CT angiography: front line for acute coronary syndromes now?

Sujith K Seneviratne, Fabian Bamberg, Udo Hoffmann

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Since coronary artery disease (CAD) is the major underlying cause of acute coronary syndrome (ACS), state of the art cardiac CT angiography (CTA), a non-invasive method that quickly and accurately determines the presence and extent of CAD, could substantially improve the early and accurate triage of patients with chest pain. A number of feasibility studies have demonstrated that the strength of cardiac CTA is its high negative predictive value (NPV), suggesting that the presence of haemodynamically significant CAD can be reliably ruled out.¹

In this issue of *Heart*, Meijboom and colleagues convincingly demonstrate that 64-slice CTA accurately excludes the presence of significant coronary stenoses compared with invasive coronary angiography (ICA) in a high-risk acute chest pain population with non-ST elevation ACS and an expectedly high prevalence of CAD (see article on page 1386).² Although the study is unique in patients with non-ST elevation ACS, the accuracy of 64-slice CTA in patients with a high prevalence of CAD has been assessed previously.¹ The authors deliver a strong message confirming the ability of CTA to safely exclude significant CAD (NPV 100%) on a per patient basis in an acute clinical setting in patients with a high prevalence of coronary artery calcification. The data also demonstrate that the specificity (75%) is only moderate and somewhat lower than in recent reports on patients with stable angina (>90%). This can be attributed primarily to the high prevalence of coronary artery calcification (in 67% of 123 false positive cases) and the inclusion of all the segments in the analysis.

Given the general need for revascularisation in patients with non-ST elevation myocardial infarction, a potential clinical benefit of cardiac CTA might be to guide subsequent revascularisation treatment (ie, percutaneous coronary intervention (PCI) vs coronary artery bypass grafting). However, the limited specificity observed by the authors, with an overestimation of lesion severity in almost half of the patients (41/104), suggests that cardiac CTA currently cannot guide these decisions, and further improvements in spatial and temporal resolution are needed to obtain a precise estimation of the severity of stenosis for each lesion.

Early and accurate triage of patients presenting with acute chest pain to the emergency department (ED) remains difficult because neither the chest pain history, a single set of biomarkers for

myocardial necrosis or initial 12-lead ECG alone or in combination identifies a group of patients that can be safely discharged without further diagnostic testing. Moreover, current strategies fail to identify patients with a high probability of ACS who have myocardial ischaemia but no objective evidence for myocardial necrosis at presentation at the ED. Although risk prediction algorithms, such as the acute cardiac ischaemia time-insensitive predictive instrument,³ have improved the ability to stratify patients according to risk, the threshold to admit patients with chest pain remains low, with about 80% of all patients with a lead symptom of chest pain admitted. However, only 10–15% of these patients develop ACS and thus >85% are discharged without a diagnosis of ACS. The resultant impact on healthcare systems worldwide is enormous and is estimated to be \$8 billion annually in the USA alone.

Patients with ACS who have raised initial troponin levels and dynamic ischaemic ECG changes require admission, and significant stenoses can be found in most patients during subsequent invasive coronary angiography. However, diagnosis of non-ST elevation ACS, and especially unstable angina, is not straightforward. Lau *et al* in a review of 109 studies found that authors rarely define unstable angina, and even in the current study seven patients were labelled as “highly suspicious for CAD” despite presumably negative stress tests.⁴ Moreover, stress testing is performed only after exclusion of non-ST elevation myocardial infarction by biomarkers and thus, in general, not considered a tool for early triage in the ED. In addition, owing to its low specificity (<75%), patients not infrequently undergo ICA to exclude CAD.

Preliminary data suggest that cardiac CTA has the potential to redefine the diagnostic and management strategies in patients with acute chest pain in the ED. Rubinshtein *et al* in a study of 58 patients with acute chest pain at intermediate risk (negative initial troponin and non-diagnostic ECG) demonstrated an NPV of 100% and specificity of 92% (n = 35/38) for diagnosis of ACS in the ED by cardiac CTA.⁵ Patients were discharged (n = 35/58) without stress testing if there was no obstructive CAD on CTA and if serial troponin measurements were negative. There were no deaths or myocardial infarctions during a

Abbreviations: ACS, acute coronary syndrome; CAD, coronary artery disease; CTA, CT angiography; ED, emergency department; ICA, invasive coronary angiography; LV, left ventricular; NPV, negative predictive value; PCI, percutaneous coronary intervention

See end of article for authors' affiliations

Correspondence to:
Dr U Hoffmann, Cardiac
MR PE CT Program,
Massachusetts General
Hospital and Harvard
Medical School, 165
Charles River Plaza Suite
400, Boston, MA 02114,
USA; uhoffmann@
partners.org

15-month follow-up but one patient required PCI in a distal coronary vessel (one false negative CTA or disease progression during follow-up).

Hoffmann *et al* in an observational cohort study of 103 consecutive patients at intermediate risk (initially negative troponin and non diagnostic ECG) performed cardiac CTA at the time of initial triage with the results blinded to caregivers.⁶ They found that 40% of the study group had no detectable CAD, 31% had non-obstructive CAD, and 29% had either significant stenosis or could not be ruled out. Both no CAD and non-obstructive CAD had an NPV of 100% for ACS (13.6% event rate on clinical criteria) during index hospitalisation and for major adverse cardiac events after 5 months.

In contrast, Goldstein *et al* randomised patients at very low risk for ACS who also had negative serial troponin values 4 hours apart into a CTA-based triage system ($n = 99$) or a nuclear stress test-based triage system ($n = 98$).⁷ CTA patients without coronary calcification (Agatston score <100 U) and stenosis $<25\%$ were discharged (68%). Patients with 26–70% stenoses underwent stress testing and those with $>70\%$ stenoses, ICA. No events were recorded during a 6-month follow-up and diagnostic efficiency was similar in both groups. However, the cost of patient evaluation was lower in the cardiac CTA arm.

Overall, these data demonstrate the potential of cardiac CTA to decrease safely hospital admissions in patients with acute chest pain. However, before the clinical use of cardiac CTA in the ED, there needs to be validation of a safe, efficient and cost-effective algorithm for a CTA-based triage system. To this end we need to agree on negativity criteria for CTA—that is, whether a negative scan is defined as the absence of any CAD or just the absence of obstructive CAD. Furthermore, the need for serial troponin measurements at 6–12 hours after presentation at the ED in the presence of a negative CTA is still unclear, given that a minority of patients do have ACS with a late rise in troponin even in the absence of CAD. Because most of these patients have at least transient left ventricular (LV) dysfunction (ie, myocarditis, apical ballooning syndrome, coronary ischaemia secondary to spasm, and LV failure), perhaps a strategy that additionally requires normal global and regional LV function, which can be assessed reliably at no additional contrast or radiation by CTA may identify the patient group suitable for early and safe discharge directly from the ED.

A potential drawback of the implementation of cardiac CTA lies in its inability to determine the haemodynamic significance of the lesions. Coupled with a relatively poor specificity, cardiac CTA might potentially lead to unnecessary ICA or interventions, or both. This becomes even more important in view of a recent study showing the limited benefit of PCI, although this was in patients with stable angina.⁸ As suggested by Meijboom *et al*, it

is conceivable that although rare, patients with high risk coronary anatomy (left main, three-vessel or proximal segments of a main coronary artery) could be referred directly for angiography while all other patients with intermediate lesions, distal vessel disease or uninterpretable scans may require further evaluation with stress testing. Regional LV dysfunction in the corresponding vascular territories may also signify the stenoses detected and may improve the specificity of CTA as has been found for nuclear stress imaging.

Radiation exposure, iodinated contrast administration and incidental non-cardiac findings potentially requiring clinical or radiological follow-up are other factors to be considered in an assessment of the efficacy of cardiac CTA in the ED.

Overall, while initial studies are promising for the use of cardiac CTA as the front line in patients with acute chest pain only randomised controlled trials that critically evaluate the cost and perform a comprehensive cost-effectiveness analysis will provide the data necessary for an evidence-based class Ia recommendation by the professional societies.

Authors' affiliations

Sujith K Seneviratne, Fabian Bamberg, Udo Hoffmann, Cardiac MR PET CT Program, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

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