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REPORTS OF ORIGINAL INVESTIGATIONS

Outcomes of hematopoietic cell transplant recipients requiring invasive mechanical ventilation: a two-centre retrospective cohort study

Pronostics des récipiendaires de transplantations de cellules hématopoïétiques nécessitant une ventilation mécanique invasive : une étude de cohorte rétrospective dans deux centres

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Abstract

Purpose *Outcomes of critically ill, hematopoietic cell transplant patients who require prolonged mechanical ventilation are not well studied. We describe the baseline characteristics, critical care management, and outcomes of this population and explore potential predictors of mortality.*

Methods *We performed a retrospective cohort study in two critical care units in Ontario. We included adult intensive care unit patients who required invasive mechanical ventilation within 90 days of receiving a hematopoietic cell transplant. The primary outcome was mortality at 90 days. Using logistic regression, we explored predictors of mortality including type of transplant (allogeneic vs autologous), severity of illness (assessed using the Sequential Organ Failure Assessment [SOFA] score), and baseline characteristics (such as age and sex).*

Results *We included 70 patients from two study sites. Ninety-day mortality was 73% (n = 51) in the entire cohort, 58% (15/26) in patients post-autologous transplant, and 82% (36/44) in those post-allogeneic transplant. Ninety-one percent (10/11) of patients who required invasive mechanical ventilation for more than 21 days died. Independent predictors of all-cause mortality*

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included allogeneic transplant, higher SOFA score, the presence of acute hypoxemic respiratory failure, and a longer interval between receiving the transplant and initiation of mechanical ventilation.

Conclusions *Our study shows high rates of mortality among hematopoietic cell transplant recipients that require invasive mechanical ventilation, particularly in those post-allogeneic transplant and in those who require prolonged ventilation for more than 21 days.*

Résumé

Objectif *Les pronostics des patients en état critique recevant une transplantation de cellules hématopoïétiques et nécessitant une ventilation mécanique prolongée sont peu étudiés. Nous décrivons les caractéristiques de base, la prise en charge de soins critiques et les pronostics de cette population et explorons des prédicteurs potentiels de mortalité.*

Méthode *Nous avons réalisé une étude de cohorte rétrospective dans deux unités de soins critiques en Ontario. Nous avons inclus les patients adultes de l'unité de soins intensifs nécessitant une ventilation mécanique invasive dans les 90 jours suivant la transplantation de cellules hématopoïétiques. Le critère d'évaluation principal était la mortalité à 90 jours. À l'aide d'une analyse de régression logistique, nous avons exploré les prédicteurs de mortalité, y compris le type de greffe (allogénique ou autologue), la gravité de la maladie (évaluée à l'aide du score SOFA - Sequential Organ Failure Assessment), et les caractéristiques de base (telles que l'âge et le sexe).*

Résultats *Nous avons inclus 70 patients provenant de nos deux sites d'étude. La mortalité à 90 jours était de 73 % (n = 51) dans la cohorte entière, 58 % (15/26) chez les patients ayant reçu une greffe autologue, et 82 % (36/44) chez les patients ayant reçu une greffe allogénique. Quatre-vingt-onze pour cent (10/11) des patients nécessitant une ventilation mécanique invasive pendant plus de 21 jours sont décédés. Les prédicteurs indépendants de mortalité toutes causes confondues comprenaient la greffe allogénique, un score SOFA plus élevé, la présence d'une insuffisance respiratoire hypoxémique aiguë, et un intervalle plus long entre la greffe et le début de la ventilation mécanique.*

Conclusion *Notre étude montre des taux de mortalité élevés chez les récipiendaires de greffes de cellules hématopoïétiques nécessitant une ventilation mécanique invasive, particulièrement chez les patients ayant reçu une greffe allogénique et chez ceux nécessitant une ventilation prolongée de plus de 21 jours.*

Hematopoietic cell transplantation (HCT) is a lifesaving procedure used to treat malignant and non-malignant diseases.[1] The HCT patient faces an increased risk of adverse events in the post-HCT period including intensive care unit (ICU) admission. This risk is primarily due to the pre-HCT conditioning regimes of high-dose chemotherapy and radiotherapy, in addition to the subsequent immunosuppression that results from the HCT.[2-5] Previous studies have shown that the rates of ICU admission and the need for invasive mechanical ventilation (MV) are high and increasing in this population.[6,7]

The prognosis of critically ill HCT patients, particularly those requiring invasive MV, has historically been poor.[8,9] Nevertheless, this may be changing with recent advances such as enhanced patient selection, safer transplantation strategies, and improved post-HCT and ICU care.[6,10] This has led to an increased demand for early and aggressive critical care interventions aimed at supporting these patients when complications arise.[7,11] Despite these recent advances, a large percentage of these patients will die, with studies showing highest risk in those requiring invasive MV or renal replacement therapy.[6,8,9]

As the overall number of patients receiving HCT is expected to increase in the coming years, this will likely lead to more HCT patients being admitted to the ICU.[10] Improved characterization and prognostication of critically ill HCT recipients who require invasive MV is thus crucial to better identify predictors of poor outcome, aid in the identification of treatable factors, and inform shared decision-making with patients and families about how aggressive life-supporting interventions should be.[12] Hence, the primary aim of this study was to describe the baseline characteristics, critical care interventions, and 90-day mortality of post-HCT patients admitted to the ICU requiring invasive MV. As a secondary aim, we explored potential predictors of mortality in this population.

Methods

Study design and setting

We conducted a retrospective cohort study among critically ill adult patients who required invasive MV within 90 days following HCT at two hospitals in Canada: Mount Sinai Hospital (Toronto, ON, Canada) and Juravinski Hospital (Hamilton, Ontario). Both hospitals' ICUs serve as referral centres for two large HCT centres in Ontario, Canada. The study period was from January 2006 to August 2016. The study was approved (November 7, 2016) for waived consent by the research ethics boards of both centres prior to initiation and was conducted in accordance with

the good clinical practice guidelines and the amended declaration of Helsinki.

Study population

We included patients if they were older than 16 years, had been admitted to the ICU at one of the participating centres during the study period, and required invasive MV within 90 days of receiving an HCT. We included patients who received any type of HCT and for any indication. We excluded patients who were intubated strictly to facilitate a procedure (such as bronchoscopy), patients who were intubated for less than 24 hr, and those who received only non-invasive ventilation.

Measurements and variables

We collected baseline demographics, ICU admission diagnosis, baseline comorbidities, data related to the HCT (underlying diagnosis, time between HCT and invasive MV requirement, type of HCT, Hematopoietic Cell Transplant Comorbidity Index,[13] and presence of graft *vs* host disease [GVHD]) from paper and electronic medical records at each institution. We calculated baseline Acute Physiology and Chronic Health Evaluation (APACHE) II and daily Sequential Organ Failure Assessment (SOFA) severity scores for all the patients by extracting data from the medical record.[14,15]

The primary outcome of the study was all-cause mortality at 90 days from the initial day of invasive MV. We also report data on ICU mortality, co-interventions received while in the ICU (e.g., ventilation parameters, neuromuscular blockade, utilization of advanced ventilatory techniques such as prone or high frequency oscillation), days of invasive MV, and types of life-support interventions (e.g., use of vasopressors and renal replacement therapy).

Statistical analysis

We summarized baseline patient characteristics using proportions for categorical variables and mean (standard deviation [SD]) or median [interquartile range (IQR)] where appropriate for continuous variables. We used bivariate analysis to compare the baseline characteristics of patients who died with those who survived. We also compared recipients of allogeneic and autologous HCT. Continuous variables were compared using *t* test for normally distributed data and the Wilcoxon rank-sum test for skewed data sets. Categorical variables were compared using the Fisher's exact test.

As an exploratory analysis to identify potential predictors of mortality, we assessed the association between the independent variables studied and the primary outcome (mortality at 90 days) by developing a multivariable logistic regression model. Initial inclusion of covariates in the model was based on: variables previously reported to be associated with the outcome (type of HCT [allogeneic *vs* autologous], presence of GVHD [yes *vs* no]), baseline variables deemed to be clinically relevant (age [as a continuous variable], sex) and those variables which were significantly different in the bivariate analysis (at the $P < 0.2$ level). For model selection, we used either Akaike's information criteria or likelihood ratio tests when appropriate. We used high-degree polynomials and cubic restricted splines to evaluate the linear relationship of all included continuous predictors with the log (odds) of the outcome. For our final model, we assessed discrimination by means of the area under the receiver operating curve and calibration by the Hosmer-Lemeshow test statistic.

Finally, we constructed non-parametric curves using the Kaplan-Meier estimator to describe the survival experience of the total sample of included patients. We also constructed adjusted survival curves for patients with autologous and allogeneic HCT. We used a $P < 0.05$ threshold to declare statistical significance, all reported *P* values are two sided and we used STATA v.14.2 (StataCorp LP, College Station, TX, USA) for all analyses.

Results

We included 70 patients who met our eligibility criteria. Table 1 summarizes the baseline characteristics for the study population at initiation of invasive MV. Median [interquartile range (IQR)] age was 55 [44–61] yr and 41% ($n = 29$) were female. The reason for MV was acute hypoxemic respiratory failure (AHRF) in 87% ($n = 61$) of the included patients. Allogeneic HCT was most common (62%, $n = 44$) and the most frequent underlying disease was acute myeloid leukemia (21%, $n = 15$). The median [IQR] HCT-Comorbidity Index was 1 [0–3], and 16% ($n = 11$) had been previously diagnosed with GVHD. The median [IQR] time from HCT to requiring MV was 16.5 [10–40] days. Regarding the severity of disease, the median [IQR] APACHE II and SOFA scores were 25 [22–30] and 11 [8–13], respectively.

Overall, all-cause 90-day mortality was 73% ($n = 51$) and ICU mortality was 63% ($n = 44$). Mortality was higher in patients who required longer duration of MV: 76% ($n = 28/37$) for those requiring MV over seven days ($n = 28/37$) and 14 days ($n = 19/25$), and 91% ($n = 10/11$) in those requiring MV for more than 21 days. The median [IQR] duration of MV was 9 [1–24] days. Mortality was also slightly higher for those requiring invasive MV and vasopressors, invasive MV, and renal replacement

Table 1 Baseline characteristics of included patients with HCT undergoing invasive mechanical ventilation

Baseline covariate		Entire cohort (n = 70)	Alive at 90 days (n = 19)	Dead at 90 days (n = 51)	P value*
Age, years, mean (SD)		51 (14)	52 (12)	51 (14)	0.59
Female sex, n (%)		29 (41)	11 (58)	18 (35)	0.09
Allogeneic transplant, n (%)		44 (63)	8 (42)	36 (71)	0.03
Underlying hematologic	ALL	9 (12.9)	0 (0)	9 (18)	0.58
malignancy, n (%)	AML	15 (21)	5 (26)	10 (20)	
	Amyloidosis	2 (3)	1 (5)	1 (2)	
	Aplastic anemia	2 (3)	0 (0)	2 (4)	
	HL	4 (6)	1 (5)	3 (6)	
	MDS	10 (14)	2 (11)	8 (16)	
	MM	10 (14)	5 (26)	5 (10)	
	NHL	10 (14)	4 (21)	6 (12)	
	Other	8 (11)	1 (5)	7 (14)	
Time from HCT to invasive MV, days, median [IQR]		16.5 (10,40)	11 (7, 15)	24 (11,54)	< 0.001
APACHE II score, median [IQR]		25 [22–30]	23 [20–33]	25 [22–29]	0.48
SOFA, median [IQR]		11 [8–13]	9 [7–12]	12 [9–14]	0.02
Hemoglobin, mean (SD)		82 (11)	82 (12)	82 (11)	0.99
Bilirubin, mean (SD)		68 (127)	35 (48)	80 (144)	0.21
Lactate, mean (SD)		3.7 (4.2)	2.7 (2.7)	4.1 (4.6)	0.24
Creatinine, mean (SD)		150 (90)	165 (100)	144 (87)	0.41
Platelet count/mL, mean (SD)		47 (79)	47 (54)	48 (87)	0.97
Neutrophil count/mL, mean (SD)		3.4 (5.7)	3.1 (7.3)	3.6 (5.1)	0.79
CMV infection, n (%)		14 (20.0)	2 (11)	12 (24)	0.23
Acute hypoxemic respiratory failure, n (%)		61 (87.1)	13 (68)	48 (94)	0.004
PaO_2/F_iO_2, mean (SD)		191 (103)	224 (125)	181 (95)	0.23
Gastrointestinal bleed, n (%)		9 (12.9)	2 (11)	7 (14)	0.72
Engraftment syndrome, n (%)		2 (2.9)	1 (5)	1 (2)	0.46
GVHD, n (%)		12 (17.1)	1 (5)	11 (22)	0.11
Febrile neutropenia, n (%)		53 (75.7)	11 (58)	42 (82)	0.03
HCT-CI, median [IQR]		1 [0–3]	1 [0–3]	1 [0–4]	0.95

*P value represents comparison between survivors and decedents. Means are compared with T tests, medians with Wilcoxon and proportions with the Fisher's exact test

ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; APACHE = Acute Physiology and Chronic Health Evaluation; CMV = cytomegalovirus; GVHD = graft *vs* host disease; HCT = hematopoietic cell transplantation; HCT-CI = Hematopoietic Cell Transplant Comorbidity Index; HL = Hodgkin's lymphoma; IQR = interquartile range; MDS = myelodysplastic syndrome; MM = multiple myeloma; NHL = Non-Hodgkin's lymphoma; SD = standard deviation; SOFA = Sequential Organ Failure Assessment

therapy, or all three life-support modalities. Figure 1 shows the survival of the entire cohort of patients, and for patients with autologous *vs* allogeneic HCT.

Table 1 also shows the univariate analysis comparing the baseline characteristics of patients who survived with the baseline characteristics of those who died. Patients who died before 90 days were more likely to be allogeneic HCT recipients (71% *vs* 42%; $P = 0.03$), had a longer time from HCT to MV (median of 24 *vs* 11 days; $P < 0.01$), and presented with a higher baseline SOFA score (12 *vs* 9; $P = 0.02$). Patients who died were more likely to be admitted because of acute hypoxemic respiratory failure (AHRF) (94% *vs* 68%; $P = 0.01$) and with febrile neutropenia (82% *vs* 58%; $P = 0.03$). The intensity of co-interventions such as the use of prone position during MV, renal replacement therapy, and neuromuscular blockade was generally greater in patients who died (data not shown), and reached statistical significance ($P = 0.05$) with regard to requirement for vasopressor therapy (73% *vs* 47%) and mean (SD) levels of positive end-expiratory pressure [12.1 (4.2) *vs* 9.9 (3.5) cmH_2O].

Table 2 shows the baseline characteristics and main outcomes for patients who underwent either autologous or allogeneic HCT. Of note, the allogeneic group was mainly

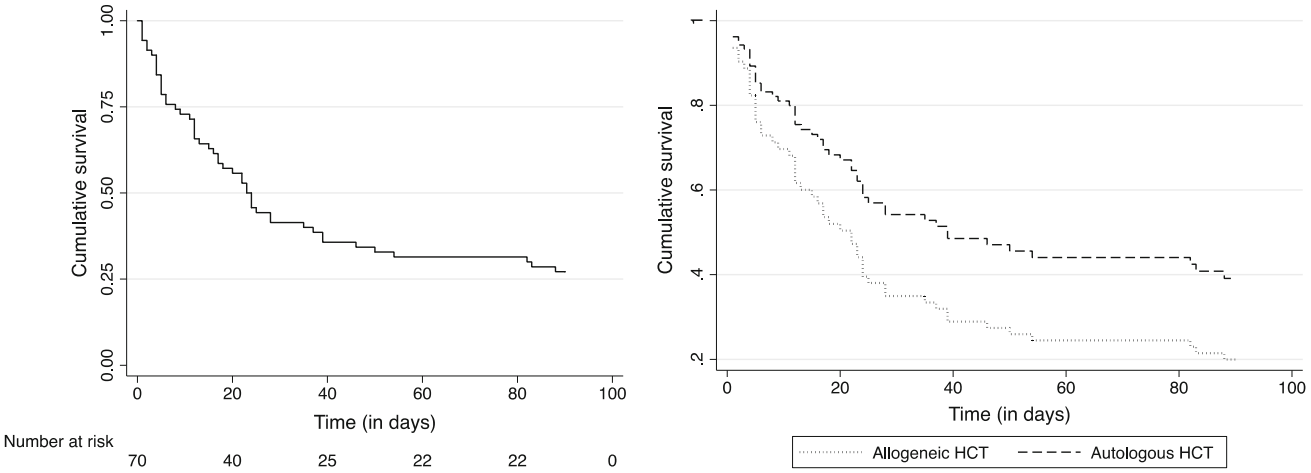

Fig. 1 Cumulative survival of hemopoietic cell transplant recipients during follow-up. Left panel shows Kaplan–Meier survival curve for the entire cohort of patients. Right panel shows post estimation, Cox proportional hazards model adjusted curves (including sex, age, and HCT-CI index as covariates) for allogeneic and autologous HCT patients. HCT = hematopoietic cell transplantation; HCT-CI = Hematopoietic Cell Transplant Comorbidity Index

comprised of patients with acute leukemia, and they had a significantly longer time from HCT to invasive MV.

Table 3 shows the results of the logistic regression model examining potential predictors of 90-day mortality among HCT patients who required MV. Allogeneic transplant (odds ratio [OR], 11.30; 95% confidence interval [CI], 1.61 to 79.3), higher severity of illness (for every point increase in the SOFA score: OR, 1.26; 95% CI, 1.01 to 1.60), the presence of AHRF (OR, 48.5; 95% CI, 3.41 to 690.8) and a longer interval between HCT and MV initiation (for every day increase: OR, 1.08; 95% CI, 1.01 to 1.14) were found to be independently associated with higher all-cause mortality at 90 days.

Discussion

We present the results of a two-centre study describing the characteristics and outcomes of 70 patients who underwent MV within 90 days of HCT. Most patients were mechanically ventilated within 30 days of HCT, illustrating that the pre-engraftment and peri-engraftment periods constitute a time-frame with a high risk of deterioration. Our study shows a very high overall 90-day mortality, particularly in patients who required invasive MV for more than 21 days. The independent factors associated with a higher risk of mortality were allogeneic transplantation, higher severity of disease, hypoxemic respiratory failure as the cause for intubation, and a longer time interval between HCT and need for MV.

While the overall survival of patients who become critically ill after receiving HCT has improved over the last years, our study nonetheless shows a very high risk of death among those receiving invasive MV. Of note, most of the deaths in our cohort occurred within the first 20 days, likely reflecting a combination of baseline and comorbid disease, profound immunosuppression, acute organ failure, and withdrawal of life-support interventions. These results are consistent with a recent French study examining 497 patients post-HCT, which showed similarly high 90-day mortality in patients who received MV.[6] In this study, factors independently associated with mortality included the presence of GVHD, and MV and renal replacement therapy.[6] In our cohort, the higher rate of GVHD and renal replacement therapy in non-survivors did not reach statistical significance possibly because of the small sample size. The specific case of GVHD should be evaluated in the context of allogeneic transplantation being one of the main risk factors for death among this cohort of patients. Autologous and allogeneic HCT remain distinct interventions, with different patient diagnoses, risks, and outcomes. Hence, despite a lack of association between GVHD and outcomes in our cohort, GVHD likely lies in the causal pathway for patients with allogeneic transplantation; most cases of GVHD occurred, as expected, among allogeneic HCT recipients. Furthermore, in addition to the type of HCT and the presence or absence of GVHD, the underlying condition is also likely a major risk factor for poor outcomes (i.e., most patients with acute leukemia included in our study died within 90 days).

The association between higher severity of disease and multiorgan failure at baseline (measured by the SOFA score and compared with single system failure) and worse outcomes has also been reported in other studies although the association remains controversial.[3,16,17] The association between respiratory failure as the indication for MV and

Table 2 Characteristics of patients with autologous and allogeneic HCT undergoing invasive mechanical ventilation

Baseline covariate	Autologous HCT (n = 26)	Allogeneic HCT (n = 44)	P value*
Age, yr, mean (SD)	52.4 (14.0)	50.3 (13.3)	0.52
Female sex, n (%)	10 (38)	19 (43)	0.70
Underlying hematologic malignancy, n (%)	0 (0)	9 (20)	< 0.001
ALL			
AML	0 (0)	15 (34)	
Amyloidosis	2 (8)	0 (0)	
Aplastic anemia	0 (0)	2 (5)	
HL	4 (15)	0 (0)	
MDS	0 (0)	10 (23)	
MM	10 (38)	0 (0)	
NHL	6 (23)	4 (9)	
Other*	4 (15)	4 (9)	
Time from HCT to IMV, days, median [IQR]	10.5 [7–28]	18.5 [12–49.5]	0.02
APACHE II score, median [IQR]	24 [22–30]	25 [21–30]	0.96
SOFA, median [IQR]	10.5 [8–13]	12 [9–14]	0.12
Hemoglobin, mean (SD)	83 (10)	81 (11)	0.66
Bilirubin, mean (SD)	32 (44)	89 (153)	0.07
Lactate, mean (SD)	2.9 (3.6)	4.2 (4.4)	0.23
Creatinine, mean (SD)	131 (94)	160.7 (87.5)	0.19
Platelet count/mL, mean (SD)	37 (46)	54 (94)	0.40
Neutrophil count/mL, mean (SD)	4.9 (8.1)	2.6 (3.8)	0.13
CMV infection, n. (%)	2 (8)	12 (27)	0.05
ARDS, n. (%)	14 (54)	16 (36)	0.15
Gastrointestinal bleed, n. (%)	3 (12)	6 (14)	0.80
Engraftment syndrome, n (%)	0 (0)	2 (5)	0.27
GVHD, n (%)	1 (4)	11 (25)	0.02
Febrile neutropenia, no. (%)	17 (65)	36 (82)	0.12
HCT-CI, median [IQR]	2 [0–3]	1 [0.5–3.5]	0.72
Acute hypoxemic respiratory failure, n (%)	25 (96)	36 (82)	0.08
Outcomes			
All-cause mortality at 90 days	15 (57.7)	36 (81.8)	0.05

*P value represents comparison between survivors and decedents. Means are compared with T tests, medians with Wilcoxon test, and proportions with the Fisher's exact test

ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; ARDS = documented diagnosis of acute respiratory distress syndrome; CMV = cytomegalovirus; GVHD = graft *vs* host disease; HCT = hematopoietic cell transplantation; HCT-CI = Hematopoietic Cell Transplant Comorbidity Index; HL = Hodgkin's lymphoma; IQR = interquartile range; IMV = invasive mechanical ventilation; MDS = myelodysplastic syndrome; MM = multiple myeloma; NHL = Non-Hodgkin's lymphoma. SD = standard deviation; SOFA = Sequential Organ Failure Assessment

*Other includes: chronic lymphocytic leukemia, Diamond Blackfan Anemia, myelofibrosis, and post-transplant lymphoproliferative disease

mortality has also been previously reported, although this finding in our study might be due to chance, given that only a small subset of patients (13%, n = 9) received MV for reasons other than AHRF.[5,6,18]

Furthermore, our study showed an association between higher mortality and greater time between HCT and initiation of MV. This finding is consistent with previous reports that showed up to 50% increased mortality in patients admitted to ICU with a longer lag-time from HCT to intubation.[9,17] Two possible mechanisms may explain this finding. First, the longer the time since the HCT, the broader the possible etiologies for acute respiratory failure due to prolonged immunosuppression, and non-infectious complications such as peri-engraftment respiratory distress syndrome.[2,19] Second, a longer duration of sub-acute illness and potentially delayed intubation may have a

Table 3 Predictors of death among Hematopoietic Cell Transplant patients undergoing invasive mechanical ventilation

Predictor variable	Adjusted odds ratio* (95% CI)
Age, yr	1.03 (0.97 to 1.10)
Female sex	0.26 (0.05 to 1.23)
Allogeneic transplant	11.30 (1.61 to 79.3)
SOFA score (per unit increase)	1.26 (1.01 to 1.60)
Acute hypoxemic respiratory failure	48.5 (3.41 to 690.7)
Time between HCT and MV (per day increase)	1.08 (1.01 to 1.14)

*Based on a multivariate logistic regression model including age, sex, allogeneic transplant, SOFA, acute hypoxemic respiratory failure, and time between HCT and MV (area under the curve AUC = 0.90)

CI = confidence interval; HCT = hematopoietic cell transplant; MV = mechanical ventilation; SOFA = Sequential Organ Failure Assessment

detrimental effect on a patient's physiologic reserve.[20,21] This finding raises the question of whether earlier intervention and escalation of therapy may be beneficial – e.g., the involvement of more engaged rapid response teams to identify patients at high risk of deterioration. It should be noted that time from HCT to invasive MV was on average longer for the allogeneic transplant group, which may further contribute to the higher likelihood of poor outcomes. Potential explanations for the discrepancy between time to invasive MV in autologous and allogeneic HCT patients may include: 1) that the latter group has prolonged neutropenia and thus remains at higher risk of opportunistic bacterial infections during longer periods of time; and 2) autologous HCT patients have a higher risk of non-infectious lung complications that usually occur early in the post-transplant period.[22] Finally, of all the variables independently associated with mortality in our study; only timing of MV is potentially modifiable. Findings of our study may thus help identify patients at very high risk of short-term mortality, such as recipients of allogeneic HCT receiving MV longer than three weeks. This finding of longer ICU stay and higher risk of all-cause death is also in keeping with data from a large, heterogeneous group of ICU patients.[23]

To our knowledge, our study presents the largest Canadian report of mechanically ventilated HCT patients from two centres with expertise in providing interdisciplinary care to these patients. Nevertheless, our study has limitations. First, the sample size was small, and it is therefore possible that certain associations were found or missed because of chance alone.[6,18] Importantly, given the relatively small sample size and considering the least frequent category of the primary outcome (in this case, survival) the multivariable model including four parameters is likely over-fitted. Thus, our secondary analysis should be considered as exploratory. Second, although we could broadly characterize the reason for MV, given the retrospective data collection we could not identify the specific etiologies for acute respiratory failure in many cases. Nevertheless, this may represent the usual clinical scenario where many of these patients remain without a clear diagnosis. Furthermore, limited data for specific laboratory values precluded us from calculating other scores such as the PICAT (prognostic index for intensive care after allogeneic hematopoietic stem cell transplantation) that may be useful for the prediction of outcomes in this population.[17] Third, this study reports the outcomes of only two centres in Ontario, potentially limiting the generalizability of the results. Reassuringly, the overall mortality was similar to cohorts from different countries suggesting that at least some of the results are comparable. Finally, although we had information on survival status of our cohort, we lack data on functional outcomes and health-related quality of life in survivors.

In conclusion, our study shows a very high 90-day mortality among HCT patients receiving MV, especially in those who require prolonged ventilation. This information can aid clinicians, patients, and surrogate decision-makers in choosing the most appropriate treatment direction based on the probability of survival. Our observations emphasize the importance of close collaboration between hematologists and intensivists at the onset of critical illness in setting expectations for clinicians, the patient, and their family members. Most importantly, it supports the need for further research in this area, including effective non-invasive interventions to manage hypoxemic respiratory failure, diagnostic strategies to improve the accuracy of the underlying diagnosis, prediction tools that incorporate the specific treatments of the underlying disease, and evidence-based treatment strategies such as safe and prompt MV in HCT patients.

Conflicts of interest The authors declare no potential conflicts of interest.

Editorial responsibility This submission was handled by Dr. Hilary P. Grocott, Editor-in-Chief, *Canadian Journal of Anesthesia.*

Author contributions *Mohammad Hamidi* and *Bruno L. Ferreyro* were involved in study conception and design, analysis and interpretation of data, and drafting of the manuscript. *Federico Angriman* was involved in data analysis and interpretation, and drafting of the manuscript. *Kira L. Gossack-Keenan* and *Bram Rochwerg* were involved in study conception and design, data acquisition, and critical revision of manuscript. *Sangeeta Mehta* was involved in study conception and design, analysis and interpretation of the data, and drafting of manuscript. All authors have read and approved the final version of this manuscript.

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