Who needs a heart transplant?

The aim of transplant assessment programmes is selecting a patient who will benefit from receiving a cardiac transplant. The recipient should be expected to live longer with a better quality of life when compared with continuing on medical (or other non-transplant) therapy. Until the mid-1990s, the management of heart failure comprised angiotensin-converting enzyme inhibitors (ACE), diuretics, and digoxin. With this limited armamentarium, there was consensus that many ambulant patients with NYHA classes III and IV chronic heart failure would benefit from heart transplantation. Since the late 1990s, there has been a dramatic change in the management of heart failure. Beta-adrenoreceptor, aldosterone and angiotensin receptor blockers, implantable cardioverter defibrillators, and cardiac resynchronization therapy have all become established therapies that reduce mortality rates.1–5 With this improvement in therapy for heart failure, we have to reassess who would benefit from heart transplantation.

How do we select patients?

Quantifying the risk of an individual with heart failure is notoriously difficult. Indeed, around 70 different variables have been identified as independent risk factors. Attempting to measure risk is crucially important and is fundamental when trying to predict who would be likely to benefit from a cardiac transplant.

Heart Failure Survival Score

When trying to decide who is likely to benefit from cardiac transplantation, one of the most commonly used measures has been the Heart Failure Survival Score (HFSS).6 This is a composite scoring system that relies on several non-invasive measures (Table 1), which has been the cornerstone of assessment of risk in many transplant services over the last 8 years. Patients with scores suggesting high risk have been listed for cardiac transplantation.

Is the HFSS relevant to patients with advanced heart failure in 2005?

Derivation and validation of the HFSS

Components of the HFSS (Table 1) were derived and validated on patient cohorts from 1986 to 1991 and 1993 to 1995, respectively.6 The characteristics of patients in both groups can be seen in Table 2. Although 93% were on ACE inhibitors and 92% were on digoxin, none were on beta-blockers, had defibrillators, or cardiac resynchronization therapy. Patients were surprisingly well for a potential transplant population with a mean NYHA of 2.8. The therapy of patients in 2006 is markedly different from that given to those from whom the HFSS was derived. Limited data from Aaronson’s group have attempted to clarify the value of the HFSS in patients on beta-blockers (but again low percentages were receiving modern therapies).7

What did the HFSS predict?

To predict a patient’s prognosis, the most appropriate event to record is mortality. The HFSS was derived from a transplant population with an endpoint not of mortality alone, but a combined endpoint of mortality or urgent transplantation. Urgent transplantation is not an ideal endpoint, as it is arbitrarily determined by whether or not the patient was listed for urgent transplant and whether or not an organ became available. Urgent transplantation, in other words, does not imply a poor prognosis in the same way that death does.

Other concerns related to the HFSS in 2006?

When individual components of the HFSS are considered, there is concern that many of the changes in the management of heart failure will have affected these variables.

- Resting pulse rate: Beta-blockers lower the resting pulse rate and will therefore influence the HFSS. Cardiac resynchronization therapy dictates the pulse rate as programmed by the operator.
- Mean arterial pressure: Beta-blockers and angiotensin receptor blockers both lower the mean arterial pressure and will influence the HFSS.
- Interventricular conduction delay: Left bundle branch block is now an indication for cardiac resynchronization therapy in patients with advanced heart failure in sinus rhythm and on optimal medical therapy. Implantation of
cardiac resynchronization therapy reduces mortality with a relative risk reduction of 36% (10% absolute risk reduction).4 Before transplantation can be considered in patients with a broad QRS complex (QRS > 120 ms), cardiac resynchronization therapy should be implanted. Although a broad QRS complex has consistently been shown to indicate a worse prognosis, that we can now intervene to ‘treat’ a broad QRS complex (‘dysynchrony’) means that the inclusion of this parameter in the HFSS needs to be reconsidered.

- Left ventricular ejection fraction (LVEF): This can be assessed by a number of techniques. In the original paper by Aaronson et al.,4 LVEF was measured by radionuclide ventriculography. It is essential to define by what method LVEF is measured, as considerable variation in scores would result from one group assessing by echo and another by nuclear or magnetic resonance techniques.

- Peak VO2: Mancini et al.4 originally demonstrated that patients with heart failure and a VO2 of >14 mL/kg/min had a 1-year mortality of 6% when compared with those below this level who had a 1-year mortality of 30%. A recent study has found that the outcome of patients with a given VO2 is better than previously documented.9 The HFSS, if derived and revalidated in the modern era, should consider these improved outcomes. It could be argued that patients well enough to perform a VO2 are too well for a transplant.

What might predict prognosis better than the HFSS?

**BNP:** alone or as part of a revalidated HFSS. NT-proBNP has been found to be the most powerful independent predictor of mortality in advanced heart failure.10 Indeed, a high NT-proBNP concentration (dichotomized around the median) in our population predicts mortality better than the HFSS.10 Perhaps a repeat derivation and validation of an HFSS equivalent in the modern era of heart failure management could include the B-type natriuretic peptides.

**Pulse pressure.** There is a growing body of evidence that pulse pressure may predict outcome in advanced heart failure better than mean arterial pressure (MAP).11 A lower pulse pressure predicts an increased mortality.

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### Table 1  The Heart Failure Survival Score

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Derivation sample</th>
<th>Validation sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery disease</td>
<td>(yes = 1, no = 0)</td>
<td></td>
</tr>
<tr>
<td>Intraventricular conduction delay</td>
<td>(yes = 1, no = 0)</td>
<td></td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart rate (b.p.m.)</td>
<td>(yes = 1, no = 0)</td>
<td></td>
</tr>
<tr>
<td>Na+ concentration (mmol/L)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VO2 (mL/min/kg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HFSS = ...

High risk <7.19 (35%, 1-year survival), medium risk = 7.20–8.09 (60%, 1-year survival), and low risk >8.10 (88%, 1-year survival).

### Table 2  Characteristics of the HFSS model derivation (n = 268) and model validation (n = 199) samples

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Derivation sample</th>
<th>Validation sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50 ± 11</td>
<td>52 ± 10</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>80</td>
<td>81</td>
</tr>
<tr>
<td>Race (% Caucasian)</td>
<td>66</td>
<td>78</td>
</tr>
<tr>
<td>NYHA class (mean)</td>
<td>2.8 ± 0.9</td>
<td>2.8 ± 0.7</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>20 ± 8</td>
<td>22 ± 8</td>
</tr>
<tr>
<td>Peak VO2 (mL/kg/min)</td>
<td>14.6 ± 5.4 (4–40)</td>
<td>15.9 ± 4.3 (7–40)</td>
</tr>
<tr>
<td>Resting heart rate (b.p.m.)</td>
<td>87 ± 16 (56–140)</td>
<td>87 ± 17 (43–150)</td>
</tr>
<tr>
<td>Mean blood pressure (mmHg)</td>
<td>86 ± 13 (57–130)</td>
<td>83 ± 12 (60–119)</td>
</tr>
<tr>
<td>Serum sodium (mmol/L)</td>
<td>137 ± 4 (119–147)</td>
<td>138 ± 4 (120–148)</td>
</tr>
<tr>
<td>IVCD (%)</td>
<td>27</td>
<td>53</td>
</tr>
<tr>
<td>Ischaemic aetiology (%)</td>
<td>45</td>
<td>47</td>
</tr>
<tr>
<td>Medical therapy (%)</td>
<td>88</td>
<td>93</td>
</tr>
<tr>
<td>ACE inhibitor (%)</td>
<td>94</td>
<td>92</td>
</tr>
<tr>
<td>Diuretic (%)</td>
<td>93</td>
<td>92</td>
</tr>
</tbody>
</table>

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### Who does need a heart transplant?

#### Hospitalized patients

**Patients with decompensated heart failure**

Although most patients hospitalized with heart failure are managed medically and then discharged, there are a proportion of patients who become shocked and whose outlook is very poor. It is for such patients that cardiac transplantation should be considered.

**Patients with cardiogenic shock complicating myocardial infarction**

Patients with ST elevation myocardial infarction complicated by shock have a high mortality rate.12 These patients should receive primary angioplasty with intra-aortic balloon pump insertion, but if they do not respond to these measures, transplantation should be considered.

Both these earlier patient groups should be managed aggressively. If they are not in a unit with cardiac transplantation capabilities, they should be transferred to one which does. When these patients are managed aggressively, they often respond well to non-transplant measures and are mobilized and discharged.

#### Outpatients

An ambulant patient with heart failure would have to have a 1-year mortality of >20% to warrant cardiac transplantation on the basis of 1-year outcomes. Recent clinical trials of patients with advanced heart failure have found 1-year mortality rates of 9.7–13.5%.4,11 There are no current studies in transplant eligible patients who have 1-year mortality rates of >20%. The argument that ambulant patients with heart failure should be transplanted because the 5- and 10-year survival is better post-cardiac transplantation than for those on medical therapy (at least with currently available...
data) is a difficult one. If the 1-year survival with medical therapy is better than transplant, can we justify transplanting a patient for the 5- and 10-year possible benefit? If the patient dies peri-operatively, this argument is difficult to justify.

Risk of morbidity and mortality post-cardiac transplantation

There are several factors recognized as predictors of mortality following cardiac transplantation. Being in hospital, requiring mechanical ventilation or dialysis at the time of transplantation, a panel reactive antibody >10%, repeat transplantation, or having adult congenital heart disease are categorical risk factors that are strong predictors of first-year mortality. Significant continuous factors include donor heart ischaemic time, age of donor and recipient, centre volume, and the recipient’s weight, and readings of bilirubin, creatinine, and diastolic pulmonary artery pressure.

However, several previously identified risk factors appear to have less impact on mortality in the current era. These include a pre-transplant diagnosis of coronary artery disease, having an intra-aortic balloon pump at the time of transplant, and having an infection requiring intravenous drug therapy within 2 weeks of transplant.

Assessment standards/medical optimization

Cardiac transplant assessment units should be staffed by cardiologists with an interest in heart failure. All patients should have optimal non-pharmacological and pharmacological management. They should be assessed for their requirements for defibrillators and cardiac resynchronization therapy. Only once they are on optimal therapy, should they be considered for transplantation. Units should clearly log their rates of use of all pharmacological therapies, implantable cardioverter defibrillators, and cardiac resynchronization therapy. If patients are not receiving these therapies, the reasons should be clearly logged.

Conclusions

The patient population that warrants cardiac transplantation has changed over the last decade because of the availability of both improved pharmacological and advanced pacemaker technologies. Fewer ambulatory patients are being transplanted. In this population, the traditional method of risk stratification, the HFSS, requires revalidation in the era of these new therapies. More hospitalized patients with either severe decompensated heart failure or with cardiogenic shock post-myocardial infarction are now being transplanted. Cardiologists should be aware of those patients who might be suitable for cardiac transplantation, and should discuss them early in the course of their admission with their regional transplant service.

Conflict of interest: none declared.

References


