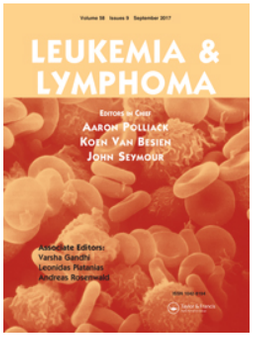

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Leukapheresis reduces 4-week mortality in acute myeloid leukemia patients with hyperleukocytosis – a retrospective study from a tertiary center

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ABSTRACT

Hyperleukocytosis in patients with acute myeloid leukemia (AML) can lead to leukostasis, which if left untreated, has a high mortality. While prompt cytoreductive chemotherapy is essential, treatment with leukapheresis is controversial. This study investigated the outcomes of patients with hyperleukocytosis who received leukapheresis. From 5596 encounters of patients with leukemia seen at Houston Methodist Hospital, we identified 26 patients who had newly diagnosed AML, WBC >50,000/μL, and received leukapheresis. We matched 26 patients who had similar baseline characteristics but did not receive leukapheresis. The primary endpoint was to compare the 28-day mortality rates between the treatment and the control groups. Secondary endpoints were 6-month, 1-year, and 2-year mortality rates. Using multivariate logistic regression analysis, leukapheresis was associated with significantly lower 28-day mortality rate (30.8% vs. 57.7%, $p = .022$). There was, however, no difference in long-term mortality rate. Our study demonstrates the short-term mortality benefit of using leukapheresis in AML patients presenting with hyperleukocytosis.

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Introduction

Hyperleukocytosis is a laboratory abnormality conventionally defined as total white blood cell count greater than 50,000–100,000/μL, often with accompanying tumor lysis syndrome, disseminated intravascular coagulation, and electrolyte abnormalities in patients with adult acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) [1–4]. Hyperleukocytosis occurs in 5–13% of AML, especially in the monocytic subtypes (M4 and M5). The phenomenon also occurs in chronic lymphocytic leukemia (CLL), prolymphocytic leukemia, and in 10–30% of acute lymphocytic leukemia (ALL) [5,6].

Leukostasis, or symptomatic hyperleukocytosis, is a less common, more catastrophic phenomenon involving end-organ damage. Pathophysiology is thought to be two-fold. The high concentration of larger, less deformable blast cells cause hyperviscosity with resultant microvasculature occlusions; locally, dividing blast cells secrete endothelial cell-damaging cytokines that can enhance the hypoxemic damage [7,8]. This is most often seen in AML patients with WBC greater than 100,000/μL, ALL greater than 400,000/μL, and CLL well above 1,000,000/μL [5,9,10]. The consequences are especially prominent in the lungs and central nervous system, causing dyspnea, hypoxia, headache, dizziness, vision disturbances, confusion, somnolence, and coma [1–3].

As leukostasis is associated with a short-term mortality rate of 20–40%, rapid cytoreduction with hydroxyurea, induction chemotherapy, and leukapheresis are crucial [11,12]. Leukapheresis aims at immediate reduction of elevated WBC and is generally well-tolerated. Most literature agrees on the importance of prompt chemotherapy, however, no prospective or large observational studies exist on the role of adjunct leukapheresis. Furthermore, there are sparse guidelines regarding when and how to utilize leukapheresis. According to the American Society for Apheresis (ASFA) guideline, the indication for therapeutic leukapheresis includes AML and ALL patients who present with leukostasis symptoms or complications (Grade 1B recommendation). The indication for prophylactic leukapheresis includes patients who do not present with

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Supplemental data for this article can be accessed here.

leukostasis, but have AML and WBC >100,000/μL or ALL and WBC >400,000/μL (Grade 2C recommendation) [1].

What constitutes 'symptomatic' leukostasis is also not completely clear. Nevertheless, clinical evidence of neurologic symptoms and respiratory distress has significant prognostic implications with even lower complete remission (CR), disease-free survival (DFS), and overall survival (OS) [11]. To facilitate clinical evaluation, Novotny et al. 2005 devised a clinical grading scale to classify hyperleukocytic leukemia patients into four stages of leukostasis – not present, possible, probable, and highly probable [13]. The probability score is based on type and severity of symptoms at presentation, emphasizing pulmonary and neurologic manifestations. Our study evaluates the role of adjunct leukapheresis in short-term and long-term outcomes, as well as the value of the leukostasis symptom grading scale in newly diagnosed AML.

Methods

Patients

Methodist Environment for Translational Enhancement and Outcomes Research (METEOR) is a clinical data warehouse and analytics environment that integrates existing business data warehouse with internal and external research databases and national registries to support clinical research and outcome studies with the aim of improving cost-effective patient care. The METEOR data warehouse contains records dating back to 1 January 2006, on patients seen at Houston Methodist Hospital with over 1 million unique patients and over 4 million unique patient encounters. The selected data included baseline demographics and overall outcomes. The METEOR database was queried for the diagnosis of leukemia, hyperleukocytosis (at least 50,000/μL), and patients receiving at least one leukapheresis procedure.

A total of 5596 leukemia patient encounters between 2006 and 2016 were reviewed. Among these, 1812 were AML patient encounters. 26 unique patients with newly diagnosed AML and hyperleukocytosis were found to have received leukapheresis during the 11-year period. The decision for giving leukapheresis treatment was based on the institutional guideline to consider leukapheresis as part of the cytoreduction therapy for AML patients when WBC >100,000 and/or when patients present with symptoms of leukostasis. Furthermore, a matched control group was constructed consisting of 26 patients with newly diagnosed AML and hyperleukocytosis (WBC >50,000/μL), who did not undergo leukapheresis. The control group was selected to match the baseline characteristics of patients in the intervention group. The median follow-up time for all 52 patients was 20.5 months. Patients in both groups confirmed the diagnosis of AML based on standard morphology, cytochemistry, and immunophenotyping by flow cytometry of bone marrow and/or peripheral blood.

Statistical analysis

Baseline characteristics were compared between patients in leukapheresis group and control group using a Pearson chi-square test for qualitative variables and the Mann–Whitney *U* test for quantitative variables. Mann–Whitney *U* test was also used to compare the number of days each group required to reduce WBC to less than 50,000/μL; chi-square test was used for all other qualitative variable analyses.

The primary endpoint was the 28-day mortality (or terminal condition leading to hospice care) between the group of patients who received leukapheresis and standard chemotherapy versus the group who received standard chemotherapy alone. Demographic and laboratory variables recorded for analysis included age, gender, race, WBC count, percentage (%) of peripheral blasts, hemoglobin, platelets, creatinine, glomerular filtration rate, uric acid, lactate dehydrogenase, prothrombin time (PT), INR, thromboplastin time (PTT), and fibrinogen. The probability of leukostasis syndrome at presentation was measured using the Symptom grading scale as per Novotny et al. [13]. The presence of acute kidney injury (AKI), clinical tumor lysis syndrome (TLS), disseminated intravascular coagulation (DIC), respiratory failure, sepsis, clinically significant bleeding, and acute coronary syndrome (ACS) were also considered in the analysis. In addition, clinical variables that potentially influence the outcome of the study such as whether the patient received hydroxyurea, the type of chemotherapy, and the difference in cytogenetic risks, were also incorporated in the analysis. Stepwise selection was used to identify the variables from the above list that most closely associated with 28-day mortality. Previously published variables known to be associated with mortality were forced into the model before selection. All the selected variables were introduced to multivariate logistic regression analysis. *p*-Values of less than .05 indicated statistical significance. SPSS version 19 (Chicago, IL) was used for all analyses.

Secondary endpoints included the effect of leukapheresis on 6-month, 1-year, and 2-year mortality, using the same multivariate logistic regression modeling.

The effect of leukapheresis on complication recovery was also evaluated using chi-square or Fisher's exact test as appropriate.

Leukapheresis

Leukapheresis was performed using a continuous-flow blood cell separator COBE Spectra (Terumo BCT™, Lakewood, CO). PMN procedure was used for myeloid cytoreduction. Acid citrate dextrose was added for anticoagulation; Formula A was added at an average ratio of 1:16 with a range between 1:12 and 1:20 based on the platelet count. Hydroxyethyl starch was not used. All the procedures were continued until at least 7–10 L of blood volume had been processed. For patients with initial WBC count greater than 100,000/μL, leukapheresis was repeated daily until WBC dropped to less than 100,000/μL. A few patients had initial WBC less than 100,000/μL and received leukapheresis due to symptomatic leukostasis. All of these patients received only one session of leukapheresis and achieved significant WBC reduction with WBC less than 50,000/μL.

Chemotherapy

All study patients received standard chemotherapy regardless of leukapheresis except 4 patients who expired before initiation of chemotherapy and 2 patients who refused induction chemotherapy. All patients who did not receive chemotherapy received hydroxyurea. Eight patients expired or went to hospice before finishing planned chemotherapy regimen (3 in control group and 5 in leukapheresis group). The categories of chemotherapy regimens are listed in Table 1. There was no significant difference in the regimens between the control and the leukapheresis groups. Detailed chemotherapy regimens and dosages can be found in the 'Supplemental material'.

In addition to chemotherapy, most patients received hydroxyurea (HU) ranging from 500 to 3000 mg daily for cytoreduction. Also, allopurinol 150–300mg daily and/or rasburicase 0.05–0.2 mg/kg were given to most patients for the prevention or treatment of TLS; this was not different between the two groups. (Table 1)

Results

Baseline characteristics

The characteristics of the patients are listed in Table 2. The median age at the time of hyperleukocytosis was 64.5 years in leukapheresis group and 60 years in the control group ($p = .18$). There were more males in leukapheresis group than in control group (69% vs. 38%, $p = .03$). The distribution of race was not statistically different between the two groups. The median WBC was higher in the patients who received leukapheresis (163.5k/μL vs. 101.3k/μL, $p = .002$). There was no significant difference in median hemoglobin, median platelets, the percentage of peripheral blasts, creatinine, uric acid, LDH, coagulation test, or the scores on Novotny's leukostasis grading scale [14].

Table 2. Baseline characteristics.

Characteristics	Control group ($N = 26$)	Leukapheresis group ($N = 26$)	p Value
Median age	64.5 (34-91)	60 (26-88)	.18
Gender			.03
Male	10 (38%)	18 (69%)	
Race			.32
Asian	1 (4%)	3 (11%)	
African American	4 (15%)	3 (11%)	
Caucasian	19 (73%)	16 (62%)	
Hispanic	0 (0%)	3 (11%)	
Other	2 (8%)	1 (4%)	
Median WBC	101.3	163.5	.002
Median peripheral% blast	75	75	.08
Median Hemoglobin	9.2	8.3	.06
Median Platelet	36	22.5	.08
Median Cr	0.7	1.15	.23
Median GFR	90	46	.18
Median uric acid	5.7	8.1	.15
Median LDH	1854	1902	.07
PT	16.7	18.4	.57
INR	1.45	1.45	.57
PTT	37.1	37.4	.77
Median fibrinogen	449	386	.23
Novotny's leukostasis grading scale [13]			.30
0	9 (35%)	4 (15%)	
1	4 (15%)	8 (31%)	
2	8 (31%)	7 (27%)	
3	5 (19%)	7 (27%)	

WBC: white blood cell; GFR: glomerular filtration rate; LDH: lactate dehydrogenase; PT: prothrombin time; PTT: thromboplastin time; INR: international normalized ratio.

Table 1. Number of patients received each type of chemotherapy, hydroxyurea, allopurinol, and rasburicase.

Chemotherapy/medications	Control group $N = 26$	Leukapheresis group $N = 26$	p Value[a]
Standard or high-dose cytarabine-based induction therapy	17 (65%)	20 (77%)	.36
Azacitidine or low-dose cytarabine	5 (19%)	4 (15%)	.71
No chemotherapy	4 (15%)	2 (8%)	.39
Hydroxyurea	17 (65%)	21 (81%)	.21
Allopurinol	20 (77%)	22 (85%)	.48
Rasburicase	7 (27%)	11 (42%)	.24

[a]Chi Square test.

Table 3. Number of patients in each ELN genetic group.

ELN genetic group	Control group $N = 26$	Leukapheresis group $N = 26$	p Value[a]
Favorable	2 (8%)	3 (12%)	.22
Intermediate-I	13 (50%)	16 (62%)	.40
Intermediate-II	3 (12%)	3 (12%)	1.00
Poor	4 (15%)	1 (4%)	.16
Unknown	4 (15%)	3 (12%)	.68

ELN: European LeukemiaNET.
[a]Chi square test.

Table 4. Complications present at the onset of hyperleukocytosis.

	Control group ($N = 26$)	Leukapheresis group ($N = 26$)	p Value[a]
AKI	11 (42%)	12 (46%)	.78
Clinical TLS	10 (38%)	13 (50%)	.40
DIC	5 (19%)	8 (31%)	.34
Respiratory failure	5 (19%)	5 (19%)	1.00
Sepsis	14 (53%)	10 (40%)	.27
Clinically significant bleeding	6 (23%)	8 (31%)	.53
ACS	2 (8%)	3 (12%)	.64

AKI: acute kidney injury ; TLS: clinical tumor lysis syndrome; DIC: disseminated intravascular coagulation; ACS: acute coronary syndrome.
[a]Chi square test.

Cytogenetic and molecular characteristics categorized based on European LeukemiaNET (ELN) standardized reporting system were available for 45 of 52 patients (Table 3).

The number of patients presenting with complications specific to hyperleukocytosis/leukostasis, such as AKI, clinical TLS, DIC, respiratory failure, sepsis, clinically significant bleeding, thrombosis, and ACS are recorded in Table 4. We found no statistically significant difference between the two cohorts when comparing these variables.

Timing of leukapheresis and chemotherapy

All patients received leukapheresis within three days of the onset of hyperleukocytosis, 23 of 26 (88%) received the procedure on the first day of the presentation. Furthermore, most of the patients received leukapheresis and chemotherapy concurrently, with 22 of 24 patients (92%) receiving chemotherapy within one day of leukapheresis. The median number of days from patient presenting in the hospital to the start of chemotherapy was one day for both leukapheresis group and control group ($p = .44$, Mann–Whitney U test, excluding patients who did not receive chemotherapy).

WBC counts reduction

Among the group of patients who received leukapheresis, 16 patients required 1 session, 8 patients required 2 sessions, and 2 patients required 3 sessions for appropriate cytoreduction. The median percentage of WBC counts reduction after 1–3 sessions of leukapheresis was 55% with a range from 19% to 94%. The combination of leukapheresis and chemotherapy reduced WBC count more effectively than chemotherapy alone; the median number of days required to reduce the patient's WBC below 50,000 was 3 days for leukapheresis group and 4 days for the control group ($p = .033$) (Figure 1).

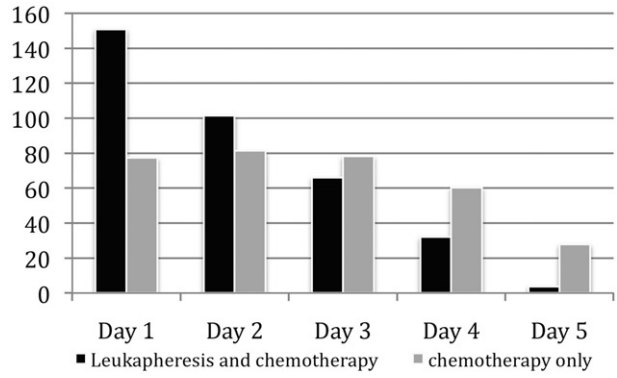

Figure 1. Median WBC counts on first 5 days.

28-Day mortality

The prognostic factors associated with 28 days mortality were identified by stepwise selection from the lists of clinical and laboratory variables described in the "Methods" section. Age >60 and WBC count were previously published to be associated with short-term mortality during induction chemotherapy [15] and thus forced into the model. The following variables were significant in the stepwise selection: treatment with leukapheresis, Novotny's leukostasis grading score [13], the presence of respiratory failure, and the presence of clinically significant bleeding.

The above variables were incorporated into a multivariate logistic regression model. The result demonstrated that patients who received leukapheresis and chemotherapy had a significantly lower 28-day mortality rate than patients who only received treatment with chemotherapy (30.8% vs. 57.7%, $p = .022$, odds ratio 0.06, Figure 2). Higher Novotny's leukostasis grading score [13] ($p = .043$, odds ratio 3.24), the presence of clinically significant bleeding ($p = .017$, odds ratio 58.82), and the presence of respiratory failure ($p = .003$, odds ratio 72.76) were also significantly associated with increased mortality (Table 5). In addition, complete remission rate after the 28 days was not statistically different between the two groups (57.7% vs. 42.3%, $p = .27$, chi-square test).

Long-term survival

We also performed analysis for 6-month, 1-year, and 2-year mortality to study the effect of leukapheresis on long-term mortality. Multivariate logistic regression was again used for statistical analysis. Patients who were lost to follow-up before 6 months, 1 year, and 2 years were excluded from the mortality analysis for that time interval. The mortality rate was lower in leukapheresis group for each studied time interval, but this was also not statistically significant (Table 6).

Impact on complications

We reviewed the impact of leukapheresis on the complications associated with hyperleukocytosis. Specifically, the number of patients who developed AKI, clinical TLS, and DIC on admission but achieved resolution within 7 days were reported (Table 7). The leukapheresis group achieved statistically significant resolution of AKI (27% in control group vs. 75% in leukapheresis group, $p = .02$) and clinical TLS (25% in control group vs. 69% in leukapheresis group, $p = .03$) within the 7-day period. DIC also resolved more frequently within 7 days in patients treated with leukapheresis, but not statistically significantly (40% in control group vs. 63% in leukapheresis group, $p = .59$).

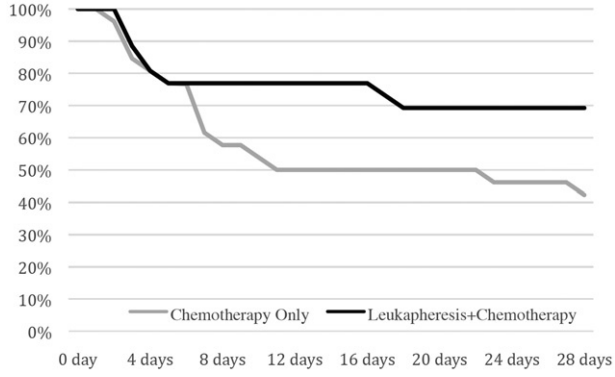

Figure 2. 28 Days survival rate.

Table 5. Multivariate logistic regression for 28-day mortality rate.

Variables in multivariate analysis	Odds ratio	*p* Value
Treatment with leukapheresis	0.06	.022
Novotny's leukostasis grading score [15]	3.24	.043
Presence of respiratory failure	72.76	.003
Presence of clinically significant bleeding	58.82	.017
Age >60 years	2.34	.078
WBC >100,000/μL	1.88	.957

Discussion

Hyperleukocytosis-induced TLS, DIC, and leukostasis-associated hypoxemic end-organ damage can cause significant early mortality and lasting comorbidities. Rapid cytoreduction can be achieved through induction chemotherapy, hydroxyurea, leukapheresis, or combinations thereof. However, the benefit of leukapheresis is still not well-established in the literature. Some representative analyses including those by Porcu et al. [3,6,14] and Chang et al. [16] showed no early mortality benefits, and Kuo et al. [17] showed no early mortality or long-term survival benefits. On the other hand, Giles et al. [12] and Bug et al. [15] showed early mortality benefits at 2–3 weeks with no long-term survival benefits, and Cuttner et al. [18] and Lester et al. [19] showed remission and long-term survival benefits, respectively. Furthermore, the heterogeneous parameter methodology makes it difficult to draw conclusions. Examples include timing of leukapheresis to induction chemotherapy (pre-induction versus concurrent), time interval defined as 'early' mortality (from days to weeks), and the concurrent use of other cytoreduction therapies such as hydroxyurea.

We chose to analyze the effect of leukapheresis concurrent with induction chemotherapy, as the latter is the standard treatment for hyperleukocytosis [20]. The decision to monitor mortality at 28 days was its correspondence to the time course of induction chemotherapy for AML. Because an overwhelming

Table 7. Number of patients recovered from AKI, TLS, and DIC.

	Control	Leukapheresis	*p* Value
AKI resolved in 7 days	3/11 (27%)	9/12 (75%)	.02[a]
TLS resolved in 7 days	3/12 (25%)	9/13(69%)	.03[a]
DIC resolved in 7 days	2/5 (40%)	5/8 (63%)	.59[b]

[a]Chi square test.
[b]Fisher's exact test.

Table 6. 28-day, 6-month, 1-year, and 2-mortality rate in control group and leukapheresis group.

	Number of patients in analysis[a]	Control group	Leukapheresis group	Odds ratio	*p* Value
28-Day mortality	52	16/26 (57.7%)	10/26 (30.8%)	0.063	.022
6-Month mortality	48	17/24 (70.1%)	12/24 (50.0%)	0.371	.284[b]
1-Year mortality	45	17/23 (73.9%)	12/22 (54.5%)	0.329	.262[b]
2-Year mortality	42	19/21 (90.5%)	12/21 (57.1%)	0.079	.110[b]

[a]Patients lost follow-up before 6 months, 1 year, and 2 years were excluded from the mortality analysis for that time interval.
[b]Variables in multivariate logistic regression: Treatment with leukapheresis, presence of respiratory failure, ELN cytogenetic group, Age >60, Novotny's leukostasis grading score [13].

24–54% mortality has been associated with this time period, we questioned whether adjunct leukapheresis given with standard chemotherapy improves clinical outcomes [12,14,21]. Our results showed that even though the complete remission rates was not statistically different between the two groups, leukapheresis treatment showed a significant reduction in 28-day mortality rate in patients with AML (57.7% in control group vs. 30.8% in leukapheresis group), and this has not been reported before. However, we did not see any statistically significant long-term mortality benefit of leukapheresis during the follow-up periods of 6-month, 1-year, and 2-years (Table 7), consistent with previous studies [12,15,22].

We could also demonstrate that leukapheresis more effectively reduced WBC and resolved hyperleukocytosis complications. Leukapheresis significantly expedited WBC reduction with median days taken for WBC to come below 50,000 as 4 days in the control group and 3 days in the leukapheresis group (Figure 1). Such increase in cytoreduction efficiency is consistent with most previous findings including but not limited to those by Giles et al. [12], Pastore et al. [22], Hasse et al. [23], and De Santis et al. [24]. Though there are exceptions, most literature agree on high WBC counts as a poor prognostic factor [11,17,21,25–28]. Specific to this study's 28-day interval of interest, Estey et al. [28] and Greenwood et al. [27] have correlated WBC $>$25k/μL and WBC $>$30k/μL with death during induction; Kuo et al. [17] echoes that WBC $>$34.1k/μL is an independent risk factor for early mortality [28]. Thus, the more efficient leukapheresis-associated cytoreduction in our study may have contributed to the early mortality benefit observed in the leukapheresis group. Interestingly, Kuo et al. [17] also found the prognostic impact of higher WBC diminishes drastically after 28 days in comparison to other known AML risk factors such as age and cytogenetics [16]. If high WBC count is indeed more of a short-term prognostic factor, it may explain the clinical observations that leukapheresis-associated rapid WBC counts reduction produce early but not long-term mortality benefits.

Furthermore, TLS, DIC, as well as leukostasis-induced hypoxemic symptoms of respiratory failure, renal failure, and CNS involvement may be other independent, substantial contributors to early mortality [3,4,6,17,19,26]. In this study, adjunct leukapheresis was associated with the superior rate of resolution of AKI (27% in control vs. 75% in leukapheresis with $p = .02$) and TLS (25% in control vs. 69% in leukapheresis with $p = .03$) within 7 days. Though not statistically significant, DIC also resolved faster in the leukapheresis group (40% in control vs. 63% in leukapheresis). Although large-scale studies are lacking, leukapheresis has been reported in the literature to expedite leukostasis-induced renal, respiratory, and cerebral vascular complications [20,29–33]. Specifically, Maurer et al. [30] found leukapheresis to be beneficial in patients with severe hyperuricemia and renal dysfunction. We were unable to draw conclusions from acute respiratory failure and CNS symptomatic improvements in this study due to fragmentary charting on complication recovery; however Piro et al. [20] and Bunin et al. [29] have reported respiratory distress reversal associated with leukapheresis. These findings lend credence to an effect of leukapheresis for rapid tumor burden reduction and ensuing early mortality and morbidity benefit, but little effect on long-term mortality rate or complete remission rate.

The leukostasis grading scale devised by Novotny et al. [13] was also evaluated for clinical practicality and correlation to early mortality. The median score in both leukapheresis and control was grade 2 with a roughly equal proportion in the low-grade (score of 0–1, 50% in control group versus 46% in leukapheresis group) and high-grade (score of 2-3, 50% in control group versus 54% in leukapheresis group) ranges. In a retrospective study Piccirillo et al. [34] has shown a correlation between Novotny's clinical grading score [13] of 3 and early mortality. Our study demonstrated a significant association between the higher grading range and 28-day mortality in a multivariate logistic regression analysis ($p = .043$, odds ratio $= 3.24$). The potential implication of such association includes the grading scale's utility as an independent prognostic factor for early mortality and as a method of standardizing clinical evaluation for leukostasis, with the goal of facilitating decision making for leukapheresis. However, the grading scale was not significant in the stepwise selection of 6-month, 1-year, or 2-year mortality analysis and thus not a prognostic factor for long-term mortality. Further studies with larger sample size may also be needed to validate this grading scale.

The study has several limitations. Long-term mortality and overall survival data was limited by a significant number of patients being lost to follow-up (19% AML patients were lost to follow-up in the 2-year mortality analysis). In addition, we are only able to obtain ECOG/WHO status for a few numbers of patients due to the nature of retrospective study. The study was also limited by small patient size and thus inability to account for all confounders especially parameters such as WBC and gender distribution, which were markedly different between the two groups. To minimize these confounder variables, we incorporated WBC count in our multivariate analysis for 28-day mortality.

Furthermore, there were 4 patients in control group and 2 patients in leukapheresis who did not receive chemotherapy secondary to early mortality or patient choice. The higher number in control group is likely a consequence of not receiving leukapheresis, and was not stastically significant. There were fewer patients receiving HU in the control group compared to the leukapheresis group. However, it was not statistically significant (65% vs. 81%, $p = .21$). Moreover, patients in control group who did not receive hydroxyurea had lower 28-day mortality rate than those who did (44.4% vs. 64.7%). Therefore, the use of hydroxyurea was not a key factor to determine short-term mortality.

Conclusions

Hyperleukocytosis and Leukostasis is a medical emergency that requires prompt diagnosis and treatment. In this retrospective study, we analyzed the impact of leukapheresis on the 28-day mortality of newly diagnosed AML patients receiving chemotherapy and leukapheresis versus those receiving chemotherapy alone. 6-Month, 1-year, and 2-year mortality, as well as cytoreduction effectiveness and hyperleukocytosis complications including TLS, DIC, and AKI, were also performed. Primary analysis did demonstrate early mortality benefit of leukapheresis in AML patients. However, there was no difference in long-term mortality between the leukapheresis group and control group. Secondary analysis demonstrated the effective role of leukapheresis in cytoreduction and faster resolution of AKI and TLS. We also validated the grading scale devised by Novotny et al. [13] as a potential prognostic tool in facilitating clinical decision-making. A prospective, multi-centered study will likely yield more conclusive guidelines.

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Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article online at http://dx.doi.org/10.1080/10428194.2016.1277386

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