Critical Review Form
Therapy

Litt HI, Gatsonis C, Snyder B, et al. CT angiography for safe discharge of patients with possible acute coronary syndromes. N Engl J Med. 2012 Apr 12;366(15):1393-403.

Objectives: **"to determine the safety and efficiency of a CCTA-based strategy" (p. 2) for the detection of coronary artery disease.**

Methods: **This randomized, controlled, multicenter study was conducted at five sites in the US between July 7, 2009, and November 3, 2011. Patients were enrolled from emergency departments at five sites, with some additionally enrolled after admission to an observation unit. Eligible patients were 30 years or older with symptoms suggestive of ACS, an initial Thrombolysis in Myocardial Infarction (TIMI) risk score of 0 to 2, and no acute ischemia on ECG. Exclusion criteria included non-cardiac symptoms, coexisting conditions necessitating admission, normal CCTA or angiography findings within the previous year, and contraindications to CCTA.**

Patients were randomized in a 2:1 ratio to CCTA or traditional care after the initial ECG but before serum creatinine and cardiac troponin results. Patients with creatinine clearance less than 60 ml per minute or requiring CT for pulmonary embolism were withdrawn. In the CCTA group, the initial evaluation performed was CCTA, while in the traditional care group, healthcare providers decided which testing to perform. All clinical decisions were made by the attending team. In the CCTA group, a second troponin measurement was taken 90 to 180 minutes after arrival.

The primary outcome was safety, as indicated by the rate of major cardiac events (cardiac death or myocardial infarction) within 30 days among patients without significant coronary artery disease on CCTA. Clinically significant coronary disease was defined as stenosis ≥50%. Secondary outcomes included discharge rate, length of stay, and 30-day rates of death, MI, revascularization, and resource utilization. Follow-up occurred by telephone at 30-days and adverse events were confirmed through record reviews. If patients were unavailable, hospital records and the Social Security Death Master File were searched.

A total of 1392 patients were enrolled; 22 were withdrawn, primarily due to newly diagnosed renal insufficiency, leaving 1370 patients. Randomization occurred in the ED for 1231 patients (90%), with remaining patients randomized post-observation unit admission. 908 patients were assigned to CCTA and 462 to traditional care. The mean age was 49 in the CCTA group and 50 in the traditional care group, and 49% and 44% were male, respectively.

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Guide	Comments
Are the results valid?	
Did experimental and control groups being the study with a similar prognosis?	
Were patients randomized?	Yes. Patients were randomized in a 2:1 ratio to CCTA or traditional care.
Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	Yes. Randomized was web-based and off-site. Per the research protocol "Upon successful participant registration and randomization to Group A or Group B, a confirmation e-mail containing the registration and case specific calendar is sent to the research staff enrolling the participant via the web." This method should ensure allocation concealment.
Were patients analyzed in the groups to which they were randomized?	Yes. "Comparisons were made according to the intention-to-treat principle." (p. 4) Of 908 subjects assigned to the CCTA-based strategy, 767 (84%) completed the CCTA examination but were analyzed according to group assignment.
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, gender, race, cardiac history and risk factors, baseline ECG findings, and TIMI risk score.
Did experimental and control groups retain a similar prognosis after the study started?	
Were patients aware of group allocation?	Yes. Given the intervention there would have been no way to blind patients or clinicians, raising the potential for performance bias, specifically as regards to earlier discharge from the ED/hospital.
Were clinicians aware of group allocation?	See above.
Were outcome assessors aware of group allocation?	Yes. The authors make no mention of blinding of outcome assessors. Given the interventions and outcome measurements this would have been difficult to achieve (observer bias).
Was follow-up complete?	Yes. Only 10 patients in the CCTA group and 5 in the traditional care group did not have clinical follow-up, representing 1.1% of the enrolled population.
What are the results?	
How large was the treatment effect?	Safety • There were no deaths or myocardial infarctions within 30 days in 640 patients with negative CCTA (0%; 95% CI 0 to 0.57). Secondary Outcomes: • There were no cardiac deaths in either group. • MI occurred within 30 days in 10 of 908 (1%) in the CCTA group and 5 of 462 (1%) in the traditional care group; difference of 0.02 percentage points (95% CI −5.6 to 5.7). • One serious adverse event (bradyarrhythmia) in each group, likely related to heart rate control medications. Efficiency and Use of Resources • Patients in the CCTA group were more likely to be discharged from the ED (49.6% vs. 22.7%; difference 26.8%; 95% CI: 21.4% to 32.2%). • Ther was a shorter length of stay in the CCTA group (median 18 vs. 24.8 hours). • Coronary artery disease was more likely to be diagnosed in the CCTA group vs. the traditional care group (9.0% vs. 3.5%; difference 5.6%; 95% CI 0% to 11.2%). 30-Day Follow-up:

	• There was no significant difference in the use of invasive angiography (5.1% vs. 4.2%; difference: 0.9%; 95% CI −4.8% to 6.6%). • There was no significant difference in revascularization rates (2.7% vs. 1.3%; difference 1.4%; 95% CI −4.3% to 7.0%). • Negative findings on invasive angiography were less likely in the CCTA group (29% vs. 53%; difference −23.7%; 95% CI −48.8% to 3.3%). • There was no significant difference in repeat ED visits, hospitalizations, or cardiologist office visits.
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	See above.
How can I apply the results to patient care?	
Were the study patients similar to my patient?	Likely yes. This study was conducted at 5 centers in the US. It seems likely that the included patients represent a sufficient sample to generalize to our patient population (external validity). Patients were included in this study if further risk stratification was deemed necessary by the physician caring for the patient. There has been increasing evidence since the inception of this study that such testing in low risk patients is often not beneficial (Foy 2015, Redberg 2015). Rates of provocative testing among patients presenting to the ED with chest pain have fallen significantly over the last 15 years, in part due to the introduction of high-sensitivity troponins (Contractor 2021), and it is unclear how these changes would impact the findings in this study.
Were all clinically important outcomes considered?	Yes. The authors considered major adverse cardiac events, discharge rate, length of stay, and 30-day rates of death, MI, revascularization, and resource utilization. They did not consider cost or patient satisfaction.
Are the likely treatment benefits worth the potential harm and costs?	This study suggests that the use of CCTA in low-risk chest pain patients is safe, with no deaths or myocardial infarctions within 30 days in 640 patients with negative CCTA (0%; 95% CI 0 to 0.57). Patients in the CCTA group were more likely to be discharged from the ED and had a median length of stay approximately 6 hours shorter than those receiving traditional care.

Limitations:

1. **While the lack of blinding is understandable, there is a risk of both performance bias on the part of clinicians and observer bias on the part of outcomes assessors.**
2. **Approximately 16% of patients randomized to CCTA did not undergo imaging as planned.**
3. **This study included a very low-risk patient population with a TIMI score of 2 or less; research suggests that provocative such testing in such patients is often not beneficial (Foy 2015, Redberg 2015).**

Bottom Line:

This multi-center randomized controlled trial found no significant risk of death or myocardial infarctions within 30 days among patients with low-risk chest pain in the ED with a subsequent negative CCTA (0%; 95% CI 0 to 0.57). The use of CCTA compared to traditional care also reduced admission rates and length of stay with no increase in the use of invasive angiography. It is possible that this study included a significant number of patients whose risk of clinically significant occlusive coronary artery disease was sufficiently low that no

additional testing was warranted as any patient with a TIMI score ≤ 2 was eligible. Additionally, this study predated the use of high-sensitivity troponins, which appear to have led to a decrease in subsequent testing among low-risk chest pain patients.