Peer Review File
Article information: https://dx.doi.org/10.21037/jlpm-22-64

Reviewer Comments
Reviewer A
Comment 1: Check sentence line 27 "The challenge …. these assays is used in..."
Reply 1: Thank you for this. The abstract has been revised request of the editor and this sentence has been clarified.

Comment 2: In line 40, 41, 100 and 119 different abbreviations for hs cTn are used.
Reply 2: Thank you for this. The manuscript has been checked to ensure that the appropriate abbreviation for hs cTn is used.

Comment 3: Check sentence in line 55 "…able.."
Reply 3: Thank you for this. The English is been corrected.

Comment 4: In line 122 suggestion to change "dysfunction" in subtitle to "challenges". To my opinion this better fits with the point to make and this expression is already used by the author in the abstract. In our and some other countries the cardiology department has its own ED, the so called cardiac emergency department, that maybe simplifies implementation of the algorithms and (relatively) keeps down the amount of non-specific testing…?
Reply 4: Thank you for this suggestion which I have adopted.

Comment 5: In line 143 cardiac troponin T was not abbreviated and % of troponins between 3-50 ng/L was not described. Also check "… is predicated by appropriate…".
Reply 5: I have added the abbreviation and the percentage of the total requests as requested.

Comment 6: Similarly with above, in line 162 "utilization of rapid assessment protocols remains low" might differ between countries, though I totally agree with the "problems" when dealing with the observe-group.
Reply 6: Thank you for this comment. Unfortunately it is very difficult to assess reliably on a country by country basis the extent to which rapid assessment protocols have been implemented. We have undertaken a more recent survey for which we are still analysing the data. A preliminary analysis of survey seems to confirm that transition to hs cTn is mostly complete. This is also the view of industry who have stopped supplying all intend to stop supplying anything other than high sensitivity troponin assays. It is more difficult to obtain a reliable assessment other than in broad brush strokes on how these assays are being used. It would be very nice to know to what extent there has been country by country uptake but it is difficult to obtain this data. In the UK as a rapid diagnostic algorithms have been endorsed by NICE, uptake is relatively high certainly. In the US with the US (from discussions with colleagues)

uptake appears less widespread. However, I do not really feel I have the data to make other than fairly general statement at this point.

Reviewer B

Comment 1: This paper concisely summarizes the definition of a high-sensitivity troponin measurement system, the problems of a conventional troponin measurement system, and the process and problems of the transition from the convention to high-sensitivity assay.

I would like to suggest only correction.

Line 39-40 and 53 There was repeated mention of abbreviations for expressions.

Reply 1: Thank you for the comment. I think I have corrected the matter though I think it's important to distinguish between hs cTnT and hs cTnI.

Reviewer C

Comment 1: The paper is well written and does not require any modification with the exemption of a very few listed below:
p4 L65 - provide the source of the Roche diagnostics cTnT assay_
Reply 1: I am not quite sure what the referee means here. The head office for Roche is in Basel but there are usually country based subsidiaries.

Comment 2: p4 L68 The majority of the existing cTnI assays provided acceptable analytical68 performance characteristics. please provide the reference
Reply 2: I have added a reference to the IFCC tables which cover the conventional sensitive troponin assays.

Comment 3: p5 L75. please provide the references for the surveys listed
Reply 3: These studies are already referenced within the manuscript.

Comment 4: p7 L 141 In the most recent audit of requesting practice at St George's Hospital... - please provide the reference
Reply 4: I have added the relevant references.

Reviewer D

Comment 1: L93-94: "Currently in Europe, there is almost complete transition to high sensitivity assays [14] with laboratories either currently using or intending to use hs cTn". Can the author include an estimation around the conversion percentage for other geographies, including the US, and Asia Pacific?
Reply 1: I would be delighted to be able to do this sadly am unable to do so. Detailed data on the US and Asia Pacific is currently difficult to obtain. We had hoped that are most recent iteration of the questionnaire would achieve more global coverage but

responses from both areas have been limited. On discussions with manufacturers (see point above) the intention is to withdraw everything other than high sensitivity assays and only retain non-high sensitivity assays where regulatory compliance is not been given for the high sensitivity version.

Comment 2: L148: "Similar problems with sample timings were seen on switching to a 0-2 hour repeat testing protocol with a diagnostic sample taken at three hours from admission". Did the author intent to write "two hours from admission"? What is meant by admission? Admission to the ED or into the hospital?
Reply 2: No. The study compare the diagnostic equivalence of the 0-2 hour protocol with samples taken on admission and at three hours. All samples were taken into far as we were aware at the time of hospital admission, this being the same as the time of admission to the ED according to our information system. I have clarified the text.

Comment 3: L150-151: "... and between the second and third samples the median interval was 1.2 hours (interquartile range 0.9-1.9 hours". What was the 'appropriate' time interval between the second and third sample? Was there a guidance around this in the protocol?
Reply 3: I have added some clarification. Anticipated time between first and second samples for a 0-2 hour protocol was two hours and between the 2 and the 3 hour sample 1 hour.

Comment 4: L161: "The major problem at present is the widespread use of non-specific troponin testing." and L162 "Currently, utilization of rapid assessment protocols remains low and problematic". These are rather strong statements, and it would be helpful if the author can elaborate on this in the body of the manuscript, including a quantitative description of the challenges.
Reply 4: Rather an assessment of where we are at present. In respect of the question of non-specific troponin testing, this is a much discussed problem. I have added some further comments within the text although I feel it is difficult to add much more to that which is already stated. I have added some further discussion of the question of what may be the barriers to introduction of these techniques, as well as suggesting some solutions.