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Extracorporeal support for trauma: A trauma quality improvement project (TQIP) analysis in patients with acute respiratory distress syndrome

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Abstract

Introduction: The use of extracorporeal membrane oxygenation (ECMO) in trauma patients with severe acute respiratory distress syndrome (ARDS) continues to evolve. The objective of this study was to perform a comparative analysis of trauma patients with ARDS who received ECMO to a propensity matched cohort of patients who underwent conventional management.

Methods: The Trauma Quality Improvement Program (TQIP) database was queried from 2013 to 2016 for all patients with ARDS and those who received ECMO. Demographics, as well as clinical, injury, intervention, and outcome data were collected and analyzed. Patients with ARDS were divided into two groups, those who received ECMO and those who did not. A propensity score analysis was performed using the following criteria: age, gender, vital signs (HR, SBP) and GCS on admission, Injury Severity Score (ISS), and Abbreviated Injury Scale (AIS) score in several body regions. Outcomes between the groups were subsequently compared using univariate as well as Cox regression analyses.

Secondary outcomes such as hospitalization (HLOS), ICU length-of-stay (LOS) and ventilation days stratified for patient demographics, timing of ECMO and anticoagulation status were compared.

Results: Over the 3-year study period, 8990 patients with ARDS were identified from the TQIP registry. Following exclusion, 3680 were included in the final analysis, of which 97 (2.6%) received ECMO. On univariate analysis following matching, patients who underwent ECMO had lower overall hospital mortality (23 vs 50%, p < 0.001) with higher rates of complications (p < 0.005), including longer HLOS. In those undergoing ECMO, early initiation (<7 days) was associated with shorter HLOS, ICU LOS, and fewer ventilator days. No difference was observed between the two groups with regard to anticoagulation.

Conclusion: Extracorporeal membrane oxygenation use in trauma patients with ARDS may be associated with improved survival, especially for young patients with thoracic injuries, early in the course of ARDS. Anticoagulation while on circuit was not associated with increased risk of hemorrhage or mortality, even in the setting of head injuries. The mortality benefit suggested with ECMO comes at the expense of a potential increase in complication rate and prolonged hospitalization.

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1. Introduction

Extracorporeal membrane oxygenation (ECMO) has been reserved for patients with severe, refractory ARDS when conventional therapy fails. Appropriate patient selection is paramount and generally relies on expert opinion and clinical guidelines published by the Extracorporeal Life Support Organization (ELSO). (1) However, consensus is lacking for the trauma subgroup and outcomes are variable. For example, one longitudinal analysis showed that between 2006 and 2010, ECMO use increased 1.68-fold in trauma patients while survival decreased from 75.8% to 62%. (2) In contrast, a systematic review published in 2016 including several case series and 31 patients in total reported an overall survival of 87%. (3) More recently, results from a National Trauma Data Bank (NTDB) study on ECMO in 2017 concluded that ECMO was safe, particularly in centers that performed ECMO frequently, with an overall survival of 64%. (4) This correlates well with two randomized controlled trials of general
patient populations with severe acute respiratory failure which report survival rates of 63–64%. (5,6)

Conventional management for adult respiratory distress syndrome (ARDS) includes the institution of lung protective ventilation using low tidal volumes and optimal positive end expiratory pressure (PEEP) settings while tolerating a degree of hypercapnia. (7) More aggressive measures, including prone positioning, neuromuscular blockade, inhaled pulmonary vasodilators, and advanced ventilator modalities have documented benefit in select cases. (8-11) Using these strategies, the prevalence of ARDS in the adult trauma population has decreased significantly in recent years, with current rates between 13.4 and 18.1%. (12,13) Despite advanced interventions, mortality in the severe ARDS subgroup remains significant, and overall hospital survival rates of patients with severe lung dysfunction range from only 26–58%. (14-17) More specifically, in the trauma population, mortality rates are between 40 and 60% with conventional therapy. (18,19)

To date, no studies evaluating ECMO using the Trauma Quality Improvement Program (TQIP) registry have been performed. The TQIP registry offers many of the advantages of NTDB but with additional information regarding anticoagulation and transfusion requirements. Our study objective was to compare outcomes of trauma patients with ARDS who received ECMO to a propensity matched TQIP population who underwent conventional management. In addition, we sought to determine whether patient injury patterns, timing of ECMO initiation, or use of anticoagulation affected these outcomes.

2. Methods

2.1. Study design

This retrospective cohort study was performed using data from the TQIP database which is maintained by the American College of Surgeons Committee on Trauma and aggregates patient data from more than 750 trauma centers across the United States. The data contained in TQIP are standardized at the time of submission using the validation system and rules defined in the National Trauma Data Standard (NTDS) data dictionary. (20) The TQIP database contains de-identified data, and the present study was approved by the Institutional Review Board of the University of Southern California.

The TQIP database was queried from 2013 to 2016 for all adult patients with a diagnosis of ARDS and those who received ECMO. Exclusion criteria included an abbreviated injury score (AIS) score of 6 in any body region, systolic blood pressure (SBP) or heart rate (HR) of 0 on arrival, cardiopulmonary arrest after admission, transfer patients, HLOS <72 h, patients leaving against medical advice, or patients with >10% missing data. Patients with significant cardiac history were also excluded as our focus was on venovenous (VV) ECMO, and the TQIP registry does not differentiate between VV and venoarterial (VA) ECMO. This included patients with prior myocardial infarction, unstable angina, and a history of congestive heart failure (CHF). Transfer patients were excluded to avoid confounding cannulation times and outcomes with respect to duration of mechanical ventilation, hospitalization, or discharge. We collected variables including demographics (age, gender, race, and comorbidities); clinical data at the time of arrival (vital signs and Glasgow Coma Scale (GCS)); injury data (Abbreviated Injury Scale (AIS) for each body region and Injury Severity Scale (ISS)); interventions (ECMO cannulation and anticoagulation); and outcomes (mortality, hospital length of stay (HLOS), intensive care unit length of stay (ICU LOS), complications, transfusion requirements, and discharge disposition).

In order to develop a non-ECMO comparator population with ARDS, we identified patients with ARDS who did not undergo ECMO who were at a similar risk of death based on a propensity matched model using primary characteristics. The patients were matched, and the analysis was performed without replacement using the nearest neighbor method, with a caliper set to 0.2, and was corrected for age, gender, vital signs (HR, SBP) and Glasgow Coma Score (GCS) on admission, injury severity score (ISS), and abbreviated injury score (AIS) in the following regions – head, face, neck, chest, abdomen, pelvis, extremity, external. A high match tolerance value was used to prevent loss of ECMO patients from analysis. Outcomes were then compared between patients that underwent ECMO for ARDS (N = 97 patients) and the matched cohort who underwent conventional management (N = 1266 patients). Patient inclusion in the study is shown in Fig. 1.
Subgroup analyses based on timing of ECMO initiation using prior published cutoffs (<48 h, 48 h to 7 days, and >7 days) and the use of anticoagulation were performed to delineate their effect on clinical outcomes. The primary outcome of interest was mortality. Secondary outcomes included duration of mechanical ventilation and hospitalization (days), complications, blood transfusions (packed red blood cells, fresh frozen plasma, platelets and cryoprecipitate), and discharge disposition – skilled nursing facility, long term rehabilitation, or home.

2.2. Statistical analysis

Descriptive statistics were used to summarize the demographics, clinical data, injury data, and outcomes. Results were reported as numbers and percentages for categorical variables and medians with interquartile range (IQR 25–75%) or means with standard deviation for continuous variables. After propensity matching, some variables demonstrated significant differences, so survival characteristics were compared between the ECMO population (N = 97 patients) and the non-ECMO population (N = 1266 patients) using a forward stepwise Cox regression model. The covariates were those with p values < 0.001, which were age (mean), mean admission SBP, mean admission HR, no history of hypertension, head, chest and lower extremity AIS scores <3, admission to an academic trauma center and finally ECMO use. Secondary outcomes such as hospital length-of-stay (HLOS), ICU LOS, and ventilation days stratified for patient demographics (age, gender, ISS, body region), timing of ECMO, and anticoagulation status were compared. Univariate comparisons were made using unpaired Student’s t-test or Mann-Whitney U test for continuous variables and Chi Square analysis or Fisher Exact for categorical variables with p values less than 0.05 deemed significant. Analysis was performed using SPSS software vers. 22.0 (IBM, Armonk, NY, USA) and R version 3.5.1 (Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1. Demographic data

Of the 1,099,022 patients in the TQIP registry over the study period, a total of 8990 patients with ARDS were identified, of which 181 (2%) underwent ECMO. After exclusion criteria were applied, a total of 3680 ARDS patients were included for analysis. Of these, 97 (2.6%) patients underwent ECMO. Compared to the non-ECMO population (N = 1266 patients) using a forward stepwise Cox regression model, the covariates were those with p values < 0.001, which were age (mean), mean admission SBP, mean admission HR, no history of hypertension, head, chest and lower extremity AIS scores <3, admission to an academic trauma center and finally ECMO use. Secondary outcomes such as hospital length-of-stay (HLOS), ICU LOS, and ventilation days stratified for patient demographics (age, gender, ISS, body region), timing of ECMO, and anticoagulation status were compared. Univariate comparisons were made using unpaired Student’s t-test or Mann-Whitney U test for continuous variables and Chi Square analysis or Fisher Exact for categorical variables with p values less than 0.05 deemed significant. Analysis was performed using SPSS software vers. 22.0 (IBM, Armonk, NY, USA) and R version 3.5.1 (Foundation for Statistical Computing, Vienna, Austria).

Table 1

| Study population. | No ECMO (n = 1266) | ECMO (n = 97) | p value |
|------------------|--------------------|---------------|---------|
| Gender (Male %)  | 1000 (79)          | 79 (81)       | 0.603   |
| Mean Age in Years (SD) | 56 (39–69)       | 35 (22–51)    | <0.001  |
| Mean Systolic Blood Pressure (mmHg) (SD) | 130 (103–152) | 118 (90–127) | <0.001  |
| Mean Heart Rate (beats/min) (SD) | 96 (79–116) | 108 (88–129) | 0.001   |
| Median Glasgow Coma Scale (IQR 25–75%) | 9 (3–15) | 14 (3–15) | 0.03    |
| Alcohol Abuse (%) | 190 (15)          | 4 (4.1)       | 0.004   |
| Drug Abuse (%)    | 82 (6.5)           | 8 (8.2)       | 0.499   |
| Bleeding Diathesis (%) | 111 (8.8)  | 2 (2.1)       | 0.02    |
| Stroke (%)        | 35 (2.8)           | 1 (1.0)       | 0.51    |
| COPD (%)          | 19 (3.9)           | 1 (2.1)       | 0.03    |
| History of Angina (%) | 2 (2.1)     | 2 (2.1)       | 0.99    |
| History of Myocardial Infarction (%) | 1 (1.0)   | 1 (1.0)       | 0.98    |
| History of Peripheral Vascular Disease (%) | 2 (4.0)   | 2 (2.1)       | 0.155   |
| Hypertension (%)  | 392 (31)           | 16 (16)       | 0.001   |
| Diabetes Mellitus (%) | 174 (14)   | 11 (11)       | 0.545   |
| Dementia (%)      | 35 (2.8)           | 2 (2.1)       | 0.97    |
| Renal Insufficiency/Failure (%) | 14 (4.1) | 1 (0.0) | 0.616  |
| Steroid Use (%)   | 10 (0.0)           | 0 (0.0)       | 0.95    |
| Smoker (%)        | 190 (15)           | 22 (23)       | 0.06    |
| Median Injury Severity Score (IQR 25–75%) | 27 (20–38) | 27 (17–34) | 0.288   |
| Head AIS 3, 4, 5 (%) | 798 (63)       | 28 (29)       | <0.001  |
| Face AIS 3, 4, 5 (%) | 47 (3.7)     | 1 (1)         | 0.251   |
| Neck AIS 3, 4, 5 (%) | 35 (2.8)      | 3 (3.1)       | 0.85    |
| Chest AIS 3, 4, 5 (%) | 760 (60)     | 74 (76)       | 0.001   |
| Abdomen AIS 3, 4, 5 (%) | 266 (21)    | 28 (28)       | 0.07    |
| Spine AIS 3, 4, 5 (%) | 215 (17)     | 16 (16)       | 0.78    |
| Upper Extremity AIS 3, 4, 5 (%) | 72 (5.7)   | 6 (6.2)       | 0.839   |
| Lower Extremity AIS 3, 4, 5 (%) | 317 (25)  | 39 (40)       | 0.001   |
| External AIS 3, 4, 5 (%) | 1 (0.1)    | 0 (0)         | 0.99    |
| Academic Center   | 747 (59)          | 83 (86)       | <0.001  |
| Level I Trauma Center | 912 (72) | 82 (85) | 0.004   |

ECMO: Extracorporeal Membrane Oxygenation, SD: Standard Deviation, IQR: Interquartile Range, COPD: Chronic Obstructive Pulmonary Disease, AIS: Abbreviated Injury Scale.

ECMO: Extracorporeal Membrane Oxygenation, SD: Standard Deviation, IQR: Interquartile Range, COPD: Chronic Obstructive Pulmonary Disease, AIS: Abbreviated Injury Scale.
ARDS. Superior survival compared to patients that underwent conventional management of gender, HR, SBP, GCS, and AIS (body regions- head, neck, face, chest, abdomen, pelvis, spine, extremity and external) the patients that underwent ECMO for ARDS had superior survival compared to patients that underwent conventional management of ARDS.

Table 2
Study population outcomes.

|                      | No ECMO (n = 1266) | ECMO (n = 97) | p value |
|----------------------|--------------------|---------------|---------|
| Acute Kidney Injury (%) | 241 (19)           | 28 (29)       | 0.02    |
| Myocardial Infarction (%) | 32 (2.5)           | 3 (3.1)       | 0.734   |
| Stroke (%)           | 51 (4)             | 4 (4)         | 1       |
| Deep Vein Thrombosis (%) | 139 (11)          | 17 (18)       | <0.001  |
| Pulmonary Embolus (%) | 51 (4)             | 16 (16)       | <0.001  |
| Central Line Infection (%) | 35 (2.8)       | 1 (1)         | 0.51    |
| Ventilator Associated Pneumonia (%) | 0 (0)            | 7 (7.2)       | <0.001  |
| Unplanned Intubation (%) | 177 (14)          | 8 (8.2)       | 0.16    |
| Reoperation (%)      | 66 (5.2)           | 10 (10)       | 0.04    |
| Readmission to ICU (%) | 81 (6.4)          | 6 (6.2)       | 0.89    |
| Sepsis (%)           | 203 (16)           | 17 (18)       | 0.64    |
| Superficial SSI (%)  | 13 (1)             | 4 (4.1)       | 0.028   |
| Deep SSI (%)         | 23 (1.8)           | 1 (1)         | 0.88    |
| Compartment Syndrome (%) | 13 (1)           | 2 (2.1)       | 0.29    |
| Days on Ventilator (median/IQR) | 12 (7–20)       | 22 (11–32)    | <0.001  |
| Hospital Length of Stay (median/IQR) | 17 (10–29)     | 29 (16–46)    | <0.001  |
| ICU Length of Stay (median/IQR) | 14 (8–22)       | 24 (14–34)    | <0.001  |
| Mortality (%)        | 633 (50)           | 22 (23)       | <0.001  |

ECMO: Extracorporeal Membrane Oxygenation, ICU: Intensive Care Unit, SSI: Surgical Site Infection, IQR: Interquartile Range.

days, p = 0.002), and fewer ventilator days (22 ± 19 vs 35 ± 16, p = 0.005). Of the survivors, there was no significant difference in discharge disposition (p = 0.31).

3.4. ECMO and anticoagulation

ECMO patients were stratified according to anticoagulation status. Patients who received anticoagulation were compared to those who did not based on matched characteristics at baseline (age, gender, co-morbidities, vital signs, GCS on presentation, injury severity, and incidence of co-occurring TBI (p > 0.1 for all)). Among ECMO patients who were anticoagulated, 5 (6%) were found to have conditions warranting therapeutic anticoagulation, 3 of which were for pulmonary emboli and 2 for symptomatic deep vein thromboses. Of all anticoagulated ECMO patients, 44% received unfractionated heparin, 51% received low molecular weight heparin, and 6% received another form of anticoagulation. Anticoagulation was started, on average, 3.9 ± 4.6 days after the initiation of ECMO. Anticoagulated patients had a prolonged HLOS (37 vs 22 days, p = 0.03), but no significant difference was observed in overall hospital mortality, ICU LOS, blood product transfusion, or number of ventilator days (p > 0.1 for all), as shown in Table 4. There was also no significant difference in discharge disposition between the groups (p > 0.1).

4. Discussion

The optimal patient demographic for the use of ECMO in the setting of severe ARDS remains to be defined, especially for trauma patients. In our study using the TQIP registry, we compared outcomes of trauma patients with severe ARDS who underwent ECMO with a propensity-matched cohort of those who underwent conventional management. The frequency of ECMO use in our study (2.6%) was consistent with a previous report using the NTDB. (4) Our analysis demonstrates that patients who underwent ECMO have lower overall mortality despite a higher rate of associated complications when compared to those undergoing conventional management. Mortality in the matched non-ECMO ARDS group was 50%, which is within the range reported in the literature. (14–19) Early initiation of ECMO, within 7 days of admission, was associated with shorter HLOS, ICU LOS, and fewer ventilator days compared to late initiation (>7 days). ECMO patients who were anticoagulated had a longer HLOS but no difference in mortality, rate of complications, or transfusion requirement.

Data is conflicting regarding the use of ECMO in trauma patients. In regard to survival, two major RCTs and one propensity-matched study demonstrated benefit when severe ARDS patients were transferred to an ECMO center (23–25). (5,6,21) The Conventional Ventilatory Support Versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure (CESAR) trial randomly assigned 180 patients with severe ARDS (defined as hypercapnic respiratory acidosis with an arterial pH of <7.2 or a Murray score greater than 3) to a single ECMO center or continued conventional management. Six-month survival without disability was improved among patients that were transferred and the authors concluded that transfer to an ECMO-capable center was associated with improved survival. This was consistent with the findings in our study although we did not have post-discharge follow-up data. Of the 90 patients that underwent ECMO in the CESAR trial, however, only five were trauma related. The most recent trial, the ECMO to Rescue Severe Lung Injury (EOLIA) trial, randomized 249 patients with severe ARDS (defined as PaO2/FiO2 < 50 for >3 h or <80 mm Hg for >6 h) to receive early VV-ECMO or conventional low-tidal volume low-pressure ventilation. Results demonstrated an improved 60-day mortality in favor of ECMO (35 vs 46%) although this difference was not statistically significant (p = 0.09). While there was no specific reference to the number of trauma patients included, a majority had either viral or bacterial pneumonia as the cause of their severe lung dysfunction. Multicenter randomized data in the trauma population is lacking.

In the first multicenter retrospective cohort analysis including only trauma patients, VV ECMO was independently associated with survival when compared to those who underwent conventional management. (22) Of the 26 patients in the ECMO group, 15 survived to discharge. Similarly, our findings demonstrate a significantly lower overall hospital mortality in favor of the ECMO group (23 vs 50%). Interestingly, mortality within ECMO cohorts appears to be decreasing when comparing studies chronologically. Guirand et al. reported 42% mortality of patients placed on ECMO from 2001 to 2009 and a more recent NTDB study reported 36% mortality in the 80 patients who underwent ECMO between 2012 and 2014. (4,22) Our study, using the most recent data from 2013 to 2016, demonstrates a continuation of this downward trend with a mortality of 23%. When compared to these two prior studies, the patients in our series had an older mean age with a similar median ISS. This decline in mortality could be attributed to several factors but potentially reflects advancements in equipment, critical care, and overall familiarity with utilizing ECMO in this population. The results are encouraging but must be interpreted with caution given the variation in patient demographics.
comorbid conditions, treating facilities, mechanisms of injury, and timing of ECMO initiation between the studies.

Despite the survival benefit seen in the ECMO group, patients were noted to have more complications throughout their hospital course. This is in contrast to an existing NTDB study which showed no significant difference in complications (4). Higher rates of acute kidney injury, venous thromboembolism, ventilator-associated pneumonia, and reoperation were observed. There are several plausible mechanisms that could explain these findings. Acute kidney injury may have caused difficulty in managing the fluid status of the patient, predisposing them to volume overload and pulmonary edema, increasing their ventilator requirements. The recumbent positioning of an ECMO patient predisposes them to venous thromboembolism, as well as the pro-thrombotic nature of the circuit. Potential interruptions in anticoagulation or running the circuit without anticoagulation could also contribute. Ventilator-associated pneumonia could have been a factor leading to ECMO use or, alternatively, could have been a consequence of prolonged treatment duration. As expected with an increased incidence of complications, we observed an increase in ICU LOS and ventilator days, both of which likely contributed to prolonged hospitalization. Unfortunately, TQIP does not provide duration of therapy, only whether a particular treatment modality was used, or a complication occurred; therefore, it becomes difficult to determine causality.

As its use becomes more widespread, many trauma centers have incorporated ECMO capability at their institutions. The majority of patients included in our study were treated at academic or level 1 trauma centers which potentially affected outcomes. Instituting therapy at high volume centers has been suggested as an important aspect for survival as multiple studies have concluded that ECMO candidates should be transferred to facilities well versed in the procedure and after-care. (4,5) A retrospective review of over 7000 pediatric patients who received ECMO demonstrated improved survival when treated at centers which perform at least 22 cases annually. (23) As similar for the adult population has yet to be described.

Early initiation of ECMO in the treatment plan appears to play a key role in reducing complications, duration of hospitalization, and number of days on the ventilator as demonstrated by our findings. Less time on the ventilator prior to cannulation has previously been shown to improve outcomes. (24) This likely represents a difference in patient

| Table 3 | Early vs. late ECMO. |
|-----------------|-----------------|-----------------|
|                | Early ≤ 7 Days (n = 71) | Late > 7 Days (n = 26) | p value |
| Gender (Male %) | 58 (82) | 21 (81) | 0.91 |
| Mean Age in Years (SD) | 39 (17) | 34 (16) | 0.15 |
| Mean Systolic Blood Pressure (mmHg) (SD) | 117 (35) | 120 (27) | 0.23 |
| Mean Heart Rate (beats/min) (SD) | 114 | 102 | 0.07 |
| Median Glasgow Coma Score (IQR 25–75%) | 14 (3–15) | 13 (4–15) | 0.19 |
| Alcohol Abuse (%) | 3 (4.1) | 1 (3.6) | 0.08 |
| Drug Abuse (%) | 4 (5.5) | 5 (19.2) | 0.09 |
| Bleeding Diathesis (%) | 3 (4.1) | 0 (0) | 0.76 |
| Stroke (%) | 1 (1.4) | 0 (0) | 0.28 |
| COPD (%) | 2 (2.7) | 0 (0) | 0.22 |
| History of Angina (%) | 0 (0) | 0 (0) | NA |
| History of Myocardial Infarction (%) | 1 (1.4) | 0 (0) | 0.43 |
| History of Peripheral Vascular Disease (%) | 1 (1.4) | 1 (3.8) | 0.2 |
| Hypertension (%) | 10 (14) | 5 (19) | 0.14 |
| Diabetes Mellitus (%) | 7 (9.6) | 4 (15) | 0.09 |
| History of Dementia (%) | 3 (4.1) | 0 (0) | 0.07 |
| Renal Insufficiency/Failure (%) | 0 (0) | 0 (0) | NA |
| Steroid Use (%) | 0 (0) | 0 (0) | NA |
| Smoker (%) | 16 (22) | 8 (31) | 0.13 |
| Median Injury Severity Score (IQR 25–75%) | 27 (17–36) | 26 (19–34) | 0.65 |

Outcomes

|                | Early ≤ 7 Days (n = 71) | Late > 7 Days (n = 26) | p value |
|-----------------|-----------------|-----------------|-----------------|
| Acute Kidney Injury (%) | 18 (26) | 11 (42) | 0.06 |
| Myocardial Infarction (%) | 2 (2.7) | 1 (3.8) | 0.44 |
| Stroke (%) | 4 (5.5) | 1 (3.8) | 0.31 |
| Deep Vein Thrombosis (%) | 13 (18) | 4 (15) | 0.16 |
| Pulmonary Embolus (%) | 8 (11) | 5 (19) | 0.25 |
| Central Line Infection (%) | 1 (1.4) | 0 (0) | 0.74 |
| Ventilator Associated Pneumonia (%) | 6 (8.4) | 4 (15) | 0.08 |
| Unplanned Intubation (%) | 3 (4.1) | 3 (12) | 0.24 |
| Reoperation (%) | 6 (8) | 3 (12) | 0.39 |
| Readmission to ICU (%) | 4 (5.5) | 2 (7.7) | 0.68 |
| Sepsis (%) | 15 (21) | 5 (19) | 0.18 |
| Superficial SSI (%) | 1 (1.4) | 3 (12) | 0.09 |
| Deep SSI (%) | 1 (1.4) | 2 (7.7) | 0.36 |
| Compartment Syndrome (%) | 1 (1.4) | 1 (3.8) | 0.13 |
| Mean Days on Ventilator (SD) | 20 (17) | 34 (15) | <.0001 |
| Mean Hospital Length of Stay (SD) | 29 (26) | 48 (24) | 0.002 |
| Mean ICU Length of Stay (SD) | 22 (16) | 40 (16) | <.0001 |
| Mortality (%) | 18 (26) | 5 (19) | 0.11 |

Comparison of survivors

n = 54 n = 21

|                | Early ≤ 7 Days (n = 71) | Late > 7 Days (n = 26) | p value |
|-----------------|-----------------|-----------------|-----------------|
| Mean Days on Ventilator (SD) | 22 (19) | 35 (16) | 0.005 |
| Mean Hospital Length of Stay (SD) | 35 (27) | 53 (23) | 0.007 |
| Mean ICU Length of Stay (SD) | 26 (17) | 43 (16) | 0.002 |

ECMO: Extracorporeal Membrane Oxygenation, SD: Standard Deviation, IQR: Interquartile Range, COPD: Chronic Obstructive Pulmonary Disorder, SSI: Surgical Site Infection.
population, with early use representing those with direct trauma to the thorax or lung parenchyma, and later use in those with severe lung dysfunction due to physiologic sequelae of their injuries and hospitalization. (4) One study from the ELSO registry suggests the optimal ECMO candidate in the setting of trauma is a younger patient with isolated blunt thoracic injury (74% survival) requiring short duration VV-ECMO. (25) This correlates well with our retrospective design of our study and use of the TQIP registry, several limitations must be acknowledged. First, we acknowledge the major limitation that there were no respiratory parameters available from TQIP, such as blood gas values, ventilator settings, or imaging to confirm ARDS diagnosis, which would have allowed for more accurate propensity matching. Additionally, we were unable to assess the use of rescue strategies for ARDS, such as recruitment maneuvers, prone positioning, neuromuscular blockade, inhaled pulmonary vasodilators, or advanced ventilator modes (airway pressure release ventilation, high frequency ventilation), which would further improved matching. Secondly, we were unable to extract whether patients required respiratory or combined respiratory and cardiopulmonary support, which hindered our ability to determine whether they received VV or VA ECMO. We attempted to control this by excluding patients with diagnoses of cardiopulmonary arrest on admission, cardiogenic shock, or a history of congestive heart failure in conjunction with ARDS, thereby narrowing the study population to those who likely required only VV ECMO. Third, there were limited details regarding patient care while on circuit. Provider variability in circuit management, cannula selection, surgical technique, and anticoagulation selection (dose, timing, interruptions, and therapeutic drug levels) could not be controlled by our database. Fourth, the TQIP database provides information on anticoagulation (timing of initiation), but the reason for initiation is not included. Therefore, we were not able to discern which patients were started on anticoagulation specifically for ECMO. It is possible that many patients were started on anticoagulation in the setting of routine DVT prophylaxis. Fifth, we were unable to extract time of ECMO discontinuation; therefore, we could not deduce a relation between duration of ECMO and HLOS or ventilator days. Although the data suggests that these indices did improve, it is difficult to determine with complete certainty that ECMO utilization alone was responsible. Additionally, those with HLOS <72 h were excluded from analysis. This may have led to selection bias, as patients who were started on anticoagulation in the setting of trauma is a younger patient with isolated blunt thoracic injury (74% survival) requiring short duration VV-ECMO. (25) This correlates well with our findings given the large percentage of patients in our ECMO cohort with significant chest injuries. Clinically, the Respiratory ECMO Survival Prediction (RESP) score could also assist in patient selection. (26)

In light of the patient population, anticoagulation is a common concern when considering ECMO in this high-risk group. Our ECMO cohort had a significant number of patients who received anticoagulation in the presence of TBI (45/85, 53%, median AIS-Head = 3 [IQR 2–5]). Additionally, there was no notable difference in the incidence of severe TBI (AIS-Head ≥ 3) between the anticoagulated and no anticoagulation groups. Overall, hesitation regarding the use of prophylactic or therapeutic anticoagulation in this setting appears to be decreasing. Case series suggest the ECMO circuit can be used successfully with or without anticoagulation, even in those with TBI and craniotomy along with other systemic injuries. (27-30) Use of ECMO in the bleeding coagulopathic patient is controversial, although case studies have shown that ECMO can also be used successfully in severe hemorrhagic shock with traumatic lung injury. (30) Advances in circuitry, specifically heparin-bonded cannulas and shorter tubing lengths, have allowed ECMO use with little or no anticoagulation. Additionally, recent large ELSO registry study suggests the benefits conferred by ECMO in terms of mortality far outweigh the risks of hemorrhage. (25)
course of ARDS. Anticoagulation while on circuit was not associated with increased risk of hemorrhage or mortality, even in the setting of head injuries. This possibility of a mortality benefit observed with ECMO may come at the expense of a potential increase in complication rate and prolonged hospitalization, both of which could improve as provider and facility experience with this treatment modality increase. A well-designed multicenter randomized study in the trauma population may eliminate the limitations of this retrospective observation study and confirm this hypothesis. However, there are many practical limitations of creating such a study until ECMO use for trauma becomes more well established.

Author contribution

- Literature review: Henry, Ghafi, Piccinini, Liassides, Matsushima, Golden, Lewis
- Study design: Henry, Ghafi, Piccinini, Liassides, Matsushima, Golden, Lewis, Inaba, Strumwasser
- Data collection: Henry, Ghafi, Piccinini, Liassides
- Data analysis/interpretation: Henry, Ghafi, Piccinini, Liassides, Matsushima, Golden, Lewis, Inaba, Strumwasser
- Writing/Critical revision: Henry, Ghafi, Piccinini, Liassides, Matsushima, Golden, Lewis, Inaba, Strumwasser

Conflicts

None of the authors have any conflicts of interest to disclose. Neither internal nor external financial support was used for this study.

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