

Peer Review File

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Reviewer A

The authors attempt to address a very common conundrum we face as operators regarding the safety and efficacy of TF TAVR in patients with concomitant aortic dilatation/aneurysm.

Overall I believe the study and results to be of value given that it suggests that TF TAVR can be done safely. However, in my humble opinion the results only address, and should be limited to suggest, that TAVR can be done safely in these patients with low peri-procedural risks.

1. There are some significant difference in baseline characteristics. For example there is a markedly higher incident of bicuspid TAVR in those with AA.

Reply 1: Yes, several variables in baseline characteristics showed statistically significant differences. For example, the incidence of BAV is higher in AA ≥ 45 mm group, which is not difficult to understand because BAV patients are prone to AA dilation (intrinsic abnormality of the aortic wall). However, we performed Cox regression analyses, and only three variables were identified as independent risk factors for mortality in multivariable analyses (paravalvular aortic insufficiency, serum creatinine, and history of cerebrovascular disease).

Changes in the text: None.

2. The overall number of patients are understandably low resulting in a non-statistical difference in overall survival but rather large % difference between the two groups ($92.5\% \pm 3.5\%$ vs. $78.3\% \pm 6.8\%$, $P=0.198$).

Reply: A major limitation is the relative short follow-up period (median 19 months) and small sample size. At 60-month interval, the number at risk in AA ≥ 45 mm group and AA < 45 mm group is only 1 and 12, respectively. Large sample size and long-term follow-up are required. Therefore, the present study only reported our early experience and mid-term results, and should be interpreted cautiously, as we mentioned in the Limitation part.

Changes in the text: None.

3. Most importantly, the real question operators have is whether TAVR in AA patients is a safe "longterm" alternative to surgery. Meaning, years post-TAVR, do these patients have a higher chance of worsening AA which require endovascular/surgical repair/replacement questioning the initial choice of AVR +/- concomitant AA repair.

Reply 3: This is a good question. In patients with AA dilation, long-term results are important, including the incidence of aortic dissection/rupture, the AA dilation rate, and the need for AA intervention (endovascular or surgery). In the present study, only one patient in AA < 45 mm group (with a preoperative AA of 39mm) experienced type A aortic dissection 10 months after the procedure. Follow-up TTE results suggested that no rapid aortic growth (more than 5mm/y) was found in any patient. Therefore, the authors believe the risk of adverse aortic events (at

least during the mid-term follow-up period) are low in this patient group. However, as the indications for TAVR expand to the younger and low-risk patients, further studies are required to evaluate the prognosis of TAVR in patients with dilated AA. We added these contents in the revision.

Changes in the text: (Page 13, Line 228-231) Fourth, as the indications for TAVR continue to expand to younger and lower-risk patients, the long-term impact of AA dilation requires more attention. Further studies comparing the outcomes of TAVR, SAVR, and SAVR plus AA repair/replacement (Wheat's procedure) in patients with dilated AA would be helpful.

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4. A few grammatical errors. Recommend polishing for ease of reading.

Reply 4: We polished the revision as requested.

Changes in the text: Minor grammatical changes.

5. Questioning validity and/or clinical applicability for reference 17 based on "the publication type of the study was the letter" needs to be rephrased.

Reply 5: We revised the content.

Changes in the text: (Page 12, Line 205-206) However, the incidence of adverse aortic events was not reported in the study.

Reviewer B

1. Authors presented baseline characteristics in 467 patients, and outcome in 451 patients. The reviewer recommends I to present these data in 451 patients.

Reply 1: We added these data in the revision (Supplementary Table 1)

Changes in the text: Supplementary Table 1.

2. How much patients received optimal medical therapies (statin, ACEI, beta-blocker)?

Reply 2: This is a good point. However, we did not have thorough details of these information. We explained these limitations in the revision.

Changes in the text: (Page 13, Line 231-234) In addition, the present study focused on the baseline characteristics and perioperative data. Other factors, such as medication, blood pressure control, and family history of AAEs, were not considered.

Reviewer C

Thank you An et. al. for writing up this important topic on FU study in patients underwent TAVR with dilated ascending aorta.

An et. al. reported that 461 patients underwent TAVR and were included in the study. However, 8 of them were excluded from follow-up analysis, because they were converted into open heart surgery. Please provide more detail explanation on this and justify the rationale behind. I assume these 8 patients underwent TAVR but was not successful and were converted to surgery. However, the outcome of these 8 patients might affect the overall result. For example, if patients with AA >45mm were more likely (2% vs 1.6%) to be converted to surgery during TAVR, they might have poorer survival outcome. Excluding these 8 patients will falsely lead to a conclusion that there are no difference in survival between the dilated AA and non-dilated AA groups,

especially when there exist a difference of overall survival rate between the 2 groups albeit statistically non-significant (92.5%±3.5% vs. 78.3%±6.8%).

Reply: This is a good point. Among 8 patients who were converted to SAVR, only 1 patient had preoperative AA ≥45mm, and excluding these patients did not affect the survival outcome. Details of these patients were added in the revision.

Changes in the text: Supplementary Table 2. Details of patients who were converted to SAVR

Patient number	Age	Gender	AA diameter	Reasons for converting to SAVR	In-hospital death
1	72y	Male	54mm	Cardiac tamponade	No
2	63y	Male	38mm	Coronary artery obstruction	Yes
3	51y	Female	38mm	Coronary artery obstruction	No
4	60y	Male	42mm	Severe paravalvular leak	No
5	70y	Male	40.6mm	THV malposition	No
6	65y	Female	41mm	THV malposition	Yes
7	63y	Male	44mm	THV malposition	No
8	56y	Male	41mm	THV malposition	Yes