DRAFT FOR CONSULTATION

Clinical Commissioning Policy Proposition:

Personalised External Aortic Root Support (PEARS) for surgical management of enlarged aortic root (adults)

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Clinical Commissioning Policy Proposition: Personalised External Aortic Root Support (PEARS) for surgical management of enlarged aortic root (adults)

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Plain Language Summary

The policy proposition aims to confirm NHS England's commissioning approach to personalised aortic root support for patients with enlarged aortic roots.

The aim of personalised external aortic root support (PEARS) is to prevent enlargement and subsequent rupture of the aorta, which is frequently fatal. The aorta is the main blood vessel that carries blood from the heart. PEARS is a bespoke, personalised, 3D printed sleeve of medically approved knitted mesh to support the aortic root and ascending aorta. It is created using computer-aided design from a special CT scan to make an individualised replica for each patient's own ascending aorta and aortic root. On this replica is manufactured a sleeve of a soft, compliant fabric that is then fitted onto the patients aorta during surgery.

Most patients presenting with enlarged aortic roots are adults and children with Marfan syndrome. Marfan syndrome is a genetic disorder of the connective tissues - a group of tissues that maintain the structure of the body and support internal organs and other tissues. In people with Marfan syndrome, the aorta is weaker than usual and prone to enlarge and widen. The widening is progressive and may lead to tears in the wall of the aorta and possibly rupture.

Other, less common, causes of enlarged aortic roots are patients with a bicuspid aortic valve (BAV), adults that have undergone complex cardiac correction in infancy, and adults that have undergone the Ross operation. BAV is a condition where the aortic valve has only two leaflets instead of the usual three. The valve may function normally for years without the patient being aware of the problem, often until they reach their 50s or 60s. The Ross procedure is a cardiac operation in which the aortic valve is replaced with the person’s own pulmonary valve. The pulmonary valve is replaced at the same time with a donor pulmonary valve.

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of personalised aortic root support for patients with enlarged aortic roots.

1. Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal to not routinely commission personalised external aortic root support for adults with enlarged aortic roots.

For the purpose of consultation NHS England invites views on the evidence and other information that has been taken into account as described in this policy proposition.

A final decision as to whether personalised external aortic root support for patients with enlarged aortic roots due to genetic diseases will be routinely commissioned is planned to be made by NHS England by May 2016 following a recommendation from the Clinical Priorities Advisory Group.

2. Proposed Intervention and Clinical Indication

The aim of personalised external aortic root support (PEARS) is to prevent enlargement and subsequent dissection and rupture of the aorta. PEARS is suitable for enlarged aortic roots measuring 40-55mm in diameter, and growing by >5mm per year, as measured by echocardiography.

Aortic roots become enlarged predominantly as a result of genetic diseases such as Marfan syndrome. Many of these patients have weak aortas that can become enlarged and progressively widen, which may lead to tears in the wall of the aorta (dissection) and possibly rupture, which is frequently fatal. Other causes of enlarged aortic roots are bicuspid aortic valve (BAV) disease and previous cardiac correction surgieries (for example, surgery in infancy and the Ross procedure).

With the PEARS procedure, a bespoke external support for the ascending aorta and aortic root is made using computer-aided design. During surgery, the support is wrapped around the aorta, which remains intact. The aortic valve must be functional.

3. Definitions

Personalised external aortic root support (PEARS) is a bespoke, personalised, 3-D printed sleeve of medically approved knitted mesh to support the aortic root and ascending aorta. It is created using computer-aided design from a special CT scan to make an individualised replica for each patient's own ascending aorta and aortic root. On this replica is manufactured a sleeve of a soft, compliant, macroporous fabric.

Annuloaortic ectasia is a cardiac anomaly that includes dilatation of the aortic sinuses and annulus in addition to the ascending aorta, leading to aortic valve insufficiency. If left untreated there is a high risk of death due to dissection or rupture of the aorta or heart failure resulting from severe aortic regurgitation.

Marfan syndrome is a genetic disorder of the connective tissues. In people with Marfan syndrome, the aorta (the main blood vessel that carries blood from the heart) is weaker than usual and prone to enlarge and widen. The widening is progressive and may lead to tears in the wall of the aorta (dissection) and possibly rupture.

A bicuspid aortic valve (BAV) is a congenital disease where the aortic valve has only two leaflets instead of the usual three. The valve may function normally for years without the patient being aware of the problem, often until they reach their 50s or 60s.

The Ross procedure is a cardiac surgery where the aortic valve is replaced with the person's own pulmonary valve. The pulmonary valve is replaced at the same time with a donor pulmonary valve.

Total root replacement (TRR), also known by Bentall procedure, is an open heart surgery where the entire aortic root and valve is replaced with an artificial fabric graft. Aortic valve can be replaced with either a mechanical or bioprosthetic valve.

The valve-sparing root replacement (VSRR) procedure preserves the functionality and superior hemodynamics of the native aortic valve while replacing the aortic root.

4. Aim and Objectives

This policy proposition aims to define NHS England's commissioning position on personalised external aortic root support (PEARS) as part of the treatment pathway for adults with enlarged aortic roots due to a genetic cause.

The objective is to ensure evidence based commissioning with the aim of improving outcomes for adults with enlarged aortic roots due to a genetic cause.

5. Epidemiology and Needs Assessment

The aim of personalised external aortic root support is to prevent enlargement and subsequent dissection and rupture of the aorta.

Annuloaortic ectasia is a cardiac anomaly that exists in about 75-85% of Marfan syndrome patients, therefore most patients presenting with enlarged aortas are adults and children with Marfan syndrome. Marfan syndrome is a genetic disorder of the connective tissues and affects about 1 in 5,000 people in the UK (Marfan foundation). Both men and women are equally affected.

Enlarged aortas also occur in patients with bicuspid aortic valve (BAV). BAV is the most common type of congenital aortic valve disease, affecting around 1-2% of the UK population. Approximately one third of BAV population also have an abnormality in the aorta which causes it to expand.

Other patients that may benefit from the PEARS procedure include patients that present with an enlarging aorta but a competent aortic valve due to having undergone complex cardiac correction in infancy and people who have undergone the Ross operation and now present with an enlarged aorta.

The PEARS procedure is appropriate for adults that have an enlarged aorta (40-55mm in diameter) that is growing by >5mm per year, as measured by echocardiography. Of the above identified sub-groups,about 40 - 50 patients per year are expected to meet these criteria. Around half (20-25) of these are expected to have Marfan syndrome, 10-15 to have BAV and 5-10 to have had cardiac correction surgery in infancy. Currently 10-12 patients per year undergo the PEARS procedure. If the number of specialised centres able to perform the procedure increases, the number of patients could rise to 40 - 50 patients per year and meet the total expected demand by eligible patients in England.

6. Evidence Base

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of personalised external aortic support (PEARS) for patients with enlarged aortic roots due to genetic diseases.

Annuloaortic ectasia is a cardiac anomaly which exists in about 75-85% of Marfan syndrome (MFS) patients. This includes dilatation of the aortic sinuses and annulus in addition to the ascending aorta, leading to aortic valve insufficiency. If left untreated there is a high risk of death due to dissection or rupture of the aorta or heart failure resulting from severe aortic regurgitation.

Currently there are three types of surgical methods to correct this anomaly including Total aortic root replacement (TRR), Valve-sparing aortic root surgery (VSARR) which includes two techniques reimplantation also called the David procedure and the remodelling as also called the Yacoub procedure. The other one is called the Personalised External Aortic Root Support (PEARS) developed by Treasure et al.
Total aortic root replacement (TRR) using a composite mechanical valve conduit by Bentall has long been considered the ‘gold-standard’ treatment in this setting, with good early and late postoperative outcomes. However, one of the limitation of this treatment is patients require long-term anticoagulation and experience complications related to anticoagulation. VSARR has emerged as an alternative to composite valve-graft aortic root replacement, particularly in patients with MFS who have isolated root pathology with functionally normal valve leaflets. This technique preserves native valves, thus avoiding the disadvantages of a mechanical prosthesis and the complication of lifelong anticoagulation. PEARS involves fitting a bespoke computer designed external support made of a fabric mesh manufactured from a macroporous textile from a medical grade polymer yarn.

Research questions:
• Is the proposed new procedure as effective as the existing procedure?
• Is the procedure better than the existing one in terms of improved outcomes for patients and for the clinical management of patients?

There are no studies reporting head-to head comparison of PEARS vs other two surgical techniques in patients with Marfan syndrome. The evidence for PEARS in Marfan syndrome mainly comes from studies published by Treasure et al and NICE Intervention Procedure Guidance 2011 https://www.nice.org.uk/guidance/ipg394/chapter/2-The-procedure authored by Treasure et al. The evidence for TRR and VSARR in Marfan syndrome is available from a systematic review by Benedetto et al 2011 and from a prospective multicentre study by Coselli et al 2014.

There are number of other studies (Liu et al 2011, Shrestha et al 2012, Hu et al 2014, Arabkhani et al 2015) comparing either TRR vs VSARR or comparing remodelling VSARR vs reimplantation VSARR which have a proportion of patients who are Marfan syndrome. As none of the studies report outcome on Marfan syndrome and are excluded from the evidence review

Short term outcomes: In a latest study by Treasure et al 2014 based on prospective case series of 30 Marfan patients undergoing PEARS had better outcomes compared to patients undergoing TRR or VSARR on number short term and long term clinical parameters as reported in studies for TRR and VSARR.The short-term 30 days peri-operative measures were better in PEARS (Treasure et al 2014) compared to TRR or VSARR (Coselli et al 2014). These included mortality, operation time, cardio pulmonary bypass time, myocardial ischemia time, blood transfusion, coagulation aid, ICU stay (hrs), major valve related and cardiac complications. However the baseline characters of patients in these two studies are different in that patients in study by Coselli had higher proportion of patients with aortic regurgitation (30% PEARS vs 78% TRR and 54% VSARR) and non-elective operations (0% PEARS vs 23% TRR and 4% VSARR). Also for number of other baseline characteristics it appears that patients who had TRR or VSARR had poorer measurements than PEARS but cannot be verified due to lack of comparative data in two papers. This difference in baseline could be because PEARS group included patients who did not have higher level of severity and did not meet European (ESC/EATS) guidelines for TRR or VSARR.

Long term outcome measures: Long term outcome measures of aortic surgery in Marfan syndrome patients are available from a systematic review by Benedetto et al (2011), Coselli et al 2014 and Treasure et al 2014 and 2015. The main long term outcome measures were re-intervention on aortic valve, thromboembolic events, endocarditis, valve related events, survival and valve related death. For all the long-term outcome measures PEARS group had better results in that this group has had no events (0%) recorded for the above indicators (pls see worksheet labelled Table -long-term outcome measure). However compared to patients in TRR and AVSRR patient groups patients in the PEARS group were on average operated upon at a younger age with smaller aortic root diameter and with no or trivial aortic regurgitation. None in the PEARS group had dissection at the time of surgery or prior to it compared to 23% in TRR and 6% in VSARR group in Coselli et al 2014 and 0.3% TRR and 0.18 VSARR in Benedetto et al 2011.

In summary it can be concluded that PEARS is a safe and effective elective intervention in carefully selected patients with Marfan syndrome who are at lower risk (smaller aortic root diameters, no aortic regurgitation, and younger age patients). However it is difficult to compare outcomes for PEARS with other intervention such as TRR or AVSRR, because of the differences in baseline characters patients undergoing TRR and AVSRR. Generally patients in TRR and AVSRR are older and are high risk in terms greater aortic root diameter, persistence of aortic dissection and aortic regurgitation which are all known risk factors that influence outcome of surgery. There are no published studies evaluating PEARS in high risk Marfan syndrome or TRR/AVSRR in low risk patients similar to patient group in Treasure et al. Also as noted in NICE IPG 2011 long term safety and effectiveness are yet to be established.

A prospective cohort study comparing PEARS alongside TRR and AVSRR as proposed by Treasure et al should be considered for further evidence generation. Also as the low complication rate in PEARS group could be due to low risk profile of patients, watchful waiting' as a comparator group need to be considered. This could provide answer to question if patients receiving PEARS have had unnecessary intervention and exposed to the risks of complication from the intervention.

Research question:
• Is the treatment more cost effective than using the existing procedure?

There are no published literature comparing the cost effectiveness of PEARS to TRR or VSARR. Treasure et al suggest that there are likely to be cost savings due to lesser complications, reduced procedural costs and avoidance of anticoagulation. However intervening early a can lead to increased number of cases treated and therefore increased costs.

Research question:
• Are any subgroups identifiable from the evidence?

There are no sub-group analysis available from Treasure et al 2014 and 2015. A subgroup analysis by aortic dimensions, aortic aneurysm, previous cardiovascular operation, and other cardiac risk factors could add to the evidence of effectiveness. However based on the reported outcome both short and long term measures in Treasure et al it appears that the current inclusions criteria appears to be safe and effective as the results for valve related deaths, survival and complication rates are at their lowest rates and for some none.

7. Documents That Have Informed This Policy Proposition

NICE interventional procedure guidance 294: external aortic root support in Marfan syndrome

8. Date of Review

This document will lapse upon publication by NHS England of a clinical commissioning policy for the proposed intervention that confirms whether it is routinely or non-routinely commissioned (expected by May 2016).