Peer Review File

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First Round Peer Review

Comment 1: I would like to congratulate the authors on this contribution. The paper is well-written and the described surgical technique very interesting. I would appreciate an in-depth description of the way the authors suture the ostia of the head vessels to the tailored openings within the prosthetic graft as 0% endoleak is 'amazing'.

Reply: We would like to thank the reviewer for this comment. Accordingly, we have rewritten the method about the suturing of s-TAR procedure in Methods section **on Page 8, line 156-170** of the revised manuscript to make sure the reader can understand how the ostia of the head vessels were sutured to the tailored openings within the prosthetic graft.

The rewritten descriptions **on Page 8, line 156-170** of the revised Methods section are "Three elliptical patches on the polyester fabric of the stent graft were separately modified around each arch branch orifice under direct visualization by a pair of surgical scissors. The modification diameter at the stent graft was similar to that of each branch orifice. (Figure 1 D1 and D2). Next, each arch branch vessel was connected to the stent graft, using the inside-to-out technique, followed by the

returning-to-the-inside technique, through all the layers of the polyester fabric and the native aortic arch wall as deeply as possible. Specifically, the polyester fabric of the stent graft at the base of the modification was first sutured around each arch branch orifice using a 5-0 polypropylene 17-mm 1/2C double-armed mattress suture. Then, the polyester fabric was stitched to the native aortic arch wall using a continuous suture. Usually, the left subclavian artery was first reconstructed, followed by the left common carotid artery and then the innominate artery. After reconstructing the aortic arch, the proximal end of the stented graft and aortic wall were anastomosed together to complete the proximal aortic arch stump plasty with a continuous suture (4-0 polypropylene suture). (Figure 1 E1 and E2)."

Comment 2: Could you please give a more detailed description of the stent technique.

Reply: We would like to express our sincere gratitude to reviewers for the helpful suggestion. We have rewritten the methodology of s-TAR procedure in Methods section **on Page 7-9, line 147-176** of the revised manuscript to make sure the reader can understand how the s-TAR procedure was performed.

The methodology of s-TAR procedure in details **on Page 7-9, line 147-176** of the revised manuscript above is "The aortic arch was transected proximal to the origin of the innominate artery. The diameter of the native mid-arch (between the left carotid

and left subclavian arteries) was measured by inserting a ball-shaped sizer to select the appropriate stent graft size. Then, the stent graft was inserted anterogradely into the aortic arch and descending aorta under direct visualization, and released once the proximal end of the self-expandable metallic stent was positioned just proximal to the inferior side of the orifice of the innominate artery. Subsequently, an occlusive balloon was inserted and deployed in the descending aorta to resume perfusion of the lower body via the femoral artery. (Figure 1 C1 and C2).

Three elliptical patches on the polyester fabric of the stent graft were separately modified around each arch branch orifice under direct visualization by a pair of surgical scissors. The modification diameter at the stent graft was similar to that of each branch orifice. (Figure 1 D1 and D2). Next, each arch branch vessel was connected to the stent graft, using the inside-to-out technique, followed by the returning-to-the-inside technique, through all the layers of the polyester fabric and the native aortic arch wall as deeply as possible. Specifically, the polyester fabric of the stent graft at the base of the modification was first sutured around each arch branch orifice using a 5-0 polypropylene 17-mm 1/2C double-armed mattress suture. Then, the polyester fabric was stitched to the native aortic arch wall using a continuous suture. Usually, the left subclavian artery was first reconstructed, followed by the left common carotid artery and then the innominate artery. After reconstructing the aortic arch, the proximal end of the stented graft and aortic wall were anastomosed together to complete the proximal aortic arch stump plasty with a continuous suture (4-0

polypropylene suture). (Figure 1 E1 and E2).

The distal end of the vessel prosthesis for replacement of the ascending aorta was trimmed as a suitable shape. Then, the end-to-end anastomosis between the proximal aortic arch containing the intraluminal stented graft and the distal ascending aortic prosthesis was accomplished with a continuous suture (4-0 polypropylene suture). To avoid tearing during anastomosis, a vascular graft strip was placed on the external wall to strengthen the aortic arch. (Figure 1 F1 and F2)."

Comment 3: The main indication is a pathological aneurysm of the ascending aorta, eventually extending to the proximal arch (zone 3) but with a preserved diameter of the distal arch (zone 2) at 35 mm. It is questionable whether this type of disease needs to be treated so rigorously by complete aortic arch replacement instead of a hemiarch procedure. From this perspective, the comparison might not completely be correct. Perhaps the authors should comment on this.

Reply: We thank the reviewers for this comment. Accordingly, we have added more discussion about why we did not compare s-TAR with hemi-arch replacement **on Page 13-14, line 277-290** of the revised manuscript.

The added part about why we did not compare s-TAR with hemi-arch replacement **on Page 13-14, line 277-290** of the revised manuscript above is following as "Currently, the conventional approaches for aortic arch replacement are the hemi-arch

replacement, island technique and Sun's procedure (8). The first one is hemi-arch replacement, which is literally described as the resection of ascending aorta, and elimination of the aortic arch wall to the orifice of innominate artery in the greater curvature and the lesser curvature as much as possible (9). Given the remnant aortic pathologies after hemi-arch replacement, this procedure may potentially place the patients at excess risk of aortic dilation, dissection, rupture and thus reoperation (10). The second one is the re-anastomosing of "island" of three supra-aortic branches with a Dacron graft. The downside is that residual aortic tissue left after "island" arch replacement may also re-dilate and result in reintervention (11). Therefore, our center has not used these two methods since 2015. The three one involves the separate anastomoses of the three supra-aortic branches and 4-branched arch graft and implantation of a stent graft into descending aorta, namely Sun's procedure, which has still been used in our center. Indeed, this procedure presents several disadvantages (12)."

Comment 4: It is difficult to understand how the supra-aortic vessels in the s-TAR technique are really connected. Is the suturing to the stent graft prosthesis done from within the lumen of the graft or is it done externally?

Reply: We appreciate the reviewer's question. Accordingly, we have added more information about how the supra-aortic vessels in the s-TAR technique are really connected **on Page 8, line 156-170** of the revised manuscript.

The information of about how the supra-aortic vessels in the s-TAR technique are really connected in details **on Page 8, line 156-170** of the revised manuscript above is "Three elliptical patches on the polyester fabric of the stent graft were separately modified around each arch branch orifice under direct visualization by a pair of surgical scissors. The modification diameter at the stent graft was similar to that of each branch orifice. (Figure 1 D1 and D2). Next, each arch branch vessel was connected to the stent graft, using the inside-to-out technique, followed by the returning-to-the-inside technique, through all the layers of the polyester fabric and the native aortic arch wall as deeply as possible. Specifically, the polyester fabric of the stent graft at the base of the modification was first sutured around each arch branch orifice using a 5-0 polypropylene 17-mm 1/2C double-armed mattress suture. Then, the polyester fabric was stitched to the native aortic arch wall using a continuous suture. Usually, the left subclavian artery was first reconstructed, followed by the left common carotid artery and then the innominate artery. After reconstructing the aortic arch, the proximal end of the stented graft and aortic wall were anastomosed together to complete the proximal aortic arch stump plasty with a continuous suture (4-0 polypropylene suture). (Figure 1 E1 and E2)."

Comment 5: Is it possible that anastomotic bleeding can result in some kind of 'endoleak'? And so yes, how can you deal with this.

Reply: We appreciate the reviewer's question. Accordingly, we have added more

information about endoleak from anastomotic bleeding **on Page 17, line 355-367** of the revised manuscript.

The information of about endoleak from anastomotic bleeding in details **on Page 17, line 355-367** of the revised manuscript above is "Endoleak from the anastomotic bleeding remains an important complication for the stent graft technique (22). CTA should be scheduled for each patient before discharge, 3 months after the surgery, and every 6 months thereafter to detect endoleak and malperfusion of the three supra-aortic vessels. For a small endoleak, no reintervention was performed except a close follow-up. However, type I endoleak should be managed with early reintervention using embolization or branched stent graft (23). In our early procedures, we did find that the margin of the left subclavian artery is generally the source of type I endoleak; thus, we updated our protocol of anastomosis in subsequent cases, which emphasized a maximum penetration through all the layers of the polyester fabric and the native aortic arch wall to confirm the tight attachment between the stent graft and native arch. Since then, type I endoleak never happened again. In our study, all surviving patients undergoing the s-TAR were confirmed to be patent without any type of endoleak during the follow-up."

Comment 6: What is done if the distal aortic arch is > 35 mm?

Reply: We thank reviewers for the helpful comment. Accordingly, we have added

more discussion about what to do if the distal aortic arch is > 35 mm **on Page 18, line 374-380** of the revised manuscript.

The added part about what to do if the distal aortic arch is > 35 mm in details **on Page 18, line 374-380** of the revised manuscript above is following as "Based on our experiences, selection of suitable patients is also the key to the success of our s-TAR technique. If the distal aortic arch is more than 35 mm before operation, two stent grafts should be inserted, one of which is in the distal aortic arch and partially overlapped. In our clinical practice, there were a small number of patients who received the s-TAR procedure using two stent grafts due to the distal aortic arch more than 35 mm, as shown in Figure 3."

Comment 7: Patients' allocation for each procedure is not clearly described. It is not done by randomization. You should mention the selection bias as a limitation of this study, because surgeon's preference or anatomical suitability could be the potential bias of this study.

Reply: We thank the reviewer for this comment. Accordingly, we have added the selection bias to the study limitations section **on Page 19, line 395-398** of the revised manuscript.

The added part about selection bias **on Page 19, line 395-398** of the revised manuscript above is following as "Patients' allocation for each procedure is not done

by randomization. Thus, surgeon's preference or anatomical suitability could be the potential bias of this study. In addition, this study is a retrospective study with a limited sample size. Further research with multiple centers and larger samples are scheduled."

Comment 8: Because I am not accustomed to this stent graft, as most of the readers all over the world, it would be better to mention the length of the stent graft. Can you select the variety of length of the stent graft according to the aortic anatomy? As you mentioned in the manuscript that "the proximal end of the stented graft was "moved forward" and positioned just proximal to the origin of the innominate artery, resulting in limited sacrifice of intercostal arteries and avoiding extensive coverage of the descending aorta." I presume that you cannot control the distal landing zone by selecting variety of graft length.

Reply: We thank the reviewer for this comment. Accordingly, we have added the information about stent graft to the Methods section **on Page 6, line 122-125** of the revised manuscript.

The added part about the information about stent graft **on Page 6, line 122-125** of the revised manuscript above is following as "The stent graft (Microport Medical Co, Ltd, Shanghai, China) was used in our surgical procedures, which consisted of a woven

Daron graft and a self-expandable metallic stent (diameter, 28–30 mm). A 10-mm stent-free sewing Dacron edge was placed on both ends, to which a conventional hand-sewn anastomosis could be done."

Comment 9: Contraindication of this modification might include severe atherosclerotic wall of the aorta at the origin of supra-aortic vessels.

Reply: We thank the reviewer for this comment. Accordingly, we have added this contraindication to the exclusion criteria **on Page 5, line 104-106** of the revised manuscript.

The added part about the exclusion criteria **on Page 5, line 104-106** of the revised manuscript above is following as "severe atherosclerosis in the aortic arch or severe calcified plaque in the origin of supra-aortic vessels which may increase the risk of endoleak and cerebral infarction."

Comment 10: When the diameter discrepancy between anastomosis site and zone 2 of the aortic arch was large, is this procedure still indicated, or is it an anatomical contraindication?

Reply: We thank the reviewer for this comment. Accordingly, we have added more discussion about what to do if the diameter discrepancy between anastomosis site and

zone 2 of the aortic arch was large **on Page 17, line 368-374** of the revised manuscript.

The added part about what to do if the diameter discrepancy between anastomosis site and zone 2 of the aortic arch was large in details **on Page 17, line 368-374** of the revised manuscript above is following as “If the diameter discrepancy between anastomosis site and zone II of the aortic arch was large, the s-TAR procedure could still be performed. When there is constant blood flow through the aortic arch, it creates pressure on the aortic wall and dilates the aortic arch. However, when the proximal end of the aortic aorta is blocked during the operation, the dilated aortic arch would shrink back. Thus, the implanted stent graft could be tightly attached to the wall of the native aortic arch. Follow-up data in this study suggested that the stent graft was attached well with the native aortic arch.”

Comment 11: Suturing the origin of the supra-aortic vessels to the stent graft might be a potential risk of endoleak, especially the size mismatch is prominent.

Reply: We thank the reviewer for this comment. Accordingly, we have added more discussion about how to do if the size mismatch is prominent **on Page 18, line 381-392** of the revised manuscript.

The added part about how to do if the size mismatch is prominent in details **on Page 18, line 381-392** of the revised manuscript above is following as “Actually, it is

important for surgeons to measure the distance between the origins of three arch branch vessels at aortic CTA. The distance between the three arch branch vessels should be more than 1.5 cm in s-TAR technique. During the procedure, the surgeon should reconfirm the distance before modifying the stent graft. If the distance between the origins of three arch branch vessels is less than 1.5 cm, the s-TAR technique should be adjusted the primary protocol as there is a high chance of endoleak. Specifically, the entire “island” patch on the polyester fabric of the stent graft were removed around the orifices of the three arch branches under direct visualization by a pair of surgical scissors. Then, the three arch branch vessels were integrally sutured to the polyester fabric of the stent graft. The other steps were the same as before. Figure 4 shows a schematic representation of the entire “island” modification in the s-TAR procedure.”

Second Round Peer Review

Comment 1: I have had the pleasure to review the revised manuscript. The authors have improved certain aspects of this paper, but I am afraid further work is necessary. Two areas need revising primarily: 1) References seem out of synch. On multiple points the reference does not backup the statements made. (Examples: ref 2,3,7,11, etc)

Reply: We thank the reviewer for this comment. Accordingly, we have updated some of the references in the revised manuscript.

Comment 2: Certain contradictions exist: Examples: 1. Line 119: you discuss primary tear and further down state acute aortic dissection was excluded?

Reply: We thank the reviewer for this comment. Accordingly, we have depleted this contraindication from the exclusion criteria **on Page 6, line 103-108** of the revised manuscript.

The rewritten part about the exclusion criteria **on Page 6, line 103-108** of the revised manuscript above is following as "The exclusion criteria were: (1) a primary tear involving the aortic arch or orifices of three supra-aortic branches; (2) severe atherosclerosis in the aortic arch or severe calcified plaque in the origin of supra-aortic vessels which may increase the risk of endoleak and cerebral infarction; (3) serious comorbidities such as ruptured aneurysm, severe coagulation disorder, and multiple organ failure".

Comment 3: Line 127: Choice of procedure was based on underlying condition but also 1:1?

Reply: We thank the reviewer for this comment. Accordingly, we have added more discussion about the choice of procedure **on Page 7, line 109-114** of the revised manuscript.

The added part about the choice of procedure **on Page 7, line 109-114** of the revised

manuscript above is following as “The decision to proceed with s-TAR or c-TAR was discretionary based on the underlying clinical conditions. In general, for each one patient from the s-TAR cohort, one control subject was recruited into c-TAR cohort. The 1-to-1 matching was based on variables identified a priori to be of interest. Matching variables included age (± 5 years), sex (exact), weight (± 20 kg), height (± 20 cm), and left ventricular ejection fraction (LVEF, ± 10%)”.

Comment 4: I am not aware of any guideline stating arch surgery should be performed at 35mm. Please reference appropriately.

Reply: We thank the reviewers for this comment. Accordingly, we have added more discussion about the surgical indication **on Page 19, line 394 and Page 20, line 395-407** of the revised manuscript.

The added information about the surgical indication **on Page 19, line 394 and Page 20, line 395-407** of the revised manuscript above is following as “Among healthy adults in China, the normal diameter of aortic arch is about 23.9-29.8 mm. A 50% increase is referred to about 35-45 mm, which is considered arch aneurysmal dilatation. In the presence of ascending aortic aneurysm, the diameter of aortic arch in zone II > 35 mm could be considered an indication for concomitant aortic arch reconstruction. If the ascending aorta is replaced alone, the residual intact arch may be at excess risk of aortic dilation, dissection, and thus reoperation. In our early experiences, patients with ascending aortic aneurysm and aortic arch dilation (Zone II,

35-45 mm) commonly received ascending aorta replacement alone, but not concomitant aortic arch reconstruction. Subsequently, a large proportion of the patients required secondary surgical management within 2-3 years as the residual aortic arch developed an aneurysmal dilatation or dissection (Supplementary Figure 1). Therefore, prophylactic reconstruction of the intact aortic arch is necessary at the time of ascending aorta replacement for ascending aortic aneurysm combined with aortic arch dilatation as long as the patient's condition permits this".

Comment 5: Hemiarch surgery is not a form of arch replacement!

Reply: We thank the reviewers for this comment. Accordingly, we have rewritten the information about the hemiarch surgery **on Page 14, line 279-284 and Page 15, line 285-287** of the revised manuscript.

The rewritten part about the hemiarch surgery **on Page 14, line 279-284 and Page 15, line 285-287** of the revised manuscript above is following as "The standard surgical procedures for ascending aortic aneurysm with extended aortic arch dilation are contemporarily the ascending aortic arch replacement combined with hemi- or total-arch replacement and classical elephant trunk or stented elephant trunk technique. The hemi-arch replacement is literally described as the resection of ascending aorta, and elimination of the aortic arch wall to the orifice of innominate artery in the greater curvature and the lesser curvature as much as possible. Given the remnant aortic pathologies after hemi-arch replacement, this procedure may potentially place the

patients at excess risk of aortic dilation, dissection, rupture and thus reoperation. Therefore, our center has not used this method since 2015”.