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## Advance Care Planning Among Hematopoietic Cell Transplant Patients and Bereaved Caregivers

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### Abstract

Younger, healthier patients contemplating high-risk (but potentially curative) hematopoietic cell transplants (HCT) may not consider advance care planning (ACP). We investigated the effect of pre-transplant ACP in surviving HCT patients and bereaved caregivers using retrospective, audiotaped telephone surveys. Subjects were identified between 2001–2003 via databases at two high-volume HCT centers. Transcripts were coded by 2 investigators, with differences resolved by consensus. HCT survivors (n=18) were interviewed a median of 13 months after HCT for acute leukemia (7), lymphoma (5), or other (6); 50% had living wills, 72% had a formal proxy. Twelve (67%) had discussed mortality risk pre-HCT with the medical team. Of those, 92% felt their hope and perception of the medical team's truthfulness was increased or unchanged (I/U) by the conversation, while all felt clinician commitment to transplant was I/U. Bereaved caregivers (n=11) were interviewed a median of 10 months post-death (median 31 days post-HCT, range 13–152). Nine (82%) had discussed mortality risk pre-HCT with the medical team; 7 (78%) felt hope was I/U, all felt clinician commitment to transplant and truthfulness was I/U, and most felt ACP reduced burden (67%). ACP discussions with patients and caregivers pre-HCT did not affect hope and supported confidence in medical teams.

### Keywords

advance care planning; caregivers; hematopoietic stem cell transplant; survivors; qualitative research; questionnaires

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## Introduction

Advance care planning (ACP) is the process of communication between clinicians, patients and caregivers regarding the health care a patient would like to receive in the future if the patient cannot speak for him or herself.(1) While a significant amount of research has addressed ACP in cancer patients with solid tumors(2–7), less is known about ACP for patients with hematologic malignancies, and particularly those undergoing hematopoietic cell transplantation (HCT).(8–10) This paucity of ACP research in HCT populations is important because patients offered HCT are typically younger, otherwise healthy individuals, who may not have considered their own mortality or their end of life (EOL) care preferences.(9–11) However HCT patients face significant risks of morbidity and mortality for the chance of cure, which transplant represents. And while early, in-hospital mortality rates are low for autologous patients, mortality rates within the first 100 days are typically 5–30% for allogeneic recipients, depending on patient donor type (related vs unrelated), comorbidities and socio-demographics, and underlying malignancies.(12–26) By one year, non-relapse mortality rates for HCT range from approximately 10% for autologous procedures to over 70% for high-risk allogeneic transplants in patients with aggressive diseases.(27, 28) Despite this, patients prior to HCT are usually relatively healthy and would have time to consider ACP issues as they prepare to undergo HCT.

How patients with hematologic malignancies think about the risk of death associated with transplantation or their desires to engage in prospective planning for the possibility of poor outcomes, including death, from transplantation is unknown.(29–33) Based on existing ACP research in cancer patients broadly, fears and concerns about death and dying may not be addressed proactively by patients, caregivers or clinicians, despite a high risk of mortality. Indeed, research demonstrates that patients, particularly those who are at high risk of dying, are overly optimistic about the likelihood of positive outcomes.(34) Furthermore, transplant clinicians may be concerned that discussing a patient's risk of mortality or EOL care preferences in advance of the patient's clinical decline may reduce patient (and caregiver) hope and create concerns that clinicians will not “do everything” possible to cure the patient.

Given the identified barriers to ACP conversations in general cancer populations, and based on our own clinical experience caring for transplant patients, we were particularly interested in the effect that pre-transplant discussions of mortality risk and ACP might have on survivors' or caregivers': 1. confidence in the truthfulness of the medical team, 2. commitment of the medical team to “get the patient through” the transplant successfully, and 3. their personal hope that the patient would survive the transplant experience. We felt that both groups were important to study because an increased effort to encourage ACP before HCT would affect not only those who die from the procedure, but also those who survive. We hypothesized that discussions of mortality risk and ACP would not diminish survivors' or caregivers' perceptions of the truthfulness or commitment of the medical team, nor would it affect their hope that the transplant recipient would survive.

## Subjects and Methods

Research was approved by the Institutional Review Board at both participating institutions (Fred Hutchinson Cancer Research Center, Dana-Farber Cancer Institute) prior to study initiation.

### Study Sample

Potential subjects were consecutively identified via clinical databases from two high-volume, tertiary HCT centers. Once identified, permission was sought to contact the potential subject from the (prior) attending HCT physician. If permission was obtained, a trained and experienced interviewer contacted the potential subject to discuss the study and obtain consent between the years 2001–2003. Analysis and publication were delayed because of personnel changes. The enrollment goal was a total of 30 participants in each group. Both autologous and allogeneic patients and their caregivers were eligible.

Participants were adults age ≥ 21 years, English-speaking and, at the time of the survey, free of major, uncontrolled psychiatric illness. HCT survivors had to have received their transplant 6–12 months prior to the survey while decedents' transplants must have occurred 6–12 months prior to the survey and he/she must have died within 6 months following HCT. Bereaved caregivers were defined as the decedent's primary support person during the transplant.

### Survey Instrument

Surveys for this study used a mixed qualitative and quantitative format, were audio-recorded, and were designed for telephone administration. The survey for bereaved caregivers captured socio-demographics, relation of the caregiver to the decedent, and the caregiver's involvement with the decedent pre-transplant, during the transplant hospitalization, and in the final week of life. The interview began with an opportunity to describe the entire transplant experience in an open-ended fashion for both caregivers and survivors. Caregiver interviews probed for when the caregiver began to realize that the decedent might die, while survivor interviews probed if there was ever a time when the respondents thought they might die.

Fourteen items captured decedent and family member interest and comfort in discussing ACP issues; the effects of such discussions on their perceptions of trust in and commitment of the medical team; and their personal perception of hope. Other topics included overall distress in the bereavement period and after-death contact by medical staff. These items were developed specifically for this telephone interview as no validated questions were available at the time of study initiation. Questions addressing the primary goals of the study are listed in Table 1 and included hypothetical versions of questions if caregivers (or survivors) did not report discussing the possibility of death during the pre-transplant period. The “medical team” was defined as “the doctors, nurses, social workers, and other medical personnel involved in your care.”

Additional items for the bereaved caregiver survey were adapted from the After-Death Bereaved Family Member Interview (35, 36) and the Edmonton Symptom Assessment

Scale.(37) The former questions addressed the decedents' last week of life, focusing on symptoms, care, physician communication, care coordination, and the caregiver's ratings of these aspects of care. Surveys for transplant survivors were adapted from the caregiver survey, using the patient perspective.

## Analysis

Analysis of the quantitative components of the surveys included counts and percentages. Surveys were audio-recorded and transcribed. After reviewing a small sample of survivor and caregiver transcripts, two investigators developed a code list/book (KC, SL) using a consensus process. The remaining transcripts were then coded by 2 investigators (KC, ETL), with differences resolved by consensus.

## Results

### Survivors Quantitative results

Of the potential survivors identified, no HCT physicians refused permission to contact the survivor. Of those approached: 18 participated (64%), 6 couldn't be contacted (21%), 3 refused (11%) and 1 was ineligible (unknown reason) (4%) (N=28 total). No information is available regarding the 3 individuals who refused to participate.

Survivor participants were a median of 47 years old, female, married, Christian, well-educated and diagnosed with leukemia or lymphoma (see Table 2). All patients reported their race or ethnicity as non-Hispanic white. Fourteen (78%) rated their current health as good or better. Sixteen (89%) survivors were comfortable or very comfortable with the survey questions and 78% reported no stress associated with the interview.

Overall, 50% (n=9) of survivors had living wills and 72% (n=13) had a formally designated proxy. All but one had discussed some aspect of ACP (living will, durable power of attorney for health care, or EOL care preferences like resuscitation or ventilation) either with family or friends prior to transplant. However, only 9 (50%) survivors had discussed their EOL care preferences with their formal proxy. Survivors' perceptions of the value of ACP were generally positive. Of those who had previously discussed any aspect of ACP, 14 (78%) felt that it relieved them of worry and reduced the burden on their family, and all but one survivor would recommend ACP to someone undergoing HCT.

Twelve survivors (67%) reported discussing their mortality risk with the medical team pre-transplantation. Of these, 11 (92%) felt hope was increased or unchanged (I/U) by this discussion (one individual felt hope was decreased). All felt clinician commitment to transplant and truthfulness was I/U, except one survivor who couldn't remember the effect of the conversation. Among the 6 survivors (33%) who had not discussed their mortality risk pre-transplant, all felt that it would not have affected their perception of the team's commitment or truthfulness and 4 (67%) felt that it would not have affected their hope. Four of the 6 who had not discussed prognosis pre-transplant either didn't know or would not have wanted the medical team to discuss their risk of death pre-transplant.

Of note, there was no discernable relationship between those who reported having discussions of their mortality risk (either with the medical team or with their family) and their reports of having had a living will or proxy. In fact only 5 of 12 (42%) who reported discussing mortality risk with the medical team reported having both a living will and a formal proxy, while 3 of 6 (50%) of those who reported not having a conversation about their risk of mortality had both. Similarly of those who reported talking with their family about the possibility of dying during the transplant, half found this upsetting -- while half did not -- and none of those who had *not* had this conversation were upset by the absence of the conversation.

### Survivors: Qualitative results

A common theme articulated by survivors (n=11) was the lack of choice in receiving a transplant given their grim prognosis and lack of other treatment options. For example, one survivor said, “And I know to someone who is healthy and never had to deal with that, that’s a scary thing. But when you’re thinking, ‘Am I going to be dead in two months or am I going to be dead in three years?’ well, three years sounds pretty good.” Another stated, “And I got a team of doctors, and they sat down with me and explained to me what the situation was. And really I had no decision to make. It was either go for the transplant or ... I would have been dead.”

However many survivors also reported not understanding or not being told the truth regarding their prognosis (n=8). Of these, many questioned whether their lack of recollection of prognostic conversations was related to denial or the stress of the situation (i.e. an inability to take it all in) in conjunction with a lack of communication (see Table 3, quotation #1, for an example quote from one survivor). Six articulated the need to “stay positive” or “ignorance is bliss” as a method of coping (see Table 3, quotations #2 and 3, for example quotations from two survivors). In contrast, 7 (39%) wished mortality risks had been impressed upon them more vigorously and 4 would have wanted better preparation for complications, post-transplant quality of life, or to have been given other treatment options. Two survivors actively regretted the decision to have a transplant.

### Bereaved Caregivers: Quantitative results

Of the identified potential bereaved caregivers, 3 HCT physicians refused permission to contact the bereaved caregiver (reasons unknown). Of those approached for participation: 11 participated (28%), 13 couldn't be contacted (33%), 5 refused (13), 2 were ineligible (reasons unknown) (5%) and 5 did not complete surveys (unknown reasons) (13%) (N=39 total). No information is available regarding the 13 bereaved caregivers who were potentially eligible but were not contacted or did not participate.

Bereaved caregivers were a median of 48 years old, female, and well-educated (see Table 4). All caregivers reported their race/ethnicity as non-Hispanic white. The majority were the spouse of the decedent (73%) and had known the decedent for a median of 23 years. All of the bereaved caregivers were the decedent's proxy, had attended most or all of the clinic visits (82%), and were involved “always” or “a lot” (63%) in medical decision-making. Decedents were more frequently older, male and diagnosed with myelodysplastic syndrome

than survivors in this study (see Table 5). Most decedents died within 1–2 months of transplantation. All bereaved caregivers reported being comfortable or very comfortable with survey questions; 55% reported little or no stress associated with the interview.

Six (55%) decedents had a living will prior to death, and all but one had a formally designated proxy per their bereaved caregivers. Nine bereaved caregivers and decedents (82%) had discussed the possibility of the decedent's death pre-transplant. Of those, 6 caregivers found this discussion “a lot” upsetting, while 2 did not, and 3 were unsure or refused to answer. Of the 2 caregivers who had not had a conversation with the decedent, both found the absence of a conversation “a lot” upsetting. Seven (78%) had discussed with the decedent their EOL preferences with respect to ventilation and 6 had discussed preferences for cardiopulmonary resuscitation. Most caregivers (82%) felt ACP reduced caregiver burden “a lot” (n=7) or “a little” (n=2). However caregivers were less positive about ACP's effect on worry (n=8 [73%], of which 5 reporting only “a little” reduction in worry).

Nine bereaved caregivers (82%) had discussed mortality risk pre-transplant with the medical team. Of these, 7 (78%) felt their hope that the decedent would make it through the transplant was I/U; two felt their hope was decreased. All felt clinician commitment to successful transplantation and truthfulness was I/U by this discussion. For the two bereaved caregivers that had not discussed pre-transplant prognosis, both felt that their hope would have been decreased but would have wanted to discuss the risk anyway. Both also felt their perception of the medical team's commitment to getting the decedent through the transplant and their truthfulness would have been I/U. Consistent with the survivor surveys, there was no consistent pattern in the relationship between prognostic conversations and the occurrence of ACP conversations or documents.

### **Bereaved Caregivers: Qualitative results**

Caregivers expressed the rush to transplant and the perceived inevitability of the intervention in light of the severity of the illness/lack of treatment options. Four caregivers expressed appreciation for “the straight story” while 6 wished to have been better prepared for death or complications (see Table 6, quotation #1, for an example quote from one bereaved caregiver). However, also like survivors, many caregivers expressed the need to stay positive (see Table 6, quotation #2, for an example quote from one bereaved caregiver).

## **Discussion**

This study investigated the relationship between pre-transplant prognostic or ACP conversations and patient or caregiver hopes, perceptions of clinician truthfulness and commitment to curative cancer care. Our results suggest that in the large majority of cases, prognostic and ACP discussions do not negatively affect patient or caregiver hopes or their perception of the medical team. In fact, most HCT survivors and bereaved caregivers appreciate pre-transplant discussions of mortality risk and view ACP as having positive effects on personal worry and family burden. All bereaved caregivers who had *not* had these conversations, wished they had, and 83% of survivors would recommend ACP to others preparing for transplantation.



However, a small but important minority of HCT survivors (22%) expressed a preference not to discuss prognosis or participate in ACP conversations pre-transplantation, even with the benefit of hindsight. The reluctance to dwell on prognosis in the pre-transplant period appears to be related to the need to stay positive as a mechanism of coping with a dire prognosis. This coping style, coupled with incomplete or inaccurate prognostic information and an inability of patients to imagine peri-transplant complications or post-transplant life, may engender limited or poor ACP -- a dynamic that should be studied in more detail in future studies. Practically, clinicians may find that asking permission of patients and caregivers to engage in ACP discussions may be a helpful method to identify this important minority, a technique also recommended for "breaking bad news."<sup>(38)</sup>

This current study does have limitations. First, it represents a relatively small number of subjects recruited from two institutions. However, the qualitative analysis suggested saturation of themes (i.e. very few additional themes were identified over time) even with the current sample size. The survey instrument performed well in both survivor and caregiver samples and will require only minor refinements prior to use in further studies. While only two institutions were included, they represent high-volume centers in geographically distant settings (Seattle, WA and Boston, MA). Subjects were predominantly non-Hispanic white; however the majority of transplant recipients are of this background. <sup>(39)</sup> Further research should consider differences by racial and ethnic status. Another limitation is the requirement to obtain transplant physician permission prior to contacting the patient or caregiver, a practice which may alter the representativeness of the sample in unknown ways. However this is a common study requirement and was viewed as necessary to ensure successful study conduct and to reduce the risk of harm to participants. Future studies should identify more clearly with whom the ACP conversations are occurring, allowing greater clarity around the effect of each medical team member's (and the number of) conversations. Doing so might also allow for investigation of how patient and/or caregiver attitudes toward ACP differ by the skill or experience level of the clinician introducing the topic. Also while the data were collected several years ago, there have not been revolutionary changes in communication approaches to suggest prognostic or ACP conversations have changed in this period of time. Finally, the retrospective nature of the study may introduce recall bias and limits our ability to verify discussions of mortality risk or ACP.

Despite these limitations, our results represent an important contribution to what is known about ACP for HCT patients and their caregivers. ACP that includes prognostic discussions enhance patient choice and provides information that is critical to informed decision-making. Furthermore, it is acceptable to most surviving patients and helpful to all bereaved caregivers without adverse effects. Future research should investigate the effect of a prospective intervention to increase ACP on decedent and caregiver preparedness to make end of life decisions as well as survivor and caregiver (bereaved and non-bereaved) outcomes- with the caveat that such a study should pay careful attention to the small, but important subpopulation of patients and caregivers who are reluctant to engage in prognostic and ACP conversations.<sup>(11)</sup> A better understanding of how such conversations may affect this subgroup's perceptions of the transplantation experience and their eventual outcomes will better inform the science of EOL decision making.

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**Table 1**

The primary study questions as asked of bereaved caregivers.

1. <i>“When the medical team discussed the possibility that (patient) could die during the transplant, did this increase or decrease your hope that (patient) would make it through the transplant?”</i>
2. <i>“When the medical team discussed the possibility that (patient) could die during the transplant, did these discussions increase or decrease your confidence that the medical team would be truthful with you?”</i>
3. <i>“When the medical team discussed the possibility that (patient) could die during the transplant, did these discussions increase or decrease your confidence that the medical team was fully committed to getting (patient) through the transplant?”</i>

Response options for all questions included: increased, did not change, decreased, do not remember and does not wish to answer.

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**Table 2**

Characteristics of hematopoietic cell transplant survivors and bereaved caregivers.

Characteristics	Survivors (N=18)		Bereaved Caregivers (N=11)	
	n	%	n	%
<b>Age at interview</b> (years; median, range)	47	33–67	48	37–65
<b>Gender (n, %)</b>				
Women	10	56%	9	82%
<b>Race/ethnicity</b>				
Non-Hispanic, white	18	100%	11	100%
<b>Marital status (n, %)</b>				
Single, never married	1	6%		
Married	13	72%		
Divorced or separated	4	22%		
<b>Education (n, %)</b>				
College or greater	9	50%	7	64%
<b>Religion (n, %)</b>				
Christian: Protestant, other	5	28%		
Christian: Catholic	10	56%		
None	1	6%		
Unknown	2	11%		
<b>Diagnosis (n, %)</b>				
Acute Myeloid Leukemia	6	33%		
Acute Lymphoblastic Leukemia	1	6%		
Lymphoma	5	28%		
Multiple Myeloma	3	17%		
Chronic Myelogenous Leukemia	2	11%		
Unknown	1	6%		
<b>Time from transplant to interview</b> (months; median, range)	13	8–24	10	6–12

**Table 3**

Example quotations from HCT survivors regarding the difficulty of retaining prognostic information and the “need to stay positive” in the peri-transplant period.

Example survivor quote #1: <i>“I felt from the way he explained...I had a really good chance of making it through. You know, I think it may be one of those situations where I may have blocked out some things, because I know I did that...And I know that I think just as a self-preservation thing, I just shut it out.”</i>
Example survivor quote #2: <i>“I don't do any reading on it. I just don't. Because, the first time I did, I read some stuff that threw some doubt my way, and I can't afford to have any doubt. It's one clear picture, one goal, one outcome is the only acceptable thing in this situation. Nothing else is acceptable, so I can't allow anything else to filter into me that might throw doubt in my mind.”</i>
Example survivor quote #3 (Survivor reported never discussing prognosis): <i>“Never brought up. Never spoken. Always positive.”</i> Interviewer asked, “And is that what you wanted with them (doctors)?” Survivor responded, <i>“That's what I wanted. When I walked into (facility), and I spoke to my leukemia doctor, he turned to me and said, “We want to cure you,” and I believed him.”</i>

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**Table 4**

Relationship of bereaved caregivers to hematopoietic cell transplantation decedents.

<b>Bereaved Caregiver Characteristics (N=11)</b>		
<b>Length of caregiver relationship</b> (years; median, range)	23	8–50
<b>Relationship to decedent</b>		
Spouse	8	73%
Parent	2	18%
Sibling	1	9%
<b>Clinic visits attended with decedent</b>		
Some	2	18%
Most	2	18%
All	7	64%
<b>Caregiver involvement in medical decision-making</b>		
Not at all	1	9%
Some	3	27%
A lot	1	9%
Always	6	54%
<b>Time in hospital during decedent's last week of life</b> (days; median, range)	7	2–7



**Table 5**

Characteristics of hematopoietic cell transplantation decedents.

<b>Decedent Characteristics (N=11)</b>		
<b>Decedent age at death</b>	56	22.08–57.66
<b>Decedent gender</b>		
Women	5	45%
<b>Decedent marital status</b>		
Single, never married	2	18%
Married	8	73%
Divorced	1	9%
<b>Decedent religion</b>		
Protestant	3	18%
Catholic	5	45%
Jewish	1	9%
Other or unknown	1	9%
Unknown		
<b>Decedent diagnosis</b>		
Lymphoma	4	36%
Myelodysplastic syndrome	4	36%
Acute Myeloid Leukemia	1	9%
Acute Lymphoblastic Leukemia	1	9%
Essential Thrombocythemia	1	9%
<b>Days between transplantation and death (days; median, range)</b>	31	13–152

**Table 6**

Example quotations from bereaved caregivers regarding the lack of preparation for the decedent's hematopoietic cell transplantation experience and the need to “stay positive” in the peri-transplant period.

Example bereaved caregiver quote #1: *“I didn't feel as well prepared as I could have been for what the picture was going to look like once he was in there. You know, I mean I knew he was going to get really sick.... if he (doctor) had said listen, this is huge thing, like this is no small thing that we are going to do to you. There is a decent chance that you will die while you are here – that you won't even make it out of here. And that you know we're going to show you a movie of someone actually going through... the post high dose chemo and radiation and transplant -- you know like their worst state and this is what it will look like.”*

Example bereaved caregiver quote #2: *“No doubt in anybody's mind what the risks were. They were very well explained to us. Explained to us very graphically, over and over, you know many different times from different people. So I mean we knew what the risks were but I think we were just focusing on positive, positive. This is what we had to do.”*

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