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Original article

Extremity fasciotomy for patients on extracorporeal membrane oxygenation is independently associated with inpatient mortality

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ABSTRACT

Introduction: Extracorporeal membrane oxygenation (ECMO) maintains end-organ perfusion in critically ill patients with cardiac or respiratory failure; however, ECMO cannulation in the extremities has been associated with significant limb ischemia and risk of compartment syndrome. Current literature on ECMO and fasciotomies is limited to small single-center retrospective studies. This study aimed to (1) compare the incidence of postoperative outcomes and mortality in patients undergoing fasciotomy while on ECMO to those of non-fasciotomy ECMO patients, and (2) assess the difference in adjusted mortality risk between the two groups.
Hypothesis: We hypothesized that patients undergoing fasciotomy while on ECMO would have significantly higher odds of in-hospital mortality than non-fasciotomy ECMO patients after adjustment for perioperative variables.
Methods: We conducted a retrospective review of NIS from January 1st, 2012-September 30, 2015 for all hospitalizations involving ECMO and stratified them into two cohorts based on whether they underwent fasciotomy after ECMO. Patient baseline characteristics, in-hospital procedures, and postoperative outcomes were compared between the two cohorts. Logistic regression was used to assess in-hospital mortality risk between the two cohorts adjusting for age, sex, Elixhauser score, and perioperative procedures and non-fasciotomy perioperative morbidity.
Results: There were 7,085 estimated eligible discharges between 2012 and 2015 identified, 149 (2.1%) of which underwent fasciotomy following ECMO. One hundred and thirteen of the 149 hospitalizations (77%) in the fasciotomy cohort resulted in in-hospital mortality, compared to 3,805 of the 6,936 (55%) in the non-fasciotomy cohort. There were no differences in rates of transfusion ($p = 0.290$), length of stay ($p = 0.282$), or discharge disposition ($p = 0.126$) between the two cohorts. In the logistic regression model, the fasciotomy cohort had a higher odds of in-hospital mortality than non-fasciotomy cohort (OR, 2.5; 95% CI, 1.1–5.6).
Discussion: Operative treatment of acute compartment syndrome for patients on ECMO therapy is associated with significantly increased mortality and morbidity. Whether fasciotomy is a marker of sickness or represents a cause-and-effect relationship is unknown and future should investigate the role of non-operative treatment of compartment syndrome on mortality in this population.
Level of evidence: III; Prognostic.

1. Introduction

Extracorporeal membrane oxygenation (ECMO) is a lifesaving method of facilitating end-organ perfusion and oxygenation during reversible cardiopulmonary failure [1,2]. Despite its potential value, there is considerable morbidity associated with ECMO reflecting the inherent complexity of ECMO therapy and host compromise [3]. Adult patients who are cannulated peripherally (as opposed to centrally) on ECMO are generally cannulated in their lower extremities (femoral vein and/or artery) [4]. Whether venovenous (VV) or venoarterial (VA), the use of peripheral ECMO often places patients at considerable risk of limb ischemia and/or compartment syndrome which may require fasciotomy [5].

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Due to flow diversion and subsequent limb ischemia (VA) or elevated venous pressure leading to congestion (VV), compartment syndrome manifests in 7–14% of patients requiring peripheral ECMO cannulation [6]. Fasciotomy for treatment is seen in 0–6% of all ECMO patients [7–15]. Inherent host factors increasing the incidence of compartment syndrome in ECMO patients include a relatively high incidence of critical peripheral vessel stenosis and concurrent vasopressor use [4]. Compartment syndrome in patients receiving VA or VV ECMO therapy is a challenging diagnosis as concurrent intubation and sedation limits clinical exam [16]. Thus, the recognition of compartment syndrome may come at a late, and terminal, stage. In patients not on ECMO, fasciotomy performed 8 hours after the inciting insult is associated with increased surgical site infection [17]. Additionally, surgical management of compartment syndrome after 12 hours is associated with a significant loss of limb function, about 8% of normal limb functionality [18]. Given the frail status of patients on ECMO the infection risk associated with fasciotomy may contribute to blood stream infection and organ failure [19]. Further potentially complicating fasciotomy in these patients is the risk of hemorrhage with extensive surgical incisions and continued systemic anticoagulation for the ECMO patient [20,21]. In critically ill patients where surgery poses a life-threatening situation, the management of acute systemic side effects (e.g. acute renal failure) and delayed limb salvage or amputation is a viable solution. Given the risks of fasciotomy in this population, understanding the overall impact of acute surgical treatment of extremity compartment syndrome in patients on ECMO is imperative.

The goal of this study was to:

- compare the incidence of mortality in patients undergoing fasciotomy on ECMO to the general ECMO population;
- to assess the difference in adjusted mortality risk between these two populations.

We hypothesize that performing a fasciotomy on a patient supported on ECMO is associated with increased inpatient mortality, even after adjustment for perioperative variables.

2. Methods

This study was determined to be exempt from review by our institutional review board.

2.1. Patients

The National Inpatient Sample (NIS) is a publicly available database consisting of a stratified sample of all hospital admissions in the United States. Diagnosis and procedure codes are coded using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) (Supplemental Table 1). A retrospective review of NIS between 2012 and 2015 was conducted for discharges requiring the need for ECMO during hospitalization. Discharges were stratified into two cohorts, fasciotomy and non-fasciotomy, based on whether patients underwent fasciotomy while on ECMO (identified by ICD-9-CM procedure codes 83.14 or 83.44 that occurred on the same day or after ECMO). NIS data encodes a maximum of 15 procedure codes per hospitalization. Therefore, discharges with 15 or more procedures were excluded from this study to eliminate potential bias from patients who may have had fasciotomy procedure codes truncated from their associated NIS discharge record. Discharges from the fourth quarter of 2015 were excluded as this represented the transition point from ICD-9-CM to ICD-10-CM coding. Finally, we excluded discharges involving patients under the age of 18 or those involving cardiotomy to remove those patients likely to be on central ECMO.

2.2. Methods of Assessment

NIS was queried for patient demographics (age, sex, race, payer status), comorbidity burden (summed Elixhauser index consisting of 30 comorbidity indices previously validated for predictive use in adult inpatient and intensive care patients [22,23]), and perioperative procedures and complications (cardiac, respiratory, or vascular procedures, dialysis, organ transplant, and enteral/parenteral nutrition, transfusion requirement, acute kidney failure, and cardiac shock), length of stay, discharge disposition, and in-hospital mortality. Elixhauser comorbidities were identified using ICD-9-CM diagnosis codes and a summed Elixhauser comorbidity index score was calculated based on previously described methodology [24]. The Elixhauser comorbidity index is a validated scale that has demonstrated high accuracy in determining mortality risk in NIS data [25].

2.3. Statistical Analysis

The two cohorts, fasciotomy and non-fasciotomy, were compared with regards to patient demographics, comorbidity burden, and postoperative course. Descriptive statistics were reported as unweighted counts and weighted percentages for categorical variables and weighted mean with standard deviation for continuous variables. Differences between the two cohorts were assessed using Chi^2 for categorical variables and *t*-tests for continuous variables. A logistic regression model controlling for age, sex, Elixhauser comorbidity index, perioperative procedures and non-fasciotomy peri-operative morbidity was used to compare adjusted mortality risk between the two cohorts. Covariate inclusion was based on clinical relevance. Results of the regression model were reported as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was accepted at $p < 0.05$. All statistical analyses were conducted using STATA Version 15 (StataCorp, College Station, TX).

3. Results

We identified 7,085 estimated discharges (95% confidence interval, 6,239-7,931) between 2012 and 2015 that met our criteria, 149 (2.1%) of which underwent fasciotomy following ECMO. The mean patient age of all included discharges was 49 ± 16 years, and 40% of hospitalizations involved female patients (Table 1). The mean Elixhauser index was 4.7 ± 2.1. The mean number of days between ECMO and fasciotomy in the fasciotomy cohort was 3.3 ± 4.6 days. Overall mortality rate was 55%.

3.1. Preoperative Characteristics

Regarding preoperative characteristics, the two cohorts were similar in age (fasciotomy, 45 ± 15; no fasciotomy, 49 ± 16; $p = 0.125$), sex ($p = 0.715$), race/ethnicity ($p = 0.756$), payer status ($p = 0.400$), and summed Elixhauser index (fasciotomy, 4.7 ± 2.1; non-fasciotomy 4.7 ± 2.1; $p = 0.944$). The non-fasciotomy group underwent a higher proportion of respiratory procedures (fasciotomy, 27%; non-fasciotomy, 51%; $p = 0.009$), but there was no significant difference in rates of cardiac procedures ($p = 0.440$), vascular procedures ($p = 0.256$), dialysis ($p = 0.741$), or organ transplant ($p = 0.064$).

3.2. Postoperative Outcomes

Regarding postoperative course, the fasciotomy group had a significantly higher rate of in-patient mortality (fasciotomy, 77%;

Table 1
Patient demographics, comorbidity burden, and postoperative course by post-extracorporeal membrane oxygenation (ECMO) fasciotomy requirement in 7,085 hospitalizations requiring ECMO. National Inpatient Sample, 2012-2015q3.

Variables	n (%)[a]			p-value
	All Discharges (n = 7,085)	Fasciotomy (n = 149)	No Fasciotomy (n = 6,936)	
Patient Preoperative Characteristics				
Age (years)[b]	49 ± 16	45 ± 15	49 ± 16	0.125
Sex: Female	2,848 (40)	64 (43)	2,777 (40)	0.715
Race/Ethnicity				0.756
White	4,223 (60)	78 (53)	4,138 (60)	
Black	1,105 (16)	28 (17)	1,077 (16)	
Other/Unknown	1,757 (25)	43 (30)	1,715 (25)	
Payer Status				0.648
Medicare	1,899 (27)	25 (17)	1,878 (27)	
Medicaid	1,247 (18)	30 (20)	1,212 (18)	
Private	3,394 (48)	78 (52)	3,316 (48)	
Other/Unknown	546 (7.7)	14 (10)	531 (7.6)	
Summed Elixhauser Index[b]	4.7 ± 2.1	4.7 ± 2.1	4.7 ± 2.1	0.944
Perioperative Procedures and Clinical Course				
Cardiac Procedures	2,820 (40)	71 (47)	2,749 (40)	0.440
Respiratory Procedures	3,543 (50)	43 (27)	3,500 (51)	0.009
Vascular Procedures	4,747 (67)	113 (77)	4,627 (67)	0.256
Dialysis	1,027 (15)	28 (17)	1,006 (15)	0.741
Organ Transplant	808 (11)	0 (0)	808 (12)	0.064
Enteral/Parenteral Nutrition	758 (11)	10 (6.7)	744 (11)	0.478
Transfusion	2,026 (29)	28 (20)	1,998 (29)	0.290
Acute Kidney Failure	4,648 (66)	120 (80)	4,527 (65)	0.086
Cardiac Shock	298 (4.2)	21 (13)	276 (4.0)	0.013
Length of Stay (days)[b]	21 ± 27	16 ± 25	21 ± 27	0.282
Discharge Disposition				0.126
Home	1,360 (19)	14 (10)	1,346 (19)	
Care Facility	1,793 (25)	21 (13)	1,771 (26)	
Died	3,918 (55)	113 (77)	3,805 (55)	
Other/Unknown	14 (0.2)	0 (0)	14 (0.2)	
In-Hospital Mortality	3,918 (55)	113 (77)	3,805 (55)	0.017

[a] Percentages may not add up to total cell counts due to sampling weight application and rounding.
[b] Reported as weighted mean ± standard deviation.

non-fasciotomy, 55%; $p = 0.017$) as well as cardiac shock (fasciotomy, 13%; non-fasciotomy, 4.0%; $p = 0.013$). There was no difference in rates of transfusion ($p = 0.290$), acute kidney failure ($p = 0.086$), length of stay ($p = 0.282$), or discharge disposition ($p = 0.126$).

3.3. *Inpatient Mortality*

After adjusting for age, sex, Elixhauser comorbidity index, inpatient procedures and complications during hospitalization, patients undergoing fasciotomy after ECMO had a significantly higher odds of in-hospital mortality than ECMO patients not undergoing fasciotomy (OR, 2.5; 95% CI, 1.1-5.6).

4. Discussion

ECMO is a lifesaving machine used in the intensive care units as a last resort to support critically ill patients suffering from cardiopulmonary failure [1]. One such morbidity in this population is lower extremity acute compartment syndrome that needs fasciotomy release [4]. In the setting of ECMO-associated compartment syndrome, limb preservation and function is one of many factors to consider when deciding treatment options with systemic effects. Our data demonstrate that when fasciotomy is performed in the setting of ECMO, it is associated with an 80% inpatient mortality, 22% absolute difference compared to ECMO patients not receiving fasciotomy, and an adjusted 2.5-times greater risk of inpatient mortality.

Previous studies regarding ECMO associated fasciotomy have been performed in small single center populations. In a study of 5 patients with thigh compartment syndrome, Kreibich et al. report a 20% inpatient mortality rate [26]. In a meta-analysis conducted by Cheng et al., they report on the combined results of 335 patients in studies evaluating fasciotomy or compartment. In this population there was a 10% incidence ($n = 33$) of fasciotomy or compartment syndrome [6]. The 2% incidence of fasciotomy in our study likely reflects the difference in definition of our population (fasciotomy only as opposed to a compartment syndrome diagnosis to assess the effect of this procedure in a critically ill population) versus the Cheng et al. meta-analysis (fasciotomy [procedure] and compartment syndrome [diagnosis]). Their study reported a heterogenous population consisting of both diagnosis and procedure with differing morbidity and mortality profiles. Other studies report an incidence of fasciotomy in the ECMO population of 0-6%. [7–15].

Conflicting evidence exists regarding limb ischemia and mortality in this population. Foley et al. did not find that limb ischemia was associated with mortality in their study of 43 patients with 4 patients experience limb ischemia requiring fasciotomy [27]. Lunz et al. found a 10% inpatient mortality difference in ECMO patients with ischemic complications compared to those without, however this was nonsignificant [28]. This data is limited by lack of data regarding treatment for limb ischemia. Tanaka et al. report the results of 84 patients requiring VA ECMO with a 20% rate of vascular complications, 12% rate of fasciotomy ($n = 10$), and significant mortality hazard ratio of 3 in this population [29]. They also report an 80% mortality rate in a population with vascular complications (ischemic and hemorrhagic complications requiring surgical treatment) and a median survival of 11 days in this population. Given the multitude of procedures encompassed under Tanaka et al., definition of vascular complications, our data expands on their findings with a larger, fasciotomy only, population. To our knowledge, the only report of the outcomes of ECMO patients receiving fasciotomy is in abstract form. Robins et. al. reported on 23 patients (4.5% of total ECMO population) who received fasciotomy following ECMO with a 70% inpatient mortality rate. Results of covariate-controlled analysis and fasciotomy indication are not available [30].

While our data demonstrates an association between performance of fasciotomy and mortality after adjustment, there are several potential confounding etiologies of this increase in mortality. The large incisions associated with fasciotomy have a significant infection and bleeding risk in this vulnerable and systemically anticoagulated population [19]. Both of these potential morbidities may be iatrogenic contributions to mortality. Fasciotomy, however, may not be the ultimate causative factor of mortality in this population. The development of compartment syndrome treated with fasciotomy may be a clinical marker of severe critical illness which drives the difference in mortality rather than the fasciotomy procedure itself. Nevertheless, regardless of potential etiology, this data is critical to informing multi-disciplinary and family discussions when deciding the management of acute compartment syndrome in this population.

The strength of our data is that to our knowledge this the first study to describe an independent association between fasciotomy and mortality in patients on ECMO, and the largest report of outcomes in this specific population. Still there are limitations to our data. Our study is a large national database study and therefore is reliant on coding accuracy. Additionally, the NIS codes for only 15 inpatient procedures. We excluded discharges involving 15 or more procedures as these observations could have involved truncated data; therefore, a small number of patients who received an extremity fasciotomy after their first 15 procedures may have been excluded. However, the ICD-9-CM administrative coding system used by NIS has previously been used in ECMO patients [31,32]. Our data also lack some of the granular detail of the small, retrospective studies, precluding our analysis from including certain variables such as VA versus VV ECMO treatment or time under ECMO. It is possible that this data would have strengthened our regression model and influenced the difference in odds of mortality between these two groups. Additionally, we cannot account for recognized compartment syndrome treated non-operatively, and duration of acute compartment syndrome prior to treatment. However, the intent of our study was to describe the systemic effect of a surgical procedure on a population with significant comorbidity rather than to understand the etiology of compartment syndrome in this population.

5. Conclusion

Surgical treatment of acute compartment syndrome in patients undergoing ECMO treatment is associated with significantly elevated mortality and morbidity. On multivariate analysis our study demonstrates a 2.5-fold increase in inpatient mortality when a fasciotomy is performed on patients undergoing ECMO treatment. Our data may help guide multidisciplinary medical and surgical teams regarding expected outcomes when deciding on compartment syndrome treatment method in this critically ill population. Further study regarding the non-operative treatment of compartment syndrome in this population is warranted.

Disclosure of interest

Erik Hasenboehler, M.D., is a paid consultant for DePuy Synthes Trauma. He receives grant support as well as a grant for a research fellow from DePuy Synthes Trauma. He is also a paid lecturer and faculty for AO North American Trauma and has stock ownership in Summit Med Ventures. For the remaining authors, no conflicts were declared.

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Authors' contributions

Y.P.C., R.M.A., and S.S.R. were involved in study design and conceptualization, data manipulation and analysis, interpretation, and writing. V.P., M.J.B., and E.E. were involved with data interpretation, writing, and critical revisions. E.A.H. was involved in study design and conceptualization, interpretation, writing, and critical revisions. All authors approve of the final article.

Appendix A. Supplemental Table 1: Diagnosis and procedure codes used in the current study. ECMO, extracorporeal membrane oxygenation; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; PR-CCS, procedure clinical classification software; OR, operating room

Diagnosis/Procedure	Code	Description
ECMO	ICD-9-CM Procedure Code 39.65	Extracorporeal membrane oxygenation
Fasciotomy	ICD-9-CM Procedure Code 83.14	Fasciotomy
	ICD-9-CM Procedure Code 83.44	Other fasciectomy
Cardiotomy	ICD-9-CM Procedure Code 35.x	Operations on valves and septa of heart
	ICD-9-CM Procedure Code 36.x	Operations on vessels of heart
	ICD-9-CM Procedure Code 37.1	Cardiotomy and pericardiotomy
	ICD-9-CM Procedure Code 37.3x	Pericardiectomy and excision of lesion of heart
	ICD-9-CM Procedure Code 441.x	Major aortic dissection or aneurysm repair
Cardiac Procedures	PR-CCS 43	Heart Valve Procedures
	PR-CCS 44	Coronary Artery Bypass Graft
	PR-CCS 45	Percutaneous Transluminal Coronary Angioplasty
	PR-CCS 46	Coronary Thrombolysis
	PR-CCS 47	Diagnostic Cardiac Catheterization; Coronary Arteriography
	PR-CCS 48	Insertion; Revision; Replacement; Removal of Cardiac Pacemaker or Cardioverter/Defibrillator
	PR-CCS 49	Other OR Heart Procedures
	PR-CCS 225	Conversion of Cardiac Rhythm
Respiratory Procedures	PR-CCS 34	Tracheostomy; Temporary and Permanent
	PR-CCS 37	Diagnostic Bronchoscopy and Biopsy of Bronchus
	PR-CCS 39	Incision of Pleura; Thoracentesis; Chest Drainage

	PR-CCS 41	Other Non-OR Therapeutic Procedures on Respiratory System
	PR-CCS 58	Hemodialysis
Other Vascular Procedures Dialysis	PR-CCS 54	Other Vascular Catheterization; Not Heart
	PR-CCS 56	Other Vascular Bypass and Shunt; Not Heart
	PR-CCS 60	Embolectomy and Endarterectomy of Lower Limbs
	PR-CCS 61	Other OR Procedures on Vessels Other Than Head and Neck
Organ Transplant	PR-CCS 176	Organ Transplantation (other than bone marrow, corneal, or kidney)
Enteral/ Parenteral Nutrition	PR-CCS 223	Enteral and Parenteral Nutrition
Transfusion	PR-CCS 222	Blood Transfusion
Acute Kidney Failure	ICD-9-CM Diagnosis Code 584.x	Acute kidney failure
Cardiac Shock	ICD-9-CM Diagnosis Code 998.01	Postoperative cardiogenic shock

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