H
ear transplantation is a very effective treatment option
for patients with many end-stage cardiac pathologies. Unfortu-
nately, a shortage of donor organs limits the number of
patients who benefit from this intervention, and many patients
die while awaiting transplantation. Per the Scientific
Registry for Transplant Recipients, the estimated overall heart
transplant wait-list mortality for 2013 was 10.7 deaths per 100
wait-list years.1 Given this, there has been great interest in
identifying the donor risk factors that are significantly associ-
ated with adverse recipient outcomes, to safely expand donor
heart utilization and to ensure that organs are not unneces-
sarily rejected.

When evaluating donor organs, there are a number of well-
defined exclusion criteria, such as use of high-dose inotropic
support during donor management, positive hepatitis/HIV
serologies, obstructive coronary artery disease, and irrevers-
ible left ventricular systolic dysfunction.2 However, there are
a number of donor risk factors that are evaluated on a case-by-
case basis. Among these are elevated donor troponin I levels.
Previous studies have shown that troponin I may be a reli-
able surrogate of donor heart function,3,4 and this biomarker
has therefore been used to help select optimal organs. What
is often not taken into consideration is the fact that donor
troponin levels are influenced by a number of clinical variables,
including mode of death and renal function.5 The Table lists
the most commonly cited reasons for nonacceptance of donor
hearts for transplantation.

Studies investigating recipient outcomes after using
hearts from donors with elevated troponin I have had mixed
results. Initial studies concluded that elevated donor tropo-
nin T levels were associated with decreased left ventricular
ejunction fraction, possibly predisposing to worse recipient
outcomes, although that end point was not specifically evalu-
at.6 Shortly thereafter, Potapov et al6 found that recipients of
hearts from donors with elevated troponin I or T had a higher
odds of developing primary graft failure. In a follow-up study,
this group found that elevated donor cardiac troponin T and
procalcitonin were independently associated with early graft
failure.8 Although the study cohorts were small, and the criteria
for primary graft failure have since been revised, this was the
longstanding belief for a number of years. Interestingly, one
subsequent study suggested that elevated donor troponin lev-
els may be protective against future recipient complications,
such as development of cardiac allograft vasculopathy.9 More
recently, our group showed that modestly elevated donor car-
diac troponin I levels are not associated with increased recipi-
ent mortality after cardiac transplantation.10 Since then, other
studies have shown that elevated donor troponin I levels are not
associated with increased incidence of acute rejection or graft
dysfunction in the transplant recipient.4 Similar findings have
also been noted in the pediatric literature, although median tro-
ponin levels were much lower at ≈0.1 ng/mL.12 Most recently,
Szarszoi et al13 used the newer high-sensitivity cardiac tropo-
nin T assay to study recipient incidence of primary graft
dysfunction after receiving hearts from donors with elevated
high-sensitivity cardiac troponin T. They found no significant
difference in high-sensitivity cardiac troponin T levels between
patients who developed primary graft failure and those who
did not. One possible explanation for the change in findings in
recent years is the reduction in mortality because of improve-
ments in perioperative care. Generally, however, hearts from
donors with elevated troponin I are subjected to more stringent
selection criteria and often excluded from transplantation.

In this issue of Circulation: Heart Failure, the study by
Madan et al14 used the national United Network for Organ
Sharing database to investigate recipient outcomes after trans-
plantation using hearts from donors with variably elevated
levels of troponin I. The authors concluded that elevated donor
troponin I levels in patients with preserved left ventricular sys-
tolic function were not associated with primary graft dysfunc-
tion, the development of cardiac allograft vasculopathy, or
increased mortality.

The study has a number of strengths that should be high-
lighted. First, it is the most comprehensive (with a cohort of
≈11000 recipients) study investigating recipient outcomes
using donors with elevated troponin. It is also relevant to our
current practice because it includes data from contemporary
years (2007 to 2014). Improvements in surgical and periope-
ratative management and immunosuppressive therapies have
led to significantly improved survival after heart transplanta-
tion in the current era, which may mitigate the effect of using
higher-risk donor hearts. Additionally, the authors used hard
definitions for primary graft dysfunction, minimizing ambigu-
ity. Finally, the authors appropriately adjusted for a large num-
ber of donor and recipient characteristics that may be potential
confounders, strengthening their findings significantly.

Although the study has many strengths, there are important
caveats to consider. The first of these is the variability of tro-
ponin measurements. The authors selected the highest reported
Elevated Troponin? Take Heart and Reconsider!

Table. Common Reasons for Donor Heart Nonacceptance for Transplantation

<table>
<thead>
<tr>
<th>Common Reasons for Donor Heart Nonacceptance for Transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older age</td>
</tr>
<tr>
<td>Female sex</td>
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<tr>
<td>Death because of cerebrovascular accident</td>
</tr>
<tr>
<td>Need for cardiopulmonary resuscitation</td>
</tr>
<tr>
<td>History of smoking</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
</tr>
<tr>
<td>Troponin &gt;1.0 μg/L</td>
</tr>
<tr>
<td>Need for high-dose inotrope/pressor support*</td>
</tr>
<tr>
<td>Left ventricular dysfunction (ejection fraction &lt;50%)</td>
</tr>
<tr>
<td>Left ventricular regional wall motion abnormalities on echocardiogram</td>
</tr>
<tr>
<td>Left ventricular hypertrophy on echocardiogram</td>
</tr>
</tbody>
</table>

*Generally defined as dopamine or dobutamine >10 μg/kg/min or any use of norepinephrine.

Adapted from Khush et al.4

troponin value during donor management for their analyses. However, it is important to consider the implications of an elevated troponin in various clinical scenarios. For example, an elevated troponin after brain stem herniation or cardiopulmonary resuscitation, which often results in catecholamine release followed by myocardial injury, may not be equivalent to a donor with stable hemodynamics and persistently elevated troponin. Furthermore, different organ procurement organizations have different protocols for donor management, including laboratory evaluation before offering organs, so the reported values may reflect differences in donor management and the timing of blood draws. In addition, different donor hospitals use various troponin assays with variable sensitivity. Therefore, the use of a single troponin value, without other temporal or clinical standardization, should be interpreted with caution.

Another point to consider is the possibility of selection bias. Only those organs accepted for transplant were included in this analysis. It is likely that those donors with elevated troponin levels had other favorable features (ie, young age, lack of additional comorbidities) that ultimately led to acceptance of their hearts for transplantation. Thus, the outcome of marginal or high-risk donor hearts with elevated troponin levels remains unknown because many of these organs were likely discarded.

Although this article concludes that troponin elevation in donors with intact systolic function does not portend poor recipient outcomes, there is still need for further investigation. Given the variability of troponin levels over time, it may be more insightful to follow trends (ie, rise, decline, or persistent elevation) rather than a single value. The timing of troponin levels relative to donor cardiopulmonary resuscitation and brain stem herniation should be considered with respect to heart utilization and recipient outcomes. It may also be worthwhile to study the association between elevated troponin levels and recipient outcomes in donors with left ventricular dysfunction (ejection fraction <55%, excluded from this study) because decisions about acceptance of these hearts for transplantation are much more difficult than acceptance of a heart with normal function. Regardless, this article should go a long way toward reassuring transplant centers when evaluating heart offers from donors with normal cardiac function in the setting of elevated troponin levels. Hopefully this will represent a concrete step toward safely expanding donor heart utilization.

Disclosures

Dr Khush is the principal investigator of a National Institutes of Health–sponsored multisite study that aims to establish evidence-based criteria for donor heart selection (R01HL125303). The other authors report no conflicts.

References


Key Words: Editorials ■ allograft ■ biomarker ■ coronary artery disease ■ incidence ■ troponin
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