

## Peer Review File

Article information: <https://dx.doi.org/10.21037/jtd-23-331>

### Reviewer A

Comment 1: The authors should specify why the patients > 75 years of age were enrolled as elderly. “Frailty or sarcopenia” rather than “age” may be one of more important factors to determine the postoperative results. Please discuss on it.

Reply 1: Thank you for your comment. I agree with your opinion that frailty or sarcopenia of patients is more important than age. However, age is an important known risk factor, and Milewski et al. (Hospital of the University of Pennsylvania) first mentioned that old age is a high-risk factor for total arch replacement and reported hybrid procedure is a safety option for elderly patients. In their report, they define old age as > 75 years old. For this reason, we define old age as >75, and we related sentence in the introduction section. (page5, line 60, 61)

Comment 2: The author excluded the patients with aortic aneurysm extending below the level of the pulmonary artery bifurcation. In the hybrid group, the distal end of TEVAR may be around at the level of the pulmonary artery bifurcation. Please provide the data of the length of the TEVAR device used.

Reply 2: We thought conventional open repair via sternotomy was available for aortic arch aneurysms not extending to pulmonary bifurcation. Therefore, we exclude aortic arch aneurysms extending pulmonary bifurcation in both groups. Accepting your opinion, we inserted the mean length of the TEVAR graft as “The length of the inserted stent graft was  $158.6 \pm 24.7$  mm.” (page 10, line 182)

Comment 3: What are the criteria for performing frozen elephant trunk or TEVAR in the hybrid group?

Reply 3: The indication of hybrid procedure was not controlled because this was a multicenter cohort study, and the preference for hybrid procedure differed in each operator and hospital. We insert this sentence in the limitation. (page13, line 269-273)

Comment 4: What are the criteria for performing zone 0-TEVAR, zone 1-TEVAR, or zone 2-TEVAR? Is this level variation associated with the level of the proximal end of the aneurysm? Please describe the detail.

Reply 4: The types of TEVAR were selected by the level of the proximal end of the aneurysm. The most important selection criteria for TEVAR type was sufficient landing zone, ranging from 15-25 mm proximally and 20-30 mm distally. In addition, and in a specific situation, the angle of patients' aorta or combined thromboembolism risk was also considered. We added this sentence in the “Methods” section. (page8, line 127-133)

Comment 5: In the section of “Surgical indications”, the authors mention that the hybrid arch procedure was considered for high-risk elderly patients with multiple

comorbidities. In patient characteristics, however, the incidence of chronic obstructive lung disease and chronic kidney disease were significantly greater in the TAR group than in the hybrid group. Please explain this discrepancy.

Reply 5: Because this is a multicenter cohort study, the indication of hybrid procedure was slightly different in each medical center or operator. Although age and comorbidities were significant factors in selecting patients, anatomical characteristics of the aorta were also critical factors for selecting patients for hybrid procedures. These factors influence the choice of procedure and the results. We added this sentence in the "Limitation" section. (page13, line 269-273)

Comment 6: Line 208: Do the words, "a distal anastomosis leak" mean pseudoaneurysm after TAR?

Reply 6: Yes, this patient had pseudoaneurysm formation at the distal anastomosis site, and this area was concealed by pleural adhesion. The angiography revealed a distal anastomosis site leak, and we performed additional TEVAR at the leakage site. To clarify, we converted "distal anastomosis leak" to "distal anastomosis leak with pseudoaneurysm formation, concealed by pleural adhesion." (page11, line 209-211)

Comment 7: In the hybrid group, 3 patients underwent late reintervention for type Ib endoleak. The author should describe the way to determine the diameter of frozen elephant trunk or TEVAR.

Reply 7: We generally select the diameter of the stent graft to be about 120% of the aortic aneurysm diameter. After TEVAR, additional ballooning or stent graft insertion is performed if there is an endoleak in post-TEVAR angiography. We added this sentence in "Surgical technique for hybrid procedure" in the "Method" section. (page 8, line 127-133)

## **Reviewer B**

Comment 1: The authors are to be commended for performing TAR in patients at rather higher perioperative risk, such as CKD, COPD, and age, than in the hybrid group, with good results. Because TAR is the gold standard but highly invasive technique for arch aortic lesions, a hybrid procedure may be indicated to reduce risk in patients with high perioperative risk, the aortic pathology of which was suitable for the hybrid procedure. In the study, patients undergoing TAR had higher perioperative risks compared with those undergoing hybrid procedures. The reviewer recommends the authors to describe the detailed indication of hybrid procedures for patients with lower perioperative risks, especially regarding anatomic characteristics. This would support their conclusion the surgical strategy should be chosen based on patient-specific demographic and anatomical characteristics.

Reply 1: Thank you for your comment. The indication of hybrid procedure was not controlled because this was a multicenter cohort study, and the indication of hybrid procedure differed in each hospital and operator. And age and comorbidities were significant factors for selecting patients, but anatomical characteristics of the aorta were

also critical factors for selecting patients for hybrid procedures. These factors influence the choice of procedure and the results. We added this sentence in the "Limitation" section. (page13, line 269-273)

Comment 2: While the reviewer understands the authors evaluate the important issue, it is necessary to address the anatomic characteristics and the rationale of the use of a hybrid approach in more detail.

Reply 2: I also agree with your opinion. However, the definite anatomical criteria were not controlled because this was a multicenter cohort study, and we mentioned this sentence in the "Limitation" section. However, in the hybrid procedure, the types of TEVAR were selected by the level of the proximal end of the aneurysm. Therefore, the most critical selection criteria for TEVAR type was sufficient landing zone, ranging from 15-25 mm proximally and 20-30 mm distally. In addition, and in a specific situation, the angle of patients' aorta or combined thromboembolism risk was also considered. We generally select the diameter of the stent graft to be about 120% of the aortic aneurysm diameter. We added this sentence in "surgical technique of TEVAR" in the "Method" section. (page8, line 127-133)

### **Reviewer C**

Comment: I appreciate the authors efforts. This is a retrospective study that evaluated outcomes between total arch replacement and hybrid operation for aortic arch aneurysm in elderly patients. This study showed no differences of postoperative complications between both groups. However, the hybrid operation required more frequent re-intervention compared to total arch replacement. These findings were not included new information compared to previous studies. Moreover, study design was not adequate because the hybrid operation included total arch replacement with frozen elephant trunk, and 3, 2, and 1 debranching thoracic endovascular aortic repair (TEVAR). Total arch replacement with frozen elephant trunk that required cardiopulmonary bypass with cerebral perfusion is apparently different from debranching TEVAR that needed no cardiopulmonary bypass, which significantly affected outcomes after the operations.

Reply: Thank you for your comment. We also agree that cardiopulmonary bypass and cerebral perfusion significantly impact the risk of surgery, which are important factors. I also agree that patients in the hybrid group are heterogeneous. However, this paper also attempted to see the effect of the stent graft and remnant aneurysmal changed aortic tissue on patients after TEVAR. The life expectancy is currently gradually increasing, and this remnant aneurysmal changed tissue with stent graft increases the reintervention rate in elderly patients as well. This is a sufficient conclusion to raise awareness about the possibility of the risk of increasing the reintervention rate in elderly patients who underwent TEVAR.

### **Reviewer D**

Comment 1: This manuscript described the comparison of the short and long-term results between TAR and hybrid repair for aortic arch aneurysm in the elderly population. The authors concluded that the treatment outcomes did not differ between the two groups, although the re-intervention rate is higher in hybrid group.

However, there are many recent reports that concluded otherwise. Seike Y et al reported significant higher hospital mortality in TAR group (Interactive Cardiac and Thoracic Surgery 2019, 29:101-108). Ikeno et al. reported that the operative mortality of TAR is significantly higher in elderly population. Moreover, Yoshitake et al, that the authors cited in the discussion (Ref No. 18) did not discuss about only the elderly population. So, their conclusion might be different for the elderly population.

The number of cases in this manuscript is too small to draw the contradictory conclusion.

Reply 1: Thank you for your comment. Our patient cohort may have been selected for older but relatively healthy patients, and we agree the number of cases in this manuscript is too small to conclude about a higher reintervention rate risk in the hybrid group. For this reason, further investigation using a larger cohort and longer follow-up is necessary. However, Iba et al. (Eur J Cardiothorac Surg. 2014, 46:32-9) and Cazavet et al. (Eur J Cardiothorac Surg. 2016, 49:134-40) also reported a higher risk of reintervention rate in hybrid group, and we want to raise awareness about the possibility of the risk of increasing the reintervention rate in elderly patients who underwent TEVAR.

Minor points:

Comment 2: TAR with frozen elephant trunk should be classified to TAR group in this kind of analysis.

Reply 2: Thank you for your comment. However, the operator can reduce the length of aorta resection by using a frozen elephant trunk, and remnant aneurysmal changed aortic tissue and stent graft in frozen elephant trunk technique is the most important risk factor for reintervention. For this reason, we concluded that TAR with frozen elephant trunk is a hybrid group rather than a TAR group.

## **Reviewer E**

Comment 1: Because 5-year follow-up is not long, please change “long” to “mid.”

Reply 1: Thank you for your comment. Accepting your opinion, we changed “long” to “mid”

Comment 2: I cannot understand “patients with aortic arch aneurysm extending below pulmonary artery bifurcation level” for exclusion criteria. Please add more explanation. CT scans? Why was TARFET required if those aneurysms were excluded. Those aneurysms were located at the very proximal aortic arch and TARFET was not necessary.

Reply 2: We thought that it is not only an aortic arch aneurysm if an aortic arch

aneurysm extends below the pulmonary bifurcation, and this is an aortic arch aneurysm combined with descending thoracic aortic aneurysm, definitely a different etiology. Therefore, we did not perform total arch replacement via a sternotomy in this situation, and additional stent graft treatment or staged operation is needed. An aortic arch aneurysm extending below the pulmonary artery bifurcation level required a different operative approach, and we excluded aortic arch aneurysm extending below the pulmonary artery bifurcation level for this reason.

Comment 3: Hybrid group had a variety of procedures: TARFET is completely different from Zone 0 TEVAR. Zone 0 TEVAR is also different from Zone 1 or 2 TEVAR, and I think that the disease is different among those groups (aneurysm location and dissecting/atherosclerotic).

Reply 3: I also agree that patients in the hybrid group are heterogeneous, and due to the small number of hybrid group, it was difficult to classify the hybrid group into each TEVAR zone. However, this paper also attempted to see the effect of the stent graft and remnant aneurysmal changed aortic tissue on patients after TEVAR. The life expectancy is currently gradually increasing, and this remnant aneurysmal changed tissue with stent graft increases the reintervention rate in elderly patients as well. This is a sufficient conclusion to raise awareness about the possibility of the risk of increasing the reintervention rate in elderly patients who underwent TEVAR.

Comment 4: Three patients underwent coil embolization for Type II endoleak. Were their aneurysms still dilating after surgery and, therefore, coil embolization was performed? Most of Type II endoleaks can be left without surgical intervention.

Reply 4: We usually perform coil embolization in the case of type 2 endoleak after TEVAR, and open repair is considered if aneurysmal dilatation continuously progresses. In these 3 cases, the aneurysmal dilatation progressed in follow-up CT and we performed coil embolization. We closely observed these patients after coil embolization and added this sentence in the “Results” section. (page 11, line 217, 218)

Comment 5: My advice

Please describe some good points of hybrid procedures: short duration of hospitalization or ICU stay? Short ventilator support time? less complications? Quick start for postoperative rehabilitation? Whatever. If you can say something better in hybrid procedure group, you can find some reasons to select hybrid procedures.

Reply 5: Thank you for your opinion. In this current study, there was no significant difference in ICU stay duration because most patients in the hybrid group needed to stay at the ICU waiting for a secondary TEVAR operation after the first debranching or aorta operation. Excluding this waiting time, the length of ICU stay was significantly shorter in the hybrid group, and we added this result in the “Results” section. (page10, line 186, 187 & page12, line 235, 236)

Comment 6: TARFET patients should be excluded from hybrid group. TARFET is completely different from TEVAR procedure.

Reply 6: Thank you for your comment. However, the operator can reduce the length of aorta resection by using a frozen elephant trunk, and remnant aneurysmal changed aortic tissue and stent graft in frozen elephant trunk technique is the most important risk factor for reintervention. For this reason, we concluded that TAR with frozen elephant trunk is a hybrid group rather than a TAR group.