Transplant outcomes are steadily improving

The use of hematopoietic cell transplantation (HCT) has been steadily increasing, especially in the last decade, and this growth has been driven by a significant improvement in outcomes. Recently published studies have found survival after unrelated donor transplant comparable to related donor transplant results in several patient populations. In some instances, unrelated transplant outcomes have even exceeded those obtained in related transplant. [1,2]

Table 1 shows unadjusted one-year overall survival of unrelated donor transplant recipients after first allogeneic HCT. In just over a decade, one-year survival has improved by 18%, rising from 42.2% to 60.3%.

<table>
<thead>
<tr>
<th>REPORT YEAR</th>
<th>TRANSPLANT PERIOD</th>
<th>ONE-YEAR SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>2007-2009</td>
<td>60.3%</td>
</tr>
<tr>
<td>2009</td>
<td>2003-2007</td>
<td>56.3%</td>
</tr>
<tr>
<td>2007</td>
<td>2001-2005</td>
<td>51.5%</td>
</tr>
<tr>
<td>2003</td>
<td>1996-2001</td>
<td>42.2%</td>
</tr>
</tbody>
</table>

Table 1. Survival of unrelated donor HCT facilitated by the National Marrow Donor Program (NMDP) at U.S. transplant centers. (NMDP data)

Clinical advances drive improved outcomes

Several factors have led to better outcomes, including refined clinical practice, enhanced patient-donor human leukocyte antigen (HLA) matching and better understanding of optimal transplant timing.

Advances in clinical practice include improvements in pre-transplant conditioning regimens, such as less-toxic reduced-intensity regimens, and better post-transplant supportive care. Several new antifungal agents have contributed to progress in treating fungal infections in HCT recipients, especially when used in preemptive and prophylactic strategies. [3]

DNA-based tissue typing has increased the accuracy and specificity of HLA typing, which allows more precise matching between patients and donors.[4] And large registry studies have resulted in a better understanding of which donor-patient HLA mismatches are better tolerated than others. [5]

These advances have made hematopoietic cell transplantation better tolerated and more effective at treating underlying diseases, thereby expanding this potentially curative strategy to increasing numbers of patients. ■
Optimal timing: Early referral improves HCT outcomes

Appropriate timing of allogeneic transplant is a critical factor in improved patient outcomes. For most diseases, transplants performed early in the disease process are associated with lower transplant-related mortality and disease recurrence.

In a study by Lee et al. of 3,857 unrelated donor transplants, patients with intermediate-stage disease had a 38% greater risk of mortality than patients with early-stage disease as seen in Table 2. Patients with advanced disease had approximately twice the mortality risk as patients with early-stage disease. [1] A major conclusion made by the authors of this study was that an early referral is perhaps the single most important step that can affect survival.

Consultation with a transplant center early in the course of a disease is the best way to ensure that if a transplant is indicated, it is performed at an optimal time for the patient. The NMDP and the American Society for Blood and Marrow Transplantation have developed guidelines for timing of transplant consultation that specify which patients are at risk for disease progression and who therefore should be referred for HCT consultation.

The guidelines are available in mobile app, print and online at marrow.org/md-guidelines.

**Table 2. Mortality risk for HCT patients with unrelated donor by disease stage.[1]**

<table>
<thead>
<tr>
<th>DISEASE STAGE</th>
<th>n</th>
<th>HAZARD RATIO</th>
<th>95% CI</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td>1454</td>
<td>1.00</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Intermediate</td>
<td>1352</td>
<td>1.38</td>
<td>1.25</td>
<td>1.53</td>
</tr>
<tr>
<td>Late</td>
<td>645</td>
<td>1.90</td>
<td>1.67</td>
<td>2.16</td>
</tr>
</tbody>
</table>

Comparable outcomes in related, unrelated HCT

Only approximately 30% of patients for whom allogeneic transplantation is an appropriate therapy will have an HLA-matched sibling. Thus, the majority of potential transplant patients will need to use an unrelated donor or cord blood unit in order to undergo allogeneic transplantation.

Between 66-93% of patients have an available and willing HLA-matched donor at ≥ 7 of 8 loci through the NMDP’s Be The Match Registry®, depending on race or ethnicity.

One study of 2,223 patients ≥21 years with acute myelogenous leukemia who underwent allogeneic HCT found that there were no significant differences in survival based on stem cell source (related or unrelated donor).

This retrospective analysis of data reported to CIBMTR (Center for International Blood and Marrow Transplant Research) for transplants between 2002-2006 compared HCT outcomes using HLA-matched related (n=624), 8/8 matched unrelated (n=1,193), and 7/8 matched unrelated donors (n=406). A multivariate analysis revealed that matched related and 8/8 unrelated donor HCT recipients had similar survival (relative risk, 1.03; p=0.62). [1]

In a single-center study by Ho et al with 433 transplants using a reduced-intensity conditioning regimen, unrelated donor (n=246) and related donor (n=187) transplant recipients had comparable 2-year overall survival: 56% vs. 50%, respectively (p=0.53). [2]

A multivariate analysis showed that unrelated donor HCT was significantly associated with a lower risk of relapse (hazard ratio [HR] 0.67, p=0.002) and superior progression-free survival (HR 0.69, p=0.002).

These studies, in addition to several others, demonstrate that not having a matched related donor should no longer be considered a contraindication for HCT.


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