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Comorbidity, age and mortality among adults treated intensively for acute myeloid leukemia (AML)

Bernard Tawfik, MD¹, Timothy Pardee, MD, PhD^{2,3}, Scott Isom, MS⁴, Sarunas Sliesoraitis, DO, PharmD¹, Allison Winter, M.D.¹, Julia Lawrence, DO², Bayard L. Powell, MD², and Heidi D. Klepin, MD, MS²

¹Department of Internal Medicine, Wake Forest Baptist Health, Winston-Salem, NC

²Department of Internal Medicine, Section on Hematology and Oncology, Wake Forest School of Medicine, Winston-Salem, NC

³Department of Cancer Biology, Winston-Salem, NC

⁴Division of Public Health Sciences, Department of Biostatistics, Wake Forest School of Medicine, Winston-Salem, NC

Abstract

Introduction—Our goal was to characterize comorbidities among adults receiving intensive therapy for AML, and investigate their association with outcomes.

Methods—We retrospectively analyzed 277 consecutive patients with newly diagnosed AML treated intensively at the Comprehensive Cancer Center of Wake Forest University from 2002–2009. Pretreatment comorbidities were identified by ICD-9 codes and chart review. Comorbidity burden (modified Charlson Comorbidity Index [CCI]) and specific conditions were analyzed individually. Outcomes were overall survival (OS), remission, and 30-day mortality. Covariates included age, gender, cytogenetic characteristics, hemoglobin, white cell count, lactate dehydrogenase, body mass index, and insurance type. Cox proportional hazards models were used to evaluate OS; logistic regression was used for remission and 30-day mortality.

Corresponding Author: Heidi D. Klepin, MD, MS, Section on Hematology and Oncology, Wake Forest School of Medicine, hklepin@wakehealth.edu, P: 336-716-5772; F: 336-716-5687.

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Study concept and design: B. Tawfik, T. Pardee, J. Lawrence, H. Klepin

Data acquisition: B. Tawfik, S. Sliesoraitis, A. Winter

Quality control of data and algorithms: B. Tawfik, H. Klepin, S. Isom

Data analysis and interpretation: B. Tawfik, T. Pardee, S. Isom, J. Lawrence, B. Powell, H. Klepin

Statistical analysis: S. Isom

Manuscript preparation: B. Tawfik, T. Pardee, S. Isom, H. Klepin

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Results—In this series, 144 patients were ≥60 years old (median age 70 years, median survival 8.7 months) and 133 were <60 years (median age 47 years, median survival 23.1 months). Older patients had a higher comorbidity burden (CCI 15.8% versus 26%, $p<0.001$). Prevalent comorbid conditions differed by age (diabetes 19.2% versus 7.5%; cardiovascular disease 12.5% versus 4.5%, for older versus younger patients, respectively). The CCI was not independently associated with OS or 30-day mortality in either age group. Among older patients, diabetes was associated with higher 30-day mortality (33.3% vs. 12.0% in diabetic vs. non diabetic patients, $p=0.006$). Controlling for age, cytogenetic characteristics and other comorbidities, the presence of diabetes increased the odds of 30-day mortality by 4.9 (CI 1.6–15.2) times.

Discussion—Diabetes is adversely associated with 30-day survival in older AML patients receiving intensive therapy.

Keywords

Acute Myeloid Leukemia; Aged; Comorbidity; Survival; Remission Induction; Diabetes

Introduction

Acute myeloid leukemia (AML) is a disease of older adults with a median age of onset of 68–72 years (1). Older age is consistently associated with worse survival and higher treatment-associated morbidity (2, 3). Poor outcomes for older adults with AML are attributable to both tumor biology and age-related patient characteristics that decrease treatment tolerance (4, 5). Identifying measurable patient characteristics that contribute to suboptimal outcomes among older adults can help individualize pre-treatment assessment and inform supportive management of those patients. One area of particular interest is the assessment of comorbidities, because they are common among older patients and can influence treatment decision-making and toxicity risk.

Older patients with AML often have a substantial comorbidity burden (6–11). Prevalence estimates of at least one major comorbid condition range from 30–70% in most studies. Furthermore, many studies of older adults with AML show a relationship between greater comorbidity burden (measured by Charlson Comorbidity Index [CCI] or Hematopoietic Stem Cell Transplantation Comorbidity Index [HCT-CI]) and worse outcomes including lower remission rates, higher risk of 30-day mortality and worse OS (6–9, 12, 13). However, not all studies have confirmed these relationships (10, 14, 15). Comparisons across studies are limited due to differences in patient selection and treatments received. In addition, accounting for patient characteristics such as physical function may attenuate some of the independent effects of comorbidity burden on outcomes (10). Finally, measuring comorbidity burden alone may miss the prognostic importance of specific conditions. Understanding which comorbidities have a greater influence on treatment tolerance would better inform management decisions for individual patients than comorbidity burden scores alone.

The aims of this study were to characterize comorbidity by age within an intensively treated AML population, and investigate associations among comorbidities and OS, remission rates, and 30-day mortality.

Methods

Study population

Using electronic medical records, we retrospectively analyzed the characteristics of consecutive patients who met the following inclusion criteria: newly diagnosed AML, receipt of intensive induction treatment at the Comprehensive Cancer Center of Wake Forest University between 2002–2009, and age > 18 years. Patients with acute promyelocytic leukemia (APL) or those receiving “less intense” regimens (including hypomethylating agents, palliative chemotherapy, or no treatment) were excluded from the study. Regimens of chemotherapy were deemed “intense” if they included cytarabine and anthracycline. Patients were also excluded if they received prior chemotherapy for another hematological malignancy or if the date of induction was not recorded. This study was approved by the Institutional Review Board of Wake Forest School of Medicine.

Measures

Predictor variables—Comorbidity data were collected using ICD-9 codes and chart review from data available in the electronic medical record on or before the date of induction chemotherapy. Comorbidity burden was measured using the modified CCI, excluding AML (8, 16). Individual comorbidities evaluated (and their respective ICD-9 codes) were myocardial infarction (410–412), congestive heart failure (398–398.99, 402–402.91, 428–428.43), peripheral vascular disease (440–447.9), dementia (290–291.5, 294–294.9), cerebrovascular accident (430–433.99, 435–435.9), chronic obstructive pulmonary disease (491–493.22), connective tissue disease (710–710.9, 714–714.33, 725), peptic ulcer disease (531–534.91), liver disease (571–573.39, 070–070.9, 570–572.4), hemiplegia (342–342.12, 434–434.11, 436, 437–437.7), renal disease (403–404.93, 580–586), diabetes (250–250.93), and malignancy (140–195.8, 196–199.2).

Covariates—We collected baseline data on age (stratified at the time of diagnosis as age 60 vs. < 60 years(4)), gender, body mass index (BMI), race, type of insurance, cytogenetic risk stratification score (17), and type and date of induction chemotherapy. We also collected laboratory data, including glucose, hemoglobin, bilirubin, white blood cell count, creatinine, and lactate dehydrogenase, from the date of presentation for induction therapy in the hospital.

Outcomes—Outcomes were OS from date of induction chemotherapy initiation, treatment response as defined by complete remission, and 30-day mortality. Complete remission (CR) was defined as absolute neutrophil count > 1000/microliter (mcl), platelets 100,000/mcl and no residual or extra medullary disease. Complete remission with incomplete count recovery (CRi) was defined as < 5% bone marrow blasts and transfusion independence with persistent cytopenia with either an absolute neutrophil count < 1000/mcl or platelets < 100,000/mcl (18). For analyses, the remission outcome included CR+CRi. Thirty-day mortality was calculated from date of initiation of induction chemotherapy. The cause of death among those who experienced 30-day mortality was abstracted from the medical record. For exploratory analyses the cause of death was defined as the primary precipitant of multi-system organ failure/death as attributed in the discharge summary.

Statistical Analysis—Data were stratified by age group (<60, ≥60 years) and descriptive statistics were calculated to examine differences between the strata. Categorical variables were compared using a Chi-squared test and a t-test was used to compare continuous measures. Some of the measures required a log transformation in order to meet the normality assumption. Cox proportional hazards models were used for bivariate analysis as well as the fully adjusted model to estimate survival. For all analyses, comorbidity burden (CCI) was categorized as none vs. 1 or more based on the distribution of comorbidity scores. We also performed analysis of prevalent individual conditions including diabetes mellitus, renal disease, myocardial infarction/congestive heart failure, and chronic obstructive pulmonary disease. Myocardial infarction and congestive heart failure were combined into a single cardiac variable due to low prevalence of each individual condition.

Cox proportional hazards models were used for bivariate analysis as well as the fully adjusted model to estimate survival. Both remission (CR+CRi) and 30-day mortality were analyzed using logistic regression models. Bivariate analyses assessed the unadjusted association between comorbidity burden or individual comorbid conditions and the outcomes of interest. Additionally, covariates which had a p-value of 0.2 or less in bivariate analyses were deemed to contribute information and thus included in the fully adjusted models. Hazard ratios from both the unadjusted and adjusted models for comorbidity burden and the comorbidities of interest are reported. The same covariates were found to be significant contributors in both the adjusted models for remission in younger patients and in older patients (age, BMI, and cytogenetic risk). Similarly, adjusted models for 30-day mortality included age and cytogenetic risk. Contributing covariates differed by age and comorbidity measure in OS adjusted models. The model for comorbidity burden in younger patients included age, BMI, cytogenetic risk, insurance type, and WBC, while the corresponding model for older patients included age, cytogenetic risk and LDH. The model assessing individual comorbidities in younger patients included age, BMI, cytogenetic risk, insurance type and WBC, while the corresponding model for older patients included age, cytogenetic risk and LDH. In each of the adjusted models considering an individual comorbid condition as a predictor, the remaining comorbid conditions were included as covariates to control for potential confounding.

Limited exploratory analyses were conducted including comparison of attributed causes of death by diabetic status using a Fisher's Exact test among older adults and logistic regression to evaluate the association between admission blood glucose values and 30-day mortality. Blood glucose was considered as a continuous variable. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC).

Results

We reviewed 368 consecutive cases of individuals with newly diagnosed AML and identified 277 patients who met our inclusion criteria (Figure 1). Baseline characteristics are presented in Table 1. The most common treatment regimens included anthracycline +cytarabine+etoposide (44% older versus 81% younger patients) and anthracycline +cytarabine (37% older versus 9% younger patients). Some patients had no cytogenetics results due to no metaphases being identified or missing verification (6.3% older, 4.5%

younger). Consistent with previous results, older patients had a lower percentage of favorable cytogenetics (low risk: 3.0% older vs. 26.0% younger, intermediate risk: 73.3% older vs. 54.3% younger and high risk: 23.7% older vs 19.7% younger, $p < 0.0001$). Compared to younger patients, fewer older patients achieved a CR (52.1% older vs. 73.3% younger, $p = 0.0003$) or CR+CRi (62.7% older vs. 81.7% younger, $p = 0.0005$). Older patients showed a trend toward higher 30-day mortality compared to their younger counterparts, (16.0% vs. 8.3, $p = 0.05$) with statistically significant shorter median overall survival (8.7 vs. 23.1 months, $p < 0.0001$).

As expected, a larger proportion of older adults had comorbidities (CCI 1) (58.3% older vs. 26.3% younger, $p < 0.0001$). Overall, the prevalence of individual major comorbid conditions was low. Older patients were more likely than younger patients to have diabetes (19.2% older vs. 7.5% younger, $p = 0.005$), cardiac disease (12.5% older vs. 4.5% younger, $p = 0.018$) and COPD (12.5% older vs. 3.8% younger, $p = 0.008$).

In this cohort, comorbidity burden (CCI 1) was not associated with OS in unadjusted or adjusted analyses in either age group (Table 2). Among older patients, after adjusted analyses, only age remained significantly associated with OS ($p = 0.018$), and cytogenetic risk group showed a trend toward significance ($p = 0.064$). In the younger cohort, cytogenetic risk group ($p < 0.0001$) was associated with survival, with BMI near significance ($p = 0.071$). None of the most prevalent comorbidities (diabetes, cardiac disease, renal disease) had a statistically significant association with OS in adjusted analysis in either age group, although point estimates in the older cohort for diabetes and renal disease suggested a negative association.

Comorbidity burden (CCI 1) was not associated with achieving CR+CRi in either age cohort in unadjusted or adjusted analyses (Table 3). Characteristics associated with complete remission were higher BMI ($p = 0.004$) and cytogenetic risk score ($p = 0.001$) in the younger cohort. Among prevalent comorbid conditions, a diagnosis of renal disease at the time of induction chemotherapy was associated with lower odds of remission for younger patients (odds ratio [OR] 0.2; 95% confidence intervals [CI] 0.03–1.0) after adjusting for age, BMI, cytogenetic risk group, diabetes, COPD, and cardiovascular disease. Among older patients there were no statistically significant associations between individual conditions and complete remission status with the point estimate for diabetes suggestive of an adverse relationship.

Comorbidity burden (CCI 1) was not associated with 30-day mortality in either age group (Table 4). The presence of diabetes was associated with over a four-fold higher odds of 30-day mortality for older adults in adjusted analyses (OR 4.9, 95% CI 1.6–15.2). Among older patients, the 30-day mortality was 33.3% versus 12.0% ($p = 0.006$) for older adults with or without diabetes (Figure 2). Among younger adults, the 30-day mortality was 20.0% versus 7.3% (with and without diabetes respectively), but was not statistically significant ($p = 0.16$).

Exploratory analyses were conducted to further evaluate the relationship between diabetic status and 30-day mortality among older adults. The attributed primary causes of early death

for diabetics were infectious complications (88.8%) and bleeding complications (11.2%) compared to infectious complications (50%), bleeding complications (21.4%), myocardial infarction (14.3%) and acute renal failure not attributed to infection (14.3%) among non-diabetics. There was a trend towards a greater proportion of diabetics dying from infectious complications which did not achieve statistical significance ($p=0.08$). The association between baseline glucose values and 30-day mortality was also explored among older adults. The mean $\pm$ standard deviation (SD) baseline glucose values were 119.8 $\pm$ 29mg/dl for non-diabetic patients and 171.8 $\pm$ 70.7mg/dl for patients with known diabetes. There was an association between baseline glucose value and 30-day mortality (OR 1.1, CI 1.0–1.2) using a 10mg/dl unit of change. Specifically, the odds of death within 30 days of induction were 1.1 times greater for each 10 mg/dl increase in baseline blood glucose.

Discussion

In this retrospective analysis of 277 adults treated with intensive induction therapy for AML, we found no statistically significant association between comorbidity burden measured by the modified CCI and clinical outcomes of OS, remission, or 30-day mortality. However, when considering individual comorbidities, we found an association between presence of diabetes and higher 30-day mortality among older adults, and presence of renal disease and lower remission rates among younger patients. These results are hypothesis-generating and provide evidence to further investigate the prognostic significance of diabetes during AML therapy, including mechanisms underlying this association which may lead to interventions.

The utility of measuring comorbidity burden (using the CCI or HCT-CI) to predict treatment outcomes for older adults with AML has been investigated in several single-institution studies and population-based analyses with mixed conclusions(5, 7–15, 19, 20). Many studies have shown an association between comorbidity burden and outcomes (specifically survival, remission, and early mortality) (5, 8, 9, 11–13, 20). For example, data from Surveillance, Epidemiology, and End Results (SEER) linked with Medicare showed an association between claims-based CCI and shorter survival among over 5,000 older adults with newly diagnosed AML(5). As with single- institution studies, treatment was not uniform. Many individuals received low-intensity therapy or supportive care, possibly due to comorbidity (5, 11, 12, 20).

Three studies that investigated the predictive value of comorbidity burden specifically among older adults treated intensively for AML showed an association with outcomes. Etienne et al. retrospectively analyzed 133 older adults (age ≥ 70 years) treated intensively and showed an association between higher CCI scores and lower remission rates (8). Two studies showed an association between higher pre-treatment HCT-CI scores and risk of early mortality and shorter survival (9, 13).

Similar to our results, a few studies of older adults treated intensively for AML did not show robust associations between comorbidity burden and outcomes (10, 14, 15). Results of a Danish population-based cohort study of adults treated intensively for AML suggested that performance status is a stronger predictor of survival than comorbidity burden (15). In a single-institution study of older adults who received geriatric assessments before intensive

induction therapy, the HCT-CI was not significantly associated with survival, whereas measures of physical function and cognition were predictive (10). Another study of AML patients 80 years of age suggested that neither the CCI or HCT-CI accurately predicted survival in this age group.

The lack of consistency in the literature regarding the importance of comorbidity burden may be in part explained by differing patient populations and treatment characteristics. The sensitivity of comorbidity measurement tools used may differ, and the use of variable cutoffs on each scale influence results. The individual conditions summed for a given comorbidity score are frequently not captured, and may influence results. In the current analysis, all patients were considered fit for intensive induction by their treating physician, likely minimizing presence of uncompensated comorbidity. Use of claims data in addition to chart review may also have influenced outcomes, resulting in a more comprehensive comorbidity assessment inclusive of conditions which were clinically compensated.

Investigating the importance of individual comorbidities in patients with AML is an important next step, not only in better refining risk stratification but also informing management strategies that may improve treatment tolerance. Our findings suggest the presence of diabetes and renal disease at diagnosis may influence treatment outcomes. While renal disease, inclusive of acute renal failure, may be a surrogate marker of disease burden, diabetes is typically a preexisting condition that may be a marker of vulnerability. The present analysis is the first to highlight a potential negative association between diabetes and early mortality among older adults with AML.

Diabetes has been associated with increased cancer incidence and higher mortality among people diagnosed with various cancers, including hematologic malignancies (21, 22). However, few studies have focused on patients with acute leukemia. In a retrospective study of 97 older adults investigating the prognostic significance of BMI during intensive therapy for acute myeloid leukemia, presence of diabetes was not significantly associated with overall survival (median survival of 268 or 321 days for those with versus without diabetes, respectively)(23). Early mortality, however, was not a reported outcome. Consistent with our results, a retrospective study by Ali et al showed higher in-hospital mortality in patients with AML who had hyperglycemia during hospitalization (OR, 1.38; 95% CI, 1.23–1.55; $P < .001$)(24). Results were adjusted for disease state, cytogenetic characteristics, treatment type, and disease response; higher mortality remained associated with hyperglycemia of above 110 mg/dL, 150 mg/dL, or 200 mg/dL (OR, 1.44 [1.27–1.63]; 1.46 [1.28–1.67], and 1.56 [1.25–1.94], respectively; all $P < 0.001$). These results are also consistent with findings from a study of patients with acute lymphocytic leukemia which showed an association between hyperglycemia, increased number of infections, and decreased disease-free survival (25). Diabetes may predispose to early mortality by increasing the risk of infectious complications (26). Hyperglycemia has known immunosuppressant effects, and increases risk of infections contributing to worse outcomes in multiple settings including intensive care unit populations (27–29). While our data must be interpreted with caution given the relatively small sample size, the exploratory analyses of cause of death would support further investigation of the hypothesis that infectious complications may be higher among diabetic patients. In addition to increased infectious risk, presence of diabetes may be a

marker of additional underlying vulnerability including subclinical cardiovascular disease which may not be reflected in a comorbidity score. Finally, the effect of hyperglycemia on tumor biology in AML is unknown. Future studies are needed to validate these observations and assess the impact of glycemic control on outcomes during induction therapy (30).

This study has several limitations. This is a single-institution study which can limit generalizability of findings. Results from retrospective studies are subject to unmeasured confounding. Similar to other retrospective studies of comorbidity, we limited our selection of comorbidities to those both well-represented and well-documented in the cohort. While comprehensive in its approach, reliance of ICD-9 codes and chart review may still under-represent present comorbid conditions which were not documented. Our modest sample size may have limited power to investigate associations, particularly among younger adults, who have fewer comorbidities. Functional status was not documented in the electronic medical record, and therefore could not be included in multivariate analyses. However, while future studies should account for functional status, evidence suggests that among older adults functional status and comorbidity provide independent information(31).

This study also has several strengths. Our study represents real-world experience of documentation of comorbidities, which increases the applicability of our findings to clinical practice. The use of ICD codes with chart review confirmation is a more inclusive methodology for capturing major comorbid conditions in this retrospective sample. Inclusion of only those patients receiving intensive therapy minimizes the confounding effects of treatment on comorbidity. Importantly, assessment of individual comorbid conditions adds to the literature.

In summary, our data suggest that a diagnosis of diabetes may represent a marker of vulnerability to treatment-related toxicity for older adults with AML. The implications of a diagnosis of diabetes in the context of AML therapy warrants further study, particularly among older adults. Future research should focus on both validation of findings and exploration of mechanisms. The link between diabetes and cancer treatment outcomes is particularly important, as it may be amenable to intervention.

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Abbreviations

AML	Acute Myeloid Leukemia
BMI	body mass index
CCI	Charlson Comorbidity Index

CR	complete remission
CI	confidence interval
HCT-CI	Hematopoietic Cell Transplantation – Comorbidity Index
OR	odds ratio
OS	overall survival
mCCI	modified Charlson Comorbidity Index

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Figure 1.
CONSORT diagram showing selection of cases for this study.

Figure 2. Relationships between diabetes, age, and 30-day mortality in older and younger patients (over or under 60 years of age, respectively) with AML who underwent intensive treatment. DM: diabetes mellitus.

Table 1

Baseline characteristics of adults with newly diagnosed AML by age

	Younger	Older	p-value
Total (n)	133	144	
Age (mean $\pm$ sd)	44.3 (11.2)	70.3 (6.6)	<0.0001
Female	68 (51.1%)	67 (46.5%)	0.55
White	109 (82.0%)	136 (94.4%)	0.001
Body Mass Index (BMI)			0.15
< 30	84 (67.7%)	93 (72.1%)	
30–34.9	16 (12.9%)	22 (17.1%)	
35 +	24 (19.4%)	14 (10.9%)	
Missing	9	15	
Charlson Comorbidity Index			<0.0001
0	98 (73.7%)	60 (41.7%)	
1	13 (9.8%)	31 (21.5%)	
2	14 (10.5%)	24 (16.7%)	
3 +	8 (6.0%)	29 (20.1%)	
Comorbidities			
Diabetes Mellitus	10 (7.5%)	27 (18.8%)	0.008
Renal Disease	12 (9.0%)	22 (15.3%)	0.14
Cardiac Disease	6 (4.5%)	18 (12.5%)	0.02
Chronic Obstructive Pulmonary Disease	5 (3.8%)	18 (12.5%)	0.009
Cytogenetic Risk Score			<0.0001
1: Favorable	33 (26.0%)	4 (3.0%)	
2: Intermediate	69 (54.3%)	99 (73.3%)	
3: Unfavorable	25 (19.7%)	32 (23.7%)	
Unknown	6	9	
Induction Regimen			<0.0001
7+3	12 (9.0%)	53 (36.8%)	
7+3+3	107 (80.5%)	63 (43.8%)	
7+3+other	10 (7.5%)	24 (16.7%)	
Other	4 (3.0%)	4 (2.8%)	
Insurance Type			<0.0001
Medicaid	31 (23.3%)	2 (1.4%)	
Medicare	12 (9.0%)	109 (75.7%)	
Commercial Insurance	86 (64.7%)	33 (22.9%)	
Uninsured	4 (3.0%)	0	
Creatinine - median (25 th , 75 th perc.)	1 (0.8, 1.1)	1.1 (0.9, 1.3)	0.028
White Blood Cell Count - median (25 th , 75 th percentile.)	16.1 (4.9, 40.2)	10.1 (2.3, 46.3)	0.088
Lactate Dehydrogenase - median (25 th , 75 th percentile)	359 (258, 601)	317 (213, 501)	0.021
Bilirubin - median (25 th , 75 th percentile)	0.8 (0.5, 1)	0.7 (0.6, 1)	0.88
Hemoglobin (mean $\pm$ sd)	9.2 (2.0)	9.4 (1.7)	0.42

Table 2

Association between comorbidity and overall mortality

Comorbidity Variable	Younger Population Hazard Ratio (95% CI)		Older Population Hazard Ratio (95% CI)	
	Unadjusted	Adjusted [*]	Unadjusted	Adjusted ^{**}
Charlson Comorbidity Index 0 vs 1+	0.7 (0.4, 1.0)	1.0 (0.5, 1.8)	0.9 (0.7, 1.3)	0.9 (0.6, 1.3)
Individual	Unadjusted	Adjusted ^{***}	Unadjusted	Adjusted ^{****}
Comorbidities Diabetes (yes vs. no)	1.2 (0.6, 2.6)	0.5 (0.2, 1.5)	1.4 (0.9, 2.1)	1.4 (0.8, 2.2)
Renal disease (yes vs. no)	0.9 (0.4, 1.9)	0.7 (0.3, 1.6)	1.5 (0.9, 2.3)	1.3 (0.8, 2.2)
Cardiac disease	1.4 (0.5, 3.9)	0.6 (0.2, 2.2)	0.7 (0.4, 1.3)	0.8 (0.4, 1.4)
Chronic obstructive pulmonary disease (yes vs. no)	2.8 (1.1, 7.0)	1.7 (0.5, 5.7)	1.0 (0.6, 1.7)	0.9 (0.5, 1.7)

* Age, BMI, Cytogenetic Risk Score, Insurance Type, White cell count

** Age, Cytogenetic Risk Score, LDH

*** Age, BMI, Cytogenetic Risk Score, Insurance Type, White cell count, other individual comorbidities

**** Age, Cytogenetic Risk Score, LDH, other individual comorbidities

Table 3

Association between comorbidity and complete remission

Comorbidity Variable	Younger Population Odds Ratio (95% CI)		Older Population Odds Ratio (95% CI)	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Charlson Comorbidity Index 0 vs 1+ Individual	2.0 (0.8, 5.0)	1.0 (0.3, 3.7)	0.9 (0.5, 1.8)	1.1 (0.5, 2.4)
Comorbidities Diabetes (yes vs. no)	0.3 (0.1, 1.1)	0.6 (0.1, 6.1)	0.6 (0.2, 1.3)	0.5 (0.2, 1.4)
Renal Disease (yes vs. no)	0.4 (0.1, 1.5)	0.2 (0.03, 1.0)	0.7 (0.3, 1.7)	1.0 (0.3, 3.3)
Cardiac Disease (yes vs. no)	1.1 (0.1, 10.1)	1.4 (0.1, 28.7)	1.2 (0.4, 3.5)	1.0 (0.3, 3.4)
Chronic obstructive pulmonary disease (yes vs. no)	0.1 (0.02, 0.8)	0.2 (0.01, 1.6)	1.6 (0.6, 4.9)	1.4 (0.4, 4.6)

* Age, BMI, Cytogenetic Risk Score

** Age, BMI, Cytogenetic Risk Score, other individual comorbidities

Table 4

Association between comorbidity and 30-day mortality from induction

Comorbidity Variable	Younger Population Odds Ratio (95% CI)		Older Population Odds Ratio (95% CI)	
	Unadjusted	Adjusted*	Unadjusted	Adjusted*
Charlson Comorbidity Index 0 vs 1+ Individual	0.6 (0.2, 2.2)	0.8 (0.2, 3.6)	1.7 (0.7, 4.1)	1.6 (0.6, 4.3)
Comorbidities Diabetes (yes vs. no)	3.2 (0.6, 17.2)	3.0 (0.5, 19.5)	3.7 (1.4, 9.8)	4.9 (1.6, 15.2)
Renal Disease (yes vs. no)	1.0 (0.1, 8.6)	0.9 (0.1, 8.0)	1.7 (0.6, 5.2)	1.3 (0.3, 5.1)
Cardiac Disease (yes vs. no)	2.3 (0.2, 22.0)	3.7 (0.3, 50.6)	0.6 (0.1, 2.9)	0.6 (0.1, 3.2)
Chronic obstructive pulmonary disease (yes vs. no)	NA	NA	0.3 (0.04, 2.2)	0.4 (0.04, 2.9)

* Age, Cytogenetic Risk Score

** Age, Cytogenetic Risk Score, other individual comorbidities