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Mortality Trends of Oncology and Hematopoietic Stem Cell Transplant Patients Supported on Extracorporeal Membrane Oxygenation: A Systematic Review and Meta-Analysis

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Abstract

Background: There is an increasing frequency of oncology and hematopoietic stem cell transplant (HSCT) patients seen in the intensive care unit and requiring extracorporeal membrane oxygenation (ECMO), however, prognosis of this population over time is unclear. **Methods:** MEDLINE, EMBASE, Cochrane and Web of Science were searched from earliest publication until April 10, 2020 for studies to determine the mortality trend over time in oncology and HSCT patients requiring ECMO. Primary outcome was hospital mortality. Random-effects meta-analysis model was used to obtain pooled estimates of mortality and 95% confidence intervals. A priori subgroup metanalysis compared adult versus pediatric, oncology versus HSCT, hematological malignancy versus solid tumor, allogeneic versus autologous HSCT, and veno-arterial versus veno-venous ECMO populations. Multivariable meta-regression was also performed for hospital mortality to account for year of study and HSCT population. **Results:** 17 eligible observational studies (n = 1109 patients) were included. Overall pooled hospital mortality was 72% (95% CI: 65, 78). In the subgroup analysis, only HSCT was associated with a higher hospital mortality compared to oncology subgroup [84% (95% CI: 70, 93) vs. 66% (95% CI: 56, 74); $P = 0.021$]. Meta-regression showed that HSCT was associated with increased mortality [adjusted odds ratio (aOR) 3.84 (95% CI 1.77, 8.31)], however, mortality improved with time [aOR 0.92 (95% CI: 0.85, 0.99) with each advancing year]. **Conclusion:** This study reports a high overall hospital mortality in oncology and HSCT patients on ECMO which improved over time. The presence of HSCT portends almost a 4-fold increased risk of mortality and this finding may need to be taken into consideration during patient selection for ECMO.

Keywords

neoplasms, immunocompromised host, intensive care units, bone marrow transplantation, extracorporeal membrane oxygenation, extracorporeal circulation

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Introduction

Extracorporeal membrane oxygenation (ECMO) serves as rescue cardiopulmonary support in patients with reversible conditions not responding to conventional treatment algorithms.[1] In the oncology and HSCT population, ECMO outcomes have been recognizably poor with mortality rates of 58%-61%[2,3] and 81%-100%,[4,5] respectively. With accelerating progress in medical therapies, the frequency of admission of oncology and HSCT patients to the ICU and who require life-sustaining therapies has increased.[6,7] These are high complexity patients with disease-related, therapy-related and infection-related complications which predispose to worsened lung injury and recovery.[8,9] Moreover, those who have received anthracyclines may have accumulated anthracycline-induced cardiomyopathy.[10] Infection, bleeding, thrombosis and severe cytopenias requiring blood product support are also more likely to complicate the ECMO course of oncology and HSCT patients.[1]

ECMO outcomes have also improved over time in the general population.[11] Advancements in technical elements (e.g. newer centrifugal pumps, integrated streamlined circuitry and polymethylpentene fiber technology), enhanced safety mechanisms, increase in team experience with high fidelity simulation and interdisciplinary team training, improvement in intensive care (e.g. ultra-protective ventilation, nutrition, physiotherapy) and comorbidity management account for this.[12-14] This improvement in outcomes is also expected in oncology/HSCT patients; however, there is a paucity of literature available on ECMO outcomes in oncology/ HSCT populations. This study aims to determine the mortality trends and complication rate in oncology and HSCT patients receiving ECMO by conducting a systematic review and meta-analysis.

Methods

This systematic review and meta-analysis was conducted in close accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[15] and is registered in PROSPERO (CRD42020177684).

Types of Studies

To be comprehensive, our study included observational studies as well as randomized controlled trials (RCT) on oncology and HSCT patients who underwent ECMO. Reviews, commentaries, letters, case reports and small case series ($n < 10$) were excluded.[16] There were no language restrictions used.

Types of Participants

Pediatric (29 days to 17 years) and adult (age 18 years and above)[17] oncology and HSCT populations treated with ECMO were included. The oncology subgroup refers to both solid tumors and hematological malignancies, without having undergone HSCT. HSCT included allogenic or autologous transplants.[18]

Types of Interventions

We included VV and VA ECMO, eCPR and extracorporeal carbon dioxide removal (ECCOR) regardless of indication. Patients requiring any form of ventricular assist devices were excluded.

Types of Outcome Measures

Outcomes

The main outcome was all-cause mortality and studies reporting mortality within any timeframe (e.g. survival to decannulation, ICU, hospital, 28-, 60- and 90-day mortality, etc.) were included. However, hospital mortality was the most clinically relevant and was used as the primary outcome in the analyzes. Secondary outcomes included bleeding, mechanical, cardiovascular, pulmonary, neurological and renal complications on ECMO, defined by the Extracorporeal Life Support Organization (ELSO) registry database definitions,[17] and duration of ECMO, mechanical ventilation (MV) and ICU stay.

Search Methods for Identification of Studies

Electronic Searches

A systematic search to identify eligible studies was conducted on MEDLINE (1950-April 10, 2020), EMBASE (1960-April 10, 2020), Cochrane (1969-April 10, 2020) and Web of Science (1977-April 10, 2020) databases. The search strategy is available in the supplementary material (Section A). Reference lists were hand searched and experts in the field were contacted for unpublished data.

Data Collection and Analysis

Selection of Studies

Two independent reviewers (PRR and BHXZ) performed the search on April 10th 2020. After removing duplicates, articles retrieved from the search were screened for eligibility based on the title and abstract. Full text articles were then retrieved for thorough examination before inclusion. Disagreements were resolved through discussion and adjudication by an independent third reviewer (JJMW). Covidence™ software (Covidence, Australia) was used to generate the final list of articles for data extraction.

Data Extraction and Management

Data extraction was performed by 2 independent reviewers (PRR and BHXZ) using a standardized data collection form. Extracted data included study characteristics, patient demographics, clinical data (pre-ECMO and ECMO) characteristics and outcomes.

Dealing With Missing Data and Overlap Studies

All studies meeting the inclusion/exclusion criteria were included in this systematic review. Corresponding authors of included studies were contacted to provide clarification on missing or unpublished individual patient level data relevant to this meta-analysis. However, since there was potential for overlap between study subjects in registry studies and individual single-center studies, a selection of subjects/studies from mutually exclusive time periods for each outcome was made to avoid database sample overlap.[19] If more than one study represented a certain time period, the largest study was selected for inclusion. Authors were contacted for clarification if there was any ambiguity in the reported time period or involvement in registries.

Assessment of Risk of Bias in Included Studies

Risk of bias was assessed using the Newcastle-Ottawa Quality Assessment Scale for observational studies.[20,21] The Cochrane Risk of Bias tool was used for randomized control studies (RCT).[20]

Statistical Analysis

All statistical analyzes were performed by a statistician. The DerSimonion-Laird random-effects meta-analysis model was used to obtain pooled estimates of primary and secondary outcomes. Pooled estimates of hospital mortality and complications were reported as proportions and corresponding 95% confidence intervals (95% CI) while ECMO duration, ICU stay and MV were reported as mean and corresponding 95% CI. Cochran's Q was used to assess presence of heterogeneity and I^2 statistics was used to quantify heterogeneity across studies. When a meta-analysis was not feasible due to an insufficient number of studies, narrative reporting was done instead. A priori subgroup meta-analyses were performed for hospital mortality comparing the following populations: adult versus pediatric, oncology versus HSCT, hematological malignancies versus solid tumors, allogeneic versus autologous HSCT, and VA versus VV ECMO. Subgroup analysis between study variability was calculated using restricted maximum likelihood methods.

Multivariable weighted logistic meta-regression was also performed for hospital mortality to account for year of study, and HSCT population. Results from logistic regression model were expressed as adjusted odds ratio (aOR) with 95% CI. The adjusted proportions of hospital mortality over the years were visualized using bubble plots in which bubble sizes were proportional to the total number of patients recruited in the study. Separate meta-regression model was fit with time as covariate to find trends for each outcome. Potential publication bias was estimated with funnel plots which showed the standard error of each study against its logit event rate. Egger's regression test was used to detect publication bias. Comprehensive metanalysis software version 3 (Biostat Inc., USA) was used for metanalysis and SAS v9.4 SAS/STAT 15.1 (SAS Institute Inc., USA) was used for meta-regression analysis. A P-value <0.05 was considered statistically significant.

Results

A total of 3470 non-duplicate studies were identified by the search, of which only 17 studies (n = 1109 before excluding overlap) fulfilled criteria for inclusion into our review (Figure 1). Characteristics of all included studies are summarized in Table 1. All studies were retrospective in nature and deemed to have a low risk of bias according to the Newcastle-Ottawa Quality Assessment Scale (Supplementary Table 1). Eight studies were registry/database studies. The funnel plot did not reveal publication bias (Supplementary Figure 1).

Baseline and pre-ECMO characteristics were summarized in Supplementary Tables 2 and 3. All studies reported emergent use of ECMO in acute cardiorespiratory failure, except for one study,[22] which reported elective ECMO use in oncology patients for advanced broncho-plastic procedures which was associated with a full survival [10/10 (100%)]. None of the studies reported the use of ECCOR.

Primary Outcome

Hospital mortality was most consistently reported throughout the included studies followed by ICU mortality (Supplementary Table 4). After excluding registry overlap, pooled hospital mortality among oncology and HSCT patients on ECMO, derived from 10 studies (n = 462)[3,23-31] was 72% [95% CI: 65, 78] (Figure 2). Pooled ICU mortality from 8 studies (n = 273)[3,24-30] was 60% [95% CI: 53, 68] (Figure 3).

Six adult (n = 250)[3,24,27-30] and 4 pediatric (n = 212)[23,25,26,31] studies reported hospital mortality. Pooled hospital mortality in adult and pediatric studies were similar [75% (95% CI: 65, 83) vs. 68% (95% CI: 56, 79); $P = 0.329$] respectively (Supplementary Figure 2). Six studies in HSCT patients (n = 82)[3,4,24,25,27,31] and 9 studies in oncology patients (n = 319)[3,23,24,26,27,29-32] reported hospital mortality. The pooled mortality risk was higher in HSCT compared to oncology patients [84% (95% CI: 70, 93) vs. 66% (95% CI: 56, 74); $P = 0.021$] (Supplementary Figure 3). Allogeneic transplant patients (n = 55)[4,25,27] had a higher pooled mortality risk compared to patients who were transplanted autologously (n = 8),[25,27,29,33] but this was not statistically significant [83% (95% CI: 70, 91) vs. 68% (95% CI: 35, 89); $P = 0.309$] (Supplementary Figure 4).

Seven studies in patients with hematological malignancies (n = 216)[3,24,26-30] and 5 studies in patients with solid tumors (n = 138)[3,26,28-30] reported hospital mortality. There was no difference in the pooled hospital mortality risk between the 2 groups [72% (95% CI: 63, 79) vs. 71% (95% CI: 61, 79); $P = 0.895$] (Supplementary Figure 5)Seven and 5 studies in patients on VV (n = 318)[3,4,23,24,27,30,31] and VA ECMO (n = 69),[3,24-26,32] respectively, reported hospital mortality. VV ECMO was associated with a higher pooled hospital

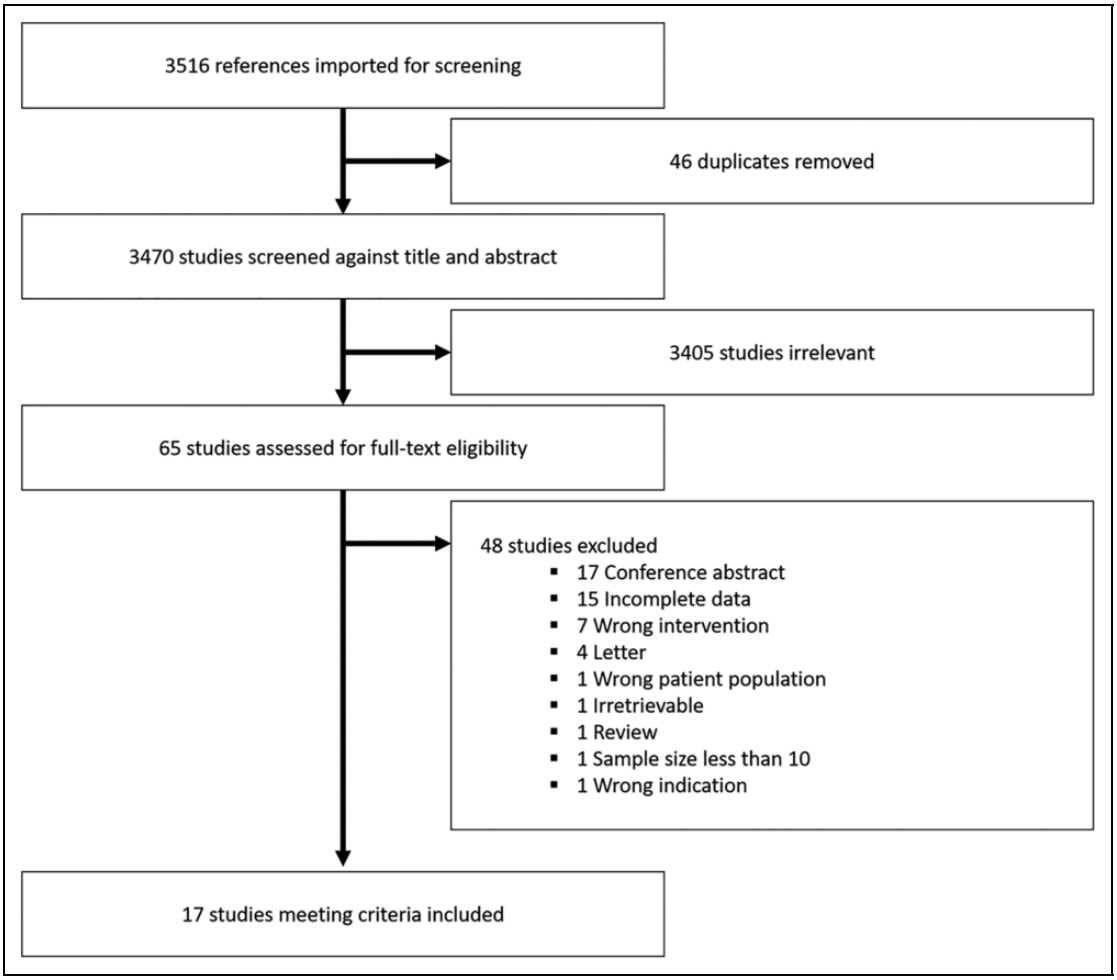

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart for this study.

mortality risk compared to VA [75% (95% CI: 63, 84) vs. 58% (95% CI: 38, 76); $P = 0.154$], though this was not statistically significant (Supplementary Figure 6).

Meta-regression showed that studies published in a more recent year were associated with improved hospital mortality (aOR: 0.92; 95% CI: 0.85, 0.99; $P = 0.026$) but patients in the HSCT population had a higher hospital mortality risk compared to patients in the oncology population (aOR: 3.84; 95% CI: 1.77, 8.31; $P < 0.001$). This trend is visualized in a bubble plot analysis (Figure 4). ICU mortality, however, did not demonstrate a reducing trend of mortality over time.

Secondary Outcomes

Seven studies reported bleeding complications (n = 77)[4,24-27,30,32] [31% (95% CI: 20, 45)] (Supplementary Figure 7) in patients on ECMO. Five studies reported mechanical complications (n = 63)[25-27,29,32] [29% (95% CI: 15, 47)] and neurological complications (n = 42)[4,25-27,32] [21% (95% CI: 14, 31)] (Supplementary Figures 8 and 9) in patients on ECMO. Meta-regression analysis indicated a downward trend in the rates of bleeding, mechanical and neurological complications with time (Supplementary Figure 10).

Five studies reported cardiovascular complications (n = 140)[4,25-27,32] [76% (95% CI: 62, 86)] (Supplementary Figure 11). Meta-regression analysis indicated an increasing rate of cardiac complications with time. Five studies reported pulmonary complications (n = 44)[4,25-27,30] [28% (95% CI: 9, 60)] and 7 studies reported renal complications (n = 142)[4,24-27,30,32] [61% (95% CI: 49, 71)] (Supplementary Figures 12 and 13). The rate of these complications did not change over time. Of note, the meta-analysis of pulmonary complications was associated with high heterogeneity ($I^2 = 88.7\%$).

Duration of ECMO was reported in 6 studies (n = 210).[4,24-27,30,32] The pooled mean duration of ECMO was 8.82 days (95% CI: 5.99, 11.65) (Supplementary Figure 14). Heterogeneity of studies was high in this metanalysis ($I^2 = 86.4\%$). MV duration reported in 3 studies (n = 54)[27,29,33] with a pooled mean of 18.28 days (95% CI: 14.98, 21.59) (Supplementary Figure 15). The pooled mean length of ICU stay from 3 studies (n = 74)[4,24,32] was 24.77 days (95% CI: 21.16, 28.38) (Supplementary Figure 16). The duration of

Table 1. Characteristics of Studies Included.

Population	Study	Study design		Total patients, n	Oncology patients, n (%)	HSCT patients, n (%)	Hospital mortality, n (%)^
		Data source	Aims/remarks				
Pediatric	Gow 2006	ELSO registry	Evaluated outcomes of a cohort of HSCT patients	19	0 (0)	19 (100)	18 (94.7)
	Gupta 2008	ELSO registry	Compared outcomes in ARF patients with and without immunocompromised conditions	2879	60 (2.1)	17 (0.6)	61 (79.2)
	Gow 2009	ELSO registry	Evaluated outcomes of a cohort of oncology patients	107	107 (100)	0 (0)	70 (65)
	Zabrocki 2011	ELSO registry	Evaluated outcomes in a general cohort of patients	3213	84 (2.6)	22 (0.7)	80 (75.5)
	Barbaro 2016	ELSO registry	Developed and validated a pediatric risk score to estimate in-hospital mortality in pulmonary ECMO	1611	83 (5.2)	0 (0)	56.6 (47)
	Bailly 2017	ELSO registry	Developed and validated a pediatric risk score to estimate in-hospital mortality in pulmonary ECMO	2495	161 (6.5)	0 (0)	101 (62.7)
	Coleman 2019	PHIS database	Compared outcomes in high-risk patient subgroups	9194	200 (2.2)	31 (0.3)	151 (65.4)
Adult	Gow 2010	ELSO registry	Evaluated outcomes of oncology and HSCT patients	72	68 (94.4)	4 (5.6)	49 (68.1)
	Lang 2014	Single center, Europe	Evaluated outcomes of a cohort of patients undergoing advanced broncho-plastic procedures performed with elective ECMO support	10	10 (100)	0 (0)	0 (0)
	Wohlfarth 2014	Single center, Europe	Evaluated outcomes of a cohort of ARF patients with hematological malignancies	14	9 (64.3)	5 (35.7)	7 (50)
	Kang 2015	Single center, Asia	Compared ECMO outcomes in patients with and without hematological malignancies	48	8 (16.7)	7 (14.6)	100 (15)
	Wu 2015	Single center, Asia	Evaluated feasibility of ECMO for oncological patients with ARDS	14	14 (100)	0 (0)	10 (71.4)
	Wohlfarth 2017	Multi-center, Europe	Evaluated outcomes of a cohort of HSCT patients with ARDS	37	0 (0)	37 (100)	30 (81.1)
	Sauneuf 2017	Multi-center, Europe	Evaluated outcomes of a cohort of patients on ECMO for pheochromocytoma crisis	34	14 (41.2)	0 (0)	3 (21.4)
	Schmidt 2018	Multi-center, Europe	Evaluated outcomes of immunocompromised patients on ECMO for ARDS	203	82 (40.4)	19 (9.4)	71 (70.3)[a]
	Stecher 2018	Single center, Europe	Evaluated outcomes of a cohort of oncology patients with ARDS	25	14 (56)	11 (44)	20 (80)
	Cho 2019	Single center, Asia	Evaluated outcomes of a cohort of patients with hematological malignancies	23	13 (56.5)	10 (43.5)	21 (91.3)

Abbreviations: ARDS, acute respiratory distress syndrome; ARF, acute respiratory failure; ECMO, extracorporeal membrane oxygenation; ELSO, Extracorporeal life support Organization; HSCT, hematopoietic stem cell transplant; and PHIS, Pediatric health information system database.

^Hospital mortality reported as a percentage of total oncology and HSCT patients.

[a]60-day mortality extrapolated from Kaplan-Meier curve (Figure 2) in paper.

ECMO therapy, MV duration and length of ICU stay did not change over time.

Discussion

This systematic review and meta-analysis which included oncology and HSCT patients on ECMO demonstrated a high ICU (60%) and hospital (72%) mortality. Pre-determined subgroup analysis identified HSCT to be associated with a higher risk of mortality (84%). After adjustment, HSCT was independently associated with an almost 4-fold increased odds of mortality, however, the overall mortality in oncology and HSCT patients on ECMO improved with time—8% lower odds of mortality with each advancing year. Oncology and HSCT patients on ECMO also displayed a high rate of ECMO complications including bleeding (31%), mechanical (29%),

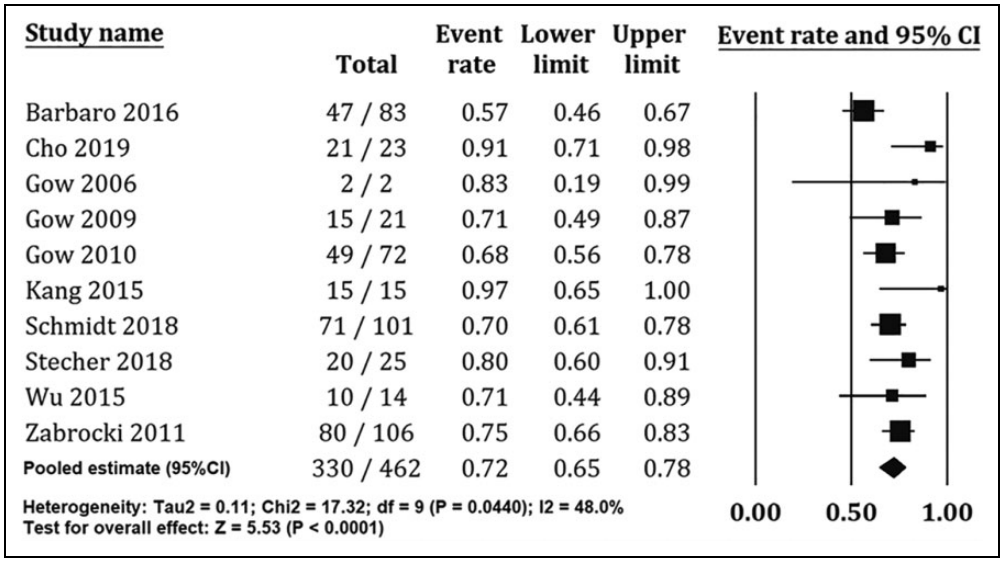

Figure 2. Overall hospital mortality in adult and pediatric studies. NB: Only non-overlapping studies were included in this metanalysis.

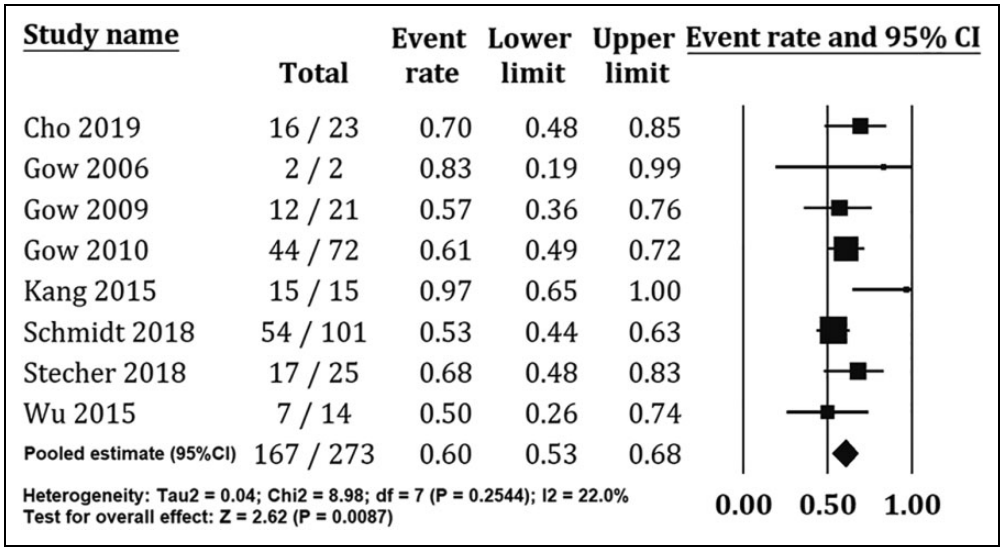

Figure 3. Overall ICU mortality for adult and pediatric studies. NB: Only non-overlapping studies were included in this metanalysis.

cardiovascular (76%), pulmonary (28%), neurological (21%) and renal (61%) complications. Survivors had a prolonged duration of MV (18 days) and ICU stay (25 days).

This study demonstrated an improving mortality trend in oncology and HSCT patients receiving ECMO over time. Nevertheless, this mortality remains high in comparison to the overall mortality provided in the most recent ELSO report, 30%.[34] Oncology and HSCT patients have unique considerations which result in reduced baseline cardiopulmonary reserves, prolonged recovery and vulnerability to all ECMO complications. Pre-ECMO characteristics such as presence of sepsis, acidosis, multi-organ dysfunction[4,25] and physiological severity scores[27] tend to be less favorable in oncology and HSCT populations, possibly accounting for the higher mortality. In our systematic review, majority of patients were on VV ECMO (318/387, 82.2%) for acute respiratory failure and undiagnosed etiologies may also pose considerable challenge for clinicians.[8] Poor outcomes in VV ECMO have specifically been associated with pre-ECMO ventilation indices and MV duration prior to cannulation.[3,26] However as these data were not reported in the majority of studies, we were not able to include them in our metanalysis. Further studies to examine pre-ECMO data and MV parameters in a more granular manner, will help in clinical decision making and counseling.[35]

From existing literature, the efficacy of ECMO in the HSCT population has been controversial.[24] Our study also demonstrated that the HSCT subgroup had a higher pooled mortality risk compared to the oncology subgroup and even though there is an improving overall mortality trend, the decision to initiate ECMO in a HSCT patient should be taken with serious

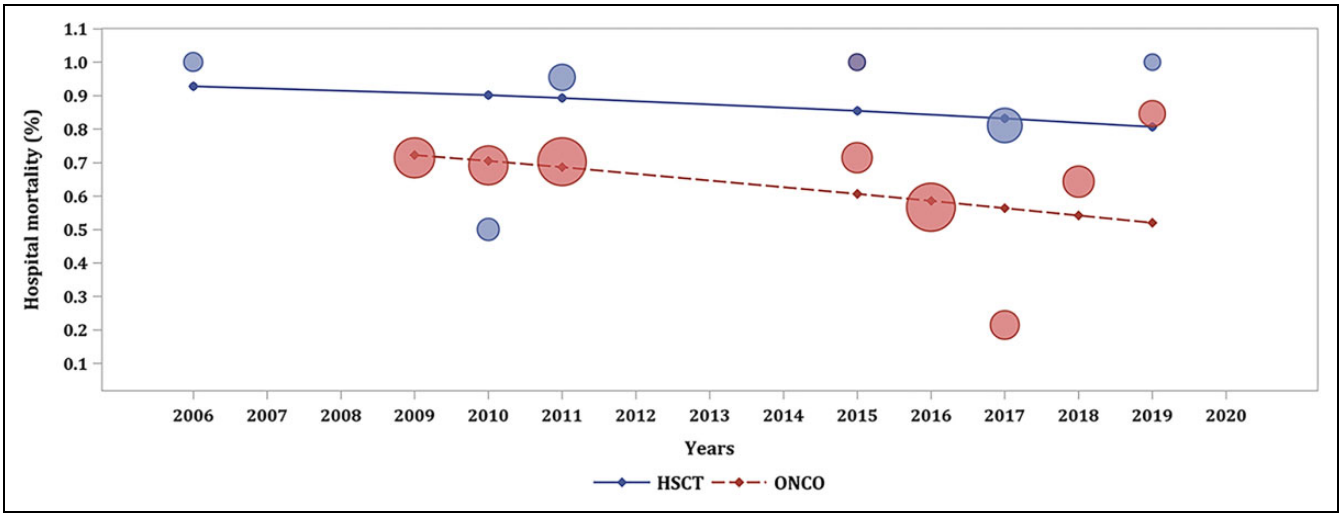

Figure 4. Bubble plot showing hospital mortality rate against year of study publication for oncology and HSCT subgroups. HSCT indicates hematopoietic stem cell transplant subgroup; ONCO, oncology subgroup. Bubble sizes were proportional to the total number of patients recruited in the study.

consideration. Severe immunosuppression, treatment toxicities, GVHD and relapse of the underlying disease are some factors which may contribute to the high mortality.[25,36] Notably, we demonstrated that pooled ECMO mortality in patients with allogeneic transplant [84% (95% CI: 70, 93)] was higher compared to those with autologous transplant [68% (95% CI 35, 89)], though not statistically significant due to the small sample size, identifying this cohort as the poor prognostic group. Though still high, the pooled mortality in autologous HSCT was similar to non-transplanted oncology patients [66% (95% CI: 56, 74)]. Further examination of the HSCT population was limited due to heterogeneity of the population and insufficient granularity of data. We acknowledge that the HSCT population included were heterogeneous and comprised of those who were in the early/late phase of HSCT transplantation with/without HSCT complications (e.g. HSCT related pulmonary complications, GVHD) and with/without remission or relapse. This is evident from the wide spread distribution of days from HSCT [151.76; (95% CI: 79.99, 223.53)] and presence of GVHD in 19% of patients (95% CI: 8, 39) (Supplementary Tables 2 and 3). There was insufficient granularity of data to stratify our analysis further to determine the contribution of each HSCT characteristic on the outcomes. Hence, clinicians should exercise caution in interpreting the results of our study.

ECMO complications in the general cohort patients were recently reviewed.[37-39] Pooled estimates were reported for bleeding (29.3%-40.8%), mechanical (10.9%-20.2%), pulmonary (6.4%-20.6%), neurological (13.3%-14.9%) and renal (14.7%-55.6%) complications. Besides a similar bleeding risk, our study indicate that complication rates in the oncology and HSCT cohort were higher than in the general cohort of ECMO patients, however, there are differences in the study design which preclude a direct comparison—definitions used in the prior studies were not consistent with our study which utilizes the ELSO categories of complications. Nevertheless, these results on complication risks may be important to prompt clinicians to re-evaluate their treatment goals for this group of patients acknowledging their risk of multi-organ dysfunction and prolonged ventilation/ICU stay. An overly aggressive approach with prolonged or recurrent ECMO runs, though not formally studied here, will likely be associated with an even higher risk of poor outcomes.[1,26,33]

The findings of our review should be interpreted in the context of its limitations. Firstly, though intending to identify RCTs and observational design studies, only retrospective observational studies were identified. These have inherent limitations such as selection bias and missing data—many studies did not report ECMO and MV parameters. Additionally, none of the studies reported a protocol for managing patients on ECMO; hence, outcomes may have been confounded by variability in management. Secondly, there is marked heterogeneity in the oncology and HSCT patient population and detailed subgroup analysis may not be sufficient to generate homogenous patient populations. Moreover, a small group of patients were identified to have received eCPR ($n = 16$), however, we were unable to retrieve data from the original publications to analyze this poor prognostic group separately. Therefore, the results of this study may not be generalizable to individual oncology and HSCT patients. Thirdly, due to inconsistent reporting, we were not able to analyze certain important factors (e.g. disease staging, therapy response, ventilation indices) which may be useful for clinical decision making. Indeed, therapy limiting decisions during the ECMO/ICU course based on stage of disease or therapy status, were not reported and therefore were unaccounted for in this analysis. Moving forward, we advocate for a minimum standardized dataset for these groups of patients supported on ECMO so as to enable

a more robust comparison, and aggregation of important clinical data. Another potential limitation of our study was the selection strategy used to avoid database sample overlap in registry studies by extraction period. Our approach may have led to the exclusion of more than necessary non-overlapping subjects for the meta-analysis resulting in a smaller sample size. However, we found that this was a reliable and transparent approach to eliminating overlap, which may have introduced even greater bias. Lastly, the cause of ICU/hospital mortality was not specified in most studies; hence, the high mortality risk may not be directly related to ECMO.

With advancements in critical care and oncological therapies the overall outcomes in these respective patient groups are improving.[40] Our study is the first to empirically show an improving mortality trend in oncology and HSCT patients receiving ECMO over time. The results of this study, however, may not be generalizable to individual oncology and HSCT patients, but rather provides a useful broad overview of prognostic trends for heme-oncologists and intensivists that may be considered in ECMO selection policies and the setting of general goals of care in this population. Future studies focusing on specific decision criteria or critical time intervals for considering withdrawal or withholding of care for such patients may be helpful.

Conclusion

This systematic review and meta-analysis, found a high overall hospital (72%) mortality rate in oncology and HSCT patients supported on ECMO. The presence of HSCT portends almost a 4-fold increased odds of mortality, whereas, a more recent year of study was associated with a decreased odds of mortality. ECMO complications were also high in this population. These findings may need to be taken into consideration during patient selection for ECMO. To enable a more detailed analysis identifying pre-ECMO and HSCT risk factors for poor outcome, future studies should report a minimum standardized dataset to facilitate more robust comparison, and aggregation of these important clinical data.

Abbreviations

ACCP-SCCM	American College of Chest Physicians-Society of Critical Care Medicine
aOR	Adjusted Odds Ratio
ARDS	Acute Respiratory Distress Syndrome
ARF	Acute Respiratory Failure
AML	Acute Myeloid Leukemia
APACHE II	Acute Physiology and Chronic Health Evaluation II
CI	Confidence Interval
CNS	Central Nervous System
CPB	Cardio-Pulmonary Bypass
ECCOR	Extracorporeal Carbon Dioxide Removal
eCPR	Extracorporeal Cardiopulmonary Resuscitation
ECMO	Extracorporeal Membrane Oxygenation
ELSO	Extracorporeal Life Support Organization
GVHD	Graft-versus-Host Disease
HSCT	Hematopoietic Stem Cell Transplantation
ICU	Intensive Care Unit
MESH	Medical Subject Headings
OI	Oxygenation Index
PEEP	Positive End-Expiratory Pressure
PIM 2	Pediatric Index of Mortality
PRISM III	Pediatric Risk of Mortality III
RCT	Randomized Controlled Trials
SAP II	Simplified Acute Physiology II
SOFA	Sequential Organ Failure Assessment
VA	Veno-arterial
VV	Veno-venous

Authors' Note

Pravin R. R., Benjamin Xiongzheng Huang, and Judith Ju-Ming Wong substantially contributed to the conception and design of this study. Pravin R. R., Benjamin Xiongzheng Huang, Judith Ju-Ming Wong, Jan Hau Lee, Mei-Yoke Chan, Rehena Sultana, Chuen Wen Tan, Heng Joo Ng, Ken Junyang Goh, and Ghee Chee Phua revised the manuscript critically for important intellectual content, approved its final version and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Pravin R. R. and Benjamin Xiongzheng Huang were responsible for performing the search, extracting the data and drafting the manuscript. Judith Ju-Ming Wong and Rehena Sultana planned the statistical approach, while Rehena Sultana conducted all statistical analysis. Pravin R. R., Benjamin Xiongzheng Huang, Judith Ju-Ming Wong, Jan Hau Lee, and Rehena Sultana were responsible for the analysis and interpretation of data. Pravin R. R. and Benjamin Xiongzheng Huang were mentored by Judith Ju-Ming Wong. Data are available on request to the corresponding author.

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Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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