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

A clinical guideline for the NHS in England and Wales

APPENDIX J: EVIDENCE TABLES

Section 7.4: Invasive Procedures - Ventricular Assist Devices

Ventricular Assist Devices

Experimental Studies

Paper	Christopher, F. & Clegg, A. 2001, *Left ventricular assist devices (LVADs) for end stage heart failure.*, The Wessex Institute for Health Research and Development, Southampton, Development and Evaluation Committee Report No.103.
Description	Systematic review
N=	n=10 studies for bridge to transplant and n=1 for bridge to recovery (all cohort studies) n=609, n=17 respectively for each study (although numbers vary for subgroup analysis)
Intervention	For both studies only 2 LVAD devices are considered technical details not given.
Outcomes	For each study the main endpoint was survival which was measured to various points in time
Results	• Bridge to transplant found benefits for survival from 71% LVAD Vs 36% control (p=0.001) to transplant, and survival to I year at 91% Vs 67% (p=0.0001) to no significant difference in survival to transplant 80% for LVADs and 84% for controls. • Survival rates reported in the region 64% -75% to transplant from non controlled cohorts • NYHA class improvement with LVAD was reported in 6 of the 10 studies with NYHA reported to be group I in up to 95% of patients to about 85% in class I which represents a good functional improvement given that most patients were in group IV pre-operation, although some studies only included analysis post transplant • One study assessed sub-maximal exercise capacity in LVAD patients showing that improved capacity was comparable with mild HF patients and significantly better than dobutamine dependant patients • As a bridge to myocardial recovery the one study reported found that 5 of 17 patients with LVAD for idiopathic dilated cardiomyopathy could be weaned off the device at up to 794 days (meanwhile 6 patients 35% had died). In the 5 patients where the device was explanted the preoperative LV internal diameter in diastole was <75mm compared to >74mm in other patients. • A quality adjusted life years gained analysis using data from one of the bridging to transplant study with the best considered methodology, assuming benefits of LVAD patients are purely those gained from the transplant itself. A benefit of 218 QALYs per 100 patients was calculated over a 20-year time period, a sensitivity analysis of different assumptions suggested a range of 98 to 361 years. • Adverse events with LVAD implants were recorded systematically in one relatively large cohort study with a control group. The most common complications were Renal dysfunction (53% of LVAD group) Infection 45%, right ventricular failure 15% and device related bleeding 12%, although only infection showed significant difference between groups 41% LVAD Vs 15 % control (p<0.008)
Comments	Excellent searching regime with wide database searching hand searching and duplicate assessment for inclusion The benefit measured in QALYs is derived from a large increase in QALY if only a few patients recover their natural heart function.

Studies included	Catanese (1996), Dasse (1992), Frazier (1992), Frazier (1994), Frazier (1995), Foray (1996), Levin (1994), Massad (1996), McCarthy (1994), Moskowitz (1997), Muller (1997), Oz (1997)

Paper	Rose, E. A., Gelijns, A. C., Moskowitz, A. J., Heitjan, D. F., Stevenson, L. W., Dembitsky, W., Long, J. W., Ascheim, D. D., Tierney, A. R., Levitan, R. G., Watson, J. T., Meier, P., Ronan, N. S., Shapiro, P. A., Lazar, R. M., Miller, L. W., Gupta, L., Frazier, O. H., Desvigne-Nickens, P., Oz, M. C., Poirier, V. L., & Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group 2001, "Long-term mechanical left ventricular assistance for end-stage heart failure. [see comments.]", *New England Journal of Medicine.*, vol. 345, no. 20, pp. 1435-1443.
Description	Randomised controlled trial
N=	n=129, LVAD =68, medical therapy =61 Age =67yrs, male =80%, LV ejection fraction =17%, all NYHA IV, Minnesota living with heart failure score 75/105 at baseline
Intervention	A LVAD implanted either into a preperitoneal pocket or the peritoneal cavity depending on the surgeons' preference, Vs best medical therapy in patients with NYHA class IV on drug therapy and LV ejection fraction <25% (or NYHA III with 14+ days of inotropic or balloon pump support).
Outcomes	Primary end point was death from any cause, to be assessed until the 92 death had occurred.
Results	• Subgroup analysis showed an increased effect of intervention with age, in the under 60yrs group 1yr survival of 74% LVAD Vs 33% medical (p=0.05), whereas in 60-69yrs survival was 47% Vs 15% (p=0.009) • Patients in LVAD group more than twice as likely to have a serious averse event (rate ratio 2.35 95% CI 1.86 – 2.95) These events included infection in 28% at three months, bleeding in 42% AT 6 months, and device failure in 35% at 24 months
Comments	Findings imply that for every 1000 device implants 270 deaths could be avoided annually, however this magnitude of effect must be considered within the context of the complexity of therapy.
Reference	183

Paper	Gracin, N., Johnson, M. R., Spokas, D., Allen, J., Bartlett, L., Piccione, W., Parrillo, J. E., Costanzo, M. R., & Calvin, J. E. 1998, "The use of APACHE II scores to select candidates for left ventricular assist device placement. Acute Physiology and Chronic Health Evaluation", *Journal of Heart & Lung Transplantation*, vol. 17, no. 10, pp. 1017-1023.
Description	Cohort study
N=	N=81, LVAD implanted =31, no LVAD =50 USA Urban cardiac medical centre
Intervention	LVAD
Outcomes	Mortality at 800 days
Results	• When LVAD and non LVAD patients with medium APACHE score were compared, LVAD treated patients had a better survival (p=0.0049) • Increasing APACHE II score by a single unit increased the relative risk of mortality RR 1.139 (95% CI 1.005 to 1.231) in multivariate analysis
Comments	Patients were well matched in demographic, laboratory physiological, and comorbid parameters. Although the LVAD group had higher serum bilirubin which suggests more severe disease. Unusual study design of retrospective sub-variable analysis of an existing cohort study. No a priori basis for assuming score efficacy Improved survival after LVAD implantation is not risk-free.
Reference	185

Non-experimental studies

Paper	Holman, W. L., Skinner, J. L., Waites, K. B., Benza, R. L., McGiffin, D. C., & Kirklin, J. K. 1999, "Infection during circulatory support with ventricular assist devices", *Annals of Thoracic Surgery*, vol. 68, no. 2, pp. 711-716.
Description	Case series
N=	
Intervention	
Outcomes	
Results	• 41 LVADs were implanted during study period • Profile of recipients was 44 yrs and for 84 days of support • Patients characteristics were similar in non implanted group • Total of 191 positive cultures were obtained, 106 class 1, 59 class II, 22 class III, and 4 class IV. • 5 patient deaths were attributed to sepsis • Class II or IV (blood stream infections) occurred in 20 patients • Mean number of cultures per day of support were 0.16 +/-2 for the first 20 LVAD implants and 0.03 +/-0.04 for the second 21 implants given ($p<0.05$) suggesting improvements over time with experience • Correlation between date of implant and number of positive fungal cultures approached significance ($r= -0.30$, $p=0.059$) • Even serious infections can be successfully managed with appropriate therapy and adjuvant surgical treatment. • The provision of antifungal prophylaxis should be as short as possible in LVAD patients to discourage the emergence of resistant fungal organisms • Measures to minimise infections include, minimising traffic in the operating theatre, leaving LVAD components in sterile packaging until the last moment. • Institutional surveillance of surgically related infections is of extreme importance.

Comments	A retrospective analysis of infections in patients supported by ventricular assist devices being used as a bridge to transplantation Patients were implanted with a LVAD if they exhibited any of:- medically refractory ventricular arrhythmias / right ventricular failing / a condition that required left atrial cannulation for a LVAD All patients in this study were accepted for transplant before LVAD placement. Infection defines as an antemortem positive culture result Infections grouped to 4 classes . Class I = patient related non blood-stream infections i.e. urine, wounds, sputum, skin. Class II = isolated blood stream infections as determined by blood culture. Class III = LVAD related infections at peri cutaneous insertion sites. Class IV = infections of blood contacting intra-corporeal LVAD components Infections grouped as fungal or bacterial (then defined by genus and species) Blood cultures performed pre 1992 used a different lab method.
Reference	184

Paper	Mancini, D. M., Beniaminovitz, A., Levin, H., Catanese, K., Flannery, M., DiTullio, M., Savin, S., Cordisco, M. E., Rose, E., & Oz, M. 1998, "Low incidence of myocardial recovery after left ventricular assist device implantation in patients with chronic heart failure.", *Circulation*, vol. 98, no. 22, pp. 2383-2389.
Description	Case series
N=	
Intervention	
Outcomes	
Results	• Average age of LVAD recipient was 50 yrs in retrospective study and 47 yrs in prospective cohort. Pre-implant LVEF <20% in both groups • Of 5 explants in original population 2 expired (3months and 27 months) 2 required re-implant (6 months and 24 months) and one alive to 15 months. • 7 of 18 patients with implants in prospective study were able to be down titrated to a fixed rate of 20 cycles / min to be assessed for cardiac function. Of these 5 were given transplant, 1 awaiting transplant and 1 successfully explanted. • Clinical parameters that suggest recovery are an ability to exercise at low fixed rate to a VO2 >20 ml/kg/min, as are consistent valve opening, normal shortening fraction, and absence of marked ventricular dilation. • Patients were often reluctant to proceed with a test that decreases device support • No attempt was made to assess the mechanism for recovery.
Comments	Study to identify patients with sufficient myocardial recovery after LVAD insertion to ex-plant the device Patients tested with respiratory gas analysis, echocardiography, and haemodynamic measurements Retrospective chart review of 111 patients for ex-plant patients, and 18 of 39 patients assessed from prospective cohort
Reference	186