Critical Review Form
Therapy

PGY-4

Goldstein JA, Chinnaiyan KM, Abidov A, et al; CT-STAT Investigators. The CT-STAT (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment) trial. J Am Coll Cardiol. 2011 Sep 27;58(14):1414-22.

Objectives: **"To determine whether CCTA has the potential to safely increase efficiency and reduce the ED costs of care…" (p. 1415)**

Methods: **This multicenter, randomized, comparative effectiveness trial comparing a CCTA-based diagnostic strategy against rest-stress myocardial perfusion imaging (MPI) for evaluating acute low-risk chest pain was conducted at 11 university and 5 community hospitals between June 2007 and November 2008. Inclusion criteria included chest pain suspicious for angina, age ≥25 years, pain onset to presentation within 12 hours, presentation to randomization within 12 hours, normal or nondiagnostic ECG without ischemia, and TIMI risk score ≤4. Exclusion criteria included known coronary artery disease, elevated cardiac biomarkers, ischemic ECG changes, ejection fraction ≤ 45%, contraindications to contrast or beta-blockers, atrial fibrillation, BMI ≥39 kg/m², elevated serum creatinine, and CT imaging or contrast administration within 48 hours.**

Patients were sequentially enrolled from the ED whenever research coordinators were present and randomized in a 1:1 ratio to CCTA or MPI. The primary outcome was diagnostic efficiency, measured as time from randomization to receiving test results. Secondary outcomes included ED costs and safety, defined by the absence of major adverse cardiac events (MACE) over six months in patients with normal or near-normal index tests. These events encompassed ACS/MI, cardiac death, or revascularization. Follow-up involved hospital records and telephone interviews 6 months after the ED visit. Mortality was confirmed by the Social Security Death Index.

Out of 6,640 patients screened, 749 were enrolled and 699 completed the protocol (361 in the CCTA group and 338 in the MPI group). Over six months, 72 patients were lost to follow-up for nonfatal MACE, leaving 627 patients with complete six-month follow-up. The mean age was 50 in both groups and 45.2% and 47.0% were male in the CCTA and MPI groups, 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 1:1 fashion to undergo CCTA or MPI.
Was allocation concealed? Was it possible to subvert the randomization to ensure a patient would be "randomized" to a particular group?	Likely yes. "The randomization scheme was generated in a 1:1 ratio stratified (by site), alternating block design. All sites received their own site-specific, randomization envelopes. Once a patient was enrolled and the consent form had been signed, the next sequentially numbered envelope was opened and included the randomization arm and the patient's unique study identification number." (p. 1417) While the use of a seemingly non-random block design may allow clinicians to deduce the sequence and hence subvert the process, this seems unlikely (allocation concealment).
Were patients analyzed in the groups to which they were randomized?	No. The authors mention that 50 patients were excluded after they either failed to complete the protocol or withdrew consent. Only patients who completed the protocol (CT vs. MPI) were included in the analysis (intention to treat vs. per protocol analysis).
Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to age, gender, weight/BMI, presence of medical comorbidities, and TIMI score. The authors do not report baseline vital signs or home medications.
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?	Somewhat. "The MACE events were adjudicated by a blinded clinical events committee using standard American College of Cardiology Foundation/American Heart Association criteria." (p 1416) There is no mention of blinding to those assessing other outcomes (observer bias).
Was follow-up complete?	Mostly yes. There were 699 patients with complete early results (including the primary outcome) included in the analysis. There were 72 (10.3%) patients lost to follow-up for nonfatal MACE at 6 months (8.3% in the CCTA group, 12.4% in the MPI group). All-cause mortality data were available from the Social Security Death Index for 698 of 699 (99.9%) patients.
What are the results?	
How large was the treatment effect?	**CCTA Group (n = 361)** o Minimal CAD ruled out in **297 (82.2%)** o ≥70% stenosis in **13 (3.6%)** o 25–70% (intermediate) stenosis in **37 (10.2%)** o Non-interpretable scans in **14 (3.9%)** • **Disposition after CCTA:** o Of 297 with normal/minimal disease, **262 (88.2%) discharged home within 6 h** o Rest-stress MPI performed in **37 (10.2%)** o ICA performed in **24 (6.6%)** • **Revascularization:** o **13 patients** underwent revascularization (9 PCI, 4 CABG) • **6-month follow-up:** o **No deaths or late ACS** o **Total MACE:** 17 of 330 (5.2%)

	▪ 14 revascularizations (1 AMI, 7 unstable angina) ▪ 3 additional unstable angina cases **MPI Group (n = 338)** • **Findings on initial MPI:** o Normal/probably normal in **304 (89.9%)** o **271 (89.1%)** of these discharged home within 6 h • **Additional testing:** o ICA in **21 (6.2%)** o **8 PCI** (4 NSTEMI, 3 unstable angina) o **3 additional** unstable angina not revascularized • **6-month follow-up:** o **No deaths or post-discharge ACS** o **Total MACE:** 12 of 297 (3.7%) ▪ 8 revascularizations (4 AMI, 3 unstable angina, 1 AMI non-revascularized) **Comparative Outcomes (CCTA vs. MPI)** • **ICA during index visit:** 6.7% vs. 6.2% (p = 0.80) • **Revascularizations:** 3.6% vs. 2.4% (p = 0.34) • **AMI:** 0.3% vs. 1.5% (p = 0.11) • **Mortality:** 0 vs. 0 • **6-month cumulative events:** 5.2% vs. 3.7% (p = 0.36) • **No late ACS or deaths in either group** **Primary Outcome — Diagnostic Efficiency** • **Time to diagnosis:** o CCTA: median **2.9 h** o MPI: median **6.2 h** o → **54% faster diagnosis** with CCTA (p < 0.0001) **Secondary Outcomes** • **ED cost of care:** o CCTA: **$2,137** median o MPI: **$3,458** median o → **38.2% cost reduction** (p < 0.0001) • **Radiation exposure:** o CCTA: **11.5 mSv** o MPI: **12.8 mSv** (p = 0.02) • **Safety (6-month MACE among normal/near-normal tests):** o CCTA: 2 of 268 (0.8%) o MPI: 1 of 266 (0.4%) (p = 0.29) o **No deaths in either group**
How precise was the estimate of the treatment effect? (i.e. what 95% CIs were associated with the results?)	The authors do not provide confidence intervals for the differences in outcomes. While the p-values suggest a statistically significant difference in several outcomes, confidence intervals would have provided additional clinical information and improve our understanding of the impact of these findings (limitations of p-values).
How can I apply the results to patient care?	
Were the study patients similar to my patient?	Likely yes. This study was conducted at 16 hospitals 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?	No. The primary outcome was time to test results, which is of unclear importance. The authors did not measure ED or hospital length of stay or patient satisfaction.
Are the likely treatment benefits worth the potential harm and costs?	Unclear. This study suggests that the use of CCTA compared to rest-stress MPI reduced the time to ED diagnosis by a median 3.3 hours with no increased risk of major adverse cardiac events and significant difference in downstream testing/treatment (i.e. ICA). 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 ≤ 4 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.

Limitations:

1. **This trial included a convenience sample of patients, with no comparison of included patients to those who were eligible but not included.**
2. **While unlikely, the use of a seemingly non-random block design may allow clinicians to deduce the sequence and hence subvert the randomization process (allocation concealment).**
3. **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.**
4. **Although the authors calculated a sample size of 704 patients, only 699 completed the protocol and 627 completed 6-month follow-up.**
5. **While the authors note a significant decrease in time to diagnosis with CCTA, they do not report ED length of stay, a more patient- (and provider-) centered outcome.**

Bottom Line:

This multi-center randomized controlled trial suggests that the use of CCTA compared to rest-stress MPI reduced the time to ED diagnosis by a median 3.3 hours with no increased risk of major adverse cardiac events and significant difference in downstream testing/treatment (i.e. ICA). 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 ≤ 4 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.