State-of-the-Art Evaluation of Emergency Department Patients Presenting With Potential Acute Coronary Syndromes

ABSTRACT: It is well established that clinicians cannot use clinical judgment alone to determine whether an individual patient who presents to the emergency department has an acute coronary syndrome. The history and physical examination do not distinguish sufficiently between the many conditions that can cause acute chest pain syndromes. Cardiac risk factors do not have sufficient discriminatory ability in symptomatic patients presenting to the emergency department. Most patients with non–ST-segment–elevation myocardial infarction do not present with electrocardiographic evidence of active ischemia. The improvement in cardiac troponin assays, especially in conjunction with well-validated clinical decision algorithms, now enables the clinician to rapidly exclude myocardial infarction. In patients in whom unstable angina remains a concern or there is a desire to evaluate for underlying coronary artery disease, coronary computed tomography angiography can be used in the emergency department. Once a process that took ≥24 hours, computed tomography angiography now can rapidly exclude myocardial infarction and coronary artery disease in patients in the emergency department.

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About 20 million patients present with symptoms possibly suggestive of acute coronary syndrome (ACS) to emergency departments (ED) in North America and Europe each year.[1–3] Patients with ACS and acute myocardial infarction (AMI) present with a wide variety of symptoms such as chest pain, shortness of breath, weakness, nausea, vomiting, and even fatigue, making the diagnosis difficult. Demographics, cardiac risk factors, chest pain characteristics, and physical examination can assist disposition decisions but are insufficient to identify who does and does not have an ACS.[4–7] Some patients may have objective evidence of a clear-cut diagnosis, but the majority do not.[8] The majority ultimately will be found not to have ACS, but symptoms caused by noncardiac and often benign disorders such as musculoskeletal pain, pleuritis, or gastroesophageal reflux make the rapid rule-out of ACS more difficult and result in huge medical expenses. Safe and early rule-out of ACS contributes to more efficient and high-value healthcare delivery.

HISTORY AND PHYSICAL EXAMINATION

Clinical features, alone or in combination with an ECG, are poorly predictive for AMI (Table 1).[9,10] In addition, they have variable reliability. Features classically associated with a lower probability of AMI such as pleuritic, positional, and sharp chest pain have poor to fair interphysician reliability (κ=0.27–0.44),[11] whereas high-risk

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Table 1. Likelihood Ratios for Clinical Features That Increase or Decrease the Risk of AMI in Patients Presenting With Chest Pain[9,10]

Clinical Feature	Likelihood Ratio (95% CI)
Increased likelihood of AMI	
Described as pressure	1.3 (1.2–1.5)
Pain in chest or left arm	2.7*
Chest pain radiation	
To right arm or shoulder	4.7 (1.9–12)
To left arm	2.3 (1.7–3.1)
To both left and right arm	7.1 (3.6–14.2)
To both arms or shoulders	4.1 (2.5–6.5)
Chest pain most important symptom	2.0*
Chest pain associated with exertion	2.4 (1.5–3.8)
Worse than previous angina or similar to prior AMI	1.8 (1.6–2.0)
History of MI	1.5–3.0†
Nausea or vomiting	1.9 (1.7–2.3)
Diaphoresis	2.0 (1.9–2.2)
Third heart sound	3.2 (1.6–6.5)
Hypotension (systolic BP <80 mm Hg)	3.1 (1.8–5.2)
Pulmonary crackles	2.1 (1.4–3.1)
Decreased likelihood of AMI	
Pleuritic chest pain	0.2 (0.1–0.3)
Described as sharp	0.3 (0.2–0.5)
Positional chest pain	0.3 (0.2–0.5)
Reproduced by palpation	0.3 (0.2–0.4)
Inframammary location	0.8 (0.7–0.9)
Not associated with exertion	0.8 (0.6–0.9)

AMI indicates acute myocardial infarction; BP, blood pressure; and CI confidence interval.

*Data not available to calculate CIs.

†In heterogeneous studies, the likelihood ratios are reported as ranges. Likelihood ratios tell us how much to modify our suspicion for a particular test result. The positive likelihood ratio tells us how much to increase the probability of disease when the test is positive. The negative likelihood ratio tells us how much to decrease when the test is negative.

features (radiation to left arm, substernal location, and history of AMI) are more reliable (κ=0.74–0.89).[11]

Traditional cardiac risk factors, derived from population-based longitudinal cohort studies of asymptomatic patients, are poor predictors of risk for AMI or ACS in symptomatic patients in the ED.[6,7] Similarly, the physical examination seldom is useful for distinguishing patients with ACS from patients with noncardiac chest pain.

Trials of medications, once thought to be useful, now are known to be unable to rule in or rule out ACS. Relief of symptoms with either nitroglycerin or a "gastrointestinal cocktail" occurs with similar frequency whether symptoms are related to or unrelated to myocardial ischemia.[12,13]

Knowledge of a previously normal stress test should not affect clinical decision making in the ED because patients with a prior normal stress test are at the same risk of 30-day adverse cardiovascular events as patients who have not previously undergone stress testing.[14,15] Stress testing does not assess whether nonobstructive plaque existing at the time of the test will subsequently rupture, leading to ischemia.

On the other hand, prior invasive coronary angiography results are useful for risk stratification of patients. Patients with no or minimal (<25%) stenosis have an excellent long-term prognosis, with 90% free from single-vessel disease and >98% free from myocardial infarction nearly a decade later.[16,17] Thus, recent coronary angiography with normal or minimally diseased vessels makes the possibility of an ACS extremely unlikely, unlike a recent negative stress test, which is still associated with a 5% event rate at 30 days.[14]

THE ECG

The ECG is the most important initial diagnostic instrument used for detecting ACS because it is the quickest means of objectively diagnosing acute ST-segment–elevation myocardial infarction (STEMI). Characteristic patterns such as ST-segment elevations or depressions, T-wave changes in anatomic distributions, a new bundle-branch block, and Q waves can all provide information on the timing, severity, and location of a lesion. However, the sensitivity of ST-segment elevation for diagnosing AMI is poor. Non-STEMI and unstable angina (UA) can occur with only nonspecific changes or with no change at all on ECG.[18]

Misinterpretation or misclassification of the ECG can hinder the diagnosis of AMI. Misclassifications rates range from 5.9% to 29%.[19,20] False-positive interpretations of the ECG occur in at least 11% to 14% of presumed STEMI cases.[21,22] Although it is true that the more significant the ECG abnormalities are, the more likely the patient is to have AMI, UA, and serious cardiovascular complications, patients with normal or nonspecific ECGs still have a 5% to 28% incidence of ACS. New electrocardiographic evidence of ischemia increases the risk of AMI to 25% to 73% and the UA risk from 14% to 43%; however, ischemic changes alone lack a high degree of specificity.[4,23] Thus, the standard 12-lead ECG is useful for risk stratification of patients with potential ACS but is not definitive. The addition of the right-sided precordial lead V4R in the setting of acute inferior myocardial infarction helps detect RV involvement.

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BIOMARKERS

The clinical assessment, even with an ECG, is not sufficient to diagnose or exclude AMI and ACS in most patients, and thus the addition of blood tests to measure the concentration of cardiac troponin (cTn) T or I forms the cornerstone for the early diagnosis of AMI. Clinicians use cTn values to estimate the likelihood of AMI and the short-term risk of adverse cardiovascular outcomes, including death.

Advances in assay technology have led to a refinement in the clinical ability to detect and quantify myocardial injury.[1–3,24–60] These assays increase diagnostic accuracy at presentation, substantially reduce the "troponin-blind" interval, and have allowed the recent development of several novel strategies for the early rule-out or rule-in of AMI.[1–3,24–61] These assays are labeled sensitive when able to detect cTn in ≈20% to 50% of healthy individuals. Assays are labeled as highly sensitive if they detect a level in >50% of apparently healthy subjects and they have a coefficient of variation of <10% at the 99th percentile upper reference limit of the assay. High-sensitivity assays can accurately detect cTn at a lower levels than older-generation assays, giving them higher sensitivity for the detection of AMI at presentation, which means that the time interval to the second measurement of high-sensitivity (hs) cTn can be significantly shortened, thereby reducing the time to diagnosis and improving efficiency in the ED.[1–3,24–33]

Although hs-cTn assays have been used in Europe, Australia, New Zealand, Canada, and many other developed countries since 2010, they have not yet received approval for use in the United States. High-sensitivity and sensitive cTn assays quantify the amount of cardiomyocyte damage and therefore should be interpreted as quantitative variables. The higher the cTn level is, the higher the likelihood of AMI is. For levels in the normal range, the same concept applies: The lower the cTn blood concentration is, the lower the likelihood of AMI is.

In an oversimplification, hs-cTn (and sensitive cTn) assays often are criticized for having a lower positive predictive value (PPV) for AMI. This relates to the use of the 99th percentile as a cutoff level, not the assay itself. The use of the 99th percentile, mandated by the universal definition, allows both the detection of AMI earlier after presentation and the detection of small AMIs. However, these beneficial effects are at least partly counterbalanced by a more challenging differential diagnosis resulting from mild elevations in cTn associated with myocardial injury unrelated to AMI (eg, resulting from chronic cardiac disorders).

It also is critical to note that there are no false-positive troponin elevations; all reflect myocardial injury and all portend a worse prognosis than otherwise similar patients without a troponin elevation. This is true regardless of whether the patient has heart failure, renal failure, gastrointestinal bleeding, sepsis, respiratory disease, pulmonary embolism, subarachnoid hemorrhage, or stroke or the patient is asymptomatic without known cardiovascular disease.[40] Any troponin is always worse than no troponin, and more troponin is always worse than less troponin.[40]

Compared with non-STEMI patients, individuals with UA do not experience myocardial necrosis, have a substantially lower acute risk of death and/or major arrhythmias, and seem to derive less benefit from intensified antiplatelet therapy and early invasive strategy.[41] Several biomarker strategies rely on serial troponin testing. Specifically, the European Society of Cardiology (ESC) has a 0- and 1-hour algorithm and a 0- and 2-h algorithm. These novel strategies have been fine-tuned to detect AMI but not UA.

It is important to highlight 5 points for the application of biomarker-based strategies in clinical practice: First, they should be used only in conjunction with full clinical assessment, including a pretest probability assessment to identify patients at high risk who are not candidates for early discharge. Second, these are risk stratification strategies rather than definitive diagnostic strategies, so additional tests (eg, invasive coronary angiography, computed tomography [CT] angiography [CTA], stress testing, perfusion imaging, or echocardiography) may be necessary for a definite diagnosis. Third, these strategies do not apply to everyone. The percentage of patients in whom they can be applied varies widely from ≈9.8% to 77%. In particular, they do not apply to patients who present so early that the troponin would not be elevated, even in the setting of AMI, nor do they apply to patients with short-lived episodes of ischemic pain who have UA without myocardial necrosis. Fourth, they can be applied only after the initial ECG has excluded a STEMI. Some apply only to patients with a completely normal ECG; others allow also for mild and nonspecific ECG abnormalities. Fifth, these strategies should optimally be embedded in the local standard ED operating procedures.

Three algorithms use the absolute change between 2 measurements of cTn in addition to the actual concentrations to take advantage of the full diagnostic information provided. Rising or falling cTn levels differentiate acute from chronic myocardial injury. Absolute rather than relative changes seem to be the best metric to differentiate AMI from other causes of chest pain.[36–39] The larger the absolute cTn change within 1, 2, or 3 hours is, the higher the likelihood of the presence of AMI is.[36–39]

Among the multitude of other biomarkers evaluated for the early diagnosis of AMI, only copeptin seems to have some clinical relevance.[3,42–47] Copeptin, the c-terminal part of the vasopressin prohormone, is secreted stoichiometrically with arginine-vasopressin from the neurohypophysis and seems to quantify the individual endogenous stress level in multiple medical conditions,

including AMI.[3,42–47] Because endogenous stress seems to be nearly invariably present at the onset of AMI, copeptin helps to improve the sensitivity of cTn at early ED presentation.[3,42–47] The less sensitive the cTn assay is, the higher the incremental value of copeptin for the early rule-out of AMI is.[3,42–47] The incremental value may be substantial if a conventional cTn assay is used that is unable to measure around the 99th percentile (eg, most point-of-care assays) but very small if a sensitive or hs-cTn assay is used. The incremental benefits of copeptin exist within the first 2 hours of arrival, after which a second troponin achieves the same sensitivity for AMI. Copeptin has neither disease (AMI) nor organ (heart) specificity and therefore is helpful only in the AMI rule-out process.[42–47] It is not useful to rule in AMI.

Biomarker-Based Strategies for Rapid Rule-Out or Rule-In of AMI

Six biomarker-based strategies have been studied and validated in large, methodologically robust, multicenter diagnostic studies including several thousand patients. The main performance metrics of the studies include safety (quantified by the negative predictive value [NPV] and sensitivity for AMI) and efficacy (percentage of patients identified) for rule-out, as well as the PPV and specificity for AMI (Table 2). Two of these strategies require the use of a predefined risk score (0- and 3-hour ESC algorithm and 2-hour advanced diagnostic protocol [ADP]), and the remaining 4 strategies do not.

0- and 3-Hour ESC Algorithm

AMI is ruled out if concentrations of hs-cTn remain in the normal range at presentation and at 3 hours later and if the patient fulfills 2 additional requirements: to be pain-free and to be at low risk of in-hospital mortality as quantified by a GRACE (Global Registry of Acute Coronary Events) score <140.[48] In patients presenting >6 hours after chest pain onset in whom the onset can be reliably quantified, a single blood draw at presentation is considered sufficient.[26,41] Patients are considered ruled in if they have a clearly elevated hs-cTn blood concentration at presentation or if the 3-hour sample shows a relevant change. This approach has been recommended by the ESC since 2011[41] and is the standard of care in many institutions in Europe (Figure, A). This approach to ruling out AMI appears to be safe for all hs-cTn assays and likely many sensitive cTn assays.[49] Assuming a 1-hour turn-around time for hs-cTn, this approach facilitates a disposition decision within ≈4 hours of presentation.

0- and 2-Hour ESC Algorithm

This approach using hs-cTn achieves a high NPV and sensitivity by also taking into account absolute concentration changes within 2 hours.[35,50,51] The lack of a relevant absolute change from presentation to 2 hours, in conjunction with the fact that both baseline and 2-hour hs-cTn concentrations are within the normal range, obviates the need to use a predefined risk score and allows one to safely rule out AMI even in patients with mild, nonspecific ECG abnormalities. This strategy allows the rapid rule-out of AMI in up to 60% of patients.[35,52] Moreover, this strategy includes a rule-in algorithm that provides a PPV of >75% for AMI and allows the early rule-in of ≈10% to 15% of patients with acute chest pain within 2 to 3 hours of presentation.

0- and 1-Hour ESC Algorithm

The concept of the 0- and 1-hour algorithm is identical to that of the 0- and 2-hour algorithm and is based exclusively on information provided by hs-cTn blood concentrations, which are assay dependent.[31,37,53–56] Again, the 1-hour algorithm obviates the need for formal use of risk scores and allows safe rule-out of AMI even in patients with mild, nonspecific ECG abnormalities. This strategy is very effective and allows an accurate disposition for ≈75% of patients: 60% rule-out and 15% rule-in of AMI. Given an average turn-around time for hs-cTn of ≈1 hour, this strategy facilitates clinical decision making within 2 to 3 hours of ED presentation for many patients. In patients assigned to observation (Figure, A), clinical decision making still requires the 3-hour measurement; in these "observe zone" individuals, final disposition can be made 4 to 5 hours after arrival.

Dual-Marker Strategy Combining cTn and Copeptin at the Time of Arrival

The dual-marker strategy combining cTn and copeptin takes advantage of the reciprocal release kinetics of both biomarkers. The combination provides incremental diagnostic value compared with a single cTn concentration when conventional cTn assays are used, albeit with a much smaller incremental benefit observed with the use of hs-cTn assays.[42–48] The NPV achieved in patients negative for both markers depends on the sensitivity of the cTn assay. Use of the 99th percentile for hs-cTnT or cTnI and a low cutoff for copeptin (eg, <10 pmol/L) achieves an NPV of 96% to 99% in studies with an AMI prevalence of 10% to 22%.[44–46,57] This strategy also has been successfully applied in a multicenter, open-label, randomized, controlled trial (RCT) in which a conventional cTn assay was used in the majority of patients in both arms. The main limitations of this strategy are the complexities related to adding a copeptin analyzer in the laboratory and a slightly lower NPV compared with the other strategies.[44–46,57,58] Two other caveats for the proper use of copeptin deserve attention. First, elevated copeptin concentrations have a very poor specificity for AMI, which creates challenges in patients with a normal first cTn but elevated copeptin. Second, in AMI, copeptin blood concentrations decline rapidly after the onset of chest pain and render its diagnostic utility low in patients presenting >6 hours after the onset of chest pain.[44–46,57,58]

Table 2. Summary of Biomarker Strategies for Rapid Assessment of Patients With Potential ACS in the ED

	Very Low cTn	cTn and Copeptin	0- and 1-h Algorithm	0- and 2-h Algorithm	2-h ADP	0- and 3-h ESC
Clinical scoring system	None	None	None	None	TIMI score ≤1 ECG normal at 0 and 2 h	GRACE <140 and pain free
Blood draws, n	1	1	2*	2*	2*	2*
Indication	Rule out	Rule out	Rule out and rule in	Rule out and rule in	Rule out	Rule out and rule in
NPV for AMI, %	98–100	92.4–99 96–99 with hs-cTn	99.1–100	99.5–99.9	99.1–100†	99.6–100
Eligible population size	+(+)	++	+++	+++	++	++(+)
Biomarker rule-out criteria‡						
Using hs-cTnT	hs-cTnT <5 ng/L	hs-cTnT <14 ng/L AND copeptin <10 pmol/L	hs-cTnT<12 ng/L AND 1-h Δ <3	hs-cTnT <14 ng/L at 0 and 2 h AND 2-h Δ <4	hs-cTnT <14 ng/L at 0 and 2 h	hs-cTnT <14 ng/L at 0 and 3 h
Using hs-cTnI	hs-cTnI <2–5 ng/L	hs-cTnI <26 ng/L AND copeptin <10 pmol/L	hs-cTnI <5 ng/L AND 1-h Δ <2	hs-cTnI <6 ng/L at 0 and 2 h AND 2-h Δ <2	hs-cTnI <26 ng/L at 0 and 2 h	hs-cTnI <26 ng/L at 0 and 3h
Biomarker rule-in criteria						
Using hs-cTnT			hs-cTnT ≥52 ng/L OR 1-h Δ ≥5	hs-cTnT ≥53 ng/L OR 2-h Δ ≥10		
Using hs-cTnI			hs-cTnI ≥52 ng/L OR 1-h Δ ≥5	hs-cTnI ≥64 ng/L OR 2-h Δ ≥15		
Feasibility	High	Low; Requires 2 biomarkers requiring different analyzers	High	High	Medium; Requires use of TIMI score	Medium; Requires GRACE score

ACS indicates acute coronary syndrome; ADP, accelerated diagnostic protocol; AMI, acute myocardial infarction; cTn, cardiac troponin; ED, emergency department; ESC, European Society of Cardiology; GRACE, Global Registry of Acute Coronary Events; hs-cTn, high-sensitivity cardiac troponin; NPV, negative predictive value; and TIMI, Thrombolysis in Myocardial Infarction. Eligible population size is quantified by the percentage of consecutive patients with chest pain eligible for this early triage strategy: +, ≈20%; ++, ≈40%; and +++, ≈50% to 75%.

*For some patients, only 1 blood draw will be necessary.

†For major adverse cardiac events (death, AMI, major arrhythmias).

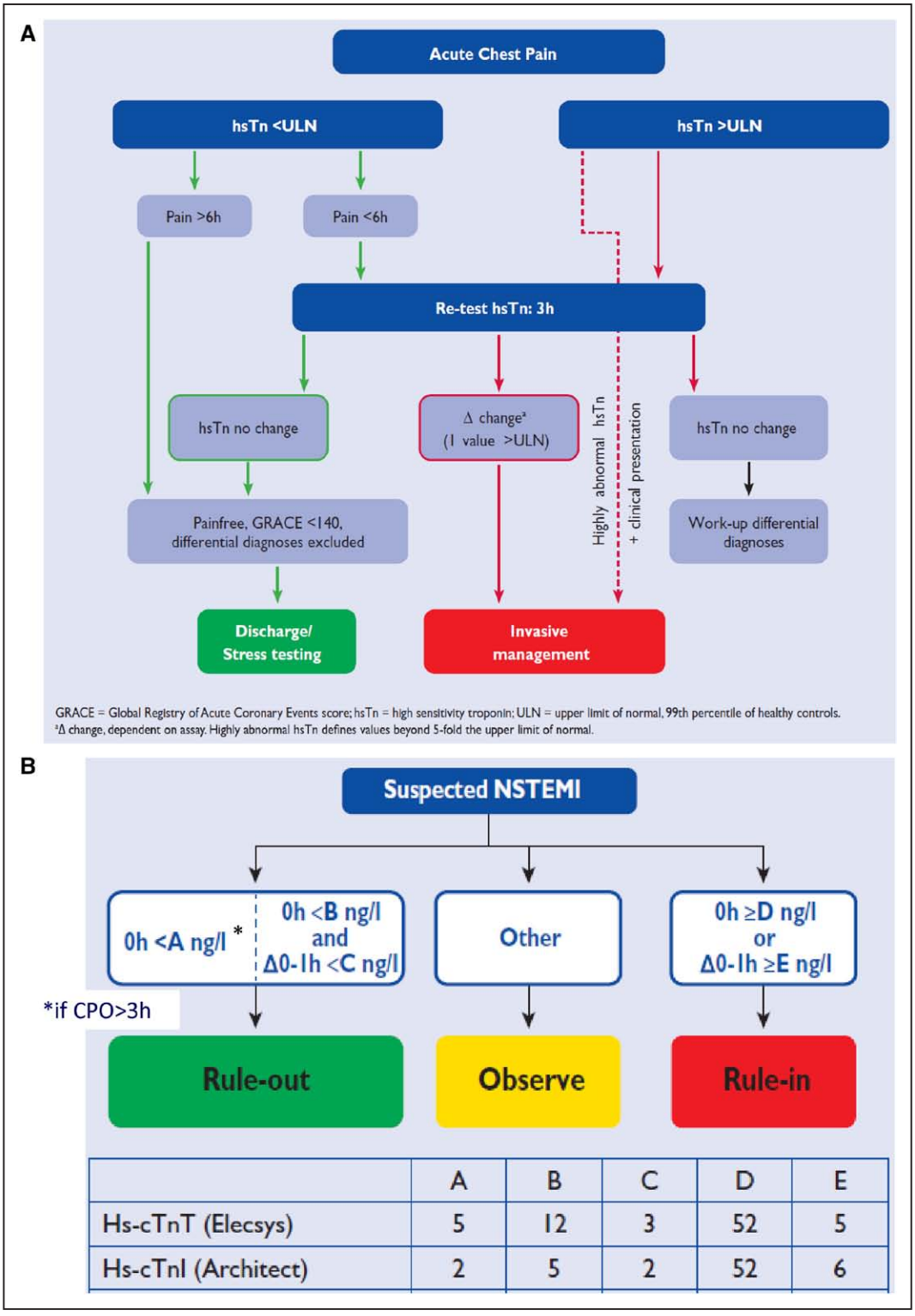
‡Characteristics are provided for the hs-cTnT (Elecsys) and hs-cTnI (Architect). Cutoff levels differ for other hs-cTn assays becoming available for clinical use in the future.

Undetectable/Very Low Levels of hs-cTn at the Time of Arrival

Very low blood concentrations of hs-cTn at presentation have a very high (98%–100%) NPV for AMI. Because the lower limit of detection is assay dependent and varies among the clinically available hs-cTn assays, defining very low concentrations using a distribution of the normal range (eg, <40% percentile of healthy individuals) may be the preferred metric to identify biologic-equivalent values. Four large studies and a recent meta-analysis have provided consistent results for hs-cTnT, whereas 2 studies showed comparable findings for 3 hs-cTnI assays.[29–34,55–60] Because the release of cTn is a time-dependent phenomenon, this approach should be used only in patients with a chest pain onset of at least 2 to 3 hours before ED presentation. In the 2015 ESC guidelines, this approach is recommended in combination with the 0- and 1-hour algorithm as the preferred rule-out strategies because of an excellent balance between speed and accuracy.[41] Because it requires only a single blood draw of an inexpensive and widely available biomarker (outside the United States), this approach has unique simplicity.

Observe Zone

Although most rapid AMI diagnostic strategies provide guidance for the rule-out only, 3 strategies also provide detailed guidance for the rule-in of AMI (0- and 3-hour ESC algorithm, 0- and 2-hour algorithm, 0- and 1-hour algorithm). In addition to the rule-out and rule-in zone, these strategies leave up to a third of patients in an observe-zone. These patients are often elderly men with pre-existing coronary artery disease (CAD) and high long-



	A	B	C	D	E
Hs-cTnT (Elecsys)	5	12	3	52	5
Hs-cTnI (Architect)	2	5	2	52	6

Figure. Algorithms.
A, The 0- and 3-hour rule-out algorithm of non–ST-segment–elevation acute coronary syndromes using high-sensitivity cardiac troponin (hs-cTn) assays.[41] **B**, The 0- and 1-hour rule-in and rule-out algorithms using hs-cTn assays in patients presenting with suspected non-ST-elevation myocardial infarction (NSTEMI) to the emergency department. Adapted from Roffi et al[41] with permission from the publisher. Copyright © 2016, European Society of Cardiology. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

term mortality. Continued serial sampling of cTn may be appropriate, with follow-up risk assessment with functional stress imaging, coronary CTA, or other diagnostic testing to help determine whether these patients may have AMI, ACS, or underlying coronary disease.

Evidence, Methodological Considerations, and Translation Into Clinical Practice

Although the continuous evaluation and possible further refinement of these strategies are necessary, appreciation of the methodology of large, prospective, multicenter diagnostic studies with meticulous and central adjudication of a final diagnosis of AMI and rather unbiased enrollment led to the strong position of the ESC advocating widespread clinical adoption. Diagnostic studies allow the precise quantification of the diagnostic performance (accuracy, sensitivity, NPV, specificity, PPV) of novel biomarkers or novel diagnostic algorithms compared with the final adjudicated diagnosis as the reference. Ideally, they are further supported by RCTs, which can add, for example, important insights into cost-effectiveness. Unfortunately, large, appropriately powered (eg, for recurrent AMI or mortality during long-term follow-up) RCTs in the diagnostic field are extremely rare. In fact, not a single such RCT has ever been performed evaluating the use of biomarkers, ECG variables, or any other inexpensive diagnostic tools in the diagnosis of AMI.

Patient Admission Despite Rule-Out Triage by the Algorithm

The disposition recommendation provided by the novel biomarker-based strategies should be used in conjunction with all other diagnostic and prognostic information available to the physician in the ED. These algorithms were designed only to safely rule out AMI and do not address the other disorders that still require admission such as UA, pulmonary embolism, aortic dissection, or pneumonia. To appropriately detect these conditions, other diagnostic tests (such as CT scans) not included in these strategies may be necessary in some patients.

COMBINING TROPONIN WITH RISK SCORING SYSTEMS FOR ACCELERATED DIAGNOSTIC PATHWAYS

Clinical decision aids have become popular to overcome cognitive biases that affect the clinician's ability to accurately predict pretest probability of disease. Physicians have difficulty in estimating risks of diseases and frequently err toward overestimation. Accelerated decision-making processes incorporating such aids can be used to facilitate safe early discharge.

Chest pain risk scoring tools in combination with cTn testing have had considerable success in identifying low-risk patients who may be suitable for early discharge (Tables 3 and 4).[61–76] Although most of the research in this area is observational, there have been 2 single-center RCTs, and there has been widespread implementation of such strategies in Australasia. The Australian state of Queensland and the country of New Zealand, with combined populations of nearly 10 million people, now have fully adopted accelerated diagnostic pathways. The strategy in Queensland (and some New Zealand sites) is based on the use of a contemporary assay such as is available in the United States rather than a high-sensitivity troponin assay.

The TIMI (Thrombolysis In Myocardial Infarction) score was developed from a high-risk group of patients but subsequently validated for use in the ED setting.[61] The ASPECT (Antithrombotics in the Secondary Prevention of Events in Coronary Thrombosis) pathway[62] (online-only Data Supplement) combined a modified TIMI risk score of 0 with a nonischemic electrocardiogram at 0 and 2 hours and multibiomarker point-of-care testing and was able to classify ≈10% of patients with chest pain as low risk for 30-day major adverse cardiac events with a >99% NPV (Table 4). The ADAPT study (2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker)[63] involved the Australasian ASPECT cohorts using just central laboratory contemporary cTns such as those available in the United States (instead of multiple biomarker testing). This study resulted in twice as many patients classified as low risk with an improved sensitivity and NPV (99.7%) (Table 4). The effectiveness of the ADAPT pathway was then validated in an RCT[64] and has been widely implemented in Queensland, Australia.

A modified ADAPT rule, incorporating results from a highly sensitive troponin assay in patients with a TIMI score of 0 or 1, found that ≈40% of patients could be identified as low risk with >99% sensitivity and NPV. This was further validated in the independent APACE (Advantageous Predictors of Acute Coronary Syndromes Evaluation) study (Table 4) cohort.[65]

A modified Goldman risk score recently was incorporated into an accelerated diagnostic pathway[67] (Table 3 and the online-only Data Supplement) in which patients were determined suitable for early discharge after a single high-sensitivity troponin measured on arrival at the ED (TRUST study). This validation study classified a percentage of patients as low risk (39.8%) similar to the ADAPT and APACE studies with good sensitivity (98.8%) and NPV (99.7%; Table 4).[63,65,66]

The HEART score[67] was derived on the basis of clinical logic and simplicity rather than statistical derivation from a prospective trial. The manner in which the score was developed is interesting. Jacob Six, a cardiologist from Utrecht, the Netherlands, was undertaking teaching rounds with medical students. In the process of ward rounds, he taught students that the key factors to consider when assessing patients with chest pain were

Table 3. Summary of Commonly Used Risk Scores

Rule	Characteristics of Risk Score	Early Discharge Criteria
Modified Goldman score and Trust ADP	8 Criteria each worth 1 point: typical new-onset chest pain at rest; pain the same as previous myocardial infarction; pain not relieved by nitroglycerin spray within 15 min; pain lasting >60 min; pain occurring with increasing frequency; hypotension; acute shortness of breath; pain within 6 wk of a myocardial infarction or revascularization	Total score ≤1, nonischemic ECG, hs-cTn <14 ng/L
HEART score	5 Criteria each graded 0, 1, or 2: history, ECG, age, risk factors, troponin	Total score ≤3
North American Chest Pain Rule		Absence of new ischemia on ECG, no history of coronary disease, not typical pain, age <40 y, and initial cTn negative; if age is 41–50 y, add repeat troponin at 6 h
Vancouver Chest Pain Algorithm		Absence of ongoing pain, angina; physical findings consistent with heart failure, murmur, or hemodynamic instability; ischemic ECG, and elevated cTn
EDACS	4 Different categories with variable point assignments	Total score ≤16, no new ischemia on ECG, both 0- and 2-h cTn negative
	Age groups, history of premature CAD, or 4 risk factors, 4 symptoms associated with pain, sex	
	Range of scores usually requiring computer or a smartphone application	
MACS Clinical Decision Rule		5 CAD symptoms; nonischemic ECG and negative serial biomarker tests (hs-cTn and H-FABP)
Modified TIMI score	5 criteria each worth one point: age, ≥3 CAD risk factors, known CAD, ASA in past 7 d, recent severe angina	ASPECT, ADAPT

ADAPT indicates 2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker; ADP, accelerated diagnostic pathway; ASA, acetylsalicylic acid/aspirin; ASPECTS, Antithrombotics in the Secondary Prevention of Events in Coronary Thrombosis; CAD, coronary artery disease; cTn, cardiac troponin; EDACS, Emergency Department Assessment Chest Pain Score; H-FABP, heart-type fatty acid binding protein; hs-cTn, high-sensitivity cardiac troponin; MACS, Manchester Acute Coronary Syndromes; and TIMI, Thrombolysis in Myocardial Infarction.

their history, ECG results, age, risk factors, and troponin test result (Table 3). He then realized that these factors actually formed a good mnemonic, and work began to determine whether a related score would be useful in clinical practice.

Backus et al[67] tested the score on 880 patients, yielding a 98.1% sensitivity and a 41.6% specificity. Mahler et al[68] tested the HEART score on a registry cohort of 1070 patients. In this population, the score achieved a 58.3% sensitivity and an 85.0% specificity; however, it must be noted that this population had a very low prevalence of disease (1%), meaning that only a small number of false-positive results (5 cases) had a large influence on the sensitivity. In 2013, a retrospective validation was published using data from 2906 patients from the Asia-Pacific ASPECT study in which the prevalence of major adverse cardiac events was 12.9%.[69] In this analysis, the sensitivity was 96.3%. In 2013, a validation published from 10 centers in the Netherlands had a combined major adverse cardiac event prevalence of 17%, also resulting in a sensitivity of 96.3%.[69] In this study, the ECG criteria were modified slightly, with 2 points also being given for negative T waves. Both analyses required retrospective determination of history parameter of the score from other data fields. There has now been a small RCT using a modified version of the HEART score that used structured criteria to categorize history and excludes patients from being classified as low risk if there is a positive troponin result from blood sampling at 0 and 3 hours from arrival at the ED.[70] In this study, the prevalence of major adverse cardiac events was 6%, and the sensitivity for major adverse cardiac events for 141 patients randomized to the modified HEART pathway was 100%.

The original troponin criteria were based on the contemporary non–high-sensitivity Beckman Access AccuTroponin I assay with a threshold for positivity of 0.04 μg/L (40 ng/L). Clinicians wishing to use the HEART score should be judicious about how best to use troponin results within the score. First, it would seem that

Table 4. Summary of Risk Score Performance

Decision Aid	n	Low Risk, %	Sensitivity, %	NPV, %	MACEs, %	Troponin Assay
Modified TIMI score=0						
ASPECT ADP[62]	3582	9.8	99.3	99.1	11.8	C
ADAPT ADP[63]	1975	20	99.7	99.7	15.3	C
Modified TIMI score=0 or 1						
ADAPT cohort[65]	1635	40	99.2	99.7	15.1	H
APACE cohort[65]	909	39	99.4	99.7	17.2	H
Modified Goldman score						
TRUST ADP[66]	960	39.8	98.8	99.7	10.1	H
HEART score						
Backus et al[67]	880	34.4	98.1	99.0	18.0	C
Mahler et al[68]	1070	84.5	58.3	99.4	1.2	C
Six et al[69]	2906	28.2	96.3	98.3	12.9	C
Mahler et al[70]	141	46.8	100	100	6	C
North American Chest Pain Rule						
Hess et al[71]	2718	18	100	100	12.0	C
Vancouver Chest Pain Algorithm						
Scheuermeyer et al[72] derivation	763	14.5	100	100	21.6	H
Scheuermeyer et al[72] validation	906	20.4	99.2	99.5	13.1	H
Cullen et al[73]	1635	13.0	99.1	98.6	20.4	H
Cullen et al[73]	1635	12.8	98.8	98.1	20.4	C
MACS Clinical Decision Rule						
Body et al[74] derivation	698	35.5	99.4	99.6	22.5	H
Body et al[74] validation	463	27.0	98.0	98.4	21.2	H
EDACS						
Than et al[75] derivation	1974	42.2	99.0	99.6	15.5	C
Than et al[75] validation	608	51.3	100	100	12.9	C
Canada[76]	763	41.0	100	100	17.4	C

ADAPT indicates 2-Hour Accelerated Diagnostic Protocol to Assess Patients With Chest Pain Symptoms Using Contemporary Troponins as the Only Biomarker; ADP, accelerated diagnostic protocol; APACE, Advantageous Predictors of Acute Coronary Syndromes Evaluation; ASPECTS, Antithrombotics in the Secondary Prevention of Events in Coronary Thrombosis; C, contemporary; EDACS, Emergency Department Assessment of Chest Pain Score; H, high sensitivity; MACE, major adverse cardiac event; MACS, Manchester Acute Coronary Syndromes; NPV, negative predictive value; and TIMI, Thrombolysis in Myocardial Infarction.

using serial troponin samples improves the sensitivity; however, prospective studies on this approach are limited. Second, it is important to recognize that all troponin assays are different from each other, and it is not clear whether the points-allocated approach for the troponin component will be the same for every troponin assay. Because several adaptations exist for using the HEART score, differences should be considered in its implementation.

In a derivation study, the North American Chest Pain Rule (Table 3 and the online-only Data Supplement)[71] was 100% sensitive for a cardiac event within 30 days and categorized 18% of patients as safe for early discharge (Table 4). The model was internally validated with statistical bootstrapping techniques but has not yet been validated in an external data set.

The new Vancouver Chest Pain Diagnostic Algorithm was derived from a single cohort implementation study with careful monitoring of patient outcomes.[72] Clinicians used their own judgment to classify patients as low risk or to continue observing and testing troponin. More than 70% of patients were classified as low risk with high sensitivity. When it was later assessed on an Australasian population with the use of high-sensitivity and contem-

porary troponin assays,[73] considerably fewer patients (13%) were classified as low risk. With the use of the high-sensitivity assay, the diagnostic sensitivity for ACS was 99.1%, specificity was 16.1%, PPV was 23.3%, and NPV was 98.6%. With the use of a contemporary non–high-sensitivity troponin assay, 208 patients (12.6%) were eligible for early discharge, with 4 of these patients being diagnosed with ACS for a sensitivity of 98.8%.

The Manchester Acute Coronary Syndromes (MACS) Decision Rule[74] differs from other accelerated chest pain diagnostic pathways in that it incorporates testing of a heart-type fatty acid binding protein in addition to high-sensitivity troponin. Biomarker concentrations are considered continuous variables, and computer software is required to calculate the probability of a major adverse cardiac event occurring within 30 days. The need for an additional assay that is not commonly available and computer software makes this unlikely to be adopted widely.

The EDACS-ADP (Emergency Department Assessment of Chest Pain Score Accelerated Diagnostic Pathway) decision aid was derived from 2 Australasia centers as preplanned parallel research to the observational ADAPT study.[75] Data were prospectively collected for 37 candidate variables commonly used in clinical care or reported as having value in predicting AMI among ED patients.[75] This protocol was validated and tested for reproducibility with prospectively collected data from separate cohorts of patients from the same centers. In the derivation and validation cohorts, the EDACS-ADP classified >40% of patients as low risk with high sensitivity.[75] A subsequent validation of the EDACS-ADP using a Canadian cohort of patients classified a similar proportion of patients as low risk with optimal sensitivity and NPV.[76] The EDACS-ADP has been validated in an RCT[77] and is now being used in multiple hospitals in New Zealand and Australia.

Clinical decision aids with or without clinical gestalt have the potential to be important tools in the assessment of patients presenting to the ED with possible AMI, and accelerated decision-making processes incorporating such aids can be used to facilitate safe early discharge. Clinicians or departments thinking of adopting an ADP for local implementation should carefully decide on the outcome of importance (ie, early rule-out of AMI versus rule-out of ACS). Consideration also should be given to the prevalence of the disease in the hospitals where ADPs were studied. An ADP that was developed and tested in a low-prevalence population must be transferred with caution to a setting where the disease prevalence is high, and for this reason, it is important to consider both the sensitivity and the NPV of the rule-out strategy. The pathways based on ADAPT, EDACS, and HEART have the most extensive evidence base behind them.

ASSESSMENT OF CAD OR MYOCARDIAL ISCHEMIA IN THE ED

Guidelines from both Europe and the United States recommend not just ruling out AMI but also risk stratifying patients who present with potential ACS and evaluating them for CAD.[41,78] Biomarker approaches detect AMI but will not be able to detect UA, which, by definition, lacks myocardial necrosis. When concerns about UA remain after ascertainment of negative biomarkers, further assessment of inducible ischemia or detection of CAD is important. Although most commonly done through the use of cardiac catheterization for the highest-risk patients and 24- to 72-hour stress testing for many low- to intermediate-risk patients, coronary CTA has been found to have a high degree of diagnostic accuracy with the additional benefit of facilitating safe and expeditious discharge of low- to intermediate-risk patients without significant CAD directly from the ED.

Coronary CTA

Coronary CTA is an appropriate option for the evaluation of low- to intermediate-risk patients with chest pain syndromes in the ED.[79] It has a high degree of diagnostic accuracy; is predictive of acute, 30-day, and 1 year event rates; and can safely and more rapidly facilitate discharge from the ED for patients who present with a potential ACS.

Accuracy

A systematic review of 41 studies totaling 2515 patients indicated a sensitivity of 95% and specificity of 85% for the detection of obstructive CAD in all types of scanners combined.[80]

Because recent cardiac catheterization with normal or minimally diseased vessels greatly reduces the possibility of an ACS and because coronary CTA correlates well with catheterization,[16,17] it makes sense that negative coronary CTA results should be similarly predictive.

Short-Term Outcomes

It has been well demonstrated that a negative coronary CTA (defined as maximal stenosis <50% in all vessels) predicts freedom from 30-day myocardial infarction, coronary revascularization, and cardiovascular death. In a recent meta-analysis of studies of 1559 patients with symptoms suggestive of ACS who presented to an ED, the sensitivity was 93.3%, specificity was 89.9%, PPV was 48.1%, and NPV was 99.3% for 30-day cardiovascular events.[81]

Two RCTs of ≥1000 patients have confirmed the benefit of this approach.[82,83] The ACRIN-PA (American College of Radiology Imaging Network) 4005 multicenter trial randomized 1370 low- to intermediate-risk ED patients to either coronary CTA or traditional care.[82] Patients with a negative coronary CTA (<50% maximal stenosis) were

free from cardiac death or myocardial infarction at 30 days (upper limit of the 95% confidence interval, 0.57%). Additionally, the coronary CTA–based strategy doubled the discharge rate (50% versus 23%) and shortened the length of stay (18 versus 25 hours) while identifying more patients with coronary disease (9% versus 3%) and simultaneously reducing the likelihood of a negative catheterization. Similarly, the ROMICAT-II study (Rule Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography) was a multicenter RCT comparing the effectiveness of coronary CTA evaluation and standard evaluation.[83] Patients who received CT evaluation had a shorter length of stay and were more likely to be discharged from the ED (47% versus 12%). Overall, there were no differences in clinical adverse events between the 2 groups and no undetected ACS at 28 days. These data support the recommendations that patients with a maximal stenosis of <50% can be safely discharged home from the ED.

Longer-Term Outcomes

Hollander et al[84] evaluated 588 low-risk patients who received coronary CTA in the ED. Of the 481 patients with <50% stenosis in any vessel who also did not have depressed left ventricular function, 53 patients (11%) were rehospitalized and 51 patients (11%) received further diagnostic testing (stress or catheterization) during the subsequent year. Only 1 patient died (0.2%) and there was no AMI during this time period.[84] Hadamitzky et al[85] enrolled 1256 consecutive patients with suspected CAD undergoing 64-slice coronary CTA and observed them prospectively for the occurrence of cardiac death, myocardial infarction, or UA requiring hospitalization. In the 802 patients without any stenosis >50%, only 1 case of UA occurred during the initial 90 days. Within a median of 18 months, there were only 4 events in these 802 patients (<0.5%), whereas there were 17 events in the 348 patients (5%) with obstructive CAD.[85]

The ACRIN-PA 4005 study followed up 1285 patients for 1 year and found that only 1 of the 640 patients with a negative coronary CTA on presentation had an adverse event.[86]

Compared with the traditional care arm, patients randomized to coronary CTA had similar rates of ED revisits, hospital admissions, and subsequent cardiac testing.[86]

Two smaller studies focused on low- to intermediate-risk patients with chest pain. The ROMICAT trial (Rule Out Myocardial Infarction Using Computer Assisted Tomography) reported 2-year outcomes for their cohort in 368 ED patients with acute chest pain, negative initial troponin, and a nonischemic ECG.[87] Cumulative probability of 2-year events increased across strata for CAD, but none occurred in patients without disease (no CAD, 0%; nonobstructive CAD, 4.6%; obstructive CAD, 30.3%).

In a European cohort of 227 patients with 2.3 years of follow-up, there were no cardiovascular events in the 96 patients without CAD (0%), 2 events in the 76 patients with nonobstructive CAD group (2.6%), and 11 in the 55 patients (20%) with obstructive CAD.[88] Abdulla et al[89] conducted a meta-analysis that included 5675 patients who were mostly intermediate to high risk in 10 studies with a mean follow-up of 21 months. The event rate was 0.5% in 2045 patients with normal CTA, 3.5% in 2068 patients with nonobstructive CAD, and 16% in 1562 patients with obstructive CAD.

Thus, it seems clear that a negative coronary CTA is associated with a very low event rate and that discharge directly from the ED is safe in the short and longer term.

Calcium Score Alone

The role of coronary artery calcium score (CACS) alone or in combination with angiography remains the subject of some debate. The American College of Cardiology Foundation/American Heart Association 2007 clinical expert consensus document on coronary artery calcium scoring by CT evaluated 6 published reports in 27 622 patients, none of whom were symptomatic ED patients.[90] The relative risk for myocardial infarction or death over 3 to 5 years was increased 4.3-fold for any measurable calcium compared with a CACS of 0. Patients without detectable calcium (or a CACS of 0) have a very low rate of death from coronary heart disease or myocardial infarction (0.4%) within this time frame. In contradiction, Gottlieb et al[91] evaluated 291 patients who were undergoing coronary CTA and invasive coronary angiography, of whom most (95%) patients were at intermediate to high probability of obstructive CAD. A total of 72 patients had a CACS of 0, among whom 14 (19%) had at least 1 stenosis ≥50%. Chang et al[92] found that 4 of 17 patients (24%) with a CACS of 0 still had CAD. Within the CONFIRM registry (Coronary Computed Tomography Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry), >5000 patients had a CACS of 0, yet 16% of these patients still had evidence of CAD on coronary CTA.[93] Freedom from CACS does not appear to provide enough information to effectively risk stratify patients in the ED for acute events.

Application in Practice

The Society of Cardiovascular Computed Tomography guidelines on the use of coronary CTA for patients presenting with acute chest pain to the ED provide detailed recommendations for patient selection, site requirements, imaging, scanning, and reader requirements, as well as details on patient preparation.[94]

Coronary CTA is not ideal for all low- to intermediate-risk patients. Up to one-third of patients may not qualify for imaging because of contrast allergy, renal insufficiency, unresolved tachycardia, or inability to receive β-blockade for heart rate control. The ideal patient is not known to be free of disease or to definitely have underlying coronary disease and but will be considered low- to intermediate-risk without significant

contraindications (Table 5). Typical patients may have a TIMI score of 0 to 2 (or equivalent other scoring system) or may be at higher risk but have had a negative stress test in the past 6 to 12 months, therefore benefiting from a different assessment of potential underlying disease.

There is a concern that the use of coronary CTA may be associated with an increased risk of coronary angiography and revascularization than seen with stress testing, but the ACRIN-PA study suggested more appropriate use of cardiac catheterization because there was a lower rate of angiographically negative coronary arteries in the coronary CTA group.[82]

Providers must continue to interpret test results in conjunction with clinical judgment. Finding coronary disease on a coronary CTA does not mean that the coronary disease is the cause of the symptoms. Although it is possible to help clarify the relevance of CAD detected by calculating fractional flow reserve on coronary CTA images, the duration of time required to process these images (up to 6 hours) makes fractional flow reserve not practical in ED patients. Similarly, reversible ischemia on a stress test does not mean that the patient has ischemic heart disease because low-risk patients have a high false-positive rate.

Future studies need to help determine which patients with coronary CTA demonstrating coronary disease benefit from interventions. Additionally, future studies need to determine the role of coronary CTA in patients with low-grade troponin elevations and in patients who do have rising or falling patterns with serial measurements.

Same-Day Stress Testing

Although a complete review of stress testing in the outpatient and hospital setting is beyond the scope of this review, it is worth noting that stress testing also can be done rapidly after negative biomarkers are obtained.[95–97] Amsterdam et al[96] found stress testing after a single negative biomarker to be safe. Kirk et al[95] demonstrated that stress testing in ED patients with chest pain without the use of serum biomarkers was safe, but the study was small and biomarkers are universally obtained early in the clinical course of patients with potential ACS. A report on 856 patients receiving stress testing after 2 troponin values 2 hours apart found this approach to be safe and efficient.[97]

Resting Sestamibi Imaging

Resting sestamibi imaging is useful for early risk stratification of patients with potential ACS. The use of early resting sestamibi imaging can reduce unnecessary hospitalizations among patients without ACS without reducing appropriate admissions for patients with ACS.[98] Tatum et al[99] found no AMIs or deaths within 12 months in 338 patients with normal scans, whereas an abnormal scan was associated with 50-fold increased risk of AMI, 14.5-fold increased risk of 30-day revascularization, and 30-fold increased risk of death over 12 months.

There are, however, significant practical issues preventing widespread implementation. Radioisotope preparation in batches makes use in a single patient costly. Decreased accuracy occurs if injection does not occur during or shortly after pain, making timely injection essential. Timely injection by certified nuclear technologists is difficult to attain at most sites.

Table 5. Appropriate Indications for Coronary CTA in Patients With Acute Chest Pain Syndromes

Indications
ECG negative or indeterminate for myocardial ischemia
Low to intermediate pretest likelihood by risk stratification tools
TIMI score of 0–2 (low risk) ideal or TIMI score of 3–4 (intermediate) in some cases
HEART score <3
≥1 Negative troponin values, including point-of-care assays
Equivocal or inadequate previous functional testing during index ED or within previous 6 mo
Equivocal indications
High clinical likelihood of ACS by clinical assessment and standard risk criteria (eg, TIMI score >4)
Previously known CAD
Known calcium score >400
Relative contraindications
History of allergic reaction to iodinated contrast
GFR <60 mL·min^{-1}·1.73 m^{-2}
Factors likely to lead to nondiagnostic scans; specifics will vary with scanner technology and site capabilities
Heart rate greater than site maximum for reliably diagnostic scans after β-blockers (usually 70–80 bpm)
Contraindications to β-blockers and heart rate not controlled
Atrial fibrillation or other markedly irregular rhythm
BMI >39 kg/m^2
Absolute contraindications
Known ACS
GFR <30 mL·min^{-1}·1.73 m^{-2} unless on long-term dialysis
Previous anaphylaxis after iodinated contrast administration
Previous episode of contrast allergy after adequate steroid/antihistamine preparation
Pregnancy

ACS indicates acute coronary syndrome; BMI, body mass index; CAD, coronary artery disease; CTA, computed tomography angiography; ED, emergency department; GFR, glomerular filtration rate; and TIMI, Thrombolysis in Myocardial Infarction.

Cardiovascular Magnetic Resonance Imaging

Cardiovascular magnetic resonance imaging has been proven to be a reliable and well-tolerated tool and is useful after ACS to focus on remodeling or for diagnosis of diseases such as myocarditis. However, in the setting of acute chest pain in the ED where rapid diagnosis is required, it is not practical. Its use in other settings is beyond the scope of this review.

Echocardiography

Resting echocardiography has insufficient sensitivity and poor specificity for the detection of AMI. It cannot distinguish old from new infarcts. Larger areas of infarction and more depressed left ventricular function predict a higher likelihood of cardiovascular complications and an increased mortality. The predictive properties of stress echocardiography and myocardial perfusion imaging are similar with respect to AMI and the presence of CAD but are typically outpatient or next-day tests and are not usually done in the ED.

No Objective Testing

An increasingly common school of thought is that objective testing for ischemia or coronary disease in some low-risk patients who currently receive testing is not necessary because it has not been shown to lower event rates or to improve outcomes compared with accelerated biomarker-based protocols alone. Unfortunately, there have not been any randomized trials comparing testing with no-testing strategies, and such a trial would require a prohibitively large number to demonstrate a difference between groups. Foy et al[100] found no difference in the hospitalization rate or AMI at 7 and 190 days between patients who did and did not have an imaging test during the ED visit using a private insurance claims database. They concluded that deferral of noninvasive testing for these patients may be reasonable. This no-testing approach might miss an opportunity for long-term CAD risk assessment and intervention (ie, statins) and does not take into account the high likelihood of an ED patient with chest pain presenting again within the next year. Additionally, it is not guideline compliant because current practice guidelines recommend testing for CAD after exclusion of myocardial infarction.

CONCLUSIONS

It is well established that the clinician cannot use clinical judgment alone to determine whether an individual patient who presents to the ED has an ACS. The improvement in cTn assays, especially in conjunction with clinical decision algorithms, now enables the clinician to rapidly exclude myocardial infarction. In patients in whom UA remains a concern or there is a desire to evaluate for underlying CAD, coronary CTA can be used in the ED. Although this process once took ≥24 hours, patients can now have myocardial infarction and CAD rapidly excluded in the ED.

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FOOTNOTES

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