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Triple Rule Out Versus Coronary CT Angiography in Patients With Acute Chest Pain

Results From the ACIC Consortium

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ABSTRACT

OBJECTIVES This study sought to evaluate the diagnostic yield of triple rule out (TRO) versus coronary computed tomography angiography (CTA) scanning in patients with acute chest pain enrolled in a large statewide registry.

BACKGROUND Although TRO scans provide simultaneous evaluation of coronary artery disease (CAD), pulmonary embolism (PE), and aortic disease (AD), their use is not well defined.

METHODS Patients undergoing TRO or coronary CTA at 53 Michigan institutions for acute chest pain (in the emergency department or inpatient setting) in the ACIC (Advanced Cardiovascular Imaging Consortium) were included. Demographic characteristics, scan findings, and image quality parameters were compared between coronary CTA and TRO scans. The primary outcome was diagnostic yield, defined as obstructive CAD (>50% stenosis), PE, or AD; secondary outcomes were radiation dose, contrast volume, and image quality.

RESULTS From July 2007 to September 2013, 12,834 patients underwent computed tomography scanning (TRO, $n = 1,555$; coronary CTA, $n = 11,279$). The TRO group had more women (57.1% vs. 47.8%, $p < 0.001$). Diagnostic yield was similar (TRO, 17.4% vs. coronary CTA, 18.3%; $p = 0.37$), driven by CAD (15.5% vs. 17.2%, $p = 0.093$); PE and AD were 1.1% and 0.4% ($p = 0.004$) and 1.7% and 1.1% ($p = 0.046$). TRO had higher median radiation (9.1 mSv vs. 6.2 mSv; $p < 0.0001$) and mean contrast (113 ± 6 ml vs. 89 ± 17 ml; $p < 0.0001$) doses. Nondiagnostic images were frequent in TRO (9.4% vs. 6.5%; $p < 0.0001$). In emergency department patients, PE and AD were more often detected on TRO. Among inpatients, there were no differences in overall yield or in that of PE, AD, or CAD.

CONCLUSIONS TRO was associated with slightly higher yield of PE and AD, specifically in the emergency department. This benefit comes with higher nondiagnostic image quality, radiation, and contrast doses. Although TRO may be of value in selected patients, its indiscriminate use is not warranted. The appropriate use of TRO needs to be further defined. (Advanced Cardiovascular Imaging Consortium [ACIC]; NCT00640068) (J Am Coll Cardiol Img 2015;8:817–25)

Annually, more than 5.5 million patients present to emergency departments (EDs) throughout the United States with acute noninjury-related chest pain, the majority of whom are discharged with a diagnosis other than acute coronary syndrome (1,2). Despite this, there has been a dramatic increase in advanced imaging for acute chest pain totaling more than $10 billion annually (1,3).

Although subjective and objective data assist in the evaluation of acute chest pain, patient history has proved unreliable (4). Care providers focus much of their efforts on the evaluation of obstructive coronary artery disease (CAD), pulmonary embolism (PE), and

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ABBREVIATIONS AND ACRONYMS

AD = aortic dissection

CAD = coronary artery disease

CTA = computed tomography angiography

ED = emergency department

PE = pulmonary embolism

TRO = triple rule out

aortic dissection (AD) (2). When left undiagnosed, these are associated with increased mortality, poor prognosis, and malpractice litigation (5,6).

In the evaluation of acute chest pain with low to intermediate risk of acute coronary syndrome, coronary computed tomography angiography (CTA) provides a time- and cost-efficient option in the evaluation of obstructive CAD, with a negative predictive value of nearly 100% (7–9). In addition to its diagnostic role in evaluating chest pain, the prognostic utility of coronary CTA is increasingly being established (10,11). Despite its improved diagnostic efficiency over traditional acute chest pain evaluation protocols, coronary CTA allows only a limited assessment of the pulmonary vasculature and aortic arch.

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A triple rule out (TRO) coronary CTA protocol has thus been implemented (12,13). This protocol allows for simultaneous assessment of the thorax for CAD, PE, and AD with similar diagnostic yield, median hospital length of stay, and cost of care as with traditional coronary CTA protocols (14,15). Although image quality has been shown to be equivalent, this often comes at the cost of increased contrast volume and radiation exposure (14–16).

This study was performed to compare the diagnostic yield of traditional CTA and TRO protocols in the evaluation of acute chest pain across a variety of medical centers participating in the ACIC (Advanced Cardiovascular Imaging Consortium).

TABLE 1 Sample Protocols (on a Dual-Source, High-Pitch Capable Scanner)

	Coronary CTA	TRO
Scan range	Start: Just below the carina End: Inferior border of the heart	1. High-pitch mode starting at the lung bases to include costophrenic angles (PE) 2. High-pitch or adaptive sequence (prospective gated) just below the inferior heart border and cranially to include the aortic arch (AD)
Scan direction	Craniocaudal	1. Craniocaudal (PE) 2. Caudocranial (AD) *For single-injection protocol, craniocaudal for PE and caudocranial for coronaries and AD
Gantry angle	No angle	No angle
Scan mode*	High-pitch, adaptive sequential, or spiral with ECG triggering (0.6-mm detector) 0.28 s rotation	High-pitch spiral and/or sequential with ECG triggering (0.6-mm detector) 0.28-s rotation
Field of view	150–200 mm	150–200 mm
Contrast	Iopamidol (Isovue 370, Bracco Diagnostics Inc., Monroe Township, New Jersey) 60 ml at 5.5–6 ml/s + 50-ml saline flush	Iopamidol (Isovue 370, BRACCO) 80 ml at 5.5–6 ml/s + 50-ml saline flush
Procedure	Care bolus at ascending aorta triggered at 90 Hounsfield units	1. Obtain topogram 2. Test bolus of 20 ml of contrast 3. Dynamic analysis of 2 regions of interest at main pulmonary artery and ascending aorta to determine the timing for each scan (time delays) 4. Scanning
Reconstruction algorithm	Filtered back projection or iterative reconstruction based on body habitus	Filtered back projection or iterative reconstruction based on body habitus

*Tube voltage is determined by body mass index and body habitus. All patients were positioned supine head first.

AD = aortic dissection; CTA = computed tomography angiography; ECG = electrocardiogram; PE = pulmonary embolism; TRO = triple rule out.

METHODS

STUDY POPULATION. The ACIC was a statewide quality improvement initiative sponsored by Blue Cross Blue Shield/Blue Care Network of Michigan and included 53 hospitals and imaging centers performing coronary CTA (17). Participating centers received internal review board approval and included a waiver of consent. The ACIC database includes demographic characteristics, risk factors, symptoms, results of previous testing, and medical history. To ensure data accuracy, patients were interviewed at the point-of-service for symptoms and medical history. Pre-test likelihood of CAD is calculated using the Diamond-Forrester criteria. Nurses and/or technologists recorded information about medication use, vital signs, and procedural times. Information was also provided about the scanner model and manufacturer and protocol parameters. Effective radiation exposure and intravenous contrast doses were recorded. Coronary artery calcium scoring scans were performed only when specifically requested by the ordering physician.

Patients undergoing computed tomography (CT) scanning in the ED or as inpatients at these centers from 2007 to 2013 were included in this analysis. Outpatient studies were excluded.

CORONARY CTA PROTOCOL AND IMAGE INTERPRETATION. Coronary CTA was performed on various types of scanners available at each institution, ranging from 64- to 320-slice scanners, with scan techniques dictated by standard clinical protocols at each site (18). Multiple manufacturers (Siemens Healthcare [Erlangen, Germany], Philips Medical Systems [Eindhoven, the Netherlands], GE Healthcare [Milwaukee, Wisconsin], and Toshiba Medical Systems [Otawara, Japan]) with single- or dual-source systems were used. Beta-blockers were typically administered before scanning with a target heart rate as close to 60 beats/min as possible. Sublingual nitroglycerin was also given before scanning to patients who had no contraindication. Typical tube

voltage was based on body mass index typically ranging from 100 to 120 kV, but as low as 80 kV on selected scans. Both prospective and retrospective scanning protocols were used (Table 1). Prospective includes both axial or "step-and-shoot" scanning and high-pitch spiral scanning. Topograms were obtained to determine scan range. Tube current, gantry rotation time, pitch, and collimation varied based on the protocol and manufacturer. Iodinated contrast infused during the scan varied based on scan length and time, patient habitus, and cardiac output. Details of bolus tracking/timing or number of contrast bolus phases were not specified. Protocols were generally determined based on the reading physician's discretion; there were no pre-specified parameters across centers with regard to heart rate, arrhythmia, body habitus and other patient-related factors.

Coronary CTA scans were interpreted at each institution by cardiologists and/or radiologists with Level II (or III) training. Coronary stenoses were evaluated using a 16-segment model. Obstructive CAD was defined as coronary stenosis >50% in major epicardial vessels (left main, proximal, and mid segments of the left anterior descending, left circumflex, and right coronary arteries and the first and second diagonal and obtuse marginal branches). At centers where a cardiologist was the primary reader, all studies were read by a radiologist for noncardiac pathology.

IMAGE QUALITY. The quality of each study was rated by the reading physician at every site on a scale of 1 to 4. Excellent (a score of 1) was defined as complete absence of motion artifacts, excellent signal-to-noise ratio, and clear delineation of vessel walls, with the ability to assess luminal stenosis as well as plaque characteristics. Good (a score of 2) was defined as nonlimiting motion artifacts, reduced signal-to-noise ratio, and/or calcifications present, with preserved ability to assess luminal stenosis as well as plaque characteristics. Adequate (a score of 3) was defined as reduced image quality due to any combination of noise, motion, poor contrast enhancement, or calcium that significantly impairs ease of interpretation, but image quality is sufficient to rule out significant stenosis. Nondiagnostic (a score of 4) was defined as reduced image quality that precludes adequate assessment of stenosis in the majority of vessels (18). Individual readers based their rating on clinical impression; sample images were not provided.

ESTIMATION OF RADIATION DOSE. Radiation doses were estimated by previously described methods (19,20). Each scanner provided a protocol summary containing the dose/length product for each image series, which integrated estimated absorbed radiation in the x, y, and z directions based on the CT dose index volume. The total dose for the entire CT examination was then used to derive the effective radiation dose using the summed dose/length product multiplied by the European Working Group for Guidelines on Quality Criteria in Computed Tomography conversion coefficient (kappa = 0.014 mSv/mGy·cm) (21).

STUDY ENDPOINTS. The primary endpoint of this study was diagnostic yield: a composite of coronary artery diameter stenosis >50%, PE, and AD. The threshold of 50% luminal narrowing was used because this often prompts further invasive or noninvasive coronary evaluation. Secondary endpoints included radiation dose, contrast volume, and image quality.

TABLE 2 Patient Characteristics

	Coronary CTA (n = 11,279)	TRO (n = 1,555)	p Value
Age, yrs	52 ± 13 (51)	53 ± 13 (52)	0.027
Women	5,380 (47.8)	888 (57.1)	<0.0001
Body mass index, kg/m^2	30 ± 6.3 (29)	30 ± 6.1 (29)	0.73
Body mass index >30 kg/m^2	4,490 (39.9)	635 (40.8)	0.49
Family history of premature CAD	3,933/10,576 (37.2)	466/1,468 (31.7)	<0.0001
Diabetes	1,500 (13.4)	194 (12.5)	0.36
Hypertension	5,220 (46.8)	767 (49.9)	0.022
Hyperlipidemia	4,907/10,617 (46.2)	625/1,445 (43.3)	0.034
History of CAD	1,784 (15.8)	215 (13.8)	0.042
Previous MI	890 (8.0)	82 (5.3)	0.0002
Previous PCI	676 (6.1)	75 (4.9)	0.062
Coronary artery bypass grafting	466 (4.2)	63 (4.1)	0.86
Smoker			<0.0001
Never	5,749 (51.2)	889 (57.5)	
Former (>12 months)	2,633 (23.4)	345 (22.3)	
Recent (within 12 months)	276 (2.5)	30 (1.9)	
Current	2,575 (22.9)	283 (18.3)	
Congestive heart failure	517 (4.7)	36 (2.3)	<0.0001
Cardiac arrest	174/11,040 (1.6)	6/1,518 (0.4)	0.0003
Atrial fibrillation	671/11,042 (6.1)	66/1,532 (4.3)	0.006
Peripheral vascular disease	298/10,909 (2.7)	22/1,511 (1.5)	0.003
Cerebrovascular accident	532/11,102 (4.8)	54/1,532 (3.5)	0.027
Chronic obstructive lung disease	1,220/11,114 (11)	159/1,534 (10.4)	0.47
Valvular heart disease	834/10,878 (7.7)	133/1,512 (8.8)	0.13
Chronic kidney disease	137 (1.2)	11 (0.7)	0.08
Patient status = ED versus inpatient	7,070 (63.0)	1,158 (74.5)	<0.0001
Chest pain risk (Diamond-Forrester criteria), n	10,583	1,503	<0.0001
Very low	397 (3.8)	71 (4.7)	
Low	906 (8.6)	170 (11.3)	
Intermediate	6,654 (62.9)	994 (66.1)	
High	2,626 (24.8)	268 (17.8)	
Framingham Risk Score, n	11,226	1,547	0.76
Low	7,292 (65.0)	990 (64.0)	
Intermediate	2,642 (23.5)	375 (24.2)	
High	1,292 (11.5)	182 (11.8)	

Values are mean ± SD (median), n (%), or n/N (%).

CAD = coronary artery disease; ED = emergency department; MI = myocardial infarction; PCI = percutaneous coronary intervention; other abbreviations as in Table 1.

TABLE 3 Findings on Coronary CTA Examination

All Patients	Coronary CTA (n = 11,279)	TRO (n = 1,555)	p Value
AD	129 (1.1)	27 (1.7)	0.046
PE	47 (0.4)	17 (1.1)	0.0004
CT stenosis >50%*	1,932 (17.2)	239 (15.5)	0.093
Diagnostic yield (any of the 3 above)	2,065 (18.3)	270 (17.4)	0.37
Uninterpretable CTA scan	725 (6.5)	145 (9.4)	<0.0001
Male Patients Only	**(n = 5,886)**	**(n = 667)**	
AD	82 (1.4)	15 (2.3)	0.083
PE	24 (0.4)	9 (1.4)	0.005
CT stenosis >50%*	1,205/5,875 (20.5)	151/663 (22.8)	0.17
Diagnostic yield (any of the 3 above)	1,286 (21.9)	168 (25.2)	0.049
Uninterpretable CTA scan	358/5,866 (6.1)	51/658 (7.8)	0.098
Female Patients Only	**(n = 5,380)**	**(n = 888)**	
AD	47 (0.9)	12 (1.4)	0.17
PE	23 (0.4)	8 (0.9)	0.071
CT stenosis >50%*	726/5,367 (13.5)	88/883 (10.0)	0.004
Diagnostic yield (any of the 3 above)	778 (14.5)	102 (11.5)	0.018
Uninterpretable CTA scan	364/5,362 (6.8)	94/886 (10.6)	<0.0001
Centers Performing Both Coronary CTA and TRO Only	**(n = 10,419)**	**(n = 1,555)**	
CT findings: AD	119 (1.1)	27 (1.7)	0.046
CT findings: PE	40 (0.4)	17 (1.1)	0.0002
CT stenosis >50%*	1,774 (17.1)	239 (15.5)	0.12
Diagnostic yield (any of the 3 above)	1,896 (18.2)	270 (17.4)	0.43
Uninterpretable CTA scan	649 (6.3)	145 (9.4)	<0.0001
Emergency Department Patients Only	**(n = 7,070)**	**(n = 1,158)**	
CT findings: AD	64 (0.9)	21 (1.8)	0.0046
CT findings: PE	7 (0.1)	11 (1.0)	<0.0001
CT stenosis >50%*	830 (11.8)	134 (11.6)	0.91
Diagnostic yield (any of the 3 above)	888 (12.6)	158 (13.6)	0.30
Uninterpretable CTA scan	403/7,060 (5.7)	95/1,152 (8.3)	0.0008
Inpatients Only	**(n = 4,162)**	**(n = 396)**	**p Value**
CT findings: AD	65 (1.6)	6 (1.5)	0.94
CT findings: PE	39 (0.9%)	6 (1.5%)	0.28
CT stenosis >50%*	1,090/4,147 (26.3)	105/393 (26.7)	0.85
Diagnostic yield (any of the 3 above)	1,165 (28.0)	112 (28.3)	0.90
Uninterpretable CTA scan	318/4137 (7.7)	50/391 (12.8)	0.0004

Values are n (%) or n/N (%). *Greater than 50% stenosis in a major epicardial vessel (left main, proximal, and mid segments of the left anterior descending, left circumflex, and right coronary arteries and first and second diagonal and obtuse marginal branches).

CT = computed tomography; other abbreviations as in Table 1.

STATISTICAL ANALYSIS. All statistical analyses were performed using version 9.3 of SAS for Windows (SAS Institute, Cary, North Carolina). The study population was divided into 2 groups based on the protocol: 1) coronary CTA; and 2) TRO. Using Pearson's chi-square where the expected frequency was >5 or the Fisher exact test, the categorical variables were reported as numbers and percentages. Continuous variables were examined using logistic regression, with TRO as the dependent variable and reported as mean ± SD or median and 25th, 75th percentiles where appropriate. Backward elimination logistic regression analysis was performed to determine whether TRO was an independent predictor of diagnostic yield as well as to determine predictors of uninterpretable scans. The following significant variables were included: sex, age, body mass index >30 kg/m^2, Framingham Risk Score, scanning mode, tube strength, radiation dose (mSv), heart rate (beats/min), contrast volume (ml), and history of atrial fibrillation, valve disease, chronic obstructive lung disease, or congestive heart failure.

RESULTS

BASELINE CHARACTERISTICS. A total of 12,834 patients from July 2007 to September 2013 at 53 institutions in Michigan met the study criteria. Of these, 11,279 (87.9%) were in the coronary CTA group and 1,555 (12.1%) were in the TRO group. Demographic characteristics were similar in both groups (Table 2). Those undergoing TRO were more often women (57.1% vs. 47.8%; p < 0.0001) with a lower CAD pre-test likelihood according to the Diamond-Forrester criteria and a lower frequency of tobacco use, family history of premature CAD, hypertension, and hyperlipidemia.

PRIMARY OUTCOME. Composite diagnostic yield determined by the presence of obstructive CAD (stenosis >50%), PE, and/or AD was 17.4% for TRO and 18.3% for coronary CTA (p = 0.37) (Table 3). This was driven by obstructive CAD: 15.5% in TRO and 17.2% in coronary CTA (p = 0.93) and accounted for 88.5% and 93.6% of diagnoses, respectively. Diagnostic yields of PE and AD were 1.1% and 0.4% (p = 0.0004) and 1.7% and 1.1% (p = 0.046), respectively. Some patients had more than 1 diagnosis. A multivariable model for diagnostic yield adjusting for the differences between the TRO and coronary CTA subjects found that having a TRO scan was not predictive (odds ratio: 0.87, 95% confidence interval: 0.71 to 1.07) of diagnostic yield.

PE and AD were diagnosed more often on TRO than on coronary CTA in centers that routinely performed TRO and coronary CTA, with no statistically significant difference in the overall diagnostic yield. Uninterpretable studies were more often reported with TRO than with coronary CTA. Similarly, PE and AD were more often detected on TRO than on coronary CTA among ED patients. Among inpatients, however, there was no difference in the detection of PE and AD between TRO and coronary CTA (Table 3).

SECONDARY OUTCOMES. The median radiation dose was 49% higher for TRO than CTA: 9.1 mSv (interquartile range: 6.4 to 13.5) versus 6.2 mSv

(interquartile range: 3.9 to 11.6) ($p < 0.0001$) (Table 4). For TRO, the median dose varied based on protocol and type of scanner; the lowest radiation dose was associated with high-pitch spiral scanning. Mean contrast volume was 27% higher for TRO than for coronary CTA: 113 ± 16 ml versus 89 ± 17 ml ($p < 0.0001$). Nondiagnostic or uninterpretable image quality was noted more frequently in TRO (9.4% vs. 6.5%; $p < 0.0001$) with similar reported reasons (Table 5). Results of the multivariable model found that the factors that contributed to poor image quality were higher heart rates, body mass index >30 kg/m^2, valvular heart disease, congestive heart failure, higher contrast volume, and higher Framingham Risk Score (Table 6).

TABLE 4 Specifics of CTA TRO Examination

	Coronary CTA (n = 11,279)	TRO (n = 1,555)	p Value
Scanner type, n	11,256	1,554	<0.0001
64-slice	3,793 (33.7)	54 (3.5)	
Dual source	2,528 (22.5)	607 (39.1)	
320	35 (0.3)	1 (0.06)	
High-pitch spiral	4,900 (43.5)	892 (57.4)	
Pre-scan heart rate–lowering medications	9,276 (82.5)	1,292 (83.3)	0.43
Average heart rate during scan	60 ± 8.4 (59)	62 ± 8.8 (61)	<0.0001
Pre-scan sublingual nitroglycerin	10,414 (92.5)	1,512 (97.2)	<0.0001
Contrast volume	89 ± 17 (85)	113 ± 16 (120)	<0.0001
Scan length	13.2 ± 2.1 (14)	16.8 ± 2.6 (17)	<0.0001
Tube potential, kV	111 ± 11 (120)	112 ± 10 (120)	0.18
ECG dose modulation	8,616 (76.8)	1,019 (65.7)	<0.0001
Total dose/length product	442 (276, 826)	651 (458, 962)	<0.0001
Effective radiation dose, mSv	6.2 (3.9, 11.6)	9.1 (6.4, 13.5)	<0.0001
CTA scan quality, n	11,237	1,544	0.0001
Excellent	4,344 (38.7)	600 (38.9)	
Good	4,492 (40.0)	570 (36.9)	
Adequate	1,676 (14.9)	229 (14.8)	
Poor/uninterpretable	725 (6.5)	145 (9.4)	

Values are n (%), mean ± SD (median), or median (25th, 75th).
Abbreviations as in Table 1.

DISCUSSION

In this statewide study, the overall diagnostic yield was similar between TRO and coronary CTA. TRO was associated with a slightly higher yield of PE and AD, but also with higher nondiagnostic image quality and radiation and contrast doses. These data suggest that although TRO is feasible, it cannot be recommended in all patients presenting with acute chest symptoms. Clinical scenarios with the suggestion of increased risk of PE and/or AD in addition to CAD may present the best use for TRO.

Although the composite diagnostic yield in both groups were comparable, this was predominantly driven by obstructive CAD, which was 15 times that of PE and AD. Although PE and AD were infrequent, they were diagnosed more frequently in the TRO group, unlike a similar study comprising a smaller cohort of patients with similar risk profiles (14). It is important to note that in that previous study, there was a lower diagnostic yield for PE in the coronary CTA group (1.1% with TRO and 0.2% with coronary CTA; $p = 0.05$) with no AD in either group. Given similar patient risk factor profiles in the present study, these differences were most likely driven by sample size as well as varied protocols across centers. The diagnostic yield for PE in this study in TRO and coronary CTA was much lower than the 9% to 19% in dedicated PE protocols (22–24). However, in those studies, patients were selected for CT examinations based on clinical presentation and/or traditional risk stratification models. Although the benefits of risk stratification for PE with D-dimer, Wells criteria, and Geneva criteria are well described (25,26), their effects on the diagnostic yield of coronary CT (CTA or TRO) are yet to be demonstrated. The standardized use of risk stratification tools would likely improve the diagnostic yield and thus prevent unnecessary use of TRO.

It is important to note that even though the rates of PE and AD on coronary CTA (with limited field of view) were lower than in dedicated protocols, they were high for unsuspected but clinically important diagnoses. However, >97% of TRO studies showed neither AD nor PE. These discordant findings between scan intention and results highlight the fact that the diagnosis of acute chest pain can be challenging, particularly because clinical presentations are often atypical or unclear.

The majority of the overall studies (64%) were performed in the ED. There was a statistically significant difference in the diagnostic yield of both PE and AD with TRO in the ED, but not among inpatients. This could reflect alternate indications for ordering the study as an inpatient (for example, further

TABLE 5 Reasons for Poor/Uninterpretable Image Quality

	Non-TRO (n = 725)	TRO (n = 145)	p Value
Calcium	173/709 (24.4)	27/140 (19.3)	0.19
Motion	486/714 (68.1)	96/142 (67.6)	0.91
Noisy image	203/714 (28.4)	42/142 (29.6)	0.78
Low vascular contrast	192/711 (27.0)	37/143 (25.9)	0.78

Values are n/N (%).
Abbreviations as in Table 1.

TABLE 6 Multivariate Analysis of Nondiagnostic/Uninterpretable Image Quality

	Odds Ratio	95% CI	p Value
Average heart rate during scan (increments of 10 beats/min)	2.013	1.858–2.181	<0.0001
Body mass index >30 kg/m^2	1.744	1.501–2.026	<0.0001
Valvular heart disease	1.467	1.158–1.857	0.0015
Congestive heart failure	1.415	1.048–1.910	0.0233
Contrast volume (every 25 ml)	1.269	1.148–1.403	<0.0001
Framingham Risk Score (increments of risk categories)	1.221	1.102–1.353	0.0001
TRO scanning	1.018	0.817–1.270	0.8717
ECG dose modulation	0.672	0.572–0.789	<0.0001

CI = confidence interval; other abbreviations as in Table 1.

evaluation of an equivocal stress test in the ED or clarification of an abnormal chest x-ray).

TRO was associated with higher median radiation doses and contrast volumes. Although the increased scan time and scan length required with TRO protocols are generally considered the main cause of an increased dose, the difference in scan length between coronary CTA and TRO in this study was only 3.6 cm. These data suggest "overscanning" on coronary CTA or "underscanning" on TRO at least at some sites; with rigid adherence to prescribed scan lengths, the difference in radiation dose could be conceivably higher. These data also demonstrate the overall ordering patterns of both protocols. Patients with higher pre-test likelihood of CAD underwent coronary CTA, whereas those with a lower likelihood underwent TRO. Thus, TRO included younger patients and more women, the specific populations in which radiation dose exposure must be limited (27). Additionally, the diagnostic yield among women was one-half of that in men. This finding highlights the fact that women more often present with atypical symptoms, but also received unnecessary radiation and contrast. Although the diagnosis of PE on TRO in the women who had the disease is a positive, the lack of such diagnoses in the majority of those scanned highlight the challenges and limitations of pre-test clinical identification of patients with potential life-threatening conditions.

There have been extensive, successful efforts by the ACIC to optimize protocols to decrease radiation dose (28). Our median radiation dose reflects both older and newer protocols. Most of the scans included in this study were performed using 64-slice scanners. Centers using dual-source scanners capable of high-pitch scanning reported <50% of the median radiation dose. Also, low-dose protocols for 320-row scanners can decrease radiation exposure to <3.5 mSv and total contrast volume to 60 ml without sacrificing image quality (29).

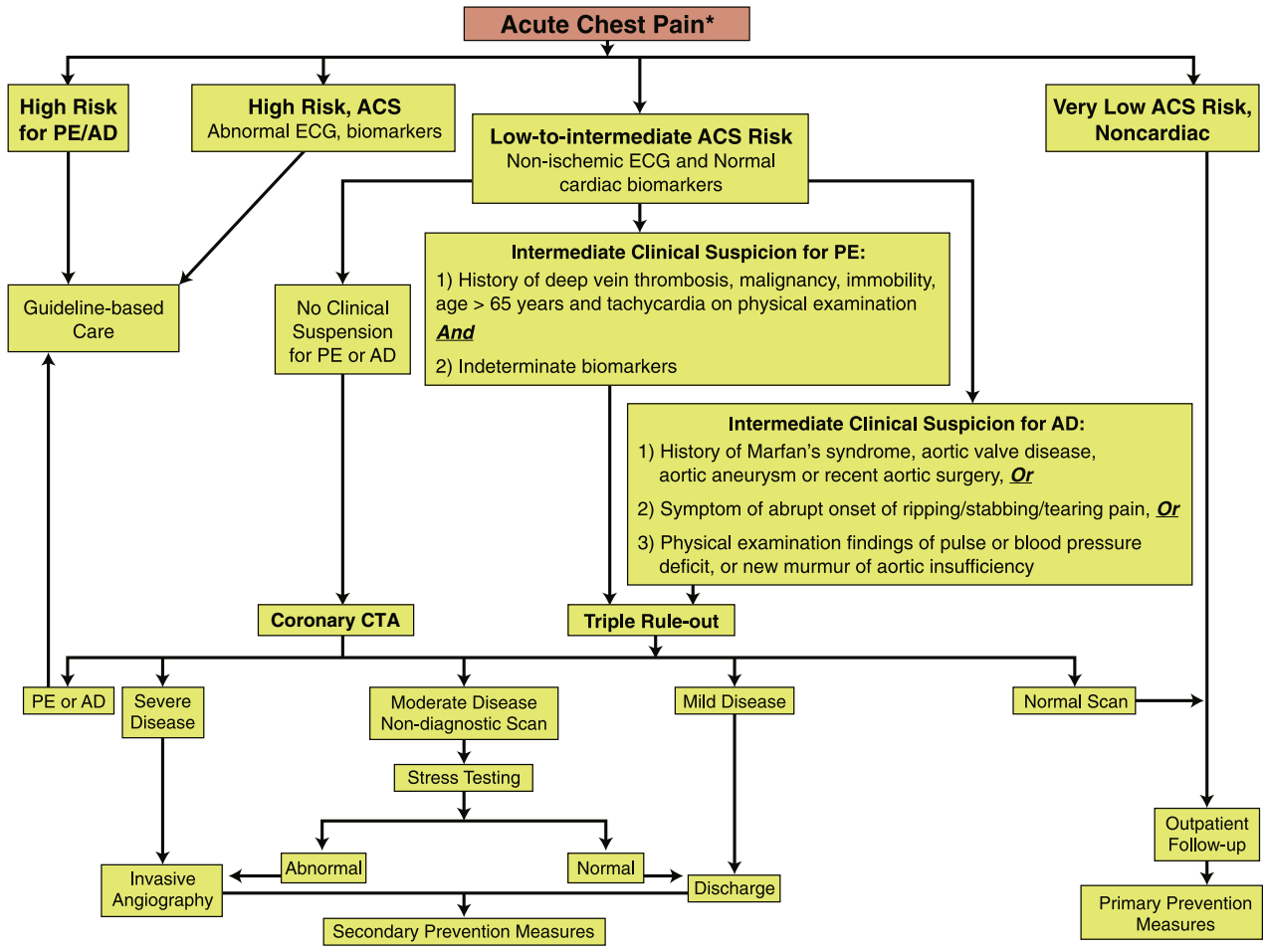
TRO was associated with a 45% higher frequency of nondiagnostic image quality compared with coronary CTA. Although the TRO scan type itself was not a significant predictor of nondiagnostic image quality on multivariate analysis, it is likely that this protocol is affected by the type of contrast bolus used as well as body habitus. Higher heart rates and ectopy (resulting in motion artifacts) and clinical conditions that may result in the patient's inability to lie flat were found to be significant predictive factors for scan uninterpretability. These results further demonstrate the need for appropriate patient selection for TRO to avoid unnecessary radiation exposure from a nondiagnostic scan, leading to additional testing with their associated risks and costs.

CLINICAL IMPLICATIONS. This large multicenter study suggests that TRO provides a slightly increased diagnostic yield for PE and AD compared with coronary CTA. It is unclear whether this is related to liberal use of TRO. Nonetheless, patients undergoing TRO are more often low-risk women with an overall low yield on CT scanning. Thus, these results do not necessarily tip the balance in favor of TRO use in all patients with acute chest symptoms.

Currently, there are no established guidelines outlining pre-scan evaluation of indications for TRO. The effects of clinical evaluation and subsequent patient selection on diagnostic yield are unknown. The results of this study suggest that although there is a potential utility for TRO in the evaluation of acute chest pain, appropriate patient selection through established clinical algorithms is necessary. TRO must be used judiciously and not indiscriminately, particularly because nearly 1 in 10 TRO scans was nondiagnostic despite the higher radiation and contrast doses necessarily associated with it. TRO may be considered when clinical features and initial laboratory data (e.g., indeterminate troponin and elevated D-dimer) raise concern for: 1) obstructive CAD; and 2) PE or AD. Therefore, we propose an algorithm that divides patients presenting with acute symptoms into 3 risk groups: high, low to intermediate, and very low (noncardiac) (**Figure 1**). Both coronary CTA and TRO are best avoided in patients with known CAD; such patients may be best suited for stress testing with/without imaging.

Among low- to intermediate-risk patients, clinical suspicion of PE must warrant additional evaluation of risk that includes the Wells criteria or Geneva criteria (e.g., history of deep vein thrombosis, malignancy,

FIGURE 1 Suggested Algorithm for the Use of TRO in Patients With Acute Chest Pain



Suggested pathway incorporating the use of TRO protocols in patients with acute chest pain. *Excludes patients with known CAD. ACS = acute coronary syndrome; AD = aortic dissection; CAD = coronary artery disease; CTA = computed tomography angiography; ECG = electrocardiogram; PE = pulmonary embolism; TRO = triple rule out.

tachycardia, immobilization, age older than 65 years) and suggestive laboratory data (increased D-dimer) (25,26). If the suspicion of PE remains intermediate with such detailed evaluation along with that for CAD, TRO may be considered after meticulous patient preparation (**Figure 2**).

Similarly, intermediate suspicion of AD (1 high-risk feature in history, symptoms, or physical examination) along with continued suspicion of CAD may warrant TRO (**Figure 3**). A double rule out protocol may be considered in patients with an overlap in diagnosis of AD and CAD with inclusion of the abdominal aorta, without the extra contrast for opacification of the pulmonary circulation. More than 1 high-risk feature in the patient's history (Marfan syndrome, aortic valve disease or recent aortic surgery, known aortic aneurysm), symptoms (abrupt onset of ripping/tearing/stabbing chest pain), and physical examination (pulse deficit, blood pressure difference in limbs, perfusion deficits, murmur of aortic insufficiency) would warrant triage to dedicated AD pathway for diagnosis and management (30).

STUDY LIMITATIONS. The most important limitation of this study is its inability to distinguish the source of the increased diagnostic yield of TRO for PE and AD. There are 2 possibilities: 1) physicians appropriately selected patients for TRO, yielding a higher incidence of PE or AD; or 2) the TRO procedure has a higher sensitivity due to a contrast bolus appropriately timed for right-sided circulation. We were able to retrospectively evaluate 8 of 17 patients in the TRO group who had PE and found that each had filling

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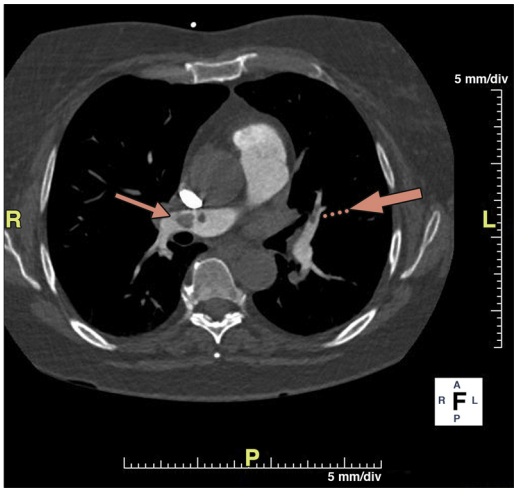
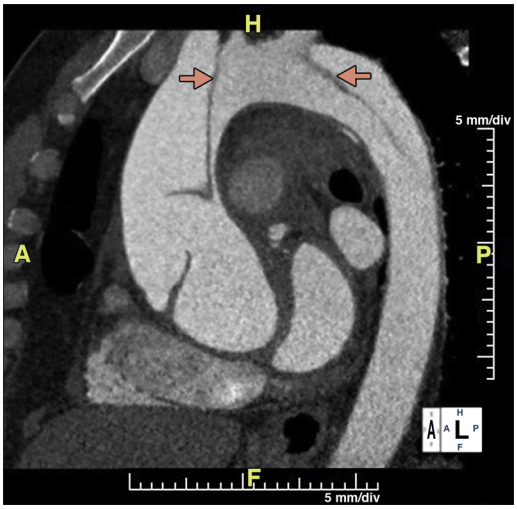
FIGURE 2 Pulmonary Emboli Noted on a TRO Scan



Triple rule out scan in a 59-year-old woman who presented to the emergency department with chest pressure, palpitations, and shortness of breath 1 week after lumbar stenosis surgery. Coronary arteries and aorta were normal on TRO, but she was found to have extensive bilateral pulmonary emboli with significant filling defects involving bilateral multiple segmental branches **(arrows)**. TRO = triple rule out.

FIGURE 3 Aortic Dissection Noted on a TRO Scan



TRO scan in a 52-year-old man with long-standing hypertension presenting to the emergency department with acute chest pain radiating to the back. TRO scan reveals aortic dissection **(arrows)**. TRO = triple rule out.

defects that fell within the imaging window of standard coronary CTA. However, it is foreseeable that PE may have been missed on coronary CTA scans due to a limited field of view and/or varying protocols.

As a retrospective study, it is difficult to make definitive comparative conclusions. There are multiple participating centers using varied chest pain and imaging algorithms; thus, this study reflects varied practice patterns. Protocols and physician threshold for ordering coronary CTA vary within and across different institutions, with the potential for selection bias. It is important to note that TRO can often be used inappropriately as a screening tool to evaluate all chest pain. Data on varying reconstruction methods that could have contributed to image quality were not collected. There is no discrimination of studies duplicated from patients receiving care at multiple medical centers.

CONCLUSIONS

In this large registry, TRO was associated with slightly higher diagnostic yield for PE and AD compared with coronary CTA, particularly in the ED, and was used more often in younger women. Additionally, TRO is associated with significantly higher radiation and contrast doses compared with coronary CTA. Thus, although feasible, clinical criteria for TRO use and appropriateness must be further defined.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with a low to intermediate likelihood of CAD and PE/AD, TRO may result in higher diagnostic yield compared with coronary CTA. Due to the significantly higher radiation and contrast doses associated with TRO, it must be judiciously applied in clinical practice.

TRANSLATIONAL OUTLOOK: Although the diagnostic yield for PE and AD was higher in TRO compared with coronary CTA, it is associated with higher radiation and contrast doses as well as more frequent nondiagnostic image quality. Thus, patient selection and appropriate use of TRO must be further defined.

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