr Treat Options Cardiovasc Med. 2021;23.
[46] Celeng C, Leiner T, Maurovich-Horvat P, Merkely B, de Jong P, Dankbaar JW, et al. Anatomical and functional computed tomography for diagnosing hemodynamically significant coronary artery disease: a meta-analysis. JACC Cardiovasc Imaging. 2019;12:1316–25.
[47] Driessen RS, Danad I, Stuijfzand WJ, Raijmakers PG, Schumacher SP, van Diemen PA, et al. Comparison of coronary computed tomography angiography, fractional flow reserve, and perfusion imaging for ischemia diagnosis. J Am Coll Cardiol. 2019;73:161–73.
[48] Lu MT, Ferencik M, Roberts RS, Lee KL, Ivanov A, Adami E, et al. Noninvasive FFR derived from coronary CT angiography: management and outcomes in the PROMISE trial. JACC Cardiovasc Imaging. 2017;10:1350–8.
[49] Nørgaard BL, Terkelsen CJ, Mathiassen ON, Grove EL, Bøtker HE, Parner E, et al. Coronary CT angiographic and flow reserve-guided management of patients with stable ischemic heart disease. J Am Coll Cardiol. 2018;72:2123–34.

[50] Ihdayhid AR, Norgaard BL, Gaur S, Leipsic J, Nerlekar N, Osawa K, et al. Prognostic value and risk continuum of noninvasive fractional flow reserve derived from coronary CT angiography. Radiology. 2019;292:343–51.
[51] Modi BN, Sankaran S, Kim HJ, Ellis H, Rogers C, Taylor CA, et al. Predicting the physiological effect of revascularization in serially diseased coronary arteries. Circ Cardiovasc Interv. 2019;12:e007577.
[52] Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, et al. Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. J Am Coll Cardiol. 2015;66:337–46.
[53] Williams MC, Moss AJ, Dweck M, Adamson PD, Alam S, Hunter A, et al. Coronary artery plaque characteristics associated with adverse outcomes in the SCOT-HEART study. J Am Coll Cardiol. 2019;73:291–301.
[54] Williams MC, Kwiecinski J, Doris M, McElhinney P, D'Souza MS, Cadet S, et al. Low-attenuation noncalcified plaque on coronary computed tomography angiography predicts myocardial infarction: results from the multicenter SCOT-HEART trial (Scottish Computed Tomography of the HEART). Circulation. 2020;141:1452–62.
[55] Ferencik M, Mayrhofer T, Bittner DO, Emami H, Puchner SB, Lu MT, et al. Use of high-risk coronary atherosclerotic plaque detection for risk stratification of patients with stable chest pain: a secondary analysis of the PROMISE randomized clinical trial. JAMA Cardiol. 2018;3:144–52.
[56] Oikonomou EK, Marwan M, Desai MY, Mancio J, Alashi A, Hutt Centeno E, et al. Non-invasive detection of coronary inflammation using computed tomography and prediction of residual cardiovascular risk (the CRISP CT study): a post-hoc analysis of prospective outcome data. Lancet. 2018;392:929–39.
[57] Antonopoulos AS, Sanna F, Sabharwal N, Thomas S, Oikonomou EK, Herdman L, et al. Detecting human coronary inflammation by imaging perivascular fat. Sci Transl Med. 2017;9.
[58] Dey D, Slomka PJ, Leeson P, Comaniciu D, Shrestha S, Sengupta PP, et al. Artificial intelligence in cardiovascular imaging: JACC state-of-the-art review. J Am Coll Cardiol. 2019;73:1317–35.
[59] van den Oever LB, Vonder M, van Assen M, van Ooijen PMA, de Bock GH, Xie XQ, et al. Application of artificial intelligence in cardiac CT: from basics to clinical practice. Eur J Radiol. 2020;128:108969.
[60] Si-Mohamed SA, Sigovan M, Hsu JC, Tatard-Leitman V, Chalabreysse L, Naha PC, et al. In vivo molecular K-edge imaging of atherosclerotic plaque using photon-counting CT. Radiology. 2021;300:98–107.
[61] Abbara S, Blanke P, Maroules CD, Cheezum M, Choi AD, Han BK, et al. SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography: a report of the Society of Cardiovascular Computed Tomography Guidelines Committee: endorsed by the North American Society for Cardiovascular Imaging (NASCI). J Cardiovasc Comput Tomogr. 2016;10:435–49.
[62] Achenbach S, Marwan M, Ropers D, Schepis T, Pflederer T, Anders K, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. Eur Heart J. 2010;31:340–6.
[63] Meijboom WB, Meijs MF, Schuijf JD, Cramer MJ, Mollet NR, van Mieghem CA, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. J Am Coll Cardiol. 2008;52:2135–44.
[64] Dai T, Wang JR, Hu PF. Diagnostic performance of computed tomography angiography in the detection of coronary artery in-stent restenosis: evidence from an updated meta-analysis. Eur Radiol. 2018;28:1373–82.
[65] Cheng VY, Berman DS, Rozanski A, Dunning AM, Achenbach S, Al-Mallah M, et al. Performance of the traditional age, sex, and angina typicality-based approach for estimating pretest probability of angiographically significant coronary artery disease in patients undergoing coronary computed tomographic angiography: results from the multinational coronary CT angiography evaluation for clinical outcomes: an international multicenter registry (CONFIRM). Circulation. 2011;124. 2423-32, 1-8.
[66] Ferreira AM, Marques H, Tralhão A, Santos MB, Santos AR, Cardoso G, et al. Pre-test probability of obstructive coronary stenosis in patients undergoing coronary CT angiography: comparative performance of the modified diamond-Forrester algorithm versus methods incorporating cardiovascular risk factors. Int J Cardiol. 2016;222:346–51.
[67] Feger S, Ibes P, Napp AE, Lembcke A, Laule M, Dreger H, et al. Clinical pre-test probability for obstructive coronary artery disease: insights from the European DISCHARGE pilot study. Eur Radiol. 2021;31:1471–81.
[68] Winther S, Schmidt SE, Rasmussen LD, Juárez Orozco LE, Steffensen FH, Bøtker HE, et al. Validation of the European Society of Cardiology pre-test probability model for obstructive coronary artery disease. Eur Heart J. 2021;42:1401–11.
[69] Lee AJ, Michail M, Quaderi SA, Richardson JA, Aggarwal SK, Speechly-Dick ME. Implementation of NICE Clinical Guideline 95 for assessment of stable chest pain in a rapid access chest pain clinic reduces the mean number of investigations and cost per patient. Open Heart. 2015;2:e000151.
[70] Goldstein JA, Chinnaiyan KM, Abidov A, Achenbach S, Berman DS, Hayes SW, et al. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. 2011;58:1414–22.
[71] Hulten E, Pickett C, Bittencourt MS, Villines TC, Petrillo S, Di Carli MF, et al. Outcomes after coronary computed tomography angiography in the emergency department: a systematic review and meta-analysis of randomized, controlled trials. J Am Coll Cardiol. 2013;61:880–92.
[72] Hoffmann U, Truong QA, Schoenfeld DA, Chou ET, Woodard PK, Nagurney JT, et al. Coronary CT angiography versus standard evaluation in acute chest pain. N Engl J Med. 2012;367:299–308.
[73] Litt HI, Gatsonis C, Snyder B, Singh H, Miller CD, Entrikin DW, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. N Engl J Med. 2012;366:1393–403.
[74] Chang HJ, Lin FY, Gebow D, An HY, Andreini D, Bathina R, et al. Selective referral using CCTA versus direct referral for individuals referred to invasive coronary angiography for suspected CAD: a randomized, controlled, open-label trial. JACC Cardiovasc Imaging. 2019;12:1303–12.
[75] Lubbers M, Dedic A, Coenen A, Galema T, Akkerhuis J, Bruning T, et al. Calcium imaging and selective computed tomography angiography in comparison to functional testing for suspected coronary artery disease: the multicentre, randomized CRESCENT trial. Eur Heart J. 2016;37:1232–43.
[76] Hamilton-Craig C, Fifoot A, Hansen M, Pincus M, Chan J, Walters DL, et al. Diagnostic performance and cost of CT angiography versus stress ECG—a randomized prospective study of suspected acute coronary syndrome chest pain in the emergency department (CT-COMPARE). Int J Cardiol. 2014;177:867–73.
[77] Nasis A, Meredith IT, Sud PS, Cameron JD, Troupis JM, Seneviratne SK. Long-term outcome after CT angiography in patients with possible acute coronary syndrome. Radiology. 2014;272:674–82.
[78] Liew GY, Feneley M, Worthley SG. Noninvasive coronary artery imaging: current clinical applications: Cardiac Society of Australia and New Zealand guidelines. Heart Lung Circ. 2011;20:425–37.
[79] Leong CL, Teoh TW, Bentley L, O'Rourke E, Allright A, Werkmeister M, et al. Resource implications following expansion of computed tomography coronary angiography: an Australian experience. J Med Imaging Radiat Oncol. 2021.
[80] Dreisbach JG, Nicol ED, Roobottom CA, Padley S, Roditi G. Challenges in delivering computed tomography coronary angiography as the first-line test for stable chest pain. Heart. 2018;104:921–7.
[81] Kempton HR, Bemand T, Bart NK, Suttie JJ. Using coronary artery calcium scoring as preventative health tool to reduce the high burden of cardiovascular disease in Indigenous Australians. Heart Lung Circ. 2020;29:835–9.
[82] Jeffries A, Costello B, Corkill W, Varghese S, Tayeb H, Gallagher C, et al. Prognostic value of coronary artery calcium scoring and computed tomography coronary angiography in remote Indigenous and non-Indigenous Australians. Int J Cardiol. 2021;328:241–6.