Reviewer’s report

Title: A Randomised Controlled Trial of Ivabradine and Atorvastatin in Emergent Orthopaedic Lower Limb Surgery: A Mechanistic Study of Peri-Operative Myocardial Injury and its Prevention Using Computed Tomography Coronary Plaque Imaging and Novel Biomarkers of Cardiovascular Stress and Lipid Metabolism

Version: 2 Date: 11 June 2014

Reviewer: Stacy O’Blenes

Reviewer’s report:

Major Compulsory Revisions:

1. When it comes to the primary outcomes tested in this study (perioperative MI incidence and magnitude after randomization to Rx therapy), the type of study (RCT) and statistical analyses used are appropriate. However, correlations between cardiac biomarkers, platelet activity markers, plaque burden and perioperative MI would have been better looked into with separate observational studies, which would have required the application of different protocols and stat methods. There are many assumptions of causality that need to be made to confirm or invalidate the complex mechanistic hypotheses formulated by the investigators. As a result, I don’t think that the study design – or at least how it is reported – adequately test them and will lead to significant conclusions.

2. Outcomes: Unclear definitions of primary outcomes. Many secondary outcomes for which patients will be screened for during follow-up don’t appear in the list. Where is the LFTs outcome coming from? I would have liked measurement units to be given for each outcome. How is plaque burden evaluated and reported (there’s a clear protocol on the acquisition technique but not on how it will be used)?

Minor Essential Revisions

1. Randomization: OK description. What about blinding? Please Clarify

2. Sample size calculations: Would have been better reported in words... e.g. “we estimated that ___ patients would be required to have a power of ___% (alpha = ____, two-tail) to identify a difference PMI incidence of ____.”

3. The writing quality is fair but there are many typo and spelling mistakes, inconsistencies in capitalization, incomplete sentences and inappropriate use of verb tenses. The overall quality of the abstract section is poor and doesn’t summarize well the full article.
4. The background section, despite being quite interesting, appears too long as compared to the methods section and lacks a clear structure as compared to other study protocols published on Trials.

5. Discussion: I would have appreciated a word on feasibility and expected impact as opposed to a summary of the background section and hypotheses.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

N/A