The echocardiographic assessment of donor heart function prior to cardiac transplantation

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Received 3 August 2004; received in revised form 12 October 2004; accepted 25 October 2004
Available online 8 December 2004

KEYWORDS
Echocardiography; Donor heart assessment; Heart transplantation

Heart transplantation is an effective mode of treatment for patients suffering from end-stage heart failure but the demand for hearts far outweighs supply. Approximately 10–20\% of potential heart-transplant recipients die on the waiting list.\textsuperscript{1} Despite public education initiatives, activity in heart transplantation has been falling, with activity in the UK dropping from >250 cases/year in 1995 to 174 in 2001–2.\textsuperscript{2} A specific problem within heart transplantation is the low yield of transplantable hearts from the existing donor pool. Once consent has been obtained, the average utilization rate of donor hearts ranges from 39 to 42\%.\textsuperscript{3}

Although the failure to use donor hearts is multifactorial, left ventricular dysfunction is the commonest single cause and is responsible for approximately 26\% of the unused organs.\textsuperscript{4} Brain stem death (BSD) is associated with intensive sympathetic nervous system activity and the release of pathophysiological amounts of catecholamines into the circulation.\textsuperscript{5} This sympathetic 'storm' may provoke both myocardial ischaemia\textsuperscript{6} and an inflammatory reaction with release of cytokines that can exacerbate organ injury. The storm is characterized by a fluctuating blood pressure due to altered vascular resistance, a variable volume status and abnormalities of myocardial wall motion. Despite differences in the demographics of the patients presenting with brain stem death from different causes (vascular, tumour, trauma, hypoxic or infective), there does not appear to be a difference either in early or late outcome of cardiac transplantation according to

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donor cause of death. Whether there are different echocardiographic appearances of the donor heart according to cause of brain stem death is not established.\(^7\)

The best method of assessing the donor heart remains controversial. Currently, selection involves a review of the present and past medical history of the donor, invasive monitoring of donor heart function with central venous and pulmonary artery catheters, and direct surgical inspection. A donor heart may be rejected on the basis of an adverse history alone. Echocardiography is a non-invasive, portable, and rapidly available investigation that is ideally suited to the accurate assessment of donor ventricular function. However, usage varies widely, partly because of the limited published evidence to support routine echocardiographic assessment of donor hearts. This paper reviews this literature and indicates potential means by which echocardiography can reduce the rejection rate of donor hearts without compromising recipient outcome.

The potential of transthoracic echocardiography (TTE) as a screening tool for cardiac donors was first identified in 1988.\(^8\) Despite the inherent difficulties of imaging ventilated subjects, TTE was successfully performed in all but one of 74 potential donors. Nine potential donor hearts with grossly abnormal echocardiograms were excluded from transplantation (8 hearts with severe left ventricular dysfunction and 1 heart with severe mitral and tricuspid regurgitation). Of the remaining 64 studied, TTE was normal in 46, 9 had pericardial effusions, 5 had mild septal hypokinesis, and 4 had possible mitral valve prolapse without significant regurgitation. In the absence of TTE, 21 (29%) of these donor hearts would have been excluded on clinical criteria (chest trauma, prolonged hypotension, cardiac arrest and prolonged catecholamine use). However, transplantation was successful in each case, including those with mild abnormalities on TTE. Therefore, TTE screening of donor hearts is feasible. It may exclude donor hearts with severe cardiac dysfunction and avoid direct surgical inspection. Perhaps more importantly, this study raised the possibility that TTE could identify donor hearts that could be used successfully in transplantation despite the presence of other clinical factors that would previously have led to exclusion.

Subsequent studies have helped to define limitations to this early promise of standard TTE to distinguish between those donor hearts with ventricular dysfunction that could proceed successfully to transplantation and those that could not. Firstly, left ventricular (LV) dysfunction is a common finding in patients with intracranial pathologies and BSD. In 147 patients with subarachnoid haemorrhage, global or regional LV dysfunction was found in 30 (20%) patients on echocardiography. Regional wall motion abnormalities tended to cover multiple arterial territories and occur in the absence of coronary artery disease.\(^9\) This frequency has been confirmed in a retrospective study of 66 patients with brain stem death, 28 (42%) of whom were found to have global or segmental LV dysfunction that was not predicted by clinical and electrocardiographic examination. It is interesting to note that in both of these studies, apical LV function was often preserved despite the presence of other regional abnormalities. This sparing is thought to be due to the relative paucity of sympathetic nerve terminals and reduced myocardial norepinephrine content in the LV apex, leading to reduced susceptibility to the catecholamine storm in BSD.\(^10\) Secondly, left ventricular dysfunction documented on echocardiography in heart donors with BSD does not appear to correspond to any demonstrable pathological abnormality at postmortem.\(^10\) Thirdly, there is clear evidence not only that donor hearts with mild abnormalities in LV function on TTE can be successfully transplanted but also that donor hearts with more severe regional wall abnormalities may improve immediately post-transplant. In one study, 9/40 hearts with severe regional wall motion abnormalities (defined as diffuse hypokinesis of all segments in a 6 segment model) were successfully transplanted with resolution of left ventricular dysfunction persisting to 15 months post transplantation.\(^11\) All these patients had normal coronary angiograms. In a further study of urgent transplantation in sick paediatric recipients, the use of donor hearts despite the presence of LV dysfunction (defined as LV fractional shortening <28%, mean LV shortening fraction 24.5±3%) and mitral regurgitation did not result in an increase in 30 day mortality or inotrope requirement compared with normal donor hearts. In each case, LV function was normal on echocardiography at 30 days post-transplantation.\(^12\) It may be that the importance of more severe left ventricular dysfunction and the impact of regional wall motion abnormalities on outcome may vary with other clinical factors such as the age of the donor heart. Clearly, the presence of regional wall abnormalities in a young donor is likely to be of less significance than those found in an older donor in whom the likelihood of ischaemic heart disease is higher.\(^13\) In summary, left ventricular dysfunction is common in donor hearts, does not correspond to a detectable pathological abnormality,
and in some cases may recover even when apparently severe.

Clearly, the challenge for echocardiography is to be able to distinguish those donor cases with abnormal function likely to be transient from those that fail the recipient. There is some evidence that low dose dobutamine (up to 20 \(\mu\)g/kg/min) stress echocardiography may be useful. In a small prospective study of 30 consecutive BSD patients, 7 donor hearts were identified with impaired LV function (FS < 30%) and proceeded to dobutamine stress echocardiography. In 3, LV function improved but there was no response in the remaining 4. Troponin T levels were markedly higher in the non-responsive group compared to the responsive patients. Although none of these hearts were used for transplantation, the inference is that DSE may identify those donor hearts with less myocardial necrosis that could proceed to successful transplantation. Such a possibility requires further study.

An alternative method to DSE of reducing the rate of rejection of donor hearts with impaired LV function is to monitor response to intensive and prolonged management with TTE. In a prospective study of 49 donor hearts with reduced ejection fraction (EF < 50%) or regional wall abnormalities sufficient for the organs to be initially rejected, prolonged donor management resulted in an improvement in EF or regional left ventricular dysfunction in 38 (78%) donors. Serial TTE was successful in identifying this improvement, resulting in the successful transplantation of 34 donor hearts. However, the natural history of changes in donor heart function as visualized by echocardiography is not known. In the studies published to date, there has been considerable variation in timing of echocardiography in relation to time of brain stem death and in relation to time of transplantation.

A critical issue for the echocardiographer in the assessment of donor hearts arises with the adequacy of image on ventilated patients sufficient for the accurate assessment of regional LV function. Firstly, comparative studies of TTE with transoesophageal echocardiography (TOE) have suggested that TTE assessment may be incomplete in up to 2%. The yield of abnormal studies was higher with TOE (9/24) compared with TTE (3/24) but numbers were inadequate to show a difference in outcome based on imaging modality. More importantly, TTE studies were performed without harmonic imaging and without contrast opacification of the left ventricle. It may be that with these improvements, TTE will remain sufficient for donor heart assessment without the need for routine invasive monitoring. Secondly, the experience of the echocardiographer in the assessment of donor heart function may be of central importance, particularly given the considerable changes in loading pressures to which the hearts are subject. Assessment at local donor hospital sites by echocardiographers not used to regular study of donor hearts may be significantly less accurate than an assessment made by an echocardiographer with experience in transplantation assessment.

In conclusion, if heart transplant activity is to be increased or even maintained, the large pool of potential donor hearts which is initially rejected should be investigated more intensively. Although the selection of an appropriate cardiac donor depends on many factors, adequate ventricular function and lack of significant valvular heart disease are of paramount importance in successful outcome. TTE can accurately and non-invasively include donor hearts for successful transplantation on the basis of preserved or mildly impaired LV function despite the presence of adverse clinical factors. TTE can accurately exclude donor hearts with severe LV dysfunction and severe valvular heart disease. Organ retrieval is costly and labour intensive, and is made more so by the 10—40% of attempted retrievals that are aborted because of donor heart malfunction. Such abortive attempts may be reduced by preliminary TTE assessment of the donor heart by an experienced observer. In those cases where TTE or TOE is unable to give a conclusive assessment of donor heart function, caution is required since regional wall abnormalities may improve. However, in these cases, echocardiography will continue to be one important part of a whole gamut of investigations, both electrocardiographic, haemodynamic, and surgical, necessary to make the final decision whether to withdraw or retrieve. Further research is needed to identify methods of assessing transient LV dysfunction that would not preclude transplantation.

Acknowledgements

R.V. Venkateswaran is supported by a financial grant from: Cardiac Surgical Trust Fund, University Hospital Birmingham NHS Trust, Edgbaston, Birmingham B15 2TH, United Kingdom.

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