Early triage of emergency department patients with acute coronary syndrome: Contribution of 64-slice computed tomography angiography

Orientation précoce des patients pris en charge dans les services d’urgences pour un syndrome coronarien aigu : apport du scanner coronaire 64 barrettes

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Summary
Background. — Multislice computed tomography coronary angiography (MSCT-CA) is feasible in the emergency department (ED) for ruling out obstructive coronary artery disease (CAD).
Aim. — To investigate a diagnostic strategy using MSCT-CA for the early triage of patients presenting to the ED with acute chest pain suggestive of acute coronary syndrome (ACS), according to the medium-term incidence of clinical events.

KEYWORDS
Cardiac CT; Atherosclerosis; Acute coronary syndrome; Coronary artery

Abbreviations: ACS, Acute coronary syndrome; BMI, Body mass index; CAD, Coronary artery disease; CI, Confidence interval; ECG, Electrocardiogram; ED, Emergency department; FFR, Fractional flow reserve; GRACE, Global Registry of Acute Coronary Events; ICA, Invasive coronary angiography; MACE, Major adverse coronary events; MSCT-CA, Multislice computed tomography coronary angiography; mSv, Millisievert; SD, Standard deviation; TIMI, Thrombolysis In Myocardial Infarction.
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Methods. — We conducted a single-centre, prospective, observational cohort study in 123 patients with low-risk to intermediate-risk acute chest pain suggestive of ACS. MSCT-CA was performed using dual-source 64-slice computed tomography with retrospective electrocardiographic gating. Patients without coronary artery lesions were discharged from the ED. The incidences of death, myocardial infarction and myocardial revascularization were collected during a mid-term follow-up.

Results. — According to MSCT-CA, 93 patients (75.6%) had no CAD or coronary artery stenosis less or equal to 50% and 28 patients (22.8%) had stenosis more or equal to 50%. Invasive coronary angiography was performed in 29 patients (23.6%). MSCT-CA accurately identified ten patients (8.13%) with obstructive CAD requiring myocardial revascularization; all had a low TIMI score (0—2) and eight had a low GRACE score. The mean estimated effective dose of MSCT-CA was 16.3 ± 6.4 mSv. Median follow-up was 15 months. No patient (95% CI 0—3.0%) had major adverse cardiovascular events during follow-up.

Conclusion. — MSCT-CA appears to be a useful initial triage tool in the ED. When the MSCT-CA result is negative, it allows safe early discharge because of its high negative predictive value. In a significant number of cases of low-risk ACS, MSCT-CA detects severe coronary lesions and allows further dedicated diagnostic and therapeutic intervention. Reduction of radiation exposure would help acceptance in clinical practice.

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Background

The investigation of patients presenting to emergency departments (EDs) with chest pain remains challenging worldwide [1—3]. Evaluation strategies include detailed clinical assessment, serum cardiac biomarkers, resting electrocardiogram (ECG) and individual determination of mortality risk [1—3]. This approach lacks diagnostic accuracy in low-risk patients and up to 8% of cases of acute coronary syndrome (ACS) are missed in the ED, with a higher mortality risk [2,4,5].

Multislice computed tomography coronary angiography (MSCT-CA) is accurate compared with invasive coronary angiography (ICA) and is feasible and practical in the ED [6—11]. MSCT-CA has a high ability to rule out obstructive coronary artery disease (CAD) [12,13]. Since 2008,
MSCT-CA has become part of the management strategy for some patients with ACS without high-risk features in our institution, in agreement with American and French recommendations [14,15]. However, the relevance of this strategy is still controversial [16], even in our institution. The paucity of data on the incremental value of further diagnostic tests and on the prognosis of patients released from the ED after a normal MSCT-CA explains why it is difficult for health institutes to develop guideline recommendations with a great level of evidence [3,16].

Therefore, we assessed a diagnostic strategy using MSCT-CA for the early triage of patients presenting to ED with acute chest pain suggestive of ACS, according to the medium-term incidence of clinical events.

**Methods**

**Population**

We conducted a single-centre, prospective, observational cohort study in low-risk to intermediate-risk ACS patients. From April 2008 to September 2009, 123 patients presenting to the ED of the University Hospital of Rangueil in Toulouse, France, were prospectively enrolled. Patients presenting to this ED with acute chest pain or other recent-onset angina-like symptoms, an ECG without myocardial ischemia-related abnormalities and without elevation of cardiac troponin could be prospectively enrolled. Standard chest pain assessment by the ED physicians included:

- detailed assessment of clinical history;
- CAD risk factors; description of symptoms;
- physical examination;
- 12-lead ECG; chest X-ray;
- and measurement of cardiac biomarkers (troponin I), repeated six hours later.

Patients could be enrolled at the ED if their Global Registry of Acute Coronary Events (GRACE) risk score was less than 119 (http://www.outcomes-unmassmed.org/grace).

Patients were excluded if aortic dissection or pulmonary embolism was particularly suspected; in these cases, a standard dedicated diagnostic algorithm was performed. Patients were also excluded if there was evidence for a cause of chest pain other than myocardial ischemia. Patients were excluded if the chest pain was related to a high-risk ACS. High-risk criteria were:

- ST-segment elevation acute myocardial infarction;
- diabetes mellitus known for more than 10 years;
- a rise in serum cardiac troponin concentration;
- ECG changes suggesting ischemia;
- GRACE risk score greater or equal to 119;
- history of CAD; and acute heart failure.

These patients were admitted to the cardiology intensive care unit and ICA was performed according to European recommendations [1].

After this evaluation, the ED physician was free to include the patient in the study if further immediate coronary evaluation was considered as being required. If the patient had no CAD risk factor, atypical chest pain and a very low GRACE score, the ED physician could allow patient to leave the ED with an appointment to see a cardiologist a few days later. The safety and efficiency of an immediate MSCT-CA has not yet been demonstrated in such cases.

At this stage, patients were not included if MSCT-CA was not feasible or was contraindicated because of: age less than 18 years; allergy to contrast agents; pregnancy; atrial fibrillation or frequent ectopy; uncontrolled heart rate; inability to perform a 20-second breath hold; body mass index (BMI) greater than 40; or renal failure (creatinine clearance less than 60 mL/min/m²). If the patient was suitable for inclusion, a cardiologist was called to provide a full explanation of the strategy. The patient was then included if they gave informed consent. Clinical history, CAD risk factors and description of symptoms were checked by a cardiologist at the ED. Thrombolysis In Myocardial Infarction (TIMI) [17] and GRACE risk scores were calculated.

**Technique and image reconstruction**

MSCT-CA was performed using dual-source 64-slice computed tomography (SOMATOM, Dual-Source Definition; Siemens Medical Solutions, Erlangen, Germany) with retrospective electrocardiographic gating. Before acquisition, the patients received beta-blockers, targeting a heart rate less or equal to 65 beats/min. The acquisition started at the level of the carina and stopped below the heart after injection of iodine contrast. Calcium scoring was not studied (i.e. only one acquisition was performed). Moreover, no delayed acquisition was performed in order to limit radiation exposure. The acquisition delay was computed automatically by placing a region of interest in the ascending aorta, with a start threshold of 150 Hounsfield units. A biphasic injection using a dual-head injector consisted of a bolus of 1.5 cc/kg of contrast agent (iomeprol) at a concentration of 400 mg/mL (iomeron 400, Bracco-Byk, Milan, Italy) followed by a saline flush. Collimation was 64 × 0.6 mm with a gantry rotation of 330 ms and a pitch of 0.36. The reference tube current was 320 mA. The tube voltage was adjusted to the patient’s body weight: 80 kV for patients less than 70 kg, 100 kV for patients weighing 70–90 kg and 120 kV for patients above 90 kg. Raw data were reconstructed with a slice thickness of 0.75 mm every 0.5 mm using a standard kernel, every 10% of the R–R interval. Current intensity modulation was systematically applied to reduce radiation during systolic phases (maximal current intensity between 30–40% and 70–80%, depending on the heart rate). The tube modulation programme CARE Dose 4D was also used (Siemens Medical Solutions, Erlangen, Germany).

For each patient, the images were uploaded to a dedicated workstation (Leonardo; Siemens, Erlangen, Germany) and interpreted by two experienced cardiac radiologists who were aware of the clinical data. One, two or three phases were kept for the analysis, depending on the heart rate of the patient and the presence of motion artifacts. Multiplanar reconstruction, curvilinear multplanar reconstruction, volume rendering technique and maximum intensity projection were used for the analysis (Circulation Software; Siemens, Erlangen, Germany). A 17-segment model of the coronary arteries and a three-point grading score (normal, mild [< 50% luminal diameter narrowing], stenosis [≥ 50%]) were used to evaluate coronary stenosis; however, only segments greater than 1.5 mm in diameter were analysed. Patients were classified according to the maximal lesion.
MSCT-CA was considered as ‘negative’ when there was no or mild CAD. MSCT-CA was considered as ‘positive’ when there was at least a single coronary artery stenosis greater or equal to 50%. MSCT-CA was also considered as ‘positive’ when it was not interpretable.

**Diagnostic pathway**

The diagnostic pathway of the patient according to the MSCT-CA result is summarized in Fig. 1. Patients without CAD or with mild lesions on MSCT-CA were discharged early from the ED without treatment after other possible causes of chest pain had been investigated. All patients with stenosis greater or equal to 50% on MSCT-CA were admitted to the cardiology unit and had ICA. Qualitative ICA was performed by one of the nine physicians from the catheterization laboratory of the University Hospital of Rangueil in Toulouse. The interventional cardiologist was aware of the results of the MSCT-CA. The ICA was visually interpreted by two observers. Automated analysis stenosis severity assessment was also applied for lesions greater or equal to 50%, with an automated edge-detection system (Medical QCA/MS; Medis Imaging System, Leiden, The Netherlands). A functional stress test (myocardial perfusion imaging, stress echocardiography or exercise treadmill test, according to availability) or fractional flow reserve (FFR) was performed to assess the haemodynamic significance of intermediate stenosis greater or equal to 50% but less or equal to 70% and direct myocardial revascularization indication. Only Lesions with an FFR less than 0.80 at maximum hyperaemia were considered functionally significant and were treated by mechanical revascularization [18]. Only severe lesions and intermediate lesions with proven myocardial ischaemia were considered for myocardial revascularization. Non-obstructive CAD is defined by stenosis greater or equal to 50% but less or equal to 70% on ICA with a negative stress test or FFR test. Medical therapy, including aspirin, beta-blockers and statins, was proposed for patients with non-obstructive CAD. Obstructive CAD is defined by stenosis greater or equal to 70% on ICA or less or equal to 50% on ICA with an abnormal functional stress test or FFR less than 0.80. A revascularization strategy associated with medical therapy was proposed for obstructive CAD patients.

**Follow-up**

All patients or proxies and general practitioners were contacted by the first investigator (S.H.) by a telephone recall between January 2010 and April 2011. Clinical status was queried. During follow-up, death or a history of myocardial infarction, myocardial revascularization or heart failure was searched for. The main outcome criteria were major adverse coronary events (MACE), defined as myocardial infarction, myocardial revascularization and cardiovascular death occurring after the primary hospitalization. For the patients followed in our cardiology department, the follow-up data in the medical information file were noted.

**Statistical analysis**

Continuous variables are expressed as mean ± standard deviation (SD) and the median is provided if the distribution of the variable departed from normality. Categorical variables are expressed as total number (percentage). The SCORE method with continuity correction was used to estimate the 95% confidence interval (CI) for proportions [19]. Student’s t test was performed to compare means of quantitative variables between groups. Fisher’s exact test was performed to compare proportions. A p value less than 0.05 was considered to be statistically significant. All calculations were done using MedCalc statistical software, version 8.0 (MedCalc Software, Mariakerke, Belgium).

**Results**

A total of 123 patients constituted our final population. Study population characteristics are listed in Table 1. Prevalence of CAD and patient course are presented in Fig. 1. In two cases (1.63%), MSCT-CA analysis was not possible because of kinetic artefacts due to high heart rate. Of these two patients, one had a negative stress echocardiography and was discharged without MACE during a median 15-month follow-up. The other patient had ICA that revealed significant stenosis of the left anterior descending artery and had myocardial revascularization by angioplasty and one stent. According to MSCT-CA results, 93 patients (75.6%) had no or mild CAD and 28 patients (22.8%) had stenosis greater or equal to 50%. ICA was performed in 29 patients (23.6%). A complementary diagnostic functional stress test or FFR was necessary in 20 patients. A negative FFR was measured in three patients. Obstructive CAD requiring myocardial revascularization was diagnosed in 10 patients (8.1%). Stenosis greater or equal to 70% was observed in nine patients; one patient had stenosis between 50% and 70% and a positive stress echocardiography. Of these 10 patients, eight were at low risk and two were at intermediate risk. Of the 28 patients with stenosis greater or equal to 50% on MSCT-CA, 19 patients had stenosis less or equal to 70% on ICA and a negative FFR/functional stress test and were classified as having non-obstructive CAD. Patient characteristics according to CAD severity are listed in Table 1. In Table 2, patients finally diagnosed with obstructive CAD are compared with the remaining sample (i.e. patients with no or mild CAD according to MSCT-CA results and those with MSCT-CA stenosis greater or equal to 50% but without obstructive CAD according to ICA and FFR/functional stress test). Chest pain thought to be typical angina pectoris was a factor significantly associated with obstructive CAD according to Fisher’s exact test (p = 0.0449). Mean age was higher in patients with obstructive CAD (p = 0.0476). The probability of having obstructive CAD after a positive MSCT-CA was 35.7%.

The mean estimated effective dose of MSCT-CA was 16.3 ± 6.4 mSv (3.0−33.7 mSv). Mean radiation exposure was higher in young people (p = 0.024), patients with a high BMI (p = 0.0386) and men (p = 0.045). No acute renal insufficiency or beta-blocker side-effects were reported.

Median follow-up was 15 (7−30) months. Follow-up data were available for every patient. No patient (95% CI 0−3.0%) had MACE during follow-up. Of the 10 patients who had myocardial revascularization at the first step, none had MACE during follow-up. Of the 93 patients who had a negative MSCT-CA, none (95% CI 0−5.0%) had MACE during follow-up. The negative predictive value of MSCT-CA...
<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 123)</th>
<th>MSCT-CA</th>
<th>ICA ± FFR/stress test</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No CAD(^a) (n = 66)</td>
<td>Mild CAD (n = 27)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>50.9 ± 13.8 (19—86)</td>
<td>47.6 ± 13.0</td>
<td>52.3 ± 12.8</td>
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<td>Men</td>
<td>87 (70.4)</td>
<td>44 (66.7)</td>
<td>19 (70.4)</td>
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<td>Weight (kg)</td>
<td>74.5 ± 13.8</td>
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<td>Body mass index</td>
<td>25.2 ± 4.2</td>
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<td>Cardiac risk factors</td>
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<tr>
<td>Hypertension</td>
<td>41 (33.3)</td>
<td>18 (27.3)</td>
<td>10 (37.0)</td>
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<td>21 (31.8)</td>
<td>11 (40.7)</td>
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<td>Diabetes mellitus</td>
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<td>7 (10.6)</td>
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<td>Family history of CAD</td>
<td>39 (31.7)</td>
<td>21 (31.8)</td>
<td>10 (37.0)</td>
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<td>Men aged &gt; 50 years or</td>
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<td>18 (27.2)</td>
<td>13 (48.1)</td>
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<td>8 (12.1)</td>
<td>1 (3.7)</td>
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<td>24 (19.5)</td>
<td>16 (24.2)</td>
<td>4 (14.8)</td>
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<tr>
<td>2</td>
<td>49 (39.9)</td>
<td>26 (39.4)</td>
<td>13 (48.1)</td>
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<td>≥ 3</td>
<td>39 (31.7)</td>
<td>16 (24.2)</td>
<td>9 (33.4)</td>
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<tr>
<td>Symptoms</td>
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<tr>
<td>Atypical chest pain</td>
<td>51 (41.5)</td>
<td>30 (45.5)</td>
<td>11 (40.7)</td>
</tr>
<tr>
<td>Typical angina pectoris</td>
<td>72 (58.5)</td>
<td>36 (54.5)</td>
<td>16 (59.3)</td>
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<td>TIMI score</td>
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<td>0</td>
<td>72 (58.5)</td>
<td>40 (60.6)</td>
<td>19 (70.4)</td>
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<td>41 (33.3)</td>
<td>22 (33.3)</td>
<td>6 (22.2)</td>
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<td>2</td>
<td>10 (8.1)</td>
<td>4 (6.1)</td>
<td>2 (7.4)</td>
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<tr>
<td>Median</td>
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<tr>
<td>Range</td>
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<td>GRACE score</td>
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<td>Low risk: ≤ 88</td>
<td>108 (87.8)</td>
<td>61 (82.4)</td>
<td>24 (88.9)</td>
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<tr>
<td>Intermediate risk: 89—118</td>
<td>15 (12.2)</td>
<td>5 (7.6)</td>
<td>3 (11.1)</td>
</tr>
<tr>
<td>Median</td>
<td>52</td>
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<tr>
<td>Range</td>
<td>18—111</td>
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<tr>
<td>Radiation dose (mSv)</td>
<td>16.3 ± 6.3 (3.0—33.7)</td>
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</tbody>
</table>

Data are mean ± standard deviation (min—max) or number (%). CAD: coronary artery disease; FFR: fractional flow reserve; GRACE: Global Registry of Acute Cardiac Events; ICA: invasive coronary angiography; MSCT-CA: multislice computed tomography coronary angiography; TIMI: Thrombolysis in Myocardial Infarction.

\(^a\) Absence of CAD on MSCT-CA.

\(^b\) The patient with non-diagnostic MSCT-CA but obstructive stenosis on ICA was counted in this group.
Figure 1. Study population.

Discussion

In the present study, MSCT-CA identified ten patients (8.13%) with obstructive CAD requiring myocardial revascularization from a sample of 123 patients with acute chest pain at low-to-intermediate risk presenting to an ED. These ten patients had a low TIMI risk score (between 0 and 2) and eight patients (80%) had a low GRACE risk score. These results confirm the need for further testing in low-risk chest pain patients and the value of MSCT-CA.

Furthermore, 75.6% of patients with acute chest pain had no CAD or coronary artery lesions less or equal to 50% on MSCT-CA and did not have an adverse coronary event or death (95% CI 0–3%) during a median follow-up of 15 months. Our results correspond with those reported by Hollander et al. in the USA and Schlett et al. in Germany [20,21]. Negative MSCT-CA could therefore allow immediate and safe dismissal from the ED of these patients with acute chest pain without ECG abnormalities or a rise in serum cardiac biomarkers. Given the large number of such patients, early MSCT-CA may significantly improve patient management in the ED.

MSCT-CA offers direct visualization of the coronary arteries but does not provide information on inducible ischemia. As we did not perform a stress test systematically, we cannot compare our results with another diagnostic strategy based on a stress test. In our institution, stress tests such as stress echocardiography, nuclear myocardial perfusion imaging, magnetic resonance imaging and the standard treadmill test are not available 24 hours/day. Conversely, MSCT-CA is available quickly. The feasibility of MSCT-CA in the ED is not currently applicable in all centres 24 hours/day. However, our results confirm that further testing in low-risk chest pain patients is necessary. According to previous studies, a diagnostic strategy with MSCT-CA could shorten the length of stay, decrease costs, reduce the need for ICA and improve prognosis compared with chest pain unit management with ICA or the stress tests in use at the moment [22–25]. Given our results and these studies, MSCT-CA may be one of the first triage examinations that should be widely available 24 hours/day, particularly in small centres.

The probability of having obstructive CAD in the presence of coronary artery stenosis greater or equal to 50% on MSCT-CA is only 35.7%. The clinical impact of a positive result is limited and may require additional non-invasive investigation before ICA. Patients with acute chest pain and coronary artery stenosis greater or equal to 50% on MSCT-CA but without haemodynamic significance on FFR or functional stress test seemed to have no coronary event or death under medical treatment. This sample of patients was low (n = 18, 15%). This observation is in agreement with the results of Pijls et al. [26]. Given these results, we would recommend performing a functional test without radiation, such as stress echocardiography, when MSCT-CA suggests the presence of coronary artery stenosis greater or equal to 50%, reserving ICA for a positive or inconclusive functional test result. For patients in whom MSCT-CA suggests severe lesions, ICA may be required to confirm the anatomy of the
lesions detected. In these cases, in our experience, FFR provides a fast assessment of the haemodynamic significance of the ambiguous lesions during the same examination and improves the myocardial revascularization indication decision. Fortuitous discoveries of non-obstructive CAD will also allow early risk factor modification, thereby potentially preventing future cardiac events. But the relevance of this approach needs to be evaluated in large dedicated studies [3].

There was variety in the patients’ ages (19 to 86 years) and levels of risk (very low risk to intermediate risk). The study population represented only a sample of all patients presenting to the ED with chest pain. This makes it difficult to define the cohort of patients that is best suited to this new technology. We excluded patients at high risk and patients with known CAD, thereby limiting applicability for many ED patients; but MSCT-CA does not improve risk stratification and early ICA is recommended [1,27]. We also excluded patients with contraindications to MSCT-CA. But it seems that approximately 80% of non-CAD patients undergoing a rule-out ACS process could be suitable for MSCT-CA [28]. Almost one-quarter of these are from very low-risk groups and the risk/cost-benefit ratio of further testing is dubious. We identified two main factors that could improve the pretest probability of having obstructive CAD: older age and typical angina-like symptoms. Therefore, in a setting of a low-risk young patient with highly atypical symptoms, no additional diagnostic evaluation may be required. The recent recommendations of the National Institute for Health and Clinical Excellence in the UK proposed that the indication for MSCT-CA in ACS at low risk should therefore be based on the pretest prevalence of CAD, according to age, sex, cardiovascular risk factors and chest pain characteristics [3]. The results of our study confirm the merits of these new recommendations.

A significant issue with MSCT-CA is radiation exposure. Mean estimated effective dose is high (estimated as 16.3 mSv) despite appropriate image acquisition protocol. Guéret et al. reported a higher mean exposure of 19 mSv in a French multicentre observational study carried out at the same time [29]. Chow et al. reported a similar estimated effective dose of 15 mSv in a similar sample of patients with acute chest pain in an ED in an experimental centre in Canada [30]. Little is still known about the long-term effects of radiation. An increasing risk of cancer is suspected above 20 mSv [31].

### Conclusion

MSCT-CA is a promising technology for chest pain evaluation in the ED. Our results suggest that it could be a useful and necessary initial triage tool. When the MSCT-CA result is negative, it allows safe and early discharge because of its high negative predictive value. In a significant number of low-risk ACS patients, MSCT-CA detects severe coronary lesions and allows dedicated further diagnostic and therapeutic intervention. Some people suggest that it should be a first-line test [32]. Our results are a validation of the French recommendations published in 2009 [15]. New guidelines from the European Society of Cardiology for the management of ACS now recommend (with a class IIa) the use of MSCT-CA as an alternative to ICA to exclude ACS when there is a low-to-intermediate likelihood of CAD and when troponin and ECG are inconclusive [33]. But the inability of anatomical findings to prove the presence of ischaemia and the cancer risk induced by radiation exposure still raise concerns about the relevance of this strategy. The results of our study deserve to be completed by multicentre analysis and compared with a diagnosis strategy based on a stress test alone.
Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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