Coping in patients with hematologic malignancies undergoing hematopoietic cell transplantation

Richard Newcomb,^{1,2} Hermioni L. Amonoo,^{2,3} Ashley M. Nelson,⁴ Joanna Choe,¹ Katherine Holmbeck,¹ Anisa Nabily,¹ Stephanie J. Lee,⁵ Thomas W. LeBlanc,⁶ and Areej El-Jawahri^{1,2}

¹Division of Hematology and Oncology, Department of Medicine, Massachusetts General Hospital, Boston, MA; ²Harvard Medical School, Boston, MA; ³Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, MA; ⁴Department of Psychiatry, Massachusetts General Hospital, Boston, MA; ⁵Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA; and ⁶Division of Hematologic Malignancies and Cellular Therapy, Department of Medicine, Duke University School of Medicine, Durham, NC

Key Points

- Coping strategies before HCT are associated with pre-HCT quality-of-life and psychological distress.
- Supportive care interventions during HCT to promote approach-oriented coping and to mitigate avoidant coping are needed.

Patients undergoing hematopoietic cell transplantation (HCT) must cope with physical and psychological symptoms. Yet, studies examining pre-HCT coping are limited. We aimed to characterize pre-HCT coping, evaluate the association of coping with baseline quality of life (QOL) and psychological distress, and identify sociodemographic factors associated with pre-HCT coping. We conducted a cross-sectional analysis of baseline data from a multisite randomized supportive care intervention trial among patients with hematologic malignancies undergoing allogeneic or autologous HCT. We assessed patient-reported QOL, psychological distress, and coping within 72 hours of admission for HCT. We used the median split method to dichotomize coping and multivariate regression analyses to characterize the association of coping with psychological distress and QOL. Of patients awaiting HCT (n = 360; mean age, 55.4 years; 49.7% autologous), 43.5% were high users of approach-oriented coping, whereas 31.3% were high users of avoidant coping. Patients reported high use of emotional support (60.9%), acceptance (51.2%), self-blame (33%), and denial (31.3%). Older age (\geq 65 years) was associated with less frequent use of avoidant coping (odds ratio, 0.5; P = .01). Approach-oriented coping was associated with better pre-HCT QOL (Beta(B) = 6.7; P = .001), and lower depression (B = -1.1; P = .001) and anxiety (B = -0.9; P = .02) symptoms. Avoidant coping was associated with worse pre-HCT QOL (B = -13.3; P < .001) and symptoms of depression (B = 1.9; P < .001), anxiety (B = 3.1; P < .001), and posttraumatic stress disorder (B = 8.1; P < .001). Pre-HCT coping is strongly associated with psychological distress and QOL. These data support the need for interventions to address coping during HCT hospitalization. This clinical trial was registered at www. clinicaltrials.gov as #NCT03641378.

The full-text version of this article contains a data supplement.

© 2024 by The American Society of Hematology. Licensed under Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0), permitting only noncommercial, nonderivative use with attribution. All other rights reserved.

Submitted 28 June 2023; accepted 9 December 2023; prepublished online on *Blood Advances* First Edition 5 January 2024; final version published online 13 March 2024. https://doi.org/10.1182/bloodadvances.2023011081.

Presented in abstract form at the 65th annual meeting of the American Society of Hematology, San Diego, CA, 8-12 December 2023.

The data that support the findings of this study are available upon reasonable request from the corresponding author, Richard Newcomb (richard.newcomb@mgh.harvard. edu).

Introduction

Hematopoietic cell transplantation (HCT) is an intensive treatment that often requires a 3- to 4-week hospitalization for conditioning chemotherapy, receipt of stem cells, recovery of blood counts, and monitoring for complications. Patients with hematologic malignancies undergoing HCT endure immense physical symptoms and must cope with significant depression and anxiety symptoms.¹⁻³ The profound symptom burden contributes to a dramatic decline in quality of life (QOL), which predicts long-term morbidity including symptoms of depression and posttraumatic stress disorder (PTSD).^{1,4,5} Heightened psychological distress before HCT augments this QOL deterioration during hospitalization, particularly in older adults undergoing HCT.⁶

Coping is critical to every aspect of the illness and the recovery experience of patients with cancer, including the challenges of diagnosis, treatment, and prognostic uncertainty.7-9 Patients may use a range of coping strategies to manage their illness experience, which can be organized into a framework of approach-oriented and avoidant coping. Approach-oriented coping strategies (eg, positive reframing, problem solving, and seeking emotional support) are cognitive-behavioral strategies patients use to directly confront stressors that commonly accompany the illness experience.¹⁰ In contrast, use of avoidant coping strategies (eg, denial, avoidance, and disengagement) involves withdrawing from the stress.¹⁰ In patients with advanced solid malignancies and acute myeloid leukemia, use of approach-oriented coping is associated with improved QOL and decreased symptoms of depression, anxiety, and PTSD, whereas avoidant coping is inversely correlated with these outcomes.^{11,12} Furthermore, approach-oriented coping moderates the effect of supportive care interventions on clinical outcomes such as QOL.^{7,13} Importantly, integrated specialty palliative care in patients with acute myeloid leukemia preserves approach-oriented coping and decreases avoidant coping, suggesting that coping strategies in patients with hematologic malignancy are modifiable.¹³ Thus, it is crucial to understand patients' use of coping strategies before HCT because hospitalization represents a time of great trepidation and distress for recipients of HCT and an opportunity for interventions to promote approachoriented coping and curb maladaptive coping.

Prior studies describing coping strategies in patients undergoing HCT, which have limitations in sample size and applicability (conducted before 2010),¹⁴⁻¹⁶ found neither associations between approach-oriented coping and pre-HCT symptoms of depression and anxiety,^{14,15} nor did they exclusively examine post-HCT coping.¹⁷ Larger and more current studies are needed to examine coping strategies before HCT. Furthermore, investigation into sociodemographic, psychosocial, and medical correlates of poor coping during early HCT hospitalization could identify patients at greatest risk of maladaptive coping and inform subsequent supportive care intervention development. For example, older HCT recipients are potentially more vulnerable to early and late complications of HCT.¹⁸⁻²¹ Coping strategies may evolve and diversify with age and could impact management of challenges associated with HCT.^{22,23} Improved understanding of the responses of older recipients of HCT to stressors is needed to better inform timely and adequate supportive care for this subpopulation.²⁴ Finally, given the role of coping in mediating benefits of supportive care interventions, identifying correlates of approach-oriented and avoidant coping in patients before HCT would be helpful in optimizing supportive care interventions throughout the care trajectory of HCT and recovery.

In this study, we sought to describe coping strategy use among patients before HCT hospitalization, identify baseline sociodemographic and clinical factors associated with coping strategies, and investigate associations of coping strategy use with psychological distress and QOL.

Methods

Study design and procedures

We conducted a secondary analysis of cross-sectional data from a multisite randomized trial of an inpatient palliative care intervention (www.clinicaltrials.gov identifier: NCT03641378) at Massachusetts General Hospital, Boston, MA; Duke University Hospital, Durham, NC; and the Fred Hutchinson Cancer Research Center, Seattle, WA from October 2018 to July 2022. The institutional review boards at all participating sites approved this study. With permission from their oncologist, we approached patients in-person within 72 hours after their admission for HCT. Study procedures were consistent across sites and during the COVID-19 pandemic.

Participants

Eligible participants were adults (aged \geq 18 years) with hematologic malignancies hospitalized to undergo allogeneic or autologous HCT. Eligibility criteria also entailed the ability to read and respond to questions and complete questionnaires in English or Spanish with assistance from an interpreter. We excluded patients undergoing HCT for classical hematologic conditions, those undergoing outpatient HCT, those with psychiatric or cognitive conditions that the transplantation clinicians believed would preclude participation in study procedures, and those who had previously seen inpatient palliative care.

Sociodemographic and clinical data

At enrollment, participants self-reported their demographic information including age, sex, education, race, ethnicity, marital status, religious beliefs, employment status, and income. Consistent with prior studies, we defined older age as \geq 65 years at the time of enrollment.^{25,26} We also collected clinical variables such as performance status, hematologic malignancy diagnosis, transplantation type, conditioning intensity, stem cell donor source, and pre-HCT disease status from the electronic health record.

Patient-reported measures

Consistent with prior studies, patients completed baseline assessments within 72 hours of admission for HCT.^{5,27} Patients' use of coping strategies was measured with the Brief COPE, a 28item questionnaire that assesses the use of 14 coping methods with 2 items for each method.²⁸ To reduce questionnaire burden for participants, we limited our assessment to 8 coping strategies previously used in other studies among patients with hematologic malignancies: use of active coping, positive reframing, acceptance, emotional support, religious coping, self-blame, denial, and behavioral disengagement.^{7,11} Scores for each scale range from 2 to 8, with higher scores indicating greater use of that coping strategies into 2 higher-order domains informed by prior literature: approach-oriented coping (ie, use of emotional support, active coping, positive reframing, and acceptance) or avoidant coping (ie, self-blame, denial, and behavioral disengagement).^{8,11,13} We reported scores for religious coping separately because it is not included in the 2 higher-order domains.

We used the 14-item Hospital Anxiety and Depression Scale (HADS) to assess depression and anxiety symptoms.²⁹ The HADS contains 2 7-item subscales that measure symptoms of depression and anxiety within the past week. Each subscale ranges from 0 to 21, with higher subscale scores indicating worse symptoms; scores >7 indicate clinically significant symptoms.

We used the PTSD checklist, civilian version (PCL-C) to assess PTSD symptoms.³⁰ The PCL-C is a 17-item self-reported measure that evaluates the severity of PTSD symptoms. Scores range from 17 to 85, with higher scores indicating worse PTSD symptoms. Scores >29 are considered clinically significant.

We assessed patient QOL with the Functional Assessment of Cancer Therapy, Bone Marrow Transplant (FACT-BMT) scale.³¹ Scores range from 0 to 148, with higher scores representing better QOL. FACT-BMT includes subscales assessing physical, functional, emotional, social well-being, and bone marrow transplantation-specific concerns during the past week.

Statistical analysis

We calculated descriptive statistics, including means or medians for continuous variables and proportions for categorical variables. As in previous studies.^{7,8,11-13} we used the median split method to dichotomize use of coping strategies in our sample, because there are no validated Brief-COPE cutoffs for low or high coping. We calculated the median scores for each of the 7 coping domains, then described the proportion of patients with a score greater than the median as "high utilizers" for each coping strategy. Patients whose score was less than, or equal to, the median, were included in the "low utilizers" group. We considered the median score (8) as the cutoff point for high utilizers for the emotional support and acceptance coping strategy use because the median scores were the same as the highest possible score (8). We similarly used the median spit method to identify high utilizers of the composite variables for approach-oriented and avoidant coping.^{11,12} Given concomitant use of approach-oriented and avoidant coping strategies, we created a categorical variable to describe overall coping. From the dichotomous variables of high use of approach-oriented and avoidant coping, we classified coping as "high use, approach-oriented only," "high use, avoidant only," "high use, approach and avoidant," and "high use, neither."

We used unadjusted logistic regression models to identify demographic and clinical variables associated with high use of approach-oriented and avoidant coping strategies. We used multivariate linear regression models to examine associations of approach-oriented and avoidant coping strategies with patientreported outcomes (QOL and symptoms of depression, anxiety, and PTSD). For all models, we adjusted for sociodemographic factors (ie, age, sex, race, ethnicity, education, relationship status, diagnosis, and time from diagnosis) associated with coping.^{8,11} Given analysis of baseline data pre-HCT and controlling for disease related factors including diagnosis and pre-HCT disease status, we did not adjust for HCT-specific variables such as conditioning intensity. Given collection of baseline data before randomization, we did not include randomization status as a covariate in regression models.

We used complete case analyses without accounting for missing data. With a low missingness rate of 1.1%, there were no observed differences in missing data by coping. We considered a 2-sided P value < .05 as statistically significant. We performed all statistical analyses using R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline characteristics

We enrolled 360 patients. Table 1 displays baseline patient characteristics. The majority of patients were male (62.8%), identified as White (77.5%), had received at least some college-level education (78.9%), and were married or living with a partner (70.6%). One-quarter (26.4%) were aged \geq 65 years. Approximately half received autologous HCT (n = 178, 49.4%). A minority (17.8%) entered HCT with refractory or untreated disease. At baseline, patients reported a mean FACT-BMT score of 107.8 (standard deviation [SD] = 19.4), mean HADS depression score of 4.4 (SD = 3.2), mean HADS anxiety score of 5.3 (SD = 3.7), and mean PCL-C (PTSD) score of 26.5 (SD = 9.4). The baseline prevalence of clinically significant baseline symptoms of depression (n = 64, 17.8%), anxiety (n = 95, 26.4%), and PTSD (n = 103, 39.6%) were notable.

Use of coping strategies

Figure 1 displays the proportion of patients scoring as high utilizers of individual coping strategies based on the median split method. Coping strategy scores had nonparametric distributions (supplemental Figure 1). Overall, 43.5% of patients identified as high utilizers of approach-oriented coping. Emotional support (60.8%) and acceptance (51.4%) had the largest proportions of patients scoring as high utilizers. Of note, the median and mode score for emotional support and acceptance was 8, which is the maximum value of the Brief-COPE measures. Overall, 31.3% of patients identified as high users of avoidant coping. Nearly one-third of patients highly used avoidant coping strategies including self-blame (33.1%) and denial (31.4%). Behavioral disengagement was infrequently used (11.9%). Finally, nearly half of patients highly used religion and spirituality (46.7%).

Use of multiple coping strategies

Figure 2 illustrates the distribution of number of highly used approach and avoidant coping strategies. Overall, most patients (62.2%) identified as high utilizers of multiple approach-oriented coping strategies. In contrast, a minority of patients (20.5%) frequently used multiple avoidant coping strategies. Only 19 (5.3%) patients highly used denial, self-blame, and behavioral disengagement. Notably, 43 (11.9%) patients identified as high utilizers of both approach-oriented and avoidant coping.

Sociodemographic and clinical factors associated with coping strategies

Education level, relationship status, employment status, pre-HCT performance status, diagnosis, time from diagnosis, transplant

 Table 1. Patient sociodemographic and clinical characteristics

Characteristic	N = 360 n (%)
Site	
Massachusetts General Hospital, Boston, MA	179 (49.7)
Duke University Hospital, Durham, NC	99 (27.5)
Fred Hutchinson Cancer Research Center, Seattle, WA	82 (22.8)
Age (y), mean (SD)	55.4 (12.5)
Female	137 (38.1)
Race	
White	278 (77.2)
African American	39 (10.8)
Asian	20 (5.6)
American Indian	7 (1.9)
Missing	16 (4.4)
Hispanic ethnicity	17 (4.7)
Relationship status	
Married or cohabitating	254 (70.6)
Noncohabitating relationship	11 (3.1)
Single, never married	42 (11.7)
Divorced or separated	35 (9.7)
Widowed	13 (3.6)
Missing	5 (1.4)
Live alone	52 (14.4)
Highest education level	
Did not complete high school	8 (2.2)
High school degree or equivalent	67 (18.6)
Some college	58 (16.1)
Associate degree	36 (10.0)
College degree	90 (25.0)
Advanced graduate degree	97 (27.0)
Missing	4 (1.1)
Employment	
Full or part-time work	143 (39.7)
Unemployed, illness or disability	105 (29.2)
Unemployed, looking for work	6 (1.7)
Unemployed, not looking for work	12 (3.3)
Student	4 (1.1)
Retired	83 (23.1)
Missing	7 (1.9)
ECOG PS	
0	176 (48.9)
1	167 (46.4)
2	7 (1.9)
Missing	10 (2.8)
Diagnosis	
Multiple myeloma	111 (30.8)
Acute leukemia (AML, ALL)	89 (24.7)
Lymphoma	88 (24.4)

Table 1 (continued)

Characteristic	N = 360 n (%)
MDS/MPN/CML	68 (18.9)
Other	4 (1.1)
Transplantation type	
Myeloablative, autologous	179 (49.7)
Myeloablative, allogeneic	119 (33.1)
Reduced intensity, allogeneic	62 (17.2)
Transplantation donor	
Autologous	179 (49.7)
Matched related	45 (12.5)
Matched unrelated	101 (28.1)
Mismatched	15 (4.2)
Cord	20 (5.6)
Disease status at HCT	
Complete response	163 (45.3)
Partial response	130 (36.1)
Refractory disease	55 (15.3)
Untreated	9 (2.5)
Missing	3 (0.8)

ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; ECOG PS, Eastern Cooperative Oncology Group performance status; MDS, myelodysplastic syndrome; MPN, myeloproliferative neoplasm.

type, and pre-HCT disease status were not associated with high use of either approach-oriented or avoidant coping. Older adults (odds ratio [OR], 0.5; P = .01) and those with income greater than \$100 000 (OR, 0.60; P = .04) were less likely to highly use avoidant coping. Female sex (OR, 1.6; P = .03) and disabled employment status (OR, 1.6; P = .04) were associated with increased likelihood of high use of avoidant coping.

Comparison of coping strategies between older and younger adults

Figure 3 displays the proportion of older and younger adults scoring as high utilizers of coping strategies. Older and younger adults similarly identified as high utilizers of approach-oriented coping strategies including emotional support (67.4% vs 58.5%; P = .12), acceptance (55.8% vs 49.8%; P = .31), active coping (42.1% vs 37.0%; P = .42), and positive reframing (36.8% vs 41.5%; P = .51). Older adults were significantly less likely to highly use self-blame (21.1% vs 37.4%; P = .005). High use of denial (25.3% vs 33.6%; P = .17) and behavioral disengagement (10.5% vs 12.5%; P = .77) were similar between older and young adults.

Association of coping strategies with QOL and psychological distress

Table 2 lists associations between approach-oriented and avoidant coping strategies and patient-reported outcomes. When controlling for baseline demographic and pre-HCT clinical factors, high use of approach-oriented coping was associated with increased baseline QOL (Beta (B) = 6.7; P = .001) and decreased symptoms Figure 1. Proportion of patients reporting high use of individual coping strategies based on median split method. Median scores for approach-oriented coping strategies: emotional support, 8; acceptance, 8; reframing, 6; and active coping, 7. Median scores for avoidant coping strategies: self-blame, 2; denial, 2; and behavioral disengagement, 2. Median score for religious coping: 5.



of depression (B = -1.1; P = .001) and anxiety (B = -0.9 P = .02). Interaction terms between high use of approach-oriented coping and clinically significant depression (B = -5.1; P = .32) and anxiety (B = 5.9; P = .14) were not associated with QOL. We did not observe a significant relationship between approach-oriented coping and PTSD symptoms (B = -1.8; P = .06). Avoidant coping was associated with decreased baseline QOL (B = -13.3; P < .001) and increased symptoms of depression (B = 1.9;

P < .001), anxiety (B = 3.1; P < .001), and PTSD (B = 8.1; P < .001). Interaction terms between high use of avoidant coping and clinically significant depression (B = -4.0; P = .38) and anxiety (B = -6.0; P = .14) were not associated with QOL.

Compared with patients with predominant profiles of avoidant coping, patients who identified as high users of both approachoriented and avoidant coping reported higher baseline QOL



Figure 2. Distribution of number of highly used approach-oriented and avoidant coping strategies.

The graphic displays the distribution of the number of highly used approach-oriented (top panel) and avoidant (bottom panel) coping strategies. High use of a coping strategy was calculated using the median split method and independently summed across approach-oriented and avoidant coping strategies to generate the number of highly used coping strategies.



Figure 3. Proportion of patients reporting high use of individual coping strategies based on median split method by age. Older age defined as ≥65 years at the time of enrollment. Median scores for approach-oriented coping strategies: emotional support, 8; acceptance, 8; reframing, 6; and active coping, 7. Median scores for avoidant coping strategies: self-blame, 2; denial, 2; and behavioral disengagement, 2. Median score for religious coping; 5.

(B = 6.9; P = .03) and similar symptoms of depression (B = 0.87; P = .15), anxiety (B = 0.86; P = .19), and PTSD (B = 3.0; P = .68). Figure 4 illustrates the proportion of patients with clinically significant symptoms of depression, anxiety, and PTSD by overall coping strategy use.

Discussion

In this secondary analysis of baseline data from a multisite supportive care, randomized clinical trial, we demonstrate that patients before HCT hospitalization frequently use approach-oriented coping strategies, even at a time of high anticipation and trepidation. Nearly one-third of patients relied on avoidant strategies such as self-blame and denial. Key sociodemographic factors including age, sex, and employment status were associated with coping style. Finally, use of coping strategies was strongly associated with baseline QOL and psychological distress.

To our knowledge, this is the largest study to characterize baseline coping strategies in patients undergoing HCT. We observed that patients frequently use approach-oriented coping before HCT hospitalization. At a time of immense physical and psychological challenge, patients' use of approach-oriented coping strategies before HCT is an inherent strength. However, use of approach-oriented coping is susceptible to decrease amidst challenging clinical circumstances. For example, patients in the control arm of a specialty

palliative care intervention during induction therapy for acute myeloid leukemia used approach-oriented coping less frequently after initiation of induction therapy.¹³ However, receipt of specialty palliative care during the course of induction therapy enabled patients with acute myeloid leukemia to maintain use of approach-oriented coping and reduce reliance on avoidant coping.¹³ In fact, changes in coping strategy use were the most important mediators of the benefit of specialty palliative care in patients with acute myeloid leukemia.¹³ These findings illustrate that coping strategies are modifiable during a 3- to 4-week hospitalization and may be crucial to improve patient outcomes and experience. Thus, identification of approachoriented coping strategies before HCT may enable focused reinforcement through use of psychosocial support resources including social workers, chaplains, psychologists, and inpatient palliative care consultants. In fact, in a previous randomized clinical trial of integrated inpatient specialty palliative care during HCT, palliative care clinicians explicitly addressed coping strategies in the majority of both initial consult and follow-up visits, which further emphasizes the feasibility and importance of this practice in supporting patients during HCT hospitalization.³² Additionally, we found that many patients relied on avoidant coping strategies, which could affect important behaviors such as medication adherence and engagement in post-HCT care and increase risk of rehospitalization.^{33,34} Indeed, coping was markedly multifaceted, with >10% of patients simultaneously using approach-oriented and avoidant coping. Prior

Table 2. Multivariate associations between coping strategies and patient-reported outcomes

	QOL			Depression			Anxiety			PTSD		
	В	SE	Р	В	SE	Р	В	SE	Р	В	SE	Р
Approach	6.7	2.1	.001	-1.1	0.3	.001	-0.9	0.4	.02	-1.8	1.0	.06
Avoidant	-13.3	2.1	<.001	1.9	0.4	<.001	3.1	0.4	<.001	8.1	1.0	<.001

Multivariate relationships between high use of approach-oriented and avoidant coping with baseline QOL (FACT-BMT) and symptoms of depression (HADS depression), anxiety (HADS anxiety), and PTSD (PCL-C). Model covariates include age, sex, race, ethnicity, education, relationship, employment, performance status, diagnosis, time from diagnosis, and pretransplantation disease status.

SE, standard error.



Figure 4. Proportion of patients with clinically significant symptoms of depression, anxiety, and PTSD by high use of approach oriented and avoidant coping strategies. Coping categories included "high use, approach oriented only," "high use, avoidant only," "high use, approach oriented and avoidant," and "neither."

studies have also identified a diversity of pre-HCT coping strategies.^{14,15} In its clinical practice guidelines, the American Society of Transplantation and Cellular Therapy recommends that BMT social workers conduct a pre-HCT psychosocial evaluation.³⁵ However, comprehensive and systematic assessment of coping strategies is not standard practice.³⁶ Based on our findings, we would advocate for consistent and comprehensive assessment of coping strategies in the pre-HCT psychosocial evaluation, which could potentially optimize psychosocial support during and after HCT hospitalization.

In our study, coping strategies were strongly associated with pre-HCT QOL and psychological distress. Interestingly, unlike older studies describing pre-HCT coping strategies, our study demonstrated that approach-oriented coping was associated with decreased baseline psychological distress.^{15,37} Our observed negative association between approach-oriented coping and psychological distress is consistent with theoretical models of stress and coping³⁸ and findings in recent studies of patients with solid and hematologic malignancies.^{11,12,39} In particular, our findings on the effect of coping style on QOL and distress are similar to those observed in patients with acute myeloid leukemia.¹¹ Given the lack of clinically meaningful cutoffs for the Brief COPE, it is difficult to quantify the clinical significance. However, in patients with hematologic malignancies receiving specialty palliative care, promotion of approach-oriented coping and mitigation of avoidant coping mediates clinically significant improvement QOL and decrease in psychological distress, suggesting modifications in coping are important to improve patient outcomes.^{13,27,40} Unfortunately, specialty palliative care remains underused in HCT because of shortages of specialty palliative care clinicians and ongoing reticence about specialty

palliative care in HCT.^{27,41,42} Thus, in order to improve patient QOL and emotional wellbeing independent of palliative care use patterns, development of alternative supportive care interventions is needed. As an important modifiable factor, coping is an appealing domain for future interventions. HCT clinicians such as social workers, psychologists, chaplains, and nurses have expertise in guiding and shaping coping strategies.^{43,44} Future supportive care interventions could leverage their expertise to optimize patient coping during HCT hospitalization. Finally, novel interventions to promote approach-oriented coping delivered through digital health applications are also potentially appealing and scalable and merit further investigation to assess feasibility and efficacy.

To facilitate development of targeted supportive care interventions to support patient coping style, identification of noteworthy subgroups is crucial. Indeed, coping in patients with cancer is a dynamic process and intrinsically related to patient circumstances, experiences, and comorbidities.^{45,46} Our study demonstrates that sociodemographic factors including age, ability to work, and income level are importantly associated with pre-HCT coping style. Our study is particularly novel in characterizing coping in older adults with hematologic cancers undergoing HCT. Resilience in older adults with cancer remains underrecognized.²⁴ Although resilience has physical, psychosocial, and cognitive domains, adaptive coping is positively associated with resilience in adults with cancer.^{47,48} Our findings demonstrate that decreased use of avoidant coping could be a key feature of resilience in older adults with hematologic malignancies and should be an area of future investigation. In addition, our study identifies income level and disability status as important sociodemographic factors associated with use of avoidant coping before HCT and affirms prior studies examining the importance of socioeconomic wellbeing and ability to work in coping style.^{46,49} Although these factors may not be inherently modifiable, they are easily identifiable pre-HCT and may help direct coping interventions to patients at highest risk of use of maladaptive coping. Furthermore, employment status is an important indicator of HCT survivors' functional recovery and socioeconomic wellbeing after HCT, and longitudinal studies are needed to assess the relationship between coping style and return to work after HCT.⁵⁰ Finally, although our study focuses on the relationship between coping style and psychiatric symptoms, it is notable that the presence of baseline psychiatric comorbidity also likely influences use of coping strategies.^{39,46,48,51} Supportive care interventions during HCT hospitalization should account for coexisting psychiatric comorbidities, and future studies are sorely needed.

The current analysis has several limitations. First, the study cohort was derived from tertiary cancer care centers that serve patient populations with limited diversity. Race, ethnicity, culture, and socioeconomic status may affect availability and use of coping strategies, and our findings may not be generalizable to broader patient groups. Similarly, our study population was predominantly male and married. Sex and marital status may influence coping, and thus may affect generalizability of study findings. Second, the cross-sectional design limits applicability across HCT clinical continuum. There are limited data on whether, and how, use of coping evolves over the course of HCT recover. In addition, the timing of baseline assessment could have affected study results. For instance, discussion of coping during pre-HCT psychosocial assessments, or prior mood disorder-related treatment may have affected pre-HCT coping strategy use. The baseline data collection window during conditioning chemotherapy could have further affected patient-reported outcomes. Future studies to evaluate longitudinal assessment of coping are needed to address these important questions. Third, coping is a multifaceted construct that is challenging to capture comprehensively with a single questionnaire, particularly in a heterogenous and complex patient population. Although we assessed coping domains previously shown to be important among patients with hematologic malignancies, it is possible that other domains of coping not assessed may also be important. Fourth, our use of the median split to dichotomize use of coping strategy may limit generalizability because other patient populations may have different distributions of coping strategy use. Finally, because patients with hematologic malignancies reported increased psychological distress during the COVID-19 pandemic, the study period, which included the peak of the COVID-19 pandemic, may have affected patient-reported outcomes.

In conclusion, most patients hospitalized before HCT use approachoriented coping strategies, although a smaller number of patients rely on avoiding coping strategies. Moreover, approach-oriented coping was associated with improved pre-HCT QOL and psychological distress, whereas patients with high use of avoidant coping strategies reported significantly worse baseline QOL and distress. Our study supports comprehensive assessment of pre-HCT coping strategies, identification of patients at higher risk of maladaptive coping during their hospitalization, and development of interventions to promote adaptive coping for patients hospitalized for HCT. Study findings highlight the ongoing need for supportive care providers with expertise in facilitating adaptive coping, including social workers, chaplains, psychologists, and palliative care clinicians, to be available and involved during early hospitalization. Hence, supportive interventions incorporating coping strategy skill building should be prioritized and studied longitudinally.

Acknowledgments

Time for data analysis and manuscript preparation was supported by National Cancer Institute through grants R01CA222014 (A.E.-J.) and K08CA251654 (H.L.A.).

The work of T.W.L. on patient experience and palliative care integration in hematologic malignancies is funded, in part, by a Scholar in Clinical Research award from the Leukemia and Lymphoma Society.

Authorship

Contribution: R.N. was responsible for conceptualization, data analysis, and manuscript writing and editing; H.L.A. was responsible for conceptualization, data analysis, and manuscript writing and review; A.M.N., J.C., K.H., A.N., S.J.L., and T.W.L. performed data analysis and manuscript review; and A.E.-J. was responsible for conceptualization, data analysis, and manuscript writing and editing.

Conflict-of-interest disclosure: R.N. reports equity reimbursement from Timedoc and Vertex Pharmaceuticals. T.W.L. reports consulting fees/honoraria from AbbVie, Agilix, Agios/Servier, Astellas, AstraZeneca, BeiGene, BlueNote, Bristol Myers Squibb/Celgene, CareVive, Flatiron, Genentech, GlaxoSmithKline, Lilly, Meter Health, Novartis, and Pfizer; speaker fees from AbbVie, Agios, Astellas, Bristol Myers Squibb/Celgene, and Incyte; equity interest in Dosentrx; and research funding from AbbVie, American Cancer Society, AstraZeneca, Bristol Myers Squibb, Deverra Therapeutics, Duke University, Jazz Pharmaceuticals, the Leukemia and Lymphoma Society, and the National Institute of Nursing Research/ National Institutes of Health, and Seattle Genetics. The remaining authors declare no competing financial interests.

ORCID profiles: R.N., 0000-0002-8251-6961; H.L.A., 0000-0001-9136-9644; A.M.N., 0000-0003-1742-3280; K.H., 0000-0003-1235-0668; S.J.L., 0000-0003-2600-6390; T.W.L., 0000-0002-0546-7895.

Correspondence: Richard Newcomb, Division of Hematology/ Oncology, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114; email: richard.newcomb@mgh.harvard.edu.

References

2. Pidala J, Anasetti C, Jim H. Quality of life after allogeneic hematopoietic cell transplantation. Blood. 2009;114(1):7-19.

^{1.} El-Jawahri A, Traeger L, Kuzmuk K, et al. Prognostic understanding, quality of life, and mood in patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant.* 2015;50(8):1119-1124.

- Pidala J, Anasetti C, Jim H. Health-related quality of life following haematopoietic cell transplantation: patient education, evaluation and intervention. Br J Haematol. 2010;148(3):373-385.
- 4. El-Jawahri A, Vandusen H, Traeger L, et al. Quality of life and mood predicts post-traumatic stress disorder after hematopoietic stem cell transplantation. *Cancer.* 2016;122(5):806-812.
- 5. El-Jawahri AR, Traeger LN, Kuzmuk K, et al. Quality of life and mood of patients and family caregivers during hospitalization for hematopoietic stem cell transplantation: QOL and Mood During HCT. *Cancer.* 2015;121(6):951-959.
- 6. Newcomb R, Johnson PC, Cronin K, et al. Quality of life, physical functioning, and psychological distress of older adults undergoing hematopoietic stem cell transplantation. *Transplant Cell Ther.* 2023;29:387.e1-387.e7.
- 7. Greer JA, Jacobs JM, El-Jawahri A, et al. Role of patient coping strategies in understanding the effects of early palliative care on quality of life and mood. *J Clin Oncol.* 2018;36(1):53-60.
- 8. Nipp RD, El-Jawahri A, Fishbein JN, et al. The relationship between coping strategies, quality of life, and mood in patients with incurable cancer. *Cancer.* 2016;122(13):2110-2116.
- 9. Nipp RD, Greer JA, El-Jawahri A, et al. Coping and prognostic awareness in patients with advanced cancer. J Clin Oncol. 2017;35(22):2551-2557.
- 10. Carver CS, Scheier MF, Weintraub JK. Assessing coping strategies: a theoretically based approach. J Pers Soc Psychol. 1989;56(2):267-283.
- 11. Amonoo HL, Bodd MH, Reynolds MJ, et al. Coping strategies in patients with acute myeloid leukemia. *Blood Adv.* 2022;6(7):2435-2442.
- 12. Amonoo HL, Daskalakis E, Deary EC, et al. Relationship between longitudinal coping strategies and outcomes in patients with acute myeloid leukemia. J Natl Compr Canc Netw. 2022;20(10):1116-1123.
- 13. Nelson AM, Amonoo HL, Kavanaugh AR, et al. Palliative care and coping in patients with acute myeloid leukemia: mediation analysis of data from a randomized clinical trial. *Cancer*. 2021;127(24):4702-4710.
- 14. Fife BL, Huster GA, Cornetta KG, Kennedy VN, Akard LP, Broun ER. Longitudinal study of adaptation to the stress of bone marrow transplantation. *J Clin Oncol.* 2000;18(7):1539-1549.
- Wells KJ, Booth-Jones M, Jacobsen PB. Do coping and social support predict depression and anxiety in patients undergoing hematopoietic stem cell transplantation? J Psychosoc Oncol. 2009;27(3):297-315.
- Mah K, Khoraych M, Lipton JH, et al. Do allogeneic bone marrow transplant candidates match coping to controllability of pre-treatment stressors? Psychol Health Med. 2008;13(3):337-345.
- 17. Barata A, Gonzalez BD, Sutton SK, et al. Coping strategies modify risk of depression associated with hematopoietic cell transplant symptomatology. *J Health Psychol.* 2018;23(8):1028-1037.
- Muffly L, Pasquini MC, Martens M, et al. Increasing use of allogeneic hematopoietic cell transplantation in patients aged 70 years and older in the United States. Blood. 2017;130(9):1156-1164.
- 19. Zuckerman T. Allogeneic transplant: does age still matter? Blood. 2017;130(9):1079-1080.
- 20. Levin-Epstein R, Oliai C, Schiller G. Allogeneic hematopoietic stem cell transplantation for older patients with acute myeloid leukemia. Curr Treat Options Oncol. 2018;19(12):63.
- 21. Rosko AE, Cordoba R, Abel G, Artz A, Loh KP, Klepin HD. Advances in management for older adults with hematologic malignancies. J Clin Oncol. 2021;39(19):2102-2114.
- Skwirczyńska E, Chudecka-Głaz A, Wróblewski O, et al. Age matters: the moderating effect of age on styles and strategies of coping with stress and self-esteem in patients with neoplastic prostate hyperplasia. Cancers (Basel). 2023;15(5):1450.
- Abdallah M, Kadambi S, Parsi M, et al. Older patients' experiences following initial diagnosis of acute myeloid leukemia: a qualitative study. J Geriatr Oncol. 2022;13(8):1230-1235.
- 24. George T, Shah F, Tiwari A, et al. Resilience in older adults with cancer: a scoping literature review. J Geriatr Oncol. 2023;14(1):101349.
- Nakamura R, Saber W, Martens MJ, et al. Biologic assignment trial of reduced-intensity hematopoietic cell transplantation based on donor availability in patients 50-75 years of age with advanced myelodysplastic syndrome. J Clin Orthod. 2021;39(30):3328-3339.
- Kennedy VE, Olin RL. Haematopoietic stem-cell transplantation in older adults: geriatric assessment, donor considerations, and optimisation of care. Lancet Haematol. 2021;8(11):e853-e861.
- 27. El-Jawahri A, LeBlanc T, VanDusen H, et al. Effect of inpatient palliative care on quality of life 2 weeks after hematopoietic stem cell transplantation: a randomized clinical trial. JAMA. 2016;316(20):2094-2103.
- 28. Carver C. You want to measure coping but your protocol's too long: consider the Brief COPE. Int J Behav Med. 1997;4(1):92-100.
- 29. Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67(6):361-370.
- Smith MY, Redd W, DuHamel K, Vickberg SJ, Ricketts P. Validation of the PTSD Checklist-Civilian Version in survivors of bone marrow transplantation. J Trauma Stress. 1999;12(3):485-499.
- McQuellon R, Russell G, Cella D, et al. Quality of life measurement in bone marrow transplantation: development of the Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) scale. *Bone Marrow Transplant*. 1997;19(4):357-368.
- Nelson AM, Johnson PC, Kavanaugh AR, et al. Palliative care for patients undergoing stem cell transplant: intervention components and supportive care measures. Bone Marrow Transplant. 2021;56(8):1971-1977.

- 33. Mumby PB, Hurley C, Samsi M, Thilges S, Parthasarathy M, Stiff PJ. Predictors of non-compliance in autologous hematopoietic SCT patients undergoing out-patient transplants. *Bone Marrow Transplant*. 2012;47(4):556-561.
- 34. Richardson DR, Huang Y, McGinty HL, et al. Psychosocial risk predicts high readmission rates for hematopoietic cell transplant recipients. *Bone Marrow Transplant*. 2018;53(11):1418-1427.
- 35. BMT Clinical Social Worker Role Description. National Marrow Donor Program Social Work Workforce Group. 2017.
- Wiener L, Sannes TS, Randall J, et al. Psychosocial assessment practices for hematopoietic stem cell transplantation: a national survey study. Bone Marrow Transplant. 2023;58(12):1314-1321.
- Fife BL, Huster GA, Cornetta KG, Kennedy VN, Akard LP, Broun ER. Longitudinal study of adaptation to the stress of bone marrow transplantation. J Clin Orthod. 2000;18(7):1539-1549.
- Wenzel L, Glanz K, Allmer C. Stress, coping and health behavior. In: Health Education and Health Behavior: Theory, Research and Practice. Jossey-Bass; 2002:210-239.
- Calderon C, Gomez D, Carmona-Bayonas A, et al. Social support, coping strategies and sociodemographic factors in women with breast cancer. *Clin Transl Oncol.* 2021;23(9):1955-1960.
- 40. El-Jawahri A, Traeger L, Greer JA, et al. Effect of inpatient palliative care during hematopoietic stem-cell transplant on psychological distress 6 months after transplant: results of a randomized clinical trial. *J Clin Orthod*. 2017;35(32):3714-3721.
- 41. Han H, Liu Y, Qin Y, et al. Utilization of palliative care for patients undergoing hematopoietic stem cell transplantation during hospitalization: a population-based national study. *Am J Hosp Palliat Care.* 2019;36(10):900-906.
- El-Jawahri A, LeBlanc TW, Burns LJ, et al. What do transplant physicians think about palliative care? A national survey study. Cancer. 2018;124(23): 4556-4566.
- 43. Kestenbaum A, Shields M, James J, et al. What impact do chaplains have? A pilot study of spiritual AIM for advanced cancer patients in outpatient palliative care. J Pain Symptom Manage. 2017;54(5):707-714.
- 44. Uwayezu MG, Nikuze B, Maree JE, Buswell L, Fitch MI. Competencies for nurses regarding psychosocial care of patients with cancer in Africa: an imperative for action. JCO Glob Oncol. 2022;8(8):e2100240.
- 45. Greer JA, Applebaum AJ, Jacobsen JC, Temel JS, Jackson VA. Understanding and addressing the role of coping in palliative care for patients with advanced cancer. J Clin Oncol. 2020;38(9):915-925.
- **46.** Bottaro R, Faraci P. The influence of socio-demographics and clinical characteristics on coping strategies in cancer patients: a systematic review. *Support Care Cancer.* 2022;30(11):8785-8803.
- 47. Macía P, Barranco M, Gorbeña S, Iraurgi I. Expression of resilience, coping and quality of life in people with cancer. PLoS One. 2020;15(7):e0236572.
- Smith MM, Saklofske DH, Keefer KV, Tremblay PF. Coping strategies and psychological outcomes: the moderating effects of personal resiliency. J Psychol. 2016;150(3):318-332.
- 49. Faraci P, Bottaro R. A cross-sectional study examining the relationship between socio-demographics and coping styles in a group of cancer patients. *Clin Neuropsychiatry*. 2021;18(1):3-12.
- 50. Bhatt NS. Prevalence and determinants of return to work as a patient-centered outcome in survivors of hematopoietic cell transplantation. Curr Hematol Malig Rep. 2022;17(6):228-242.
- 51. Jacobs JM, Fishman S, Sommer R, et al. Coping and modifiable psychosocial factors are associated with mood and quality of life in patients with chronic graft-versus-host disease. *Biol Blood Marrow Transplant.* 2019;25(11):2234-2242.