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Quality of life and physical function in adults treated with intensive chemotherapy for acute myeloid leukemia improve over time independent of age†



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ABSTRACT

Objectives: Intensive chemotherapy (IC) is the primary treatment of acute myeloid leukemia (AML) but is associated with significant toxicity, particularly in older adults. We characterized the impact of AML and its treatment on quality of life (QOL) and physical function in younger (age 18–59) and older (age 60+) patients with AML over 1 year from diagnosis.

Materials and Methods: AML patients undergoing IC without stem-cell transplant at two tertiary care centers were enrolled in a prospective, longitudinal study. Assessments were done pre-IC and at 7 time points over the next year. QOL, fatigue, and physical performance (grip strength, 2-minute walk test (2MWT), timed chair stands) were measured in all patients whereas daily function was measured only in older patients. Data were analyzed using mixed effects regression models.

Results: 237 patients were recruited (140 younger and 97 older, 56% male). One-year survival was 79% and 60% among younger and older patients, respectively. For patients in remission, global QOL and fatigue improved significantly over time ($p < 0.001$ for both); trends were similar between older and younger patients. Grip strength did not change over time ($p = 0.58$) whereas both the 2MWT ($p < 0.001$) and timed chair stands ($p < 0.001$) improved significantly. Daily function improved significantly over time ($p = 0.003$).

Conclusions: Survivors of AML in remission after IC achieve significant improvements in QOL, fatigue, and physical function over time with similar trajectories for older and

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younger patients. These data suggest that appropriately selected older patients do well following IC.

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1. Introduction

Acute myeloid leukemia (AML) is an aggressive hematological malignancy primarily occurring in older adults, with a median age of onset of 68 years, and a 3-year survival below 20% in adults over age 60.¹ There are three main initial treatment options: intensive chemotherapy (IC), supportive care, and investigational agents, with IC being preferred for most otherwise fit patients in terms of disease control and improved survival.² IC consists of one or two cycles of induction followed by several cycles of consolidation chemotherapy. Although IC is associated with improved survival, it is also associated with significant toxicity and long periods of hospitalization, which may negatively affect quality of life (QOL) and physical function.

Older adults with AML have a poorer prognosis than younger adults and higher treatment-related morbidity and mortality.³ Moreover, aging is associated with significant declines in physiologic function and reparative ability across a wide range of organ systems.^{4,5} This leaves older adults particularly vulnerable to treatment toxicity and prolonged hospitalization, which may reduce QOL and worsen physical function. This perception of major declines in QOL and physical function may contribute to the significantly lower rates of IC in older versus younger adults with AML.^{6,7}

To date, relatively few studies have analyzed QOL and physical function in patients undergoing this treatment. One prospective study ($n = 27$) found that induction treatment was associated with physical and psychological distress, as well as decreased QOL.⁸ Another study involving 61 patients aged 16–70 undergoing IC concluded that subjective benefits reported by patients outweighed the adverse effects,⁹ although data were not analyzed by age group. We are aware of only one study that prospectively compared QOL and physical function in older and younger adults undergoing IC.¹⁰ We previously reported a preliminary analysis of the first 103 patients included in the present study who were assessed over the first three cycles of chemotherapy. We found small improvements in global QOL and physical function, with no change in fatigue, over these three cycles. In general, younger and older adults had similar trajectories of QOL over time, although physical function improved more in younger adults.¹⁰

Understanding QOL and physical function in survivors of AML is important for several reasons. First, there have been slow but steady improvements in longer-term survival, particularly among younger patients, over the past few decades.^{6,11,12} As survival continues to improve, longer-term survivorship issues become more pertinent. Second, the prognosis of older adults lags significantly behind younger adults, and clinicians continue to debate the merits of offering IC to newly diagnosed older adults with AML. This is particularly important with the availability of non-intensive therapies such as hypomethylating agents. Understanding the level of QOL and physical function in older adults who achieve remission with IC is important, since these two areas are paramount in the minds of older adults with cancer.¹³

Our objectives were: (1) to investigate the impact of the treatment of AML with IC on QOL, fatigue, and physical function over 12 months from diagnosis; (2) to compare changes in these outcomes between older (aged ≥ 60 years) and younger (18–59 years) patients; and (3) to examine the impact on daily activities in older adults.

2. Methods

2.1. Patient Population

This prospective longitudinal cohort study was conducted at two university-affiliated tertiary care cancer centers in Toronto, Canada: the Princess Margaret Cancer Centre and the Odette Cancer Centre. The study was reviewed and approved by respective institutional research ethics boards. Patients were recruited from May 2008 to March 2012. Consecutive adult patients age 18 years or older who were newly diagnosed with AML, and who opted to undergo IC were eligible. Patients were recruited before or within three days of starting cycle 1 of IC, which consisted of daunorubicin 60 mg/m²/day for three days plus cytosine arabinoside (Ara-C) 200 mg/m²/day (100 mg/m²/day for patients aged ≥ 60) as a continuous infusion for seven days. Patients achieving a complete remission (CR) then received two cycles of consolidation therapy as described previously.¹⁰ Patients who did not achieve CR with one cycle of IC could receive a second induction, consisting of mitoxantrone, etoposide, and Ara-C.¹⁴

Patients who consented were seen at eight time points over 12 months: pre-IC, after each of the first three cycles of chemotherapy, which were roughly at 4–6 weeks, 9–12 weeks, and 13–16 weeks, and then at six months, eight months, ten months, and 12 months after diagnosis.

Demographic information, disease characteristics, performance status (PS) using the Eastern Cooperative Oncology Group (ECOG) scale, and co-morbidities were obtained from the patient's hospital record. Cytogenetic risk group was categorized using the Medical Research Council system.¹ At each visit, patients completed a series of self-administered questionnaires and three physical function tests. We recorded when patients were present for the visit but too unwell or unwilling to complete physical function tests. Patients were censored from the study if they went on to bone marrow transplantation (BMT), at the time of disease relapse, or if they did not achieve CR after one or two cycles of IC with no further plans for IC.

2.2. Patient-reported Outcomes

Patient-reported outcomes completed at each visit included the European Organisation for the Research and Treatment of Cancer (EORTC) 30-item questionnaire (QLQ-C30)¹⁵ and the Functional Assessment of Cancer Therapy fatigue subscale (FACT-Fatigue).¹⁶ The EORTC QLQ-C30 is a validated generic QOL scale for patients with cancer that has been widely

translated and is broadly used. It contains 30 questions covering global health, five QOL domains (physical, role, emotional, social, and cognitive function), and several symptom scales/items. The QLQ-C30 is scored from 0 to 100, with higher scores representing better QOL. The FACT-Fatigue

Table 1 – Baseline patient demographics and disease characteristics.

Baseline characteristic	Younger patients (<60)	Older patients (≥60)	p
N	140	97	
Age range, years	21–59	60–81	–
Gender, % male	69 (49%)	64 (66%)	0.01
First language, % English	83 (59.3%)	52 (53.6%)	0.38
Marital status			0.01
Married	102 (72.9%)	71 (73.2%)	
Divorced/separated	11 (7.9%)	15 (15.5%)	
Single	23 (16.4%)	5 (5.2%)	
Widowed	4 (2.9%)	6 (6.2%)	
Race			0.15
White	94 (67.1%)	73 (75.3%)	
Black	5 (3.6%)	8 (8.3%)	
Oriental	21 (15.0%)	8 (8.3%)	
South Asian	16 (11.4%)	7 (7.2%)	
Other	4 (2.9%)	1 (1.0%)	
Smoking status			0.04
Current smoker	6 (4.3%)	5 (5.2%)	
Never smoked	81 (57.9%)	40 (41.2%)	
Quit smoking	53 (37.9%)	52 (53.6%)	
ECOG performance status			0.40
0	64 (45.7%)	39 (40.2%)	
1	49 (35.0%)	44 (45.4%)	
2	23 (16.4%)	13 (13.4%)	
3	4 (2.9%)	1 (1.0%)	
Mean Karnofsky score % (SD)	80.6% (15.2)	80.9% (13.4)	0.85
Median Charlson index score (range)	0 (0–3)	0 (0–3)	0.32
Median number of comorbidities (range)	1 (0–7)	2 (0–7)	<0.001
Cytogenetic risk group			0.02
Favorable	35 (25.0%)	9 (9.3%)	
Intermediate	20 (14.3%)	12 (12.4%)	
Normal	49 (35.0%)	48 (49.5%)	
Unfavorable	25 (17.9%)	21 (21.6%)	
Inconclusive	11 (7.7%)	7 (7.2%)	
AHD	17 (12.1%)	30 (30.9%)	<0.001
Mean hemoglobin (SD)	94.0 (18.8)	92.8 (18.1)	0.60
Mean WBC count (SD)	23.0 (48.1)	27.4 (45.5)	0.48
Mean neutrophil count (SD)	2.9 (7.7)	2.6 (4.1)	0.71
Mean platelets (SD)	91.2 (111.8)	94.6 (80.3)	0.79
Mean peripheral blast % (SD)	32.3 (31.8)	31.4 (32.1)	0.84
Mean bone marrow blast % (SD)	58.2 (30.0)	55.4 (26.6)	0.47

Abbreviations: ECOG = Eastern Cooperative Oncology Group; AHD = antecedent hematologic disorder; SD = standard deviation; WBC = white blood cell. Only values less than 0.05 should be italicized.

Table 2 – Baseline quality of life and physical performance by age group.

Measurement [mean (SD)]	Younger patients (<60)	Older patients (≥60)	p
Quality of life	140	97	
Global health	45.7 (26.9)	45.5 (26.7)	0.93
Physical functioning	74.2 (25.8)	75.3 (28.2)	0.76
Role functioning	44.9 (33.2)	48.7 (37.4)	0.41
Emotional functioning	64.9 (25.0)	72.6 (23.9)	0.02
Cognitive functioning	74.9 (24.7)	76.9 (24.9)	0.65
Social functioning	42.2 (33.3)	55.1 (34.5)	0.005
FACT-F score (/52)	29.0 (12.9)	30.3 (13.9)	0.11
Beck Depression Inventory (/63)	11.7 (6.9)	8.8 (6.1)	0.003
Physical performance			
Grip strength (kg)	30.6 (12.5)	28.4 (11.4)	0.18
Unable to do, n	1	5	
2-minute walk distance (ft)	383.8 (118.6)	357.9 (128.7)	0.16
Unable to do, n	25	23	
Chair stands/min	25.5 (9.8)	23.5 (8.7)	0.14
Unable to do, n	21	22	

FACT-F = Functional Assessment of Cancer Therapy Fatigue subscale. Notes: Quality of life measures are scored out of 100 except where otherwise indicated. p-Values are bolded where <0.05. Domain values are bolded where differences are potentially clinically important. See text for minimum clinically important differences.

consists of 13 items exploring fatigue. Overall scores range from 0 (maximal fatigue) to 52 (no fatigue).

Mood was assessed using the Beck Depression Inventory, a psychometrically valid measure consisting of 21 items (range of scores 0–63).¹⁷ Higher scores indicate greater depressive symptoms.

Patient-reported daily function was assessed with the Lawton–Brody Index of instrumental activities of daily living (IADL), consisting of eight IADL items and a score ranging from 0 to 17.¹⁸ Higher scores indicate greater independence.

Other than the IADL measure, all questionnaires were administered to younger and older patients at each visit. The IADL measure was restricted to older adults and was administered at six time points. This is summarized in Supplementary Table 1.

2.3. Objective Physical Function Tests

Three measures were chosen to assess fitness and deconditioning, while being sensitive to the challenges of assessing patients with cancer undergoing active chemotherapy. Grip strength was measured three times in each hand with a Jamar dynamometer.¹⁹ Grip strength correlates well with upper-body muscle strength and is a significant predictor of disability²⁰ and mortality in older adults.²¹ Endurance was assessed with the two-minute walk test (2MWT),²² a shorter version of the six-minute walk test.²³ Timed walking tests are validated sub-maximal endurance measures of fitness in all age groups.^{22–24} Lower body fitness was measured with ten timed chair stands^{25,26} and is predictive of lower extremity disability and function in older adults.

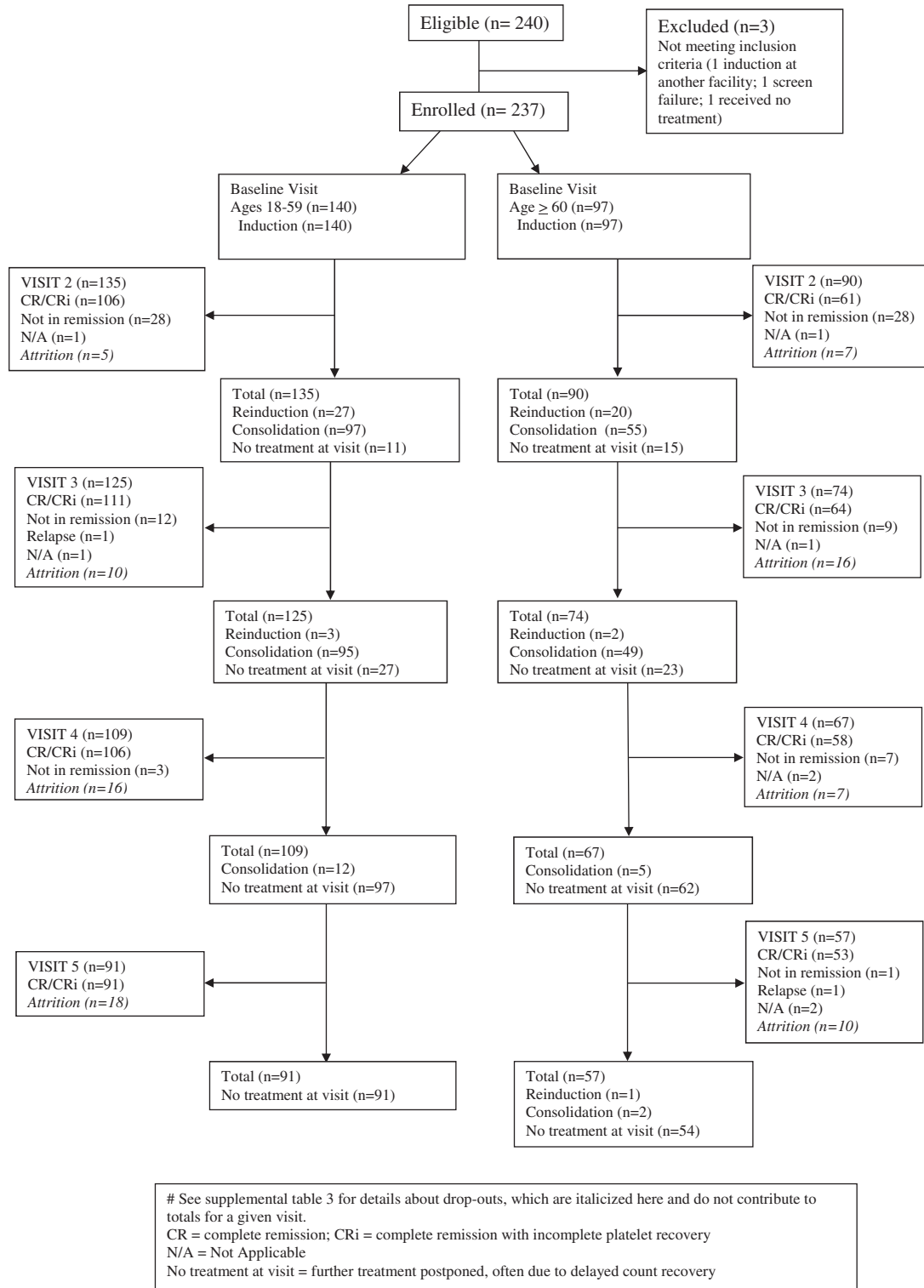
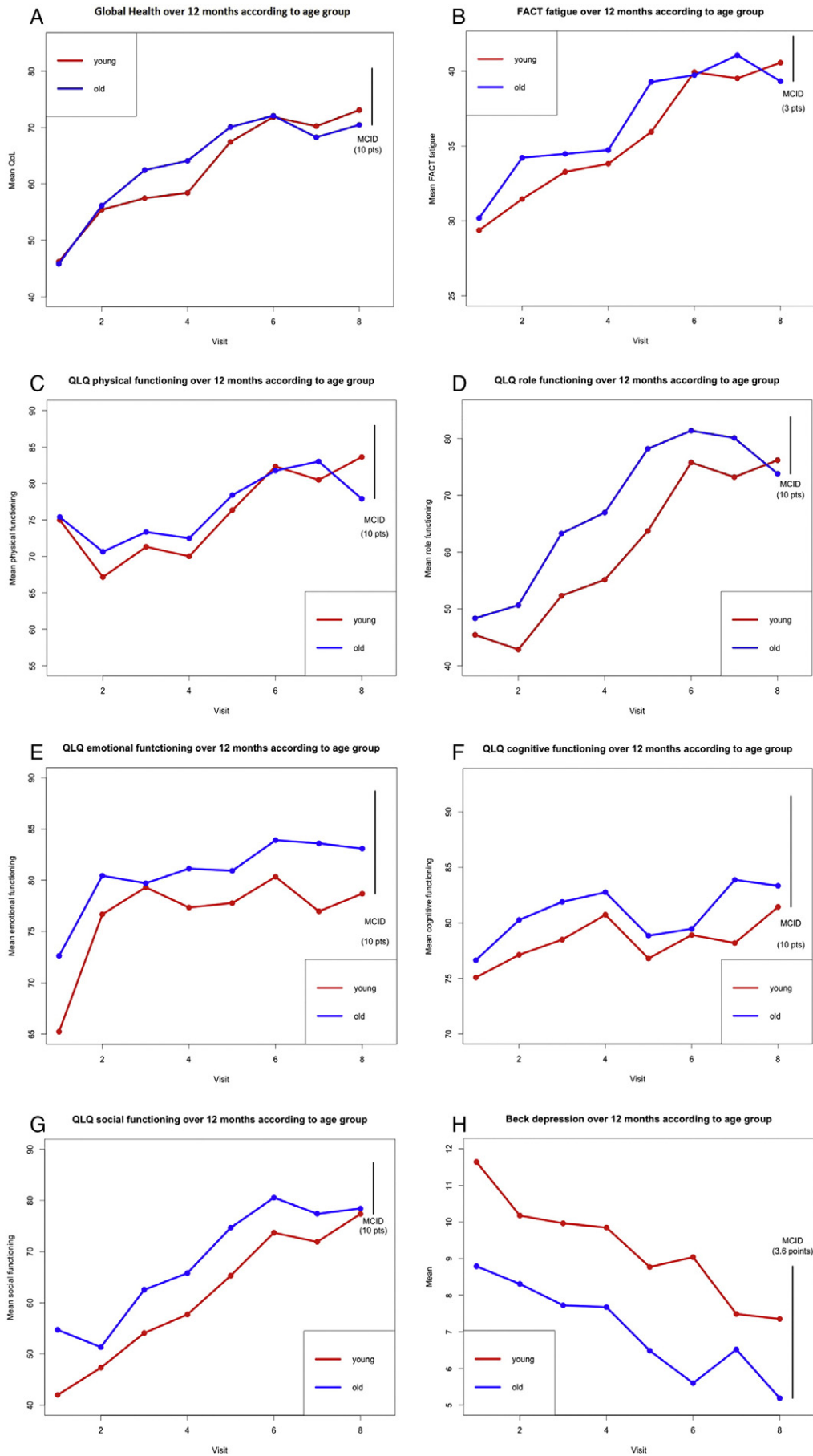


Fig. 1 – Flow sheet of treatments and remission status among younger and older patients on study. This figure shows treatment between visits and remission status per visit among younger and older patients on study. Details on attrition are provided in Supplementary Table 4; summary information is given here and these patients do not contribute to totals for a given visit. CR = complete remission; CRi = complete remission with incomplete platelet recovery; N/A = not applicable/available; no treatment at visit = further treatment postponed, often due to delayed count recovery.



2.4. Other Outcomes

As measures of health care utilization, we captured the number of hospitalizations, emergency room visits, and intensive care unit admissions per patient.

2.5. Primary Outcomes and Minimum Clinically Important Differences

Our co-primary outcomes were Global Health (from the QLQ-C30) and FACT-fatigue. For all outcomes, we determined the minimum clinically important difference (MCID) based on published literature. The MCID was 10 points for all QLQ-C30 scale scores,²⁷ 3–4 points²⁸ for the FACT-F, and 3.6 points²⁹ for the Beck Depression Inventory.

2.6. Statistical Analyses

Baseline characteristics were described using means for continuous data and counts for categorical data. Differences in baseline characteristics between older and younger patients were compared using Student's t-test for continuous variables and the chi-square test for categorical variables.

To examine changes over time in our primary and secondary outcomes (QOL and physical function), we used linear mixed effects regression models with subject-specific random effects for visit, and fixed effects for age group, gender, smoking status, baseline performance status, and hemoglobin. Hemoglobin was modeled as a time-dependent covariate. To test for differences between age groups in slopes over time, we added an age-by-time interaction term. Other outcomes were described as counts and medians. For all statistical comparisons, a p-value of 0.05 was considered significant. No correction was made for multiple significance testing.³⁰ Analyses were performed using the nlme package in R 3.1.0 (Statistical Computing, Vienna, Austria).

2.7. Sensitivity Analysis for Missing Data

Given the likelihood that patients who drop out or do not provide outcome data tend to be sicker than participating subjects,³¹ we formally assessed the impact of missing patient data on our outcomes.³² Any patient who missed a visit, who did not fill in a QOL questionnaire, or was unable to complete a physical function test due to fatigue or illness was assigned a score equal to the median of the worst quintile of scores from the patient's age group at that particular visit for the specific test. Data that were missing because a patient died or withdrew from the study due to disease progression were not imputed. We used Rubin's rule to combine between-subject and within-subject variances to get a summary estimate and

standard errors. We used these to derive an approximate p-value.

2.8. Exploratory Analyses

We performed two exploratory analyses. First, we examined age as a categorical variable rather than dichotomous variable. Thus we compared multivariable models using the approach detailed above with a four-level categorical age variable (age 50 or younger, 51–60, 61–70, over age 70) to models using a dichotomous age variable (under age 60 versus age 60+). Model performance was compared using the Akaike Information Criterion. Second, we examined the effect of baseline ECOG PS on outcomes by age group. For this analysis, PS was dichotomized into PS 0–1 versus 2–3 and adjusted for covariates as detailed above.

3. Results

Among 393 potentially eligible patients, we approached 355 (90%), of whom a total of 237 patients (140 younger, 97 older) were enrolled (67%). The most common reasons for lack of enrolment were lack of interest or feeling overwhelmed. Further details and a breakdown by age group are provided in Supplementary Fig. 1.

The median ages for the younger and older groups were 52.9 and 69.7 years, respectively. A higher proportion of younger patients had favorable risk cytogenetics, although this was not statistically significant ($p = 0.12$). Older patients had a higher number of comorbidities and were more likely to be male, retired, and have an antecedent hematologic disorder. Other baseline and demographic characteristics were similar between the two age groups (Table 1).

At baseline, there was no difference between older and younger patients in either global health or fatigue (Table 2). On average, patients reported moderate fatigue. Among QOL domains, emotional functioning and social functioning were higher in older adults; other domains were similar among older and younger patients. Mood was also better in older patients (Table 2). Younger and older patients had similar performance on grip strength ($p = 0.18$), the 2MWT ($p = 0.16$), and chair stands ($p = 0.14$) (Table 2).

3.1. Clinical Outcomes

Of the 237 patients, 166 (70%) achieved CR after one or two cycles of induction chemotherapy (74% and 65% among younger and older patients, respectively, $p = 0.22$). Treatments received per cycle and remission status of patients are shown by age group in Fig. 1. One-year survival was 71% overall (79% versus

Fig. 2 – Changes over time in self-reported outcomes by age group. Vertical axes of panels were scaled to correspond to 1.5 standard deviations in height, and the minimal clinically important difference for each measure is shown as a vertical bar. Panels show the European Organisation for the Research and Treatment of Cancer core 30-item questionnaire (EORTC QLQ-C30) global health scale (panel A), the Functional Assessment of Cancer Therapy fatigue subscale (panel B), physical functioning (panel C), role functioning (panel D), emotional functioning (panel E), cognitive functioning (panel F), and social functioning (panel G) from the EORTC QLQ-C30, and the Beck Depression Inventory (panel H).

60%, respectively, $p = 0.003$). Survival curves by age group are shown in Supplementary Fig. 2.

3.2. Changes in QOL, Fatigue, and Depression Over Time

QOL, fatigue, and depression results over time are shown in Fig. 2. Global health and fatigue scores both improved over time (both $p < 0.0001$). Among QOL domain scores, all but the physical function and cognitive function domains improved over time. The greatest improvements occurred in global health, role functioning, and social functioning. Depression scores also improved significantly over time ($p < 0.0001$).

3.3. Age-based Differences in Patient-reported Outcomes Over Time

In adjusted mixed effects models, there was no difference in slopes over time (i.e., recovery) by age group for any of the primary or secondary patient-reported outcomes (Fig. 2, data not shown).

3.4. Objective Physical Function Over Time and by Age Group

Objective physical function results are shown in Fig. 3. Overall grip strength remained stable over time ($p = 0.74$ for effect of time in adjusted model) with no difference by age group ($p = 0.059$ for the age-by-time interaction). Visual inspection of the actual values suggested an initial decline with subsequent recovery in both age groups over time (Fig. 3). Performance on both the 2MWT and timed chair stands improved over time ($p < 0.001$), although there was an age-by-time interaction for the latter outcome ($p = 0.048$ in adjusted model), suggesting greater recovery in younger adults.

3.5. Daily Function Over Time

IADL improved significantly over time in older adults ($p = 0.003$, Supplementary Fig. 3).

3.6. Other Outcomes

Health care utilization by age group is shown in Supplementary Table 2.

3.7. Impact of Missing Data

By the end of the 12-month follow-up, slightly more than half the patients (144 of 237, 60.7%) had died, were censored, or withdrew from the study (Supplementary Table 3). Although attrition was greater among older adults, retention was excellent among eligible participants; the majority of the dropouts were due to death (16 younger, 21 older) or undergoing BMT (30 younger, 12 older). Seven younger patients dropped out voluntarily. Similarly, only six older patients dropped out voluntarily. No patient was lost to follow-up.

After imputing data for patients who were alive and still in remission but too unwell to provide outcome data, findings were not materially different from our primary analysis for any of our patient-reported outcomes (data not shown).

Among objective physical function measures, the age-by-time interaction for timed chair stands was attenuated ($p = 0.071$); findings for grip and 2MWT were unchanged (data not shown). Supplementary Table 4 provides details on the number of patients per age group who had data imputed at each time point and reasons for missing data among patients remaining on study.

3.8. Exploratory Analyses

We examined the impact of substituting a 4-level categorical age variable instead of a dichotomous age variable on our main outcomes. This approach confirmed the main analysis for all PROs. In contrast, for physical performance measures, findings suggested that the best recovery in all 3 physical performance measures was seen among those age 50 or younger. Patients age 51–60 and 61–70 had similar recoveries, and patients over age 70 had the worst recovery. However, for all 3 physical performance measures, differences among all but the youngest age group were smaller than the MCID (data not shown).

We also examined the effect of baseline ECOG PS on our main one-year outcomes. This analysis was restricted to younger patients as there were too few older patients with PS 2–3 to facilitate analysis. In general, a PS of 2–3 was associated with significantly worse global health, fatigue, physical functioning, role functioning, and all 3 measures of physical performance over time than a PS of 0–1 (data not shown).

4. Discussion

AML is often a rapidly progressive disease associated with significant symptoms and a large impact on QOL. Our results showed a similar symptom burden for older and younger patients at the time of diagnosis. IC is associated with significant treatment-related morbidity and mortality.³³ With increasing age there is a greater incidence of treatment toxicity, lower CR rates, higher rates of relapse, and shorter survival.² This has led to a pervasive pessimistic attitude towards treating AML with IC in older adults, coupled with an intense effort to find alternative less-intensive treatment approaches in these patients.³³ Despite this, there has been little published data regarding the effects of IC on QOL over the ensuing months post-treatment in both younger and older patients. Our findings should reassure clinicians, as we demonstrated statistically significant and clinically important improvements in QOL, fatigue, and mood in both younger and older AML survivors over the first year after the start of IC. Of particular note is the remarkably similar course of recovery in these parameters among older and younger patients, with comparable improvements in patient-reported outcomes.

With respect to objective physical function, our data suggest a lesser degree of improvement in these measures among older adults, particularly for grip strength. This is likely for two reasons. First, otherwise healthy older adults have less physiologic reserve, leading to greater toxicity and slower recovery after IC. Second, sarcopenia (reduced muscle mass) is common in older adults, which would lead to lower expected normative values than a younger cohort. Importantly, physical function results for all patients, particularly younger adults, were

significantly below the expected results for the general population. For example, normative data for grip strength is 50.6 kg for patients under 60, and 41.7 kg for adults over

60.¹⁹ Mean grip strength was below 35 kg at all time points in our study, indicating relatively profound loss of upper extremity strength, particularly among younger patients. This is likely due to the combination of significant weight loss, with its resultant loss of muscle mass, physical inactivity during IC, and fatigue. Grip strength is a significant predictor of overall survival and disability in middle-aged and older cohorts,³⁴ and our results emphasize the need to examine exercise-based interventions to counteract reductions in fitness and potentially improve longer-term recovery.

Our prior study reported on the first four time points (i.e., during chemotherapy) for the first 103 patients.¹⁰ The current study significantly extends those prior findings, by including a much larger cohort, more sophisticated analyses, and four additional time points of follow-up (approximately 8 months) post-treatment. Our findings regarding QOL are similar to smaller series in predominantly younger cohorts with AML.^{9,35,36} They are also similar to those from a prior pilot study conducted by our group among 65 older adults with AML treated with either intensive or non-intensive therapies.³⁷ With respect to objective physical function, our findings of reduced physical function during and after IC extend those of several small exercise intervention studies in patients with AML.^{38–41} Changes in daily self-reported function have not been reported previously in AML patients.

An important future direction of this work will be to correlate our findings with serum cytokine levels, which were collected at four time points over one year in consenting participants. This will be used to examine cytokine signatures as predictors of QOL recovery as well as relapse among older AML patients./ relapse among older AML patients.

We recognize several important limitations to our study. First, our study was limited by both referral and selection bias. All of the patients received IC at two specialized tertiary care centers. Although the vast majority of patients with AML in our large catchment area (approximately 6 million people) are referred to these centers for evaluation, some very old patients with co-morbidities are likely not referred.⁶ In addition, older patients at our centers are more carefully selected to undergo induction on the basis of disease biology, comorbidities, and performance status compared to younger patients.⁴² In particular, few patients age 70 or older with adverse-risk cytogenetics were offered IC outside a clinical trial setting.³⁷ This may partially explain the observed outcomes in both QOL and physical function among older adults in our study.

A second limitation was survivorship bias. Our cohort consisted of only individuals who remained in CR. This is because we do not intend to predict the trajectory of all those who complete IC, but those who are still alive and in remission over time. Patients who relapsed, died, withdrew, or underwent BMT were not included in subsequent visits. Although few

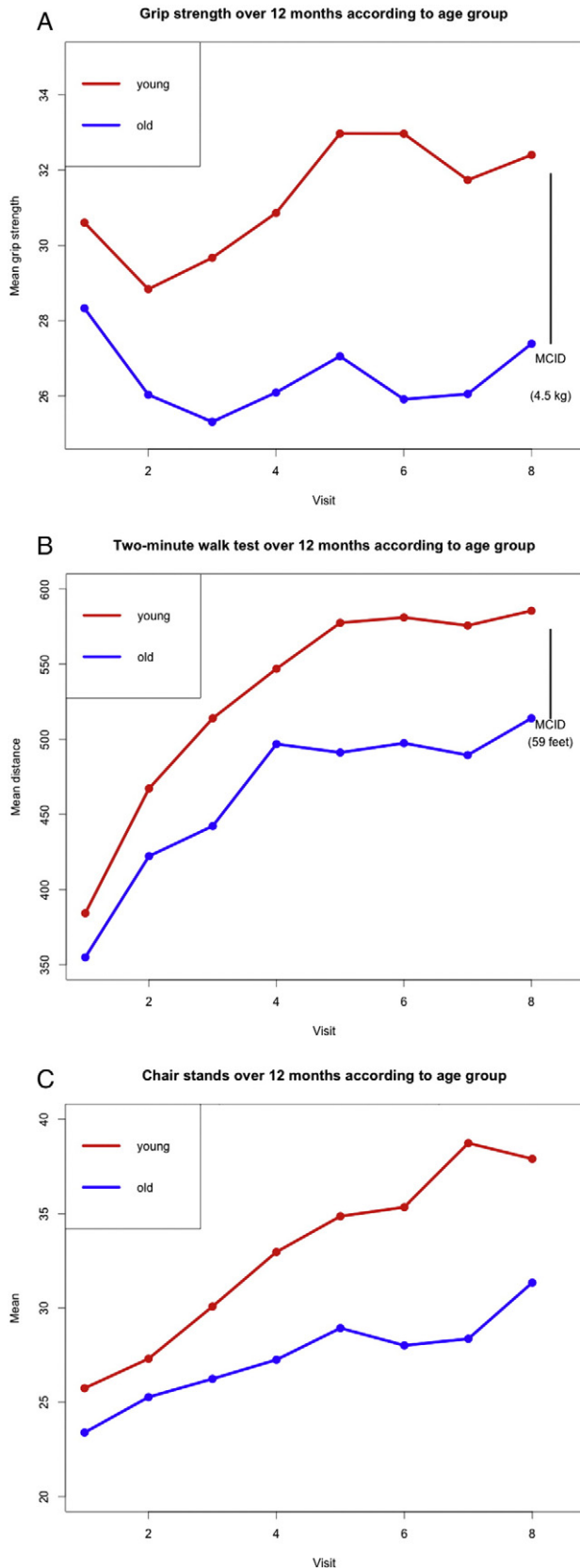


Fig. 3 – Changes over time in objective physical function by age group. Vertical axes of panels were scaled to correspond to 1.5 standard deviations in height, and the minimal clinically important difference for each measure is shown as a vertical bar. Panels show grip strength (panel A), 2-minute walk test distance (panel B), and timed chair stands (panel C).

people dropped out for voluntary reasons, this cannot eliminate the possibility of survivorship bias. We explored the possible impact of data that were missing because patients were doing poorly by running a second set of analyses with missing values replaced by values chosen from the worst quintile of observed scores at the corresponding visit. Although this sensitivity analysis is a standard approach and reinforced our primary findings, it is still an imperfect method of dealing with missing data.³²

Our analyses of the impact of performance status and exploration of age as a categorical variable should be viewed as exploratory, since these were post-hoc analyses and limited by small sample sizes, particularly among older adults. Finally, despite being the largest study to date in this area our sample size is still modest, particularly given the predictable attrition in the older age group over time. Thus, small changes over time or differences between age groups may have been missed.

5. Conclusion

In conclusion, QOL and physical function are similarly affected in older and younger patients by a diagnosis of AML and treatment with IC. While older adults may recover physical function more slowly than younger adults, appropriately selected older adults have similar QOL to younger adults during and after IC. IC should not be precluded in older adults on the basis of concerns around excess toxicity or detrimental effects on patient well-being. The impact of exercise interventions during or after IC on QOL and functional recovery should be explored.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.jgo.2015.04.002>.

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