Author's response to reviews

Title: Early prediction of survival after open surgical repair of ruptured abdominal aortic aneurysms

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Author's response to reviews: see over
Ref.: MS: 1662475542124919; “Early prediction of survival after open surgical repair of ruptured abdominal aortic aneurysms“

Dear Dr. Carlo Banfi,

We are very grateful to the editorial team and the reviewers for their insightful and helpful comments on our manuscript MS: 1662475542124919 entitled “Early prediction of survival after open surgical repair of ruptured abdominal aortic aneurysms”. We appreciated that the reviewers recognized the importance of this work. In this revision, we made every effort to comprehensively and thoroughly address all concerns, and believe that the present manuscript benefited from the reviewers’ insights and as a result is considerably improved. The revision fully addresses all of the specific concerns.

We have enclosed our statements to the reviewers’ along with the revised manuscript. We hope that you will accept our article for publication. Thank you very much for giving us the opportunity to address the reviewers’ comments and to submit a revised manuscript.

Yours sincerely,

Felix Krenzien, M.D.
Peter Fellmer, M.D.
Reviewer #1:

Remarks to the Author

"The authors report a retrospective analysis of multi organs failure score used to predicted ICU mortality after RAAA. The present study is interesting, but some other studies are already published in the literature in the same topic. Thus the authors should include the results of these previous studies in their discussion, and the additional value of their analysis, particularly regarding their advanced statistical analysis."

Response:

Thank you very much for your comment. We revised our discussion and compared our results to additional previous published studies and extended our references. In conclusion, the value of the present study is the advanced analysis of the proposed scores and the comparative comparison. The analysis showed the clinical application in RAAA and can encourage the physician in decision making since mortality and morbidity are still high and challenging.

"Line 126: An advanced age is known to be major risk factor of death after RAAA. As the median age among patients who died in ICU is very high, maybe it could be relevant to exclude patients of more than 80yo for the statistical analysis."

Response:

We appreciate your comment. We totally agree, that an advanced age is a negative predictor for survival [1,2]. Of note, the rates of RAAA in Germany are low from the 5th to the 7th decade.
of life but show a peak in the 8th and 9th decade [3]. This is even more pronounced in females, where the median age of RAAA ranges from 80-89 years.

The median age of the present cohort was 75.9 (IQR; 64.6 – 80.7), what is consistent to large epidemiological studies [1,3,4]. Obviously, to exclude patients older than 80 years would neglect a major part of the study population and would exclude the typical patient, who suffer from a rupture. Again, older patients have a higher likelihood to die. Interestingly, age is not considered in the SOFA and TISS-28, but these scores were able to predict patients, who will die and would be older. The discussion was modified in regards to the median age and their relevance.

"Line 74/75 : The scores of multiple organ failure evaluation have already been evaluated in the literature during ICU after RAAA. This sentence should be modified, according to the additional value of the present study."

Response:
Thank you for your comment. The sentence was modified according to your advice. The additional value of the present study is the competitive comparison of the proposed scores and the day by day analysis of each score, whether a patient will survive or die.

"Line 164/165 : Several studies already analysed the impact of multi organ failure scoring on post operative mortality after RAAA :


The results of this study should be compared with these previous studies in the discussion.”

Response:

Thank you very much for the literature. The discussion was revised and the results were compared to APACHE II score and further studies.

"Discussion : Danuta Gierek et al demonstrated that the most significant correlation between post operative death and score was demonstrated for APACHE II. Some of the parameters required to calculate APACHE II scores are levels of pH and HCO3 in arterial blood gasometry, serum concentrations of creatinine and potassium and age. According to literature, abnormalities in gas exchange, acid-base imbalance and low arterial blood pressure are the key risk factors in RAAA patients. Why the authors didn’t choose to analyse the APACHEII score in their study? If possible, it would add some value to the present study."

Response:

We thank the reviewer for this comment. The APACHE and APACHE II were built by a subjective method. Experts selected and weights variables from a panel to build up the score [5,6]. In contrast, SAPS II, TISS-28 and SOFA were developed with assistance of statistical modeling technique [7–9], why they might be superior. Furthermore, the mentioned parameters (pH, HCO3, PaO2, FiO2, creatinine, potassium, age, systolic blood pressure) are included in the SAPS II score and abnormalities in gas exchange and acid-base imbalance are considered.
Moreover, every score was exclusively assessed prospectively in our study. That means every score was calculated daily at 6 a.m. in the morning. All parameters were available based on recent results. A retrospective calculation of APACHE II would include a further confounder in terms of a retrospective calculation prone to missing values.

Reviewer #2:

Remarks to the Author

This article is well written. The scoring and prediction of short, mid-term prognosis for those patients is still an issue. Nevertheless, several literature reviews and propensity scores have been proposed.

Response:

We thank the reviewer for this comment. We totally agree, that there are several evaluations available of different scoring models as well as literature reviews. We revised our discussion and our results were discussed in more depth in regards to the literature. The high mortality of RAAA and severity of postoperative course are still challenging for the physicians in particular for vascular surgeons. Therefore, the use of scoring systems may be important in those patients and scoring systems can be used not only to track patients, but possibly to predict survival.

However, the proposed scoring systems and their applicability for RAAA are still not fully evaluated and which score might be superior remain unclear. The present study evaluated SAPS, SOFA II and TISS-28 and compared them to each other. We revealed superiority for SOFA and SAPS II for early (48h) prediction of survival after surgery. We think, this is of high interest.
as high mortality and morbidity are demanding in decision making and scoring models can complete the clinical of a patient.

*The description of methodology is appropriate even if the description of the chosen scores - that are not well known for vascular physicians – should be more developed.*

**Response:**

Thank you for your comment. The methods were revised and every score was explained in particular.

*You presented the predictive scores as “independent of the chosen treatment” so why did you decide to remove endo repair from your score evaluation? Do you think those scores are not relevant and/or consistent for those latter patients? It should be discussed further*

**Response:**

We decided to remove EVAR from our analysis for a certain reason. The objective of our study design was to reduce confounders and to test the proposed scores exclusively in patients' who underwent open surgery, as a single treatment option. Clearly, patients who underwent major surgery or endovascular repair have major differences in the postoperative course. The median laparotomy lead to a major trauma, while the endovascular approach is minimal invasive even sometimes performed in local anesthesia. Hence, patients have different physiological changes and post-therapeutically complications. For example, patients who underwent EVAR are considered to suffer more from abdominal compartments and have different postoperative morbidities [10–12]. Moreover, patients who undergo EVAR are
selected and biased. EVAR suitability is determined by the anatomic configuration of the aortic neck and iliac arteries, while OSR is not limited by the aneurysm morphology. Thus, patients, who are not suitable for EVAR, usually undergo surgery, as reflected in observational studies [13–15]. Therefore, we excluded these patients of our analysis.

Nevertheless, we agree, that scoring models should be tested in patients, who undergo EVAR. The applicability of these scoring models in the era of endovascular techniques is very interesting, whether survival can be predicted and critical illness can be tracked. The discussion was revised and the consideration of EVAR for scoring models was discussed.

Several scoring methods (Glasgow...) have previously been described and proposed to predict mortality for ruptured AAA? How did you consider them in comparison to yours?

Response:

The main difference between Glasgow Aneurysm Score (GAS), Edinburgh Rupture Aneurysm Score (ERAS), Hardman Index or the recent developed VSGNE RAAA risk score is, that they rely on preoperative/ intraoperative parameters [16–19]. They can be calculated in the emergency department to determine the likelihood whether a patient will survive or die. Moreover, these scores were developed exclusively in patients with RAAA.

In contrast, the proposed scores are based on postoperative parameters. They can not only be used to predict outcome, but critical illness can be tracked day by day. They were developed on huge cohorts and not exclusively in patients with RAAA, what might limit their universal use for other pathologies. To mix up preoperative and postoperative scores would be interesting but was not scope of the present analysis.
Results are not clearly exposed – and are bit confusing; we understood that you achieved to define a higher sensitive cut-off within your scoring system. I suggest that you should present your results “score-by-score” and then go through with the comparison.

Response:
The results were revised according to your comment and the results were presented score by score.

How do you explain that the scores proposed are not discriminant after 3 days?

Response:
There are several limiting factors, why discriminative power is less after 3 days. Following surgery, patients suffer from hemodynamic shock, hemorrhage and invasive trauma. After certain days, this differ from patient to patient. Some patients need re-intervention because of thromboembolic events, some patients are threatened by infections and some patients recover in a different manner of time. Therefore, the calculated score are based on different underlying clinical problems, which leads to an interindividual calculation and gradual shift of sensitivity and specificity. This is, why the highest discriminative power was found in the early postoperative stage, what was not evident after certain days. Moreover, patients who die or discharged from the ICU minimizing the cohort and the power of the statistical analysis. The discussion was modified, and this issue was briefly discussed.
The significant difference of the age of patients between both cohorts remains a major bias in the final analysis – and should more discussed and documented (results of open AAA surgery with octogenarians...).

Response:

Thank you for this comment. The discussion was revised and the age of the patients were discussed in more depth.

Line 127: Results regarding the length of stay in the ICU are not relevant – patients in the second group are dead.

Response:

The results were adjusted. Thank you for your comment.

Line 189: I do not agree, You cannot say that: we all know that the use of a score in clinical practice is always complicated – the more items you need to include the less the score will be applicable. Those scores have already been evaluated and compared with other evolving pathologies (missing references) – discussion of those previous reports, their consistency and their applicability to the vascular field should be included and debated in the present discussion.

Response:

We appreciate your comment. The discussion was revised and previous reports were discussed in more detail. We agree, that the general use of scores is an issue and time consuming. According line 189, the sentence was modified.
Interestingly, when clinical information system are used, implementation and automatic assessment of scores are possible and less time consuming. In our department, the calculation is successful performed since 2005 and proved its applicability in the daily routine. Nevertheless, we agree to your comment, that you need additional effort, to implement and calculated those scores in the daily routine.

*The bibliography and the literature review are a bit light – and should be enhanced with major references regarding AAA rupture and recent review of scoring systems.*

**Response:**

The discussion and references were revised. Thank you, for your comment.

**Reviewer #3:**

Remarks to the Author

*The question posed by the authors is well defined and the methods are well described. Data are well collected and exposed and basically the manuscript seems to adhere to the standard for reporting and data deposition. The discussion is well balanced and the analysis of the results is objective. The authors show a good knowledge of the papers close to their topic.*

**Response:**

Thank you very much for your comment.
What should be interesting in my opinion is to know how many of the patients involved in this study were hemodynamically unstable at the moment of surgery and many were tamponade or hemodynamically stable. How this two different conditions can influence the scores?

Response:

Thank you for this interesting comment. We totally agree, that intraabdominell bleeding may have an impact on critical illness and that hemodynamic shock is the overall survival limiting factor [20]. Clearly, hemodynamic parameters are considered in many preoperative scoring models, most of them assessed and calculated in the emergency department preoperatively (e.g. ERAS, GAS, Hardman Index, VSGNE RAAA risk score) [16–19].

In contrast, the present study validated scores based exclusively on postoperative parameters. The analysis was focused on the survival and the early prediction of survival on ICU. The consideration of preoperative parameters would include major confounder and mix up preoperative and postoperative variables. To our mind, an additional analysis would be more appropriate, but of high interest to evaluate the impact of preoperative parameters like hemodynamic shock on critical illness and available scoring models (e.g. systolic blood pressure, hemoglobin level, loss of consciousness, cardiac arrest et cetera).
References


