Characteristics and Outcomes of Patients with Hematologic Malignancies Receiving Chemotherapy in the Intensive Care Unit

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Abstract

Background: To evaluate the short- and long-term outcomes of adult patients with hematologic malignancies receiving chemotherapy in the intensive care unit (ICU).

Methods: Retrospective single center study comparing the outcomes of patients with hematologic malignancies who received chemotherapy in the ICU with a matched cohort of ICU patients who did not receive chemotherapy. Conditional logistic regression and shared frailty Cox regression were used to assess short-term (ICU and hospital) mortality and death by 12-months post-hospital discharge, respectively.

Results: One hundred eighty one patients with hematologic malignancies received chemotherapy in the ICU. ICU and hospital mortality rates were 25% and 42%, respectively. Higher severity of illness score on ICU admission were significantly associated with higher ICU (OR 1.07, p<.001) and hospital mortality (OR 1.05, p=<.001). Six and 12-month survival estimates post-hospital discharge were 58% and 50%, respectively. When compared to the matched cohort of patients who did not receive chemotherapy, patients who received chemotherapy had a significantly longer length of stay in the ICU (median 6 vs. 3 days, p<0.001) and hospital (median 22 vs. 14 days, p=0.024). The relationship between mortality by 12-months and receiving chemotherapy approached, but did not reach statistical significance in multivariable analyses (HR 1.45, p=0.08).

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Conclusions: Short-term mortality was similar among patients with hematologic malignancies who did or did not receive chemotherapy in the ICU although patients who received chemotherapy had increased resource utilization. These results may inform ICU triage and goals of care discussions with patients and their families regarding the outcomes of patients receiving chemotherapy in the ICU.

Condensed Abstract

Our study is the first and largest study to date of patients with hematologic malignancies who received chemotherapy in the ICU at a US tertiary cancer center. Our data can assist oncology and critical care teams when discussing goals of care and prognosticating outcomes of patients who receive chemotherapy in the ICU and in dealing with triaging scarce ICU resources.

Keywords

chemotherapy; cancer; hematologic; intensive care unit; outcomes

INTRODUCTION

A complex host of factors influences the decision to administer oncologic therapies in the intensive care unit (ICU) for patients with hematologic malignancies. These include the improved short-term (ICU and hospital) and long-term (post-hospital discharge) survival rates associated with this patient cohort,[1-3] the type and status of the underlying malignancy, concern for potential for adverse effects due to oncologic therapies and the presence of life-threatening critical illness syndromes. Other important considerations include the capabilities of the ICU to support active treatment of oncologic patients and the negative biases of the ICU towards patients with a perceived poor outcome due to their cancer or need for oncologic therapies.

While the prognostic factors and outcomes in patients with hematological malignancies admitted to oncologic ICUs have been extensively examined,[4-14] only four studies (three retrospective and one prospective) specifically address the outcomes of patients receiving chemotherapy in the ICU.[4-7] All four studies were based in oncologic ICUs at single centers outside the United States (US), retrospective in design, had relatively small number of patients (<100 patients with hematologic malignancies), and except for one study[7], reported only short-term outcomes (<6 months). Notably, these studies [4-7] focused on patients receiving initiation chemotherapy for newly diagnosed hematologic malignancies and did not address the clinical factors and outcomes of patients receiving continuation chemotherapy.

The purpose of this study was to improve our understanding of the characteristics and outcomes of patients with hematologic malignancies receiving chemotherapy in the ICU. Our goals were to describe reasons for ICU admission, the timing and types of chemotherapy regimens given, whether the regimens were initial or part of ongoing oncologic treatment, and both short-term (ICU and hospital mortality) and long-term (death by 12 months) outcomes. We also compared the outcomes of these patients with a cohort of

matched patients with similar hematologic malignancies who were admitted to the ICU during the same time period, but did not receive chemotherapy.

METHODS

This retrospective study was conducted between January 1, 2010 - December 31, 2015 in the 20-bed, adult ICU of Memorial Sloan Kettering Cancer Center. The ICU is staffed by intensivist-led multidisciplinary teams and all patients are cared for in collaboration with the patient's primary oncologist or surgeon. Consultations for ICU admission are all triaged through the admitting intensivist attending physicians. Patients are admitted primarily with one or more organ dysfunctions and for life extending therapeutic options associated with potentially severe adverse effects.

The decision to administer chemotherapy in the ICU is jointly agreed upon by oncologists and intensivists after discussions with the patients and/or their authorized representatives. These medications are solely prescribed by oncologists, and prepared by specialty pharmacists. Intravenous agents are administered by chemotherapy nurses; in contrast, oral agents are administered by ICU nurses. In this study, we define chemotherapy as any combination of traditional cytotoxic chemotherapy, biologic or immune therapy directed at a hematologic malignancy. Radiation therapy alone was not considered. A waiver of authorization for this study was obtained through our Institutional Review Board.

Data Sources

Using hospital-wide and ICU databases, we identified all ICU patients with hematologic malignancies who received chemotherapy in the ICU. We included for analysis only the first ICU admission during which the patient received chemotherapy; subsequent ICU admissions for chemotherapy were excluded. We also excluded patients receiving chemotherapeutic agents as part of the conditioning regimen for autologous or allogeneic hematopoietic stem cell transplantation (HSCT); concomitantly administered with major surgical procedures; instilled in body cavities to facilitate sclerosis (i.e., pericardial and pleural spaces); or given for non-cancerous conditions (e.g., autoimmune or viral diseases). Similarly, patients receiving corticosteroids only were also excluded due to the extensive use of many types of corticosteroids for a myriad of conditions in our ICU.

Demographics and outcomes

Demographic and clinical data included age, gender, severity of illness score using the Mortality Probability Model at ICU admission version 2 (MPM_0-II), history of HSCT, primary ICU admission diagnosis as noted in the admission day critical care attending physician note, the Charlson comorbidity index[15], dates of hospital and ICU admissions, Sequential Organ Failure Assessment (SOFA) score at the start of chemotherapy, use of mechanical ventilation, vasopressor medications, and renal replacement therapies (hemodialysis or continuous renal replacement therapy) on admission and during ICU stay, and ICU and hospital length of stay (LOS). Primary outcomes were ICU and hospital mortality and survival by 6 and 12 months post-hospital discharge.

Cancer diagnoses and chemotherapy

Hematologic malignances were classified as newly diagnosed (within 30 days of ICU admission) or older diagnosed (>30 days; includes relapse/progression). We coded chemotherapy as initiation (initial administration) or continuation (part of an ongoing regimen). Patients who were treated with their first chemotherapy within 5 days prior to ICU admission with carry-over into the ICU were also included in the initiation category.

Chemotherapy data collected included the ICU start date, type (cytotoxic, biologic or immune), number (single or multiple), and route of administration (parenteral, oral, intrathecal, or subcutaneous). We also determined the dates of the original cancer diagnosis, and the last chemotherapy administered prior to ICU admission for the continuation group.

Statistical Analysis

Patients who received chemotherapy were 1:1 individually matched to non-chemotherapy patients on age, gender (male vs. female) and disease type (leukemia, lymphoma, and other). Exact matches were used for gender and disease type, while a 0.25 caliper match was used for age and a greedy match algorithm was employed. Patients who were not matched were dropped from the analyses. Characteristics between chemotherapy and non-chemotherapy patients were compared with McNemar's Test and the Wilcoxon Signed Rank test where appropriate.

We assessed three outcomes: death in ICU, death in hospital, and death by 12-months post-hospital discharge. Death in ICU and death in hospital were treated as binary covariates.[16] The relationships between covariates and short-term outcomes were assessed with univariable and multivariable conditional logistic regression with matched pair serving as strata. All factors were adjusted for in multivariable models regardless of significance; however, as the MPM II score on ICU admission incorporates the need for mechanical ventilation and vasopressor agents, only the MPM II score was included in multivariable models. Death by 12-months was assessed from the time of hospital discharge until death. Patients alive at 12 months were censored. Only patients who were alive at hospital discharge were included in this analysis. Kaplan Meier methods were used to estimate survival, and univariable and multivariable shared frailty Cox regression were used to assess the relationship between covariates and death by 12-months. The proportional hazards assumption was assessed through residual plots.

To analyze the effect of initiation versus continuation chemotherapy on ICU and hospital mortality and survival by 12-months in the chemotherapy cohort, standard logistic regression and Cox proportional hazards regression were used. Fisher's Exact test and Wilcoxon Rank Sum test were used to check for differences between the initiation and continuation chemotherapy groups. Two-sided p-values less than or equal to 0.05 were considered statistically significant. All analyses were performed with SAS 9.4 (The SAS Institute, Cary, NC).

RESULTS

During the study period, 4973 patients were admitted to the ICU. Of these, 186 patients (3.7%) with hematologic malignancies received chemotherapy in the ICU (Figure 1). Of the 186 patients, 181 were successfully matched to ICU patients who did not receive chemotherapy (Table 1). Cancer type and gender were identically matched. The cohorts did not differ in age (p>0.95). The five patients who were not matched were female leukemia patients aged 30 or younger. Median Charlson comorbidity index was similar in both groups (p=0.55). Median MPM-II score on ICU admission was 39 (range, 7-95) in the chemotherapy cohort and 46 (range, 8-94) in the non-chemotherapy cohort (p=0.57).

Patient Characteristics: Chemotherapy Patients (n=181)

Patients who received chemotherapy in the ICU were primarily male (n=115 [64%]) with a median age of 62 years (18-86) (Table 1). One hundred three patients (57%) were treated for lymphoma and 78 (43%) for leukemia. Sixty-nine (38%) patients were treated for newly diagnosed hematologic malignancies. Twenty patients (11%) had prior HSCT and two patients (1%) received radiation therapy during their ICU stay. Primary ICU admitting diagnoses were sepsis/septic shock (n=47 [27%]), chemotherapy administration (n=45 [25%]), respiratory insufficiency/failure (n=33 [19%]), renal insufficiency/failure (n=23 [13%]), and bleeding (n=11 [6%]) (Table 1). Median MPM II score on ICU admission was 39 (7-95). Median SOFA score at start of chemotherapy was 6.0 (range: 0-15). During ICU stay, 38% of patients (137/181) needed mechanical ventilation, 34% (123/181) required vasopressor therapy and 7% (25/181) underwent renal replacement therapy. Median ICU LOS was 6 days (range: 1-47) and median hospital LOS was 22 days (range: 2-121).

Treatment Characteristics: Chemotherapy Patients

Cytotoxic chemotherapies were given to 135 patients (75%), immunotherapy agents to 21 patients (12%) and combined regimens to 25 patients (14%). One hundred three patients (57%) received multiple agents. Median time between the diagnosis of cancer and ICU admission was 5 months (range: 0-318). Sixty eight patients (38%) were diagnosed with cancer within 30 days of ICU admission.

Fifty six patients (31%) received chemotherapy within 5 days of ICU admission, 33 patients (18%) received chemotherapy greater than 5 days before admission, and 92 patients (51%) did not receive chemotherapy prior to ICU admission. Seventy two patients (40%) received initiation and 109 patients (60%) received continuation therapies in the ICU (Table 2). Of the 56 patients who received chemotherapy within 5 days, only 8 (14%) were from the initiation cohort. In those patients who received chemotherapy after ICU admission, the median time was 1.5 days overall (range: 1-17 days) with a median of 1 day (range: 1-16) for patients in the continuation cohort and 2 days (range: 1-17) in the initiation cohort.

Chemotherapy Patients Compared to Non-Chemotherapy Patients (N=362)

ICU and Hospital Mortality—ICU mortality was 25% (46/181) in the chemotherapy cohort and 22% (40/181) in the non-chemotherapy cohort. Receiving chemotherapy in the ICU was not significantly associated with worse ICU mortality (p=0.61) after adjustment for

known mortality confounding factors (Table 3). Overall hospital mortality was 42% (76/181) in the chemotherapy cohort and 33% (59/181) in the non-chemotherapy cohort (Table 1). Although as a univariable factor, patients who received chemotherapy in the ICU had higher odds of dying in the hospital that approached statistical significance (OR: 1.52, 95% CI: 0.98-2.35, p=0.06), after adjusting for known mortality predictors, there was not enough evidence to suggest that patients who received chemotherapy had significantly worse hospital mortality (OR: 1.58, 95% CI: 0.85-2.92, p=0.14) (Table 3). Additionally, higher MPM II scores on ICU admission were associated with higher risk of ICU (OR: 1.07, 95% CI: 1.03-1.10, p<0.001) and hospital mortality (OR:1.05, 95%CI: 1.03-1.07, p<0.001) (Table 2).

Post-hospital Survival Outcomes—Of the 362 patients, 227 patients (63%) were discharged alive: 105 from the chemotherapy cohort and 122 from the non-chemotherapy cohort. At 6-months, the estimated survival was 58% (95% CI: 48-67%) for chemotherapy patients and 73% (95% CI: 64-80%) for non-chemotherapy patients. At 12-months, the estimated survival was 50% (95% CI: 40-59%) for chemotherapy patients and 59% (95% CI: 50-67%) for non-chemotherapy patients (Figure 2). Patients who received chemotherapy demonstrated a lower survival distribution compared with non-chemotherapy patients (Supplemental Figure 1). Further, in multivariable analyses, patients who received chemotherapy in the ICU had a trend of higher risk of dying by 12 months (OR: 1.45, 95% CI: 0.95-2.19, p=0.08) (Table 4). In contrast to ICU and hospital mortality, MPM II score on ICU admission was not significantly associated with death by 12 months (p=0.14) (Table 3).

Initiation (n=72) versus Continuation (n=109) Chemotherapy Patients

The proportion of patients with a history of HSCT was higher (18/109 [17%]) for the continuation chemotherapy patients compared to the initiation patients (2/72 [3%]) (p=0.003). Additionally, initiation chemotherapy patients were more likely to be newly diagnosed (67/72 [93%]) compared with continuation patients (2/109 [2%]) (p<0.001) (Table 2). No other differences were found between the initiation and continuation groups (p=0.12->0.95).

ICU and Hospital Mortality—ICU mortality was 28% (31/109) in the continuation cohort and 21% (15/172) in the initiation cohort. In multivariable analyses, no significant differences in ICU mortality were found between continuation and initiation chemotherapy patients (p=0.27) (Supplemental Table 1). Overall hospital mortality was 48% (52/109) in the continuation cohort and 33% (24/72) in the initiation cohort. Although patients who received continuation chemotherapy had a trend of higher odds of hospital mortality than initiation patients in univariable analyses (OR: 1.82, 95% CI: 0.98-3.38, p=0.056), no significant difference in hospital mortality was found between continuation therapy patients after adjusting for known mortality predictors (OR: 1.80, 95% CI: 0.89-3.64, p=0.10).

Post-hospital Survival Outcomes—At 12 months, estimated survival was 42% (95% CI: 29-54%) in the continuation cohort and 58% (95% CI: 43-71%) in the initiation cohort (Supplemental Figure 2). In multivariable analyses, continuation chemotherapy patients had

a significantly higher risk of death by 12 months (HR: 1.77, 95% CI: 1.21-2.60, p=0.003) than initiation patients.

DISCUSSION

Our study is the first and largest study to date of patients with hematologic malignancies who received chemotherapy in the ICU at a US tertiary cancer center. Moreover, to our knowledge, we are the first to describe the short- and long-term outcomes of patients receiving initiation or continuation chemotherapy in the ICU.

The main findings of our study are that patients with hematologic malignancies who receive chemotherapy in the ICU were not found to have differences in short term mortality outcomes, but had a significantly longer ICU and hospital LOS and higher risk of death by 12 months than matched patients not on chemotherapy. There were no significant differences in ICU mortality between the initiation and continuation chemotherapy patients. The trend towards higher odds of hospital mortality among patients who received continuation chemotherapy may reflect their underlying disease severity.

Our ICU and hospital mortality rates of 25% and 42% respectively, for the chemotherapy cohort are comparable to the 25%-40% and 41%-43% ICU and hospital mortality rates, respectively, reported in four previous studies of patients undergoing chemotherapy in the ICU.[4-7] We also found that the severity of illness score (MPM-II) on ICU admission was significantly associated with worse short-term outcomes. Three of the four prior studies reported the severity of illness score (i.e., Simplified Acute Physiology Score [SAPS] II) as strongly associated with short-term outcomes.[4, 6, 7] Studies of critically ill cancer patients have consistently shown that short-term survival is primarily determined by the extent of organ failures at ICU admission, particularly the need for mechanical ventilation and vasopressors.[17-28] In our chemotherapy cohort, 38% and 34% required mechanical ventilation and vasopressors, respectively. We were unable to provide a precise reason for why despite a lower MPM score on ICU admission the patients in the chemotherapy group had a higher in-hospital mortality (albeit non-statistically significant). We can only speculate that some of the patients who received chemotherapy in the ICU were already on third or fourth line regimens and although they survived the ICU admission, they were more likely to have been designated as DNR on ICU discharge, not return to the ICU, and because of the nature of their malignancy, had a higher hospital mortality. We also included for analysis only the first ICU admission during which the patient received chemotherapy. Readmissions of patients who had earlier received chemotherapy in the ICU were not analyzed.

We also found that patients who had the same day hospital and ICU admission had lower odds of ICU and hospital mortality, possibly related to their pre-emptive ICU admission in anticipation of possible deterioration. A small retrospective singe center study showed that direct admission to the ICU of patients with high-risk acute myelogenous leukemia receiving chemotherapy and with physiological disturbances but no organ dysfunction was associated with improved outcomes.[29]

Only one previous study analyzed long-term survival of cancer patients receiving chemotherapy in the ICU.[7] That analysis involved 56 cancer patients (87.5% with hematologic malignancies) and reported survival rates of 49% and 41% at 6 and 12 months, respectively, which is lower than the 66% and 55% survival rates in our chemotherapy cohort (Supplemental Figure 1). Their survival may have been lower for a few reasons related to sample selection and treatment. First, our patients may have been less sick on ICU admission thus positively impacting their long term survival.[30] Second, it is possible that our cancer center offers superior post-hospital oncologic care and therapies. Lastly, there were underlying differences in study sample selection (i.e., inclusion of solid and hematologic malignancies in the earlier study).

Our study findings may offer guidance for triage for oncologic patients being considered for ICU admission. Recent literature demonstrates that oncologic patients with critical illness have far better outcomes than previously[1-3] thus encouraging their admission to the ICU. However, recent national society guidelines[31] do not specifically address the triage question of admitting cancer patients for therapeutic processes such as chemotherapy. In our study, we found that this specific group of oncological patients admitted for chemotherapy had equal outcomes to the matched group. This suggests that outcomes alone should not affect triage or the administration of chemotherapy. However, we also found that the patients who received chemotherapy had a significantly longer ICU and hospital LOS than patients who did not. The correlation between chemotherapy treatment duration and ICU LOS was weak to moderate (rho=0.28, p=0.001), so treatment alone did not fully explain the difference in LOS. This increase in resource utilization may certainly play a role in the triage and therapeutic decisions when ICU beds are severely limited or within non-cancer hospitals which do not specialize in oncologic therapeutic administration in the ICU.

A major strength of our study is the comparison with a matched cohort of ICU patients with similar malignancies who did not receive chemotherapy. This allowed us to control for the influence of three possible confounding factors (age, gender and type of malignancy) on the outcomes of hematologic cancer patients receiving chemotherapy in the ICU. First, we demonstrated that in contrast to the patients who did not receive chemotherapy in the ICU, the patients who received chemotherapy were more likely to have a longer ICU and hospital LOS, greater need for mechanical ventilation (during ICU stay), and higher risk of death by 12 months. Our study also reinforces the crucial role of understanding the capabilities and the triage approaches of the ICU to support these seriously ill patients.

Our study has several limitations. First, despite the large number of patients and analysis of prospectively collected clinical data, the study was retrospective and observational in nature and conducted at a single center with an ICU staff that is dedicated to supporting oncological therapies. This is a similar limitation to the previous studies [4-7] that were also performed in specialized oncologic ICUs. Second, it is possible that there was selection bias in the triage of patients admitted to the ICU for chemotherapy. However, even among oncologists and intensivists, there is variability in ICU triage of cancer patients with favorable and unfavorable prognosis[32] that may compensate for this limitation. Third, while it was obvious why chemotherapy were given in the initiation group, it was not possible for us to determine the reasons why the chemotherapy were administered (compassionate/end-

of-life, heroic, others) in the continuation group. Finally, we did not collect quality of life outcomes, including functional status and ability to receive continued oncologic treatment after ICU discharge.

In conclusion, our study showed that there were no differences in short-term mortality among patients with hematologic malignancies who did or did not receive chemotherapy in the ICU. However, patients who received chemotherapy had increased ICU and hospital resource utilization and a marginally higher risk of death by 12-months. The severity of illness score on ICU admission was significantly associated with ICU and hospital mortality and death at 12 months. Our data can assist oncology and critical care teams when discussing goals of care and prognosticating outcomes of patients who receive chemotherapy in the ICU and in dealing with triaging scarce ICU resources.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS:

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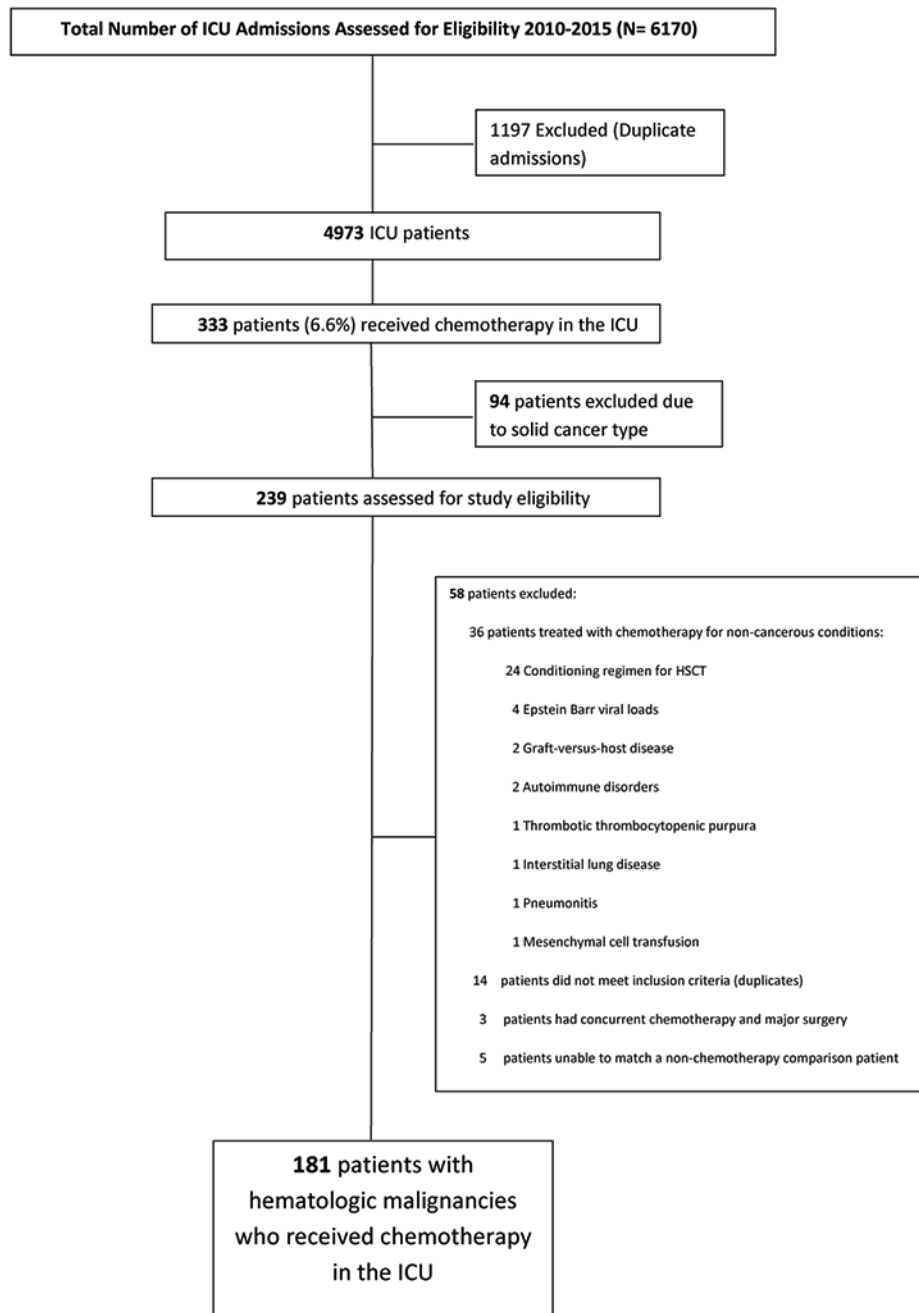
Figure 1.
CONSORT Diagram – Flowchart of ICU Admissions

Overall Survival from Discharge
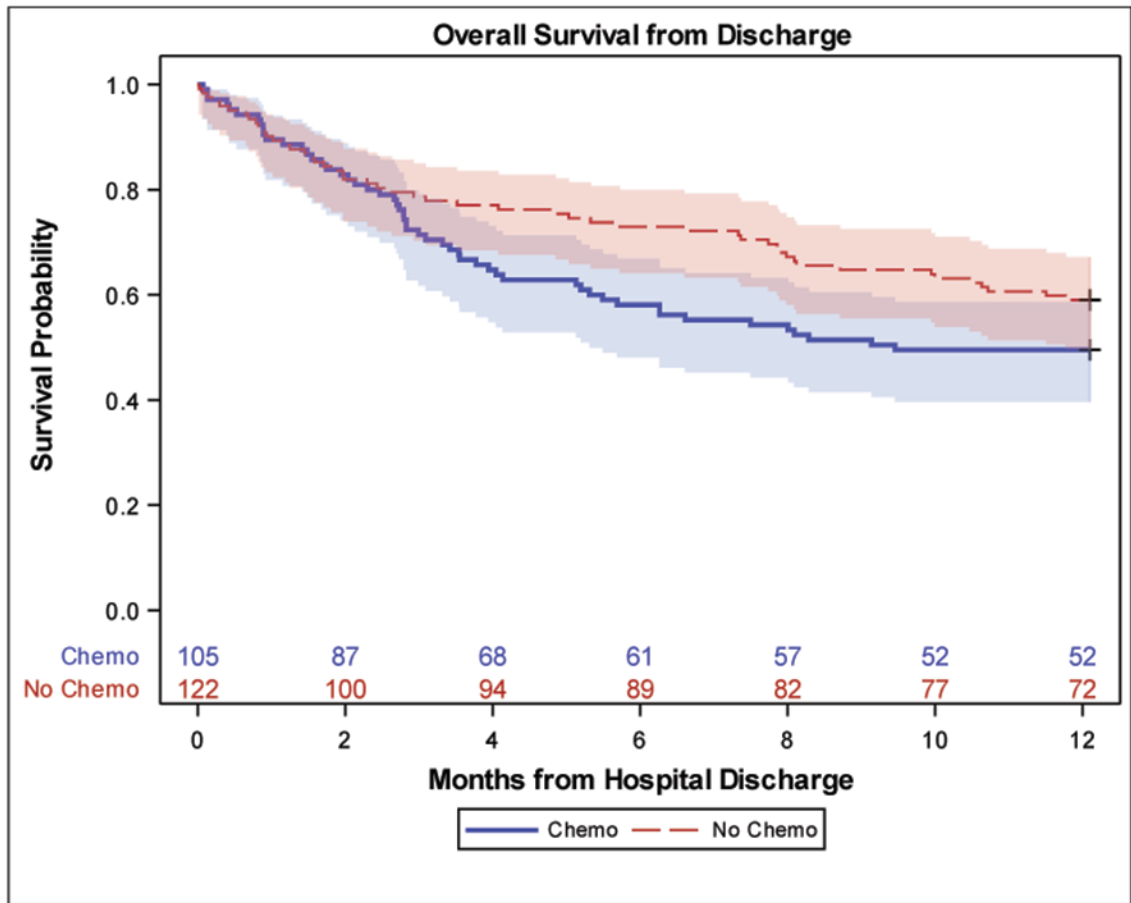
		N(#E)	KM Est	[95% CI]
6 Month	Chemo		0.58	[0.48 - 0.67]
	No Chemo		0.73	[0.64 - 0.80]
12 Month	Chemo	105 (53)	0.50	[0.40 - 0.59]
	No Chemo	122 (50)	0.59	[0.50 - 0.67]

Figure 2.
Overall Survival from Hospital Discharge Stratified by Chemotherapy Status (N=227)

Table 1.

Patient Characteristics and Cohort Comparisons

		Chemotherapy in ICU			
		All N (%)	Chemotherapy N (%)	No Chemotherapy N (%)	p-value
Sample Size		362	181	181	
Age at Admission, years	Median (range)	62 (18-87)	62 (18-86)	62 (19-87)	0.81
Gender	Male	230 (63.5)	115 (63.5)	115 (63.5)	
	Female	132 (36.5)	66 (36.5)	66 (36.5)	
MPM II Score	Median (range)	42.3 (7.40-94.7)	39.1 (7.40-94.7)	45.6 (8.28-94.0)	0.57
Cancer Type	Lymphoma	206 (56.9)	103 (56.9)	103 (56.9)	
	Leukemia	156 (43.1)	78 (43.1)	78 (43.1)	
Primary Admit Diagnosis	Bleeding	25 (7.6)	11 (6.2)	14 (9.1)	
	Cardiac	19 (5.7)	7 (4)	12 (7.8)	
	Chemotherapy Admin	45 (13.6)	45 (25.4)	0 (0)	
	Hematologic	4 (1.2)	4 (2.3)	0 (0)	
	Neurological	9 (2.7)	6 (3.4)	3 (1.9)	
	Renal	32 (9.7)	23 (13)	9 (5.8)	
	Respiratory	59 (17.8)	33 (18.6)	26 (16.9)	
	Sepsis	128 (38.7)	47 (26.6)	81 (52.6)	
	Other	10 (3)	1 (0.6)	9 (5.8)	
Charlson Comorbidity Index	Median (range)	6.0 (2.0-13.0)	6.0 (2.0-11.0)	6.0 (2.0-13.0)	0.55
Mechanical Ventilation, on Admit	Yes	42 (11.6)	17 (9.4)	25 (13.8)	0.26
	No	320 (88.4)	164 (90.6)	156 (86.2)	
Mechanical Ventilation, During Stay	Yes	137 (37.8)	75 (41.4)	62 (34.3)	0.15
	No	225 (62.2)	106 (58.6)	119 (65.7)	
Vasopressors, on Admit	Yes	41 (11.3)	16 (8.8)	25 (13.8)	0.19
	No	321 (88.7)	165 (91.2)	156 (86.2)	
Vasopressors, During Stay	Yes	123 (34)	59 (32.6)	64 (35.4)	0.63
	No	239 (66)	122 (67.4)	117 (64.6)	
CRRT/HD	Yes	25 (6.9)	17 (9.4)	8 (4.4)	0.11
	No	337 (93.1)	164 (90.6)	173 (95.6)	
Same Day Hospital/ICU Admit	Yes	86 (23.8)	34 (18.8)	52 (28.7)	**0.036**
	No	276 (76.2)	147 (81.2)	129 (71.3)	
ICU LOS, days	Median (range)	5 (0-47)	6 (1-47)	3 (0-28)	**<.001**
Hospital LOS, days	Median (range)	18 (0-126)	22 (2-121)	14 (0-126)	**0.024**
Hx of Transplant	Yes	33 (9.1)	20 (11)	13 (7.2)	0.30
	No	329 (90.9)	161 (89)	168 (92.8)	
Newly Diagnosed	Yes	89 (24.6)	69 (38.1)	20 (11)	**<.001**
	No	273 (75.4)	112 (61.9)	161 (89)	
Radiation during ICU stay	Yes	2 (0.6)	2 (1.1)	0 (0)	
	No	360 (99.4)	179 (98.9)	181 (100)	

		Chemotherapy in ICU			
		All N (%)	Chemotherapy N (%)	No Chemotherapy N (%)	p-value
# Deaths by ICU Discharge	Yes	86 (23.8)	46 (25.4)	40 (22.1)	
	No	276 (76.2)	135 (74.6)	141 (77.9)	
# Deaths by Hospital Discharge	Yes	135 (37.3)	76 (42)	59 (32.6)	
	No	227 (62.7)	105 (58)	122 (67.4)	

No comparison was done for gender or cancer type as these were perfectly matched.

Table 2.

Conditional Logistic Regression for ICU Mortality and Hospital Mortality (N=362)

Death in:			N(#D)	Univariable OR [95% CI]	p-value	Multivariable OR [95% CI]	p-value
ICU	Chemotherapy in ICU	Chemo	181 (46)	1.20 [0.74-1.95]	0.46	0.82 [0.39-1.75]	0.61
		No-Chemo	181 (40)	REF		REF	
	MPM II Score			1.03 [1.02-1.04]	**<.001**	1.07 [1.03-1.10]	**<.001**
	Charlson Comorbidity Index			0.99 [0.89-1.11]	0.88	0.80 [0.56-1.15]	0.22
	Mechanical Ventilation, on Admit	Yes	42 (18)	5.50 [1.22-24.81]	**0.027**	----	
		No	320 (68)	REF			
	Vasopressors, on Admit	Yes	41 (17)	3.67 [1.02-13.14]	**0.046**	----	
		No	321 (69)	REF			
	Same Day Hospital/ICU Admit	Yes	86 (14)	0.64 [0.28-1.49]	0.30	0.27 [0.08-0.91]	**0.035**
		No	276 (72)	REF		REF	
	CRRT/HD	Yes	25 (14)	2.75 [0.88-8.64]	0.08	6.16 [1.02-37.26]	**0.048**
		No	337 (72)	REF		REF	
	Hx of Transplant	Yes	33 (10)	2.00 [0.60-6.64]	0.26	1.17 [0.19-7.24]	0.86
		No	329 (76)	REF		REF	
Hospital	Chemotherapy in ICU	Chemo	181 (76)	1.52 [0.98-2.35]	0.06	1.58 [0.85-2.92]	0.14
		No-Chemo	181 (59)	REF		REF	
	MPM II Score			1.03 [1.02-1.04]	**<.001**	1.05 [1.03-1.07]	**<.001**
	Charlson Comorbidity Index			0.98 [0.89-1.08]	0.74	0.90 [0.70-1.14]	0.37
	Mechanical Ventilation, on Admit	Yes	42 (26)	4.33 [1.23-15.21]	**0.022**	----	
		No	320 (109)	REF			
	Vasopressors, on Admit	Yes	41 (22)	3.25 [1.06-9.97]	**0.039**	----	
		No	321 (113)	REF			
	Same Day Hospital/ICU Admit	Yes	86 (22)	0.48 [0.22-1.01]	0.053	0.27 [0.10-0.74]	**0.011**
		No	276 (113)	REF		REF	
	CRRT/HD	Yes	25 (17)	1.67 [0.61-4.59]	0.32	1.06 [0.31-3.64]	0.92
		No	337 (118)	REF		REF	
	Hx of Transplant	Yes	33 (17)	3.33 [0.92-12.11]	0.07	2.03 [0.37-11.03]	0.41
		No	329 (118)	REF		REF	

N = total number, #D = number of deaths, OR = Odds Ratio, REF = Reference Level (OR=1), 95% CI=95% Confidence Interval

Table 3.

Shared Frailty Cox Regression for 12 Month Survival from Discharge (N=227)

Death by:			Univariable			Multivariable	
			N(#D)	HR [95% CI]	p-value	HR [95% CI]	p-value
12 month	Chemotherapy in ICU	Chemo	105 (53)	1.37 [0.93-2.04]	0.11	1.45 [0.95-2.19]	0.08
		No-Chemo	122 (50)	REF		REF	
	MPM II Score		227 (103)	1.01 [1.00-1.02]	**0.013**	1.01 [1.00-1.02]	0.14
	Charlson Comorbidity Index		227 (103)	1.12 [1.03-1.22]	**0.011**	1.09 [0.98-1.20]	0.11
	Mechanical Ventilation, on Admit	Yes	16 (7)	0.94 [0.42-2.07]	0.87	----	
		No	211 (96)	REF			
	Vasopressors, on Admit	Yes	19 (11)	1.37 [0.72-2.63]	0.34	----	
		No	208 (92)	REF			
	Same Day Hospital/ICU Admit	Yes	64 (31)	1.04 [0.67-1.62]	0.85	1.16 [0.74-1.82]	0.53
		No	163 (72)	REF		REF	
	CRRT/HD	Yes	8 (5)	1.44 [0.56-3.68]	0.45	1.14 [0.43-3.05]	0.79
		No	219 (98)	REF		REF	
	Hx of Transplant	Yes	16 (9)	1.45 [0.71-2.98]	0.31	1.48 [0.71-3.08]	0.29
		No	211 (94)	REF		REF	

N = total number, #D = number of deaths, HR = Hazard Ratio, 95% CI=95% Confidence Interval

Table 4.
Patient Characteristics for Initiation versus Continuation Chemotherapy Patients

Chemotherapy Cohort Only (N=181)

			Chemotherapy in ICU		
		All 181 (100%)	Continuation 109 (60%)	Initiation 72 (40%)	p-value
Age at Admission, years	Median (range)	62 (18-86)	61 (18-86)	65 (22-86)	0.14
Gender	Male	115 (63.5)	68 (62.4)	47 (65.3)	0.75
	Female	66 (36.5)	41 (37.6)	25 (34.7)	
MPM II Score	Median (range)	39.1 (7.40-94.7)	42.7 (7.40-94.7)	34.2 (8.30-94.1)	0.19
SOFA Score	Median (range)	6.0 (0.0-15.0)	6.0 (0.0-15.0)	5.5 (0.0-14.0)	0.27
Cancer Type	Lymphoma	103 (56.9)	58 (53.2)	45 (62.5)	0.22
	Leukemia	78 (43.1)	51 (46.8)	27 (37.5)	
Primary Admit Diagnosis	Bleeding	11 (6.2)	8 (7.5)	3 (4.2)	
	Cardiac	7 (4)	3 (2.8)	4 (5.6)	
	Chemotherapy Admin	45 (25.4)	20 (18.9)	25 (35.2)	
	Hematologic	4 (2.3)	3 (2.8)	1 (1.4)	
	Neurological	6 (3.4)	5 (4.7)	1 (1.4)	
	Renal	23 (13)	14 (13.2)	9 (12.7)	
	Respiratory	33 (18.6)	22 (20.8)	11 (15.5)	
	Sepsis	47 (26.6)	30 (28.3)	17 (23.9)	
	Other	1 (0.6)	1 (0.9)	0 (0)	
Charlson Comorbidity Index	Median (range)	6.0 (2.0-11.0)	5.0 (2.0-11.0)	6.0 (2.0-9.0)	0.75
Mechanical Ventilation, on Admit	Yes	17 (9.4)	12 (11)	5 (6.9)	
	No	164 (90.6)	97 (89)	67 (93.1)	0.44
Mechanical Ventilation, During Stay	Yes	75 (41.4)	46 (42.2)	29 (40.3)	
	No	106 (58.6)	63 (57.8)	43 (59.7)	0.88
Vasopressors, on Admit	Yes	16 (8.8)	12 (11)	4 (5.6)	
	No	165 (91.2)	97 (89)	68 (94.4)	0.29
Vasopressors, During Stay	Yes	59 (32.6)	37 (33.9)	22 (30.6)	
	No	122 (67.4)	72 (66.1)	50 (69.4)	0.75
CRRT/HD	No	164 (90.6)	102 (93.6)	62 (86.1)	0.12
	Yes	17 (9.4)	7 (6.4)	10 (13.9)	
Same Day Hospital/ICU Admit	Yes	34 (18.8)	21 (19.3)	13 (18.1)	
	No	147 (81.2)	88 (80.7)	59 (81.9)	>0.95
ICU LOS, days	Median (range)	6 (1-47)	5 (1-44)	7 (1-47)	0.13
Hospital LOS, days	Median (range)	22 (2-121)	21 (2-92)	23 (2-121)	0.64
Hx of Transplant	Yes	20 (11)	18 (16.5)	2 (2.8)	**0.003**
	No	161 (89)	91 (83.5)	70 (97.2)	
Newly Diagnosed	Yes	69 (38.1)	2 (1.8)	67 (93.1)	**<.001**
	No	112 (61.9)	107 (98.2)	5 (6.9)	
Prior Radiation	Yes	2 (1.1)	2 (1.8)	0 (0)	
	No	179 (98.9)	107 (98.2)	72 (100)	

| | | Chemotherapy in ICU | | | |
		All 181 (100%)	Continuation 109 (60%)	Initiation 72 (40%)	p-value
# Deaths by ICU Discharge	Yes	46 (25.4)	31 (28.4)	15 (20.8)	
	No	135 (74.6)	78 (71.6)	57 (79.2)	
# Deaths by Hospital Discharge	Yes	76 (42)	52 (47.7)	24 (33.3)	
	No	105 (58)	57 (52.3)	48 (66.7)	