Personalized external aortic root support (PEARS): A narrative review

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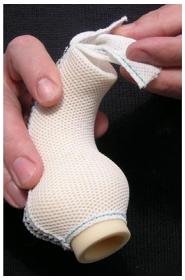
We review the development and present status of personalized external aortic root support (PEARS) in a chronological narrative.



The ExoVasc pliable macroporous mesh sleeve as presented to the surgeon for implantation.

CENTRAL MESSAGE

PEARS is an operation to prevent dilatation and to maintain aortic valve function in Marfan and other aortic root aneurysms.

PERSPECTIVE

As the result of patient and family awareness and access to echocardiography and radiologic imaging, individuals with genetically triggered aortopathy with root aneurysm present earlier. For them, PEARS complements root replacement surgery.

THE GENESIS OF A NOVEL APPROACH

PEARS was first proposed to the UK Marfan Association in 2000 by Tal Golesworthy, a developmental engineer with Marfan syndrome. His aortic diameter had increased from 44 mm to 49 mm over 12 years. He questioned what had been told by his cardiologist—that he should have his ascending aorta and aortic valve replaced, followed by lifelong anticoagulation. He had heard Tom Treasure's annual lecture to families with Marfan syndrome, which included timing of surgery with reference to correspondence with Vincent Gott in the *New England Journal of Medicine*.[1] In the postlecture Q&A, Golesworthy challenged the need for extirpative surgery. He envisaged the application of modern science to revisit the then 30-year-old idea of externally supporting an aortic aneurysm.[2] He foresaw computer modeling, with data from digital images being used to generate a physical replica of the individual's aorta by 3-dimensional printing. On that former, a personalized well-fitting sleeve would be fashioned to prevent further expansion.

PRECLINICAL BASIC SCIENCE

During the following few years, Golesworthy and Treasure investigated the feasibility of the idea. Golesworthy came to the operating theaters to see what was entailed in total root replacement. Together, they went to Robert Anderson to take a focused look at the morphology of the aortic root. Golesworthy collaborated with Michael Lampérth and Warren Thornton of Imperial College London to develop computer-aided design modeling for rapid prototyping, now known as 3-dimensional printing.

Because the intention was to support rather than to replace the aorta, a porous knitted fabric was chosen to avoid graft migration and vascular erosion,[3] the known consequences of wrapping with stiff low-porosity material. It was decided to use the same polymer, polyethylene terephthalate (Dacron), because of its proven biocompatibility.

DEVELOPMENT AND CLINICAL TRIAL OF THE PEARS OPERATION

With John Pepper, we discussed the surgical method of implantation, repeatedly and in detail. Pepper negotiated with the Royal Brompton Hospital a trial of the new procedure

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Abbreviation and Acronym
PEARS = personalized external aortic root support

in 20 patients, conducted in accordance with the requirements of the Research Ethics Committee. All patients were informed that this was innovative surgery and discussed risks and benefits with the operating surgeon. The first operation, on Golesworthy, appeared as a research letter in *The Lancet*.[4]

Surgeons embarking on PEARS are proctored by experienced operators and must study the instructions for use. In addition to the published method of implantation,[5] 2 teams in the PEARS diaspora have contributed "How to do it" papers, which provide further expert insights.[6,7] The ExoVasc device and the steps in the operation have remained unchanged, which we attribute to the time spent in basic research collaboration and careful planning. Bentall's total root replacement[8] and David's valve sparing operation[9] were conceived at the operating table and then progressively evolved in clinical practice.

OPERATIVE METHOD

The aorta is mobilized from the aortoventricular junction to beyond the brachiocephalic artery. Dissection is straightforward in the noncoronary sinus. It is more difficult in the right coronary sinus because of the proximity of the muscular free-wall of the right ventricular. The challenge in the left coronary sinus is the close proximity of right ventricular outflow tract and the pulmonary artery. Details are shown in elegant and informative drawings in Kenny's description.[6]

Dissection is made easier by avoiding cardiopulmonary bypass and anticoagulation—as has been done in 79% of cases to date—and by lowering the blood pressure and heart rate, and exercising great patience. It is also facilitated by the greater length of aortic root proximal to the coronary origins, which is a feature of Marfan morphology. Once the ExoVasc sleeve is in place, laminar flow in the coronary arteries is confirmed by transesophageal echocardiography.

In 2 instances, the surgeon did not properly dissect the aortic root and the root aneurysm continued to enlarge. At repeat operations, it was discovered that the critical area of the aortic root, proximal to the coronaries, had never been dissected or supported. These breaches of the operative protocol—effectively sham operations—are mentioned to emphasize the importance of strict adherence to the method.[10]

ESTABLISHING TECHNICAL EFFICACY OF THE PEARS IMPLANT

In a study designed and implemented in the Clinical Operational Research Unit at University College London, magnetic resonance imaging scans of the aortic root, before and at 6, 12, 24, and/or 36 months after the first 10 PEARS operations, were cropped to remove identifiers and dates. They were placed in random sequence with duplicate images of 37 unoperated patients with Marfan syndrome. Three commissure-to-sinus measurements were made "blind" by an independent vascular radiologist. No supported root had further enlarged, and 8 of 10 were markedly reduced, and remained so, with preservation of the sinus morphology.[11]

In studies in the Department of Engineering at Imperial College London 2015-2016, the characteristics of the neoaorta created by mesh incorporation were explored with finite element modeling. Both circumferential and axial wall stress were seen to be reduced by up to 52% after PEARS implantation.[12] Most type A dissections originate from a transverse tear close to the sinotubular junction.[13] PEARS eliminates this process by reducing the axial displacement.

INVESTIGATING PERIOPERATIVE BENEFITS OF PEARS

The first 20 patients who received PEARS were matched for age and root size with patients having conventional root replacement at other hospitals where PEARS was not available. Only 1 of 20 patients who received PEARS (the first) had cardiopulmonary bypass; none had myocardial ischemia. They had shorter operation times, markedly less blood loss, and only one had a blood transfusion. None needed platelets or clotting factors.[14]

EVIDENCE OF INCORPORATION OF THE MESH TO FORM A NEOAORTIC WALL

Surgeons and scientists in Leuven, Belgium, performed recovery experiments (2013-2017) in sheep[15,16] and found that the PEARS mesh was densely and consistently incorporated in the vascular adventitia.[15,17] There has been only one opportunity to confirm incorporation in humans. The 16th PEARS patient operated on in 2008 at the Royal Brompton Hospital died in his sleep of a presumed arrhythmia in 2013.[18] The aortic valve was normal and competent. On histologic examination, the mesh was incorporated into the aortic adventitia. Characteristic medial degeneration was seen distal to the support but within the implant, there was normal histology.[18] The pathologic interpretation was that absence of stress in the media of the supported part of the aorta allowed recovery of collagen formation.

EVOLVING INDICATIONS AND NEW APPLICATIONS OF PEARS

The tenth PEARS recipient was referred because her Marfan-related aneurysm had expanded during pregnancy. She wanted a PEARS operation to protect her during a subsequent planned pregnancy. She described her "patient's journey" in the *BMJ*.[19] We know of 13 would-be mothers

TABLE 1. Data on the first 200 primary PEARS operations[22] and a matched comparison of PEARS and VSSR[23]

Variable	PEARS 200 N (% or IQR)	PEARS 80 N (% or IQR)	VSRR 80 N (% or IQR)	*P* value
Male	138 (69%)	57 (71.3%)	57 (71.3%)	1.00
Age	33 (23-45)	31.7 (21.5-42.5)	32 (26.25-38)	.63
Root diameter	47 (44-49)	48 (46-50)	48 (46-49)	1.00
Marfan	147 (74%)	77 (96.3%)	64 (80.0%)	
Reoperation for bleeding		0 (0%)	6 (7.5)	.03
Stroke	2 (1%)	1 (1.3%)	1 (1.3%)	1.00
Death	1 (0.5)	0 (0%)	0 (0%)	1.00
Length of stay, d		6 (5-7)	7 (6-9)	<.001
AR grade 0-1/preoperative		80 (100%)	80 (100%)	
AR grade 0/4 postoperative		69 (83.6%)	62 (77.5%)	NS
AR grade last F-U				<.01
0/4		64 (85.4%)	41 (57.8%)	
1/4		10 (13.3%)	25 (35.2%)	
2/4		1 (1.3%)	2 (2.8%)	
≥3/4		0 (0%)	3 (4.3%)	

P values are for the 2 right-hand columns. *PEARS*, Personalized external aortic root support; *VSSR*, valve-sparing root replacement; *IQR*, interquartile range; *AR*, aortic regurgitation; *NS*, not significant; *F-U*, follow-up.

who have had PEARS without evidence of further aortic enlargement and 14 subsequent successful pregnancies. One had her operation (off-pump) during her second trimester. All are well and the number of pregnancies may be an underestimate because pregnancy and childbirth are not routine items for enquiry after aneurysm surgery.

Early in the experience, 2 patients had a PEARS implant and mitral valve repair during the same operation.[20] A total of 43 patients have had both procedures. In some cases, mitral regurgitation is the driving indication.

PEARS has also been used to support the pulmonary autograft in the Ross operation. The first 50 patients to have a Ross PEARS operation by Conal Austin were presented at The American Association for Thoracic Surgery and are published.[21]

PATIENT NUMBERS, CASE MIX, AND RESULTS

The thousandth patient landmark was reached in Spring 2024, but because of an exponential increase in case numbers, only 218 are 5 or more years after operation, so analysis of long-term outcomes would be premature. However, in the 20 years of clinical experience to date no patient in whom the ExoVasc PEARS device has been correctly implanted has demonstrated subsequent dilatation or dissection of the supported ascending aorta. The follow-up study of the first 200 patients who had PEARS for aortic root aneurysm[22] and a matched-pairs comparison with valve-sparing root replacement are summarized in Table 1.[23]

THE AUTHORS' CONCLUSIONS

Increased awareness of the possibility of root aneurysms in families affected by inherited connective tissue disease has resulted in people presenting early in the natural history of their disease. The PEARS operation is designed precisely for these patients. Outcomes in the matched comparison are similar, but there is a significant difference in progression of aortic valve regurgitation.

We cannot predict aortic dissection. PEARS may be ideal for patients whom we consider to be at high risk of dissection because of family history, a period of rapid enlargement, or a wish to become pregnant at an aneurysm size lower than a commonly accepted threshold. When we embarked on PEARS, the range that we set for operation was an aortic root diameter between 40 and 50 mm. We are acutely aware that in an important minority of aortic dissections the ascending aorta is not enlarged. Therefore, in our assessment of a prospective patient, we advise operative intervention if there is enlargement of 5 mm in 1 year even if the aortic diameter is less than 40 mm.

Conflict of Interest Statement

T.G. is Technical Director of Exstent, Ltd. All other authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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