Author's response to reviews

Title: Aortic stiffness as a marker of cardiac function and myocardial strain in patients undergoing aortic valve replacement

Authors:

Emaddin Kidher (e.kidher@imperial.ac.uk)
Leanne Harling (leanne.harling@imperial.ac.uk)
Hutan Ashrafian (h.ashrafian@imperial.ac.uk)
Hatam Nasse (hatam.naase@imperial.ac.uk)
Darrel Francis (d.francis@cheerful.com)
Paul Evans (paul.evans@sheffield.ac.uk)
Thanos Athanasiou (t.athanasiou@imperial.ac.uk)

Version: 2
Date: 28 May 2014

Author's response to reviews: see over
Reviewer 1 (Yasir Abu-Omar):

**Reviewer's report:** This paper is very well-written.

**Major Compulsory Revisions:** None

**Minor Essential Revisions:**
1. The potential confounds on PWV measures should be discussed - e.g. Aortic atherosclerosis, drugs etc.
2. The outcome measure of leg oedema is subjective and may be seen in many patients following cardiac surgery.
3. The conclusions are somewhat too optimistic in that the measure in question still needs further validation before being implemented as a marker of clinical functional status. As such, it remains a research tool.

**Discretionary Revisions:** None

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

- **Comment 1:** The potential confounds on PWV measures should be discussed - e.g. Aortic atherosclerosis, drugs etc.

**Response to comment 1:**
Unfortunately, we did not assess these particular confounders in this study, however, we agree with the reviewer on the importance of this issue and as such have added a discussion on this to our study limitations.

**Changes in response to comment 1:**

“Limitations”, Page 13, the following has been added: “Future larger studies should also examine the role of potential confounders not assessed here that may affect the relationship between PWV, cardiac function and myocardial strain. These include the degree of aortic atherosclerosis, aortic calcification, type and duration of pharmacotherapy.”

- **Comment 2:** The outcome measure of leg oedema is subjective and may be seen in many patients following cardiac surgery.

**Response to comment 2:** We thank the reviewer for this comment. We agree with the reviewer that leg oedema may be a subjective marker after cardiac surgery. However, we do believe that further investigation into the possible relationship between PWV and post-operative leg oedema may be of interest for future research. As such, we have retained leg oedema as a secondary finding in our results. However, we have now added a discussion as to the subjective nature of this assessment and thus the limitations imposed on further interpretation of this outcome in the current study.
Changes in response to comment 2:
“Discussion”, page 13, the following has been added: “Third, despite the significant relationship between PWV cut-off and post-operative leg oedema (r=0.38, OR 11.77, 95%CI [1.26–109.77]), leg oedema is a subjective measure with the potential to be influenced by several potential confounders arising during the perioperative period. Furthermore, the exact mechanism of this relationship is unknown, and further research is therefore required to evaluate this association in more detail.”

☐ Comment 3: The conclusions are somewhat too optimistic in that the measure in question still needs further validation before being implemented as a marker of clinical functional status. As such, it remains a research tool.

Response to comment 3: We thank the reviewer for this comment and agree with the suggested correction. We have now made the necessary changes to our ‘Conclusions’ section to reflect this.

Changes in response to comment 3:
In the “Abstract” (page 2), and “Conclusion” (page 14), the following amendments have been made: “These findings provisionally support the use of perioperative PWV as a non-invasive marker of clinical functional status, which when used in conjunction with biomarkers of myocardial strain such as BNP, may provide a holistic functional assessment of patients undergoing aortic valve surgery. However, in order for PWV assessment to be translated into clinical practice and utilised as more than simply a research tool, further validation is required in the form of larger prospective studies specifically designed to assess the relationship between PWV and these functional clinical outcomes.”

Reviewer 2 (A Protopapas):

Reviewer's report: Thank you for the opportunity to read your manuscript
Major Compulsory Revisions: None
Minor Essential Revisions: None
Discretionary Revisions: None
Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Response to Reviewer 3: We thank the reviewer for the positive comments.
Changes in response to Reviewer 3: No changes are required.
Reviewer 3 (Vanash Patel):

Reviewer's report: There are no English language errors. The paper is well written and has an important message and supports novel markers of cardiac function. The statistical analysis is sound.

Major Compulsory Revisions: None

Minor Essential Revisions: None

Discretionary Revisions: None

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Response to Reviewer 3: We thank the reviewer for the positive comments.

Changes in response to Reviewer 3: No changes are required.