DEM Journal Club

Article Appraisal

Article: Coronary Angiography after Cardiac Arrest without ST-segment Elevation (COACT)

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Background and Study Objective(s):

Cardiac arrest is common and has high morbidity and mortality. Ischemic heart disease is the most common cause of cardiac arrest, and is present in approximately 70% of these patients. Early coronary angiography (CAG) and percutaneous coronary intervention (PCI) have been shown to be beneficial in patients presenting with ST-elevation Myocardial Infarction (STEMI) on ECG after cardiac arrest as compared to delayed treatment, and this is supported by current guidelines. However, it is unknown whether immediate CAG and PCI is of benefit versus delayed treatment in patients presenting with cardiac arrest but who do not have ST elevation on their ECG. In previous studies 25-58% of patients in this group have unstable coronary lesions, so it has been theorized that early CAG and PCI may be of benefit to this group as well. There have been no prior RCTs on this topic and prior observational studies indicated a potential benefit to early CAG +/- PCI.

This study aimed to answer the following question: In patients who are successfully resuscitated after cardiac arrest in the absence of STEMI, is a strategy of immediate coronary angiography with PCI if necessary better than delayed angiography with respect to overall survival?

Study Design:

This was a multi-center, open label, randomized controlled trial that took place at 19 tertiary care hospitals based in the Netherlands between January 2015 and July 2018. Patients were randomized 1:1 into each group, immediate vs delayed angiography and PCI. Informed consent was waived for the intervention and obtained later for use of trial data. The immediate angiography group aimed to received CAG +/- PCI within 2 hours of randomization, while the delayed angiography group received CAG and PCI after neurologic recovery, which was usually after ICU discharge (median 120 hours). Aside from the intervention both groups received the same standard of critical care management as per the treating physician. The trial protocol was published prior to initiation of the study and there were no major alterations in the protocol during the trial. The trial was industry sponsored but industry was not involved in the design, implementation, manuscript preparation or publication processes.

Participants were recruited consecutively from OHCA patients arriving at participating emergency departments. Inclusion criteria were out-of-hospital cardiac arrest with initial shockable rhythm found to

be unconscious after return of spontaneous circulation. Exclusion criteria included STEMI on ECG, sustained shock, GFR <30, pregnancy, obvious non-coronary cause of arrest, suspected intracranial hemorrhage or stroke, refractory arrhythmia, poor premorbid status (CPC 3 or 4), and known DNR.

Results:

There were 552 patients enrolled in the trial, with 273 in the immediate and 265 in the delayed coronary angiography groups. Data from 14 patients (2.5%) data was not available because the patient did not provide deferred informed consent. Baseline characteristics were similar between the two groups, except for a long median time to target temperature of 5.4 hours vs 4.7 hours in the immediate and delayed groups, respectively.

Treatment with CAG was received by 97% of the immediate group and 65% of the delayed group. PCI was performed in 33% fo the immediate angiography group and 24.2% of the delayed angiography group. The rate of unstable coronary lesions on aniography was 12.1%, and the rate of acute thrombotic occlusion was 4.1%. Median time from randomization to treatment was 0.8h in the immediate group and 120h in the delayed group. In terms of crossover, 13 patients in the immediate group were treated with a delayed strategy, and 3 patients in the delayed group were treated with an immediate strategy. 38 patients in the delayed group underwent urgent aniography for clinical deterioration. Over 90% in both groups were treated with targeted temperature management.

The primary outcome of survival at 90 days was 64.5% in the immediate angiography group compared to 67.2 in the delayed angiography group (OR 0.89, 95% CI 0.62-1.27, p=0.51). No differences were found in any of the secondary outcomes. In both groups, three times as many patients died of neurologic causes as from cardiac causes. A sensitivity analysis was performed which showed no significant difference between the groups in the primary outcome. Subgroup analyses were performed and showed a difference in treatment effect based on age greater than or less than 70 years (P = 0.007 for interaction), or based on a prior history of coronary artery disease (P= 0.009 for interaction).

Validity of Results:

This study addressed a clear and focused question, has strong internal validity, and the methodology was robust. The protocol was published prior to the trial, and no significant alterations were made. The randomization was appropriate, with minimal cross-over between arms, and they had a high rate of follow-up. One limitation was that the trial was not blinded, though with this type of intervention it is likely not feasible. Groups were similar at baseline, and outside of the intervention treatment was predominantly the same. Of note, the time to targeted temperature management was longer in the immediate angiography group, perhaps because it is more difficult to effectively cool a patient while simultaneously attempting CAG. This may have influenced the results in favour of the delayed angiography group if some of the benefit of TTM was lost, though we have no strong data to suggest that delays of a few hours change the effect of that treatment. They used reasonable and appropriate statistical methods to analyse their data, and presented it well. Ideally, a risk ratio be better used in an RCT than an odds ratio, though in this study it would not have affected the results.

Generalizability of Results:

There are a few significant limitations to the generalizability (external validity) of the trial. This was a large multi-center trial, however it was only performed in one country. Likely the Netherlands has a similar standard of healthcare seen in developed countries. Most importantly, the rate of unstable and acute thrombotic coronary lesions in this population was much lower than seen in previous observational studies. The rate of unstable lesions was 15-20% in this trial, while in similar populations previous rates have been between 25-58%. As a result, PCI was only performed in 30%% of patients, despite more than 80% receiving CAG. This is extremely important when evaluating the efficacy of an intervention that is dependent on lesions present to treat in order to have a benefit. If you don’t have patients with the disease, the treatment will not be effective.

The Bottom Line:

This is the first randomized controlled trial comparing immediate versus delayed coronary angiography after cardiac arrest without ST-elevation. This was a well designed trial showing no difference between these two strategies with respect to the primary outcome of 90 day survival. While it has strong internal validity, there are several limitations to external validity of these results and additional trials to confirm or refute these results are ongoing. Clinicians should have a conversation with their local interventional cardiologist and advocate for their patients to receive optimal treatment if clinical assessment indicates that CAG may be of benefit.