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ORIGINAL ARTICLE

The relationship between emotional well-being and understanding of prognosis in patients with acute myeloid leukemia (AML)

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Abstract

Purpose Adults with acute myeloid leukemia (AML) face considerable distress and often have a poor prognosis. However, little is known about these patients' perceptions of prognosis and how this relates to emotional well-being (EWB).

Methods We conducted a prospective, observational study of 50 adult patients with AML initiating chemotherapy, and surveyed them longitudinally for 6 months about their prognosis, treatment goals, quality of life, and EWB (by FACT-G). We derived a prognostic estimate for each patient based on data from published trials summarized in National Comprehensive Care Network Guidelines. We used descriptive statistics and longitudinal modeling to test the hypothesis that more accurate prognostic awareness is associated with worse EWB.

Results Most patients ($n=43$; 86%) had an objectively poor prognosis attributable to relapsed disease, complex karyotype, or FLT3 mutation. Yet, 74% of patients reported expecting a 50% or greater chance of cure. Patients with a poor prognosis more often had discordant prognostic estimates, compared to those with favorable risk AML (OR = 7.25, 95% CI 1.21, 43.37). Patient-reported prognostic estimates did not vary significantly over time. At baseline, patients who better understood their prognosis had worse EWB and overall quality-of-life scores (EWB 12 vs. 19.5; $p=0.01$; FACT-G 65 vs. 75.5; $p=0.01$).

Conclusion Patients with AML overestimate their prognosis, and awareness of a poor prognosis is associated with worse emotional well-being. Efforts are needed to improve patients' understanding of their prognosis, and to provide more psychosocial support and attention to well-being as part of high-quality leukemia care.

Keywords Acute myeloid leukemia · Emotional well-being · Prognosis · Prognostic understanding · Distress

Introduction

Acute myeloid leukemia (AML) is the most common adult acute leukemia, affecting an estimated 19,940 individuals in 2020 [1]. AML yields 1.8% of all cancer deaths, and 5-year survival rates are poor at 28.7%, especially in older or high-risk adults where long-term survival rates are just 3–5% [1–4]. Evidence also suggests that patients with AML are likely to overestimate their prognosis. For example, many patients estimate their likelihood of survival as 90% at 5 years, when their oncologists have estimated their chances of 5-year survival at just 10%[5, 6].

Prognostic understanding may be especially important in informing treatment decisions near the end of life. In the solid tumor population, patients' understanding of the likelihood of cure impacts their decision-making about chemotherapy. For example, those who overestimate their chances of survival will often choose more aggressive therapies[7,

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8]. However, very little is known about prognostic understanding in hematologic malignancies, and there are important differences in treatments, outcomes, and quality of life in these diseases. For instance, patients with hematologic malignancies are more likely to choose aggressive therapies and to die in the hospital, while accessing palliative care services less frequently, as compared to patients with advanced solid tumors[9, 10]. Improving prognostic understanding is an important step toward facilitating goal-concordant care and shared decision-making in hematologic malignancies[11].

However, there is also concern that enhanced prognostic awareness may cause distress, and data are lacking regarding the relationship between leukemia patients' understanding of prognosis and their emotional well-being. Patients with AML face considerable distress from symptoms, information overload, and psychological challenges[12, 13]. A recent study assessing quality of life and mood in older patients with AML found that over one third suffer from significant depression or anxiety symptoms through their illness course[12, 14]. In the bone marrow transplant population, these stressors have been linked to higher risk of acute graft-versus-host disease and even decreased overall survival[15]. We do not know if a similar relationship exists between well-being and prognostic understanding in patients with AML. Better understanding this relationship could yield important insights to inform approaches to improving shared decision-making and enhancing the overall patient experience of AML treatment and survivorship.

In this single-institution, longitudinal study of patients undergoing active treatment for recently diagnosed or relapsed AML, we aimed to describe the relationship between prognostic understanding and emotional well-being. More specifically, we described prognostic understanding in patients at diagnosis and over time. We evaluated patient concordance with prognostic estimates determined by established, disease-related prognostic factors, both at time of diagnosis and repeatedly during the treatment course. In addition, we assessed levels of emotional well-being at similar intervals. We also evaluated the relationship between patients' prognostic understanding and their self-reported emotional well-being over time.

Methods

Study design

This was a longitudinal, prospective study conducted between February 2014 and March 2015. We enrolled 50 English-speaking adults with newly diagnosed or recently relapsed/refractory AML who had started inpatient or outpatient chemotherapy at Duke University no more than 1 week prior to enrollment, and who had not undergone a prior stem cell transplant. During the 6-month follow-up period (or until death), patients completed surveys about symptoms, prognosis, and treatment goals. Surveys were administered weekly when participants were inpatients, or monthly during outpatient treatment periods. The Institutional Review Board of the Duke University School of Medicine approved this protocol, and signed informed consent was obtained from all participants.

Assessment of prognostic understanding and emotional well-being

To assesses patients' prognostic understanding, we formed a two-question survey based on the 10-item Prognosis and Treatment Perception Questionnaire, a validated survey assessing patient beliefs regarding likelihood of cure, the importance of prognostic understanding, and preferences for information about treatment[16]. The first question assessed treatment intent by asking: "What is the goal of your current or most recent leukemia treatment," with a multiple-choice answer: "to cure, to live better, to live longer, to live better and longer, or I don't know." The second question asked: "Imagine 100 other people who have leukemia just like yours. Roughly how many of them would be cured if they received the same treatment as you?" with answers being: "over 90 people, 75 people, 50 people, 25 people, and less than 10 people," equating to a patient's expected chance of cure.

The validated Functional Assessment of Cancer Therapy family of questionnaires were used to evaluate patients' self-reported well-being. This includes an oncology-specific overall quality of life (QOL) scale (FACT-G) and a leukemia specific subscale, which together make up the FACT-Leu[17]. The FACT-G includes 27 items measuring physical, emotional, functional, and social well-being, while the leukemia subscale includes 17 items specific to patients with leukemia. Each item features a 0- to 4-point ordinal response scale and is then scored according to the published schema on facit.org[18, 19]. For example, on the FACT-Leu, one of the survey questions asks "I worry that my condition will get worse" with a response 0 reflecting not at all and 4 reflecting very much. Higher scores indicate a better QOL, and published data report clinically minimally interpretable differences for each scale and subscale[17, 19, 20]. A difference of 4–7 points on the overall FACT-G score is considered clinically meaningful, while a difference of just 1–2 points on the subscales signifies a clinically important difference[21]. The FACT-Leu and its subscales demonstrate high internal consistency ($\alpha = 0.75–0.96$) and adequate test–retest reliability (intraclass correlation range 0.765–0.890)[17]. Our analysis focuses on the EWB subscale.

Prognosis based on objective criteria (composite prognostic estimate)

A risk-stratification schema was used to generate objective estimates of each patient's prognosis, informed by data from published trials as summarized in the National Comprehensive Care Network Guidelines for AML[22]. This schema was based on factors known to be important in AML prognosis at the time of this study, including age, chromosomal abnormalities, FLT3-ITD and NPM1 mutation status, and whether the patient had primary versus secondary AML[23–25]. Patients with complex karyotypes or FLT3-ITD mutations were classified as "poor/adverse risk" ($N=32$), while those with normal chromosomes with no other abnormalities were classified as "intermediate risk," ($N=9$) and those with favorable chromosomal rearrangements (or normal chromosomes plus only an NPM1 mutation) were classified as "favorable risk" ($N=9$). These risk categories were then combined with disease status (relapse vs. newly diagnosed) to create estimated prognostic subgroups. Given the limited sample size and the overall predominance of poor/adverse-risk patients in our study, we dichotomized the sample into favorable ($N=7$) and unfavorable ($N=43$) estimated prognosis groups for analysis.

Comparison of patient and estimated prognosis

Based on the above definitions, patients were said to be in agreement with their estimated prognosis according to the following schema: (1) if their estimated prognosis was favorable and their survey response indicated a 50% or higher chance of surviving 5 years; or (2) if their estimated prognosis was unfavorable and their survey response indicated a < 50% chance of 5-year survival. This schema is based on published data showing better overall survival in patients with favorable risk cytogenetics versus intermediate or unfavorable risk cytogenetics, where survival rates are often cited at < 50% for the latter[26–28]. Other combinations of patient-assessed and estimated prognoses were considered discordant. Of note, the estimated prognosis was fixed for this analysis for each patient, and only the patients' self-reported chance of 5-year survival was variable over time, based on their response to each longitudinal survey question about their prognosis. In other words, we did not recalculate the estimated prognosis over time, even in cases when patients suffered a relapse during the study period.

Statistical methods

We used descriptive statistics to assess baseline patient characteristics. We then examined the frequency of prognostic discordance at baseline, wherein the patient-reported expected chance of 5-year survival did not agree with the estimated prognostic range for their AML risk group as defined above. We also described the association between discordance and patient-reported well-being, per the emotional well-being subscale of the FACT-Leu, at the baseline assessment. Chi-square and Wilcoxon rank-sum tests were used to compare characteristics of patients who agreed or disagreed with their estimated prognosis, and to compare measures of well-being between these two groups at enrollment. We then conducted three analyses to evaluate longitudinal trends in patients' prognostic understanding and emotional well-being. In the first analysis, we plotted the frequency of patients' discordance with their estimated prognosis during the treatment course, according to whether that estimated prognosis was favorable or unfavorable. In the second analysis, we evaluated trends in emotional well-being over time by plotting emotional well-being scores within strata of estimated prognosis, favorable or unfavorable. Finally, to assess the relationship between prognosis understanding and emotional well-being over time, we modeled emotional well-being scores as the outcome with discordance as the primary predictor longitudinally. The frequency of patient contact was variable in our cohort, because patients were followed through inpatient and outpatient treatment periods. To facilitate analysis at more discrete time points from the baseline visit, we grouped patient contacts into baseline (0–6 days), 1-month (7–28 days), 2-month (29–60 days), 3–4-month (61–120 days), 5-month (121–150 days), and 6-month (151–210 days) windows after the start of treatment. Statistical inference for all three longitudinal models were based on generalized estimating equations (GEE), to account for repeated observations from the same patient. We did not control for other demographic covariates due to the small sample size.

Results

A total of 67 eligible consecutive patients were approached, and 50 were enrolled. Table 1 shows baseline characteristics of the 50 enrolled patients, demonstrating a mean age of 63.1 years, an equal distribution of males and females, and a majority being Caucasian (42/50, 84%). A total of 43 (86%) patients were receiving an intensive induction regimen, while 7 (14%) received a palliative, low-intensity treatment regimen with azacitidine or decitabine, which was the standard of care at the time of data collection. The estimated prognosis was unfavorable for 43 (86%) patients and favorable for 7 (14%) patients.

A total of 455 surveys were completed amongst the 50 patients, averaging 9 surveys per patient. One patient with favorable risk AML did not respond to the survey question regarding prognosis estimation and was thus excluded from the analysis. The prognostic question was otherwise

Table 1 Participant characteristics and baseline data

	Total ($N = 50$)
Age, years	
Median (IQR)	63.1 (53.3, 68.4)
Gender	
Female	25 (50.0%)
Male	25 (50.0%)
Highest level of education completed	
Some high school	1 (2.0%)
High school diploma or equivalent	16 (32.0%)
Some college	8 (16.0%)
Vocational-technical degree	4 (8.0%)
Associate's degree	8 (16.0%)
Bachelor's degree	4 (8.0%)
Some graduate school	1 (2.0%)
Graduate degree	8 (16.0%)
Marital status	
Married	36 (72.0%)
Divorced	5 (10.0%)
Single	5 (10.0%)
Widowed	4 (8.0%)
Race	
Caucasian/White	42 (84.0%)
Black or African American	4 (8.0%)
Asian	1 (2.0%)
American Indian/Alaska Native	2 (4.0%)
More than one race	1 (2.0%)
Patient-reported treatment goal (per baseline survey)	
Cure	27 (54.0%)
Longevity	11 (22.0%)
Palliation of symptoms only	1 (2.0%)
No response	11 (22.0%)
Treatment regimen	
Induction chemotherapy (like the 7 + 3 regimen)	43 (86.0%)
Palliative chemotherapy (such as hypomethylating agent)	7 (14.0%)
Disease status	
Newly diagnosed	43 (86.0%)
Relapsed	7 (14.0%)
Composite estimated prognosis	
Favorable/good	7 (14.0%)
Unfavorable/poor	43 (86.0%)

answered 375 times, amounting to a 92% response rate. Eighteen (36.7%) patients felt that they had > 90% chance of cure, 6 (12.2%) felt they had > 75% chance of cure, and 12 (24.5%) felt they had > 50% of cure. Since most participants were classified into the estimated unfavorable prognosis group, we therefore found that most patients overestimated their prognosis at the baseline assessment (Fig. 1). Most strikingly, 15 of 43 (34.8%) patients with estimated unfavorable risk disease estimated a > 90% chance of cure. At baseline, 27 (54%) patients reported a treatment goal of "cure," 11 (22%) to "live longer," 1 (2%) "palliation of symptoms," and 11 (22%) did not respond to this particular question.

Overall, only 15 of 49 (30.6%) patients agreed with their estimated prognosis at the time of treatment initiation (Table 2). Of note, patients with favorable risk disease were more likely to agree with their estimated prognosis (4/6 patients, or 67%) compared to patients with unfavorable

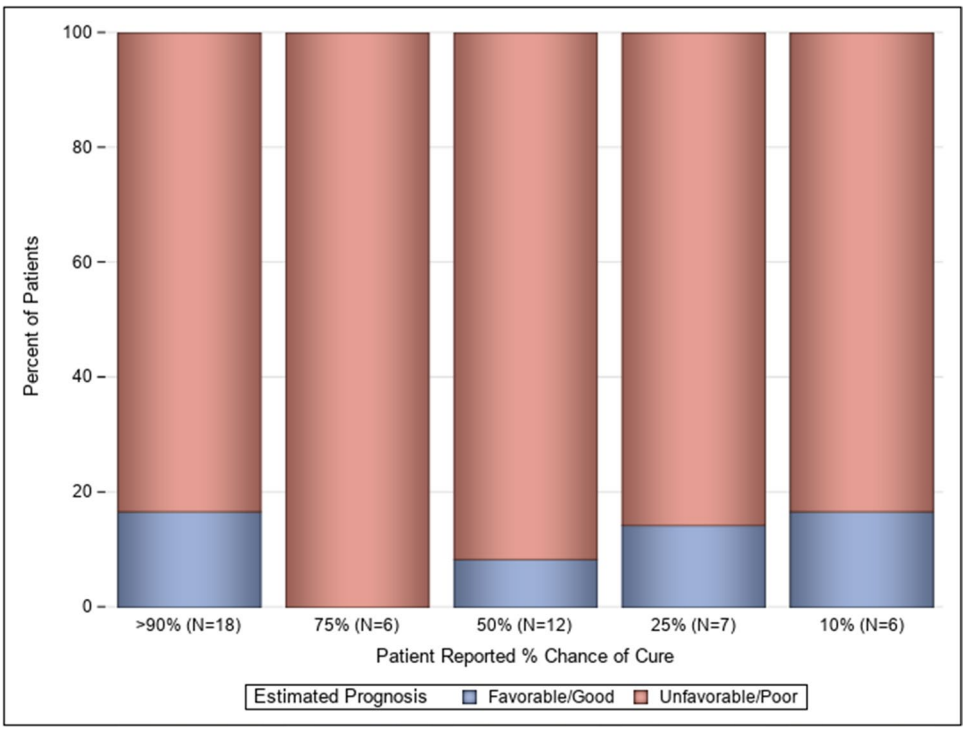

Fig. 1 Patients' estimate of survival probability at treatment initiation, by estimated prognosis. For the estimated favorable prognosis group, 3/6 (50%) of patients estimated > 90% of cure. However, for those with estimated unfavorable risk, 15/43 (34.8%) estimated > 90% chance of cure, 6/43 (13.9%) 75% chance of cure, and 11/43 (25.6%) 50% chance of cure, vastly overestimating their prognosis

Table 2 Patient prognosis at time of treatment initiation

	Concordant patient-reported prognosis ($N=15$)	Discordant patient-reported prognosis ($N=34$)	Total ($N=49$)	*P* value
Composite estimated prognosis				0.0408[1]
Favorable	4 (26.7%)	2 (5.9%)	6 (12.2%)	
Unfavorable	11 (73.3%)	32 (94.1%)	43 (87.8%)	
Patient-expected chance of 5-year survival				0.0001[1]
Over 90%	3 (20.0%)	15 (44.1%)	18 (36.7%)	
75%	0 (0.0%)	6 (17.6%)	6 (12.2%)	
50%	1 (6.7%)	11 (32.4%)	12 (24.5%)	
25%	6 (40.0%)	1 (2.9%)	7 (14.3%)	
Less than 10%	5 (33.3%)	1 (2.9%)	6 (12.2%)	
FACT-Leu total score	102.0 (90.0, 125.3)	125.5 (105.0, 143.0)	117.0 (101.0, 137.0)	0.0151[2]
FACT-Leu subscale	41.0 (33.0, 51.0)	47.5 (39.3, 57.0)	44.0 (37.0, 54.0)	0.0967[2]
FACT-G total score	65.0 (52.0, 73.3)	75.5 (68.0, 87.0)	73.0 (64.8, 86.0)	0.0104[2]
Emotional well-being subscale	12.0 (8.0, 19.0)	19.5 (17.0, 22.0)	19.0 (11.0, 21.0)	0.0057[2]
Functional well-being subscale	8.0 (6.0, 14.0)	14.5 (12.0, 20.0)	13.0 (8.0, 18.0)	0.0103[2]
Social well-being subscale	23.0 (18.0, 26.0)	23.0 (22.0, 25.0)	23.0 (20.0, 25.0)	0.5416[2]
Physical well-being subscale	20.0 (15.0, 23.0)	21.5 (18.0, 25.0)	21.0 (15.0, 24.0)	0.3671[2]

[1]Chi-square, [2]Wilcoxon

risk AML (11/43, or 25.6%). At treatment initiation, patients who agreed with their prognosis at treatment initiation had lower (worse) median emotional well-being scores (12 [IQR 8, 19] vs. 19.5 [IQR 17, 22]; $p=0.01$), as well as overall lower (worse) FACT-G scores (65 [IQR 52, 73.3] vs. 75.5 [IQR 68, 87] $p=0.01$), and FACT-LEU total scores (102 [IQR 90, 125.3] vs. 125.5 [IQR 105, 143]; $p=0.02$). Each of these differences is larger than published minimally clinically important difference thresholds for these scales/subscales.

In longitudinal analyses, patients with an unfavorable prognosis exhibited consistently higher rates of prognostic discordance (~80%) over time compared with patients who had a favorable prognosis (~50% discordance) (Fig. 2) (OR = 7.25, 95% CI 1.21, 43.37, adjusted for time of assessment; $p = 0.03$).

At baseline, both estimated prognostic groups had similar mean emotional well-being subscale (EWB) scores ($p = 0.07$). At 1 month, patients with a favorable prognosis had an increased (better) mean EWB score, which remained stable for the remainder of the study period. In contrast, the unfavorable prognosis group did not change notably from baseline. While modeling emotional well-being, we did not find a statistical association between emotional well-being and prognostic understanding longitudinally (mean difference, unfavorable − favorable = −0.39 [95% CI −0.81, 0.03]; $p = 0.07$) (Fig. 3); however, the low p value and appearance of separation in curves in Fig. 3 suggests there was not adequate power to detect this difference.

Discussion

These prospective data support findings from cross-sectional studies showing that many patients with AML overestimate their prognosis. We also found, however, that these prognostic perceptions do not appear to change significantly over time. This is surprising and important. Studies to date have not examined this relationship longitudinally; thus, our analysis adds important new insights to the literature on prognostication and highlights areas for further study. Most striking was the persistence in prognostic discordance in the subset of patients with an unfavorable prognosis, many of which felt that they had a > 90% chance of cure. The chance of cure in high-risk AML cases like these is 10–25%, at best, and is under 10% in the highest risk subgroups, particularly among older patients or those with relapsed disease[2–4]. Considering that many patients likely experienced a relapse and/or serious complication during the study, it is even more surprising that prognostic estimates did not adjust downwards over time in the unfavorable prognosis group, as more clinical complications and setbacks occurred in their illness course over time. This is concerning, and warrants further research and ultimately the development and testing of interventions to improve AML patients' understanding of prognosis.

We also found that patients with AML demonstrate a wide range of emotional responses to their illness, which was associated with patient understanding of their prognosis. This too is an important and new finding. At baseline, patients who exhibited worse emotional well-being tended to also better understand their prognosis. The small subset of patients who correctly understood their poor prognosis experienced significantly lower (worse) emotional well-being scores on the FACT-G, and even had worse overall quality of life by total FACT-G score and by the FACT-Leu. In contrast, patients who disagreed with their estimated prognosis and overestimated their chance of survival exhibited higher

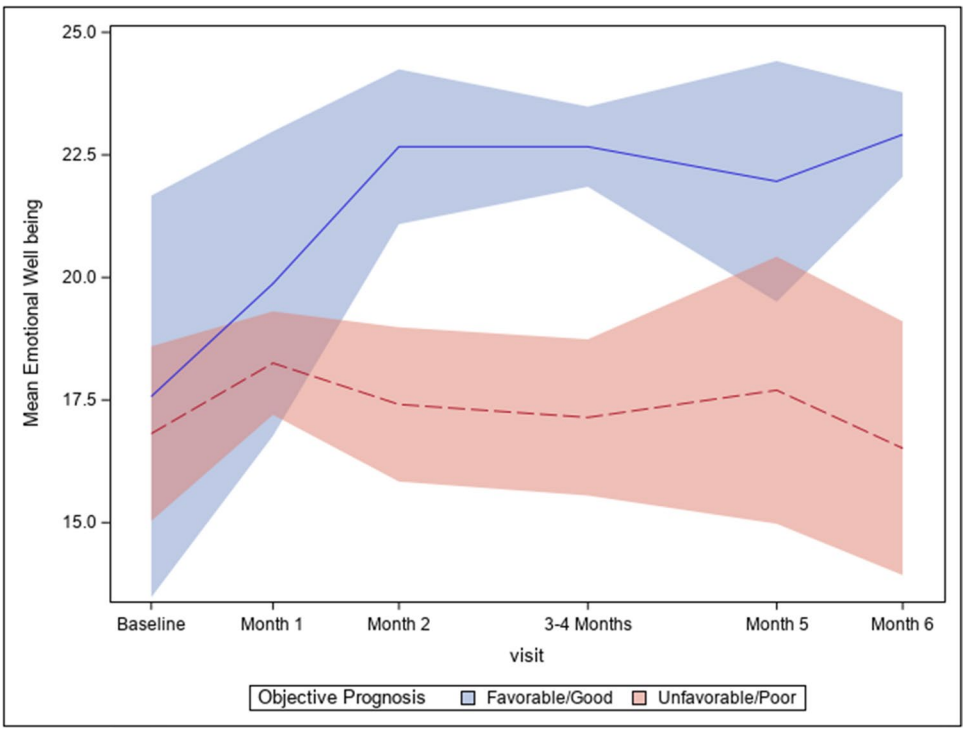

Fig. 2 Prognostic discordance over time, by estimated prognostic group. The figure below represents the rates of prognostic discordance and the 95% confidence limits across all encounters for a given prognostic group. The lines represent the rates, and the shaded regions represent the 95% confidence limits. Patients with unfavorable prognosis consistently exhibited higher rates of prognostic discordance compared to patients with favorable prognosis. For the favorable group, there were 6 patients at baseline, 13 observations at month 1, 4 observations at month 2, 13 between 3 and 4 months, 5 at month 5, and 10 at month 6. For the unfavorable group, there were 43 patients at baseline, 82 observations at month 1, 59 observations at month 2, 59 between 3 and 4 months, 20 at month 5, and 30 at month 6

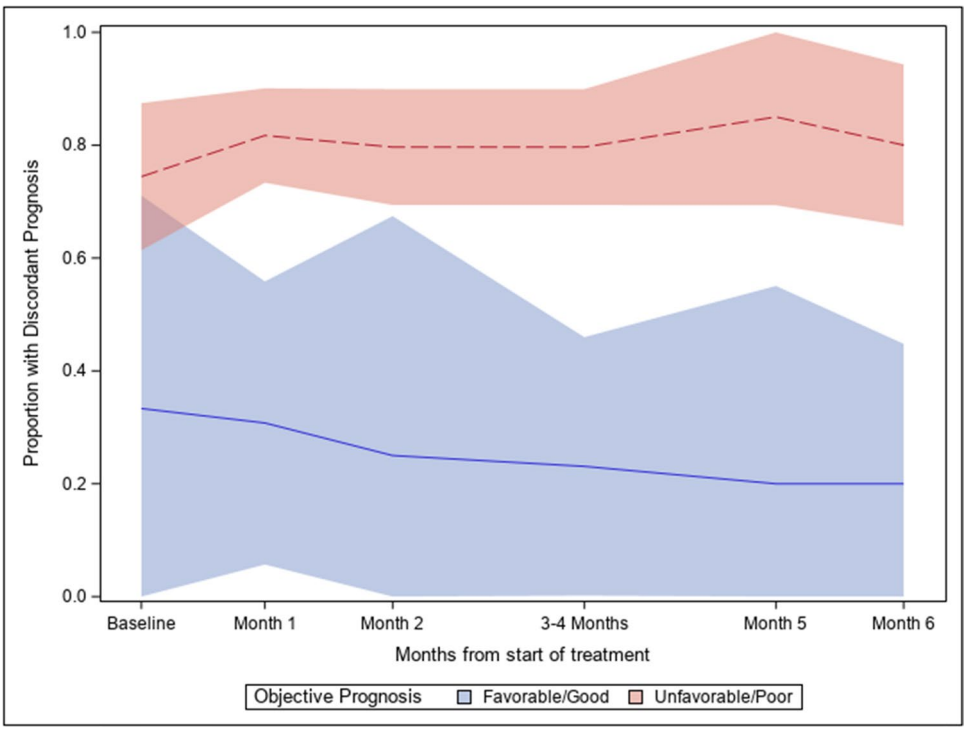

Fig. 3 Emotional well-being over time, by prognostic group. The figure below represents the mean EWB scores and the 95% confidence limits across all encounters for a given prognostic group. The lines represent the estimated means and the shaded regions represent the 95% confidence limits. Initially, patients in both prognostic groups had similar EWB scores (meaningful clinical difference 1–2 points). However, patients with favorable prognosis had improved EWB scores over time, whereas those patients with unfavorable prognosis did not change significantly from baseline, although we did not find that emotional well-being varied by prognosis over the study period (mean difference, unfavorable − favorable = −0.39 [95% CI −0.81, 0.03]; $p = 0.07$). For the favorable group, there were 7 patients at baseline, 17 observations at month 1, 6 observations at month 2, 18 between 3 and 4 months, 5 at month 5, and 14 at month 6. For the unfavorable group, there were 43 patients at baseline, 87 observations at month 1, 61 observations at month 2, 62 between 3 and 4 months, 20 at month 5, and 32 at month 6

(better) emotional well-being. While our methods cannot prove causation, these findings suggest that prognostic overestimation may be emotionally protective, and that correct prognostic understanding may be associated with emotional distress. In addition, as our cohort included mostly unfavorable risk patients, we were unable to do further analyses examining whether it is prognostic discordance, or simply acknowledging a poor prognosis, that is associated with worse EWB. It may be that those patients who knew that their disease was higher risk exhibited less emotional well-being as they knew that they had a higher chance of complications and death, rather than the discordance itself. This calls for further study and intervention development to improve the psychological care of patients with poor prognosis AML.

These findings outline two important unmet needs in AML care. First, prognostic overestimation remains a significant challenge for patients and clinicians. With the growing number of therapies offered in AML, each with their own set of toxicities and quality-of-life implications or other tradeoffs, prognostic understanding is only becoming more difficult to facilitate, yet it remains necessary to make informed decisions regarding a patient's course of care. In addition, we must appreciate the significance of psychological distress that patients may face in light of a cancer diagnosis. For some, using denial as a defense mechanism may reduce the anguish associated with a cancer diagnosis, which in of itself can be traumatic. We must work to improve patient understanding of prognosis, but how to best do that requires further study. Knowing now that prognostic discordance remains relatively fixed over time, we should recognize the need to address prognosis at diagnosis, treatment initiation, and longitudinally. This may lead to improved prognostic awareness for our patients, which is linked to goal-concordant care at the end of life.

Second, emotional well-being is generally poor in AML and may be even worse in patients who better understand their prognosis. Normative data from the US population, and from patients with cancer, show mean EWB scores of 19.9 and 18.1, respectively[29]. Thus, even our prognostically discordant AML population, with a median score of 19, is worse off than the general US population, and our

concordant population's median score of 12 is quite markedly worse than even other patients with cancer. This suggests there are important and unmet emotional needs in the AML patient population, calling for attention and intervention. We must routinely identify and offer more psychosocial support to those patients with emotional distress, and arguably to patients with AML overall.

Supportive care services must be in place to improve patients' overall distress and well-being levels through their treatment course. Integrated palliative care interventions have yielded improvements in emotional well-being in other cancer populations[30–32]. Models of integrated palliative care should be tested in AML to examine the impact on prognostic understanding and emotional well-being. In a randomized clinical trial of integrated palliative care in patients with high-risk AML, we saw marked improvements in overall quality of life, symptoms of anxiety and depression, and symptoms of post-traumatic stress, at 2 weeks into the induction chemotherapy hospitalization, and sustained at 6 months[33]. However, the impact of such interventions on prognostic awareness remains unknown. One might also ask the question of whether this detriment to emotional well-being is worth the improved prognostic understanding; more research is needed into this important question. Regardless, given that those with more accurate perceptions of curability had worse emotional well-being, the current study suggests a need for adequate psychosocial support alongside efforts to improve prognostic understanding in AML. Further efforts are needed to improve emotional well-being and prognostic understanding in AML.

While our research demonstrates unique findings, it has a few limitations. First, we had a small patient population at a single-site academic center, mostly representing inpatients receiving high-intensity induction chemotherapy. In addition, the population accrued was younger and less racially diverse than what is otherwise reported. That said, since AML is a rare disease, these 50 patients reflect the majority of adults with AML who were treated in this hospital during the study period. Regardless, it is important to replicate this work in other contexts, including outpatient settings. In addition, there were limitations in the estimated analyses grouping patients based on a literature- and guideline-derived definition of favorable and unfavorable risk, which were necessary due to the small sample size. In our cohort, we had few favorable risk patients, but had we had more of these patients, comparisons of prognostic concordance/discordance would be expected to be different than those of unfavorable risk patients, which was not reflected in our analysis. We were therefore unable to examine whether unfavorable risk disease itself is simply associated with worse EWB overall. Of note, we did not recalculate estimated prognostic estimates over the study period, even in cases when patients suffered relapses. This was the most conservative approach to the issue, yet we still found significant prognostic discordance regardless of time period, and observed that patient perception did not vary significantly over time. In addition, it is important to note that what and how much patients were told by their oncologists was not assessed as part of this study; this should be a focus of future research. Furthermore, while these findings suggest that patients who accurately understand their prognosis may be more emotionally unwell, we are unable to establish causality. Lastly, several novel therapies have been approved since we completed this study, with significant impacts on remission rates and treatment patterns. Further studies are needed to assess the impact of novel therapies on prognostic understanding and emotional well-being in AML. Despite these stated limitations, our analysis has yielded important new insights and generated hypotheses that are essential to explore further, to inform enhancements to AML patient care.

To our knowledge, this longitudinal observational study is the first to examine AML patients' understanding of prognosis over time and to explore its association with emotional well-being. We found that emotional well-being is generally poor in this population, and that prognostic overestimation persists over time. Patients with a more accurate understanding of prognosis may have worse emotional well-being. Further efforts are needed to improve patients' understanding of their prognosis both at diagnosis and over time, and to improve their emotional well-being.

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Author contribution All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by A.S., S.L., S.W., J.T., and T.W.L. The first draft of the manuscript was written by A.S., and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Availability of data and material These data have not been deposited into any central repository. Requests for access can be made in writing to the corresponding author, and are subject to Duke University rules and regulations for data protection and access.

Code availability Statistical code can be made available on written request to the corresponding author.

Declarations

Ethics approval The Institutional Review Board of the Duke University School of Medicine approved this protocol. Informed consent was obtained from all individual participants included in the study.

Consent to participate Participants provided signed informed consent to participate in the parent study that led to the dataset analyzed for this report. No consent could be provided for this secondary analysis, which was approved and within the scope of the IRB's approval of this study and the analysis of resulting data.

Consent for publication Participants provided signed informed consent to participate in the parent trial, which includes acknowledgment that resulting insights may be published. No separate consent could or should be contained for this secondary analysis of previously conducted data, nor is this required by the IRB.

Conflict of interest T.W.L. reports the following disclosures from the past 24 months: personal fees for consulting or advisory boards from AbbVie, Agios, AstraZeneca, Amgen, Astellas, CareVive, BMS/Celgene, Daiichi-Sankyo, Flatiron, Heron, Pfizer, and Seattle Genetics; royalties from UpToDate; speakers bureau fees from Agios, AbbVie, and BMS/Celgene; grants and/or research contracts from the American Cancer Society, AstraZeneca, BMS, Jazz Pharmaceuticals, the NINR/NIH, and Seattle Genetics.

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