

Relationship Between Longitudinal Coping Strategies and Outcomes in Patients With Acute Myeloid Leukemia

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ABSTRACT

Background: Patients with acute myeloid leukemia (AML) face an abrupt life-threatening illness and experience immense physical and psychological symptoms. However, no data describe how patients with AML cope longitudinally with their illness or the relationship between longitudinal coping and outcomes. **Methods:** We conducted a secondary analysis of longitudinal data from 160 patients with high-risk AML enrolled in a supportive care intervention trial to describe coping strategies longitudinally across the illness course. We used the Brief COPE questionnaire, the Hospital Anxiety and Depression Scale, the Post-Traumatic Stress Disorder (PTSD) Checklist-Civilian Version, and the Functional Assessment of Cancer Therapy-Leukemia to measure coping strategies, psychological distress, and quality of life (QoL) at baseline and at weeks 2, 4, 12, and 24 after diagnosis. Electronic health records were used to assess healthcare utilization and end-of-life (EoL) outcomes, and multivariate analyses were used to assess the relationship between coping and outcomes. **Results:** Longitudinal utilization of approach-oriented coping strategies was significantly associated with less distress (anxiety: β , -0.18 ; $P < .001$; depression symptoms: β , -0.42 ; $P < .001$; PTSD symptoms: β , -0.60 ; $P < .001$) and better QoL (β , 2.00 ; $P < .001$). Longitudinal utilization of avoidant coping strategies was significantly associated with greater distress (anxiety: β , 0.64 ; depression symptoms: β , 0.54 ; PTSD symptoms: β , 2.13 ; $P < .001$ for all) and worse QoL (β , -4.27 ; $P < .001$). Although the use of approach-oriented and avoidant coping strategies was not significantly associated with hospitalization, chemotherapy administration, or hospice use in the last 30 days of life, approach-oriented coping was associated with lower odds of ICU admissions (odds ratio, 0.92 ; $P = .049$). **Conclusions:** Longitudinal use of approach-oriented coping strategies was associated with less psychological distress, better QoL, and a lower likelihood of ICU admission, suggesting a possible target for supportive oncology interventions. Coping strategies did not impact EoL outcomes, and further research is needed to elucidate which patient factors impact EoL decision-making.

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Background

Coping with a sudden-onset life-threatening illness, intensive chemotherapy, and numerous physical adverse effects can be challenging for many patients with acute myeloid leukemia (AML).^{1,2} The demands of treatment and recovery after an AML diagnosis include managing a prolonged 4- to 6-week hospitalization, disease and therapy complications (eg, infections), high symptom burden, and an uncertain prognosis.^{1,3,4} In addition to the sizeable clinical burden, AML is characterized by poor response to standard chemotherapy, high rates of relapse/refractory disease, and limited effective therapy for relapsed disease.⁴ Although patients with AML also report a high burden of psychological distress and behavioral symptoms, including anxiety, depression, and sleep disturbance, there are limited supportive resources for patients and their caregivers.^{4–9} The accumulation of these challenges adversely impacts quality of life (QoL) and overall function in this population.^{1,7–10}

Unsurprisingly, coping plays a significant role in how patients with AML navigate the demands of treatment and recovery.^{11–13} For most patients with cancer, coping strategies may evolve over the course of their illness and treatment, as indicated by the transactional theory of coping. This theory suggests that coping evolves in response to changes in patients' internal and external demands.^{14,15} Coping flexibility (ie, adjusting and changing coping strategies to enhance desirable outcomes based on a given context) relies on the availability and utilization of a variety of coping

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strategies.¹⁶ Although we know that patients with newly diagnosed AML use a variety of coping strategies both in the avoidant and approach-oriented coping domains,¹⁷ there are limited data from this population characterizing longitudinal patterns of coping and investigating whether longitudinal changes in coping are associated with clinical outcomes and healthcare utilization.

Patients with AML have high healthcare utilization compared with other cancer populations.¹⁸ For example, approximately 15% of this population requires admission to the ICU to manage potentially life-threatening complications.^{18–20} However, studies exploring how patients with AML cope with high healthcare utilization are lacking. Although avoidance coping has been associated with the suppression of cellular immune function (ie, an independent predictor of ICU admissions) and approach-oriented coping seems to modulate immune function in patients with cancer, the association between coping, biologic or inflammatory factors, and healthcare utilization in patients with AML should be further explored.²⁰ Current evidence suggests that coping mediates the impact of palliative care interventions on psychological distress during the induction chemotherapy hospitalization for patients with AML.^{21–25} Hence, coping may modify inflammation and improve distress, which can consequently reduce healthcare utilization and improve end-of-life (EoL) outcomes in this population.^{26–28} Therefore, studies that describe the association between coping and healthcare utilization would be foundational and hypothesis-generating for research describing the biologic and immune implications of coping in the AML and other oncology populations.

A nuanced understanding of the direct impact of coping (ie, a positive or negative association) on patient-reported, clinical, healthcare utilization, and EoL outcomes across the AML illness course will provide critical evidence to enhance the incorporation of coping in supportive oncology interventions. Hence, for this study, we describe patterns of coping throughout the illness course for patients with AML and examine the longitudinal associations of coping with outcomes. A comprehensive depiction of longitudinal coping in patients diagnosed with AML will add to ongoing efforts to support this vulnerable population as they manage a life-threatening illness accompanied by demanding treatments and recovery trajectories.

Methods

Study Procedures

We conducted a secondary analysis of longitudinal data from 160 hospitalized patients with high-risk AML enrolled in a multisite randomized palliative care intervention trial (ClinicalTrials.gov identifier: NCT02207322) at Massachusetts General Hospital, Duke University Hospital,

Hospital of the University of Pennsylvania, and The Ohio State University from January 2017 to July 2019.²¹ The study was approved by all participating sites' Institutional Review Boards. All participants provided written informed consent.

Study Design

Prospective longitudinal data were obtained from participants at baseline and weeks 2, 4, 12, and 24 after AML diagnosis. Full details of the study procedures and design have been previously reported.²¹ Briefly, we screened consecutive eligible hospitalized patients with AML from admission databases in participating institutions. With permission from the treating oncologist, eligible patients were approached within 72 hours of chemotherapy initiation. Willing patients were then enrolled after consent procedures. Enrolled participants were randomized to integrated palliative care versus usual care (ie, supportive care by the oncology team) using a 1:1 computer-generated schema stratified by study site and disease status. For this secondary analysis, we combined data from participants in the intervention (n=86) and usual care control (n=74) groups for a more robust sample size.

Participants

Our sample included hospitalized adults (aged ≥ 18 years) with high-risk AML receiving intensive chemotherapy who were English-speaking and had the ability to read and complete surveys with minimal assistance. High-risk AML was defined as (1) newly diagnosed patients aged ≥ 60 years, (2) patients of any age with an antecedent hematologic disorder or therapy-related disease, or (3) patients with a diagnosis of relapsed or primary refractory AML. Intensive chemotherapy was defined as a combination of anthracycline and cytarabine (the 7 + 3 regimen) or a modification of this regimen in a clinical trial with additional drugs added or other similar intensive chemotherapy regimens requiring a 3- to 6-week hospitalization. We excluded patients who (1) were diagnosed with acute promyelocytic leukemia, (2) were receiving nonintensive chemotherapy or palliative care, or (3) had a comorbid disease or history of major psychiatric disease that the treating oncologist believed would interfere with their adherence to informed consent and study procedures.

Sociodemographic and Clinical Data

At enrollment, participants reported demographic information, including age, race, ethnicity, sex, marital status, religious beliefs, education, and income. We used the electronic health record (EHR) to confirm the disease, treatment, and clinical information.

Healthcare Utilization and EoL Outcomes

We used the EHR to obtain healthcare utilization (ie, ICU admission, days alive and out of hospital [DAOH]) and EoL information (ie, hospice and chemotherapy utilization, hospitalization in the last 30 days of life). DAOH is a well-validated healthcare utilization metric that has been shown to be an accurate quality-of-care metric, especially in a population at risk for mortality.^{29,30} We chose EoL outcomes that are commonly used in the literature to describe the intensity of EoL care for patients with hematologic malignancies.^{21,28,31,32}

Patient-Reported Measures

Participants completed self-reported measures at baseline and at weeks 2, 4, 12, and 24 after diagnosis. We evaluated patients' use of coping strategies with the Brief COPE. The Brief COPE, a 28-item questionnaire, assesses patients' use of 14 methods of coping, with 2 items for each method.³³ To reduce the questionnaire burden for participants, we followed a similar approach used in previous studies, which considered the following 7 coping strategies: emotional support, self-blame, positive reframing, active coping, acceptance, denial, and behavioral disengagement.^{17,33,34} Scores for each scale range from 2 to 8, with higher scores indicating greater use of a particular coping strategy. We grouped coping strategies into 2 higher-order domains based on prior literature using an aggregate of individual domain scores: approach-oriented coping (ie, use of emotional support, active coping, positive reframing, acceptance) or avoidant coping (ie, self-blame, denial, behavioral disengagement).^{16–18,34} We defined "last reported coping strategy used" for either approach-oriented or avoidant coping as the last coping strategy on record (ie, at baseline or at weeks 2, 4, 12, or 24 after diagnosis) for a given patient in the dataset.

We measured depression and anxiety symptoms using the 14-item Hospital Anxiety and Depression Scale,²¹ which consists of two 7-item subscales that measure symptoms of depression and anxiety, respectively. Scores range from 0 to 21, with higher scores indicating worse mood symptoms. Clinically meaningful cutoffs are 1 to 2 points.

We used the 17-item Post-Traumatic Stress Disorder Checklist-Civilian Version to evaluate posttraumatic stress disorder (PTSD) symptoms. The 17 items on the checklist assess 3 categories of PTSD symptoms as follows: intrusion (items 1–5), avoidance (items 6–12), and hypervigilance (items 13–17). The PTSD symptom severity score was obtained by summing the scores from each of the 17 items. Clinically meaningful cutoffs are 1 to 2 points, with higher scores indicating worse clinically significant PTSD symptoms (score range, 17–85).^{35,36}

We used the 44-item Functional Assessment of Cancer Therapy-Leukemia, which includes 5 subscales assessing physical, functional, emotional, and social well-being and

leukemia-specific concerns during the past week (score range, 0–176) to measure QoL. Clinically meaningful cutoffs are 5 to 7 points, with higher scores indicating better QoL.³⁷

Statistical Analysis

We performed all statistical analyses using Stata, version 16.0 (StataCorp LLC). First, to summarize participants' baseline characteristics, we used descriptive statistics (eg, mean, standard deviation) for continuous variables, depending on the normality of the data, and proportions for categorical variables. A 2-sided *P* value <.05 was considered statistically significant for all analyses. For all models, we controlled for age, sex, marital status, diagnosis type (ie, newly diagnosed vs relapsed/refractory disease), and random assignment (yes vs no) to the palliative care intervention. We computed mixed linear-effects models using maximum likelihood to account for missing data and characterize the trajectories of changes in the utilization of approach-oriented and avoidant coping strategies over time (ie, baseline, week 2, week 4, week 12, and week 24 after diagnosis). We also used mixed linear-effects models using maximum likelihood to account for missing data to describe the associations between the longitudinal utilization of coping strategies (ie, approach-oriented, avoidant) and patient-reported outcomes (anxiety, depression, PTSD, and QoL). Given the potential collinearity between anxiety, depression, PTSD, and QoL, these outcomes were modeled separately. To assess the relationship between coping strategies and healthcare utilization, we used the last reported approach-oriented and avoidant coping strategy and used logistic regression to explore the relationship between coping strategies and ICU admission (yes vs no). We used linear regression models to examine the relationship between the last reported approach-oriented and avoidant coping strategy with DAOH. We also used logistic regression models to explore the relationship between the last reported approach-oriented and avoidant coping strategies with these EoL outcomes (hospitalizations in the last 30 days of life, chemotherapy use, and hospice use).

Results

Demographics and Patient Characteristics

A total of 235 eligible patients with AML underwent screening, and 160 (68.1%) enrolled. Table 1 summarizes participants' baseline characteristics. Participants were mostly non-Hispanic White (n=138; 86.3%), with a median (range) age of 64.4 years (19.7–80.1 years). Forty percent (n=64) were female, 73.8% (n=118) were married/in a relationship, and 45.0% (n=72) were college-educated. Although most of the participants had newly diagnosed AML (n=109;

Table 1. Participant Baseline Characteristics

Characteristic	n (%)
Total, n	160
Age, median (range), y	64.4 (19.7–80.1)
Sex	
Female	64 (40.0)
Male	96 (60.0)
Race/Ethnicity	
Non-Hispanic White	138 (86.3)
Black	15 (9.4)
Hispanic	5 (0.3)
American Indian	4 (2.5)
Asian	2 (1.3)
Other	1 (0.6)
AML diagnosis type	
Newly diagnosed	109 (68.1)
Relapsed	37 (23.1)
Refractory	14 (8.8)
Relationship status	
Married/Relationship	118 (73.8)
Divorced	20 (12.5)
Single	12 (7.5)
Widowed	9 (5.6)
Missing	1 (0.6)
Religion	
Catholic	60 (37.5)
Non-Catholic Christian	53 (33.1)
None	22 (13.8)
Jewish	7 (4.4)
Muslim	2 (1.3)
Atheist	2 (1.3)
Other	13 (8.1)
Missing	1 (0.6)
Education	
High school	42 (26.3)
College	72 (45.0)
Postgraduate	44 (27.5)
Missing	2 (1.3)
Income (USD)	
<\$25,000	21 (14.2)
\$25,000–\$49,999	32 (21.6)
\$50,000–\$99,999	45 (30.4)
\$100,000–\$149,999	23 (15.5)
>\$150,000	27 (18.2)

Abbreviation: AML, acute myeloid leukemia.

68.1%), 23.1% (n=37) had relapsed AML and 8.8% (n=14) had refractory AML. The proportion of patients with missing data at the follow-up assessments for weeks 2, 4, 12, and 24 were as follows: 13 (8.1%), 23 (14.4%), 23 (14.4%), and 55 (34.4%), respectively.

The median (range) number of DAOH in this cohort was 119.5 days (97.5–154.5 days). Approximately 28.8% (n=46) of patients were admitted to the ICU. Overall, 84 participants died during the study period. Among the deceased, 35.7% (n=30) used hospice in the last 30 days of life and 50% (n=42) used chemotherapy in the last 30 days of life.

Longitudinal Coping Strategies and Patient-Reported Outcomes

The utilization of both approach-oriented (β , -0.190 ; $P=.066$) and avoidant coping (β , -0.075 ; $P=.072$) strategies declined over time, but the changes were not statistically significant (Figure 1).

Although the proportion of participants who reported high use of approach-oriented coping consistently decreased over time (ie, baseline = 47.5%; weeks 2, 4, 12, and 24 = 40.6%, 33.1%, 30.0%, and 24.4%, respectively), the proportion of participants who reported high use of avoidant coping increased over the first month (ie, baseline = 33.1%; weeks 2 and 4 = 38.8% and 40.0%, respectively) and then decreased at the 12-week (30.0%) and 24-week (21.2%) follow-up. There was no significant association between sociodemographic and disease factors (ie, age, sex, race, ethnicity, relationship status, religion, education, income, and diagnosis type) and high use of either approach-oriented or avoidant coping.

The use of approach-oriented coping longitudinally was significantly associated with less distress (anxiety: β , -0.18 [95% CI, -0.25 to -0.12]; $P<.001$; depression symptoms: β , -0.42 [95% CI, -0.49 to -0.35]; $P<.001$; PTSD symptoms: β , -0.60 [95% CI, -0.77 to -0.43]; $P<.001$) and better QoL (β , 2.00 [95% CI, 1.59 to 2.42]; $P<.001$). The use of avoidant coping longitudinally was significantly associated with more distress (anxiety: β , 0.64 [95% CI, 0.49 to 0.78]; $P<.001$; depression symptoms: β , 0.54 [95% CI, 0.41 to 0.68]; $P<.001$; PTSD symptoms: β , 2.13 [95% CI, 1.77 to 2.49]; $P<.001$) and worse QoL (β , -4.27 [95% CI, -5.14 to -3.40]; $P<.001$) (Table 2).

Approach-Oriented Coping and Healthcare Utilization at EoL

Patients' use of approach-oriented coping was significantly associated with lower odds of ICU admission (odds ratio [OR], 0.92; 95% CI, 0.841–0.999; $P=.049$). There were no associations between the use of approach-oriented coping with DAOH or EoL outcomes (Table 3).

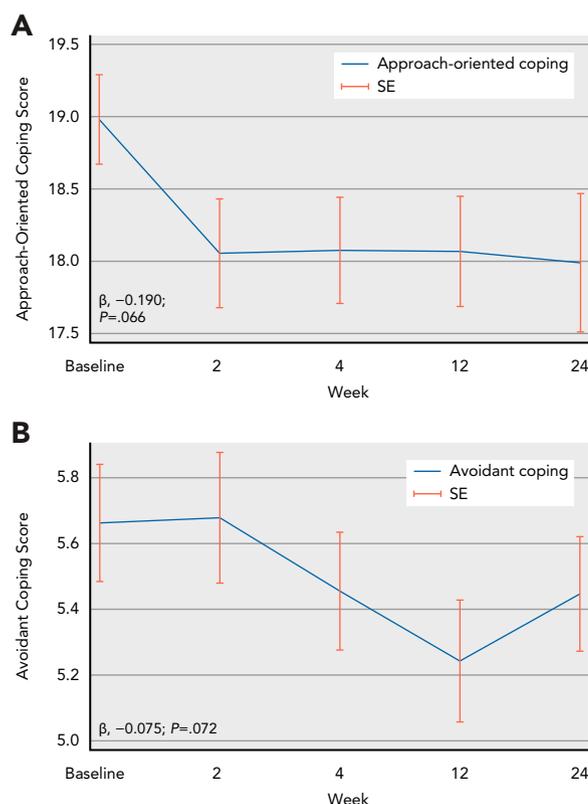


Figure 1. Longitudinal changes in (A) approach-oriented and (B) avoidant coping strategies over time.

Avoidant Coping and Healthcare Utilization at EoL

Patients' use of avoidant coping was not associated with likelihood of ICU admission (OR, 1.15 [95% CI, 0.96 to 1.37]; $P=.128$), DAOH (β , -1.13 [95% CI, -4.56 to 2.30]; $P=.515$), chemotherapy use in the last 30 days of life (OR, 1.04 [95% CI, 0.83 to 1.29]; $P=.742$), hospitalization in the last 30 days of life (OR, 0.95 [95% CI, 0.67 to 1.34]; $P=.768$), or hospice use (OR, 1.24 [95% CI, 0.99 to 1.55]; $P=.059$) (Table 3).

Discussion

In this study of patients with high-risk AML, we described longitudinal patterns of coping and comprehensively examined the association of coping with patient-reported

outcomes, healthcare utilization, and EoL outcomes. Although longitudinal approach-oriented coping was associated with less psychological distress (eg, symptoms of anxiety) and better QoL, longitudinal avoidant coping was associated with more psychological distress and worse QoL. In our assessment of links between coping and healthcare utilization, only approach-oriented coping was associated with lower odds of ICU admissions. There were no associations between the use of approach-oriented or avoidant coping with DAOH or EoL outcomes. Additional research is needed to unpack how coping impacts clinical, healthcare utilization, and EoL outcomes throughout the illness and treatment course of patients with high-risk AML.

Despite strong evidence that coping is associated with a variety of important clinical outcomes in patients with hematologic malignancies,³⁸ there are no data that examine coping longitudinally in patients with AML. Although prior work in noncancer populations suggests that coping may change over time,^{14,15} our observed variations in both approach-oriented and avoidant coping strategies over time were not statistically significant. Given the heterogeneity of the clinical course and treatments for patients with AML, our sample size was likely inadequate to explore the relationship between clinical course and coping strategies. Such research would inform the development of well-timed supportive interventions for maximum impact in the AML population. Although few studies have highlighted sociodemographic factors (eg, sex, education) that could influence coping strategy use,^{39,40} data describing factors that influence coping or coping evolution are limited. Thus, a nuanced understanding of patient- and disease-specific factors that influence coping evolution during the illness course of AML will also help identify patients at risk for underusing coping strategies that have known beneficial effects on health outcomes.

Approach-oriented coping was longitudinally associated with a reduction in distress symptoms and an improvement in QoL during the first 6 months of the illness

Table 2. Association Between Longitudinal Coping Strategies and Patient-Reported Outcomes

	Approach-Oriented Coping			Avoidant Coping		
	β	95% CI	P Value	β	95% CI	P Value
QoL	2.00	1.59 to 2.42	<.001	-4.27	-5.14 to -3.40	<.001
Depression	-0.42	-0.49 to -0.35	<.001	0.54	0.41 to 0.68	<.001
Anxiety	-0.18	-0.25 to -0.12	<.001	0.64	0.49 to 0.78	<.001
PTSD	-0.60	-0.77 to -0.43	<.001	2.13	1.77 to 2.49	<.001

Abbreviations: PTSD, posttraumatic stress disorder; QoL, quality of life.

Table 3. Association Between Last Reported Coping Strategies, Healthcare Utilization, and EoL Outcomes

Variable	Approach-Oriented Coping Strategies		Avoidant Coping Strategies	
	OR (95% CI)	P Value ^a	OR (95% CI)	P Value ^a
ICU utilization	0.92 (0.841 to 0.999)	.049	1.15 (0.96 to 1.37)	.128
DAOH	-0.38 ^a (-1.927 to 1.172)	.631	-1.13 ^a (-4.56 to 2.30)	.515
Hospice used	1.01 (0.890 to 1.14)	.928	1.24 (0.99 to 1.55)	.059
Chemotherapy last 30 days	0.92 (0.811 to 1.03)	.157	1.04 (0.83 to 1.29)	.742
Hospitalization last 30 days	0.86 (0.698 to 1.07)	.177	0.95 (0.67 to 1.34)	.768

All analyses were controlled for randomization, age, sex, marital status, and diagnosis type. The variables of hospice utilization, chemotherapy in the last 30 days, and hospitalization in the last 30 days were only examined in patients who died.

Abbreviations: DAOH, days alive and out of hospital; EoL, end of life; ICU, intensive care unit; OR, odds ratio.

^aBold indicates statistically significant P value.

^bβ coefficient rather than OR.

course. However, avoidant coping was longitudinally associated with an increase in distress and decline in QoL. These results expand on our previous work, which illustrated that baseline coping strategies were significantly associated with distress and QoL outcomes.⁴¹ Although coping and its associations with patient-reported outcomes have been studied to a limited degree in the hematologic malignancy population, our results suggest that coping is essential throughout the illness and recovery course in this population. Hence, a thorough understanding of how coping impacts psychological well-being and QoL will help tailor supportive resources in the care of patients with hematologic malignancies such as AML.

We show that approach-oriented coping is associated with lower odds of ICU admission. However, studies describing the association between coping and healthcare utilization, such as ICU admission in the AML and other cancer populations, are limited.²⁶ One potential mechanism explaining the links between coping and healthcare utilization (eg, ICU admission) is the relationship between coping and systemic inflammation; for example, in 41 men with prostate cancer, emotional approach coping seemed to modulate inflammatory processes.²⁶ In noncancer populations, although positive dyadic coping (eg, problem-solving) has been associated with lower circulating levels of C-reactive protein, negative coping was unrelated to C-reactive protein levels in caregivers of children with autism spectrum disorder.⁴² It is also possible that patients who use approach-oriented coping strategies make different decisions regarding their willingness to accept an ICU level of care. Additionally, the relationship between approach-oriented coping and fewer distress symptoms provides further insights given that distress has been significantly associated with greater healthcare utilization in cancer populations.^{43,44} These findings are hypothesis-generating and require further validation in larger studies to better understand the relationship

between coping and healthcare utilization in patients with AML.

It has been previously shown that coping mediates the beneficial effects (eg, better QoL, fewer symptoms of depression and anxiety) of palliative care interventions in this population.²⁵ However, we found no direct relationships between coping and EoL outcomes. Although a small sample size and experimental manipulation of the sample could have contributed to our negative findings, other factors (eg, disease characteristics) could also affect the role of coping on EoL outcomes. Overall, further research with more robust sample sizes is needed to understand the essential elements of coping that could impact EoL outcomes in this population.

Limitations of this study should be noted. First, our sample from academic cancer centers included predominantly non-Hispanic White, married, and educated patients with AML who could consent to study procedures in English. This limitation impacts the external validity of our findings to patients from ethnic minorities and lower socioeconomic backgrounds; variations in coping strategies in these groups compared with affluent White patients are well established.^{45,46} Larger prospective studies in more socioeconomically diverse populations are needed to validate our findings for generalizability. In addition, spirituality and geography should be assessed in future work because they may impact coping. Second, although the direction of relationships investigated in the present study is supported by other longitudinal studies of coping and distress over time in medical populations,^{16,47} the association between coping and psychological health could be bidirectional. Although our current analyses preclude the establishment of causality between coping and distress, future studies focused on interventions to promote effective coping may allow us to examine mediation and potential causal relationships between coping and distress in patients with AML. Third, we may

have been underpowered to detect the associations between coping and EoL outcomes, given the small subset of patients who died during the study. Given the role of coping in palliative care interventions, the association of coping and EoL outcomes should be assessed with larger sample sizes to understand the nuanced association between coping and EoL outcomes. Fourth, although we controlled for group assignment in our analyses, half of our sample was exposed to an intervention that targeted coping, which could impact the pattern of changes observed for coping longitudinally. Fifth, although we lacked data on treatment course and were unable to properly explore the relationship between treatment course and longitudinal trends in coping, future studies with robust samples should assess how treatment response impacts coping in this population.

Conclusions

Our study shows that for patients with high-risk AML, the longitudinal use of approach-oriented coping is associated with fewer symptoms of distress, better QoL, and lower odds of ICU admission. Hence, cultivating approach-oriented coping via supportive oncology interventions in the early phases of the illness experience of patients with high-risk AML could yield immediate and long-term benefits over the course of their illness, treatment, and recovery. Furthermore, despite the potential impact of coping in palliative care interventions, our negative findings for the direct association between coping and EoL outcomes suggest the need for more rigorous

studies characterizing the elements of coping that could positively influence EoL care in the AML population.

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References

- Zimmermann C, Yuen D, Mischitelle A, et al. Symptom burden and supportive care in patients with acute leukemia. *Leuk Res* 2013;37:731–736.
- Albrecht TA, Boyiadzis M, Elswick RK Jr, et al. Symptom management and psychosocial needs of adults with acute myeloid leukemia during induction treatment: a pilot study. *Cancer Nurs* 2017;40:E31–38.
- Sekeres MA, Guyatt G, Abel G, et al. American Society of Hematology 2020 guidelines for treating newly diagnosed acute myeloid leukemia in older adults. *Blood Adv* 2020;4:3528–3549.
- Wiese M, Daver N. Unmet clinical needs and economic burden of disease in the treatment landscape of acute myeloid leukemia. *Am J Manag Care* 2018;24(16 Suppl):S347–355.
- Schumacher A, Kessler T, Büchner T, et al. Quality of life in adult patients with acute myeloid leukemia receiving intensive and prolonged chemotherapy—a longitudinal study. *Leukemia* 1998;12:586–592.
- Yang CFJ, Aibel K, Meyerhoff R, et al. Actigraphy assessment of sleep quality among patients with acute myeloid leukaemia during induction chemotherapy. *BMJ Support Palliat Care* 2018;8:274–277.
- El-Jawahri A, Abel GA, Traeger L, et al. Quality of life and mood of older patients with acute myeloid leukemia (AML) receiving intensive and non-intensive chemotherapy. *Leukemia* 2019;33:2393–2402.
- Rodin G, Yuen D, Mischitelle A, et al. Traumatic stress in acute leukemia. *Psychooncology* 2013;22:299–307.
- Gheihman G, Zimmermann C, Deckert A, et al. Depression and hopelessness in patients with acute leukemia: the psychological impact of an acute and life-threatening disorder. *Psychooncology* 2016;25:979–989.
- Zittoun R, Achard S, Ruzsniwski M. Assessment of quality of life during intensive chemotherapy or bone marrow transplantation. *Psychooncology* 1999;8:64–73.
- Ghodraty-Jabloo V, Alibhai SMH, Breunis H, et al. Keep your mind off negative things: coping with long-term effects of acute myeloid leukemia (AML). *Support Care Cancer* 2016;24:2035–2045.
- Ghodraty-Jabloo V, Alibhai SMH, Breunis H, et al. One day at a time: improving the patient experience during and after intensive chemotherapy for younger and older AML patients. *Leuk Res* 2015;39:192–197.
- Loh KP, Abdallah M, Kumar AJ, et al. Health-related quality of life and treatment of older adults with acute myeloid leukemia: a Young International Society of Geriatric Oncology review paper. *Curr Hematol Malig Rep* 2019;14:523–535.
- Hulbert-Williams NJ, Morrison V, Wilkinson C, et al. Investigating the cognitive precursors of emotional response to cancer stress: re-testing Lazarus's transactional model. *Br J Health Psychol* 2013;18:97–121.
- Lazarus RS, Folkman S. Transactional theory and research on emotions and coping. *Eur J Person* 1987;1:141–169.
- Heffer T, Willoughby T. A count of coping strategies: a longitudinal study investigating an alternative method to understanding coping and adjustment. *PLoS One* 2017;12:e0186057.
- Amonoo HL, Bodd MH, Reynolds MJ, et al. Coping strategies in patients with acute myeloid leukemia. *Blood Adv* 2022;6:2435–2442.
- El-Jawahri AR, Abel GA, Steensma DP, et al. Health care utilization and end-of-life care for older patients with acute myeloid leukemia. *Cancer* 2015;121:2840–2848.

19. Pohlen M, Thoennissen NH, Braess J, et al. Patients with acute myeloid leukemia admitted to intensive care units: outcome analysis and risk prediction. *PLoS One* 2016;11:e0160871.
20. Schellongowski P, Staudinger T, Kundi M, et al. Prognostic factors for intensive care unit admission, intensive care outcome, and post-intensive care survival in patients with de novo acute myeloid leukemia: a single center experience. *Haematologica* 2011;96:231–237.
21. El-Jawahri A, LeBlanc TW, Kavanaugh A, et al. Effectiveness of integrated palliative and oncology care for patients with acute myeloid leukemia: a randomized clinical trial. *JAMA Oncol* 2021;7:238–245.
22. El-Jawahri A, Greer JA, Pirl WF, et al. Effects of early integrated palliative care on caregivers of patients with lung and gastrointestinal cancer: a randomized clinical trial. *Oncologist* 2017;22:1528–1534.
23. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med* 2010;363:733–742.
24. Temel JS, Greer JA, El-Jawahri A, et al. Effects of early integrated palliative care in patients with lung and GI cancer: a randomized clinical trial. *J Clin Oncol* 2017;35:834–841.
25. 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;127:4702–4710.
26. Hoyt MA, Stanton AL, Bower JE, et al. Inflammatory biomarkers and emotional approach coping in men with prostate cancer. *Brain Behav Immun* 2013;32:173–179.
27. Master SL, Amodio DM, Stanton AL, et al. Neurobiological correlates of coping through emotional approach. *Brain Behav Immun* 2009;23:27–35.
28. Vaughn DM, Johnson PC, Jagielo AD, et al. Factors associated with health care utilization at the end of life for patients with acute myeloid leukemia. *J Palliat Med* 2022;25:749–756.
29. Manzano JGM, Gadiraju S, Hiremath A, et al. Unplanned 30-day readmissions in a general internal medicine hospitalist service at a comprehensive cancer center. *J Oncol Pract* 2015;11:410–415.
30. El-Jawahri A, Chen YB, Brazauskas R, et al. Impact of pre-transplant depression on outcomes of allogeneic and autologous hematopoietic stem cell transplantation. *Cancer* 2017;123:1828–1838.
31. Johnson PC, Markovitz NH, Yi A, et al. End-of-life care for older adults with aggressive non-Hodgkin lymphoma. *J Palliat Med* 2022;25:728–733.
32. Petrillo LA, El-Jawahri A, Gallagher ER, et al. Patient-reported and end-of-life outcomes among adults with lung cancer receiving targeted therapy in a clinical trial of early integrated palliative care: a secondary analysis. *J Pain Symptom Manage* 2021;62:e65–74.
33. 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;122:2110–2116.
34. 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;36:53–60.
35. Smith MY, Redd W, DuHamel K, et al. Validation of the PTSD Checklist-Civilian Version in survivors of bone marrow transplantation. *J Trauma Stress* 1999;12:485–499.
36. Blanchard EB, Jones-Alexander J, Buckley TC, et al. Psychometric properties of the PTSD Checklist (PCL). *Behav Res Ther* 1996;34:669–673.
37. McQuellon RP, Russell GB, Cella DF, 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;19:357–368.
38. Ernst J, Hinz A, Niederwieser D, et al. Dyadic coping of patients with hematologic malignancies and their partners and its relation to quality of life—a longitudinal study. *Leuk Lymphoma* 2017;58:655–665.
39. Hudson K. Coping Complexity Model: coping stressors, coping influencing factors, and coping responses. *Psychol* 2016;7:300–309.
40. Zyga S, Mitrousi S, Alikari V, et al. Assessing factors that affect coping strategies among nursing personnel. *Mater Sociomed* 2016;28:146–150.
41. Reynolds MJ, Lavoie MW, Jones BT, et al. Associations of coping strategies with quality of life (QOL) and mood in patients with acute myeloid leukemia (AML) [abstract]. *J Clin Oncol* 2021;39(Suppl):Abstract e19012.
42. Gouin JP, Scarcello S, da Estrela C, et al. Dyadic coping and inflammation in the context of chronic stress. *Health Psychol* 2016;35:1081–1084.
43. Nipp RD, El-Jawahri A, Moran SM, et al. The relationship between physical and psychological symptoms and health care utilization in hospitalized patients with advanced cancer. *Cancer* 2017;123:4720–4727.
44. Hildenbrand JD, Park H, Casarett D, et al. Patient-reported distress and healthcare utilization in patients with advanced cancer [abstract]. *J Clin Oncol* 2020;38(Suppl):Abstract 12093.
45. Culver JL, Arena PL, Antoni MH, et al. Coping and distress among women under treatment for early stage breast cancer: comparing African Americans, Hispanics and non-Hispanic Whites. *Psychooncology* 2002;11:495–504.
46. Yoo GJ, Levine EG, Pasick R. Breast cancer and coping among women of color: a systematic review of the literature. *Support Care Cancer* 2014;22:811–824.
47. Seiffge-Krenke I. Causal links between stressful events, coping style, and adolescent symptomatology. *J Adolesc* 2000;23:675–691.