2015 ACR/ACC/AHA/AATS/ACEP/ASNC/NASCI/SAEM/SCCT/SCMR/SCPC/SNMMI/STR/STS Appropriate Utilization of Cardiovascular Imaging in Emergency Department Patients With Chest Pain

A Joint Document of the American College of Radiology Appropriateness Criteria Committee and the American College of Cardiology Appropriate Use Criteria Task Force

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INTRODUCTION

The 2010 National Hospital Medical Care Survey reported nearly 130 million emergency department (ED) visits [1]. The second largest component, 5.4%, were patients presenting with chest pain (CP) [1]. In the patient presenting with undifferentiated CP, the spectrum of potential etiologies ranges from serious, immediate, life-threatening pathologies such as acute coronary syndromes (ACS), pulmonary embolism (PE), or acute aortic syndromes (AAS) to relatively benign illness without long-term consequences (such as costochondritis) and poses a great challenge to the caregiving physician. The initial strategy focuses on rapidly and accurately excluding diagnoses with the greatest short-term mortality risk. Much of the initial diagnosis is determined by the clinical presentation as assessed by the history, physical examination, and basic ancillary testing. However, diagnostic imaging may be used to identify or exclude a potential life-threatening condition when the clinical presentation does not reveal an obvious cause.

RATING GUIDE

Methods for Establishing Appropriate Use of Imaging in ED Patients With CP

Clinicians, payers, and patients are interested in the incremental value offered by imaging to both the diagnosis and clinical management of disease conditions and, alternatively, when imaging does not offer this value. This document addresses the appropriate use of imaging in patients who present to an ED with CP. Imaging appropriateness explicitly considers two questions: (1) Is any imaging justified for 20 clinical scenarios that categorize patients after history, physical examination, and ancillary testing? and (2) If justified, what meaningful incremental information will an imaging procedure provide? This document combines evidence-based medicine, guidelines, and practice experience by engaging a rating panel in a modified Delphi exercise [2]. This document follows the methods as described in a joint publication by the American College of Cardiology and the ACR [3]. When more than one imaging study is considered appropriate for a clinical scenario, the methods do not consider preferred individual modalities among all of those rated appropriate. Clinicians should include all factors including costs as well as local availability and expertise when ordering imaging studies.

Clinical Scenario and Indication Identification by Writing Group

The Emergency Department Patients With Chest Pain Writing Panel comprised practicing emergency medicine, cardiology, and radiology representatives from the relevant professional societies. The writing panel recognized key diagnoses related to patients who present to the ED with CP for which imaging may be relevant to diagnosis and management. Because the charge of the writing group is to describe common clinical scenarios seen in contemporary practice, the document is organized with respect to diagnostic algorithms from four key clinical entry points that direct imaging (see Fig. 1):

1. Suspected non—ST-segment elevation ACS (clinical scenarios 1-10)
2. Suspected PE (clinical scenarios 11-15)
3. Suspected acute syndrome of the aorta (clinical scenarios 16-18)
4. Patients for whom a leading diagnosis is problematic or not possible (clinical scenarios 19 and 20)

Definition of Appropriateness

The ACR and American College of Cardiology definition of an "appropriate" imaging test is as follows [4]:

> The concept of appropriateness, as applied to health care, balances risk and benefit of a treatment, test, or procedure in the context of available resources for an individual patient with specific characteristics. Appropriateness criteria provide guidance to supplement the clinician's judgment as to whether a patient is a reasonable candidate for the given treatment, test or procedure.

This definition highlights the central pursuit of the greatest yield of clinically valuable diagnostic information from imaging with the least negative impact on the patient.

On the basis of available evidence, the Emergency Department Patients With Chest Pain Rating Panel members assigned a rating to each imaging procedure for each of the 20 clinical scenarios on a scale ranging from 1 to 9 as follows:

> **Appropriate rating 7, 8, or 9:** An appropriate option for the management of patients in this population because of benefits generally outweighing risks; an effective option for individual care plans although not always necessary depending on physician judgment and patient specific preferences (ie, the procedure is generally acceptable and is generally reasonable for the indication).
>
> **May be appropriate rating 4, 5, or 6:** At times an appropriate option for the management of patients in this population because of variable evidence or agreement regarding the benefit/risk ratio, potential benefit on the basis of practice experience in the absence of evidence, and/or variability in the population; effectiveness for individual care must be determined by a patient's physician in consultation with the patient on the basis of additional clinical variables and judgment

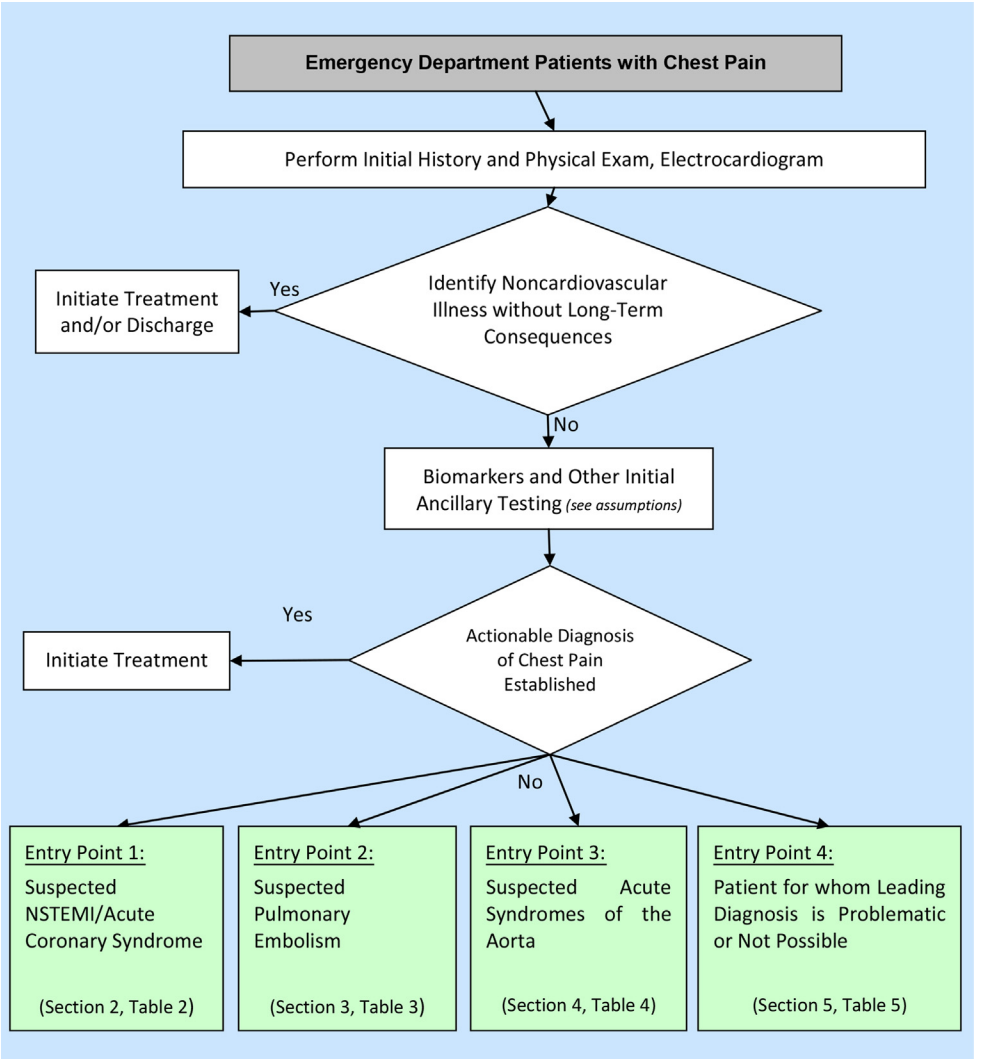

Figure 1. Entry points for clinical scenarios under consideration.

along with patient preferences (ie, the procedure may be acceptable and may be reasonable for the indication).

Rarely appropriate rating 1, 2, or 3: Rarely an appropriate option for the management of patients in this population because of the lack of a clear benefit/risk advantage; rarely an effective option for individual care plans; exceptions should have documentation of the clinical reasons for proceeding with this care option (ie, the procedure is not generally acceptable and is not generally reasonable for the indication).

Consensus was reached when 60% or greater of the panel members assigned a rating within one of the three categories: appropriate (A), may be appropriate (M), or rarely appropriate (R). When consensus was not reached for a study within a particular clinical scenario, regardless of the rating panel scores, the rating was assigned M*, or may be appropriate*, with the asterisk referring to the fact that the rating of M* was from absence of consensus as opposed to M, indicating that consensus was reached in the may be appropriate category.

DEFINITIONS

Non–ST-Segment Elevation ACS

Any group of clinical symptoms compatible with acute myocardial ischemia, including unstable angina and non–ST-segment elevation myocardial infarction (NSTEMI).

AAS

Any group of clinical symptoms compatible with aortic dissection, intramural hematoma, and symptomatic aortic ulceration.

CP Related to ACS

Any constellation of anginal or anginal-equivalent symptoms that the physician feels may represent a condition resulting from obstructive coronary artery disease (CAD). Examples of such symptoms include but are not exclusive to CP, chest tightness, burning, shoulder pain, and jaw pain or "angina equivalents" such as dyspnea.

ABBREVIATIONS (SEE APPENDIX 1)

ASSUMPTIONS

General Clinical Assumptions

To limit inconsistencies in interpretation, specific assumptions were considered by the writing group in development and were used by the rating panel. Assumptions associated with specific presentations are also reviewed in the following respective sections.

Practice Parameters/Standard of Care

All imaging is performed by qualified personnel in an accredited laboratory using standardized imaging protocols.

Clinicians should consider ionizing radiation when choosing an imaging modality for a patient in a specific clinical scenario. Radiation exposure should be minimized in all patients according to the principle of "as low as reasonably achievable." Tests involving radiation should use protocols [5] that deliver the least possible radiation dose but preserve image quality and sensitivity [6].

Cost/Value

From the standpoint of the practicing emergency medicine physician caring for an individual patient, the potential clinical benefits of an appropriate imaging study should be the highest priority, and these are weighed against potential risks of performing either no imaging study or an alternative study.

As related to societal benefits, costs should also be considered in relation to potential benefits in order to better understand comparative value. However, there is a relative paucity of data to assess cost-effectiveness among multiple studies. When available, these data are noted by the writing panel, and cost/value data are considered, if deemed appropriate, by rating panel members.

Guidance Specifically for Appropriate Use Criteria Users

Reducing imaging that is "rarely appropriate" is considered a potentially valuable means to reduce costs and population risks in cardiovascular imaging among patients who present to emergency medicine physicians with CP.

The category "may be appropriate" should be used when insufficient clinical data are available for a definitive categorization or there are substantial differences in opinion regarding the appropriateness of that indication. The absence of definitive data supporting a specific imaging study for a particular subset of patients does not imply a lack of benefit, and in such cases, careful investigation of the particulars of the clinical scenario is warranted. The designation "may be appropriate" should not be used as the sole grounds for denial of reimbursement for a given examination for a specific clinical scenario.

Entry Criteria Into Algorithms

1. All adult patients presenting to EDs with potential CP syndromes will undergo evaluations that generally include history and physical examination, immediate electrocardiography (ECG) to identify or exclude ST-segment elevation myocardial infarction (STEMI), and cardiac and/or pulmonary biomarker analysis (troponin and/or D-dimer) (Fig. 1). Some patients will be diagnosed with noncardiovascular illnesses that exclude ACS, PE, and AAS, and in general, no imaging is required. Patients with evidence of STEMI on initial ECG or initial biomarkers and/or ECG clearly consistent with ACS or NSTEMI are admitted and treated according to evidence-based guidelines. These patients are, in general, not the subjects of this document.
2. Table 1 evaluates the role of imaging in the process of the initial workup, with two common scenarios that include patients for whom ECG is diagnostic for STEMI and patients for whom an alternative, noncardiac diagnosis is likely.
3. After the initial evaluation, it is assumed that the physician will be able to clinically risk-stratify the majority of those remaining patients into one of the three suspected diagnoses of concern: ACS (section 2), PE (section 3), and AAS (section 4). Section 5 includes the minority of patients for whom a leading diagnosis is not possible. Sections 2 through 5 assume that the initial workup and ancillary testing, including cardiac and/or pulmonary biomarkers, are completed (Fig. 1).
4. Some patients who enter the clinical scenarios and undergo imaging studies will have inconclusive data to confirm or exclude a leading diagnosis after imaging. Although ratings for sections 2 through 5 may have more than one imaging study that may be considered appropriate, this document does not specifically

Table 1. Imaging of Patients for Whom the Initial Workup Is Diagnostic for STEMI or for Whom a Noncardiac Diagnosis Is Likely

Indication	Chest Radiography	Echocardiography Rest	CMR Rest	SPECT Rest	CCTA	CCath
1. Diagnostic ECG for STEMI	M	R	R	R	R	A
2. Initial history/physical examination and/or chest radiography identifies a likely noncardiac diagnosis (eg, pneumothorax, costochondritis, lesion in the esophagus)		R	R	R	R	R

Appropriate use key: A = appropriate; M = may be appropriate with rating panel consensus; R = rarely appropriate.
CCath = catheter-based coronary angiography; CCTA = coronary CT angiography; CMR = cardiovascular MR; ECG = electrocardiogram; SPECT = single-photon emission computed tomography; STEMI = ST-segment elevation myocardial infarction.

address the appropriate use of a second imaging study. The writing group acknowledges that although such patients can present a diagnostic dilemma, there are limited or no data on which to establish appropriate use criteria for the second study, particularly because findings from the first study may influence the best choice for subsequent imaging.

5. One-third of patients with confirmed acute myocardial infarction (AMI) will not have typical CP; section 2 includes those patients.
6. Imaging in the ED alone, or during evaluation in an observation unit, is considered in this document. Some patients may be candidates for outpatient referrals for follow-up imaging in lower intensity settings. The clinical scenarios in this document in general do not cover these referrals, nor does this document include imaging for patients who do not present to the ED.
7. Miniaturization of ultrasound technology has enabled the use of focused cardiac ultrasound (FOCUS), or bedside ultrasonography performed by the emergency medicine physician, using highly portable equipment that lends itself well to use in an ED setting when a rapid evaluation is required. The writing panel gave specific consideration to FOCUS as an expedited method for bedside diagnoses [7]. FOCUS is recognized as a universal part of emergency medicine training and practice. It is valuable in selected patients considered in this document, in particular those who present with CP or shortness of breath. Although it can assess left and right ventricular dysfunction, determine volume status, evaluate the fluid status of the lungs, and exclude some items in the initial differential diagnosis, its main utility for patients covered by the current guidelines is to detect pericardial fluid in patients with suspected cardiac tamponade [8].

With respect to ACS, although FOCUS can accurately estimate ejection fraction with good interrater reliability, FOCUS alone is not useful in ruling in or out an ACS. Echocardiographers have found that the absence of regional wall motion abnormalities has a negative predictive value (NPV) of 82% to 98% for AMI [9-12]. One study reported that sensitivity among patients with NSTEMI was only 86% [10]. Thus, like echocardiography, FOCUS is not considered sufficient to allow safe discharge from the ED. Similarly, FOCUS should not be used alone as the basis for decisions about the disposition of patients with possible ischemic CP. With respect to acute PE, a right ventricle larger in size than the left ventricle and paradoxical septal motion can suggest PE, but this observation on FOCUS should not preclude additional imaging. With respect to acute syndromes of the aorta, other than detecting tamponade, FOCUS is unlikely to provide diagnostic help in patients with suspected aortic dissection.

Although appropriate for patients who present to emergency medicine physicians with CP, FOCUS was not considered by the rating panel because it is inherently the initial examination performed by emergency medicine physicians, and subsequent imaging as noted in this document is also appropriate. FOCUS is indicated for the proper, rapid identification and exclusion of key cardiovascular diagnoses as indicated by existing guidelines [7].

Testing Considerations

1. This report considers exercise treadmill testing without imaging and stress testing with imaging, including the following: echocardiography, cardiovascular MR (CMR), and nuclear imaging, including single-photon emission computed tomography (SPECT). This report considers CT for the coronary arteries (coronary CT

angiography [CCTA]), for the pulmonary arteries (CT pulmonary angiography [CTPA]), and for the aorta (CT aortography [CTAo]). The report also considers CT scans tailored to identify all three diagnoses, or "triple-rule-out" (TRO) CT. This report considers invasive diagnostic catheterization that can be tailored to evaluate patients with clinically suspected ACS (CCath), PE (PCath), or AAS (catheter-based aortography [AoCath]). Although invasive catheterization can be coupled with an intervention, for the purposes of this document, *catheterization* refers only to the diagnostic portion of an overall procedure.

2. Although ratings for TRO studies (Table 5) include specific scenarios, it is acknowledged that more generally, no single test provides optimal performance for all three diagnoses (ACS, PE, and AAS).
3. All tests considered in this document have multiple capabilities, both as stand-alone technologies and for use in combination during the evaluation of individual patients. This document is not intended to describe imaging technologies; descriptions are intended to reflect the capabilities of modern imaging for emergency medicine patients.
4. The quality of the imaging data in clinical use will be reflective of the quality of the imaging data demonstrated in representative clinical trials. The quality of imaging data is a result of many steps, including data acquisition, processing, interpretation, and reporting.
5. Improvements in the analytic performance of cardiac troponin (cTn) assays have resulted in improved sensitivity and precision, resulting in the ability to measure 10-fold lower concentrations of cTn with high precision. These "high-sensitivity" cTn assays, defined as those that can measure cTn in at least 50% of healthy individuals, are not currently available in the United States, although they are already in clinical use throughout most of the world [13]. The increased sensitivity of newer cTn assays allows potentially more rapid diagnosis of patients with myocardial infarction (MI), particularly early after symptom onset, compared with contemporary assays currently in wide use. However, the higher sensitivity may lead to the detection of cTn in a substantial proportion of patients who do not have ACS but have other underlying cardiovascular diseases, such as heart failure [14]. Given the absence of widespread availability in the United States at the time of development of this document, recommendations contained herein regarding the use of troponins in the evaluation pathway of patients will generally reflect data from currently available assays [13,14]. However, as literature on the use of this type of testing is emerging, this document includes one clinical scenario that incorporates high-sensitivity troponin testing, scenario 6 in Table 2.1. Several studies have shown that patients with Thrombolysis in Myocardial Infarction (TIMI) risk scores of 0 and negative results for high-sensitivity troponin at presentation or presentation after 2 hours are at very low risk for ACS [15].

Table 2.1. Suspected Non–ST-Segment Elevation ACS: Early Assessment Pathway Based on Initial ECG, Biomarker Analysis, and Symptoms

Indication	Echocardiography Rest	CMR Rest	SPECT Rest	CCTA	CCath
Positive initial diagnosis of NSTEMI/ACS					
3. Initial ECG and/or biomarker analysis unequivocally positive for ischemia	R	R	R	R	A
Equivocal initial diagnosis of NSTEMI/ACS					
4. Equivocal initial troponin or single troponin elevation without additional evidence of ACS	M*	M*	A	A	R
5. Ischemic symptoms resolved hours before testing	R	M	M*	A	R
Low/intermediate likelihood initial diagnosis of NSTEMI/ACS					
6. TIMI risk score = 0, early hsTrop negative	R	R	R	A	R
7. Normal or nonischemic on initial ECG, normal initial troponin	R	R	M*	A	R

Appropriate use key: A = appropriate; M = may be appropriate with rating panel consensus; M* = may be appropriate as determined by lack of consensus by rating panel; R = rarely appropriate.

ACS = acute coronary syndrome; CCath = catheter-based coronary angiography; CCTA = coronary CT angiography; CMR = cardiovascular MR; ECG = electrocardiography; hsTrop = high-sensitivity troponin T; NSTEMI = non–ST-segment elevation myocardial infarction; SPECT = single-photon emission computed tomography; TIMI = Thrombolysis in Myocardial Infarction.

Comorbidities and Contraindications

Patients under consideration for rating among imaging tests do not have specific comorbidities or contraindications as noted below.

1. Unless otherwise stated, the following absolute or relative contraindications that would preclude certain types of imaging are assumed not to be present: claustrophobia, pregnancy, iodine allergy, renal dysfunction, and high resting heart rate.
2. Imaging studies that deliver ionizing radiation are, in general, relatively contraindicated during pregnancy.
3. Gadolinium-enhanced MRI is, in general, not performed in patients who are pregnant.

Availability and Expertise

1. Geographic or regional variability: issues of local availability and of skill in conducting each potential imaging study are not considered by the rating panel. Specifically, it is assumed that credentialed laboratories staffed by skilled imagers are locally available.
2. Radiotracers for nuclear imaging studies and interpreting personnel may not be available at all hours for testing, although some centers with significant off-hours volume have set up mechanisms for 24/7 testing.
3. Although the technology and expertise are generally available on an institutional basis, a qualified technologist (eg, a sonographer) may not be readily available to an ED, and it may be less likely that a reader is immediately available for studies performed after hours.
4. CCTA using 64-channel or greater cardiac CT systems [16] is now available for many emergency medicine services. Although CT scanners and expertise are generally available on an institutional basis and often include 24/7 service to the ED for CTPA and CTAo, specific capabilities for CCTA may not be readily available to the ED, especially for studies performed after hours.

Assessing the Risk for ACS in Patients With Suspected ACS

In many studies cited in this document and throughout section 2, reference is made to "low", "intermediate," or "high" risk. Although the term *risk* is used, the term refers to the likelihood that an ACS is present given a certain set of clinical findings (or alternatively risk for short-term ACS "events") [17]. For patients with suspected ACS, determination of likelihood of disease on the basis of any of the traditional methods such as those recommended by the American Heart Association scientific statement can help direct further testing and imaging in this group.

From the literature, there are no widely agreed-upon, post hoc, numerical thresholds that distinguish these categories, as there are for categories of risk for coronary heart disease using the Framingham risk score, for instance. The Rule-Out Myocardial Infarction/Ischemia Using Computer Assisted Tomography trials aimed to enroll patients with suspected ACS at "low to intermediate" risk [18,19]. The prevalence of a final diagnosis of ACS among the enrolled population was approximately 8%, and this was considered an intermediate-risk population. In a study of 2,271 patients presenting with CP to EDs, initial clinical criteria were able to identify what was termed a low-risk group, with a 30-day major cardiovascular event rate (death, MI, stroke, or revascularization) of 2.5% [20].

Clinical risk assessment involves evaluation of symptoms, initial ECG, and initial biomarkers [21]. Several scoring systems have been developed and validated in this population to various degrees, including the Agency for Health Care Policy and Research (now the Agency for Healthcare Research and Quality) CP score [20] and the TIMI score [22,23]. For the purpose of this document, reference is made to specific scoring systems in clinical scenarios on the basis of published literature that would inform ratings of imaging tests. Regarding these scoring tools, it is important to note that initial validation often occurs in a population of patients from clinical trials for which the diagnosis of ACS is definitive. Whether these tools all translate into the lower risk population of ED patients with suspected ACS is not always as yet well validated [22].

SECTION 1: IMAGING OF PATIENTS FOR WHOM THE INITIAL WORKUP IS DIAGNOSTIC FOR STEMI OR FOR WHOM A NONCARDIAC DIAGNOSIS IS LIKELY

Clinical and Imaging Rationale

Much of the initial triaging of patients presenting with CP comes from defining the clinical presentation as assessed by the history and physical examination and initial ECG. Patients not easily placed into one of these scenarios from additional information and/or risks are considered in subsequent sections and tables.

Description of Clinical Scenarios

Clinical Scenario 1: Diagnostic Electrocardiogram for STEMI. In patients for whom ECG shows STEMI, CCath has been shown to be beneficial when delivered rapidly [24]. Portable chest radiography has been studied for limited use in this setting of suspected ACS [21], on the basis of the individual patient care environment, and

found to be of low yield. Although no study should delay the "door-to-balloon" time, unless a potential contraindication, such as aortic dissection, is suspected [25], portable chest radiography may be appropriate because it can exclude a secondary pathology (eg, pneumonia, pneumothorax, abnormal line placement) important to communicate with the catheterization staff.

Clinical Scenario 2: Initial History or Physical Examination and/or Chest Radiography Identifies a Likely Noncardiac Diagnosis. Diagnoses with high short-term mortality risk, such as ACS, PE, and AAS, may be ruled out at this stage on the basis of patient history, physician examination, and chest radiography. In this scenario, all imaging modalities under consideration are considered rarely appropriate.

SECTION 2: IMAGING OF PATIENTS WITH CP AND A LEADING DIAGNOSIS OF NON–ST-SEGMENT ELEVATION ACS

Clinical Rationale

CP and other conditions consistent with possible myocardial ischemia (or rule-out ACS) are among the most common ED presentations. CP represents a high-volume, potentially high-risk scenario in which the majority of patients are actually at low risk for ACS. Over the past 20 years, there has been substantial progress on improving methods that can accurately and rapidly identify the relatively few high-risk ACS patients among the large presenting volume of low-risk patients.

Obtaining a history is of critical importance in the initial evaluation of ED CP patients. Although often not sufficient to exclude myocardial ischemia in a particular patient, a history allows risk stratification into high-, intermediate-, and low-risk groups in which additional diagnostic testing, such as cardiac marker analysis and imaging techniques, can be more appropriately targeted. The characteristics of the pain and the presence of associated symptoms are useful for risk stratification [17,20]. Although risk factors for coronary disease are often assessed, they have limited value for identifying patients with MI because they are frequently outweighed by the CP characteristics, history of coronary disease, and findings on ECG [26].

A number of risk stratification models that combine clinical and electrocardiographic findings have been shown to predict short-term outcomes in patients with symptoms suggestive of myocardial ischemia [17,20,21]. These algorithms have similar sensitivity but significantly higher specificity than physicians' evaluations, potentially identifying lower risk patients who could be evaluated in lower intensity settings or discharged home. Despite these potential advantages, few algorithms have been incorporated into standard practice. One risk stratification algorithm is the TIMI risk score, which is composed of seven variables of equal weight. Although the TIMI score was initially derived and validated in a clinical trial population with definite ACS, subsequent studies in lower risk ED patients have also shown that it can assist in risk stratification, although to a lesser degree [27]. Recent studies have suggested that when contemporary troponin testing at 0 and 2 hours is combined with a TIMI risk score of 0 (adapted to include only the initial troponin value), occurring in approximately 10% of all ED CP patients, such a strategy may identify patients at very low risk [28,29].

ECG is the initial test in patients with CP or suspected ACS because it can be performed rapidly, is inexpensive, and can readily identify STEMI patients who will benefit from early reperfusion. The presence of ischemic changes, including ST-segment depression [21], identifies a high-risk patient group, while conversely, completely normal findings on ECG identify a group of patients at relatively lower risk for MI and ischemic complications, the majority of whom can be evaluated in lower intensity settings, such as observation units. The presence of normal electrocardiographic findings on initial presentation in those patients eventually ruling in for MI identifies a group at lower risk for mortality and unfavorable outcomes compared with those with ischemic changes, but the absolute event rates are not low enough to drive discharge triage decisions [17,30].

In all patients with suspected ACS, the early determination of biomarker (troponin) status is very important because many diagnostic and treatment decisions will be, in part, determined by troponin positivity or negativity. Although the previous description of the acquisition of information implies serial determination of history, physical examination, chest radiography, and biomarker analysis, in practice, many of these are done in parallel.

The presence of clear ischemic changes on initial ECG, either ST-segment elevation or depression, identifies an ACS patient in whom admission and rapid management are mandatory; in this case, the initial triage and treatment strategy is guideline driven [24]. However, diagnostic initial electrocardiographic findings are present in only a minority of patients. The remaining clinically stable patients have possible myocardial ischemia and suspected NSTEMI ACS. It is this group in which subsequent risk stratification evaluation and potential use of additional diagnostic tools such as imaging modalities are needed.

Because of the limitations of historical, physical examination, and electrocardiographic data, many of these patients are admitted or placed into observation units, though most are later determined to have nonischemic causes of their symptoms. Despite this low threshold for admission, some patients with AMI are inadvertently discharged [31], with subsequent morbidity and mortality 2 to 3 times that of those AMI patients who are admitted, on the basis of older studies [32]. Although some of these inadvertently discharged patients may have infarctions, it is likely that some have unstable angina that may subsequently evolve into MI, underscoring the importance of identifying these patients. The findings that 2% of patients with AMI are inadvertently discharged from EDs are based on studies that used less sensitive troponin assays. In current practice, with more sensitive troponin assays, this number is likely to be smaller. In addition, patients with unstable angina who were troponin negative with old assays might be identified by elevated troponin using contemporary assays.

Thus, if the history, initial electrocardiographic results, and troponin biomarkers with or without the use of risk scores are diagnostic for ACS, a triage decision to admit and treat should be made and an evidence-based treatment strategy initiated [21]. If the initial data are sufficient to confirm a diagnosis that is not ACS (such as pericarditis, a diagnosis not considered in this document), direct early discharge from the ED with appropriate follow-up may be warranted. However, after this initial information, uncertainty often continues to exist regarding an ACS diagnosis. It is in this population—patients with suspected NSTEMI or ACS—that further workup and risk stratification are warranted. In this document, we consider two pathways of further workup: an early assessment pathway and an observational pathway.

Early Assessment Pathway and Observational Pathway

For the purpose of this document, to frame the appropriate use of cardiovascular imaging techniques within the clinical context of their use in this setting, we adopt two pathways for the evaluation of ED patients with suspected ACS. The first evaluation pathway is referred to as the early assessment pathway. With this strategy, imaging may be used early in the evaluation process, with the goal of ruling in or ruling out ACS or MI through the identification of wall motion abnormalities, perfusion defects, or obstructive CAD without the need to wait for serial biomarker analysis. Imaging tests in this pathway do not require stress physiology but rather image anatomy (CCTA), function (echocardiography, CMR), or perfusion (resting SPECT, CMR) at rest. Stress examinations were not considered by the rating panel in the early assessment pathway. Patients in the ED with CP syndromes and history of MI or revascularization (ie, known CAD) may have evidence of resting wall motion or resting perfusion abnormalities, as well as abnormal coronary anatomy by definition, which would confound the evaluation of a new symptom complex suspicious for ACS by these testing modalities. Clinical scenarios 3 to 7 considered in the early assessment pathway appear in Table 2.1.

The second pathway is referred to as the observational pathway, and it involves serial analysis of cardiac biomarkers to rule in or out myocardial necrosis and MI. Testing in this pathway may involve stress physiologic testing, and thus stress examinations were considered by the rating panel in clinical scenarios 8 to 10. Assessments at rest are generally less appropriate for patients managed in the observational pathway. Patients in the ED with CP syndromes and history of MI or revascularization (ie, known CAD) may have evidence of resting and/or stress wall motion or perfusion abnormalities, as well as abnormal coronary anatomy, which, as noted previously, would complicate the evaluation of a new symptom complex suspicious for ACS, although stress testing would identify currently existing ischemia. Ratings for the observational pathway appear in Table 2.2.

Description of Clinical Scenarios in the Early Assessment Pathway

The early assessment pathway uses tests to inform the ED physician regarding ACS for purposes of triage decision making. Some tests provide information that may be generally useful for management purposes (eg, assessment of ejection fraction), but these are not directly useful for the diagnostic purpose of identifying a patient with an ACS. Patients considered in this pathway may or may not have ongoing symptoms. Some physiologic testing, such as analysis of wall motion abnormalities, is, importantly, influenced by whether ischemia is ongoing, whereas other modalities, such as coronary CT angiographic assessment of coronary anatomy, are not. Studies have suggested that perfusion imaging test results may remain positive for a resting perfusion abnormality several hours after symptom resolution [33].

Clinical Scenario 3: Initial ECG and/or Biomarker Analysis Unequivocally Positive for Ischemia. CCath is beneficial in patients in whom initial ECG and/or biomarker analysis is unequivocally positive for ischemia, as revascularization may be associated with more favorable outcomes [21,34-36]. Thus, CCath is considered

Table 2.2. Suspected Non–ST-Segment Elevation ACS: Observational Pathway—After Assessment of Serial Cardiac Troponin

Indication	Exercise ECG	Echocardiography Rest	Echocardiography Stress/Rest	CMR Rest	CMR Stress/Rest	SPECT/PET Rest	SPECT/PET Stress/Rest	CCTA	CCath
8. Diagnosis unequivocally positive for NSTEMI/ACS	M*	M*	M*	M*	M*	M*	M*	M*	A
Serial troponins or ECG not positive for NSTEMI/ACS									
9. Serial ECG and troponins negative for NSTEMI/ACS	A	R	A	R	A	R	A	A	R
10. Serial ECG or troponins borderline for NSTEMI/ACS	M*	M*	A	R	A	R	A	A	M*

Appropriate use key: A = appropriate; M* = may be appropriate as determined by lack of consensus by rating panel; R = rarely appropriate.
ACS = acute coronary syndrome; CCath = catheter-based coronary angiography; CCTA = coronary CT angiography; CMR = cardiovascular MR; ECG = electrocardiography; NSTEMI = non–ST-segment elevation myocardial infarction; SPECT = single-photon emission computed tomography.

appropriate, whereas all other rest imaging modalities are considered rarely appropriate.

Clinical Scenario 4: Equivocal Initial Troponin or Single Troponin Elevation Without Additional Evidence of ACS. In such patients, the diagnosis of ACS remains uncertain. Both rest SPECT and CCTA are appropriate and have been evaluated in randomized trials [19,37,38]. Rest echocardiography and rest CMR may be appropriate, and CCath is rarely appropriate.

Clinical Scenario 5: Ischemic Symptoms Resolved Hours Before Testing. Assessment for wall motion abnormalities by echocardiography or other testing is dependent on the presence of ongoing ischemia. Thus, if symptoms have resolved many hours before assessment, such tests will be insensitive for the diagnosis of ACS. Resting perfusion abnormalities may persist for several hours after ischemia resolves, although it is unknown at what time point sensitivity decreases [33]. Clinical trials using rest perfusion imaging to distinguish ACS versus non-ACS CP and improve triage have allowed enrollment of patients up to 3 hours after symptom resolution [37,39]. In this setting, CCTA is considered appropriate, whereas rest CMR and rest SPECT may be appropriate. Rest echocardiography and CCath are rarely appropriate.

Clinical Scenario 6: TIMI Risk Score = 0, Early hsTrop Negative. As noted under "Testing Considerations," although high-sensitivity troponins [13] are, at the time of rating, not approved for use in the United States, they are increasingly used outside the United States. Moreover, an emerging body of literature suggests that incorporating these biomarkers can identify a group of patients already at very low clinical risk whose ACS prevalence and event rate are very low. Conceptually, in such a setting, no further testing may be considered, as the yield would likely be low. The rating panel has considered CCTA appropriate in this setting, as some of the extant trials of CCTA versus standard-of-care evaluation have generally included relatively low-risk populations. In one study, there were no cardiac deaths, and only 1% of patients had MIs within 30 days [38]. In this population, CCTA was rated as appropriate, and all other imaging modalities were rated as rarely appropriate.

Clinical Scenario 7: Normal or Nonischemic Initial ECG, Normal Initial Troponin. This scenario refers to patients in whom the initial electrocardiogram is not diagnostic for ischemic changes and the initial troponin result (not high-sensitivity assay) is also not diagnostic for NSTEMI or ACS. This scenario represents a large proportion of patients seen in this setting, in whom there generally remains uncertainty about the diagnosis after initial ECG and biomarker analysis. Such patients have been considered at low to intermediate risk for ACS. CCTA is appropriate, and rest SPECT may be appropriate, with data based on randomized trials [19,37,38]. Rest echocardiography, rest CMR, and CCath are rarely appropriate.

Description of Imaging Modalities

Resting SPECT Myocardial Perfusion Imaging. A number of studies have examined the use of resting myocardial perfusion imaging in the setting of suspected

ACS [37,39-43]. Several reports have concluded that the use of resting SPECT in the ED in such patients is associated with shorter length of stay and lower costs and can reduce unnecessary hospital admissions [37,39,43,44]. A large body of observational literature established a high NPV for a normal resting perfusion image to rule out an MI or short-term cardiac events [45]. Two randomized trials have been reported. In a smaller trial, in which management after imaging was protocol directed, a strategy incorporating resting SPECT was associated with shorter length of stay and lower cost, with similar safety [44]. In a much larger trial, in which management after imaging was left to the discretion of the ED physician ("effectiveness," ie, how a test performs in real life to influence decisions), the incorporation of resting SPECT resulted in fewer unnecessary admissions, with an unnecessary admission defined as those patients admitted from the ED whose final diagnoses were not ACS [37]. There was, however, no outcome difference 30 days after ED presentation compared with those who underwent standard ED care. In this latter trial, patients were enrolled if they were within 3 hours of symptom resolution. Resting SPECT is limited in distinguishing chronic from acute ischemia.

Echocardiography. Resting 2-D echocardiography is rapid and noninvasive. Two-dimensional echocardiography provides information about myocardial ischemia by evaluating segmental wall motion and ejection fraction [9,46], but the positive predictive value (PPV) is not high [9,47]. It may detect other possible pathologies that may be associated with CP, such as valvular disease, pericarditis, and cardiomyopathy. Like resting SPECT, 2-D echocardiography is limited in distinguishing chronic from acute ischemia. In addition, resting echocardiography cannot determine the presence of an underlying high-grade coronary stenosis in the absence of impaired myocardial perfusion at rest that results in wall motion abnormalities. Thus, most studies have shown that resting echocardiography to detect acute ischemia is useful only if there are ongoing symptoms at the time of imaging.

When contrast agents are used to assess myocardial perfusion, echocardiography is reported to achieve higher sensitivity than wall motion analysis alone with both rest and stress [48-52]. Although not currently used in routine practice, these methods have moved from research-only tools to clinical availability in some centers of expertise.

CCTA. Coronary calcium scoring was not considered by the rating panel because there are few data on coronary calcium scoring using multidetector CT hardware in patients who present to the ED in whom ACS is the leading differential diagnosis. Moreover, in patients at intermediate to high risk for CAD, a calcium score of 0 is often associated with myocardial ischemia on provocative testing [53]. For patients with coronary calcium detected by CT, the examination would require additional imaging, such as CCTA, that interrogates the coronary lumen.

For patients with CP in the ED, using stenosis detection as a surrogate for ACS and ACS events, CCTA has reported high sensitivity (86%-100%) and NPV (93%-100%), although the PPV using invasive coronary angiography as the reference standard is still limited (50%-90%) [54-58]. CCTA has been used to evaluate not only the severity of stenosis but also plaque characteristics associated with vulnerability and risk for events [18]. However, CCTA is limited in patients with extensive coronary calcium, which generally increases with the risk for ACS as well as with age. Initial reports suggested that a CT-based strategy decreases time to diagnosis (compared with SPECT), length of hospital stay, unnecessary admissions, total costs, and repeat evaluations for recurrent CP, while allowing safe discharge after a negative evaluation [18,56,59,60]. Two large randomized strategy-controlled trials have evaluated the early use of CCTA (ie, before the completion of serial troponin assessments) in patients with low to intermediate likelihood for ACS in the ED setting. Litt et al [38] compared a CCTA pathway with traditional care for safety, defined as absence of MI or cardiac death within 30 days of presentation. Both pathways were found to have a <1% rate of major adverse cardiovascular events (MACEs). Secondary end point analysis demonstrated earlier and more direct ED discharges in the patient group randomized to undergo CCTA as part of their evaluation strategy. Hoffmann et al [19] conducted a randomized controlled trial of 1,000 patients seen at nine US centers, with patients randomized to an early CCTA pathway or standard evaluation. They found as the primary end point that length of stay was shorter among patients randomized to a strategy incorporating early CCTA compared with a standard evaluation strategy. There were no undetected cases of ACS and no significant differences in MACEs. Secondary end points, including time to diagnosis and direct ED discharges, were also favorably affected by CCTA. In a subgroup of patients with full cost information, ED costs were lower in the CCTA strategy group, though overall costs at 30 days were similar.

Radiation exposure was higher in the CCTA group, and there was more downstream testing in the CCTA group. Also, patients in the CCTA arm underwent more revascularization procedures, some of which may have occurred in the absence of a stress test to judge ischemic burden of a lesion. In both of these trials, MACE rates for the CCTA arm and standard of care were less than 1%. The results of the studies of the use of CCTA in the ED have undergone meta-analysis [61] confirming the reduction in length of stay and cost but with slightly increased resulting use of invasive angiography and revascularization downstream.

CMR. Rest CMR can image regional and global ventricular function and myocardial perfusion and identify scar. When it has been used in ED patients, generally in observational studies with modest numbers of patients, contrast-enhanced perfusion, delayed enhancement, and cine evaluation of wall motion have been shown to have sensitivity of 70% to 85% to detect ischemic conditions [62-64]. Normal results on CMR have been associated with a low-risk prognosis. Imaging coronary anatomy has not been done routinely in these studies and is not widely performed; most of the information in the literature involves analysis of perfusion, scar, and function.

CCath. Although catheter angiography remains the clinical standard for the diagnosis of CAD, it has been found to be more limited in value for the initial evaluation of patients at less than high risk for ACS [21]. It can be used to confirm ACS in patients with positive screening results and interventions in the case of perfusion or wall motion abnormalities suggestive of hemodynamically significant stenosis or occlusion or in patients for whom noninvasive testing cannot provide a definitive diagnosis.

Description of Clinical Scenarios in the Observational Pathway

Although the evolution of imaging modalities has enabled the potential use of imaging tests early in the evaluation process, the majority of patients currently seen for assessment of ED CP syndromes—and who do not have initially diagnostic electrocardiographic or biomarker evidence of NSTEMI or ACS—are evaluated in the observational pathway. By definition, patients in this pathway have undergone initial ECG and biomarker testing that has not led to a clear diagnosis of ACS, but ACS is still a consideration. Thus, serial ECG and troponin biomarker analysis are used to rule out NSTEMI or ACS (or rule it in), and if ruled out, stress testing with or without imaging may be performed to assess for the potential of induction of ischemia. Anatomic testing for CAD with CCTA may also be appropriate in this pathway. The protocol of serial biomarkers followed by more definitive testing in the observational pathway has been evaluated in nonrandomized studies [65] as well as in randomized clinical trials [66,67].

The rating group considered two different groups of patients. The first group comprised patients for whom the diagnosis was unequivocally positive for NSTEMI or ACS from the analysis of serial biomarkers and ECG. The second group of patients comprised those for whom serial troponin and ECG were not positive for NSTEMI or ACS.

By definition of being in the observation pathway and having undergone serial ECG and biomarker assessments, these patients would be at least 9 to 24 hours out from ED presentation. They may still be in the ED, but by the nature of the observational pathway and practices at different hospitals, they also may have been moved to CP evaluation units or telemetry floors.

The intention for this indication was that such patients are clinically stable, having likely received initial guideline-directed medical therapy for possible ACS or NSTEMI. These patients are considered similar to those enrolled in ACS clinical trials examining strategies of routine invasive versus selective invasive ("ischemia-guided") strategies, such as TACTICS—TIMI 18 (Treat Angina With Aggrastat and Determine the Cost of Therapy With an Invasive or Conservative Strategy—TIMI 18) or ICTUS (Invasive Versus Conservative Treatment in Unstable Coronary Syndromes). Regarding the specifics of the stress testing choices, a wide range of stress testing modalities and timing of stress testing has been reported among numerous randomized trials [68-73]. Thus, we have used the word *stress* generically so as not to create numerous additional categories of exercise (maximal or submaximal) or pharmacologic stress for each modality, and we could not specify optimal timing of testing. It should be assumed that the type of stress used and the timing of testing would not be clinically contraindicated in the specific situation.

Clinical Scenario 8: Any Electrocardiogram and/or Serial Troponins Unequivocally Positive for NSTEMI or ACS. If serial troponins demonstrate positive evidence of myocardial necrosis in the setting of ischemic symptoms or electrocardiographic changes, the diagnosis of NSTEMI or ACS is made, and management can follow existing guidelines [21]. Often this will involve a strategy incorporating catheter angiography and potential

revascularization, as numerous randomized trials have shown that patients with biomarker-positive NSTEMI or ACS generally have more favorable outcomes when managed with an "invasive strategy" consisting of invasive angiography followed by revascularization. Thus, CCath is considered appropriate in this scenario. However, for NSTEMI patients in the presence of certain comorbidities, particularly abnormal renal function, the outcome benefit of a direct invasive angiography and revascularization strategy compared with a "conservative" strategy narrows [74]. In clinical trials of patients with ACS that have randomized patients to either an "invasive" or a "conservative" initial strategy (now also referred to in guidelines as an "ischemia-guided" strategy), the conservative strategy usually consists of stress testing with imaging, often stress SPECT, to assess the presence and extent of ischemia [68,69]. Although many, but not all, such trials showed an outcome advantage for the routine invasive strategy, it is also recognized that in real life, many patients covered by this indication may have comorbidities that might have excluded them from the randomized control trials, such as renal dysfunction mentioned previously, or may be elderly or frail, or simply would prefer a potentially less aggressive management direction. In these situations, clinical consideration could be given to an ischemia-guided strategy, using stress testing with or without imaging, to identify those patients with very extensive ischemia who might have a larger benefit from revascularization, while others could be treated medically. Because these scenarios generally fall outside of the clinical trials, the rating panel did not come to consensus on the alternative strategies besides invasive catheterization, and thus all are rated as "may be appropriate."

Clinical Scenario 9: Serial ECG and Troponins Negative for NSTEMI or ACS. Patients in this scenario have no evidence of myocardial necrosis. The diagnosis of NSTEMI is ruled out, and the remaining diagnostic considerations include the possibility of troponin-negative unstable angina and CP not due to an ACS. It is in this situation that stress testing to assess for the induction of inducible ischemia is useful (all rest and stress studies are appropriate), as is imaging for anatomic CAD (CCTA is appropriate). Exercise electrocardiographic testing is also appropriate if it is anticipated that the patient can attain an adequate level of exercise stress and if the electrocardiogram is interpretable for stress-induced ischemia. As these tend to be low-risk patients, particularly in the setting of low pretest probability of ACS [75,76], outpatient testing can be considered.

Clinical Scenario 10: Serial ECG or Troponins Borderline for NSTEMI or ACS. Because the assays for troponin have varying precision, at times, results are reported that are detectable but not clearly elevated in a manner consistent with NSTEMI [77]. In such a scenario, NSTEMI has neither been completely ruled in nor ruled out, and further testing is indicated. In this situation, stress testing for inducible ischemia or anatomic testing for the presence of CAD are appropriate, with all rest and stress studies as well as CCTA being considered appropriate.

Description of Diagnostic Studies

Exercise ECG Without Imaging. For low-risk patients with interpretable electrocardiograms, stress ECG without imaging has been reported to be associated with a decrease in unnecessary admissions [21,76,78,79]. The excellent NPV of 98% to 99% has been confirmed, although the PPV is limited for obstructive CAD [80-87]. The lower PPV may be due to the lower risk population being studied. Use of the Duke treadmill score reduces the false-positive rate of exercise electrocardiographic testing rather than relying on ST-segment changes alone [88-91]. Patients with normal stress test results at a high level of exertion have an excellent prognosis and can be safely discharged [92]. Thus, for patients with normal results on ECG and the ability to exercise adequately, stress tests without imaging can be useful [17]. For patients with potentially uninterpretable stress electrocardiograms (left ventricular hypertrophy with secondary ST-T changes, paced rhythms, left bundle branch block) or those who do not achieve an adequate stress heart rate, stress ECG will not be useful.

Stress Echocardiography. Stress echocardiography may involve exercise or pharmacologic (dobutamine or atropine) stress, and it increases myocardial oxygen consumption such that the presence of a flow-limiting lesion will impair perfusion and create segmental systolic and diastolic dysfunction in the underperfused region. The presence and extent of an induced wall motion abnormality are more sensitive and specific than stress-induced electrocardiographic abnormalities alone [81,82,86] and have higher NPV for excluding obstructive CAD [93-97]. Achievement of an adequate heart rate/demand response from exercise or from dobutamine stress is important to optimize sensitivity to detect underlying CAD. Thus, if exercise or tachycardic stress is felt to be clinically contraindicated, pharmacologic vasodilator stress with myocardial perfusion imaging by SPECT or CMR would be preferable. Visualization of endocardial borders for all

myocardial segments is a prerequisite for optimal test accuracy. Stress echocardiography also detects the presence of prior infarction and provides information about cardiac hemodynamics, structure, and function.

Stress SPECT and PET. Stress myocardial perfusion imaging, with exercise or pharmacologic stress, may be used to detect the presence and extent of inducible perfusion abnormalities suggestive of ischemia, as well as the presence of prior infarction. Perfusion may be assessed with the use of widely available SPECT tracers and cameras or may be performed using PET imaging if tracers, equipment, and expertise are available. PET imaging may be useful in patients with larger body mass indexes because of its inherently better spatial resolution. Electrocardiographically gated SPECT or PET acquisition allows simultaneous evaluation of regional and global left ventricular function for this population [98,99]. NPV is also high (96%-100%). The annualized event rate after normal results on stress SPECT is low over follow-up [40,87,98-100].

Stress CMR. A small randomized trial assessed outcomes and costs in patients with suspected ACS and intermediate likelihood of CAD randomized to an observation unit strategy of serial biomarkers followed by adenosine stress CMR compared with an inpatient evaluation strategy [101]. There were no differences in missed ACS from the index visit and no differences in outcome events between the two strategies over one year [102]. Costs associated with the index visit, as well as costs out to one year of follow-up were lower with the observation unit/stress CMR strategy. These investigators reported, however, that among low-risk patients, a mandated CMR strategy incurred higher costs than a "provider-directed" imaging strategy, in which clinicians most often chose stress echocardiography [103].

SECTION 3: IMAGING OF PATIENTS WITH SUSPECTED PE

Clinical Rationale

Venous thromboembolic disease includes both PE and deep venous thrombosis (DVT). PE accounts for 100,000 to 180,000 deaths annually in the United States and afflicts millions of individuals worldwide. The 15% case fatality rate for PE exceeds the mortality rate for AMI [104,105]. PE survivors may have impaired quality of life due to chronic thromboembolic pulmonary hypertension.

PE affects patients of widely varying ages, from teenagers to the elderly. Its onset is usually unpredictable, but associated risk factors may include prolonged immobility, trauma, recent surgery, cancer, oral contraceptive use, pregnancy, and postmenopausal hormone replacement.

Clinicians must remain vigilant to detect PE because of the diverse presenting signs and symptoms. For example, PE can present like other illnesses, such as pneumonia and congestive heart failure.

ECG is insensitive for PE but may raise suspicion or help confirm the diagnosis in patients with electrocardiographic manifestations of right-heart strain. Right-heart strain, however, may not be present, is not specific, and may be observed in patients with asthma, idiopathic pulmonary hypertension, or other etiologies of cor pulmonale. Patients with massive PE may have sinus tachycardia, slight ST- and T-wave abnormalities, or even entirely normal findings on ECG [106]. Other abnormalities include incomplete or complete right bundle branch block and an S1Q3T3 complex. T-wave inversion in leads V_1 to V_4 has the greatest accuracy for identifying right ventricular dysfunction in patients with acute PE.

The results of echocardiography are normal in about half of unselected patients with acute PE [107], and thus it was not considered by the rating panel for the diagnosis of PE. However, positive findings such as elevated right ventricular systolic pressure, a dilated right ventricle, and a hypokinetic right ventricle with apical sparing [108] can raise suspicion for PE. More important, echocardiography with supporting biomarkers can identify those patients with potentially poor prognoses and thus guide management [104,109,110]. For those patients, echocardiography is an important "second" examination; the role of echocardiography for prognosis is beyond the scope of this document.

Imaging Rationale

Chest radiography is insensitive to PE and was not rated. However, radiography plays a major role in initial patient management and exclusion of competing disease conditions. Major chest x-ray abnormalities are uncommon in PE. Focal oligemia (Westermark sign) may indicate massive central embolic occlusion [111]. A peripheral wedge-shaped density above the diaphragm (Hampton hump) usually indicates pulmonary infarction [112], but this finding is uncommon. Subtle abnormalities suggestive of PE include enlargement of the descending right pulmonary artery. The vessel often tapers rapidly after the enlarged portion. For patients who are not pregnant, the following three clinical scenarios were considered by the rating panel. Two additional scenarios were considered for patients who are pregnant (Table 3).

Table 3. Suspected PE

Indication	CTPA	CompUS	VQ	PMRA	PCath
Likelihood by clinical scoring algorithm alone, patient not pregnant					
11. D-dimer negative	R	R	R	R	R
Not high likelihood by a clinical scoring algorithm					
12. D-dimer positive	A	M	A	R	R
Not high likelihood by a clinical scoring algorithm					
13. High likelihood by a clinical scoring algorithm	A	A	A	R	R
Pregnancy					
14. Patient with leg symptoms	M*	A	A	R	R
15. Patient with no leg symptoms	A	M*	A	R	R

Appropriate use key: A = appropriate; M = may be appropriate with rating panel consensus; M* = may be appropriate as determined by lack of consensus by rating panel; R = rarely appropriate.

CTPA = CT pulmonary angiography; CompUS = compression ultrasonography of the deep veins; PCath = catheter-based pulmonary angiography; PMRA = pulmonary MR angiography; VQ = ventilation-perfusion scan.

Description of Clinical Scenarios

Clinical Scenario 11: D-Dimer Negative and Not High Likelihood by a Clinical Scoring Algorithm. When the clinical likelihood of DVT and PE, on the basis of clinical probability scoring systems such as the Wells criteria [113-115] or revised Geneva score [116,117], is low and the results of plasma D-dimer assay [118] are normal, the exclusion of PE is usually straightforward and accurate [119,120]. In this scenario, all imaging modalities under consideration are considered rarely appropriate.

Clinical Scenario 12: D-Dimer Positive and Not High Likelihood by a Clinical Scoring Algorithm. CTPA has supplanted ventilation-perfusion scan (VQ) as the initial study to confirm or exclude clinically suspected PE [121-123]. Both are considered appropriate studies for this scenario. PCath, once considered the reference standard, has been shown to be less useful as the initial examination [124], although it is used in planning intervention. The rating panel did not consider the role of catheterization for the intervention itself.

Clinical Scenario 13: High Likelihood by a Clinical Scoring Algorithm. The rating panel considered high-risk patients, independent of D-dimer, as a separate scenario. The panel also considered that some patients in this group may not be hemodynamically stable. CTPA, VQ, and compression ultrasonography of the deep veins (CompUS) are all appropriate initial studies.

Description of Imaging Modalities

CTPA. Multidetector-row CT scanners rapidly image the entire chest with high spatial resolution [121-123,125,126], and extant guidelines [120,127] have demonstrated CTPA as a useful diagnostic strategy to exclude or confirm the presence of a filling defect in a patient for whom there is clinical suspicion for PE. In a meta-analysis of 3,500 patients undergoing CTPA and followed for at least three months, the overall NPV of CT was 99.4% [128]. A validated outcome strategy is D-dimer testing followed by CTPA for patients with abnormally elevated D-dimer levels. Using this strategy, only 1.5% of patients with negative findings developed DVT or PE during 3-month follow-up [129]. A systematic review of management outcome studies showed that patients with low or moderate pretest probability and normal D-dimer levels had a very low 3-month thromboembolism rate [130]. CTPA also identifies other pulmonary diseases, including pneumonia, atelectasis, pneumothorax, and pleural effusion, that might not be well visualized on chest radiography.

The latest generation scanners can image thrombus in sixth-order vessels [131]. These thrombi are so tiny that their clinical significance is uncertain [132]. The presence of right-heart strain is a poor prognostic factor for patients with PE; therefore, the interpreter should compare the size of the right ventricle with that of the left ventricle in positive cases [133], as a normal right ventricle's diameter is smaller than that of the left ventricle.

CTPA using rapid imaging protocols can include additional scanning to identify DVT in the subclavian veins and other major upper extremity veins that might contain thrombi and serve as the source of PE. Although protocols have been developed and tested for imaging the venous system in the abdomen, pelvis, thighs, and knees for pelvic vein thrombosis and proximal leg DVT [134], CT venography is not routinely used at the time of pulmonary angiography, as it increases radiation exposure and rarely changes clinical management [131,135,136]. Combined CTPA and CT venography were not considered by the rating panel.

The accuracy of CT is lower when the imaging results and clinical probability assessment are discordant, particularly

in those patients with negative results on CT but high clinical probability of PE, even though this group constituted only 3% of the PIOPED (Prospective Investigation of Pulmonary Embolism Diagnosis) II cohort [134]. This finding was similar to the initial PIOPED study, which focused on pulmonary scintigraphy [137]; therefore, clinicians should be cautious in the unusual circumstance in which imaging results are discordant with clinical likelihood of PE.

Pulmonary Scintigraphy/VQ. Nuclear lung scans use radiolabeled aggregates of albumin or microspheres that lodge in the pulmonary microvasculature. Patients with large PEs have multiple perfusion defects. If ventilation scanning is performed on a patient with PE but no intrinsic lung disease, a normal ventilation study result is expected, yielding a ventilation-perfusion mismatch. This combination of findings is interpreted as indicative of high probability for PE. The initial PIOPED study showed that, of the small minority of patients with low-probability scans but high clinical suspicion for PE, up to 40% will have PE proved by PCath [137]. PE is unlikely in patients with low-probability VQ combined with low-probability clinical assessment. Conversely, a high-probability VQ combined with a high-probability clinical assessment is highly predictive of PE. With other combinations, further evaluation is often needed.

Pulmonary MR Angiography. Although single-center studies of gadolinium-enhanced MR angiography have been promising [138-140], the PIOPED III study demonstrated a lack of sensitivity to detect PE [141].

PCath. Invasive pulmonary angiography was a former reference standard for the diagnosis of PE. It has a small but defined risk for major complications [142], and reliably identifying smaller filling defects can be difficult [124]. Although the rating of catheter angiography as part of PE treatment is beyond the scope of this document, it is required when interventions—such as suction catheter embolectomy, mechanical clot fragmentation, or catheter-directed thrombolysis—are planned.

CompUS. CompUS is appropriate to evaluate the lower extremity deep venous system in high-risk patients, particularly those with leg symptoms. Compression is used to confirm the presence or absence of DVT. However, at least half of patients with PE have no imaging evidence of DVT.

SUSPECTED PE IN PREGNANCY

Imaging Rationale

In pregnancy, D-dimer testing is of limited use to exclude PE [143]. Pregnant women with suspected PE are divided into those with DVT symptoms in the legs and those without such symptoms. Although most pregnant women with clinical suspicion do not have leg symptoms [144,145], CompUS does not deliver ionizing radiation, and when there are signs and symptoms of DVT, a positive result may eliminate the need for further testing that uses ionizing radiation [146]. Current guidelines suggest that chest radiography can be used to suggest an initial test [146], but because x-ray findings do not confirm or exclude PE, chest radiography was not considered by the rating panel.

Pulmonary MR angiography generally requires the use of gadolinium and is strongly contraindicated in pregnancy. There are emerging MR methods that do not use gadolinium, but because these are limited to specialized centers, they were not considered by the rating panel. PCath is also contraindicated because of the contrast and radiation burden.

Description of Clinical Scenarios

Clinical Scenario 14: Pregnant Patient With Leg Symptoms. For hemodynamically stable pregnant patients with suspected PE and signs and/or symptoms of DVT, CompUS is an appropriate initial study because it delivers neither ionizing radiation nor intravenous contrast material. VQ was also considered appropriate, and CTPA may be appropriate.

Clinical Scenario 15: Pregnant Patient With No Leg Symptoms. For patients with no signs and symptoms of DVT and for whom clinical suspicion warrants an imaging study, both CTPA and VQ are appropriate initial examinations. Of note, when scintigraphy is performed, lung perfusion can be done as the initial study, and if the results are normal, the ventilation portion of the examination can be averted. CompUS may be appropriate.

SECTION 4: IMAGING OF PATIENTS WITH SUSPECTED ACUTE SYNDROMES OF THE AORTA

Clinical Rationale

Aortic dissection is a common pathology among the AAS; the other diagnoses include penetrating ulcer, intramural hematoma, and unstable thoracic aortic aneurysm. These diagnoses are challenging, in part because patients may have no apparent risk factors for the condition; another reason is that the clinical presentation is quite variable and therefore not readily recognized. However, because these diagnoses, including acute aortic dissection, are life threatening, with an early mortality rate of as high as 1% to 2% per hour, a high suspicion for the diagnosis and prompt

Table 4. Suspected AAS

Indication	CTAo	MRAo	TTE	TEE	AoCath
Hemodynamically unstable patient					
16. Prior or no prior aorta intervention	A	M*	M*	M*	M*
Hemodynamically stable patient					
17. No prior aorta intervention	A	A	M	A	R
18. Prior aorta intervention	A	A	M	M*	M*

Appropriate use key: A = appropriate; M = may be appropriate with rating panel consensus; M* = may be appropriate as determined by lack of consensus by rating panel; R = rarely appropriate.

AoCath = catheter-based aortography; CTAo = CT aortography; MRAo = MR aortography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

diagnostic evaluation are keys to a timely diagnosis and a favorable outcome. In the acute setting, chest radiography is commonly performed, primarily to identify other causes of a patient's symptoms but also to screen for a dilated aorta or evidence suggestive of bleeding. Normal results on chest radiography do not exclude an AAS [147], and radiography was not considered by the rating panel.

The presence of any of the known risk factors for aortic dissection in a patient with acute pain should heighten suspicion of aortic dissection and other AAS such as intramural hematoma [148]; these risk factors include a known thoracic aortic aneurysm, connective tissue disorders that result in aortic medial degeneration (eg, Marfan syndrome, vascular Ehlers-Danlos syndrome, Loeys-Dietz syndrome), a bicuspid aortic valve, family history of thoracic aortic aneurysms or dissection, advanced age, male gender, and a long-standing history of hypertension. However, the absence of these risk factors should not deter the ED physician from pursuing the diagnosis.

Unlike the pain associated with ACS, the pain of aortic dissection is usually of sudden onset (rather than a crescendo), severe, and sharp or stabbing and frequently radiates to the back or left shoulder. Patients often present with abnormal hemodynamic status, either hypertension or hypotension. There is no specific biomarker for the detection of aortic dissection, and although D-dimer levels are significantly elevated in most cases of acute dissection [149], D-dimer is generally not used in a decision algorithm that includes imaging. Thus, the definitive diagnosis of aortic dissection requires dedicated imaging of the aorta.

Imaging Rationale

Selection of the most appropriate imaging study for diagnosis and evaluation of an AAS depends on patient-related factors and the probability of an aortic syndrome versus other explanations for a patient's clinical presentation [150]. The main distinction considered by the panel was patient hemodynamic stability (Table 4). Even for a relatively unstable patient who is being strongly considered for intervention such as surgery, anatomic imaging with CT is important for planning the procedure [151,152]. However, patients with type A dissection can present with hemopericardium, and there is a distinction in these patients regarding an assessment of the pericardium as the first imaging study that can then be used to guide emergent evacuation of the pericardium.

Description of Clinical Scenarios

Clinical Scenario 16: Hemodynamically Unstable Patient, Regardless of Prior Aortic Intervention. In this scenario, hemopericardium with subsequent tamponade is a strong clinical concern. Imaging of the full anatomy with CTAo, after stabilization, is considered appropriate. All other studies may be appropriate and will be guided by the presentation and the degree of hemodynamic instability. For example, in the scenario of a patient too unstable to be transported and imaged in a CT scanner, a bedside test such as TEE may be quite appropriate and provide comprehensive and critical information regarding the underlying cause of the instability.

Clinical Scenario 17: Hemodynamically Stable Patient, No Prior Aorta Intervention. This scenario accounts for the large majority of patients with suspected aortic dissection for whom imaging is performed. CTAo, MR aortography (MRAo), and transesophageal echocardiography (TEE) are considered appropriate.

Clinical Scenario 18: Hemodynamically Stable Patient, Prior Aorta Intervention. In this scenario, the patient is stable, but a complication of the surgical or percutaneous intervention such as a pseudoaneurysm is important in the differential diagnosis. CTAo and MRAo are both appropriate, although artifacts in MR images may be challenging. The other studies may be appropriate; in

particular, echocardiography may have interference, as the prior intervention often includes metal that causes artifacts.

Description of Imaging Modalities

CTAo. CTAo rapidly images the entire aorta and its branches and identifies specific AAS. Multiplanar and 3-D image reformations can be used to plan interventions. Electrocardiographically gated techniques facilitate motion-free images of the aortic root and coronary arteries. Modern CTAo has very high accuracy for life-threatening pathology of the aorta [153,154]. Although unenhanced imaging [155] can identify findings of AAS, dedicated CTAo is used when there is a clinical suspicion for AAS, and the rating panel considered only contrast-enhanced CT.

MRAo. MR is very accurate, with sensitivities and specificities essentially equivalent to those of CT. Like CT, advantages of MR include the ability to image the entire vascular system, to identify anatomic variants of aortic dissection, and to display the aorta and branch vessels in multiple planes and three dimensions. In addition, MR can diagnose concomitant aortic valve pathology and evaluate left ventricular function. Disadvantages include prolonged duration of imaging acquisition, during which the patient is relatively inaccessible to care providers. For this reason, MR can be limited for patients who are not hemodynamically stable. Other relative contraindications are noted for patients with claustrophobia and those with either metallic implants or pacemakers. Noncontrast MR techniques are emerging as a method to provide good-quality MR angiographic images without contrast. However, because these methods are limited to research studies and large academic centers, the rating panel considered only contrast-enhanced MR.

Transthoracic Echocardiography. The advantage of echocardiography is the ability to image at the bedside when a patient is relatively unstable to undergo CT. The main use of transthoracic echocardiography (TTE) is to assess the pericardium and provide dynamic information on value (eg, the presence or absence of aortic regurgitation) and ventricular function. TTE has limitations [156] compared with TEE for visualizing an intimal flap because it can be difficult to obtain an acoustic window to assess the full extent of the aorta. Moreover, the frequent appearance of artifacts that mimic a dissection flap can arise from a mirror image or reverberation artifact that appears as a mobile linear echo density overlying the aortic lumen. The operator must make certain to distinguish any artifact from a true dissection flap.

TEE. TEE provides a superior assessment of the visualized aorta and the aortic valves compared with TTE [156,157]. Like TTE, TEE can be performed at the bedside. The main limitation is difficulty in evaluating the length of the aorta and all branch vessels in three dimensions. Obtaining high-quality transesophageal echocardiographic images of the arch behind the trachea can be technically challenging. TEE is also relatively invasive and is contraindicated in patients with some pharyngeal and esophageal abnormalities.

AoCath. AoCath was once considered the reference standard for diagnosis of the aorta, including aortic dissection, penetrating ulcer, and unstable aneurysm [158-160]. Although beyond the scope of this document and not considered by the rating panel, catheter-based approaches are now used to manage AAS patients [161], and in this setting diagnostic AoCath is performed.

SECTION 5: IMAGING OF PATIENTS FOR WHOM A LEADING DIAGNOSIS IS PROBLEMATIC OR NOT POSSIBLE

Clinical Rationale

CP patients who present to the ED with complex patterns of signs, symptoms, and clinical data (eg, laboratory assessment, ECG) can undergo a variety of imaging strategies. The ED physician typically places such patients into one of the three diagnostic pathways as detailed in sections 2 to 4. It is also assumed that alternative imaging pathways may be necessary if the initial, tentative diagnosis is not confirmed. For this reason, such complex patients often undergo more than one imaging study to arrive at a diagnosis or to exclude all diagnoses considered to be life threatening. As noted previously, this document does not consider a "second" imaging study, as there are very few data and the choice of the second study may be influenced by the findings of the first.

Imaging Rationale and Description of Imaging

Another option is to implement so-called TRO CT angiography (CTA) [162,163] to potentially evaluate or exclude CAD, PE, and aortic disease in a single examination [164,165]. Initial, small, single-center studies have reported an NPV (final diagnosis is the reference) of 99.4% to 100%, and image quality and diagnostic accuracy have reports that are equivalent to dedicated CCTA, CTPA, and CTAo [164-166].

The majority of published studies have performed TRO CTA by modifying a coronary CT protocol to image more of the chest (either from the aortic arch to the base or the entire chest) and using additional contrast to maintain pulmonary artery enhancement, resulting in reported increases in

Table 5. Imaging of Patients for Whom a Leading Diagnosis is Problematic or Not Possible

Indication	"Triple-Rule-Out" CTA
19. Overall likelihood of ACS, PE, or AAS is low	R
20. Overall likelihood of ACS, PE, or AAS is not low	A

Appropriate use key: A = appropriate; R = rarely Appropriate.
AAS = acute aortic syndrome; ACS = acute coronary syndrome; CTA = CT angiography; PE = pulmonary embolism.

radiation dose from 25% to 150% and in contrast volume from 20% to 50%. For these reasons, dedicated CT imaging is preferred when the differential diagnosis can be narrowed. However, large-volume detectors [167] and high-pitch, helical, dual-source CT [168] may reduce the radiation and contrast dose penalties of TRO CTA, potentially allowing more widespread application [169]. The rating panel considered two scenarios for those patients who could be considered for TRO CTA (Table 5).

Description of Scenarios

Clinical Scenario 19: Overall Likelihood of ACS, PE, or AAS Is Low. The increased diagnostic yield of a TRO study over dedicated coronary CT is quite small, and when the overall likelihood of both PE and AAS is low, TRO CTA is considered rarely appropriate.

Clinical Scenario 20: Overall Likelihood of ACS, PE, or AAS Is Not Low. TRO CTA is considered appropriate in patients for whom the overall likelihood of ACS, PE, or AAS is not low. As CT technology continues to improve, additional studies are anticipated that will simultaneously assess the coronary plus pulmonary arteries as well as the aorta.

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APPENDIX 1: ABBREVIATIONS

AAS = acute aortic syndrome
ACS = acute coronary syndrome
AMI = acute myocardial infarction
AoCath = catheter-based aortography
CAD = coronary artery disease
CCath = catheter-based coronary angiography
CCTA = coronary CT angiography
CMR = cardiovascular MR
CompUS = compression ultrasonography of the deep veins
CP = chest pain
CTA = CT angiography
CTAo = CT aortography
cTn = cardiac troponin
CTPA = CT pulmonary angiography
ECG = electrocardiography
DVT = deep venous thrombosis
ED = emergency department
FOCUS = focused cardiac ultrasound
MACE = major adverse cardiovascular event
MI = myocardial infarction
MRAo = MR aortography
NPV = negative predictive value
NSTEMI = non–ST-segment elevation myocardial infarction
PCath = catheter-based pulmonary angiography
PE = pulmonary embolism
PPV = positive predictive value
SPECT = single-photon emission computed tomography
STEMI = ST-segment elevation myocardial infarction
TEE = transesophageal echocardiography
TIMI = Thrombolysis in Myocardial Infarction
TRO = triple-rule-out
TTE = transthoracic echocardiography
VQ = ventilation-perfusion scan

APPENDIX 2: ACR/ACC/AHA/AATS/ACEP/ASNC/NASCI/SAEM/SCCT/SCMR/SCPC/SNMMI/STR/STS 2015 Appropriate Utilization of Cardiovascular Imaging in Emergency Department Patients With CP Writing Group, Rating Panel, Task Force, and Indication Reviewers—Relationships With Industry and Other Entities (Relevant)

A standard exemption to the American College of Cardiology's policy regarding relationships with industry is extended to appropriate use criteria writing committees that do not make recommendations but rather prepare background materials and typical clinical scenarios and indications that are rated independently by a separate rating panel.

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This table represents the relevant relationships with industry and other entities that were disclosed by participants at the time of participation. It does not necessarily reflect relationships with industry at the time of publication. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity or ownership of $10,000 or more of the fair market value of the business entity or if funds received by the person from the business entity exceed 5% of the person's gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships in this table are modest unless otherwise noted. Names are listed in alphabetical order within each category of review. Participation does not imply endorsement of this document.

*Significant (greater than $10,000) relationship.

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