Reviewer’s report

Title: Routine Creatine Kinase Testing Does Not Provide Clinical Utility in the Emergency Department for Diagnosis of Acute Coronary Syndromes

Version: 0 Date: 22 May 2019

Reviewer: Arash Mokhtari

Reviewer's report:

In this study by Wiens et al. they aimed to evaluate the utility of CK in a setting where hs-cTnT is used. This was a retrospective review of patients seeking care in their hospital with cardiac complaints, where they focused on patients with a non-diagnostic hs-cTnT and positive CK, and conclude that routine CK testing has no added benefit.

The manuscript is well written, and I agree with the conclusion. I do however have some comments:

1. Did you evaluate CK or CK-MB? I'm assuming CK-MB, but please specify. If CK, then this should be properly addressed in the limitations section. If it was CK-MB, please change "CK" to "CK-MB" throughout the manuscript.

2. You mention "bloodwork as per a regional protocol". Please describe the protocol used in your institution: Do you recommend 1h, 2h, or 3h hs-cTnT and CK testing? How do you define a significant change in hs-cTnT in your protocol? What is the cut-off you use for CK? Since you are relying on diagnoses made by the attending cardiologist, it would be helpful for the reader to get a better understanding of how the diagnoses were made.

3. Please specify the characteristics of the assays used (hs-cTnT and CK) such as the upper reference limit of the assay and if you have a institutional specific decision limits.

4. You specified a significant change as an increase of ≥5 ng/L. Although this is the preferred delta for a 1h hs-cTnT measurement, it is lower than recommended delta values for 2h, 3h, or 6h hs-cTnT (Mueller et al. Clinical chemistry. Jan 2012;58(1):209-218; Biener et al. International journal of cardiology. 2013;167(4):1134-1140; Reichlin et al. The American Journal of Medicine. 2015;128:369-379). You could have thereby possibly missed patients with a non-significant change on a 2h, 3h or 6h hs-cTnT who should have been included with the 2012 patients you assessed as TnT-/CK+. You should consider addressing this in the limitations section.

5. As per my previous comment, you defined a significant change as an increase ≥5 ng/L. Did you not consider an elevated hs-cTnT showing a significant fall on serial testing as significant and were these patients not diagnosed with acute myocardial injury or AMI?

6. The primary outcome of index visit AMI, was this based on the discharge diagnosis?
7. For both the primary and secondary outcomes, you describe a process of thorough chart review. Did the reviewers adjudicate the final diagnoses, or just extract specific discharge diagnoses? If diagnoses were adjudicated, were the reviewers blinded to the CK levels? I'm assuming they were not, which would then introduce potential bias in the adjudication process.

8. Do you have any data on baseline characteristics for the patients? Age, gender and especially AMI prevalence at least would be helpful.

9. A total of 2012 patients had a non-diagnostic hs-cTnT and positive CK. How many of these had a hs-cTnT >14 ng/L? One could argue that this is the group were it would be most important to evaluate whether CK has a role. Among these 2012 patients, some patients must have had negative serial hs-cTnT, and in these patients AMI is ruled out with a very high negative predictive value and CK is not needed. It's those with elevated hs-cTnT without significant change where the evaluation of the potential role of CK (-MB) is most interesting. Since only 1 patient among these 2012 was diagnosed with AMI, I'm wondering whether the proportion of patients with a hs-cTnT >14 was actually very small? Do you also have data on renal function on these patients?

10. You state in your discussion that, except for the 1 missed AMI, all patients with AMI had a trending hs-cTnT. Does that mean that patients with elevated hs-cTnT without significant change as a rule were never diagnosed with AMI? It is not completely uncommon to see this pattern in late presenters and in some studies they constitute 10-25% of all AMIs (Morrow et al. J Am Coll Cardiol. Oct 1 2013;62(14):1239-1241). It therefore makes me wonder if there could be some misdiagnosed patients in your TnT-/Ck+ group?

11. Among the 2012 patients, what was the most common final diagnoses?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
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