EVMS EM Critical Review Form
Therapy Articles

Resident: JD LANDON Date: 11/27/20

Citation: Newby D, et al. Coronary CT Angiography and 5-Year Risk of Myocardial Infarction. SCOT-HEART Investigators. N Engl J Med. 2018 Sep 6;379 (10):924-933

Objectives: To determine whether including CCTA in addition to the standard of care in patients with "stable chest pain" is associated with either death from CAD or non-fatal MI over a 5-year follow-up period.

Methodology: open-label, randomized, multi-center, parallel-group trial that took place in Scotland and extended the follow-up period from SCOT-HEART (6 weeks early up to 1.7 yrs)

Guide		Comments
I.	**Are the results valid?**	**.**
A.	**Did experimental and control groups begin the study with a similar prognosis (answer the questions posed below)**	Yes. Baseline characteristics of the two groups were similar on all recorded demographic datapoints (Table 1).
1.	Were patients randomized?	Yes. Patients were randomized using 1:1 computer generated randomization but ALSO, incorporated the use of minimization to balance distribution of age, sex, body-mass index, diabetes mellitus, history of coronary heart disease, and atrial fibrillation among the groups.
2.	Was randomization concealed (blinded)?	No. The patients and providers were aware who was receiving standard care vs standard care +CCTA which predisposes to ascertainment bias.
3.	Were patients analyzed in the groups to which they were randomized?	Unclear. Authors claim to use intention to treat analysis (pp. 926) however then add "Missing data were removed from the analyses" which is not typically how ITT analysis is performed.
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Except for the fact that who was referred to cardiology outpatient clinic for 'stable chest pain' was entirely based on the PCP impression and was not externally adjudicated. There was mention of patients referred directly from the ER (more likely to represent acute vs. "stable" CP) however, these patients were not clearly identified or analyzed separately.
B.	**Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)**	
1.	Were patients aware of group allocation?	Yes.
2.	Were clinicians aware of group allocation?	Yes.
3.	Were outcome assessors aware of group allocation?	Uncertain. No mention specifically whether those doing data analysis were blinded to the study objectives. Regarding outcome

		adjudication, "*in cases of uncertainty, events and causes of death were categorized by two of the authors, who were unaware of the trial assignments"*
4.	Was follow-up complete?	Unclear. Follow-up is reported as a median of 4.8 years range 3-7 years. All of the follow-up was by EMR and no in-person or phone f/u occurred.
II.	**What are the results (answer the questions posed below)?**	
1.	How large was the treatment effect?	Primary: The rate of the primary long-term end point (death from coronary heart disease or nonfatal myocardial infarction) was lower in the CTA group than in the standard-care group 2.3% in the CTA group vs. 3.9% in the standard-care group; The Absolute Risk Reduction ARR is 1.6%. The relative difference or the hazard ratio 2.3/3.9 = 0.59; 95% CI, 0.41 to 0.84; P = 0.004) the NNT to identify one person likely to benefit from CCTA = 1/1.6 x 100 is 62 patients. Secondary: Patients assigned to CTA were more likely than patients assigned to standard care alone to have commenced preventive therapies (19.4% vs. 14.7% odds ratio, 1.40; 95% confidence interval [CI], 1.19 to 1.65) Patients assigned to CTA were more likely than patients assigned to standard care alone to have antianginal therapies (13.2% vs.10.7% odds ratio, 1.27; 95% CI, 1.05 to 1.54). At 5 years, there was no difference between the groups in the frequency of invasive coronary angiography; the procedure was performed in 23.6% in the CTA group and in 24.2% in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13) Though there was an increase in invasive studies in the initial SCOT-HEART analysis @ 6weeks, there was no difference in the frequency of coronary revascularization between the groups at 5 years 13.5% in the CTA group and 12.9% on the standard care group
2.	How precise was the estimate of the treatment effect?	As above.
III.	**Can I apply the results to patient care (answer the questions posed below)?**	
1.	Were the study patients similar to my patient?	No. These are outpatient referrals from PCP office for 'stable chest pain.' Pre-test probability in these patients was likely higher than in our CP Obs. patient population which would likely portend an even lower event rate for identifying significant CAD. Additionally, the prevalence of obesity and metabolic syndrome is higher in our local population. Also, the quality and consistency of primary care and preventative medicine is likely better in Scotland as compared to Norfolk, VA.

2.	Were all clinically important outcomes considered?	No. The primary endpoint seemed reasonable and was patient-centered. There was no economic analysis. There was no assessment on LOS. Excluded patients >75 y/o. They perhaps could have analyzed whether one group had more ED visits after starting on treatment.
3.	Are the likely treatment benefits worth the potential harm and costs?	In general, I would argue yes. However, this study evaluated a test not a treatment and is only connected to the primary outcome via 'preventative medical management'. This presents a huge number of potential confounding variables regarding what was actually the true treatment effect of 'did people actually take their medications or not?" A coronary CTA in a sicker population that utilizes the ED for much of their primary care may in fact be more effective at diagnosing CAD and starting appropriate therapy. Additionally, it seems to be a highly sensitive testing resource for ruling out CAD which in our population has significant utility when the return for similar complaints multiple times. That stated it may lead to more overtesting in the initial 6 weeks and an NNT of 63 CCTA's to prevent 1 fatal or non-fatal MI over 5 years may be considered high by some.

Limitations:

- Measurement Bias - They used ICD10 codes to determine outcomes, no adjudication group to evaluate for error in identification of cases
- High risk of random error = Underpowered
    - Sample size calculated based on 13% incidence of primary endpoint, only had 3.9% incidence in the trial
    - This reduces statistical power from 80% to roughly 35%
    - Only 42% of all eligible patients were enrolled predisposing to selection bias
- Ascertainment bias: Open-label study – who decides what is 'stable chest pain' (aka PCP referral). Non-EM study
- No standardization of "standard medical treatment"
- No measurement of lifestyle alterations over time which likely played a sig. role in a slightly smaller event rate.
- Study predates high sensitivity troponin and almost universal use of 320 slice scanners.
- Fragility Index
    - If 10 cases of MI/CAD death were added to CTA group or 10 cases removed from standard care the p value would be greater than 0.05.

Bottom Line:

- In non-ED patients with evidence of "stable" chest pain and intermediate CAD risk, CCTA can favorably impact preventative strategies for the development of clinically significant CAD.
- There is insufficient evidence to compel the use of CCTA in low risk ED patients when compared to standard care.
- I would suggest that the coronary CTA may end up playing a larger role in the ED to help definitively rule out unknown CAD though in the population represented, 63 CCTA's would need to be performed to prevent one MACE
- At the end of the day, the evidence in support of quality preventative health care and appropriate medical management remains fundamental in preventing CAD death and MI. The population best served by ED CCTA as yet does not appear to be clearly defined.