NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of left ventricular assist devices as a bridge to transplant or to recovery

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2005

Procedure name

- Left ventricular assist devices
- LVAD

Specialty societies

- Society of Cardiothoracic Surgeons of Great Britain and Ireland
- British Cardiovascular Intervention Society
- College / Society of Clinical Perfusion Scientists of Great Britain and Ireland

Description

Indications

Short-term circulatory support with LVAD may be indicated for patients with end-stage heart failure (of any aetiology) who are scheduled for heart transplantation pending the availability of a suitable donor heart; and for patients with a severe acute heart failure syndrome for whom myocardial recovery is anticipated as the cause of heart failure is thought to be, at least to a degree, naturally reversible. LVADs are sometimes used for patients who fail to wean from cardio-pulmonary bypass after cardiac surgery.

Current treatment and alternatives

The management of patients with end-stage heart failure or acute heart failure syndromes from a naturally reversible cause, is challenging, and

may include combination medical therapy (including inotropic support), intra-aortic balloon pumping, and heart transplantation.

What the procedure involves

A number of left ventricular assist devices (LVADs) are available which increase cardiac output by providing mechanical support to the failing left ventricle. The choice of device may depend on the patient's body size, the length of support time required, the degree of support needed, and the type of flow desired.

Implantation of an LVAD is done under general anaesthesia through a chest incision in an operation which usually lasts for several hours. The inflow pipe of the LVAD is inserted into the left side of the heart, usually the left ventricle, and its outflow pipe into the systemic arterial system, usually the aorta. The LVAD pumps oxygenated blood from the failing left ventricle to the systemic arterial system under pressure.

Efficacy

Results from case series included within a systematic review[1] showed that between 60% (12/20) and 83% (5/6) of patients survived to transplant or were still alive awaiting transplant on LVAD support. In the active arm of a non-randomised controlled study 78% (32/41) of patients survived during LVAD support[2], for a mean length of 215 days. In another comparative study 81% (13/16)[3] of patients survived to transplant (length of support not stated). One case series demonstrated that at 30 days of bridging to transplant with an LVAD survival was 83%, falling to 19% after 24 months of support[4]. Overall mean support time of 78 days was achieved with survival of between 64% (33/52) and 72% (126/174) of patients (depending on the type of device used) in a case series with long term follow-up[5].

Post-transplant survival in a non-randomised controlled trial was 66% (21/32) at 41 months in cases bridged on LVAD support, compared to 67% (98/146) at 36 months of patients who had a transplant without circulatory support. However, patients in the latter group were significantly older[2]. One case series of 243 patients bridged to transplant with an LVAD found actuarial post-transplant survival was 91% at 1 year, 70% at 5 years, and 40% at 10 years[5]. Another case series found composite survival (during LVAD bridging and post transplant) to be 64% at 1 year, and 55% at 4 years[4].

The New York Heart Association (NYHA) class of patients during bridging to transplant improved to Class I in between 94% and 70% of cases reported in a systematic review[1], and a case series found that 47% (15/32) of successfully bridged LVAD cases were assessed to be NYHA class I, and 19% (6/32) were class II[2].

Safety

Definitions of infection vary among the studies identified, and rates have been reported at between 0% (0/10) and 100% (5/5) of cases during LVAD

support in series documented in a systematic review. A non-randomised controlled trial noted infection in 8% (1/13) of cases during LVAD bridging[3], and case series report infection rates of 18% (43/243) of cases, or infection to have occurred at a cumulative rate of 1.88 incidents per patient at 6 months of follow-up[4].

Cerebrovascular infarction was found to have occurred in 21% (55/264) of cases in one series[4]. In a second case series a cerebrovascular accident occurred in 5% (13/243) of patients and stroke in the same number during mean support time of 78 days[5]. In a third series a neurological event (not defined) occurred in 8% (1/13) of cases[3].

Significant haemorrhage occurred in between 10% (1/10) and 30% (6/20) of cases reported in a systematic review[1], and reoperation due to bleeding was required in 31% (4/13) of cases in one series[3].

Other complications reported during LVAD support include renal failure, respiratory failure, and heamolysis.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to LVADs for short-term circulatory support. Searches were conducted via the following databases, covering the period from 1996 to 20/07/2005: Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See Appendix B for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good-quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with end-stage heart failure or other left ventricular compromise
Intervention/test	Left ventricular assist devices, with intention of short-term circulatory support as bridge to transplant or myocardial recovery. Studies of the use of LVADs as a destination therapy were not included.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on one systematic review, and in addition one randomised controlled trial, two non-randomised controlled trials, and two case series that were published after the search period used in the systematic review.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (Table 2) have been listed in Appendix A.

Existing reviews on this procedure

A Health Technology Assessment systematic review on the clinical and cost effectiveness of left ventricular assist devices for end-stage heart failure has been produced by the Wessex Institute for Health Research and Development, published in November 2005. Key safety and efficacy findings relating LVAD use as bridge to transplant and bridge to recovery are collated in Table 2. The conclusions of this review are as follows.

LVADs as bridge to transplant

LVADS appear to provide some benefit to patients awaiting heart transplantation, increasing their chance of surviving both to, and following, transplantation. Benefits are evident through improvements in both functional status and quality of life with an LVAD and appear to exceed those gained from inotropic agents or usual care. There are risks associated with the use of LVADs, with adverse events related to device failures, infections and thromboembolic events. There is sparse evidence to inform judgements about the comparative efficacy and safety of different devices.

LVADs as bridge to recovery

The evidence of the clinical effectiveness of LVADs as a bridge to recovery is limited and of poor methodological quality. The systematic review shows that LVADs do appear to benefit patients who would be likely to die from their condition. There was no evidence to judge the effects on the patients' quality of life or functional status. Adverse events associated with the devices provide a risk to patients. Although evidence was limited from the studies, infections and bleeding associated with the LVADs are the main concern, because when considered with the poor health of the patients these may lead to multiple end-organ failure. These studies provide insufficient good-quality comparative evidence to identify whether any of the LVADs was more clinically effective than another LVAD or another form of care.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional procedures

N/A

Technology appraisals

N/A

Clinical guidelines

Chronic heart failure: management of chronic heart failure in adults in primary and secondary care

http://www.nice.org.uk/CG005

Public health

N/A

Table 2 Summary of key efficacy and safety findings on left ventricular assist devices for short-term circulatory support

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Clegg AJ (2005)[1] Systematic review UK (including international studies) 23 studies focusing on short-term circulatory support. The review included 6 nonrandomised controlled studies, 8 case series, and 2 case reports for bridge to transplant, and 2 case series and 5 case reports for bridge to recovery. Data pertaining to the use of LVADs as a destination therapy are not extracted here. n = 349 bridge to transplant, 12 bridge to recovery. Age = mean range 24–56 years (total range 17–66 years) for bridge to transplant, mean range 16–71 years (total range 16–73) for bridge to recovery. Male = 85% bridge to transplant, 83% bridge to recovery. Diagnoses included idiopathic cardiomyopathy, ischaemic cardiomyopathy, myocarditis, valvular heart disease, dilated cardiomyopathy, MI and coronary heart disease, for bridge to transplant; and cardiogenic shock secondary to myocarditis, myopericarditis, dilated cardiomyopathy and MI for bridge to recovery. Follow-up = range 2 days–48 months for bridge to transplant, 3–45 months for bridge to recovery. HTA funded research.	**Survival** (Bridge to transplant) Survival to transplant ranged from 60%(12/20) to 84% (16/19), with first-generation devices, and survival post transplant of those successfully bridged ranged from 60% (3 years) to 100% (2 years). Survival to transplant or still awaiting transplant ranged from 67% (2/3) to 83% (5/6), with second-generation devices. (Bridge to recovery) Of the total cases reported 58% (7/12) of cases survived to final follow-up, and 58% (7/12) had the device successfully explanted or were weaned from support. However, one of these patients subsequently died from infection and cerebral haemorrhage 149 days after explantation. **Functional status** (Bridge to transplant) The NYHA class of all patients was IV prior to implantation. In one study of a first-generation device 94% of patients were class I after transplantation, and in another study 94% were class I at 60days post transplant. The NYHA class improved to class I in 70% of patients receiving a second-generation device. (Bridge to recovery) Only one case report included functional status outcomes. The patient was NHYA class I at 6 months follow-up after explant of LVAD at 46 days.	**Complications while on LVAD support** (bridge to transplant) <u>First-generation devices</u> Infection rates were reported at between 20% (4/20) and 100% (5/5). Bleeding occurred in between 35% (7/20) and 40% (8/20) of cases, and bleeding requiring re-exploration was reported in between 0% (0/34), and 30% (6/20). The rate of thromboembolic events ranged from 5% (1/20) to 805 (4/5); however, the definition of these events Is not clear. <u>Second-generation devices</u> Major haemorrhage was reported in 10% (1/10) of cases in one series, whereas in another postoperative bleeding was 'minimal'. There were no reports of thromboembolism. No infection was reported in one series of 10 cases, while death from sepsis was reported in one of six cases in another study.	Systematic review used a detailed and broad search strategy, with bibliographies of included studies cross referenced, and manufacturers contacted for unpublished data. Data extraction and study quality assessment was done independently in duplicate with disagreements resolved through a third independent reviewer. Many different devices were used in the studies included. Different definitions/categorisations were used for complications between studies. There is potential heterogeneity between studies with regard to length of follow-up, generation of device, and reporting of outcomes prior to or post transplant. Authors state that included studies were often methodologically weak. There may be difficulties with the generalisability of the study findings owing to patient selection, and the range of aetiologies of patients included.

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Clegg AJ (2005) Cont.	**Quality of life** (Bridge to transplant) Only one study of 30 cases fitted with a first-generation LVAD included quality of life outcomes, at 1–2 weeks post implant. The overall QOL index on a scale of 0 to 1 (higher scores more satisfied) improved from a mean of 0.66 (±0.14) at baseline to 0.73 (±0.13) ($p = 0.037$). Total heart failure symptoms including cardiopulmonary, gastrointestinal, psychological, genitourinary, neurological, dermatological and physical symptoms decreased from 0.23 (±0.10) at baseline to 0.16 (±0.10) at follow-up ($p = 0.002$). There was no significant difference between functional disability score at baseline or follow-up. (Bridge to recovery) No studies reported quality of life outcomes.	(Bridge to recovery) <u>First generation devices</u> In one case report the patient developed infection problems with repeated sepsis requiring explantation. In one series of 3 cases one patient had an infectious aneurysm requiring LVAD support to be stopped, and died of sepsis 2 months later. The other two patients developed cerebral embolisms and died of multiple organ failure. One series of two cases reported kidney complications 'requiring special treatment' , and one case had lung complications also.	Few controlled studies are included, and these use a range of comparators.

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Thiele H (2005)[6] Randomised controlled trial Germany n=41 (21 LVAD, 20 intra-aortic balloon pumping as a bridge to recovery) August 2000 to December 2003 Patients with cardiogenic shock complicating AMI with the intent to revascularise by percutaneous coronary intervention (PCI). Tandem heart or Intra-aortic balloon pump. Both groups IV administration of dopamine and dobutamine if the systemic vascular resistance was high. Diuretics and fluids given to standard intensive care guidelines. All patients with PCI were given clopidogrel for at least 4 weeks and aspirin indefinitely. Age =64yrs, Male =76%, LVEF =26%, Cardiac power index = 0.22 w/m^2 Follow up = 30 days Study part supported by a grant from Cardiac assist (USA)	**Heamodynamics** Cardio power index was calculated at between 35 and 40 minutes after completion of the operation. P value for inter-group comparison	**Operative complications** There was a trend towards longer time on mechanical ventilation following LVAD implant (4 days) than with a balloon pump (2.5 days) but this was not statistically significant. **Adverse events**	Randomisation by drawing of sealed envelopes 45 of 86 patients did not meet inclusion criteria Analysis by intention to treat principle All demographic and clinical characteristics were similar at baseline except for pulmonary capillary wedge pressure which was significantly higher in the balloon group (p=0.02) No statistically significant difference in overall mortality between groups to 1 month follow up. Reasons for giving blood products not stated No indication of blinding of outcome assessment Figures are presented with average and inter-quartile ranges (not transcribed here) Considerable concomitant treatment both interventional, and pharmacological. 100% of the IABP group and 95% of the LVAD group received mechanical ventilation (method not stated), 95% of each group had PCI plus stenting, and 5% of each group had a coronary artery bypass graft.

Outcome	Balloon baseline	LVAD baseline	Post-op balloon	Post-op LVAD	P value
Cardiac output (l/min)	3.0	3.5	3.3	4.5	0.007
Blood pressure (mmHg)	64	63	67	74	0.38
Cardiac power index (w/m^2)	0.22	0.22	0.28	0.37	0.004
Systemic vascular resistance (dyn x s / cm^5)	1440	1049	1388	1153	0.08
Pulmonary capillary wedge pressure	27.0	20.0	21.5	16.0	0.003

Event	IABP	LVAD	P value
Limb ischemia	0	7	0.009
Red blood cell transfusion	8	19	0.002
Blood plasma required	4	15	0.003
Platelets required	0	5	0.04
Disseminated intravascular coagulation	3	13	Not stated
Fever	10	17	>0.05
Peak white blood cell count	15.1	19.1	>0.05
Mortality during support	4	4	>0.05
Mortality after weaning	5	5	>0.05
Overall mortality	45% (9/20)	43% (9/21)	0.86

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Schmid C (2003)[2] Non-randomised controlled trial Germany n = 187 (41 LVAD prior to transplantation, 146 transplantation without prior LVAD) Patients with chronic heart failure who were mechanically supported for > 100 days before transplant. LVAD Male = 88%, age = 42 years, dilated cardiomyopathy =22, ischemic heart disease=13, arrythmogenic right ventricular cardiomyopathy =1. Of the patients with ischemic heart disease, 5 suffered from post cardiotomy failure after coronary artery bypass, Acute MI = 3, fulminant myocarditis = 2,. No LVAD Male = 84%, age = 53 years. Either Novocor, HeartMate, DeBakey or Thoratec device, as selected on device availability and patient body size. All patients had anticoagulants except those given a HeartMate, and all received aspirin after introduction during the recruitment period. Follow-up = 41 months LVAD, 36 months no LVAD. Post transplant. Disclosure of interest not stated.	**LVAD support period** Mean interval support was 215 (±86 days). 78% (32/41) survived to transplantation. Weaning from LVAD was not possible in any case, prior to transplantation. 22% (9/41) of patients died during LVAD support, 5 from multiple organ failure, 2 from cerebral failure, and 2 from cardiac causes. **Follow-up post transplant** LVAD pre-transplant (n=32) / No LVAD pre-transplant (n=146) Alive at last follow-up: 66% (21/32) / 67% (98/146) Survival at 1 yr: 75% / 74% No statistically significant differences between groups NYHA grade I: n = 15 NYHA grade II: n = 6 Cardiac index: 3.7 ± 0.8 litres/min/m^2 Capillary wedge pressure: 11 ± 4 mmHg Systolic pressure: 33 ± 7 mmHg	**Post-transplant complications** LVAD pre-transplant (n=32) / No LVAD pre-transplant (n=146) Pacemaker for bradycardia: n = 4 Impaired kidney function: n = 6 Impaired liver function: n = 3 ISHLT grade III rejection: 31% (10/32) / 22% (32/146) ISHLT grade II rejection: 25% (8/32) / 14% (21/146) No statistically significant differences between groups In the LVAD-treated group transplant vasculopathy evaluated by coronary angiography was present in 2 cases. One patient required retransplant for chronic rejection.	Retrospective analysis. 100 day support period was chosen arbitrarily. Only 32 of original 41 (78%) patients allocated to LVAD support as a bridge to transplant underwent transplantation. Patients in non-LVAD group only evaluated for survival and rejection rate. Patients in non-LVAD group were significantly older than those given LVAD (p > 0.001). Other demographic and baseline clinical variables not provided for non-LVAD group. Authors comment that mortality rate and postoperative complications depend on patient selection and urgency of device placement.

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Carrier M (2004)[3] Non-randomised controlled trial Canada n = 36 (16 LVAD prior to transplantation, 20 without LVAD prior to transplantation) LVAD (prior to receiving transplant) Male = 46%, age = 40. All patients given LVAD were in cardiogenic shock. Acute MI = 6, congestive cardiomyopathy = 5, acute viral cardiomyopathy = 2, postpartum myopathy = 1, failure to wean from bypass = 2, Becker's muscular dystrophy related cardiomyopathy = 2. 62% had intra-aortic balloon pump, 54% required mechanical ventilation. Non-LVAD prior to transplant Male = 70%, age = 47. Ischaemic cardiomyopathy = 7, congestive cardiomyopathy = 5, acute viral cardiomyopathy = 2, congenital and rheumatic disease = 4. 5% had intra-aortic balloon pump. Thoratec LVAD implanted. Both groups administered a standard regimen of immunosuppressants. Follow-up = 9 months. Post transplant.	**Pre-transplant** 19% (3/16) of cases given LVAD died prior to transplant of multiple organ failure. **Survival** 8% (1/13) of LVAD patients and 20% (2/20) of non-LVAD patients died at transplant, and 8% (1/13) of LVAD patients died from lung infection at 7 months post transplant. Patient survival averaged 84 ± 10% in the LVAD group, and 90 ± 7% in the non-LVAD group (p = 0.6).	**Complications** LVAD pre-transplantation (n=13) / No LVAD pre-transplantation (n=20) Pretransplant Renal failure: 23% (3/13) Respiratory failure: 15% (2/13) Reoperation due to bleeding: 31% (4/13) Infection: 8% (1/13) Neurological event: 8% (1/13) Post transplant Renal failure: 15% (2/15) / 10% (2/20) Respiratory failure: 15% (2/15) / 5% (1/20) Reoperation due to bleeding: 0% / 5% (1/20) Infection: 23% (3/13) / 205 (4/20) Acute rejection events to 1 year: 23% (3/13) / 25% (5/20) No statistically significant differences between groups	LVAD patients were younger (p = 0.001), were more likely to be female (p = 0.001), donor heart ischaemic time was longer (p = 0.02). Patient selection for LVAD support is not stated. Interval to transplant for LVAD = 17±19 days, and for non-LVAD = 87±66 days (p = 0.01). No classification of outcome of transplant rejection is provided. Patients who died on LVAD prior to transplant are not included in survival analysis.

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Morgan JA (2004)[5] Case series USA n = 243 (LVAD as bridge to transplant) Patients with end-stage heart failure with the following aetiology: coronary artery disease (57%), idopathic cardiomyopathy (36%), other (7%). Age = 50 years, male = 81%. All patients received Thoratec HeartMate devices, either pneumatic (21%), dual lead vented (7%), or single lead vented (72%). Follow-up = up to 12 years. Disclosure of interest not stated.	**Bridging characteristics** Overall mean mechanical support time was 78.1 ± 82.9 days. Successful bridge to transplant was achieved in 64% (33/52) of pneumatic devices, and 72% (126/174) of single lead vented electrical devices. Multivariate analysis found only clinical status at LVAD implantation an independent predictor of survival to transplant OR 1.21 (95% CI 1.12 to 1.32; $p < 0.001$). **Device explantation** Over the 12-year study 10 devices were explanted in 3% (7/243) of cases due to infection, and 1% (3/243) of cases due to left ventricular recovery. **Post-transplant survival** Overall actuarial survival for all LVAD-treated cases Post-transplant time – Survival 1 year – 90.5% 3 years – 85.1% 5 years – 69.6% 10 years – 39.6% Post-transplant survival was not statistically different for patients who were bridged to transplant without LVAD at the same institution. Data not provided.	**Complications** For all cases irrespective of device type up to transplant **Infection and malfunction** – Incidence Overall infection – 17.7% (43/243) Device malfunction – 12.8% (31/243) **Neurological** Cerebrovascular accident – 5.3% (13/243) Transient ischaemic attack – 8.2% (20/243) Stroke (within 30 days) – 5.3% (13/243) **Right ventricular failure** Requiring assist device – 7.0% (17/243) Of these cases bridging to transplant was achieved in 64.7%.	Prospective data collection and retrospective analysis. Inclusion criteria not stated and may have varied across the study period. Concomitant treatment while on LVAD support not stated. Mean length of follow-up not stated. Overall bridge to transplant success not stated, only by device. Not clear that length of bridge to transplant was the same in non-LVAD-treated patients. Duration of support to transplant was statistically longer for dual lead devices than single lead or pneumatic devices. Authors state that improvement in outcome variable over study time is multifactorial, and not solely attributable to changes in device design. Influential factors may include patient selection, surgical technique, treatment for RV dysfunction, establishing intraoperative haemostasis, and use of intensive care units.

Abbreviations used: LVAD, left ventricular assist device; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; ISHLT, international society for heart and lung transplantation, AMI – Acute myocardial infarction.

Study details	Key efficacy findings	Key safety findings	Comments
Navia JL (2002)[4] Case series USA n = 264 Patients treated as a bridge to transplant Dec 1991 to Dec 2001. Age = 55 years, male = 84%, mean right atrial pressure = 18.1 mmHg, ischaemic myopathy = 65%, idiopathic dilated myopathy = 30%, other = 5%. LVADs used were either HeartMate electrical or pneumatic, or Novacor. 9 patients received 2 devices and 2 received 3 devices. All HeartMate cases received aspirin (and occasionally warfarin for other reasons). Novacor cases were treated with heparin, and aspirin before transition to chronic warfarin. Follow-up = 4 years. Disclosure of interest not stated.	**Survival to transplant** Survival until transplant was 83% at 30 days, 73% at 3 months, 60% at 12 months, and 19% at 24 months. **Post-transplant survival** Total survival including mortality during LVAD support and post transplant was 84% at 30 days, 74% at 3 months, 64% at 1 year, and 55% at 4 years.	**Complications** Cumulative number of infections per patient 30 days / 6 months Total 0.56 / 1.88 Driveline infections 0.26 / 0.94 Pump pocket infections 0.07 / 0.43 Overall incidence to 6 months 107% (282/264) Cerebral bleeds 0.04 / 0.15 Overall incidence to 6 months 7% (19/264) Cerebral infarction (presumed embolic) 0.15 / 0.30 Overall incidence to 6 months 21% (55/264) 30 days / 12 months Failure free support 96% / 82% Overall incidence to 12 months 8% (21/264)	Prospective data collection. No details are given as to whether a consecutive case series or method of case accrual. No details of blinding of outcome assessors. Method of selecting type of LVAD for each case not defined, some historical cross-over in device use. Survival outcomes have longer follow-up than safety findings. Cardiac related and overall mortality are not analysed separately. Denominators are not provided for survival outcomes. It can be assumed that few cases were supported on LVADs for more than 30 days. Comparison of outcomes for different devices, and risk factors for death are described in the study report.

Validity and generalisability of the studies

There is generally poor reporting of length of follow-up.

Some studies 'discount' patients that died on LVAD support for analysis of outcomes post transplant.

Infection rates may depend on where the device control and energy unit are inserted.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

No advisor was identified who had not undertaken the procedure

Prof C Di Mario, Mr E Gamel, Dr D Keenan, Dr M Baker, Mr S Tsui, Prof J Pepper.

The advisors commented that LVADs intend to preserve adequate blood flow and pulmonary capillary wedge pressure to restore end organ function. They may improve quality of life and survival in an other wise fatal condition

The majority of the advisors considered this to be a novel procedure of uncertain safety and efficacy, while one advisor each would classify it as a minor variation on an existing procedure or established.

Reported adverse events relating to the procedure include bleeding, infection, device malfunction, haemolysis, peripheral ischemia, and perforation of a ventricle or aorta. One advisor also stressed the psychological trauma inherent in undergoing such a procedure.

In addition advisors though theoretical complications might include device related thrombosis, device related strokes. It is also possible that implantation of a LVAD may unmask previously sub-clinical right ventricular dysfunction.

Advisors noted that many devices are available and technology is changing rapidly with potentially fewer complications in newer devices.

Emphasis was placed on patient selection, and particularly with respect to age. Also selection of appropriate device for each individual may be important.

Advisors thought that care should be given through a multi-disciplinary team, and that specialist centres should act as a network to support others.

Training is provided by device manufacturers, who also maintain their own device specific registries.

Advisors suggested that the title of guidance may be changed to highlight treatment as a bridge to recovery or transplantation.

This procedure is likely to be provided at a minority of hospitals, however with 12,000 patients <65 years in the UK the potential impact on the NHS is large.

Issues for consideration by IPAC

- This overview includes data on use of LVADs for short-term circulatory support (as a bridge to transplant or recovery) only, rather than as a destination therapy**.**

References

1 Clegg AJ, Scott DA, Loveman E et al. (2005) The clinical and cost-effectiveness of left ventricular assist devices for end-stage heart failure: a systematic review and economic evaluation. *Health Technol Assess* 9: 1-148.

2 Schmid C, Welp H, Klotz S et al. (2003) Outcome of patients surviving to heart transplantation after being mechanically bridged for more than 100 days. *Journal of Heart & Lung Transplantation* 22: 1054-1058.

3 Carrier M, Perrault LP, Bouchard D et al. (2004) Effect of left ventricular assist device bridging to transplantation on donor waiting time and outcomes in Canada. *Canadian Journal of Cardiology* 20: 501-504.

4 Navia JL, McCarthy PM, Hoercher KJ et al. (2002) Do left ventricular assist device (LVAD) bridge-to-transplantation outcomes predict the results of permanent LVAD implantation?[erratum appears in Ann Thorac Surg. 2004 Jan;77(1):383]. *Annals of Thoracic Surgery* 74: 2051-2062.

5 Morgan JA, John R, Rao V et al. (2004) Bridging to transplant with the HeartMate left ventricular assist device: The Columbia Presbyterian 12-year experience. *Journal of Thoracic & Cardiovascular Surgery* 127: 1309-1316.

6 Thiele H, Sick P, Boudriot E et al. (2005) Randomized comparison of intra-aortic balloon support with a percutaneous left ventricular assist device in patients with revascularized acute myocardial infarction complicated by cardiogenic shock. *Eur Heart J* 26: 1276-1283.

Appendix A: Additional papers on left ventricular assist devices for short-term circulatory support not included in summary table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (Table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Bentz B, Hupcey JE, Polomano RC, Boehmer JP. A retrospective study of left ventricular assist device-related infections. Journal of Cardiovascular Management 2004; 15(1):9-16.	n = 90 FU = ?	Device-related infections in 20% of cases.	Comparison of devices.
Ferrari M, Kadipasaoglu KA, Croitoru M, Conger J, Myers T, Gregoric I et al. Evaluation of myocardial function in patients with end-stage heart failure during support with the Jarvik 2000 left ventricular assist device. Journal of Heart & Lung Transplantation 2005; Vol. 24(2):-228	n = 2 FU = 2 months	In one case LVEF was increased by 75% while on support. And the E-max was improved 107% and 155%.	Case reports, larger series are included.
Grady KL, Meyer PM, Dressler D et al. (2004) Longitudinal change in quality of life and impact on survival after left ventricular assist device implantation. *Annals of Thoracic Surgery* 77(4):1321.	n = 78 FU = 12 months	QOL outcomes were 'fairly good'.	Have larger series in table 2.
Hetzer R, Weng Y, Potapov EV, Pasic M, Drews T, Jurmann M et al. First experiences with a novel magnetically suspended axial flow left ventricular assist device. European Journal of Cardio-Thoracic Surgery 2004; 25(6):964-970.	n = 24 FU = ?	No perioperative deaths. 30-day mortality 8%. 2 patients weaned from the device.	Have larger series in table 2.
Kohmoto T, Oz MC, Naka Y (2004) Late bleeding from right internal mammary artery after HeartMate left ventricular assist device implantation. [Review] [5 refs]. *Annals of Thoracic Surgery* 78(2):689.	n = 5 FU = 2 months	4 of 5 cases survived to transplant.	5 selected cases demonstrating bleeding from right internal mammary artery.
Kucukaksu DS, Sener E, Undar A et al. (2003) First Turkish experience with the MicroMed DeBakey VAD. *Texas Heart Institute Journal* 30(2):114.	n = 3 FU = ?	2 of 3 patients bridged to transplant. I case had pump thrombosis and died on LVAD support.	Case reports, larger series are included.
Letsou GV, Myers TJ, Gregoric ID, Delgado R, Shah N, Robertson K et al. Continuous axial-flow left ventricular assist device (Jarvik 2000) maintains kidney and liver perfusion for up to 6 months. Annals of Thoracic Surgery 2003; 76(4):1167-1170	n = 10 FU = 6 months	LVAD maintained excellent renal and hepatic function during bridge to transplant.	Have larger series in table 2.
Letsou GV, Shah N, Gregoric ID, Myers	n = 3	2 of 3 cases	Case reports, have

TJ, Delgado R, Frazier OH. Gastrointestinal bleeding from arteriovenous malformations in patients supported by the Jarvik 2000 axial-flow left ventricular assist device. Journal of Heart & Lung Transplantation 2005; Vol. 24(1):-109.	FU = ?	bridged to transplant, one patient died. 2 patients has severe GI bleeding while on LVAD support	larger series in table 2.
Martin J, Siegenthaler MP, Friesewinkel O, Fader T, Van De LA, Trummer G et al. Implantable left ventricular assist device for treatment of pulmonary hypertension in candidates for orthotopic heart transplantation-a preliminary study. European Journal of Cardio-Thoracic Surgery 2004; 25(6):971-977.	n = 6 FU = 16 months	All patients survived to transplant, one case died three months thereafter	Have larger series in table 2.
Morgan JA, Park Y, Kherani AR et al. (2003) Does bridging to transplantation with a left ventricular assist device adversely affect posttransplantation survival? A comparative analysis of mechanical versus inotropic support. *Journal of Thoracic and Cardiovascular Surgery* 126(4):1188–90.	n = 226 (121 LVAD. FU = 5 years	Actuarial survival at 5 years 75% post transplant following LVAD support similar to that with medical therapy	Same cases as in Morgan (2004) in table 2.
Rinaldi M, Pagani F, Gazzoli F et al. (2004) Left ventricular assistance from bridge to transplantation to destination therapy. The Pavia experience. *European Heart Journal Supplements* 6(6):	n = 54 FU = ?	17/54 cases died while on support 9/32 cases died after transplant. 2 cases of device malfunction.	Have larger series in table 2.
Salzberg S, Lachat M, Zund G, Oechslin E, Schmid ER, DeBakey M et al. Left ventricular assist device as bridge to heart transplantation--lessons learned with the MicroMed DeBakey axial blood flow pump. European Journal of Cardio-Thoracic Surgery 2003; 24(1):113-118	n = 15 FU = 27 months	Successful transplant in 11 of 15 cases. Survival was 100% among transplanted patients.	Have larger series in table 2.
Strauch JT, Spielvogel D, Haldenwang PL et al. (2003) Recent improvements in outcome with the Novacor left ventricular assist device. *Journal of Heart and Lung Transplantation* 22(6):674.	n = 43 FU = ?	9 patients died while on support.	Have larger series in table 2. Comparing devices.
Vitali E, Lanfranconi M, Bruschi G et al. (2003) Left ventricular assist devices as bridge to heart transplantation: The Niguarda Experience. *Journal of Cardiac Surgery* 18(2):107.	n = 53 FU = 45 months	72% of cases supported to transplant. Major bleeding in 17% of cases and neurological event in 25%.	Have larger series in table 2.

Appendix B: Related published NICE guidance for left ventricular assist devices for short-term circulatory support

Guidance	Recommendation
Interventional procedures	N/A
Technology appraisals	N/A
Clinical guideline	Chronic heart failure guideline (2003) No specific recommendations are provided for LVADs, but the evidence available at the time was summarised thus: The worldwide experience of using implantable ventricular assist devices is steadily increasing, with a small number of patients continuing with such mechanical support for more than one year in one prospective trial and in case series. Although some patients appear to recover during VAD therapy, there are insufficient data on the mechanisms of response and the identification of patients in whom devices can be safely removed to justify recommendation of more widespread use of VADs as a bridge to recovery or as chronic therapy.
Public health	N/A

Appendix C: Literature search for left ventricular assist devices for short-term circulatory support

Procedure Number: 059 Date Completed: 21/7/2005	Procedure Name: Left ventricular assist devices for short-term circulatory support

Action	Comments	Version searched (if applicable)	Date searched
Search for similar NICE topics	Guidelines: Chronic heart failure: Management of chronic heart failure in adults in primary and secondary care (p.119-121 in particular) IP 041: Partial left ventriculectomy	N/A	20/7/2005
Consult notification and specialist advisors questionnaires for additional papers	• Tandem Heart : Thiele and Schuler, Circulation 2001;104:2917-2922 • Thiele et al Eur Heart J, 2005;26:1276-83 • IMPELLA: Valgimigli & Serruys: Cathet Cardiovasc Interv 2005;65:263-67	N/A	20/7/2005
Conduct general internet search for background	• British Heart Foundation information on LVAD • American Heart Association information on LVAD. • BCBS Technology assessment report Left-Ventricular Assist Devices as Destination Therapy for End-Stage Heart Failure • BCBS Technology assessment report Special Report: Cost-Effectiveness of Left-Ventricular Assist Devices as Destination Therapy for End-Stage Heart Failure	N/A	20/7/2005
Search for Cochrane systematic review	No Cochrane reviews	N/A	20/7/2005
ASERNIP website	No information of relevance found.	N/A	20/7/2005
FDA website	Information on LVADs. Follow links on the page to view safety information on a number of approved devices	N/A	20/7/2005
Search conferences websites	17th Annual Meeting of the Mediterranean Association of Cardiology and Cardiac Surgery American Heart Association conference listings European Society of Cardiology conference listings World Heart Foundation events listings	N/A	20/7/2005
Search Databases:			
The Cochrane Library	14 hits	2005 Issue 3	21/7/2005
CRD Databases	18 hits	June 2005	21/7/2005
Embase	126 hits	1996 to 2005 Week 29	20/7/2005
Medline	242 hits	1996 to July Week 1 2005	20/7/2005
Premedline	20 hits	July 19, 2005	20/7/2005
CINAHL	22 hits	1982 to July Week 3 2005	20/7/2005
BLIC (limit to current year only)	28 hits	2004-2005	21/7/2005
National Research Register	7 hits	2005 Issue 2	21/7/2005
Controlled Trials Registry	9 hits	N/A	20/7/2005

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

Database: Medline 1996 to July Week 1 2005	Date searched: 20/7/2005
1 left ventric$ assist device$.tw. (875)	
2 lvad$.tw. (499)	
3 left ventric$ assist system$.tw. (154)	
4 lvas$.tw. (132)	
5 axial flow pump$.tw. (67)	
6 continuous flow device$.tw. (17)	
7 displacement blood pump$.tw. (1)	
8 "AB-180 iVAD".tw. (0)	
9 abiomed BVS.tw. (32)	
10 lionheart VAD.tw. (0)	
11 axiPump.tw. (2)	
12 "berlin heart".tw. (32)	
13 "berlin Incor I".tw. (1)	
14 biomedicus pump.tw. (21)	
15 cora valveless pulsatile pump.tw. (0)	
16 corAide Heart Assist device.tw. (0)	
17 DeltaStream.tw. (7)	
18 Gyro pump.tw. (11)	
19 heart Quest VAD.tw. (0)	
20 heartMate II.tw. (8)	
21 heartMate III.tw. (5)	
22 HeartMate IP.tw. (3)	
23 HeartMate VE.tw. (11)	
24 Heartquest.tw. (5)	
25 Hemopump.tw. (36)	
26 Impella.tw. (21)	
27 Jarvik 2000.tw. (43)	
28 Medos HIA-VAD.tw. (6)	
29 MicroMed Debakey VAD.tw. (16)	
30 Nippon-Zeon.tw. (1)	
31 Novacor.tw. (153)	
32 Pierce-Donachy pediatric VAD.tw. (1)	
33 Rotodynamic pump.tw. (3)	
34 Evaheart.tw. (4)	
35 TandemHeart pVAD.tw. (1)	
36 Terumo DuraHeart.tw. (1)	
37 Thoratec.tw. (110)	
38 Toyobo.tw. (11)	
39 Ventrassist.tw. (11)	
40 "VERSUS LV recovery support system".tw. (0)	
41 World heart heartSaver VAD.tw. (0)	
42 or/1-41 (1424)	
43 or/8-41 (481)	
44 *Heart-Assist Devices/ (2116)	
45 42 and 44 (1113)	
46 exp Heart Failure, Congestive/ (22283)	
47 short term circulatory support.tw. (6)	
48 46 or 47 (22288)	
49 left ventric$.tw. (36320)	
50 45 and 48 and 49 (365)	
51 43 and 49 (290)	
52 50 or 51 (557)	
53 limit 52 to humans (516)	
54 limit 53 to yr = "2002-2005" (242)	
55 from 54 keep 1-242 (242)	