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Invited review

The role of coronary CT angiography for acute chest pain in the era of high-sensitivity troponins

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ABSTRACT

Accurate and efficient diagnostic triage for acute chest pain (ACP) remains one of the most challenging problems in the emergency department (ED). While the proportion of patients that present with myocardial infarction (MI), aortic dissection, or pulmonary embolism is relatively low, a missed diagnosis can be life threatening. Coronary computed tomography angiography (CCTA) has developed into a robust diagnostic tool in the triage of ACP over the past decade, with several trials showing that it can reliably identify patients at low risk of major adverse cardiovascular events, shorten the length of stay in the ED, and reduce cost associated with the triage of patients with undifferentiated chest pain. Recently, however, high-sensitivity troponin assays have been increasingly incorporated as a rapid and efficient diagnostic test in the triage of ACP due to their higher sensitivity and negative predictive value of myocardial infarction. As more EDs adopt high-sensitivity troponin assays into routine clinical practice, the role of CCTA will likely change. In this review, we provide an overview of CCTA and high-sensitivity troponins for evaluation of patients with suspected ACS in the ED. Moreover, we discuss the changing role of CCTA in the era of high-sensitivity troponins.

1. Introduction

Acute chest pain (ACP) is one of the most common reasons that patients present to the emergency department (ED), accounting for more than 8 million annual ED visits in the U.S. and over $10 billion in diagnostic health care expenditures.[1–3] Physicians regard ACP as a challenging diagnostic dilemma, as only 2–8% patients with ACP are eventually diagnosed with acute coronary syndrome (ACS).[4] However, the consequences of inappropriate discharge can be detrimental.[5–7] Conventional triage strategies typically incorporate the clinical presentation, conventional cardiac biomarker assays, serial electrocardiograms (ECG), and rest and/or stress imaging, but these methods struggle to meet the expected safety target of less than 1% missed ACS cases.[8,9] In addition, the triage of patients with ACS using conventional troponin assays is lengthy and requires repeated testing over 6–12 h. The rationale for the use of CCTA in the ED is to both rule out ACS (based on the absence of coronary artery disease), and allow for safe and early discharge of patients. CCTA has thus evolved into a viable alternative for the exclusion of ACS among patients presenting with ACP. Recently, however, high-sensitivity troponins have been increasingly incorporated as a biomarker to rule out coronary artery disease (CAD) and acute myocardial infarction. It is currently uncertain whether the role of CCTA for ACP assessment will be affected in the era of high-sensitivity troponins.

1.1. Current role of CCTA in acute chest pain

In the last two decades, computed tomography (CT) has rapidly evolved. Contemporary scanner technology allows for high-resolution, motion-free imaging of the coronary arteries at a well-tolerated scan duration, which allows for non-invasive assessment of CAD.

1.2. Observational studies and randomized trials

Several observational studies have demonstrated the feasibility of CCTA among patients with ACP.[10–15]The ROMICAT (rule-out myocardial infarction/ischemia using computer-assisted tomography) trial, for example, enrolled 368 low-to-intermediate risk participants with ACP, who underwent 64-slice CCTA prior to hospital admission from May 2005 to May 2007.[14] In this study, 50% of patients had no

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Abbreviations

ACP	acute chest pain
ACS	acute coronary syndrome
ED	emergency department
ECG	electrocardiograms
CCTA	coronary computed tomography angiography
CAD	coronary artery disease
CT	computed tomography
SOC	standard of care
SPECT	single-photon emission computed tomography
MPI	myocardial perfusion imaging
ICA	invasive coronary angiography
AMI	acute myocardial infarction
FFR	fractional flow reserve

evidence of CAD by CCTA and ultimately did not have an acute myocardial infarction (AMI), corresponding to a sensitivity of excluding ACS of 100% in this population. In contrast, however, only half of the patients with obstructive CAD by CCTA were eventually diagnosed with ACS, limiting the positive predictive value of subsequent diagnoses of ACS and major adverse cardiovascular events. As the largest single-center observational study of CCTA for ACP, the ROMICAT study indicated CCTA could improve patient management in the ED by reliably excluding ACS in low-to-intermediate risk patients. Similarly, several other observational studies have confirmed CCTA's excellent negative predictive value (95–100%) and relative modest specificity (40–99%) for detection of ACS (Table 1).[10–15]

To prospectively test these observations, several randomized trials have been performed to evaluate the safety, accuracy, and effectiveness of CCTA compared with the standard of care (SOC) or other non-invasive tests for patients presenting to the ED with ACP (Table 2).[16–24] Goldstein et al.[16] randomized 197 participants at a single center to either CCTA or single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) and found that a diagnostic workup based on CCTA, which included the use of MPI if intermediate lesions were present, was equally safe but resulted in a shorter time to diagnosis and lower cost of care in the ED. In the subsequent multicenter CT-STAT trial,[17] the investigators randomized 699 patients at 16 different sites to either CCTA or SPECT MPI and showed that CCTA allows for more rapid evaluation and decreased cost compared to MPI. CT-STAT also confirmed that CCTA, as well as rest-stress MPI, are safe diagnostic methods that permit early discharge in most low-risk patients. Published in 2012, the ACRIN[18] and the ROMICAT II[19] trials compared CCTA with the current SOC and found that the length of stay was significantly shorter in the CCTA arm and the incidence of major adverse cardiovascular events during follow-up was equivalently low. Unlike the studies by Goldstein et al.,[16,17] the CCTA arm did not lead to significantly increased invasive coronary angiography (ICA) or revascularization rates. The estimated radiation exposure of CCTA was higher than the SOC arm in the ROMICAT II trial, while in the CT-STAT trial, radiation exposure was similar in a direct comparison of CCTA and MPI testing.

In the last few years, further studies with longer follow-up or in different geographical areas have been published to validate the value of CCTA for ACS triage. The PROSPECT trial directly compared CCTA and MPI in intermediate-risk chest pain patients with a relatively long follow-up (median 40 months).[20] However, in contrast with prior studies, the PROSPECT trial did not show significant differences in length of stay, downstream resource utilization, and clinical events between the two arms. Contrary to other trials, in PROSPECT immediate dedicated CT was not available, which likely affected the length of stay in the CT arm. In Australia, the CT-COMPARE trial[21] compared CCTA with exercise stress ECG in low-intermediate-risk patients with ACP and showed that CCTA improved diagnostic performance and reduced cost of care.

By pooling all of these studies, Gongora et al.[25] recently published a meta-analysis of 10 randomized clinical trials included 6285 participants with acute chest pain, comparing the efficacy and clinical outcomes between CCTA-based strategy and other SOC approaches. In this study, CCTA reduced length of stay and ED cost but increased the rate of ICA and revascularization. Nevertheless, there were no significant differences of clinical outcomes between the two group.

In summary, these trials demonstrate that the early use of CCTA in patients presenting with ACP allows for reliable ACS rule-out and safe discharge from the ED compared with SOC. Whether or not the increased use of invasive procedures following CCTA leads to better long-term outcomes requires further investigation.

1.3. Current guidelines on cardiac CT in the emergency department

In 2010, appropriate use criteria for cardiac CT deemed the utility of CCTA as a reasonable diagnostic approach in patients at low-to-intermediate risk for ACS.[26] Several other guidelines also discuss the application of cardiac CT.[27–29] Based on recent randomized controlled trials,[18,19] the 2014 AHA/ACC guidelines for management of patients with non-ST-elevation ACS stated that CCTA results in a faster, more cost-effective diagnosis than stress MPI in low-risk patients with chest pain.[28] Similarly, the 2015 ESC guidelines stated that CCTA should be considered as an alternative to invasive angiography to exclude ACS when there is a low to intermediate likelihood of CAD with inconclusive ECG or cardiac markers.[27]

2. High-sensitivity troponin assays

Cardiac troponins, which are structural proteins unique to the heart, are specific and sensitive biomarkers for early detection of myocardial infarction.[30,31] Measured by fully automated standard assays, cardiac troponins are superior to other clinical biomarkers for the diagnosis for acute myocardial infarction.[32,33] However, due to a delayed rise in measurable cardiac troponin from the time of myocardial injury, the sensitivity of conventional assays is low for detection of AMI when performed at the onset of symptoms. Confidently ruling out AMI therefore requires prolonged in-hospital monitoring (typically more than 6 h) as well as serial blood sampling.[34] Monitoring of patients with possible ACS is costly and contributes to overcrowding of ED.

Over the past years, high-sensitivity cardiac troponin assays have become more widely available. These new assays have a much higher degree of precision with the ability to detect serum troponin levels at the 99th percentile of a reference population with less than a 10% coefficient of variation.[27] (Fig. 2) The ability to accurately measure low concentrations of serum troponin has clinical and logistic advantages. Detection of small and previously undetectable changes in serum troponins allows for earlier detection (by lower thresholds) and fewer missed infarctions in the ED.[35] (Fig. 1) Higher precision allows for reliable exclusion of ACS at very low concentrations and retesting at shorter time intervals for patients with troponins in the grey zone[36] Nevertheless, the increased sensitivity and reporting of lower elevations in troponins come at the cost of a lower positive predictive value. More sensitive troponin assays will detect myocardial injury (or leakage) in more patients with renal disease, cardiomyopathies, pulmonary hypertension, stroke or after extreme exertion.[35] Although elevated high-sensitivity troponins are associated with worse outcomes in various clinical contexts, not all patients with elevated troponins have actionable CAD that would benefit from immediate revascularization.

A systematic review and meta-analysis of 8644 patients from 17

Table 1
Performance of coronary CTA in the triage of patients with acute chest pain in observational studies.

Study	N	Scanner	ACS risk	Inclusion criteria	ACS definition	ACS rate	Outcome (follow-up)	CT criterion	SE (%)	SP (%)	PPV (%)	NPV (%)
Rubinshtein[10]	58	64-CT	Intermediate	Negative troponin; normal ECG	CAG ≥ 50%, positive troponins or positive stress test	34%	MACE (15 months)	Stenosis ≥ 50%	100	92	87	100
Gallagher[11]	85	64-CT	Low	Negative troponin; normal ECG	AMI, UA + CAG > 70%	8%	Cardiac death or ACS (30 days)	Stenosis > 50% CS > 400	86	92	50	99
Johnson[12]	109	64-DSCT	All	Negative troponin; non-ischemic ECG	CAG > 50%	14%	CAG (6 months)	Stenosis > 50% (per segment)	100	99	79	100
Beigel[13]	340	MDCT	Low-intermediate	Negative troponin; non-ischemic ECG	CAG significant stenosis	4.4%	MACE (5 months)	Stenosis > 50%	100	97	65	100
ROMICAT[14]	368	64-CT	Low	Negative troponin; non-ischemic ECG	AMI, UA	8.4%	MACE (6 months)	Plaque Stenosis > 50%	100 77	92 87	87 35	100 98
Dedic[15]	111	64-DSCT	All	TnT ≤ 0.15 μg/mL	AMI, UA	17%	AMI or revascularization (3 months)	Calcium Any plaque Stenosis	89 100 89	41 40 79	24 26 47	95 100 97

ACS, acute coronary syndrome; AMI, acute myocardial infarction; CAG, invasive coronary angiography; CS, calcium score; ECG, electrocardiogram; SE, sensitivity; SP, specificity; UA, unstable angina; MDCT: multi detector CT; DSCT: dual-source computed tomography.SE: sensitivity; SP: specificity; PPV: positive predictive value; NPV: negative predictive value.

different studies compared high-sensitivity troponin assays with conventional assays on their diagnostic accuracy for AMI in patients with chest pain.[37] While the high-sensitivity troponin assays had greater sensitivity and negative predictive value for AMI, conventional assays had greater specificity and positive predictive value. In addition, patients with baseline elevation of high-sensitivity troponins but negative baseline conventional troponins had an increased risk for death or nonfatal MI during follow-up. Registry data indicate that high-sensitivity troponins reduce the overall length of stay, and that patients discharged early after rule out of an ACS by high-sensitivity troponins have fewer adverse events compared to conventional troponins.[38] Recently, a multi-center, cluster-randomized trial, the HighSTEACS trial, evaluated implementation of a hs-troponin assay in 48,282 patients in Scotland and demonstrated higher MI detection rates but no differences in clinical outcomes after implementation of hs-troponins. Only a third of patients reclassified to MI based on hs-troponins had the diagnosis of type 1 myocardial infarction within 1-year follow-up.

The use of high-sensitivity troponins has been incorporated into diagnostic algorithms in recent guidelines, particularly for the triage of suspected ACS patients in the ED. The 2015 ESC Non-STE-ACS guidelines recommend the use of high-sensitivity troponins due to their higher sensitivity, diagnostic accuracy, and reduced "troponin-blind" interval for earlier detection of acute MI (Fig. 3). However, the recommended 0/1 h rule-out algorithm for selected troponin assays has not been universally adopted[39] In North America, the 2014 ACC/AHA guidelines still recommend measuring conventional troponins at presentation and 3–6 h later in all patients with suspected ACS. Reluctance to introduce high-sensitivity troponins appears based on their lower specificity and subsequent risk of ACS overdiagnosis. Whether or not new high-sensitivity assay-based protocols improve clinical effectiveness and outcomes in the workup of ACP has yet to be determined in prospective studies.

3. CCTA in the era of high-sensitivity troponins

The introduction of high-sensitivity troponins has allowed faster retesting and thus more rapid discharge of patients from the ED. Due to their high negative predictive value and ability to detect MI earlier than before, these assays have become part of standard practice in the EDs in many countries around the world, potentially eroding previously reported logistic advantages of CCTA in this context.[35,40] Ferencik et al.[41] retrospectively assessed 160 patients from the ROMICAT II trial with available high-sensitivity troponin and CCTA data, and compared the diagnostic accuracy of traditional risk stratification (using CCTA or troponins only) with an approach that integrated CCTA and high-sensitivity troponin assays for ACS. It showed that the measurement of high-sensitivity troponins at presentation followed by early advanced CCTA assessment improves risk stratification and diagnostic accuracy for ACS as compared to the traditional assessment (AUC 0.84 vs 0.74, $p < 0.001$). In 2016, Dedic et al.[22] published the BEACON (Better Evaluation of Acute Chest Pain with Coronary Computed Tomography Angiography) trial, the first clinical effectiveness study to compare a diagnostic strategy supplemented by early CCTA with SOC encompassing high-sensitivity troponins for patients presenting with ACP. Between July 2011 and January 2014, the study enrolled 500 patients with symptoms suggestive of ACS at seven sites in the Netherlands. Participants were randomly assigned to either a CCTA-based diagnostic strategy or SOC, and high-sensitivity troponin results available in 80% of patients in both arms. The trial showed that the CCTA group had lower direct medical cost and less outpatient testing after the index ED visit (4% vs. 10%, respectively, $p < 0.01$), as well as a comparable rate of coronary revascularization (9% vs 7%, respectively $p = 0.4$). However, in contrast to prior studies, in BEACON, CCTA did not improve the early ED discharge rate nor reduce the length of stay (6.3 h in both groups, $p = 0.80$) (Fig. 4).[17–19] Against a background of standard care including high-sensitivity troponins, early CCTA avoids downstream

Table 2
Randomized controlled trials of early cardiac CT in the emergency department (ED) for the evaluation of patients with ACP.

Study	Site	Cohort	Study arms	N (ratio)	ACS rate (FU period)	MACE during FU	LOS (h)	ED discharge	ED cost
Goldstein et al.[16]	1	ED ACP	CTA vs MPI	197 (1:1)	5.1% (6 months)	0% vs 0%	3.4 vs 15*[a]	88.9% vs 96.9%*	$1586 vs $1872*
CT-STAT[17]	16	ED ACP	CTA vs MPI	699 (1:1)	1.7% (6 months)	0.8% vs 0.4%	2.9 vs 6.2*	82.2% vs 89.9%	$2137 vs $3458*
ACRIN[18]	5	ED ACP	CTA vs SOC	1370 (2:1)	3.5% (30 days)	1.2% vs 1.3%	18.0 vs 24.8*	49.6% vs 22.7%*	NA
ROMICAT II[19]	9	ED ACP	CTA vs SOC	1000 (1:1)	7.5% (28 days)	0.4% vs 1.2%	8.6 vs 26.7*	46.5% vs 12.4%*	$4289 vs $4060
PROSPECT[20]	1	IP	CTA vs MPI	400 (1:1)	NA (40 months)	4.5% vs 7.5%	28.9 vs 30.4	NA	NA
CT-COMPARE[21]	1	ED ACP	CTA vs ExECG	562 (1:1)	4.2% (12 months)	0.9% vs 0.4%	13.5 vs 19.7*	NA	$2101 vs $2566* (AUD)
BEACON[22]	7	ED ACP	CTA vs SOC	500 (1:1)	8.6% (30 days)	10% vs 9%	6.3 vs 6.3	65% vs 59%	€337 vs €511*
PERFECT[23]	1	IP	CTA vs MPI or stress Echo	411 (1:1)	0.9% (1 year)	1.5% vs 0.4%	48 vs 49	NA	NA
Nabi et al.[24]	1	IP	CTA vs MPI	598 (1:1)	3.0% (6 months)	3.8% vs 2.3%	19.7 vs 23.5*	96.4% vs 86.9%	$4242 vs $5104*

ACS: acute coronary syndromes; MACE, major adverse cardiovascular events, defined as cardiac death, myocardial infarction or unstable angina; LOS, length of stay; FU: follow-up; ED: emergency department; ACP: acute chest pain; IP: inpatient; CTA: computed tomography angiography; MPI: myocardial perfusion imaging; SOC, standard of care; Echo: echocardiogram; NA: non-assessable; vs: versus.
a: time to diagnosis instead of length of stay.
*: $P < 0.05$.

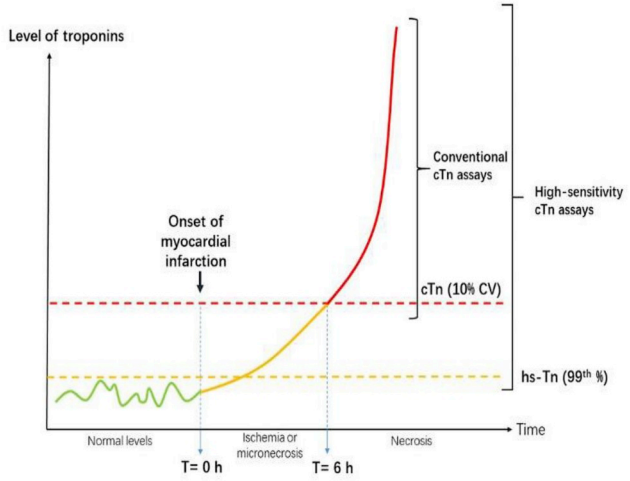

Fig. 1. Detection of cardiac troponins after myocardial infarction by conventional (cTn) and high-sensitivity assays (hs-Tn).

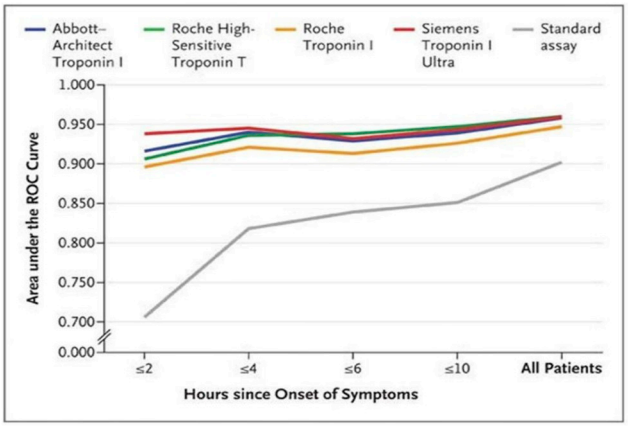

Fig. 2. Diagnostic performance by area under the ROC curve of different high-sensitivity troponin assays versus a standard troponin assay over time after presentation [Reproduced from Reichlin et al.[33] NEJM 2009].

testing and potentially reduces cost. However, available data suggest that high-sensitivity troponins expedite the triage of patients with ACP, which reduces prior logistic advantages of early CCTA when offered in an unselected manner.

4. Future challenges and opportunities

4.1. Integration of CT and biomarkers

High-sensitivity troponins and perhaps other biomarkers will change the utility of CCTA in the ED. Particularly in low-risk patients, hs-troponins are safe and implementation of these biomarkers is associated with earlier hospital discharge and fewer downstream stress tests, which will probably be cost-effective compared to advanced imaging. However, a more sensitive biomarker results in more positive results, some registries have shown increased rates of catheterizations and revascularizations[42,43] with uncertain clinical consequences for low-level elevations. The possible future role of cardiac CT in the context of acute chest pain may be summarized into three categories (Fig. 5).

4.1.1. Risk stratification of patients with a non-conclusive conventional workup of ACS

Patients with mildly elevated (intermediate) high-sensitivity troponins at presentation pose a new challenge that may require further diagnostic evaluation. Guidelines recommend combining various tools to improve accuracy and cost-effectiveness of the diagnostic process by including chest pain units, novel cardiac biomarkers, and noninvasive cardiac imaging.[44] High-sensitivity troponins are sensitive to myocardial injury but cannot identify the cause. In clinical practice, it may be difficult to distinguish dynamic troponin changes caused by a non-ST-elevation MI versus other cardiac or non-cardiac conditions. The HighSTEACS trial demonstrated that reclassification of patients to myocardial infarction based on high-sensitivity troponins did not affect outcome, and only a minority of reclassified patients suffered a type 1 myocardial infarction. Within this group of patients with low troponin elevations, or otherwise conflicting test result, cardiac CT may be able to identify those patients with clinically relevant coronary obstruction who may benefit from early intervention. The RAPID-CTCA trial aims to demonstrate the clinical and cost effectiveness of early CCTA in suspected ACS in the era of high-sensitivity troponins, and will recruit 2500 participants with suspected or confirmed ACS across the UK who are at intermediate risk by high-sensitivity troponins concentrations.[45]

4.1.2. Alternative causes of acute chest pain

CCTA can be valuable to detect other life-threatening conditions such as a pulmonary embolism or aortic dissection, but also to rule out CAD when elevated troponins are caused by a tachyarrhythmia, myocarditis or after major surgery (Fig. 6). In case of suspected non-coronary pathology CCTA provides reassurance that no ACS is missed without the need for cardiac catheterization.

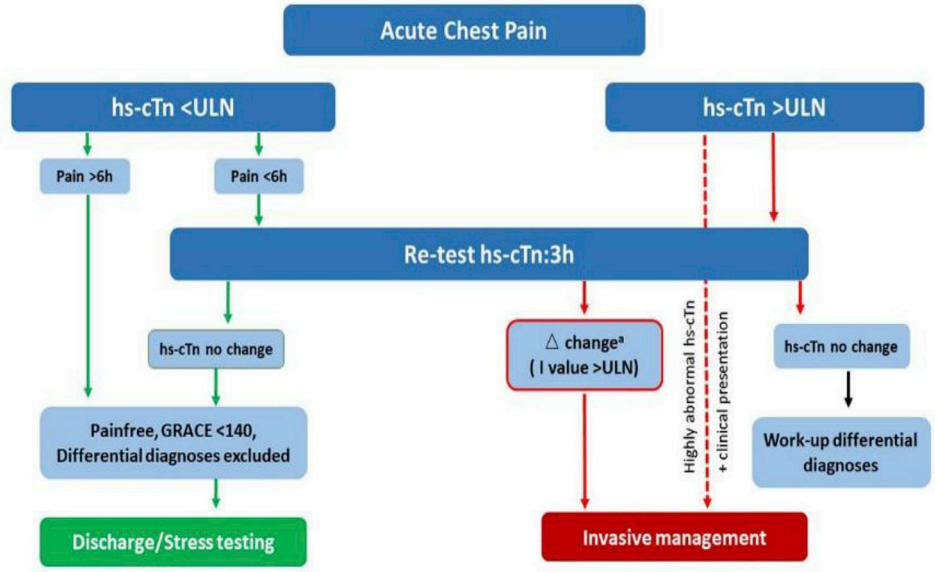

Fig. 3. The 0/3-h acute chest pain algorithm as recommended by the ESC in 2015[25] [With permission of Oxford University Press (UK)© European Society of Cardiology, www.escardio.org]. GRACE: Global Registry of Acute Coronary Events score; hs-cTn: high sensitivity cardiac troponin; ULN: upper limit of normal 99th percentile of healthy controls; a: △change, dependent on assay; Highly abnormal hs-cTn defines values beyond 5-fold the upper limit of normal.

4.1.3. Semi-elective rule-out of coronary artery disease

For certain patients in whom ACS has been ruled by negative biomarkers, it may still be relevant to identify the presence of (stable) CAD.[24, 46]In several cohorts with stable chest pain, elevated troponins were associated with the presence and severity of CAD on CT[46,47] Low elevated troponin levels may guide downstream diagnostic testing for coronary artery disease. Diagnostic testing, which includes CCTA as one of several options, may be performed during the acute chest pain admission, or later in an outpatient setting, depending on local logistics and healthcare policies. From a technical point of view, CCTA performed during office hours at a dedicated facility (most experienced team, pre-medication) will maximize image quality and potentially offer an opportunity to complement noninvasive angiography with functional CT applications, as discussed below.

4.2. Advanced functional CT applications

The high negative predictive value of CCTA allows for confident exclusion of CAD and ACS in the majority of patients. However, CCTA tends to overestimate angiographic severity compared to invasive angiography, and angiographic stenosis severity provides only a modest indicator of physiologic significance. The effectiveness of CCTA in prior studies is based at least to a degree on the low (obstructive) disease burden encountered in patients at low-intermediate risk for ACS. If CT were to be applied in cohorts with a higher probability of obstructive CAD, the ability to assess the hemodynamic significance of coronary lesions would be valuable. There are several established stress imaging tests that could be used in patients with an abnormal CCTA to establish the presence of myocardial ischemia. Alternatively, stress myocardial perfusion imaging may also be performed using CT, and meta-analyses suggest the diagnostic performance of CT perfusion imaging is comparable to other modalities.[48] In the CATCH trial, Sorgaard et al. performed CT perfusion imaging using a static acquisition scan protocol shortly after an ACS had been excluded in the ED, and demonstrated lower rates of invasive angiography and revascularization compared to CCTA alone.[49]

CT-derived fractional flow reserve (CT-FFR), by applying computational fluid dynamics onto standard CT images, represents an alternative approach to determining the functional significance of coronary lesions. The diagnostic accuracy of CT-FFR against invasive FFR has been demonstrated in several prospective cohorts of patients with stable CAD.[50–52] CT-FFR correctly re-classifies a substantial proportion of coronary stenosis considered to be of potential hemodynamic significance on CCTA, and decreases the rate of normal invasive angiograms.[53–55] Clinically available CT-FFR solutions have not yet been validated to rule out ACS and turn-around times of remote analyses may limit applicability for very early discharge. However, after an ACS has been ruled out by novel biomarkers, CT-FFR could be a valuable complementation to CCTA to assess the presence of stable CAD.

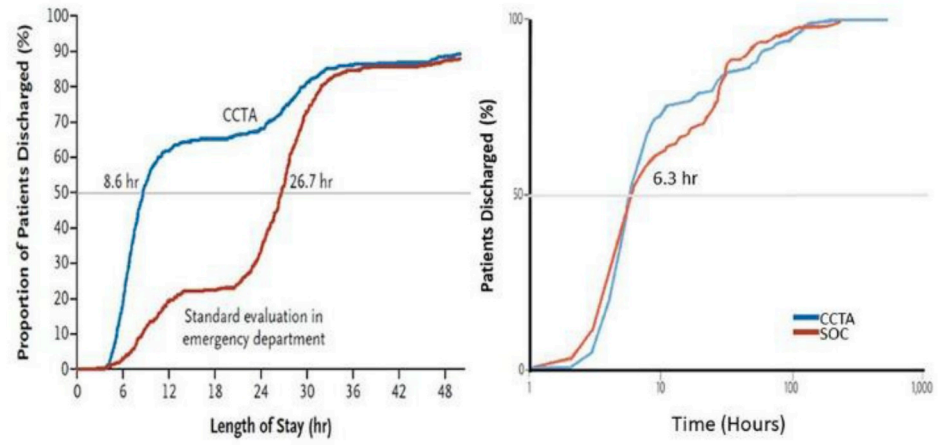

Fig. 4. Length of stay and proportion of patients discharged in the ROMICAT II and BEACON trials. The horizontal line indicates the median length of stay. In the ROMICAT II trial, length of stay was shorter in the CCTA arm compared to standard care (8.6 h vs 26.7 h, $p < 0.001$). However, in the BEACON trial, which was performed during the introduction of high-sensitivity troponins, length of stay was comparable in the CCTA and standard care arm (6.3 h in both groups; $p = 0.80$) [Reproduction from Hoffmann U et al.[19] NEJM. 2012 and Dedic et al.[22] JACC. 2016.].

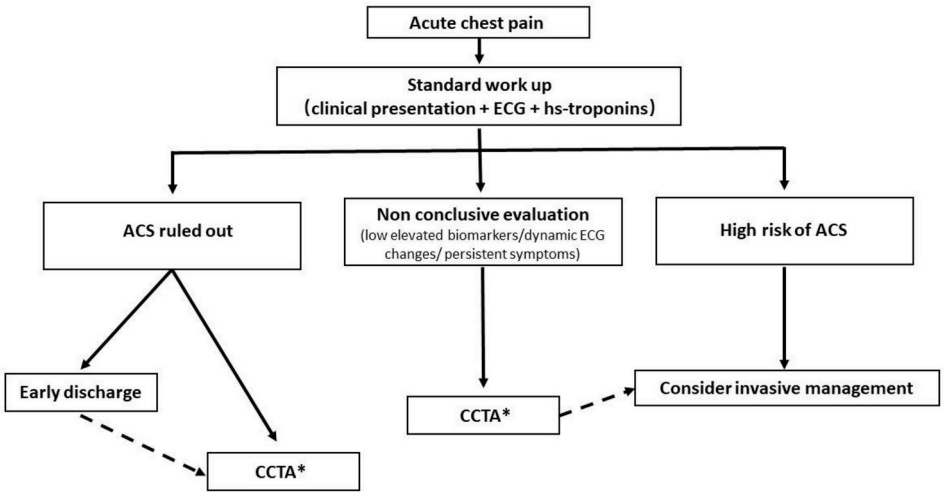

Fig. 5. A potential flow diagram with suspected acute chest pain in the era of high-sensitivity troponins. ECG: electrocardiograph; hs-troponins: high sensitive troponins. ACS: acute coronary syndrome; CCTA: coronary computed tomography angiography; *: or other available non-invasive diagnostic tests.

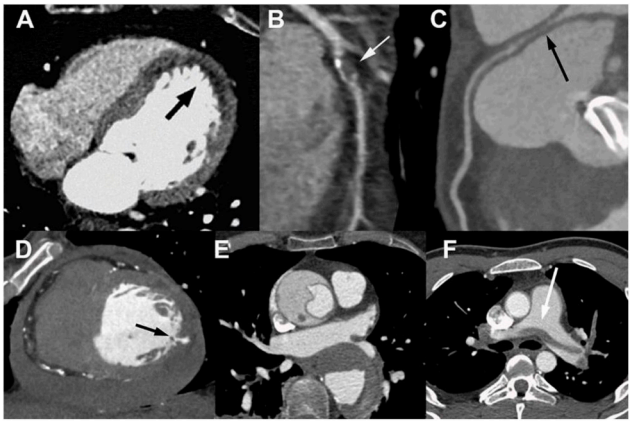

Fig. 6. Examples of cardiovascular disease in the context of acute chest pain imaged by cardiac CT. Resting myocardial perfusion defect in the left anterior descending (LAD) coronary territory (A); Thrombotic lesion in the LAD (B); external compression left main coronary artery (C); Pericardial hemorrhage secondary to free wall rupture after lateral wall infarct (D); Type A aortic dissection (E); pulmonary embolism (F).

5. Conclusions

The role of CCTA for evaluation of patients with ACP is expected to change in the era of high-sensitivity troponin. Cardiac CT may be most valuable for intermediate-risk patients with non-conclusive troponins and ECG results, or in a semi-elective setting after an ACS has been ruled out by negative biomarkers. For whom and at what stage CCTA is most helpful, combined with more sensitive biomarkers or other novel diagnostic tools, will require further investigation and new prospective trials.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcct.2019.05.007.

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