Heart transplantation (HTx) provides a substantial survival advantage in selected patients with advanced heart failure (HF) (1), transforming a very limited prognosis into a 1-year survival rate of ≥80% and a 5-year survival of 65% (2).

Many patients on a list for HTx die while awaiting a satisfactory donor heart. The shortfall in donor heart supply obliges HTx centers to consider older, so-called marginal donor hearts with less assured post-transplantation outcomes (1). Each time a donor heart is considered for transplantation, the candidate and his or her physicians must weigh the balance between the continued risks of medical therapy and the risk of HTx. The most significant early risk after HTx is the primary dysfunction of the donor heart. Although treatable in a minority by mechanical circulatory support, in the majority, such dysfunction is manifest as primary graft failure leading to death or dysfunction with secondary organ failure, which may be lethal. Despite the great need for donor organs, the proportion of hearts ultimately retrieved from the initial pool of donor hearts is low (2).

Donor hearts mainly arise from victims of trauma, intracranial hemorrhage, intracranial primary tumors, and a small number of miscellaneous causes. The cause of death per se does not affect post-transplantation survival or likelihood of being used as a donor heart if adjusted for age. As traumatic brain death is declining, the fraction of brain death from intracranial hemorrhage is increasing, along with an increase in the mean age of the eligible donor pool, increasing from 23 years in 1983 to 30 years in 2005 to 2007. Although the mean age remains only 30 years, the proportion of donors older than 50 years now makes up 12% of the donor population, and this underscores the importance of careful donor assessment (2–4). Although older donor hearts can be safely transplanted, increasing donor age worsens post-transplantation prognosis at 1 and 5 years (2) and is associated with an increasing prevalence of donor coronary artery disease.

The best way to assess the donor heart is an issue of debate. Most protocols of assessment are based, at least in part, on a consensus report that highlighted an algorithm of assessment and management commencing with an initial echocardiogram dichotomizing donors based on a threshold left ventricular ejection fraction (LVEF) of 45% (5). In donors with an LVEF ≥45%, progression to retrieval for transplantation was recommended, whereas donors with an LVEF <45% were subjected to hormonal resuscitation and hemodynamic management based on pulmonary artery catheter assessment of cardiac index, filling pressures, and vascular resistance (Fig. 1) (6).

If echocardiography is the initial assessment investigation, echocardiographically detected left ventricular (LV) systolic dysfunction in the absence of a history of heart disease is the single most common cause for nontransplantation of an organ (7). However, ventricular dysfunction may be transient (8,9), and arbitrary thresholds of LV function may exclude hearts that could be resuscitated to transplantable status. This exclusion is compounded by the fact that in practice, pulmonary artery catheter assessment,
although defining the hemodynamic status of the donor heart and facilitating management of ventricular filling and afterload (3,10), is usually reserved for the heart donor already provisionally accepted for transplantation and attended by a retrieving team. However, the achievement of defined hemodynamic performance criteria of mean arterial pressure >60 mm Hg, central venous and pulmonary capillary wedge pressures <12 mm Hg with cardiac indices ≥2.4 l·min⁻¹·m⁻² and normal vascular resistance is associated with very satisfactory outcomes and appears to be the cornerstone of the final assessment of donor pre-retrieval (8,11).

As many as two-thirds of hearts offered for transplantation are rejected as being unsuitable or likely to fail if transplanted. This rejection occurs before detailed organ inspection, and in 90% of cases is based on an anticipation of poor donor organ function in the recipient. The clinical decision to discount these organs is based on data regarding blood pressure, electrophysiographic change, periods of hypotension, periods of cardiopulmonary resuscitation, drug history, history of hypertension, and the need for inotropic support (12). However, none of these factors alone necessarily precludes successful HTx. Thus, there is a pool of unused hearts, for which permission for heart donation has been granted, from which additional transplants could be generated if we could be more confident of their post-transplantation performance.

Furthermore, between 10% and 50% of attempted retrievals are aborted because of donor heart malfunction detected on inspection. This cohort raises the matter of generation if we could be more confident of their post-transplantation performance and staffing. These issues reaffirm the requirement for improved evaluation of the donor to define those hearts in which satisfactory function is maintained and achievable and should be subjected to further assessment and direct inspection.

**The Brainstem-Dead Heart Beating Multiorgan Donor Physiology**

The process of brain death leads to intensive sympathetic nervous system activity followed by a vasoparesis (13–15). In the heart, this intense catecholamine release is believed to cause at least transient myocardial ischemia and injury. Such injury might be exacerbated by changes in endocrine homeostasis, metabolism, and the development of a proinflammatory state.

In patients with subarachnoid hemorrhage (SAH), plasma catecholamine levels have been demonstrated to reflect the severity of the neurological insult acting as a physiological marker of patient outcome in both the acute and chronic phases of traumatic brain injury (16).

This intensive sympathetic activity and catecholamine release associated with brain death (17,18) may result in myocardial ischemia and injury (9,19–22), calcium overload (21,23,24), a possible reduction in high-energy phosphates (18,25–27), beta-adrenoreceptor desensitization (28–30), endothelial damage (22,25,27,31,32), and altered gene expression (33). Elevated cytosolic calcium levels are believed to activate enzymes such as lipase, protease, endonuclease, and nitric oxide synthase (22), disrupting high-energy phosphate production and resulting in oxygen free radical generation and further contributing to organ damage. The recovery of cardiac function is further limited by a decrease in the coronary reserve (34).

**Endocrine Changes**

A euthyroid sick state may occur together with hypothalamic-pituitary failure, resulting in neurogenic diabetes insipidus (17) with an associated decrease in vasopressin. Further decreased thyroid hormone (especially triiodothyronine [T₃]), insulin, and cortisol levels are seen (35). Pituitary failure produces abnormal temperature homeostasis, and eventually a catecholamine-deficient vasoparetic state occurs. All these phenomena may further affect cardiac function (13,21,36–44). Brain death is also followed by release of the proinflammatory cytokines, tumor necrosis factor (TNF)-α, and interleukin (IL)-1 and -6 (45,46), which may exacerbate organ injury.

The impact of these biochemical and endocrine changes on the recipient outcome is unclear. A low T₃ in itself does not portend impaired ventricular function or a failure to respond to hemodynamic management (11,47). Although T₃ administration has been recommended by some groups (48), the relevance of this remains a subject of debate and controversy (3,49,50).

**Electrocardiographic Assessment in the Heart Donor**

A large number of donors (47% to 100%) have abnormalities on the electrocardiogram (51,52), but no specific electrocardiographic abnormality has been found to be a sensitive indicator of donor heart outcome. In SAH, electrocardiographic changes similar to those of myocardial infarction have been reported (53–56), which correlate with the extent of neurological injury and higher mortality (57,58). In SAH, T-wave inversion or severe QTc prolongation is highly predictive of concomitant LV dysfunction, myocardial injury, and increased mortality (59–61). Further studies have associated electrocardiographic changes in SAH with wall motion abnormalities (62), and female sex
and hypokalemia have been demonstrated as independent risk factors for prolonged QTc (63). These reports and others showing a potential association between the severity of SAH-related neurological deficit and cardiopulmonary dysfunction (60,64) give rise to the suggestion that the electrocardiography may potentially be utilized to assess the brainstem-dead donor. Although of promise in identifying a high-risk donor, electrocardiography as a solitary investigation is unlikely to define a heart that is suitable or unsuitable for transplantation unless definitive pathological abnormalities (Q waves, left bundle branch block) are identified.

Echocardiographic Assessment of the Donor Heart

A normal LVEF in the potential donor is predictive of heart use and satisfactory recipient outcome (8). Echocardiographic myocardial dysfunction is, however, common, and occurs in 10% to 42% of donor hearts (65–67). The impairment is reported as severe in as many as 20% (68), and LV impairment constitutes the main reason for hearts being declined for transplantation (3,69,70). However, the echocardiographic dysfunction of the donor heart can improve either within the donor or within the recipient. This improvement includes resolution of subdued LV function, regional wall motion abnormalities, and ventricular hypertrophy (2,68,71,72). Thus, the utility of echocardiography in donor heart assessment has been questioned because adherence to strict limits of function may inappropriately exclude hearts that could be used successfully. The presence of LV hypertrophy may also deter the use of donor hearts (73). However, recent studies demonstrated that hearts with mild to moderate left ventricular hypertrophy have similar short- and longer-term outcomes provided other risk factors are simultaneously considered (e.g., ischemic time) (74). There are few data comparing echocardiographic findings and pulmonary artery catheter measurements, but recent reports suggest that many hearts with adverse initial hemodynamics or echocardiography can be successfully managed to a state where transplantation is possible (8). Recent evidence suggests that dobutamine stress echocardiography may be useful in assessing hearts with echocardiographic abnormalities and may alert the retrieval team to the presence of undiagnosed coronary artery disease (75).
Thus, a significant number of hearts are rejected on limited clinical and echocardiographic criteria. At least some of these should progress to direct assessment and invasive monitoring, and some could probably be used successfully if preliminary assessments could be more predictive of a successful retrieval and transplantation. The objective, therefore, is to identify markers that indicate that hearts that are likely to have good function or be manipulatable to satisfactory hemodynamic status and transplantation suitability. This could increase the yield of hearts from the existing donor pool, increase transplantation rates, and improve recipient outcomes.

The Potential for Biomarker Assessment of the Donor Heart

The demographic, clinical, electrocardiographic, and echocardiographic features of the potential heart donor are each disappointingly insensitive or nonspecific in determining whether an individual heart should be used or rejected for transplantation. Apart from donor age and ischemic time, there are few donor-related risk factors that are predictive of poor outcome. Despite this, there is evidence that primary transplant organ dysfunction in hearts, lungs, and kidneys may all occur when organs are from a single donor (76). This suggests that as-yet unidentified donor factors may be important both in terms of assessing organ usability and predicting graft failure in the recipient. Each of the phenomena that may lead to or increase cardiomyocyte injury in association with brain death lends itself to biochemical assessment. Therefore, it may be possible to use biomarkers to predict donor heart dysfunction or suitability for transplantation.

The Search for a Biomarker to Assess the Donor Heart

A heart donor biomarker should have a high sensitivity and specificity to predict which hearts can have a satisfactory hemodynamic outcome in a recipient and conversely to identify those hearts that should not be transplanted (i.e., predicting nonuse or primary graft failure in the recipient). The added dimensions of donor and recipient variables and their interaction add to the complexity of the assessment use of markers in this situation. Nevertheless, the likely biochemical abnormalities that occur after brain death may in fact yield important predictive information, allowing risk stratification of the potential heart donor just as can occur in myocardial infarction, acute coronary syndromes, and HF (77,78).

Cardiac troponins. The cardiac-specific troponins cTnI and cTnT have replaced creatine kinase-myocardial bound fraction as the preferred biomarkers in patients with myocardial infarction (77) and may have an important role in the assessment of the cardiac donor. Cardiac troponin elevation is prevalent in patients with SAH and in this setting is associated with increased LV dysfunction, pulmonary edema, hypotension requiring drug support, and worse patient outcome (79). In potential heart donors, a degree of cTnI elevation appears to be universally present and 37% have cTnI levels >1 µg/l (3). Higher levels have been observed after intracranial hemorrhage rather than trauma as a cause of brain death (80). Higher troponin levels have been noted in donor hearts with a worse LVEF or hemodynamic function (3,81–83). As expected, levels of cTnT and cTnI show a strong correlation.

The phenomenon of troponin elevation and cardiac dysfunction in the donor may be transient, suggesting altered sarcolemmal integrity rather than myocyte necrosis. In SAH, high troponin levels are associated with reversible cardiac dysfunction (84), and similar reversibility of dysfunction has been observed in heart donors (3,85).

The time from coning at which troponins are measured appears to influence their levels. Higher levels are recorded closer to the coning event, and as time from coning increases, troponin levels fall and cardiac function improves (3). This may suggest a reversible stunning phenomenon and has implications for donor management and procurement services.

Thus, troponin levels may act as a surrogate marker of ventricular function in the donor, but what happens when the heart from a donor with elevated troponin is transplanted? The evidence here is mixed. Andersen et al. (82) reported that higher troponin levels were associated with an increased need for inotropes in the recipient, and other studies found that donor troponin may be predictive of early graft failure in the recipient (83,86). This finding has been corroborated in the pediatric population in which donor sera cTnI concentration has been shown to be strongly related to the subsequent presence of fatal primary graft failure in infants (86).

In contrast, Khush et al. (87) demonstrated that a moderately elevated cTnI in the donor was not associated with the need for mechanical support post-operatively or survival at 30 days or 1 year in the recipient. However, there was a tendency for a longer in hospital stay in recipients whose hearts were from donors with higher cTnI.

The incidence and severity of cardiac rejection in the recipient have also been demonstrated to be associated with an elevated donor cTnT (88). Thus, from these studies, it is apparent that troponin levels in the donor may relate to the function within the recipient, the outcome of the donor heart, and the outcome both early and mid-term in the recipient. A discriminatory cutoff in troponin levels that suggests that an individual donor heart should not be used remains undefined. Although cTnI levels >1 µg/l may be predictive of subnormal donor heart function (3), certain hearts with troponins above these criteria have been associated with successful transplantation. cTnT levels also predict donor heart function (89) (Fig. 2). One flag in the field is a cTnT >0.1 µg/l or a cTnI >1.6 µg/l, each of which has been reported to have a high sensitivity and specificity for the prediction of early graft failure (83).
TNF-α

The up-regulation of proinflammatory cytokines seen in HF also occurs after brain death (67,90). The most studied cytokine is TNF-α, which is synthesized by nucleated myocardial cells in response to cardiac stress including myocardial infarction and LV pressure or volume overload (32,91,92). Neither TNF mRNA or TNF protein is constitutively expressed in the nonfailing heart but are uniformly expressed in the failing myocardium (93,94). When administered exogenously in experimental models, TNF provokes cardiomyocyte hypertrophy and triggers apoptosis. It also blunts responsiveness to adrenoreceptor agonists and impairs contractile function (95) via a number of possible mechanisms (29,96,97). Elevated levels of TNF-α are seen in and may antedate HF. TNF-α correlates with disease severity and can predict mortality, independent of age, sex, or HF etiology (98,99). The relationship between elevated TNF-α and mortality is believed to be a direct toxic effect rather than an epiphenomenon (32,67).

In heart donors, myocardial expression of TNF-α mRNA and serum TNF levels may be increased (45,46) (Fig. 3). Elevation occurs in nearly 30% of potential cardiac donors, and higher levels are observed in donors with marginal heart function (46). The greatest increase is in donor hearts rejected due to poor function (100). In these donors, TNF-α levels exceed those seen in advanced HF.

IL-6

The circulating level of another cardiotoxic cytokine, IL-6, may also be important. In HF, increased IL-6 has been demonstrated to be associated with decreased cardiac functional status, low ejection fraction, high right atrial pressure, and poor prognosis. Significant elevation of IL-6 occurs in probably all heart donors (3), and some studies have shown it to be higher in both the myocardium and serum of donor hearts rejected for transplantation due to poor heart function (Fig. 3) (46). Expression of IL-6 and its receptor components in donor hearts is comparable to that observed in advanced HF (101).

Procalcitonin

Procalcitonin (PCT) is a precursor of the hormone calcitonin and is systemically released in sepsis. Increased PCT levels have been found in 87% of potential heart donors, and higher levels correlate with deteriorating indices of heart function; LVEF, right ventricular ejection fraction, and cardiac index (3). The serum level above which PCT appears to be associated with adverse heart function and recipient outcome is approximately 2 ng/ml. This cutoff reasonably discriminates between those hearts matching or not matching functional suitability criteria for transplantation after donor management with a sensitivity of 88%, but a poor specificity (Fig. 4) (3,102). PCT levels >2 ng/ml may also be a predictor of early graft dysfunction after transplantation. Wagner et al. (103) investigated 81 consecutive donors and found that PCT >2 ng/ml was associated with a 16% increase in the risk of early graft dysfunction.
brain-dead heart donors reporting a mortality from early graft failure of 10%. Higher donor PCT levels were noted, and a PCT level >2 ng/ml predicted early graft failure–related mortality (103).

Interestingly, donor PCT levels appear to correlate strongly with other potential biomarkers. In 79 potential heart donors investigated, PCT levels correlated with biomarkers involving different noninflammatory patterns of injury (cTnI: r = 0.346, p = 0.005; cTnT: r = 0.387, p = 0.0014; N-terminal pro-B-type natriuretic peptide [NT-proBNP]: r = 0.368, p = 0.0025; and heart type fatty acid binding protein: r = 0.45, p < 0.001) (V.B. Dronavalli et al., unpublished observations, 2009). Potapov et al. (82) combined PCT and cTnT levels as potential predictors of early graft failure in 92 donor hearts, of which 14 had early graft failure. PCT >2 ng/ml together with elevated cTnT had a high sensitivity in identifying hearts associated with early graft dysfunction (82).

**B-Type Natriuretic Peptide (BNP) and NT-proBNP**

BNP and NT-proBNP are released from ventricular myocardium in response to increased wall stress (36,104,105). BNP is produced as a prohormone that is cleaved toward the N-terminal to produce BNP and the terminal portion NT-proBNP. Both aid the diagnostic and prognostic assessment of HF and myocardial infarction and correlate with ventricular dilation, remodeling, dysfunction, HF development, and death after acute myocardial infarction (78,105,106) and acute coronary syndrome (77,78,107,108).

In addition, elevated BNP is predictive of diastolic dysfunction even in the presence of normal systolic function (109,110).

In SAH, BNP levels are elevated in accordance with neurological severity and the presence of cardiac dysfunction (3,111,112). In the brain-dead potential heart donor, BNP levels are higher in those hearts with worse echocardiographic function and those unsuitable for transplantation (113). We recently studied NT-proBNP levels in potential heart donors and found that levels closely correlate with indices of cardiac function, both hemodynamic and echocardiographic, and are also predictive of which hearts achieve hemodynamic suitability criteria (114). The likely mechanism of cardiac dysfunction after severe brain injury or brainstem death is excessive myocardial catecholamine release leading to cardiac ischemia (18). Even transient ischemia results in an immediate increase in BNP, and the magnitude of the increase is proportional to the severity of the ischemia. The BNP prohormone is probably synthesized in ventricular myocytes in response to the cardiac wall stress and pressure overload that occur at the time of cerebral injury or coning. After SAH, BNP levels are elevated in plasma but not in cerebrospinal fluid. This suggests a nonbrain source of BNP, and the heart is a likely source (114).

Thus, as a marker of myocardial stress, BNP or its analogues represents a further possible biomarker tool in the assessment of the heart donor.

**SMARCAL1**

SMARCAL1 (SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin subfamily A-like 1) is an intracellular protein that acts as a DNA-dependent ATPase involved in transcription, DNA repair, and chromatin dynamics (115). Donor serum levels of SMARCAL1 were recently demonstrated to be elevated in donors whose grafts develop primary graft dysfunction. Ahrinejad et al. (116) demonstrated in a cohort of 336 heart donors that SMARCAL1 levels were significant predictors of 3-month, 1-year, and 5-year survival and primary graft dysfunction. Using a donor serum cutoff of ≥1.25 ng/ml, they demonstrated 96% sensitivity and 88% specificity for predicting primary graft dysfunction, with a corresponding positive predictive and negative predictive values of 83% and 97%, respectively, identifying a potential role of SMARCAL1 in organ selection even before the surgical retrieval. Although the serum analysis methodology for SMARCAL1 is available commercially, the main limitations for clinical use would be the duration taken for serum analysis. In addition, whether this assay is of utility in identifying potentially suitable donor hearts is not yet established.
Predictors in Combination

None of these potential biomarkers fully discriminate between donor hearts that should or should not be used for transplantation. Interestingly, they describe different modes of myocyte injury and stress and the proinflammatory environment and have therefore the potential to be used in combination to aid donor heart assessment. Preliminary findings have demonstrated that levels of NT-proBNP, troponins, and PCT correlate significantly, and thus multimarker assessment has the potential to act as an important assessment tool. There are a few studies addressing combined variables. In 1 study, the combination of troponin and BNP assessment increased the discrimination of hearts destined to have early graft failure (117), whereas another suggested added discriminant value by adding troponin and PCT (82). In the United Kingdom, a large study (approximately 1,200 potential heart donors) is currently under way to ascertain whether such biomarkers can predict the usability of donor hearts and to explore whether certain hearts currently rejected for transplantation on limited clinical information may have a biomarker signature that suggests suitability. Overall, biomarker assessment to assess whether hearts should be used for transplantation and the development of models to predict early graft failure in the recipient show significant promise and have the potential to widen the pool of donors available for transplantation, to direct donor management, and to improve outcomes in the recipient (Table 1).

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Ref./Year</th>
<th>Groups (n)</th>
<th>Type of Study</th>
<th>End Points</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>cTnT</td>
<td>82/2003</td>
<td>Donor hearts with good recipient function (77) Donor hearts with early graft failure (14)</td>
<td>Prospective, observational</td>
<td>64% sensitivity, 97% specificity; OR: 68.4 (p &lt; 0.0001) for development of early graft failure after heart transplantation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>88/1998</td>
<td>Donor heart used Low cTnT (6) Intermediate levels (8) High cTnT (2)</td>
<td>Prospective, observational</td>
<td>Significant linear correlation between donor TnT and grade of rejection (r = 0.943, p &lt; 0.0001)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>89/1995</td>
<td>Donor hearts with severely decreased LVEF (14) Donor hearts with moderately decreased LVEF (25) Donor hearts with normal LVEF (61)</td>
<td>Prospective, observational</td>
<td>cTnT significantly higher in group with severe decrease in LVEF (p &lt; 0.01). cTnT ≥ 0.5 μg/l had sensitivity = 1, specificity = 0.84 for predicting severe decrease in LVEF</td>
<td></td>
</tr>
<tr>
<td>cTnI</td>
<td>86/1994</td>
<td>Pediatric heart donors cTnI &gt; 3 ng/ml (8) cTnI &lt; 3 ng/ml (11)</td>
<td>Prospective, observational</td>
<td>Relationship between high cTnI and graft failure (p &lt; 0.005)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>83/2001</td>
<td>Good donor graft (68) Grafts with impaired function (11) Grafts not accepted for transplantation (39)</td>
<td>Prospective, observational</td>
<td>cTnI &gt; 1.6 μg/l 94% specificity as a predictor of early graft failure; OR for development of graft failure: 42.7</td>
<td></td>
</tr>
<tr>
<td>TNF-α</td>
<td>46/2000</td>
<td>Donor hearts used (31) Donor hearts not used (15)</td>
<td>Prospective, observational</td>
<td>Used/unused donor heart</td>
<td>Serum TNF-α higher in unused hearts compared with used hearts (p &lt; 0.05)</td>
</tr>
<tr>
<td>IL-6</td>
<td>46/2000</td>
<td>Donor hearts used (31) Donor hearts not used (15)</td>
<td>Prospective, observational</td>
<td>Used/unused donor heart</td>
<td>IL-6 level significantly higher in both groups compared with normal</td>
</tr>
<tr>
<td>PCT</td>
<td>103/2001</td>
<td>Donor hearts when recipient died within 30 days (8) All other donors (71)</td>
<td>Prospective, observational</td>
<td>Mortality within 30 days after transplantation as a result of early graft dysfunction</td>
<td>PCT &gt; 2 ng/ml: 50% sensitivity and 98% specificity for predicting early graft dysfunction with OR: 43.8 (p = 0.031)</td>
</tr>
<tr>
<td>BNP/NT-proBNP</td>
<td>114/2010</td>
<td>Donors with hemodynamics suitable for donation (40) Donors hemodynamically unsuitable for donation (39)</td>
<td>Prospective, observational</td>
<td>A high plasma NT-proBNP was associated with poor cardiac function. Some of the parameters assessed were pulmonary capillary wedge pressure, cardiac power output index, LVEF, and specific echo parameters</td>
<td></td>
</tr>
<tr>
<td>SMARCAL1</td>
<td>116/2009</td>
<td>Heart donors (336)</td>
<td>Prospective</td>
<td>3-month, 1-yr survival and primary graft dysfunction</td>
<td>Using a donor serum cutoff ≥ 1.25 ng/ml, they demonstrated 96% sensitivity and 88% specificity for predicting primary graft dysfunction, with corresponding positive predictive and negative predictive values of 83% and 97%, respectively</td>
</tr>
</tbody>
</table>
References


74. Golland S, Czer LS, Kass RM, et al. Use of cardiac allografts with milder and moderate left ventricular hypertrophy can be safely used in heart transplantation to expand the donor pool. J Am Coll Cardiol 2008;51:1214–21.

Key Words: donor assessment • heart transplantation • biomarkers.