


COMMENTARY

ESR Bridges: CT builds bridges in coronary artery disease



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Imagine if we could non-invasively, reliably, and quantitatively detect coronary atherosclerosis and coronary luminal narrowing early in the development of coronary artery disease (CAD). We could fundamentally change the way CAD is diagnosed and treated. Such non-invasive and quantitative imaging of CAD using computed tomography (CT) is increasingly becoming a clinical reality worldwide, based on evidence generated in a multidisciplinary manner. The two key areas in which evidence has accumulated are the high diagnostic accuracy of CT when compared with invasive coronary angiography (ICA) as the reference [1–5] and improved patient outcomes using CT for comparative effectiveness in clinical trials [6–8].

This effort required technical developments towards multislice CT and cardiac-phase reconstruction [9, 10], as well as clinical evidence from multicentre registries [11–13], meta-analyses [1–5] and randomised

controlled trials [6–8]. Three large multicentre clinical trials in stable chest pain patients with intermediate likelihood of CAD have been published (PROMISE, SCOT-HEART and DISCHARGE) and one large trial is ongoing (CLEAR-CAD). PROMISE indicated that CT is associated with a lower rate of death or non-fatal myocardial infarction compared to functional testing [6]. SCOT-HEART found fewer deaths from CAD or non-fatal myocardial infarction with CT and standard care compared to standard care alone at 5 years of follow-up [7]. DISCHARGE showed fewer major procedure-related complications in the CT compared to the ICA group [8].

Three fundamental changes

Evidence has been generated primarily through close multidisciplinary collaboration between radiologists, cardiologists, cardiac surgeons, statisticians, epidemiologists, trialists and engineers. However, translating this evidence so that CT can truly begin to build bridges in CAD will require further multidisciplinary clinical collaboration to achieve real clinical impact through improved patient lives and well-being. What are the main arguments for integrating CT into the clinical pathways for patients with stable chest pain and suspected CAD? Based on the evidence described above, three fundamental changes in the approach to CAD are suggested [14] (Table 1).

First, CT can better detect non-obstructive CAD and therefore early coronary atherosclerosis compared to ICA [8]. This may lead to increased use of preventive therapy with CT. In SCOT-HEART, more patients in the CT group used aspirin (52% vs 41%) and statins (59% vs 50%) at 5-year follow-up compared with the standard care group [15], which was associated with 50% reduction in CAD mortality or non-fatal myocardial infarction [7]. In addition, patients in the CT group of the CAD-Man trial had higher

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Table 1 Three fundamental changes in the approach to CAD

| Fundamental change | What CT provides | Evidence for change |
|--|--|---|
| 1. Better prevention of cardiovascular events with the help of non-invasive imaging for the characterisation and quantification of coronary atherosclerosis | Early detection of coronary atherosclerosis by CT may lead to increased use of preventive therapy which results in fewer cardiovascular events | SCOT-HEART: more patients in the CT group used aspirin and statins at 5-year follow-up CAD-Man: higher statin adherence in the CT group at follow-up |
| 2. Individual determination of treatment strategy becomes possible using non-invasive imaging for determining individually the presence and extend of CAD | Non-invasive assessment of obstructive CAD by CT for individualised decision-making about who may benefit most from revascularisation with additional functional tests | DISCHARGE: 50% greater use of additional invasive or non-invasive functional testing with 25% fewer revascularisation but similar angina reduction at follow-up |
| 3. Improved procedural planning for the revascularisation strategy in patients with obstructive CAD | CT provides imaging biomarkers that could be used to guide revascularisation planning in individual patients in the future | Early, non-randomised studies; future randomised trials are needed |

statin adherence (60%) compared with the ICA group (39%), resulting in greater cholesterol reduction at 3.3 years [16]. Better prevention contributes to a long-term reduction in myocardial infarction and stroke and is facilitated by the ability of CT to more accurately identify non-obstructive CAD when compared with ICA (36% versus 22%) [8].

Second, CT is well suited for determining the best treatment strategy in patients with suspected obstructive CAD [14]. The DISCHARGE trial showed a 50% greater use of additional invasive or non-invasive functional testing in the CT group compared with the ICA group, which was associated with a 25% reduction in revascularisation with no difference in angina reduction at 3.5 years of follow-up [8]. Non-invasive assessment of obstructive disease and individualised decision-making about who may benefit most from revascularisation is therefore an important part of the potential future success story of CT in CAD.

Third, improved procedural planning can be achieved in patients with obstructive CAD confirmed by CT. In patients with high-risk anatomy in whom revascularisation provides a prognostic benefit, the route of revascularisation (i.e. percutaneous or surgical or both) could in the future be determined based on quantitative coronary artery imaging biomarkers generated from CT [17–23]. It is just a matter of time before coronary artery bypass graft surgery can be planned based on CT, provided the image quality is high and taking into account additional functional testing and accepted severity (SYNTAX) criteria. For instance, an initial study showed that heart team decisions based on CT for the route of revascularisation were in high agreement when compared with ICA [24]. Furthermore, an ongoing nonrandomised study analyses the safety and feasibility of CT guidance for planning and executing coronary artery bypass grafting [25].

Directions for future research

However, there are several limitations to the current evidence base for coronary CT. First, in patients with acute presentation, CT compared with established standard care reduced ICA rates but did not improve clinical outcomes [26]. Second, while artificial intelligence (AI) has potential to assess images and reduce workload of radiologists with high accuracy, there is limited implementation because little is known about which AI approaches might work best to individualise preventive (lipid lowering, anti-inflammatory and anti-thrombotic) therapy based on CT findings [17, 18]. Third, the current evidence in favour of CT is limited to patients with stable chest pain and an intermediate likelihood of obstructive CAD [14], suggesting that further multidisciplinary research is needed to assess patients on other ends of the clinical spectrum in which the use of CT in suspected CAD can be expected to be beneficial.

Despite these limitations, it is clear that multidisciplinary research has already built important bridges in the diagnosis and treatment of CAD and can serve as a bridgehead to further link radiology with the other disciplines to undertake even more ambitious efforts of non-invasive and quantitative cardiovascular imaging research to improve the care of our cardiovascular patients in the future.

Recommendations for clinical practice and directions for future research

- *Better prevention of cardiovascular events* with the help of non-invasive imaging for the characterisation and quantification of coronary atherosclerosis. Early detection of coronary atherosclerosis by CT may lead to increased use of preventive therapy which results in fewer cardiovascular events.

- *Individual determination of treatment strategy* becomes possible using non-invasive imaging for determining individually the presence and extent of CAD. Non-invasive assessment of obstructive CAD by CT for individualised decision-making about who may benefit most from revascularisation with additional functional tests.
- *Improved procedural planning* for the revascularisation strategy in patients with obstructive CAD. CT provides imaging biomarkers that could be used to guide revascularisation planning in individual patients in the future.

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Declarations

Guarantor

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Conflict of interest

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Ethical approval

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Study subjects or cohorts overlap

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- commentary

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References

- Gatti M, Gallone G, Poggi V et al (2022) Diagnostic accuracy of coronary computed tomography angiography for the evaluation of obstructive coronary artery disease in patients referred for transcatheter aortic valve implantation: a systematic review and meta-analysis. *Eur Radiol* 32:5189–5200
- Wieske V, Walther M, Dubourg B et al (2022) Computed tomography angiography versus Agatston score for diagnosis of coronary artery disease in patients with stable chest pain: individual patient data meta-analysis of the international COME-CCT Consortium. *Eur Radiol* 32:5233–5245
- Mohamed M, Bossert M, Wieske V et al (2023) Combination of computed tomography angiography with coronary artery calcium score for improved diagnosis of coronary artery disease: a collaborative meta-analysis of stable chest pain patients referred for invasive coronary angiography. *Eur Radiol* <https://doi.org/10.1007/s00330-023-10223-z>
- Haase R, Schlattmann P, Gueret P et al (2019) Diagnosis of obstructive coronary artery disease using computed tomography angiography in patients with stable chest pain depending on clinical probability and in clinically important subgroups: meta-analysis of individual patient data. *BMJ* 365:11945
- den Dekker MA, de Smet K, de Bock GH, Tio RA, Oudkerk M, Vliegthart R (2012) Diagnostic performance of coronary CT angiography for stenosis detection according to calcium score: systematic review and meta-analysis. *Eur Radiol* 22:2688–2698
- Douglas PS, Hoffmann U, Patel MR et al (2015) Outcomes of anatomical versus functional testing for coronary artery disease. *N Engl J Med* 372:1291–1300
- SCOT-HEART Investigators, Newby DE, Adamson PD et al (2018) Coronary CT angiography and 5-year risk of myocardial infarction. *N Engl J Med* 379:924–933
- DISCHARGE Trial Group, Maurovich-Horvat P, Bossert M et al (2022) CT or invasive coronary angiography for stable chest pain. *NEJM* 386:1591–1602
- Ohnesorge B, Flohr T, Becker C et al (2000) Cardiac imaging by means of electrocardiographically gated multislice spiral CT: initial experience. *Radiology* 217:564–571
- Lapp RM, Kachelriess M, Ertel D, Kyriakou Y, Kalender WA (2009) Cardiac phase-correlated image reconstruction and advanced image processing in pulmonary CT imaging. *Eur Radiol* 19:1035–1042
- Foldyna B, Uhlig J, Gohmann R et al (2022) Quality and safety of coronary computed tomography angiography at academic and non-academic sites: insights from a large European registry (ESCR MR/CT Registry). *Eur Radiol* 32:5246–5255
- Chow BJ, Small G, Yam Y et al (2015) Prognostic and therapeutic implications of statin and aspirin therapy in individuals with nonobstructive coronary artery disease: results from the CONFIRM (CORonary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter CONFIRM (CORonary CT Angiography Evaluation for Clinical Outcomes: An International
- Min JK, Dunning A, Lin FY et al (2011) Age- and sex-related differences in all-cause mortality risk based on coronary computed tomography angiography findings results from the International Multicenter CONFIRM (CORonary CT Angiography Evaluation for Clinical Outcomes: An International

- Multicenter Registry) of 23,854 patients without known coronary artery disease. *J Am Coll Cardiol* 58:849–860
14. QCI Study Group, Mezquita AJV, Biavati F et al (2023) Clinical quantitative coronary artery stenosis and coronary atherosclerosis imaging: a Consensus Statement from the Quantitative Cardiovascular Imaging Study Group. *Nat Rev Cardiol*. 20:696–714. <https://doi.org/10.1038/s41569-023-00880-4>
 15. Adamson PD, Williams MC, Dweck MR et al (2019) Guiding therapy by coronary CT angiography improves outcomes in patients with stable chest pain. *J Am Coll Cardiol* 74:2058–2070
 16. Feger S, Elzenbeck L, Rieckmann N et al (2021) Effect of computed tomography versus invasive coronary angiography on statin adherence: a randomized controlled trial. *JACC Cardiovasc Imaging* 14:1480–1483
 17. van den Oever LB, Vonder M, van Assen M et al (2020) Application of artificial intelligence in cardiac CT: from basics to clinical practice. *Eur J Radiol* 128:108969
 18. QCI Study Group, Follmer B, Williams MC et al (2023) Roadmap on the use of artificial intelligence for imaging of vulnerable atherosclerotic plaque in coronary arteries. *Nat Rev Cardiol*. <https://doi.org/10.1038/s41569-023-00900-3>
 19. Ayx I, Froelich MF, Baumann S, Papavassiliu T, Schoenberg SO (2023) Radiomics in cardiac computed tomography. *Diagnostics (Basel)* 13(2):307. <https://pubmed.ncbi.nlm.nih.gov/36673115/>
 20. Mannil M, Eberhard M, von Spiczak J, Heindel W, Alkadhi H, Baessler B (2020) Artificial intelligence and texture analysis in cardiac imaging. *Curr Cardiol Rep* 22:131
 21. Vliegenthart R (2023) Future trends in CT for coronary artery disease: from diagnosis to prevention. *Radiology* 307:e223285
 22. Kolossvary M, Bluemke DA, Fishman EK et al (2022) Temporal assessment of lesion morphology on radiological images beyond lesion volumes—a proof-of-principle study. *Eur Radiol* 32:8748–8760
 23. Lin A, Manral N, McElhinney P et al (2022) Deep learning-enabled coronary CT angiography for plaque and stenosis quantification and cardiac risk prediction: an international multicentre study. *Lancet Digit Health* 4:e256–e265
 24. Andreini D, Modolo R, Katagiri Y et al (2019) Impact of fractional flow reserve derived from coronary computed tomography angiography on heart team treatment decision-making in patients with multivessel coronary artery disease: insights from the SYNTAX III REVOLUTION Trial. *Circ Cardiovasc Interv* 12:e007607
 25. Kawashima H, Pompilio G, Andreini D et al (2020) Safety and feasibility evaluation of planning and execution of surgical revascularisation solely based on coronary CTA and FFR(CT) in patients with complex coronary artery disease: study protocol of the FASTTRACK CABG study. *BMJ Open* 10:e038152
 26. Gray AJ, Roobottom C, Smith JE et al (2021) Early computed tomography coronary angiography in patients with suspected acute coronary syndrome: randomised controlled trial. *BMJ* 374:n2106

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