Discrepancies Between Patient and Physician Estimates for the Success of Stem Cell Transplantation

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Context  Stem cell transplantation is associated with considerable morbidity and mortality. The extent to which patients and their physicians correctly estimate these risks is unknown.

Objective  To measure the expectations of patients and physicians prior to stem cell transplantation and correlate them with actual outcomes after transplantation.

Design  Prospective cohort study with baseline questionnaire administered July 1996 through November 1999 and follow-up to May 2000.

Setting  Tertiary care transplant center in the United States.

Participants  Of 458 surveys mailed, evaluable returned surveys were included for 313 autologous and allogeneic stem cell transplantation patients and their physicians.

Main Outcome Measures  Patient and physician expectations prior to transplantation (measured on 6-point Likert scales) of treatment-related mortality, cure with transplantation, and cure without transplantation; actual treatment-related mortality and disease-free survival among patients with at least 1 year of follow-up after transplantation (n=263).

Results  Both patients and physicians were fairly accurate in estimating treatment-related mortality when actual mortality was less than 30%. However, in situations in which mortality was higher than 30%, such as with allogeneic transplantation for intermediate or advanced disease, physician expectations were lower, while patient remained optimistic. Similarly, physicians provided lower estimates of disease-free survival in cases of intermediate or advanced disease while patient expectations remained high and constant regardless of disease stage.

Conclusions  Patients and their physicians have the most concordant and accurate expectations when the outcome of stem cell transplantation is likely to be favorable. However, patients with more advanced disease fail to recognize the higher risks associated with their situations.

JAMA. 2001;285:1034-1038 www.jama.com

M O D E L S F O R O P T I M A L shared (or informed) medical decision making encourage open discourse between patients and physicians regarding the pros and cons of treatment options. However, whether patients actually emerge from these discussions with accurate expectations for the chosen therapy has rarely been studied. Hematopoietic stem cell transplantation (SCT) for hematologic diseases offers an ideal opportunity to study this question in a high-stakes setting since SCT offers the potential of life extension or cure, but at substantial risk of treatment-related death. We measured the expectations of 313 patients and their physicians prior to transplantation, then conducted follow-up longitudinally to compare expectations with actual outcomes.

METHODOLOGY

Study Population
Patients were enrolled at the Brigham and Women’s Hospital and the Dana-Farber Cancer Institute. Eligibility criteria included age older than 18 years, ability to read English, and planned autologous or allogeneic transplantation within 3 months of study enrollment but not less than 1 week. Patients were contacted by telephone by a study investigator (S.J.L.) to introduce the study, then mailed questionnaires, consent forms, and self-addressed, stamped envelopes. Some patients could not be contacted due to logistic reasons. Others elected not to participate in the study or did not return baseline questionnaires and thus were not enrolled. Baseline surveys were administered July 1996 through November 1999.
analysis were collected as part of a much larger, prospective, longitudinal questionnaire study evaluating expectations and quality of life.

Disease status was categorized at the time of study enrollment into 3 groups. Early stage patients were those with leukemia in first complete remission, stable phase chronic myelogenous leukemia, or aplastic anemia. Intermediate patients had leukemia in second or greater complete remission, accelerated phase chronic myelogenous leukemia, chemotherapy-responsive lymphoma or myeloma, or had myelodysplastic syndrome, which was either untreated or in remission. Advanced patients had relapsed or refractory diseases.

The specific conditioning regimen and graft manipulation, if any, was according to protocol requirements and attending physician or patient preference. Patients were to receive autologous or allogeneic grafts. Graft-vs-host disease prophylaxis consisted of T-cell depletion or methotrexate and cyclosporine. Details of the transplant regimens and graft-vs-host disease prophylaxis have been previously published.5-10

Patient Education and Informed Consent Prior to Transplantation

Each patient’s physician determined the appropriateness and type of transplantation and was responsible for communicating the risks and benefits of the procedure. However, educational practices were not controlled, and individual physicians determined the depth and format of medical information discussed. All patients signed informed consent documents for transplantation that provided only general information as required by the institutional review board, not quantitative estimates of morbidity or mortality.

Data Collection

Patients were surveyed by mail before transplantation to record expectations for the outcome and collect additional sociodemographic characteristics. Predictions about cure with and without transplantation were captured by specific reference to personal outcome (What do you think is your chance of being cured with a stem cell transplant? and What do you think is your chance of cure without a stem cell transplant?), whereas the question about treatment-related mortality invoked population estimates (What percentage of people do you think die during the transplant hospitalization or from complications within the first year?). Responses were measured on 6-point Likert scales offering paired verbal and numeric information (eg, almost all [>90%], most [75%-90%], the majority [50%-74%], less than half [25%-49%], few [10%-24%], or almost none [<10%]).

The physician of each enrolled transplant patient was asked to estimate the patient’s chance of cure with and without transplantation and treatment-related mortality within the first year. Response categories were identical to patient options. Physician information was collected as soon as possible after patients returned their surveys and prior to transplantation.

Statistical Methods

The SAS system was used for all statistical calculations.11 Syngeneic patients were combined with the autologous group for analysis. Responders were compared with nonresponders using χ², Mantel-Haenszel χ², and Wilcoxon rank sum tests with P<.05 declared as significant.

Correlation between patient and physician expectations was evaluated using Bowker 2-tailed tests of symmetry and weighted κ statistics. Mean expectations for treatment-related mortality and cure were calculated for each subgroup using the midpoint (eg, 37%) when response options were ranges of probabilities (eg, 25%-49%). Discrepancies between estimates for chance of cure with transplantation were quantified by calculating the minimal difference between response options selected. For example, if a patient thought he/she had 75% to 90% chance of cure while his/her physician reported 25% to 49%, we assigned a conservative discrepancy of 26% (75% minus 49%).

Analysis of treatment-related mortality and disease-free survival was limited to the 263 patients who received transplants before May 1999 and for whom 1-year follow-up was possible. Disease-free survival at 2 years was calculated using the Kaplan-Meier method with surviving patients censored if in remission at last follow-up.

RESULTS

Patient Characteristics

A total of 458 surveys were sent to patients who underwent transplantation, and 320 were returned of which 313 (68%) were evaluable. Characteristics of the population are shown in Table 1. Responders were more likely to be white than nonresponders (93% vs 88%; P=.004) but were otherwise similar in sex, disease stage, and type of transplant procedure performed (including donor type, graft-vs-host disease prophylaxis, and degree of match, if allogeneic).

Expectations for Cure and Treatment-Related Mortality

Patient and physician estimates of chance of cure with transplantation,
chance of cure without transplantation, and 1-year treatment-related mortality were compared with each other and with actual outcomes. There were 15 physicians who saw at least 2 patients. Four physicians accounted for 64% of the patients (11%-25% each). We compared these physicians with each other and with the remaining 11 physicians; no evidence for a physician effect was seen.

The Figure shows concordance of paired patient-physician expectations. Agreement occurred only 17% to 52% of the time, and overall correlation was poor (weighted κ, 0.08-0.22). Patients were significantly more optimistic than their physicians on all measures (P≤.001). Anticipated chance of cure with transplantation showed the greatest discordance with 78% of patients estimating their chance of cure with transplantation higher than their physicians. In fact, 48% of the population indicated an anticipated cure rate at least 2 prognostic categories higher than their physician, corresponding to an absolute discrepancy of 16% to 82% (median, 26%) using conservative assumptions.

Table 2 shows patient and physician mean estimates compared with actual treatment-related mortality according to type of transplantation and disease stage. Discrepancies between estimated and actual mortality rates for each group can be seen by comparing percentages across rows. When treatment-related mortality was lowest, as for autologous transplants, related-donor T-cell–depleted procedures, or related and unrelated donor, methotrexate and cyclosporine transplants performed for early stage diseases, predictions were most concordant with actual outcomes.

![Figure. Comparison of Patient and Physician Estimates for Cure With Transplantation, Cure Without Transplantation, and 1-Year Treatment-Related Mortality](image-url)

SCT indicates stem cell transplantation.

### Table 2. Treatment-Related Mortality at 1 Year: Expectations and Actual Outcomes*

<table>
<thead>
<tr>
<th>Type of Transplant</th>
<th>Total No. of Patients</th>
<th>No. of Respondents</th>
<th>No. of Nonresponders</th>
<th>No. Mismatched</th>
<th>Estimate, % Patient</th>
<th>Estimate, % Physician</th>
<th>Actual Treatment-Related Mortality, %†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous</td>
<td>94</td>
<td>89</td>
<td>5</td>
<td>NA</td>
<td>12</td>
<td>10</td>
<td>10</td>
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<tr>
<td>Allogeneic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methotrexate/cyclosporine‡</td>
<td>71</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>21</td>
<td>33</td>
<td>42</td>
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<tr>
<td>Related to donor</td>
<td>35</td>
<td>33</td>
<td>2</td>
<td>0</td>
<td>20</td>
<td>25</td>
<td>29</td>
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<td>Disease status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>25</td>
<td>24</td>
<td>1</td>
<td>1</td>
<td>24</td>
<td>40</td>
<td>56</td>
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<tr>
<td>Intermediate</td>
<td>11</td>
<td>11</td>
<td>0</td>
<td>1</td>
<td>18</td>
<td>43</td>
<td>55</td>
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<tr>
<td>Advanced</td>
<td>54</td>
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<td>NA</td>
<td>NA</td>
<td>23</td>
<td>34</td>
<td>39</td>
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<tr>
<td>Unrelated to donor</td>
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<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Disease status</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>30</td>
<td>27</td>
<td>3</td>
<td>3</td>
<td>28</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>Intermediate</td>
<td>18</td>
<td>17</td>
<td>1</td>
<td>4</td>
<td>19</td>
<td>38</td>
<td>44</td>
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<tr>
<td>Advanced</td>
<td>6</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>15</td>
<td>55</td>
<td>67</td>
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<tr>
<td>T-cell depletion‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Related to donor</td>
<td>30</td>
<td>29</td>
<td>1</td>
<td>1</td>
<td>19</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Unrelated to donor</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>23</td>
<td>34</td>
<td>57</td>
</tr>
</tbody>
</table>

*NA indicates not applicable.
†At 1 year.
‡Type of prophylaxis for graft-vs-host disease.
comes. When treatment-related mortality was higher (>30%), as for patients with intermediate and advanced disease or those undergoing unrelated donor, T-cell–depleted, allogeneic procedures, patient (and to a lesser extent, physician) predictions greatly underestimated actual mortality.

Table 3 shows the expectations for disease-free survival with or without SCT, stratified by type of transplantation and disease stage. Most autologous patients had intermediate stage disease (90 intermediate, 4 advanced). Results for allogeneic patients are presented by disease stage only because expectations and disease-free survival were not affected by donor status or type of graft-vs-host disease prophylaxis. For each group, patient expectations were high and overly optimistic. Physician expectations were closer to actual outcomes and differed by stage of disease (90 intermediate, 4 advanced).

Results for allogeneic patients are presented by disease stage only because expectations and disease-free survival were not affected by donor status or type of graft-vs-host disease prophylaxis. For each group, patient expectations were high and overly optimistic. Physician expectations were closer to actual outcomes and differed by stage of disease (P<.001) with lower estimates assigned to intermediate and advanced patients.

**COMMENT**

We found discrepancies between patients and their physicians regarding anticipated and actual outcomes of SCT. Estimates were most concordant and correct when observed outcomes were favorable. However, as the likelihood of poor outcomes increased, physicians adjusted their expectations while patients did not.

Discrepancies between patient and physician expectations have been observed in several other settings and attributed to both patient and physician factors. Our findings show that while most transplant patients are aware they have some chance of treatment-related death and relapse, those at highest risk do not appreciate the true likelihood of these possibilities. It is easy to imagine that as a prognosis worsens, both patients and physicians may avoid discussions involving discouraging statistics, instead focusing on the curative potential of the procedure. Clinicians may be concerned that full awareness of grim prognostic information will destroy hope and increase distress, possibly decreasing a patient’s will to live. To prevent this, they may selectively withhold or minimize some details, use qualitative terms (such as frequent or possible) instead of numeric figures, emphasize optimistic information, or suggest to patients that grim prognostic estimates apply to populations and may not be meaningful to them as individuals. Patients considering transplantation may have powerful psychological incentives to view their prognoses with an optimistic bias, and it is conceivable that any attempts by physicians to force patients to acknowledge unfavorable statistics may be met with anger, denial, or mistrust, in addition to anxiety and despair.

However, there may also be costs of allowing discrepancies between expectations and reality to persist. At one level, complete respect for the principle of patient autonomy requires that each patient be given the means to make medical decisions for themselves unless they explicitly assign this role to someone else. In some cases, an unbridled understanding of the risks might change treatment decisions (alternatives include chemotherapy only or best supportive care). Even if treatment choice is not altered, a more realistic understanding of prognosis could encourage attention to financial and family arrangements, affect personal preparations prior to transplantation, or prepare families for the most likely outcome, which is death. Indeed, there is evidence to suggest that concordance of expectations with actual outcomes promotes better psychological adjustment.

There are a number of limitations to this study and its findings. Most importantly, this study was conducted at a single institution with a high percentage of well-educated and white patients, and other centers may have different populations and procedures for counseling patients. Nonetheless, we suspect that our observations might be relevant to other transplant programs and even other situations in medicine where patients accept substantial risks in the hope of a cure. Second, we began our observation period after the decision to undergo transplantation had already been made. We did not study the process leading up to those expectations. In particular, physician-patient interactions were not observed, so we do not know how prognostic information was communicated. Finally, we did not measure other parameters that would al-

**Table 3. Disease-Free Survival**

<table>
<thead>
<tr>
<th>Type of Transplant</th>
<th>No. of Patients*</th>
<th>Cure Without Stem Cell Transplantation, %</th>
<th>Cure With Stem Cell Transplantation, %</th>
<th>Actual Percentage With Disease-Free Survival (95% Confidence Interval)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous‡</td>
<td>94</td>
<td>20</td>
<td>7</td>
<td>70, 32 (44, 58)</td>
</tr>
<tr>
<td>Allogeneic</td>
<td>169</td>
<td>78</td>
<td>20</td>
<td>8, 80 (62, 52)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>8</td>
<td>80, 62 (52, 40)</td>
</tr>
<tr>
<td>Disease status</td>
<td></td>
<td></td>
<td>80</td>
<td>80, 62 (52, 40)</td>
</tr>
<tr>
<td>Early</td>
<td>78</td>
<td>13</td>
<td>7</td>
<td>73, 42 (32, 44)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>71</td>
<td>19</td>
<td>7</td>
<td>80, 42 (32, 44)</td>
</tr>
<tr>
<td>Advanced</td>
<td>20</td>
<td>19</td>
<td>7</td>
<td>80, 31 (10, 23)</td>
</tr>
</tbody>
</table>

*Five patients did not provide an estimate of cure without stem cell transplantation and 3 did not provide an estimate of cure with stem cell transplantation.
†At 2 years.
‡Ninety patients with intermediate and 4 patients with advanced disease.

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low us to assess whether overly optimistic expectations meaningfully affect treatment choices, are necessary to preserve hope, interfere with realistic preparations prior to transplantation, or adversely affect adjustment following transplantation. These hypotheses will be addressed in future studies.

Our findings should caution clinicians that many patients proceeding to SCT harbor quite optimistic expectations regarding anticipated survival, cure, and recovery that may not be supported by actual outcomes. How should a clinician respond to these data? One practical suggestion is that physicians try to ascertain their patients’ expectations early in the decision-making process and identify reasons for any misperceptions. To the extent that patients simply lack information, this would be an opportunity for education. If more active avoidance or denial is present, greater care may be required to ensure that these defensive mechanisms are not compromising the patient’s ability to make appropriate treatment choices and to be prepared for transplantation.

**Author Contributions:** Dr Lee participated in study concept and design, acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and provided statistical expertise. Dr Antin participated in acquisition of data, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript for important intellectual content, and supervised conduct of the study.

**Funding/Support:** This research was supported in part by National Institutes of Health grant CA75267-03 and the Amy Strelzer-Manasevit Scholars Program.

**Acknowledgment:** We thank Taiye Odedosu, BA, and Marisa Bueno, BA, for their help with study coordination, and the stem cell transplant physicians of the Dana-Farber/Partners Cancer Care for providing physician predictions. We especially wish to thank our patients for their participation.

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