Author’s response to reviews

Title: EuroScore 2 for identification of patients for transapical aortic valve replacement - a single center retrospective in 206 patients.

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Author’s response to reviews: see over
Dear Editorial Board, Dear Reviewers,

we would like to thank you for giving us the opportunity of revising our manuscript. Please find below specific answers to all of your raised objections. We tried to implement all of your suggestions into the enclosed manuscript and hope to have met your expectations.

For the authors
With best regards

Andreas Goetzenich

Reviewer 1:
Major Compulsory Revisions

1. The results- and discussion parts are somewhat difficult to read. The analyzed issues, i.e. predicted mortality, sensitivity, specificity, cut-off , are inconsistently compared between the different scores. “Discriminate power and calibration” are raised as new aspects in the discussion part. It would be easier to understand if they would be directly opposed with the aforementioned issues.

We added a tabular overview to the manuscript and added the missing calculations. In fact, we hesitated on presenting these facts in the first place because of a simple statistical detail: As our study is not large enough to allow calibration of such a complex score system, the determination of a useful cut-off value is statistically not permitted. Of course it can be calculated ignoring this fact and we tried our best to clarify this in our rephrased limitations of the study.

2. In the discussion the results of the study are not really discussed. Especially the advantages or disadvantages of the EuroScore 2, the main issue according to the manuscript title, are not clearly mentioned. Only the abstract-conclusion is about the better correlation of EuroScore 2. From numeral values one gets the impression that the ACEF score performs best.

We rephrased large parts of the discussion according to suggestions given by reviewer 1 & 3.

3. The conclusion section should be concise and short (like the abstract conclusion). It contains issues better considered as limitations or future perspectives.
To allow an emphasis of our study’s limitations, a separate subchapter was created. This allowed a condensed form of the study’s conclusion.

**Minor Essential Revisions**

1. There are no references about the new EuroScore 2.
   At the moment of submission, even the introducing paper itself was not yet Medline listed. As for now, several articles have been published and are cited in the re-edited discussion.

2. Sensitivity and specificity of the EuroScore 2 should be included into the results-section of the abstract.
   As already stated, sensitivity and specificity of the EuroScore 2 can only be judged using a pre-defined cut-off or by calibration. Due to the small number of patients compared to the high number of variables in the EuroScore2, a calibration is statistically not permitted. To present the desired numbers, we determined the maximal Youden’s Index and calculated sensitivity and specificity according to this deliberately chosen cut-off – emphasizing that this is not a statistically legal procedure.

3. Why are no transfemoral cases included? Is this procedure not performed, are these patients excluded because it is a surgical unit study?
   Both procedures are performed in our clinic, yet our department is only involved in the transapical approach. As patient statistics and perioperative risk might differ significantly between the two groups, we decided to keep the study limited to one implantation method, although a central register exists to compare both approaches.

4. Many references are about CoreValve, thus transfemoral TAVI, which is known to reflect be a different patient population.
   These references were partially removed. In cases where they were only mentioned to state facts about preoperative risk scoring, they were kept, as to our opinion, the process of risk evaluation is still equally performed in both patient populations.

5. It should be mentioned that each patient treated with the alternative procedure, i.e. TAVI instead of cAVR and vice versa, would have experienced a different mortality.
   The fact was added to the limitations of the study.

6. The authors convey the impression that the log EuroScore 1 served as a true estimate of operative mortality of cAVR/AVI patients. It is known that the absolute values of the log EuroScore 1 score do not reflect the true operative mortality, but they serve more as an estimate to classify patients as high risk rather TAVI candidates (>20) and lower risk rather
cAVR patients.

This was not our intention. In fact, we tried to emphasize that probably two different score systems are needed to fulfil two separate tasks: one to best estimate perioperative mortality and one to classify patients as low or high risk. We hope this fact is now made clear in our restructured discussion.

7. Material and Methods-Section: ...that were later included into the aforementioned guidelines.... There are no aforementioned “guidelines”, (5) is a review of the literature, (2) are no guidelines on TAVI.

The citation referred to the recommendations expressed in citation (5), also falsely named guidelines at the first occurrence in the manuscript. The nomination was altered in both positions.

Discretionary Revisions

1. TAVI is rather an aortic valve implantation than a replacement.

Nomination was changed in the manuscript.

2. Not only the American, but also the newer European guidelines on patients with valvular heart disease should be considered and mentioned: A Vahanian et al.: Guidelines on the management of valvular heart disease. European Heart Journal (2007) 28, 230–268

Citation was altered in the manuscript.

Reviewer 3:

Major Compulsory Revisions:

To become acceptable for a re-review, the paper should be thoroughly revised:

1. From the title, one would expect an analysis of risk stratification in a TAVI population based on the EuroSCORE 2. Although the authors provide ES2 data in the Abstract and in the Results, the remainder of the manuscript emphasizes the comparison of EuroSCORE 1, STS scores, and ACEF. This issue needs to be rectified. On the same token, all four scores should be compared regarding their respective calibration and discriminative power for the given group of 206 patients, because readers would like to see an answer to the question: “Which of the four scores is the most suitable one for differentiating which patients in this population end up surviving TAVI and which ones do not?“ Next, the authors should discuss and analyze if the answer is also applicable to other populations.

(see also the answer to question 1 of the first reviewer)
The discussion was rephrased to fulfil these criteria.

2. The manuscript needs to be evaluated by a statistician who should make corrections if needed. The ROC curves ought to be shown. PPV and NPV as well as the f-score from Table 2 should be addressed.

We decided against the presentation of the ROC curves as little information is gained by mere graphical presentation. Predictive values were further emphasized within the discussion.

3. The English diction and grammar should be completely revised by a native speaker.

The manuscript was revised by professional language editing.

Minor Essential Revisions:

4. The Abstract contains abbreviations. Amend this, please.

The abstract does not contain unexplained abbreviations. To our opinion, the persisting abbreviations account for a better readability. As all are explained on first mentioning within the abstract, we would like to confer the decision of keeping them to the Editorial Board.

5. The title is incomplete: “... - a single center retrospective analysis/study in 206 patients“

The use of “retrospective” as a noun instead of an adjective was not criticised by our language editors and was therefor kept. Again, we would accept both versions and would like to leave the decision to the Editors.