

Advance Care Planning in Patients Undergoing Hematopoietic Cell Transplantation

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ABSTRACT

Few data are available on the prevalence of advance care planning (ACP) in patients undergoing hematopoietic cell transplantation (HCT). We surveyed adult patients pre-HCT to ascertain completion of various elements of ACP. We also reviewed medical records for documentation of discussions regarding ACP and for the presence of written advance directives. Evaluable surveys were returned by 155 of 335 patients (46%) who underwent HCT during the study period; we obtained permission for medical record review from 137 of these 155 survey respondents (88%). We found that 69% of the respondents reported having designated a health care proxy, 44% had completed a living will, 61% had prepared an estate will, and 63% had discussed their wishes regarding life support with family and friends. In contrast, only 16% had discussed their wishes regarding life support with their clinicians. Documentation of discussions between clinicians and patients regarding most elements of ACP was rare. Written advance directives were present in the charts of 54 patients (39%). ACP was more common in older, college-educated, and allogeneic transplant patients. Even though ACP was more prevalent among this sample than in the general population, its use still could be enhanced, given the high risks of decisional incapacity and death that HCT patients face.

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KEY WORDS

Advance care planning • advance directives • living will • health care proxy • end-of-life care • hematopoietic cell transplantation

INTRODUCTION

Hematopoietic cell transplantation (HCT) is a therapeutic option for patients with various life-threatening malignant and nonmalignant disorders of the lymphohematopoietic system. For many such conditions, HCT offers the only possibility of long-term survival. However, HCT involves high risks of short- and intermediate-term mortality and morbidity, primarily from direct toxic effects of conditioning regimens, infectious complications, and acute and chronic graft-versus-host disease (GVHD). In adults undergoing HCT, mortality within the first 100 days after transplantation varies from 7% to 47%, depending on clinical and other factors [1]. Mortality from recurrence of underlying disease is also high.

Given the substantial risks of life-threatening

short- and intermediate-term complications, advance care planning (ACP) is especially relevant for patients considering HCT [2]. Elements of ACP might include designation of a health care proxy, completion of a living will, preparation of an estate will, and conversations with loved ones and health care providers about the patient's wishes in various circumstances. Beyond the substantial risks from both underlying disease and its treatment, several factors might be expected to foster high levels of ACP in patients considering HCT. These include the elective nature of the procedure (typically, weeks to months elapse between initial consideration of and admission for HCT); the predictability of potentially fatal post-HCT complications, which are generally associated with loss of decision making capacity due to critical illness; and the fact that many patients undergoing

HCT have lived with life-threatening illness for months or years.

Despite these grounds for advocating ACP before HCT, some patients might prefer not to undertake preparations for or discuss end-of-life contingencies. In particular, for most patients considering HCT, the procedure represents a last hope for long-term survival. Patients who decide to undergo the procedure may have strong psychological motivations to avoid dwelling on the substantial risks. In addition, living wills are problematic instruments for extending patients' autonomy to times of decision making incapacity, although their deficiencies are mitigated somewhat when complications are predictable [3]. Furthermore, patients and clinicians might not view formal designation of a health care proxy as essential if a patient's preferred proxy (eg, spouse) already receives priority under state laws regarding surrogate decision making for medical care. Similarly, patients may view estate wills as superfluous if their wishes regarding distribution of assets are consistent with state intestacy laws, which establish rules for distributing the assets of individuals who die without valid wills.

Few systematic data are available regarding ACP in patients undergoing HCT [4]. Consequently, we explored the prevalence and correlates of ACP as defined both by self-report and by review of documentation available in hospital charts.

METHODS

Study Population

The data presented here derive from a longitudinal quality-of-life survey study in adult patients undergoing HCT in the Dana-Farber Cancer Institute/Brigham and Women's Hospital (DFCI/BWH) program. All patients who underwent transplantation between July 30, 2001 and June 3, 2003 ($n = 335$) were eligible for inclusion in this analysis. (Accrual was interrupted between August 2, 2002 and February 10, 2003, however, to permit recruitment for a separate pilot study of psychosocial screening [5].)

We characterized disease status at the time of study enrollment into 3 prognostic groups based on risk of death by 1 year. Good-risk patients were those with acute leukemia in first complete remission, stable-phase chronic myeloid leukemia, early myelodysplastic syndrome (ie, refractory anemia with or without ringed sideroblasts), or aplastic anemia. Poor-risk patients were those in relapse or with refractory disease. All other patients were considered intermediate risk.

Patients considering HCT were generally seen by a single attending physician during their evaluation and preparation for transplantation. Evaluation by a

social worker was variable and sometimes occurred only after a patient was admitted for HCT unless a physician or nurse raised psychosocial concerns. Before or at the time of their first visit, patients received a binder with general information about HCT, which included a section on ACP.

The specific conditioning regimen and graft manipulation, if any, was according to protocol requirements or physician and patient preference. Conditioning regimens typically involved cyclophosphamide, carmustine, and etoposide for autologous transplants for lymphoma; melphalan for multiple myeloma; total body irradiation plus cyclophosphamide for myeloablative allogeneic transplants; and fludarabine plus busulfan for nonmyeloblastic allogeneic transplants. GVHD prophylaxis typically involved either T-cell depletion or calcineurin inhibitors, with additional agents (eg, steroids, mycophenolate, sirolimus, methotrexate) determined by protocol requirements. Details of the transplantation regimens and GVHD prophylaxis are described elsewhere [6-10].

Survey Methods

The study was approved by the DFCI Institutional Review Board (IRB). Surveys, along with self-addressed stamped return envelopes, were included in clinical information packets mailed to patients after the decision was made to proceed with HCT but before hospital admission for transplantation. These packets also contained patient schedules and information about the admission process and the hospital, but did not contain information about ACP. As approved by the IRB, return of the survey constituted evidence of informed consent; there were no explicit consent discussions regarding this study between physicians or study staff and eligible patients.

A total of 160 patients (48%) returned the survey. Of these, 5 were inevaluable due to missing responses to all 5 questions related to ACP. Thus, of the 335 patients who underwent transplantation during the study period, 155 (46%) were included in the present analysis.

Survey Instrument

The survey instrument is a 189-item questionnaire addressing quality of life, functional status, mental and physical health, expectations about prognosis and toxicity, treatment decision making, steps taken to prepare for transplantation, and demographic information. Data from an earlier version of the survey, along with a description of its development, have been published previously [11,12].

The major survey-based outcome variables for the present analysis were patients' responses to 5 questions about preparation for HCT:

1. Have you designated a health care proxy (someone to make medical decisions on your behalf)?
2. Have you prepared a will?
3. Have you completed a living will?
4. Have you discussed your wishes regarding life support with your family or friends?
5. Have you discussed your wishes regarding life support with your doctor or nurse?

Completion of these 5 actions was rated as important by more than 70% of participants in a national survey on end-of-life care [13] and provides objective data on behavioral preparations for life-threatening illness. Response options included “no,” “no, but plan to,” and “yes.”

Medical Records Review

For the present analysis, we sought separate written consent from living survey respondents to review their hospital charts. The IRB did not require permission from next-of-kin to review charts of deceased patients. Eighteen survey respondents denied or did not respond to our request for permission to review their medical records; thus, we reviewed the records of 137 respondents (88%).

We developed a standardized abstraction form to facilitate systematic chart review. Charts were abstracted by a trained research assistant, with key elements related to ACP (eg, documentation of discussions between clinicians and patients, presence of written advance directives) reabstracted by a second research assistant to increase sensitivity. Because patients received their outpatient care at DFCI and their inpatient care at BWH, we abstracted both clinic and hospital charts for each patient. Review of the clinic chart encompassed all physician, nurse, and psychosocial visits occurring during the 4-month period before the date of admission for transplantation. If a patient had fewer than 3 visits during the 4 months before admission, the review period was extended to include at least 3 visits, if possible. Review of the hospital chart encompassed attending physician, resident, fellow, nursing, and psychosocial clinician admitting notes only; later notes during the index hospitalization or during subsequent admissions were not reviewed. Relevant discussions were noted and classified as addressing 1 or more of 8 prespecified subjects related to ACP (possibility of dying from transplant complications, possibility of losing decision making capacity, wishes if seriously ill and incapacitated, discussion with family or friends about patient’s wishes, who should speak for the patient if incapacitated, completion of an advance directive, completion of an estate will, and do-not-resuscitate orders). We also recorded the presence of written advance directives in patients’ charts. DFCI policy in force at the time required that copies of advance directives be placed in

the medical record, but did not require documentation of discussions regarding ACP. In contrast, BWH policy required that attending physicians, house staff, and admitting nurses explain to patients the purpose and uses of advance directives and document the existence and substance of advance directives and the nature of patients’ wishes in the hospital admission notes.

Statistical Analysis

Using descriptive statistics, we report patients’ survey responses regarding ACP, the proportions of patients with documentation of discussions about ACP in the outpatient and inpatient medical records, and the proportion of patients with written advance directives in their medical records. To examine predictors of the intensity of ACP, we created a composite dependent variable by summing the responses to the 5 survey questions about ACP. For each question, a “no” response was assigned 0 points, “no, but plan to” was assigned 1 point, and “yes” was assigned 2 points. The resulting summary score could range from 0 (no elements of ACP completed) to 10 (all elements completed). This summary scale had high internal reliability (Cronbach’s $\alpha = 0.76$). Because of the ambiguity of “no, but plan to,” we also created an alternative composite score in which this response was assigned 0 points. Results using this alternative endpoint were similar and are not reported here.

We constructed an ordinary least squares linear regression model that included demographic, clinical, and other variables as candidate predictors of the ACP summary score. Variables included in the initial model included age, sex, college education, marital status, presence of children, income, transplant risk group, type of transplant (allogeneic vs autologous), patients’ and physicians’ estimates of 1-year treatment-related mortality (from the patient survey and an accompanying physician survey) [11], mental and physical composite score from the Medical Outcomes Study Short-Form 12 (SF12) [14], and Eastern Cooperative Oncology Group (ECOG) performance status [15]. Ordinal independent variables were dichotomized at as close to the sample median as permitted by the data. Using backward stepwise elimination, we sequentially removed from the model independent variables that were not associated with the summary score at $P < .05$. Because we viewed the analysis as hypothesis-generating, we did not adjust for multiple comparisons.

In our second analysis, we examined factors associated with the presence of an advance-care directive, dated on or before the date of transplantation, in either the clinic or hospital chart. A patient was considered to have an advance directive if we found a health care proxy form, a living will, or both in the chart. We constructed a logistic regression model that

Table 1. Demographic and Clinical Characteristics of Respondents (*n* = 155)

Characteristic	Respondents		Nonrespondents		P Value
	Number	Percent	Number	Percent	
Age at transplantation, mean (SD)	48.5 (11.8)		46.5 (12.0)		.12
Female	66	43%	73	41%	.71
Nonwhite race	5*	3%	20	11%	.006
Married/living as married†	119	77%	N/A		–
College degree	90	58%	N/A		–
Household income ≥\$50,000/year	100	67%	N/A		–
Has at least 1 child	126	81%	N/A		–
Allogeneic transplant	109	70%	110	61%	.09
Risk group					
Low	24	15%	17	9%	.07
Intermediate	108	70%	122	68%	
High	23	15%	41	23%	
Symptomatic (ECOG performance status ≥1)	101	65%	N/A		–
Days between survey completion and HCT, median (IQR)	20 (6-34)		N/A		–

SD, standard deviation; N/A, not available; IQR, interquartile range.

*Includes African-American (*n* = 3), Hispanic/Latino (*n* = 1), and Asian-American (*n* = 1) patients.

†Data on marital status, education, income, number of children, and self-reported performance status were not available for patients who did not return the baseline survey and could not be obtained by other means.

included the candidate predictor variables listed earlier, then sequentially eliminated variables from the model that did not achieve $P < .05$. As before, we made no adjustment for multiple comparisons.

All analyses were conducted using Stata 8 software (Stata Corp, College Station, TX).

RESULTS

Study Participants

Table 1 lists demographic and clinical characteristics of the survey respondents and nonrespondents. The mean age was 48.5 years, and almost half were female. Most were white, college-educated, married or living as married, had household incomes of at least \$50,000 per year, and had at least 1 child. Clinically, most were undergoing allogeneic transplantation, were in the intermediate-risk group, and were symptomatic from their disease or its treatment. Respondents completed surveys a median of 20 days before the date of HCT.

Nonrespondents and respondents were of similar age and sex, but nonrespondents were more likely to

be nonwhite (11% vs 3%; $P = .006$). Nonrespondents were slightly more likely than respondents to be in the high-risk group and to be undergoing autologous rather than allogeneic transplantation, though these differences did not achieve statistical significance. Respondents and nonrespondents had similar survival experiences ($P = .65$; log-rank test).

Self-Report of ACP

Most respondents (69%) reported having designated a health care proxy, and 61% reported having prepared an estate will (Table 2). Fewer (44%) reported having completed a living will. Of the 148 patients for whom data were available, 28% had neither a health care proxy nor a living will. Although most (63%) reported having discussed their wishes regarding life support with family or friends before admission for HCT, only 16% reported having discussed these wishes with their doctor or nurse. Among those who had not discussed their wishes with their doctor or nurse, only 42% reported planning to do so.

The mean ACP score among respondents was 5.9 (standard deviation, ± 3.0 ; range, 0–10). Older age,

Table 2. Self-Report of ACP Among Patients Undergoing HCT (*n*=155)

Have You...*†	Yes Number (Percent)	No, But Plan to Number (Percent)	No Number (Percent)
Designated a health care proxy (someone to make medical decisions on your behalf)?	106 (69)	20 (13)	27 (18)
Discussed your wishes regarding life support with your family or friends?	98 (63)	25 (16)	32 (21)
Prepared a will?	94 (61)	12 (8)	49 (32)
Completed a living will?	66 (44)	16 (11)	69 (46)
Discussed your wishes regarding life support with your doctor or nurse?	24 (16)	54 (35)	76 (49)

*“Please tell us if you have done any of the following in preparation for your transplant.”

†Totals may not add to 155 due to missing responses to individual questions.

Table 3. Correlates of Self-Reported ACP and a Pretransplantation Advance Directive in the Hospital Chart Inpatients Undergoing HCT

Patient Characteristic	Self-Reported ACP Score*			Pretransplantation Advance Directive Available in the Hospital Chart†		
	Increment‡	95% Confidence Interval	P Value	Odds Ratio	95% Confidence Interval	P Value
Age, per decade	1.2	0.9-1.6	<.001	1.9	1.3-2.7	<.001
College education	1.1	0.3-2.0	.01	—		
Allogeneic transplantation	1.3	0.3-2.2	.008	—		

*Independent variables that were not significantly associated with higher planning scores at $P < .05$ in the linear regression model included sex, marital status, presence of children, household income greater than the sample median, transplantation risk group, patient estimate of likelihood of treatment-related mortality (TRM), physician estimate of TRM, mental composite score of the SF12, physical composite score of the SF12, and ECOG performance status. R^2 of the final model = 0.28.

†Independent variables that were not significantly associated with presence of an advance directive in the hospital chart at $P < .05$ in the logistic regression model included sex, college education, marital status, presence of children, household income greater than the sample median, type of transplant, transplantation risk group, patient estimate of likelihood of TRM, physician estimate of TRM, mental composite score of the SF12, physical composite score of the SF12, and ECOG performance status.

‡Absolute increment in planning score (ie, beta coefficient) associated with a 1-unit increase in the independent variable.

college education, and allogeneic transplantation were associated with greater intensity of ACP in the multivariate model (Table 3). These 3 factors jointly explained more than 1/4 of the variance in ACP scores ($R^2 = .28$; model $P < .0001$). The association between age and most elements of ACP was especially strong (Figure 1).

Documentation of ACP in the Medical Record

Among the 8 elements of ACP that we abstracted from patients’ medical records, discussions about the possibility of dying from transplantation-related complications were documented in either the clinic or the

hospital charts of 82 patients (60%), and discussions about advance directives were documented in the charts of 61 patients (45%) (Table 4). In 45/61 cases, documentation of discussions about advance directives was limited to completion of relevant fields in the preprinted inpatient nursing intake form. Documentation regarding do-not-resuscitate orders was present in the charts of 25 patients (18%); in 22 of 25 cases, this documentation was limited to a statement about “code status” in the resident’s admission note. Documentation of discussions about each of the other 5 elements of ACP was present in < 6% of charts.

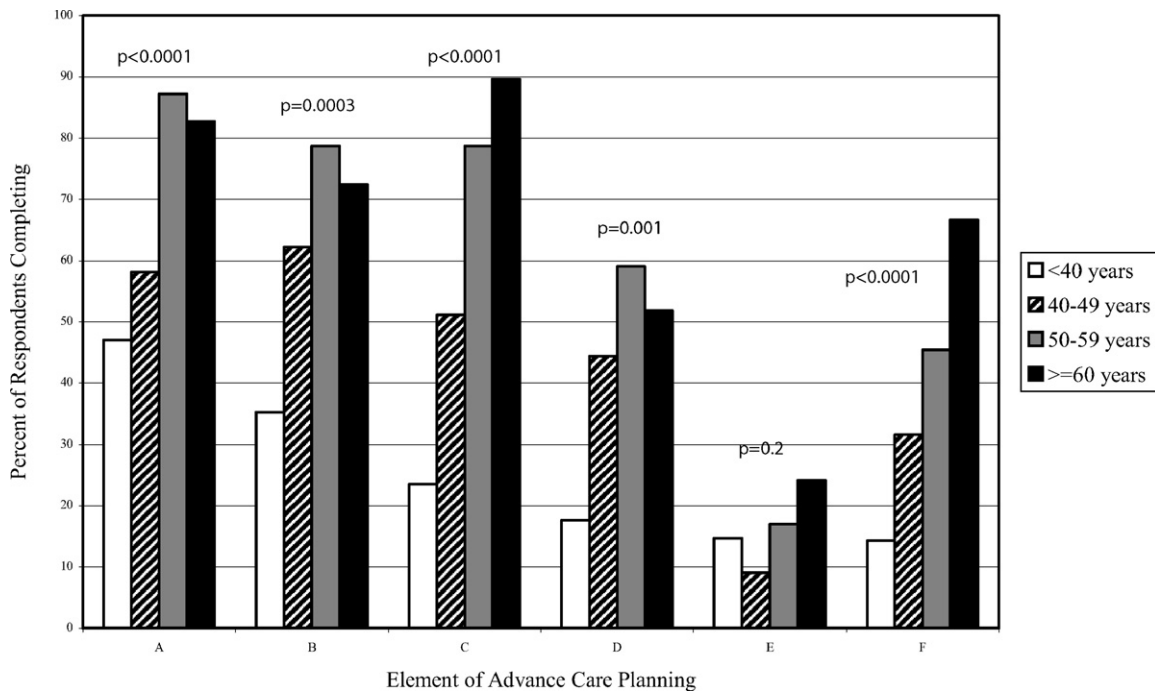


Figure 1. Completion of elements of ACP, by age group. A, designating a health care proxy; B, discussing one’s wishes with loved ones; C, completing an estate will; D, completing a living will; E, discussing one’s wishes with physician or nurse; F, copy of written advance directive available in clinic or inpatient chart. P values are computed using Wilcoxon rank-sum tests.

Table 4. Prevalence of Advance Care Discussions and Written Advance Directives Among Patients Planning to Undergo HCT, as Documented in the Medical Record ($n = 137$)

Documentation of Discussion*	Number	Percent
Possibility of dying from transplantation-related complications	82	60%
Completion of an advance directive	61†	45%
Do-not-resuscitate order	25‡	18%
Person who should speak for the patient if incapacitated	8	6%
Discussion with family or friends about patient's wishes if incapacitated	5	4%
Patient's wishes if seriously ill and incapacitated	3	2%
Possibility of losing decision-making capacity	0	0%
Completion of an estate will	0	0%
Written advance directive present§		
Any advance directive	54	39%
Health care proxy or durable power of attorney	54	39%
Living will	30	22%

*Discussion documented, or written advance directive located, in either clinic (DFCI) or inpatient (BWH) chart.

†45 of 61 instances of documentation about advance directives reflected completion of relevant fields in the preprinted nursing hospital intake forms.

‡22 of 25 notes describing do-not-resuscitate status were resident hospital admitting notes documenting the patient's "code status."

§Limited to advance directives completed on or before the date of HCT.

We identified a written advance directive (ie, health care proxy and/or living will) in the clinic or hospital chart of 54 patients (39%). Advance directives were completed a median of 116 days (interquartile range, 12–522 days) before the date of transplantation. In the logistic regression model, older patients were more likely to have an advance directive in the medical record (Table 3); patients under age 40 rarely had an advance directive (Figure 1).

We noted a statistically significant but imperfect association between self-report of a health care proxy or living will and presence of an advance directive in the chart. Of the 104 patients who reported designating a proxy or completing a living will, 50 (48%) had an advance directive in the chart, compared with 4 of the 33 patients (12%) who reported not having completed a proxy or living will ($P < .001$).

DISCUSSION

Several notable findings emerged from our analysis of self-reported and documented ACP among adult patients undergoing HCT. First, even though many patients reported having engaged in various aspects of ACP, including designating a proxy, discussing their wishes with loved ones, and completing an estate will, a substantial minority had not taken these steps. Second, patient-reported and documented discussions between patients and clinicians about most elements of ACP were rare [16]. Third, although a sizeable minority of patients had written advance directives available in their hospital charts, most did not. Finally, younger patients—especially those under age 40—were much less likely than older patients to have engaged in ACP. Other factors that might be expected to predict completion of ACP, such as being married, having children, disease risk group, perceived mortal-

ity risk, and performance status or physical functioning before HCT, were not associated with ACP.

Rates of completion of written advance directives observed in the present cohort are higher than those found in most other studies, although few data from analogous settings involving seriously ill patients undergoing high-risk elective procedures are available [17]. Many studies have documented limited use of ACP in various populations, despite the fact that most patients say that they desire advance directives [18]. In the Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment (SUPPORT), which enrolled patients with a median predicted life expectancy of 6 months, 20%–24% of patients had advance directives at the time of the index hospitalization [19]. The prevalence of advance directives varies across studies, although most demonstrate completion rates comparable to or lower than those observed in SUPPORT [16,18,20–29]. Several studies suggest that the prevalence of advance directives may be higher in patients with cancer than in other groups [20,24,30,31]. Completion of advance directives and other elements of ACP also varies by race and ethnicity [25,29,30,32]. With few exceptions [28], interventions to increase the use of advance directives have shown limited success [33,34].

The data presented here suggest that many patients considering HCT neither discuss nor plan to discuss end-of-life contingencies with their clinical team. This finding might be expected if frank discussion of end-of-life contingencies threatened the hope for cure that many patients invest in HCT [11]. Among respondents who had not discussed their wishes regarding life support with their physician or nurse, most reported no plans to do so. It is unclear from these data what proportion of these patients would welcome such conversations if initiated by cli-

nicians and what proportion would prefer that no such conversations take place. Data from other studies suggest that some patients with serious illness do not wish to discuss ACP with their physicians [31,32,35]. Nevertheless, given that approximately 40% of patients will die within 1 year of HCT, clinicians arguably should routinely offer to discuss the subject, to meet the needs of patients who welcome such conversations but hesitate to initiate them [18,36].

In considering our findings, it is necessary to acknowledge the existence of skepticism about the effectiveness of ACP at achieving its intended aims. There is limited evidence that advance directives substantially alter the course of end-of-life care [20,37-39], although some studies suggest improved psychological outcomes in survivors with whom patients previously discussed their end-of-life preferences [20,40]. Proxies have also been found to be poor judges of patients' preferences regarding end-of-life decisions, although this finding may simply highlight the need for more explicit discussion between patients and proxies [30,41-44]. Consequently, Fagerlin and Schneider recently argued that living wills have not fulfilled their promise of "extend[ing] patients' exercise of autonomy beyond their span of competence" [3]. Despite these caveats, however, there is general agreement that a comprehensive approach to ACP, including the use of written advance directives as well as conversations between patients and their loved ones and clinicians, is an integral part of high-quality care for patients with life-threatening illness [45].

It is important to explicitly address the objection that formal designation of a health care proxy may be superfluous when state law regarding the priority of surrogate decision makers is consistent with patients' wishes. If this were the case, then we might expect discussions of ACP or completion of advance directives to be more common in unmarried patients, for whom the appropriate proxy is less clear, than in married patients. That we observed no such a difference argues against such targeting of ACP.

Our study has several limitations. First, the data characterize the experience of a single institution and may not reflect practices in other settings. For example, the average socioeconomic status (SES) of patients treated in the DFCL/BWH program is high; overall rates of ACP completion might be even lower in other populations that include more patients with low SES. Also, because Massachusetts does not grant statutory recognition to living wills, their use by patients in our cohort may be more limited than would be observed in other regions. However, within our cohort, Massachusetts residents were no less likely than residents of other states to complete living wills (data not shown). Second, the response rate to the survey was lower than we would have liked, even though respondents were generally similar to nonre-

spondents with respect to measured characteristics. In addition, there is no reason to suspect that the major associations that we observed—particularly the strong relationship between young age and lack of ACP—should differ in patients who did not respond. Third, the limited evidence of discussions regarding ACP found in patients' charts may reflect a lack of documentation rather than of actual discussion [16]. Finally, the survey question regarding designation of a health care proxy did not clearly distinguish between informal and written assignment, although responses to this question did strongly predict the presence of a written advance directive in the medical chart.

In conclusion, despite the many reasons favoring ACP among patients undergoing HCT, there is room for increased attention by both patients and clinicians to this issue. The lack of ACP is especially striking in younger patients. Whether missed opportunities for ACP are due to clinicians' reluctance to raise the subject or to patients' preferences not to engage in these conversations or perform the relevant actions remains unclear. More studies are needed to examine whether our observations generalize to other settings, to clarify the factors responsible for the underuse of ACP in HCT, and to correlate ACP with important outcomes. Finally, although interventions that successfully boost rates of ACP in the medical setting are elusive, our findings suggest the importance of renewed efforts to identify such interventions, particularly for patients undergoing high-risk procedures such as HCT.

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