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

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

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Policy Statement

NHS England will not routinely commission Personalised External Aortic Root Support (PEARS) for surgical management of enlarged aortic root (adults) in accordance with the criteria outlined in this document. In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources. This policy document outlines the arrangements for funding of this treatment for the population in England.

Equality Statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities

Plain Language Summary

About enlarged aortic root

The aorta is the main blood vessel that carries blood from the heart. The 'aortic root' is the section of the aorta attached to the heart. The aim of personalised external aortic root support (PEARS) is to stop the aorta getting larger and then splitting (rupture). Most patients with enlarged aortic roots are adults and children with 'Marfan syndrome'.

- Marfan syndrome is a genetic illness of the connective tissues – these are 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 it tends to enlarge and widen. The widening gets worse and worse – and may lead to tears in the wall of the aorta and possibly splitting which will often lead to death.

Other, less common, causes of enlarged aortic roots are:

- Patients with a bicuspid aortic valve (BAV) – where the aortic valve (the valve between the heart and the main blood vessel coming out of the heart) has only two leaflets instead of the usual three. The valve may work normally for years without the patient being aware of the problem – often until they reach their 50s or 60s.
- Adults that have had complex heart surgery as a baby.
- Adults that have had the Ross operation – a heart operation where the aortic valve is replaced with the person's own pulmonary valve (the valve between the heart and the main vessel which moves blood from the heart to the lungs). The pulmonary valve is replaced at the same time with a donor pulmonary valve.

About the new treatment

PEARS is specially designed for each patient. It is a 3D printed 'sleeve' of medical grade knitted mesh. It supports the aorta, including the aortic root and the part of the aorta closest to the heart ('ascending aorta').

- It is made using computer-aided design from a special CT scan of the patient.
- This scan is used to make an individualised copy of each patient's own ascending aorta and aortic root.
- A sleeve of soft, flexible fabric can then be made around the copy.
- This is then fitted onto the patient's aorta during surgery.

What we have decided

NHS England has carefully reviewed the evidence to treat enlarged aortic roots with personalised external aortic root support (PEARS). We have concluded that there is not enough evidence to make the treatment available at this time.

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.

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 surgeries (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.

NICE has reviewed the procedure and published Interventional Procedure Guidance 394 'External aortic root support in Marfan syndrome' in May 2011.

2 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.

3 Aims and Objectives

This policy 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 in the use of PEARS for the treatment of adults with enlarged aortic roots due to a genetic cause.

4 Epidemiology and Needs Assessment

The aim of PEARS 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 (The 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 (Congenital Heart Defects UK). 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, it is estimated that about 40 - 50 patients per year are expected to meet these criteria. Around half (20-25) of these are estimated to have Marfan syndrome, 10-15 to have BAV and 5-10 to have had cardiac correction surgery in infancy. Currently, it is estimated that 10-12 patients per year undergo the PEARS procedure. However, clinical experts estimate that the number of patients could rise to 40 - 50 patients per year based on the probable number of eligible patients in England.

5 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; re-implantation also called the David procedure and remodelling also called the Yacoub procedure. The other one is called the Personalised External Aortic Root Support (PEARS) developed by Treasure et al (2012).

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 limitations 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 versus the 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 (2014, 2012, 2012) and NICE Intervention Procedure Guidance 2011[1] authored by Treasure et al (2012). 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

[1] https://www.nice.org.uk/guidance/ipg394/chapter/2-The-procedure

remodelling VSARR vs re-implantation VSARR which have a proportion of patients who have Marfan syndrome. As none of the studies report outcome on Marfan syndrome they are excluded from the evidence review

Short term outcomes: In the latest study by Treasure et al (2014) based on a prospective case series of 30 Marfan patients undergoing PEARS they had better outcomes compared to patients undergoing TRR or VSARR on a number of 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 a study by Coselli et al (2014) had a 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 a number of other baseline characteristics it appears that patients who had TRR or VSARR had poorer measurements than PEARS but this cannot be verified due to lack of comparative data in two papers. This difference in baseline could be because the PEARS group included patients who did not have higher levels 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 the PEARS group had better results in that this group had no events (0%) recorded for the above indicators. However compared to patients in the 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 interventions such as TRR or AVSRR, because of the differences in baseline characteristics of the patients undergoing TRR and AVSRR. Generally patients in TRR and AVSRR are older and are at higher 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 the patient group in Treasure et al (2012). 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 (2012) in the NICE IPG Guidance should be considered for further evidence generation. Also as the low complication rate in the PEARS group could be due to the low risk profile of these patients, watchful waiting as a comparator group would need to be considered. This could test if patients receiving PEARS have had an unnecessary intervention and exposed to the risks of complications 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 (2012) suggest that there are likely to be cost savings due to lesser complications, reduced procedural costs and avoidance of anticoagulation. However intervening early could lead to an increased number of cases being 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.

6 Documents which have informed this Policy

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

7 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision.

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