

Int J Cardiovasc Imaging (2009) 25:327–330  
DOI 10.1007/s10554-008-9381-6

EDITORIAL COMMENT

## Triple rule-out CT coronary angiography: three of a kind?

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Received: 20 October 2008 / Accepted: 20 October 2008 / Published online: 11 November 2008  
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A considerable number of patients present at the emergency department with acute chest pain complaints [1–7]. In these patients the accurate diagnosis of acute coronary syndrome (ACS) remains clinically challenging. More than 60% of patients with chest pain who are admitted to the hospital do not turn out to have ACS, emphasizing the need to improve the early triage of patients with acute chest pain. In general, triage is based on the initial clinical assessment including an electrocardiogram (ECG), serial serum markers measurements, echocardiography, myocardial perfusion scintigraphy or cardiovascular magnetic resonance (CMR) [8–19]. While management is relatively straightforward in case of ECG changes and elevated serum markers, a considerable number of patients presents with both serum markers and an ECG that are either within normal limits or inconclusive. Recently, noninvasive visualization of the coronary arteries has become possible with computed tomography (CT) techniques. Both electron beam CT (EBCT) and multi-slice CT (MSCT) allow assessment of coronary calcium burden as a marker of coronary artery disease (CAD). More recently, noninvasive coronary angiography can also be performed, for which MSCT in particular is increasingly used [20–27]. Potentially these

techniques are useful in the clinical work-up of patients presenting with suspected ACS. Haberl et al. [28] showed that MSCT was powerful enough to act as a filter before invasive angiography; in 133 symptomatic patients with suspected CAD, MSCT angiography, but not calcium scoring alone, the number of invasive angiography procedures was reduced by up to one-third with minimal risk for the patient. Olivetti et al. [29] showed in 31 patients reporting chest pain with a medium to low probability of ACS that the MSCT technique can rule out significant coronary stenoses provided that image quality is excellent. In patients with a medium to low coronary risk, MSCT proved to be a more accurate indicator of the need for coronary angiography than exercise stress testing, which is less expensive but has lower predictive values, emphasizing that MSCT has a high negative predictive value for exclusion of coronary artery stenoses. Goldstein et al. [30] compared the safety, diagnostic efficacy, and efficiency of MSCT with standard diagnostic evaluation of low-risk acute chest pain patients. The authors randomized patients to MSCT ( $n = 99$ ) versus standard care ( $n = 98$ ) protocols. Both approaches were completely safe. MSCT alone immediately excluded or identified coronary disease as the source of chest pain in 75% of patients, including 67 with normal coronary arteries and 8 with severe disease referred for invasive evaluation. The remaining 25% of patients required stress testing, owing to intermediate severity lesions or non-diagnostic scans. MSCT

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evaluation reduced diagnostic time compared with standard care (3.4 vs. 15.0 h,  $P < 0.001$ ) and lowered costs. It was concluded that MSCT coronary angiography can definitively establish or exclude coronary disease as the cause of chest pain. However, inability to determine the physiological significance of intermediate severity coronary lesions and cases with inadequate image quality are present limitations. Rubinshtein et al. [31] found that 64-slice cardiac MSCT is a potentially valuable diagnostic tool in emergency department patients with chest pain of uncertain origin, providing early direct noninvasive visualization of coronary anatomy. MSCT had high positive predictive value ( $>95\%$ ) for diagnosing ACS, whereas a negative MSCT study predicted a low rate of major adverse cardiovascular events and favorable outcome during follow-up. Consequently, MSCT-based detection of significant coronary stenoses has tremendous potential to decrease the number of unnecessary hospital admissions, without reducing appropriate admission rates, in patients with chest pain who have non-diagnostic ECG results and normal cardiac enzymes. In 22 patients with ACS, Schuijff et al. [32] showed that significantly less calcifications were present as compared to observations in patients with stable CAD. Moreover, even in non-culprit vessels, multiple non-calcified plaques were detected, indicating diffuse rather than focal atherosclerosis in patients with ACS. Compared to other noninvasive imaging techniques, Gallagher et al. [33] showed that the accuracy of MSCT was at least as good as that of stress nuclear imaging for the detection and exclusion of an acute coronary syndrome in low-risk chest pain patients. Bussel et al. [34] recently demonstrated that delayed-enhanced MSCT allowed differentiation between myocardial infarction and myocarditis with the same accuracy at acute phase compared with CMR.

In the present issue of the International Journal of cardiovascular imaging, Lee et al. [35] showed in a review article that major life-threatening causes of acute chest pain (i.e. acute aortic syndrome and pulmonary embolism as well as ACS) can simultaneously be assessed by the so-called 'triple rule-out' protocol with a single CT scan. In patients with acute chest pain and low to intermediate risk, the triple rule-out protocol may be preferred, especially in older patients who have relatively lower risk of lifelong radiation-induced cancer. However, the increased

radiation dose resulting from the extended volume coverage with this protocol should be fully considered prior to performing this protocol. Therefore, in emergency department patients who have a low clinical suspicion of pulmonary embolism and acute aortic syndrome, especially younger patients, dedicated coronary CT angiography accompanied by modifications to reduce radiation dose is recommended.

The use of triple rule-out protocol has been reported in several studies [36–40]. In a previous study from the same group [35], it was already demonstrated that MSCT appeared to be logistically feasible and showed promise as a comprehensive method for evaluating cardiac and noncardiac chest pain in stable emergency department patients [36]. Haidary et al. [37] showed that the triple rule-out 64-slice biphasic injection breath-hold CT angiography protocol provided significantly higher attenuation of aortic and pulmonary vasculature compared with our current 10- and 16-slice protocols. Rogg et al. [38] used the triple rule-out protocol and concluded that a significant number of emergency department patients who are evaluated for at least one of these three major chest pain syndromes received simultaneous testing for one of the other syndromes. Takakuwa and Halpern [39] demonstrated that triple rule-out coronary CT angiography of low to-moderate risk ACS patients presenting to the emergency department provided a noncoronary diagnosis that explained the presenting complaint in 11% of patients, suggested the presence of significant moderate-to-severe coronary disease in 11% (22 of 197) of patients, and precluded additional diagnostic cardiac testing in the majority of patients with no adverse outcomes at 30 day follow-up. It should however, be realized that the triple rule-out protocol differs from dedicated coronary CT angiography in several important aspects such as the larger field of view with the triple rule-out protocol, imaging of the entire length of the thorax, and the delivery of additional contrast, resulting in increased radiation burden to the patient.

In conclusion, the high negative predictive value ( $>95\%$ ) found in the above-mentioned studies suggests that CT coronary angiography is an attractive option for exclusion of CAD in properly selected emergency department patients with acute chest pain. CT angiography is a well-established and accurate tool for the diagnosis of acute aortic dissection and pulmonary embolism. Recent technical developments

now permit acquisition of well-opacified images of the coronary arteries, thoracic aorta and pulmonary arteries from a single CT scan. While ‘triple rule-out’ acquisition protocol can potentially exclude fatal causes of chest pain in all three vascular beds, the attendant higher radiation dose of this method precludes its routine use except when there is sufficient support for the diagnosis of either aortic dissection or pulmonary embolism [40]. Furthermore, the protocol is yet not fully optimized to exclude acute aortic syndrome or to assess the full extent of aortic dissection into the abdomen and beyond. These observations are also underscored by the NASCI-ESCR position paper on the use of MSCT Imaging for the Assessment of Acute Chest Pain, questioning the true clinical need for a triple rule-out protocol [41]. In the majority of patients a single rule-out protocol will do, and—unless there is a high index of suspicion for acute aortic syndrome or pulmonary embolism—the triple rule-out protocol should be avoided. Currently there are no large prospective studies where MSCT has been used for this purpose and further research is therefore desirable to better define the role for triple rule-out coronary CT angiography. So the triple rule-out protocol is still far from three of a kind.

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