Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-1509

Reviewer A

Comment:

"Global appreciation:

The authors aim at evaluating QoL after minimal-invasive treatment (PUMS-SAVR or TF-TAVI) of aortic valve stenosis in elderly. Though the title does not reflect the comparative nature of the study, the authors clearly state the aim of the study in the abstract as well as in introduction and study design paragraphs. The question they address is actually unanswered in the current literature since QoL comparative studies only compare outcomes after conventional SAVR versus TAVR. Though they use a sophisticated statistical tool (propensity score), the study is flown by the small number of patients in each comparative group, a still significant difference in mean age after PSM and a confuse primary outcome. Besides, the high rate of definitive PM implantations in the TAVI group is not considered as a variable of QoL, neither is the higher rate of paravalvular leakage for which we need more quantitative precisions. Mortality rate at one year was 3 time higher after TF-TAVI (overall population) and equal to 0 in both groups after PSM but the authors do not fulfill appropriate answer to the secondary outcome which also includes morbidity at one year (and especially strokes which have a certain impact on QoL)."

Answer:

Thank you for the thoughtful analysis of our manuscript.

We are aware of the fact that our manuscript is presenting the outcome of small patient groups. This circumstance is primarily a consequence of the one-to-one propensity matching.

We apologize for the vague and misleading description of the primary outcome. We elucidated the definition below, in the answer to your comment nr. 2.

We also agree with the reviewer that the QoL is a subjective measure of the health level that does not include relevant objective measures, such as stroke and pacemaker implantation. However, we believe that patient perception is also important in evaluating the outcome of the

medical therapy, especially because patient`s wish and satisfaction are increasingly used by cardiologist when indicating TF-TAVI as a treatment option in low-risk young patients.

Based on the present results, it also seems that older patients do not perceive pacemaker-implantation negatively.

We agree with the reviewer that unfortunately age is still differed in the two groups after propensity matching. However, from a medical-clinical point of view the "73-years-old" and "70-years-old" after the propensity matching could be regarded as more comparable than "78-years-old" and "66-years-old" before the matching.

Comment 1:

"a) Study group, methods and sample size.

As a single center observational study, the authors included all patients undergoing PUMS-SAVR or TF-TAVI with some exclusions criteria which did not include endocarditis. Precise how much patients with endocarditis were included in the PUMS-SAVR.

Clearly, the authors did not focus on elderly patients, therefore patients form the PUMS-SAVR were much younger even after PSM. How do you explain results in Table 1 which are inconsistent with what you stated L 103-104?"

Answer 1:

Thank you for this comment. Indeed, we did not included endocarditis in our primary exclusion criteria, however we included "prior stroke with persistent neurological impairment, dementia, motoric dysfunction of any cause". Consequently, patients with acute neurological symptoms as such eventually caused by florid endocarditis had been excluded from the study.

Patients without neurological symptoms, but with microbiologically ascertained valve endocarditis in the examinations of the removed aortic valve (6 cases from 137) were excluded from the propensity matching.

We agree with the reviewer that unfortunately age is still differed in the two groups after the propensity matching. However, from a medical-clinical point of view the "73-years-old" and "70-years-old" after the propensity matching could be regarded as more comparable than the "78-years-old" versus the "66-years-old" before the matching. In addition, chronological age can often differ from the biological age. Frailty is playing an increasing role in determining

surgical risk in the aging population. Therefore, we would not confer an extraordinary importance to the age difference in the PSM subgroups.

Changes 1:

A sentence on endocarditis was added in the lines 136-137, on page 7 of the redline manuscript.

A comment on age difference was added in the lines 275-277, on page 14 of the redline manuscript.

Comment 2:

"b) Outcome measures.

Primary outcome measures (post-treatment cardiac function and in hospital morbidity) is difficult to measure. Appropriate definitions are lacking.

Secondary outcome is not investigated in its morbidity dimension. Strokes are not considered."

Answer 2:

We apologize for this mistake. We redefined correctly the outcome measures of our study. The primary outcome measures are procedural success and early revision. The secondary outcome measures are in-hospital atrioventricular block requiring pacemaker implantation and mortality at 1-year follow-up.

Morbidity was investigated in terms of early complications, including pneumonia, TIA/stroke, delirium and need for transfusion, and the findings are presented in table 2. These findings are also described in the manuscript on page 9, lines 170-180. The incidence of stroke post-treatment is presented in table 2 as "TIA/stroke" incidence, and did not differ between the groups.

Changes 2:

The outcome measures are correctly defined on page 8, lines 145-150 of the redline manuscript.

Comment 3:

c) Presentation of results.

Presentation of QoL results are synthetic and nice but the authors (discussion and conclusion) rely on a significant difference in SF36 which is not explicit in results or figures.

Table 1 results are inconsistent with the description of the PUMS-SAVR population.

Answer 3:

The SF36_LQ questionnaire is complex, especially in German language. The evaluation is described in detail on page 11, lines 210-217 of the manuscript. The findings of the questionnaire, including the significant differences between percentages in the two groups are described in detail on page 11, lines 220-229 of the manuscript. In addition, Figure 2 depicts percentages of each patient group reporting on the questioned dimensions of satisfaction. A scale of percentages from 0 % to 100 % is depicted on each artwork of Figure 2, at 12 o'clock.

Similarly, scales of percentages from 0 % to 50 % and from 0% to 80% are depicted on the artworks of Figure 3, at 12 o'clock.

Changes 3:

Explanations are added to the Figure Legends of Figure 2 and Figure 3, on page 22 of the redline manuscript.

Comment 4:

"d) Discussion and interpretation.

Discussion is far too long and should focus on study results since no other paper is supposed to address the issue of QoL comparison after PUMS-SAVR or TF-TAVI. For instance it would be useful to put some light on quantitative assessment of paravalvular leaks after TF-TAVI (which affects 40% of PSM patients)."

Answer 4:

The length of the manuscript is in conformity with the requirements of the "Journal of Thoracic Disease".

Although we agree with the reviewer that there are no previous publications on a similar topic, we consider that the detailed discussion emphasizes the novelty of our study and increases the scientific value of the manuscript.

We entirely agree with the reviewer on that the percentage of the PVL in the TF-TAVI group is relevant. However, transforming high degree aortic valve stenosis into a low degree aortic valve insufficiency by the means of less-invasive TF-TAVI treatment confers a feeling of clinical health improvement, especially in the early post-treatment period, which explains the findings of the HrQoL questionnaire in our study.

The advantages of open surgical PUMS-SAVR treatment over TF-TAVI are described on page 13, lines 254-265 of the initial manuscript.

Changes 4:

In accordance, additional explanations on PVL after TF-TAVI are added on page 13, lines 260-264 of the redline manuscript.

Comment 5:

"It is not reasonable to pretend what is stated L 244-46 when mean life expectancy of patients receiving TF-TAVI in that study exceeds 5 years."

Answer 5:

Thank you. Our intention was to describe the causes of death of the patients who did not survive at 5 years.

Changes 5:

The sentence is corrected accordingly, on page 13, lines 255-257 of the redline manuscript.

Comment 6:

"More conclusion appears more supported by the author's beliefs than it is by study results which is against scientific methodology. Not only PUMS-SAVR offer better procedural outcomes and probably a better survival but immediate postoperative extubation after full sternotomy is a performed accomplishment since years by many centres worldwide."

Answer 6:

Thank you for this observation. We agree with the reviewer that many centers perform immediate postoperative extubation in PUMS-SAVR patients. This is easy to perform in younger patients. However, we have to point out that our patient cohort consists of older patients comparable to the TAVI group (aprox. 70 years old). These PPM groups are even more multimorbide when compared to the entire cohort. The risks of postoperative bleeding and of pulmonary dysfunction also increase with age.

Therefore, early extubation in our patient cohort might not be as successful as it is published in younger patient cohorts.

Changes 6:

We changed the conclusion in accordance with the findings of the study. Since the "highlight box" as proposed by the "Journal of Thoracic Disease" includes "what should be changed", we maintained the last sentence of our "Conclusions".

Reviewer B

Comment 1:

"In this paper Andrasi et al. compared TF-TAVI and PUMS-SAVR to assess health perception and quality of life after aortic valve procedure. This is a really hot topic in recent literature because the most important randomized trials compared TAVR to full sternotomy SAVR which nowadays is certainly not the frontier in surgical aortic valve replacement. It focuses on aspects that go beyond the obvious differences between the two procedures (procedural time, ICU-stay etc.). For these reasons, this paper, which is well structured in

each part, could add important evidence to the modern literature. The study is well conducted."

Answer 1:

Thank you. We are grateful to address the thoughtful critiques and suggestions.

Comment 2:

"There's a flaw that it's important to solve or clarify: one of the endpoints is to compare complains and HrQoL between the two procedures; both differences are not statistically significant ("On average, 25.46% (maximal value less than 50%) of the PUMS-SAVR patients and 14.75% (maximal value less than 30%) of the TF-TAVI patients reported complains after treatment. This difference was no statistically significant (p=0.371). Similarly, perceived health level after treatment (Figure 3) was described as "excellent" in 11.4% vs. 8.5% (p= 0.991) and as "very good" to "good" in 80% vs. 74.3% (p= 0.776) of the TF-TAVI and PUMS-SAVR patients, respectively").

Answer 2:

Thank you for this observation. We entirely agree with the reviewer that PUMS-SAVR is neither a dangerous treatment nor a treatment offering suboptimal outcome.

The perceived health level was indeed not "poor", and there were no differences in the percentage of patients describing it as "excellent". Indeed, health level revealed as similar in TF-TAVI and PUMS-SAVR when the "very good" and "good" outcomes were added together.

Importantly in the independently stratified quantification as it is depicted in Figure 3, 34.29 % of the TF-TAVI patients reported "very good" health level vs. 0 % "very good" health level found in the PUMS-SAVR group ($p < 0.01$) and 42.85 % of the TF-TAVI patients reported "good" health level vs. 77.14 % "good" health level found in the PUMS-SAVR group ($p < 0.01$). These findings reflect more satisfaction in the TF-TAVI group.

Although PUMS-SAVR has less PML and requires lower Pacemaker implantation is still associated with longer ventilation-time, ICU-time and longer hospital stay when compared to TF-TAVI. These later factors might explain the subjective feeling of sickness reflected in the findings of our HrQoL questionnaire.

Changes 2:

In accordance, additional explanations are added to the results, on page 13, lines 260-264 of the redline manuscript.

Comment 3:

"I think conclusions should be revised ("In conclusion, our study has demonstrated that in elderly, PUMS-SAVR achieves inferior quality of life compared to TF-TAVI. Furthermore, partial sternotomy reveals as the strongest risk factor of less-satisfactory health level after PUMS-SAVR compared to TF-TAVI, as perceived by the patients") in order to make them consistent with results; indeed results only suggest superiority of TF-TAVR in terms of complains and perceived quality of life."

Answer 3:

Thank you. We entirely agree with the reviewer that TF-TAVI treatment suggests superiority only in terms of complains and perceived quality of life.

As described above in our answer to your Comment nr. 2, the presentation of the results is now detailed and the conclusion are therefore supported by the results.

The conclusions are improved based on the recommendations made by the reviewers.