UK guidelines for referral and assessment of adults for heart transplantation

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An up-to-date list of UK heart transplant centres is available on the National Health Service Blood and Transplant website: http://www.organdonation.nhs.uk/ukt/about_transplants/transplant_units/transplant_units.jsp
Referrals may be made to any centre but should take into account geographical access for patients when attending for assessment, transplantation and post-transplant follow-up.

Endorsements Cardiothoracic Advisory Group of the National Health Service Blood and Transplant, the British Society for Heart Failure and the Society for Cardiothoracic Surgery in Great Britain and Ireland.

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ABSTRACT

Patients with advanced heart failure have a dismal prognosis and poor quality of life. Heart transplantation provides an effective treatment for a subset of these patients. This article provides cardiologists with up-to-date information about referral for transplantation, the role of left ventricular assist devices prior to transplant, patient selection, waiting-list management and donor heart availability. Timing is of central importance; patients should be referred before complications (eg, cardiorenal syndrome or secondary pulmonary hypertension) have developed that will increase the risk of, or potentially contraindicate, transplantation. Issues related to heart failure aetiology, comorbidity and adherence to medical treatment are reviewed. Finally, the positive role that cardiologists can play in promoting and facilitating organ donation is discussed.

INTRODUCTION

Despite progress in heart failure (HF) treatment, patients who have progressed to the advanced stage have a dismal prognosis and poor quality of life.[1–3] Heart transplantation (HTx) can provide effective treatment for a subset of these patients.[4 5] Guidelines on the assessment of patients for transplantation have been published.[6–8] While the principles are universal, clinical practice is affected by donor heart availability, health care funding and the availability of ventricular assist devices (VADs); ethical and legal considerations also influence the process. Transplantation commits the patient to a long-term programme of treatment including pharmacological immunosuppression; therefore, clinical decisions must take into account the patient's ability to tolerate and adhere to the ongoing treatment.

This document provides information relevant to the UK about patient referral, the role of left VADs (LVADs) prior to transplantation, the assessment process, waiting-list management and donor heart availability. It provides a consensus view from the UK Heart Transplant Centres, the Cardiothoracic Advisory Group of the National Health Service (NHS) Blood and Transplant, the British Society for Heart Failure and the Society for Cardiothoracic Surgery in Great Britain and Ireland. It is a general guide and is not intended to replace good clinical judgement or discourage the discussion of individual cases with a transplant centre.

PATIENT SELECTION

The decision to recommend HTx depends on weighing up the benefits, risks and alternatives. However, the scarcity of suitable donor hearts makes it necessary also to consider the population of potential heart transplant candidates; selection is based both on the patient's clinical need and on their capacity to benefit. Decision making should be as fair and transparent as possible. Transplant centres make a list of decisions in a multidisciplinary team meeting and in the light of relevant guidelines. Nevertheless, selection cannot be an exact science, and any patient who is dissatisfied with the decision made in his/her case is entitled to an opinion from a second transplant centre.

TRANSPLANT ACTIVITY AND OUTCOME

There are currently six UK adult heart transplant centres located in Birmingham, Glasgow, Harefield, Manchester, Newcastle and Papworth. During the last 5 years, an average of 105 adult heart transplants have been performed each year; organ allocation prioritises highly urgent patients receiving mechanical or pharmacological support at imminent risk of death.[9] There has been a marked decline in activity over the last 20 years, from a peak of nearly 300 transplants a year in the early 1990s.[10] This has been attributed to a decreasing number of patients dying from brain stem death coupled with increasing age and comorbidity within the remaining potential organ donors. In 2008, the Organ Donation Taskforce made 14 recommendations,[11] with the aim of increasing deceased donation; however, while early results have demonstrated an increase in donation after cardiac death, there has been a limited effect on the number of donors after brain stem death, that is, the donors who could donate their heart.

In selected patients, HTx improves survival and quality of life. Data on over 78 000 transplants from the Registry of the International Society for Heart and Lung Transplantation show that half of the patients survive for more than 10 years and that the median survival for those who survived the first year after transplantation is currently 13 years.[5] However, advances in the medical management have led some to question the benefit of transplantation in certain patient groups. The German Comparative Outcome and Clinical Profiles in Transplantation study found a survival benefit only in the group at highest risk of dying without transplantation (as defined by the HF survival score).[12]

However, survival after transplantation in that study was lower than that seen in the UK, and a similar UK study found that while patients with refractory HF and high-risk ambulatory patients had the most to gain from transplantation, there was also a survival benefit in populations with lower HF survival scores (albeit appearing later after transplantation).[4]

Health-related quality of life improves rapidly after transplantation. Improvement in activities of daily living and pain-discomfort has been observed using the EQ-5D (European Quality of Life - 5 Dimension quality-of-life measure)[13] and the SF-36 (Medical Outcomes Study 36 item Short Form Health survey) questionnaires.[14]

However, long-term morbidity after transplantation remains a concern. At 5 years, approximately 90% have hypertension or hyperlipidaemia, and 30% have renal dysfunction (with 7% having a serum creatinine above 200 μmol/l or renal replacement treatment). Diabetes mellitus occurs in 38%, and cardiac allograft vasculopathy (diagnosed by coronary angiography), in 28%.[5] Malignancy is an important long-term problem in immunosuppressed patients. Patients transplanted in the last 15 years have a 30% prevalence of cancer, with skin cancers comprising more than half the total.[5]

MEDICAL TREATMENT FOR HF

Medical treatment for patients with chronic HF due to systolic LV dysfunction approximately doubles life expectancy, and it is important that patients should be established on optimum treatment before considering transplantation.[15 16] However, all effective drugs have side effects, and in patients with advanced HF, worsening renal function and hypotension can limit their use. The need for 'down-titration' of medication is an ominous sign. If a patient's symptoms are not well controlled, a number of manipulations can be helpful. Discontinuing adjunctive medication (such as statins and nitrates which may no longer be beneficial) may improve adherence to a more essential medication; for example, nicorandil and calcium channel antagonists may worsen hypotension, and discontinuation will allow 'room' for effective drugs. Some drugs, such as non-steroidal anti-inflammatory drugs, including aspirin, may be harmful and should be stopped. Stopping non-steroidal anti-inflammatory drugs may both allow a diuresis in a patient with refractory congestion and help to preserve renal function.[17 18]

Whenever possible, patients should be on a β-adrenoceptor antagonist and an inhibitor of the renin–angiotensin system as well as an aldosterone antagonist using agents and, if possible, doses proven in clinical trials. Failure to tolerate these medications indicates a very adverse prognosis. Hypotension should only limit medication if it is symptomatic. If hypotension is limiting, it is probably better to use a smaller dose of agents from all three classes than a large dose of just one.

Although digoxin does not improve long-term outcome, it reduces HF hospitalisation and so is used to give symptomatic benefit in patients with advanced HF.[19] Ivabradine may be considered in patients who have a resting sinus tachycardia despite maximally tolerated doses of a β-blocker.[20]

For patients with refractory congestion, diuretic manipulation is worthwhile; a furosemide infusion and then adding a thiazide to the loop diuretic should be considered. Control of fluid and sodium intake is important, and bed rest with leg elevation can be helpful. Ultimately, mechanical fluid removal with ultrafiltration may be necessary.[21] Exacerbating factors such as anaemia, arrhythmia and thyroid dysfunction should be corrected whenever possible. Increasing resistance to diuretics or failure to tolerate conventional treatment with neurohormonal antagonists should prompt consideration of referral.

While there is no evidence that treatment with intravenous inotropic drugs improves the long-term outcome of patients with advanced HF, and they almost certainly worsen the cardiac prognosis, they can play a useful short-term role to improve tissue perfusion and organ function and so should be used when necessary. Patients with HF who have become inotrope dependent to maintain organ function have a dismal prognosis,[3] and so such treatment should only be regarded as temporary 'first aid' and should trigger referral in appropriate cases. Inotropes are used prior to transplantation when a heart is likely to become available soon under the urgent heart allocation scheme and prior to the insertion of an LVAD.

ELECTRICAL DEVICE TREATMENT

Cardiac resynchronisation treatment (CRT) improves symptoms, reduces hospitalisations and improves survival in patients with class III/IV HF, LV ejection fraction ≤35% and a broad QRS complex.[22 23] CRT does have a benefit in class IV HF[24] and may have a role in inotrope-treated patients with a broad QRS.[25] While most of the evidence for CRT is in patients with sinus rhythm, patients with AF and a controlled ventricular rate (achieved by drugs or atrioventricular node ablation) may also respond.[26]

CRT should be undertaken in patients who fulfil accepted international criteria[27] prior to transplant assessment. The implantation of a transvenous CRT system or implantable cardioverter defibrillator (ICD) does not preclude subsequent transplantation.[28]

ICDs decrease sudden cardiac death and mortality in selected patients with HF due to LV systolic dysfunction, especially when the aetiology is ischaemic.[29–31] While NICE guidance does not cover the use of ICDs in patients with a non-ischaemic cardiomyopathy, European guidelines do.[27] Patients with class IV HF were not included in the clinical trials of ICD treatment, and so, the role of ICD treatment in these patients remains unproven. An ICD is unlikely to benefit inpatients being treated for refractory HF.

NICE guidance regarding combined CRT and ICD treatment reflects the indications for each mode of treatment. European guidelines do, however, allow the use of CRT and ICD treatment in ambulant class IV HF.[16 27 32]

TRANSPLANT CANDIDATES

Ambulatory patients

Most patients will have an established diagnosis of chronic HF due to LV systolic dysfunction, that is, not attributable to correctable structural, valvular or coronary artery disease, and will fulfil the criteria in box 1.[8] While the main indication is HF due to systolic ventricular dysfunction, transplantation may also be considered on a case-by-case basis in other situations (box 2). Although cardiopulmonary exercise testing plays a central role in decision making, all the clinical data should be synthesised rather than focusing solely on the peak oxygen uptake.[2 8 33–37] A low LV ejection fraction alone is insufficient reason to consider transplantation. Patients who have near-normal resting haemodynamics (cardiac index and filling pressures) after medical treatment generally have a good prognosis, and if other indictors are favourable, transplantation may be deferred.[38 39]

The timing of referral is of central importance, and the aim should be to refer patients before complications (such as cardiorenal syndrome or secondary pulmonary hypertension) have developed, which will increase the risk of, or potentially

Box 1 Conventional criteria for heart transplantation

- Impaired LV systolic function
- NYHA III (eg, patient cannot climb one fight of stairs without symptoms) or IV symptoms
- Receiving optimal medical treatment (including target or maximum tolerated doses of β-adrenergic antagonists, ACE inhibitors and aldosterone antagonists)
- CRT, ICD or CRTD device implanted (if indicated)
- Evidence of a poor prognosis, for example,
  i. Cardiorespiratory exercise testing (VO_2 max $<$12 ml/kg/min if on β-blockade, $<$14 ml/kg/min if not on β-blockade, ensuring respiratory quotient $\geq$1.05)
  ii. Markedly elevated BNP (or NT-proBNP) serum levels despite full medical treatment
  iii. Established composite prognostic scoring system, such as the HFSS or SHFM

BNP, B-type natriuretic peptide; CRT, cardiac resynchronisation treatment; CRTD, CRT and ICD treatment; HFSS, Heart Failure Survival Score; ICD, implantable cardioverter defibrillator; LV, left ventricular; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA class IV, New York Heart Association; SHFM, Seattle Heart Failure Model.

contraindicate, transplantation. Indications for prompt referral are outlined in box 3.

Inotrope-dependent patients

Urgent assessment should be considered for hospital inpatients who fulfil the criteria in box 4. The aim should be to refer such patients before the development of complications such as secondary organ dysfunction or sepsis that may be a contraindication to transplantation or VAD implantation.

Aetiology

The most frequent indications for HTx in adults are HF due to dilated cardiomyopathy and ischaemic heart disease.[5 10] A small number of patients with valvular disease and severe secondary ventricular dysfunction also undergo transplantation.

An increasing number of patients with adult congenital heart disease (ACHD) present in adult life with advanced HF. Although the evidence base is sparse, most specialists extrapolate from clinical trials in patients with acquired disease to guide optimal care. Assessment for transplantation is challenging because symptoms often occur late and because the prognostic tools used in acquired heart disease have not been validated in ACHD. Patients with ACHD may present additional complexities for the transplant team such as human leucocyte antigen (HLA) sensitisation, complex surgery (abnormal anatomy and previous surgery), elevated or uncertain pulmonary vascular resistance and, sometimes, profound cyanosis and erythrocytosis.[40] These lead to a higher early mortality after transplantation,[41] although the long-term outcome is more encouraging.[10 42] Multidisciplinary discussion between the specialist ACHD unit and the transplant service is needed during referral and assessment.[43]

Patients with a specific heart muscle disease may be candidates for transplantation and need to be considered on a case-by-case basis. A detailed discussion of individual diseases is beyond

Box 2 Uncommon indications for transplantation

- Persistent haemodynamically compromising ventricular arrhythmias, refractory to all usual therapies (including antiarrhythmic drugs, catheter ablation, electrical device treatment, revascularisation)
- Refractory angina, where there is clear objective evidence of recurrent significant (debilitating) myocardial ischaemia that is not amenable to conventional treatment (including all forms of revascularisation and full anti-anginal treatment)
- Restrictive and hypertrophic cardiomyopathy with persisting NYHA III or IV symptoms refractory to conventional treatment and/or recurrent admissions with decompensated HF. Patients should have clear echocardiographic evidence of restrictive filling that can be confirmed by invasive haemodynamic studies, and the aetiology should be clearly identified to ascertain the presence of a systemic disease and the risk for recurrence following transplantation

HF, heart failure; NYHA class IV, New York Heart Association.

Box 3 Clinical indicators that should prompt consideration for referral

- Two or more admissions for treatment of decompensated HF within the last 12 months
- Persistent clinical evidence of overt heart failure after optimised medical treatment
- Calculated SHFM score indicating a $\geq$20% 1-year mortality
- Echocardiographic evidence of right ventricular dysfunction or increasing pulmonary artery pressure on optimal treatment (aim to refer before the PA systolic pressure exceeds 50 mm Hg)
- Anaemia, involuntary weight loss, liver dysfunction or hyponatraemia attributable to heart failure
- Deteriorating renal function attributable to heart failure or inability to tolerate diuretic dosages sufficient to clear congestion without change in renal function (aim to refer before creatinine clearance falls below 50 ml/min or the eGFR falls below 40 ml/min/1.73 m^2)
- Significant episodes of ventricular arrhythmia despite full drug and electrophysiology/device treatment
- Increasing plasma BNP or NT-proBNP levels despite adequate HF treatment

BNP, B-type natriuretic peptide; HF, heart failure; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PA, pulmonary artery; SHFM, Seattle Heart Failure Model.

Box 4 Indications for urgent inpatient referral

- Requirement of continuous inotrope infusion (or/and intra-aortic balloon pump (IABP)) to prevent multiorgan failure
- No scope for revascularisation in the setting of ongoing coronary ischaemia
- Persisting circulatory shock due to a primary cardiac disorder
- An absence of contraindications to transplantation

the scope of this paper. General considerations include the following: systemic manifestations of the disease and the likely impact on organ function, perioperative risk and overall prognosis; the patient's ability to tolerate pharmacological immunosuppression and the possibility of disease recurrence in the cardiac allograft.

RISK FACTORS AND CONTRAINDICATIONS

Related to HF

Advanced HF can lead to dysfunction in other organs, which will increase the risk associated with transplantation and may eventually become irreversible; referral should be considered before these complications become established. Whenever possible, intrinsic organ damage should be differentiated from potentially reversible abnormalities secondary to HF.

Cardiorenal syndrome

Impaired renal function is an independent predictor of mortality in HF[44] and following transplantation.[5 45] Intrinsic renal damage should be distinguished from reversible dysfunction secondary to congestion and low cardiac output. Ultrasonography is essential to assess renal shape and size as well as excluding obstruction. Any albuminuria should be assessed. Functional reassessment following a reduction in neurohormonal antagonists or after inotropic support to improve cardiac output may be required. Irreversible renal dysfunction, defined as creatinine clearance persistently <50 ml/min or an estimated glomerular filtration rate <40 ml/min/1.73 m^2, may preclude transplantation.[6 8]

Hyponatraemia

Mild hyponatraemia is relatively common in patients with chronic HF. Studies have consistently shown that it is a powerful independent predictor of poor prognosis across a spectrum of HF severities, including patients with severe or decompensated HF. Persistent hyponatraemia may, therefore, help identify patients who should be considered for advanced HF assessment.[46 47]

Liver dysfunction

Abnormal liver function tests are common in HF; liver dysfunction is a predictor of adverse outcome following transplantation, and an elevated bilirubin is a predictor of mortality both in chronic HF and after transplantation.[5 48] Standard liver 'function' tests are insensitive for detecting cardiac cirrhosis, and specialist investigation may be required in patients with chronic right HF causing severe systemic venous hypertension or refractory ascites.

Secondary pulmonary hypertension

High pulmonary vascular resistance is associated with an increased risk of right HF and mortality after HTx.[5] Concomitant lung disease, obstructive sleep apnoea and pulmonary embolic disease should be excluded. Pulmonary hypertension that is irreversible despite treatment with pulmonary vasodilators is a contraindication to HTx, and pharmacologically reversible hypertension is an incremental risk factor.[8 49] A number of variables need to be assessed, and the acceptable limits vary between centres; however, a pulmonary vascular resistance >5 Wood units, a transpulmonary gradient >15 mm Hg and a pulmonary artery systolic pressure >60 mm Hg are regarded as a contraindication by most centres.

Anaemia of HF and cardiac cachexia

Anaemia is common in HF and is an independent predictor of hospitalisation and mortality.[50] Exclusion of haematinic deficiency (including functional iron deficiency) is necessary.[51] Absolute iron deficiency may reflect gastrointestinal pathology and must be investigated. Intravenous iron is associated with short-term symptomatic improvement in iron-deficient patients and may benefit patients prior to transplantation.[52]

Involuntary weight loss (>7.5%) is an adverse prognostic factor in HF,[53] and other causes should be excluded. However, a low body mass index (BMI) does not adversely affect the outcome of transplantation.[54]

Comorbidity

Some comorbidities constitute an absolute contraindication to transplantation, and others are incremental risk factors. Relative contraindications, when present in combination, may become absolute barriers to surgery.

Age is not a contraindication to transplantation, but increasing age is an incremental risk factor,[5] and it is often associated with other comorbidity; few UK patients have been transplanted above the age of 65 years. Previous cardiac surgery is not a contraindication with outcomes typically comparable to patients undergoing transplantation as their primary procedure. However, multiple prior sternotomies are an incremental risk factor.[45]

Diabetes is not a contraindication but is a risk factor; good diabetic control must be established (glycosylated haemoglobin below 7.5%).[8 45] Microvascular complications other than non-proliferative retinopathy are usually considered an absolute contraindication to transplantation. A pre-transplant BMI >30 kg/m^2 is a risk factor.[8] Obese patients are required to lose weight, and those with a BMI >32 kg/m^2 are unlikely to be accepted by UK centres.

Symptomatic peripheral or cerebrovascular diseases are relative contraindications, given their impact on patient prognosis.[55 56] Extracardiac vascular disease is an important risk factor for perioperative mortality after HTx.[45]

Sepsis and active infection are absolute contraindications. Chronic infections should be eradicated by appropriate antimicrobial and surgical treatment. Chronic viral infections are relative contraindications, given the potential for organ injury, disease exacerbation by pharmacological immunosuppression and drug interactions between antiviral and immunosuppressive drug treatment.

Recent pulmonary embolism is a contraindication because it may increase pulmonary vascular resistance and result in postoperative right ventricular failure. Additionally, if there has been pulmonary infarction, there is a risk of the patient developing a lung abscess or other septic complication.[57] Transplantation, therefore, should normally be delayed until the infarct has healed.

Pharmacological immunosuppression is associated with an increased incidence of malignancies and by more aggressive tumour biology.[58] Active malignancy, other than localised non-melanoma skin cancer, is a contraindication to transplantation. However, patients who have achieved a sustained remission following cancer treatment may become transplant candidates.[8] Decision making should include advice from a cancer specialist, and the outcome will be influenced by the nature of the malignancy and the patient's expected prognosis for survival free of relapse.

Autoimmune disorders (eg, systemic lupus erythematosus, rheumatoid arthritis and ulcerative colitis) are relative contraindications owing to the expectation of higher complication rates and disease recurrence[59]; however, such diseases often respond well to the immunosuppression used after

transplantation, and so, decisions should be made on a case-by-case basis. Infiltrative cardiac diseases such as systemic amyloidosis and sarcoidosis are associated with a risk of progression of extra-cardiac disease or of recurrence in the cardiac allograft.[60–62] Transplantation may be appropriate when there is limited extracardiac disease and when other treatment can control the underlying disease.

Some forms of non-ischaemic dilated cardiomyopathy are associated with a skeletal myopathy. Patients suitable for transplantation will have mild skeletal involvement with a good medium-term outlook (eg, Becker muscular dystrophy).[63] More aggressive skeletal myopathies are unsuitable for transplantation.

Psychosocial factors have an important impact on the outcome of transplantation.

Substance abuse (including tobacco and excessive alcohol consumption) is a relative contraindication. Relapse of smoking is associated with poor outcome after cardiac transplantation by increasing coronary allograft vasculopathy and malignancy.[64] Tobacco abstinence for 6 months before transplantation is normally required. Abuse of alcohol or drugs may be associated with other problems such as poor adherence to treatment.

Non-adherence after transplantation is an important predictor of poor long-term outcome. A history of prior non-adherence to treatment or follow-up needs further evaluation and may represent a relative or absolute contraindication. Such patients need psychological/psychiatric evaluation.[65] Adequate, stable accommodation and family or social support are essential for successful outpatient care of both patients with transplant and patients with VAD.

Unlike most types of surgery, transplantation commits the patient to a lifelong programme of monitoring and drug treatment. Therefore, all potential recipients should have mental capacity to give their informed consent.

LVAD SUPPORT

LVADs have been used for over 25 years to 'bridge' patients to HTx. The larger, pulsatile devices proved reliable for this purpose but are not suitable for long-term support. Newer continuous flow devices have been used for nearly 10 years; implantation is easier, as the pumps are much smaller. These devices were designed for long-term use and have a much lower mechanical failure rate. All current continuous flow devices require anticoagulation with warfarin and an anti-platelet agent, and so, bleeding and thromboembolic events are a problem in a minority of patients. Infection remains a significant long-term problem, often associated with the driveline. Nevertheless, for selected patients, the introduction of LVADs is a major advance in the treatment of advanced HF.[66–68]

At present, the NHS supports the use of LVADs as a bridge to transplantation but does not fund 'destination therapy' or chronic LVAD support. While implanting a long-term VAD as a bridge to transplantation requires the patient to have a clear potential to become a transplant candidate, the decreasing number of transplants has resulted in some patients being supported for more than 2 years, and some are likely to be supported for the rest of their lives.

Some patients with non-ischaemic dilated cardiomyopathy experience an improvement in LV function during LVAD support.[69] Recovery can be promoted by a standard HF treatment and, perhaps, other drug treatments. In a minority of cases, the recovery has been sufficient for the LVAD to be explanted without transplantation. It is not possible to predict which patients will experience myocardial recovery, and LVADs are not implanted with the aim of inducing recovery, but recovery is a welcome bonus when it occurs.

Transplant-eligible patients may be considered for implantation of an LVAD if their clinical condition is deteriorating and if they are unlikely to receive a donor heart in time. LVAD support may also be used to reverse problems such as renal dysfunction and pulmonary hypertension secondary to HF, thereby making the patient a better candidate for transplantation.[70] In emergency situations, support with a low-cost, short-term device may be used as a 'bridge to decision' to allow full assessment of the patient.

The patient's overall health influences the outcome of LVAD implantation,[71] and, as with transplantation itself, the timing of the referral is of crucial importance (box 5). LVAD support is less appropriate for certain categories of HF patient (box 6), and primary HTx should be performed in these situations if possible.

Box 5 Risk factors for mortality after LVAD implantation

- Sepsis
  - Temperature >38.5°C
  - WBC $>15\times10^9$/l
- Haematology
  - Platelet count $<148\times10^9$/l
  - Prothrombin time >16 s
  - Haematocrit <34%
- Hepatic
  - Hyperbilirubinaemia
  - Elevated transaminase level
  - Albumin <33 g/l
- Renal
  - Oliguria
  - Urea>18 mmol/l
- Respiratory
  - Respiratory failure
  - Mechanical ventilation
- Age >65 years
- Cardiac surgery
  - Reoperation
  - Postcardiotomy (salvage)
- Cardiac
  - Acute myocardial infarction
  - Right heart failure
  - CVP >16 mm hg
  - Mean PAP < 25 mm Hg

CVP, central venous pressure; PAP, pulmonary artery pressure; LVAD, left ventricular assist device; WBC, white blood cell.

Box 6 Situations where LVAD implantation may be less appropriate

- Predominant right ventricular failure
- Non-dilated (hypertrophic or restrictive) cardiomyopathy
- Congenital heart disease (with complex anatomy or potential for a 'right to left' shunt)
- Prior prosthetic valve replacement (especially aortic)
- Multiple previous cardiac operations

LVAD, left ventricular assist device.

Box 7 Factors determining heart allocation

- Biological matching
  - Blood group compatibility
  - Appropriate size matching (accounting for recipient sex and pulmonary hypertension)
  - Need to avoid specific donor HLA antigens in sensitised recipients
- Clinical need
  - Severity of heart failure
  - Anticipated prognosis without transplantation
- Logistic factors influencing operative cardiac ischaemia time
  - Distance of donor from recipient centre
  - Prior surgery in the recipient (multiple sternotomies)
  - Surgical complexity (eg, prior VAD, ACHD)
- Fairness
  - Time on the waiting list

ACHD, adult congenital heart disease; HLA, human leucocyte antigen; VAD, ventricular assist device.

Severe right HF is associated with a high mortality after LVAD implantation. Patients should be referred before they develop high central venous pressure, ascites or raised bilirubin.[72] Some patients may require biventricular support, which is associated with higher perioperative mortality than univentricular support. There is a similar rate of subsequent HTx.[73]

WAITING-LIST MANAGEMENT

Allocation of donor hearts is based on the principles of the biological need for donor–recipient matching, clinical priority, the need to limit operative cardiac ischaemia time and fairness (box 7).

An Urgent Heart Allocation Scheme has been established for more than 10 years. Survival of patients transplanted on the urgent list is similar to that of other transplants. The Cardiothoracic Advisory Group periodically reviews and recommends the criteria for urgent listing to NHS Blood and Transplant (box 8).

Patients on the non-urgent waiting list are allocated hearts when there are no suitably matched patients on the urgent list. Hearts are offered first to the transplant centre in the local zone and then to other centres through a national scheme. In practice, patients of blood group O, large patients and those who are HLA sensitised tend to have long waiting times. Unfortunately, not all patients listed for transplantation will receive a heart. Patients who are highly HLA sensitised may effectively be untransplantable.

Box 8 Simplified schema of the current Cardiothoracic Advisory Group of NHS Blood and Transplant (CTAG) criteria for urgent listing

- Need for continuous inotropic treatment at high dose or in combination
- Intraaortic balloon pump with or without inotropic support
- Mechanical circulatory support with a short-term device including venoarterial extracorporeal membrane oxygenation
- Long-term LVAD support with device-related complications
- Exceptional cases out with these criteria may be listed with permission from the chair of the advisory group

LVAD, left ventricular assist device.

ROLE OF THE NON-TRANSPLANT CARDIOLOGIST

The HF cardiologist plays a vital role in identifying and referring potential transplant candidates at the appropriate time. This requires an understanding of the assessment process and an ability to give the patient realistic expectations about transplantation. Ultimately, each centre's ability to perform transplants depends on the availability of donor hearts and the ability to assess those hearts effectively. Here, again, the non-transplant cardiologist can make an important contribution.

The willingness of individuals and families to consider organ donation is of crucial importance, so too is the willingness of staff outside the transplant centre to support the donation process. HF cardiologists can increase their colleagues' awareness of the very favourable effect of transplantation on patients with advanced HF. Non-transplant cardiologists can also help with the assessment of the hearts of organ donors.

Echocardiography is the primary investigation of donor heart suitability. Unfortunately, many hospitals are currently unable to provide this basic investigation in a timely fashion. A transthoracic echocardiogram can identify valvular or structural abnormalities that may preclude donation. It can quantify any LV hypertrophy and this facilitates decision making when the donor has a history of hypertension; mild hypertrophy is not a contraindication to transplantation,[74] whereas more severe hypertrophy represents a substantial risk. Normal LV systolic function is predictive of a good post-transplant outcome for the recipient,[75] but impaired function in the initial echo does not preclude a subsequent improvement or eventual transplantation. Such cases may require further investigations including a second echocardiogram, invasive haemodynamic assessment using a pulmonary artery flotation catheter (to measure both cardiac output and the LV filling pressure; key factors in decision making) and, sometimes, invasive or CT coronary angiography.[76]

The increasing age of potential organ donors raises concern about occult donor coronary artery disease. Like hypertrophy, this need not always preclude heart donation. Coronary angiography is necessary in older donors and in those with multiple coronary risk factors as well as when there is reduced LV systolic function, regional wall motion abnormalities or ECG evidence of ischaemia. Current evidence indicates that a significant number of donor hearts are not used because of a lack of echocardiographic or angiographic data (RS Bonser, unpublished data), and further effort is needed in this area.

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