Clinical Commissioning Policy Proposition: Long term left ventricular assist device therapy for advanced heart failure (all ages)

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NHS England Reference: 1693

Prepared by NHS England Specialised Services Clinical Reference Group for Cardiac Services

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1 Executive Summary

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 advanced heart failure

Heart failure means that the heart is unable to pump blood around the body properly. It usually occurs because the heart has become too weak or stiff.

The function of the heart is to pump oxygen-full blood to muscles and vital organs such as the brain, kidney and liver. In heart failure, the heart is not strong enough to do this well. Symptoms of fatigue and breathlessness increase. In advanced heart failure patients are breathless even at rest, and organs such as the kidney and liver start to fail.

About current treatments

Heart transplantation is a definitive treatment for heart failure but not all patients are eligible. Drug treatment is effective in early heart failure but in advanced heart failure even continuous infusion of drugs administered into the veins (intravenous) fails to halt the advance of disease.

About the new treatment

Ventricular Assist Devices (VADs) are mechanical blood pumps that support or take over the pumping function of a failing heart (the right, left or both ventricles) to improve blood flow to muscle and other vital organs. Most of these devices assist the left ventricle of the heart and so are referred to as left ventricular assist devices (LVADs).

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What we have decided

NHS England has carefully reviewed the evidence for treating advanced heart failure with long term LVAD therapy. We have concluded that there is not enough evidence of either clinical or cost effectiveness to consider making this treatment available for a selected group of patients.

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2 Introduction

This document describes the evidence that has been considered by NHS England in formulating a proposal of long term left ventricular assist device (LVAD) therapy for advanced heart failure.

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 long term LVAD therapy for advanced heart failure will be routinely commissioned will be made by NHS England following a recommendation from the Clinical Priorities Advisory Group.

3 Proposed Intervention and Clinical Indication

The healthcare problem

Heart failure means that the heart is unable to pump blood around the body properly. It usually occurs because the heart has become too weak or stiff.

Conditions that can lead to heart failure include:

- coronary heart disease – where the arteries that supply blood to the heart become clogged up with fatty substances (atherosclerosis), which may cause angina or a heart attack
- high blood pressure – this can put extra strain on the heart, which over time can lead to heart failure
- cardiomyopathy – conditions affecting the heart muscle
- heart rhythm problems (arrhythmias) – such as atrial fibrillation
- damage or other problems with the heart valves
- congenital heart disease – birth defects that affect the normal workings of the heart.

Signs and symptoms, existing treatment

The main symptoms of heart failure are:

- breathlessness after activity or at rest
- feeling tired most of the time and finding exercise exhausting
- swollen ankles and legs

Some people also experience other symptoms, such as a persistent cough, a fast heart rate, and dizziness. The more advanced the heart failure, the more likely patients are to have many symptoms and treatments used previously are proving less effective.

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Patients with advanced heart failure would have progressed through treatment with optimal medical therapy, cardiac re-synchronisation therapy and non-transplant cardiac surgery if indicated before being considered for heart transplantation.

For patients with advanced heart failure who are not heart transplant candidates, the alternative treatments available include:

a) repeated hospital readmission for
   - intravenous therapy e.g. diuretics
   - intravenous inotropes (Level 2 or 3 care)
   - haemofiltration (Level 2 or 3 care)

b) palliative care until death

The proposed intervention and rationale for its use

Ventricular Assist Devices (VADs) are mechanical blood pumps that support or take over the pumping function of a failing heart (the right, left or both ventricles) to improve the haemodynamics and end-organ blood flow. Most of these devices assist the left ventricle and are referred to as left ventricular assist devices (LVADs).

VADs are commissioned by NHS England as a 'bridge to transplant' (BTT) for heart transplant candidates: LVAD implantation is used to support transplant eligible patients at risk of dying until a suitable donor is available.

This policy proposition is to describe a not for routine commissioning position for the use of LVAD implantation as a permanent life-long therapy to patients with advanced heart failure who are not heart transplant candidates. This is sometimes known as 'destination therapy'.

4 Definitions

Cardiac ejection fraction – this refers to the percentage of blood that is pumped (or ejected) out of the ventricles with each contraction.

Inotropes – a positive inotropic agent increases the strength of muscular contraction of the heart.

Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS). This is a North American registry established in 2005 for patients who are receiving mechanical circulatory support device therapy to treat advanced heart failure. It is sponsored by The National Heart, Lung and Blood Institute (NHLBI) and housed at the University of Alabama.

Revascularisation – this refers to procedures that aim to restore blood flow to the

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heart muscle that is supplied by narrowed coronary arteries. These include balloon angioplasty and coronary artery bypass graft.

Symptomatic hypotension – this refers to fall in blood pressure resulting in symptoms of discomfort, such as a feeling of weakness, fatigue, dizziness or loss of consciousness.

Level 2 critical care - patients requiring more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care.

Level 3 critical care - patients requiring advanced respiratory support alone or monitoring and support for two or more organ systems. This level includes all complex patients requiring support for multi-organ failure.

Continuous flow left ventricular assist devices (CFVAD) – a blood pump with a rapidly rotating impeller generating a continuous stream of forward blood flow.

WHO functional classes – a standard classification of disease severity of heart failure which places patients in one of four categories based on how much they are limited during physical activity. Patients in class I have no symptoms at physical activity; patients in class IV are symptomatic even at rest. Classes II and III are intermediate.

5 Aims and Objectives

This policy proposition considered: the use of LVAD therapy in adult patients with advanced heart failure.

The objectives were to review the evidence for LVAD in the treatment of patients with advanced heart failure who are not eligible for heart transplant.

6 Epidemiology and Needs Assessment

The proposal was considered for patients with advanced heart failure with a cardiac ejection fraction of 25% or less, not eligible for transplant and requiring continuous inotrope therapy. There is no direct epidemiological evidence about the size of this target population. Evidence is available from the North American INTERMACS registry and from other countries where LVAD destination therapy is funded. Expert opinion in the UK suggests that the best comparator is the United States, where the rate of destination LVAD implant is 4.2 per million population in 2015-16. Germany

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is a recognised outlier with a rate of 12 per million population.

From the US data 82.6% of patients were in Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) Profile 1-3, i.e. inotrope dependent. Applying the US rate to England suggests a steady state of 3.5 per million population destination therapy (DT) implants (it would take several years to build up the programme), suggesting about 190 DT LVAD per annum in England.

7 Evidence Base

The evidence review found no controlled studies which reported the outcomes for continuous flow left ventricular assist devices (CFVAD) compared to optimal medical therapy (OMM) in patients ineligible for transplant and dependent on inotropes who were implanted with a device as destination therapy.

There was one prospective controlled study (patients not dependent on inotropes), one prospective controlled study (control was pre-approval CFVAD, not OMM as per scope of this review), three systematic reviews of uncontrolled studies (or out of scope controlled studies) and seven large retrospective uncontrolled studies suitable for inclusion.

The main outcome of interest was survival. The survival of CFVAD recipients is 74% and 59% at one and two years for people with a baseline INTERMACS profile 1-3 (Jorde et al 2014). There is INTERMACS registry data reporting 57% survival at 3 years (Kirklin et al 2015). CFVAD appears to offer clear improvement in survival compared to OMM for people needing continuous inotropes since their estimated survival is only 20% at 1 year (Boothroyd et al 2013). Other key outcomes reported were function, quality of life and adverse events.

Improvements in function were measured using the 6 minute walk distance test (6MWD). In the prospective post approval HMII DT study (Jorde et al 2014), 19% of the 247 HMII recipients were able to complete a 6MWD test. Before HMII implant, the mean baseline 6MWD was 183±97m. Two years post implant, this had increased to 297±118m. It is not known what proportion of HMII recipients became ambulatory after device implant or how an improvement of 114m over six minutes translates to activities of daily living or independence.

In addition, a large proportion (at least 80%) of HMII recipients who are alive at 6 months and at 2 years achieve and sustain NYHA class I or II, from an initial NYHA IV health state (Boothroyd et al 2013).

Improvements in quality of life (QoL) have been reported using a wide variety of measures including KCCQ, EQ5D and MLHFQ. KCCQ has been shown to improve from a mean score of 24 at baseline to 68 and 74 at 3 months and 24 months

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respectively post implant (equivalent to NYHA class II) (Rogers et al 2010, reported in McIlvennan et al 2014). EQ5D was also shown to improve significantly with a 33-35 point improvement between baseline and 12 months (Grady et al 2015). All studies which reported quality of life outcomes reported significant improvements although it was noted that some of these were highly selective in recruiting subjects for analysis (i.e. those who died or were too unwell to complete a QoL assessment were excluded from the analysis). This may lead to an over optimistic understanding about the QoL that can be achieved outside of a study environment.

Adverse events were significant with the most common being bleeding. A significant proportion of HMII recipients will experience a bleed during the first 24 months after device implant. Jorde et al reported that over 54% of recipients had a bleed which required transfusion and 13% needed further surgery.

Other common adverse events included infection (sepsis, local device related, non-device related), stroke (haemorrhagic stroke, ischaemic stroke) and device related events such pump thrombosis and device malfunction.

The three cost effectiveness studies identified were based on outcomes at 2 years modelled over a lifetime (approximately 5 years). The model will have estimated a projected survival as well as QoL (including the impact of adverse events on QoL) based on indirect data from more than one study, and based on assumptions beyond the period of observed data. There was a wide variation in the estimated quality adjusted life years (QALY) and life years gained (LYG) over a lifetime. Despite the weakness of the models, the estimated ICER was consistently high in all studies (£91,299 to £162,388 per QALY). This is not surprising as the LYGs are associated with numerous and serious adverse events which in turn reduce quality of life for the patient and increase the ongoing cost of care.

The published literature on the use of CFVAD as DT compared to OMM for patients with NYHA class IV dependent on inotropes is of low quality. There is a large volume of uncontrolled, small, observational studies, none of which are suitable for meta-analysis. Most studies report the ‘as treated’ outcomes only and often exclude some with the poorest outcomes, increasing the uncertainty of the findings.

NHS England has concluded that there is not sufficient evidence to support a proposal for the routine commissioning of this treatment for the indication given the uncertainty regarding the magnitude of net clinical benefit, the significant harms associated with their use and the likelihood that the introduction of this technology as destination therapy into the NHS would displace treatments and services for patients of greater value. NHS England considered the evidence of cost effectiveness and noted the high Quality Adjusted Life Year estimates.

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8 Proposed Criteria for Commissioning

The use of LVAD implantation as a permanent life-long therapy to patients with advanced heart failure who are not heart transplant candidates is not recommended for routine commissioning by NHS England.

9 Proposed Patient Pathway

Not applicable

10 Proposed Governance Arrangements

The use of LVAD implantation as a permanent life-long therapy to patients with advanced heart failure who are not heart transplant candidates is not recommended for routine commissioning by NHS England.

11 Proposed Mechanism for Funding

Not applicable

12 Proposed Audit Requirements

Not applicable

13 Documents That Have Informed This Policy Proposition

In March 2015 NICE issued guidance IPG 516: Implantation of a left ventricular assist device for destination therapy in people ineligible for heart transplantation.

14 Date of Review

This document will be reviewed when information is received which indicates that the policy requires revision. Notably evidence regarding longer term outcomes that demonstrated continued survival and quality of life benefits. Evidence will need to support an estimated cost-effectiveness / value that offers value to patients and the NHS

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15 References

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INTENSIVE CARE SOCIETY STANDARDS © 2009 Levels of Critical Care for Adult Patients.

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