DEM Journal Club

Article Appraisal

Article: Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay

Date of Journal Club: January 7, 2016

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Background and Study Objective(s):

The diagnosis or exclusion of an MI is an essential branch point in some patients' pathway of care in the ED. With standard troponin (trop) assays, this process can take up to 6 to 8 hrs depending on the approach used, however in the era of high sensitivity (HS) trop, increasing numbers of studies have attempted to assess how this modality could improve the precision or speed with which MIs are diagnosed in the ED.

This study is a validation of a 1hr HS trop algorithm previously published by the same authors. This algorithm aims to rule in or rule out an MI using the HS trop at presentation and the absolute change at 1-hr and has been touted as an approach to potentially shorten ED stays, and thus lessen ED crowding, while maintaining patient safety. The data for this paper comes from a currently ongoing, larger trial called the APACE trial.

Study Design:

A European prospective cohort study 1320 subjects was carried out. This evaluated based on baseline trop and rise after 1hr. Baseline <12ng/L and change within 1hr of <3ng/L ruled out MI. Baseline >52ng/L or change within 1hr of >/= 5ng/L ruled in MI. Anything in between was deemed the observational zone. Inclusion criteria were patients presenting with non-traumatic chest pain with onset or peak <12hrs or “other symptoms of MI.”

The lead author was contacted in an attempt to obtain a more precise description of “other symptoms of MI” and he indicated this term referred to other anginal pain patterns eg: radiating to back, shoulder or jaw, but not other symptoms such as dyspnea. Exclusion criteria were: renal disease requiring hemodialysis and STEMI on ECG.

Results:

The authors found that 75.9% of subjects were able to be dispositioned using the algorithm and 17.3% of subjects ruled in for MI. Cumulative mortality in the rule-out group at 30 days was 0.0%. The following test characteristics of the HS trop 1-hr algorithm were reported by the authors:

Sensitivity: 99.6% (95%CI: 97.6%-99.9%)
Specificity: 95.7% (95%CI: 94.3%-96.8%)
Negative Predictive Value: 99.9% (95%CI: 99.3%-100%)

Positive Predictive Value: 78.2% (95%CI: 72.1%-83.6%)

The authors did not report likelihood ratios, however we calculated them from the data provided in the paper and found the following:

+LR = 0.996/(1-0.957) = 23.2
-LR = (1-0.996)/0.957 = 0.004

Validity of Results:

The general sentiment of Journal Club attendees was that this study investigated an important question and its power of this study led to impressively narrow 95% confidence intervals. Three major potential sources of bias were raised and discussed in detail.

1. Incorporation Bias:
The final diagnosis of MI was determined by two independent cardiologists who included the HS troponin being tested in their assessment of the final diagnosis. Being aware of the presentation and 1-hr HS trops had the potential to influence their final diagnosis, and thus artificially improve the determined accuracy of the test.

2. Losses to Follow Up:
The number of patients lost to follow up was not reported and these missing numbers may be masking a higher mortality than the study reported.

3. Study Population:
The inclusion criteria meant that atypical presentations of MI, and the wide range of patients trop is applied to in North America, may not have even been included in the study. As a result, there may have in fact been more MI's in patients going through the ED than accounted for, potentially altering the test characteristics in a different population.

Generalizability of Results:

Significant concerns were raised over the very high prevalence of MI in the studied patient population. The 17.3% rate was felt by Journal Club attendees to be significantly higher than the prevalence of MI in the population we apply trop testing to in North American EDs (as an aside, there was some discussion as to whether this reflected a more judicious use of diagnostic testing in Europe, or a more judicious use of EDs and thus a different population than we see in North American EDs).

Using this test in our ("lower pre-test probability") population would be anticipated to result in worse specificity and a significantly lower PPV than the 78.2% reported, however, using this test in our population would also be anticipated to increase the NPV potentially making it a very good "rule out test" when negative, with a major time-savings advantage over current approaches. It was noted that this study was funded by an HS trop assay company and it is not clear whether or not this algorithm would be reproducible using HS assay machines from other companies.

The analogy of various d-Dimer assays, and their different diagnostic performances was raised. Finally, it was noted that the study looked only at diagnosing NSTEMI and not all ACS. As such, the results cannot and should not be extrapolated to be applicable to rule in or out unstable angina. Concerns were raised by Journal Club attendees that a misunderstanding of this could cause misuse of the algorithm and could also make referrals to cardiology for unstable angina more challenging. It was noted that St. Paul's Hospital will be switching to an HS trop assay in the very near future and Vancouver General Hospital is embarking on a study of this modality.

The Bottom Line:

The results of this study add to the increasing amount of promising information regarding the potential for HS trop to accelerate the diagnosis of MI in ED patients. However, the generalizability of the precise diagnostic test performance results to our population is questionable, in particular because the prevalence of MI we obtain a trop on is much lower than that of the studied population. Although the test performance (specifically the low specificity) precludes this to be used as the sole rule in test without a significant number of false positives, the algorithm

proposed may be applicable to our population as more rapid rule out MI test.

The bottom line impression of Journal Club attendees was that implementation of this or any similar algorithm at a given site would require a multidiscliplinary approach that includes EM, Lab Medicine and Cardiology to establish clear and collectively agreed upon parameters for use and interpretation. Further research, and real world experience in BC sites who are already implementing HS trop, will likely help clarify the future role of this modality and whether or not it replaces standard trop, as some suspect it will.