Has personalised surgery made another advancement in aortic root surgery?

Yuanjia Zhu, Joseph Woo

The valve-sparing aortic root replacement (VSARR) operation using the remodelling and reimplantation techniques were first described in 1979 and 1988, respectively.[1 2] This procedure was designed to preserve the aortic valve cusps in patients who have aortic root aneurysm with or without associated aortic regurgitation (AR) by replacing the aneurysmal root segment with an artificial aortic graft. Since the debut of the VSARR procedure, it has gained popularity in experienced surgeons and is an excellent choice for patients whose ARs are functional without calcification or fenestration and are mainly due to functional aortic annulus dilation.[3 4] A variety of graft configurations with different graft geometries and neosinus construction techniques have also been described.[3] In patients whose aortic valve cusps require further repair, standard aortic valve repair techniques can also be applied at the same time of VSARR.[4]

The personalised external aortic root support (PEARS) technique was first described by Pepper *et al* in 2013.[5] Briefly, to perform this procedure, each patient's aortic measurements are obtained from three-dimensional (3D) imaging, such as MRI or CT, and are rendered into a computer-aided design model. This 3D reconstruction of the individual patient's aorta is wrapped with a customised external support mesh made from medical grade polymer fabric with a pore size of 0.7 mm. To implant this support mesh, extensive dissection must be performed first to completely free the aorta from the aortoventricular junction proximally to the origin of the brachiocephalic artery distally. Both the left and right coronary arteries must also be dissected circumferentially. Next, coronary artery openings are made in the support mesh, and the axial seam is opened longitudinally, followed by an incision to connect the axial seam to the coronary opening. The mesh is then carefully placed around the aorta with locating sutures through the seam at the lower margin of the mesh, the nadir of aortic cusp attachments, and in line with the commissures to prevent migration. Early results after PEARS appeared promising with low morbidity and reoperation rates.[6 7]

In this issue's matched comparison of PEARS versus VSARR conducted by Van Hoof *et al*,[8] the authors investigated patients in the "PEARS 200" database and patients in the "Aortic Valve Insufficiency and Ascending Aorta Aneurysm International Registry" who underwent VSARR. Only patients with connective tissue disease operated electively for root aneurysm <60 mm with AR of <1/4 were included. In general, patients undergoing VSARR were further along in their aortic aneurysm disease progression or had a more severe connective tissue disease phenotype than those undergoing PEARS (49 vs 46 mm, $p<0.001$). Additionally, VSARR patients compared with PEARS patients were older, had higher EuroSCORE II, and were more likely to have preoperative AR. Propensity score was calculated using the following variables: gender, age, height, weight, a previous history of cardiac surgery, EuroSCORE II, left ventricular ejection fraction, maximal aortic root diameter, preoperative AR grade, and scheduled concomitant procedure. Propensity score matching of 1:1 was then conducted, and 80 pairs were generated. Median follow-up for the PEARS and the VSARR groups were 25 and 55 months, respectively. Seven (4.4%) patients who had PEARS required intervention for coronary injury or impingement, resulting in one death (0.6%), whereas one coronary intervention and zero death were reported after VSARR. In the matched cohort, survival at 5 years was similar for PEARS and VSARR at 98.3% and 98.6% ($p=0.27$), respectively. Freedom from aortic valve or aortic intervention as well as freedom from AR of ≥2/4 up to 5 years were also similar in the matched cohort ($p=0.67$ and $p=0.40$, respectively). No type A dissections were reported during the study period.

Though the results following PEARS were equivalent to those after VSARR, some questions remained unanswered and to be explored. In the study, the authors acknowledged that the unmatched cohorts were inherently different between those who underwent PEARS and those who underwent VSARR. Although propensity score matching was conducted, certain differences cannot be adjusted. For example, the VSARR patients appeared to present at a later stage of the aortic disease or had more aggressive connective tissue disease phenotypes with AR prior to operation. Additionally, for the VSARR patients, 57% were operated on using the reimplantation technique, and 37.4% underwent remodelling with aortic annuloplasty. Although this study may not be powered to investigate differences between these two groups compared with PEARS, stratification on postoperative AR based on the specific VSARR technique employed is warranted. We suspect that the outcomes following VSARR using the remodelling versus reimplantation technique may be quite different. Since a randomised control trial cannot be performed, a selection bias is potentially present when deciding which procedure a patient should undergo. The results reported in this article at least demonstrated excellent decision making by the surgeons included in the databases.

The VSARR procedure has the important advantage of replacing the diseased aortic segment with Dacron grafts, taking late aortic dilation and disease progression out of the equation. At the same time, surgeons can choose the appropriate graft size from a wide range of graft diameters to reproduce the native, non-diseased geometry of the aortic root. In the PEARS cohort, downsizing of the aorta was also achieved by manufacturing the implant scaled to 95% or 100% luminal diameter. Though this may be adequate for patients with mild aortic aneurysms, PEARS is not suitable for those with advanced aneurysmal disease or fragile aortic tissue. Furthermore, even implanting the device at 100% luminal diameter, the aortic tissue is still constricted and under constant circumferential tension. Further downsizing of the diameter may greatly affect tissue viability in the long term. What is happening biologically to the aortic wall that is under continuous circumferential stress? How much does the aorta grow over time after PEARS? Additionally, since the seam has to be opened in order to wrap the aorta with the implant and only a few sutures are placed to secure the implant, there are large areas of weak points mechanically, and each anchor suture becomes a stress concentration. These can lead to device failure or may even allow for pseudoaneurysm formation through the weak points. The authors also acknowledged that

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dissecting around the left coronary artery is the most dangerous manoeuvre in the operation. In fact, high incidences of coronary injury from PEARS were reported in several publications.[5–7] One may ask if it is worth it in the end to not be able to definitively address the aortic pathology while compounding the risk of coronary injury that requires coronary artery bypass grafting.

The VSARR procedure overall is highly versatile and can also be personalised according to patients' root geometries and pathologies. For example, aortic cusp repairs can be performed simultaneously when the aortic valves are exposed. Naturally, patients would not be selected to undergo PEARS if extensive aortic cusp repairs are anticipated, further limiting the candidate pool for PEARS. In fact, nearly 40% of VSARR patients in this study required some form of aortic cusp repair. Additionally, any malalignment in the aortic commissures can also be addressed when posting the commissures onto the Dacron graft. A biomechanical engineering study confirmed the important and intricate relationship of commissure rotational angle and height to AR.[9] Minor aortic cusp prolapse can potentially be corrected by adjusting aortic commissure positions on the Dacron graft. The VSARR procedure also provides structural support around the functional aortic annulus and the sinotubular junction to ensure long-term durability of the optimised aortic root geometry.

Overall, the article presented an interesting procedure to address aortic root aneurysms. Though one may be excited about this personalised surgical approach, we have to bear in mind that PEARS may only be suitable for select patients. There are still many questions to be answered. We are looking forward to seeing the long-term outcomes following PEARS and are excited to see efforts made to drive early surgical intervention for patients with aortic diseases.

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Correspondence on "Has personalised surgery made another advancement in aortic root surgery?" by Zhu and Woo

To the Editor A matched comparison of personalised external aortic root support (PEARS) and valve-sparing root replacement (VSRR)—to which two of the present authors contributed (JP, TT)—has recently been published.[1] In an accompanying editorial, Zhu and Woo ask whether PEARS is an advancement in aortic root surgery.[2] We have been involved in the development and evaluation of PEARS and would like to provide further information and clarify some points in response to this editorial.

The PEARS procedure was proposed in 2000 by a patient and developed with academic engineers and surgeons. The inventor was the first recipient as published in The Lancet in 2004.[3] This was followed by a succession of technical and clinical papers cited in an Editorial in Heart in 2011.[4] In 2014, outcomes in the first 30 patients, 1–9 years after operation, were published in Heart.[5] A study of patients' values published in Heart[6] showed that patients with inherited root disease, who often have family histories to inform them, have very clearly expressed preferences. The exponential rise in the overall number of PEARS operations[7] has in large part been driven by patients finding their own information.

Biological incorporation of the PEARS mesh and its effect on circumferential stress and aortic expansion over time have been answered in published evidence from animal experiments[8] and cardiac MRI.[9] These show that incorporation of the mesh into the aortic wall consistently provides a thicker neoaorta with no increase in luminal diameter over time. Laplace's law states that wall tension is inversely related to the wall thickness and directly related to diameter, so the aortic wall stress is reduced by PEARS.

By January 2022, there had been no record of pseudoaneurysm formation in 570 PEARS operations in 12 countries though not yet in the USA.[7] The precise method of dissection and placement of the mesh is designed to preclude all suture lines as has been described and illustrated by Czech authors.[10]

There have been no published reports of PEARS device failure. Continued enlargement has only been seen in cases where a surgeon deviated from the protocol, discarding the proximal portion of the mesh thus performing 'an inadvertent 'double-blind' trial of a sham operation after which the aortic root continued to expand'.[11] Of note are the histological findings after a coincidental death 4.5 years after PEARS which showed restoration of normal collagen in the aortic media in the *supported* compared with the *unsupported* aorta.[12] Surgery cannot replace missing fibrillin but healing of collagen in ligaments and tendons is achieved by physically supporting tissues to reduce tension as occurs in PEARS.

AVIATOR (Aneurysm InternATiOnal Registry) is a register of completed operations, by surgeons and centres with a commitment to VSRR. Registries provide an opportunity for an unrecorded number of patients to be diverted to other operations, which is more likely when technical difficulties such as coronary injury are encountered, thus reducing the record of adverse events. PEARS is manufactured to measure from each patient's imaging allowing complete intention-to-treat data capture.

We consider that the intention of early diagnosis and monitoring of congenitally determined aortic root disease is to offer truly prophylactic interventions. As set out in the editorial, VSRR is more versatile than PEARS[2] but stability of aortic dimension and aortic valve function were comparable in the propensity-matched comparison.[1] In the survey of patients' values,[6] most placed high value on the reduced burden of anxiety and freedom to enjoy an unrestricted active lifestyle. We suggest that PEARS is a means towards those two objectives so we do regard it to be an advance.

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Response to: Correspondence on "Has personalised surgery made another advancement in aortic root surgery?" by Zhu and Woo

We appreciate the letter from Austin and colleagues regarding our article 'Has personalised surgery made another advancement in aortic root surgery?'.[1] In the previous article, we briefly summarised the excellent results from the matched comparison study performed by Van Hoof and colleagues regarding personalised external aortic root support (PEARS) versus valve-sparing aortic root replacement.[2] We had several questions regarding the inherent limitations from a study that used propensity score matching, biological changes to the aortic wall after PEARS, rates of aortic growth and device failure post-repair, and concerns for coronary injury. In the correspondence letter, the authors adequately addressed our questions with data nicely summarised from other studies from the group.[3–12] Overall, the article presented by Van Hoof *et al* conveyed exciting results and represents another step forward towards personalised surgery.[2] We would like to congratulate the authors again for their hard work and the thoughtful interpretation of their results. We are excited to see that computer-aided design and a personalised surgical approach have important roles in the field of aortic surgery. We are optimistic that early surgical intervention in patients with aortic disease via advanced repair techniques and innovative technology will markedly improve long-term outcomes.

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