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ORIGINAL RESEARCH ARTICLE

Effect of body mass index on the outcome of surgical patients receiving extracorporeal devices (VV ECMO, pECLA) for respiratory failure

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ABSTRACT

Introduction: To determine whether obese surgical patients are at a significant disadvantage in terms of outcomes after extracorporeal device (ECD) support, such as veno-venous extracorporeal membrane oxygenation (VV ECMO) or pumpless extracorporeal lung assist (pECLA), for respiratory failure, the relationship between body mass index (BMI) and hospital outcomes was analyzed.
Methods: This retrospective study included data on patients who were supported with an ECD between January 1, 2008 and December 31, 2014. The analysis included 89 patients (74 male).
Results: The median BMI was 30 kg/m^2 (19-88.5). The median duration of the ECD support was 9.0 days, with a maximum of 37.1 days. The median LOS (length of stay) in the intensive care unit (ICU) was 21 days (range 0.06-197.6). The median hospital LOS was 34.9 days (range 0.1-213.8). VV ECMO was performed 72 times, and pECLA was performed 18 times. The number of patients successfully weaned off the ECD was 54 (60.6%). Survival at the discharge from the hospital was 48.3%.
Conclusions: 54 (60.6%) patients were successfully weaned off the ECD; 43 (48.3%) patients survived and were discharged from the hospital. The analysis of correlations between BMI and outcomes of surgical patients treated with ECD showed no association between BMI and mortality. Complications (especially oxygenator clotting) were not more frequent in obese and extremely obese patients. We hypothesized that patients with higher or morbid BMIs would have increased mortality after ECD support. A BMI of 30.66 kg/m^2 corresponded to the desired sensitivity and specificity to predict mortality. This finding applied only to the study group. Treatment with ECD in obese patients presents unique challenges, including percutaneous cannulation and increased staff requirements. However, based on these data, obesity should not be an exclusion criterion for ECD therapy.

Keywords: BMI, ECMO, Outcome, pECLA, Respiratory failure, Surgical patients

Introduction

The number of morbidly obese intensive care unit (ICU) patients is increasing globally, and research into the management and outcomes of these patients, many of whom are critically ill, is both germane and timely (1, 2). Chen et al reported that obesity was associated with an increased risk of hospitalization (3). Obesity has also been identified as a risk factor for the development of acute respiratory distress syndrome (ARDS) (4).

The obesity paradox has been used to describe the observed phenomenon of improved or nonimpaired survival for critically ill patients with moderate obesity (5, 6). Obese survivors required longer durations of mechanical ventilation and longer stays in the ICU (7, 8). Increased body mass index (BMI) is associated with increased length of hospital stay but not with mortality (4). Some studies suggest that certain groups of overweight patients exhibit reduced hospital mortality (9-14). However, paradoxical and conflicting effects of obesity on ICU outcomes and the outcomes of specific critical illnesses, such as lung failure and septic shock, have been reported in studies of the BMI of critically ill patients (9, 15-17).

The overall outcomes after extracorporeal life support (ECLS) may have improved over the last decade, and the indications for ECLS, such as sepsis, trauma or cardiac arrest, are generally accepted. VV ECMO has a survival rate of up to 71% in patients with severe respiratory failure (18).

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Aim of the study

Our hypothesis was that patients with higher or morbid obesity have increased mortality after extracorporeal device (ECD) support. If this is true, it should be possible to identify a cut-off BMI value that is associated with an increase in hospital mortality.

Methods

Study design

This single-center retrospective study was performed from January 1, 2008 to December 31, 2014 in a surgical ICU with more than 2,500 admissions per year.

Inclusion and exclusion criteria

Patients over the age of 16 years who received ECD support (VV ECMO and pECLA) during the study period were enrolled.

Outcome measures

In-hospital mortality was defined as the primary outcome, and ICU LOS and hospital LOS and ECD run time were defined as the secondary outcomes in order to evaluate additional effects of the intervention.

Statistical analysis

IBM® SPSS® Statistics Version 22 was used. Statistical regression (binary logistic regression) models were constructed based on factors found to be associated with outcomes at a p value <0.05. In the mortality models, factors that were available at the time of starting ECD were considered in a prognostic model; a p value of 0.05 was considered to be statistically significant. A receiver operating curve (ROC) was used to determine the BMI cutoff value for mortality prediction.

Privacy policy

All patient data were collected in a pseudonymous form using continuous study numbers. The data were saved in a database on an access-controlled PC.

Cannulation criteria

The criteria for the VV ECMO treatment of respiratory failure were defined as follows: severe hypoxemia (pO_2/FiO_2 ≤200 mmHg, FiO_2 0.8-1.0); tidal volume ≥4-6 mL/kg ideal body weight; inspiratory pressure (P_{insp}) ≥32-34 mmHg; respiratory acidosis (pH ≤7.25) and/or arterial oxygen saturation ≤90%. pECLA use was limited from 2008 to 2009 because of a trend away from this option, which was replaced by centrifugal systems in the later years. The precise indication was to enable lung-protective ventilation due to extracorporeal CO_2 removal ($ECCO_2R$).

All patients were cannulated percutaneously. Eighteen (20.2%) patients were cannulated in the referral hospital by a transfer ECMO team (Tab. I). VV ECMO was initiated through cannulated jugular-femoral (mostly 21 and 23 French) cannulae or double lumen cannula (31 French). PECLA cannulation was always veno-arterial femoro-femoral (mostly 17 and 15 French).

The iLA® Membrane Ventilator (Novalung) and the CardioHelp HLS® or Maquet Rotaflow ELS® (Maquet) were used. Once the gas exchange has been initiated via ECMO, the invasiveness of the mechanical ventilation was reduced during the first 4 to 6 hours, targeting tidal volume on 4 mL/kg ideal body weight and P_{max} less than 28 mmHg to facilitate lung healing. PEEP was maintained regarding the ARDS network recommendations. FiO_2 flow on the ventilator was decreased accordingly to the preset goals for oxygenation, which were targeted at PaO_2 of 60 mmHg and an arterial SaO_2 >90%. $PaCO_2$ was adjusted to achieve a pH level >7.2. Oxygen was used as the sweep gas, with a flow rate maintained between 1 to 10 L/min. Spontaneous breathing efforts with ventilator support were allowed in awake patients after the sedation was reduced during the first 48 hours postcannulation. The circuit was monitored once daily for its gas transfer, and the presence of blood clots was evaluated by the perfusionist.

In cases where the underlying disease was treated successfully and lung function improved, the blood flow rate was reduced in a stepwise fashion to 2.0 L/min. Thereafter, the sweep gas was finally switched off. If the arterial gas exchange parameters remained stable, the cannulas were removed, and manual compression of the vessels followed.

Anticoagulation

During the cannulation, 5,000 units of heparin were applied. Without risk of bleeding pTT was aimed at 50 to 60 seconds. In cases of traumatic brain injury with intracranial bleeding but also in the absence of increased bleeding risk due to cranial CT, no heparin was given for at least 48 to 72 hours following the traumatic incident. In cases of severe bleeding or consumption coagulopathy after trauma, 400 units of heparin per hour were administered with a delay of 3 to 5 days, depending on the recovery of the coagulation system. Surgical procedures on ECD (Tab. II) were performed without heparin, with antifibrinolytic therapy, and after normalization of the platelet count and clotting indices. The perioperatively targeted values were quick >50%, pTT <50 sec, fibrinogen >250 mg/dL, platelets >50,000/nL; in brain injured patients, the following target values were used: platelets >80,000/nL.

Results

Patients

The study group was divided into 4 groups according to the World Health Organization (WHO) classification (1, 2). The WHO defines a BMI greater than or equal to 25 as overweight (group 2) and a BMI greater than or equal to 30 as obese (group 3). Group 4 (BMI of >35) was defined as extremely obese (Tab. I). The study cohort consisted predominantly of male patients (85.2%) who experienced major trauma (52.3%).

TABLE I - Patient characteristics by BMI group

	ECD	BMI <25	25< BMI <30	30< BMI <35	35< BMI
Number of patients (n; % of 89 patients)	89 (100%)	13 (14.6%)	31 (34.8%)	24 (27.0%)	21 (23.6%)
Sex (male) (n; %)*	74 (83.1%)	10 (76.9%)	26 (83.9%)	22 (91.6%)	16 (76.1%)
Age (years)**	55 (17-86)	49 (18-75)	54 (17-86)	58 (16-75)	56 (28-75)
BMI (kg/m^2)**	30.0 (19.0-88.5)	23.4 (19.0-24.9)	27.3 (25.3-29.4)	30.9 (30.0-33.9)	41.5 (35.0-88.5)
Respiratory failure in thoracic trauma patients (n; %)*	47 (52.8%)	10 (76.9%)	20 (64.5%)	12 (50.0%)	5 (23.8%)
Respiratory failure in non-trauma patients (n; %)*	18 (20.2%)	2 (15.4%)	6 (19.3%)	3 (12.5%)	7 (33.3%)
Extra-pulmonary sepsis (n; %)*	25 (28.0%)	1 (7.7%)	5 (16.1%)	9 (37.5%)	10 (47.6%)
Other (alveolitis) (n; %)*	5 (5.6%)	1 (7.7%)	2 (6.4%)	1 (4.1%)	1 (4.8%)
vv ECMO (n; %)*	72 (80.9%)	10 (76.9%)	24 (77.4%)	19 (79.1%)	19 (90.5%)
pECLA [#] (n; %)*	18 (20.2%)	3 (23.1%)	8 (25.8%)	5 (20.8%)	2 (10.5%)
ECD cannulation in referral hospitals (n; %)	18 (20.2%)	0 (0%)	8 (25.8%)	5 (20.8%)	5 (23.8%)
Use of double lumen cannula (n; %)*	13 (14.6%)	4 (30.8%)	5 (16.1%)	1 (4.1%)	3 (14.2%)
Murray score before ECD cannulation**	2.76 (1.25-3.75)	2.5 (1.5-3.75)	2.75 (1.25-3.75)	2.75 (1.5-3.5)	2.5 (1.25-3.75)
SOFA score before ECD cannulation**	13 (6-20)	11 (9-17)	12 (6-18)	13.5 (9-20)	12 (7-17)
Ventilation time** (hours)	438. (0-4992)	384 (72-1332)	623.5 (0-1167)	361.5 (14-4992)	413 (0-1782)
Extubation on ECD*	2 (2.2%)	1 (7.7%)	0 (0%)	0 (0%)	1 (4.8%)
Extubation after ECD* (without tracheostomy)	4 (4.5%)	0 (0%)	3 (9.6%)	0 (0%)	1 (4.8%)
T-piece on ECD*	5 (5.6%)[&]	0 (0%)	2 (6.4%)[&]	1 (4.1%)	2 (9.5%)
Died before indication of tracheostomy was a concern*	17 (19.1%)	1 (7.7%)	4 (12.9%)	8 (33.3%)	4 (19.0%)
Percutaneous tracheostomy during ECD*	60 (67.4%)[###]	10 (76.9%)	23 (74.1%)[###]	15 (62.4%)	12 (57.1%)
	ECD	BMI <25	25< BMI <30	30< BMI <35	35< BMI
Duration of ECD run (days)**	9.0 (0.1-37.1)	11.8 (2.9-21.3)	8.9 (0.9-33.9)	9.1 (0.7-37.0)	7.3 (0.1-26.8)
Post-ECD days in ICU**	14.2 (0-110.9)	19.1 (0-75.9)	27.9 (0-110.9)	0.9 (0.-94)	6.8 (0-91.1)
Weaned from ECD*	54 (60.6%)	9 (69.2%)	22 (77.4%)	10 (41.6%)	13 (61.9%)
LOS in ICU (days)**	21 (0.6-197.6)	21 (5.0-63.0)	24 (3.9-197.6)	14.8 (0.5-80.0)	16.6 (3.4-88.6)
Patients discharged from the ICU (n; %)*	45 (50.5%)	8 (61.53%)	19 (61.2%)	8 (33.3%)	10 (47.6%)
LOS in hospital (days)**	34.9 (0.1-213.8)	41.9 (8.5-108)	42.6 (2.9-126.6)	24.9 (0.6-213.8)	26.7 (0.1-110.6)
Patients discharged from the hospital (n; %)*	43 (48.3%)	8 (61.53%)	18 (58%)	7 (22.5%)	10 (47.6%)

* Within each BMI group.
** All values are expressed as the median (with range).
[&] 1 ECD without ventilation (in awake patient).
[#] Thoracic trauma patients cannulated for pECLA. 2008-2009.
[##] Multiple uses.
[###] 1 patient discharged to referral center for assist device (intubated, without tracheotomy).
ECD = extracorporeal device; BMI = body-mass index; VV ECMO = veno-venous extracorporeal membrane oxygenation; pECLA = pumpless extracorporeal lung assist.

TABLE II - Surgery during ECD run

Number of patients with surgical interventions	8 (8.9% of n = 89)
Laparotomy in post-traumatic abdomen	6 (6.7%)
Reconstruction of lower extremity arteries (popliteal, femoralis superficialis)	3 (3.4%)
Craniectomy	2 (2.2%)
Hemipelvectomy in sepsis	1 (1.1%)
Embolectomy	1 (1.1%)
Thoracotomy	2 (2.2%)
Amputation of the lower extremity	1 (1.1%)
All surgical interventions during ECD run	16 (17.9%)

ECD = extracorporeal device.

Patient characteristics in relation to the BMI groups

The group with 25 kg/m^2< BMI <30 kg/m^2 (31 patients) constituted the largest percentage of all patients. The proportion of trauma patients (76.9%) in the group with BMI <25 kg/m^2 was largest. The group with 35 kg/m^2< BMI showed the lowest percentage of trauma and the highest rates of respiratory failure and sepsis as ECD indications. Statistical tests revealed no significant differences between the BMI groups in terms of precannulation scores, ECD run, LOS in the ICU or in hospital mortality.

Weaning

The aim in all the patients was to wean mechanical ventilation in parallel with weaning from the ECD. In 7 patients (7.8%), rapid weaning was successful; 2 patients were extubated while on the ECD, and an additional 4 patients were weaned after the ECD run without requiring a tracheotomy (Tab. I).

Complications

Continuous renal replacement therapy (CRRT) was performed in renal failure in 59.5% of the patients.

Bleeding, oxygenator clotting and complications during cannulation were the most common complications (Tab. III). There were no significant differences in the incidence of complications between the BMI groups.

Outcomes

Fifty-four (60.6%) patients were successfully weaned off the ECD; 43 (48.3%) patients survived and were discharged from the hospital (Tab. I). We hypothesized that patients with higher or morbid BMIs would have increased mortality after ECD support; however, this hypothesis could not be confirmed. A BMI of 30.66 kg/m^2 corresponded to the desired sensitivity and specificity to predict mortality (Fig. 1). BMI had no decision-making power because the ROC curve lay not exactly on the diagonal, but near it, indicating a random process (Fig. 1). The AUC was 0.564, indicating the poor classification ability of BMI. This finding applied only to the study group.

As predictive factors for hospital mortality, multivariate regressions analysis found the following: age, p<0.008; admission SOFA score, p<0.035; days in hospital after disconnection from the ECD, p<0.01.

Conclusions

Effects of obesity on outcomes in the ICU

Martino reported that extreme obesity (BMI >40) is not associated with worse survival than normal weight (7). Compared with normal-weight patients, obese patients had a 26% and 43% lower risk of mortality at 30 days and 1 year after ICU admission, respectively (10). ICU mortality was influenced more strongly by the severity of illness and failed extubation rather than BMI (19). The effects of obesity on the pathogenesis of acute lung injury are poorly understood. Kordonowy demonstrated that obesity attenuates the development of acute lung injury in mouse models and implicated obesity-associated neutrophil chemotactic dysfunction (20). Obese patients who develop acute lung injury (ALI) exhibit lower levels of several proinflammatory cytokines, which indicates that the inflammatory response may be altered in patients with ALI and a high BMI (21). Stapleton suggested that lower levels of surfactant protein D decreased epithelial injury and increased endothelial injury in the lungs of obese patients (21). Slynkova observed that obesity is not a significant predictor of either acute organ failure or death during or after acute organ failure in critical illness (22). However, the presence of diabetes mellitus, which is associated with obesity, is a strong predictor of both acute organ failure and death after acute organ failure. Fonarow et al (12) observed paradoxical results in obese persons with heart failure in early stage due to greater protection against malnutrition-inflammation-cachexia.

Effects of obesity on outcomes after ECD therapy

Pham reported that a higher BMI was protective in an analysis of factors that were associated with death in 122 patients treated with ECMO for H1N1 influenza (23). Increased body weight was also not a risk factor for hospital mortality in adult patients who required support with ECMO for respiratory failure in the ELSO Registry analysis (24). A growing number of studies regarding the factors that determine outcomes in adult ECLS patients have been published (24-26). Of all the reported adverse events that occur during ECLS, coagulopathy is the most common and has a significant impact on mortality (26). In the group of ECLS patients with lung failure, only the preoperative serum creatinine levels were correlated with survival (25).

Challenges of extracorporeal circulation in obese patients

Theoretically, the increase in cardiac output that is associated with a higher BMI may surpass the oxygenation capacity

TABLE III - Complications during ECD treatment

Complications*	ECD n = 89	BMI <25** n = 13	25< BMI <30 n = 31	30< BMI <35 n = 24	35< BMI n = 21
Frequency of CRRT	53 (59.5%)	6 (46.1%)	14 (45.1%)	16 (66.6%)	17 (80.9%)
Total complications	33 (37%)	8 (61.5%)	6 (19.3%)	10 (41.6%)	9 (42.8%)
Cerebral bleeding	2 (2.2%)	1 (7.7%)	0	1(4.1%)	0
Diffuse bleeding	4 (4.5%)	0	0	2 (8.2%)	2 (9.5%)
Low flow complication during prone positioning	1 (1.1%)	0	0	0	1 (4.8%)
Complications during cannulation	3 (3.3%)	0 (%)	0	2 (8.2%)	1 (4.8%)
Oxygenator clotting or need for replacement (number of patients)	16 (17.9%)	3 (23.1%)	5 (16.1%)	4 (16.6%)	4 (19%)
Oxygenator clotting or need for replacement (number of oxygenators)	25	5	6	6	8
Accidental cannula removal with CPR	1 (1.1%)	1 (7.7%)	0	0	0
Arterial ischemia on iLA	1 (1.1%)	1 (7.7%)	0	0	0
ILA to VV ECMO	2 (2.2%)	0	1 (3.2%)	1 (4.1%)	0
DIC	1 (1.1%)	1(7.7%)	0	0	0
HIT	1 (1.1%)	0	0	0	1(4.8%)
In-cannula thrombosis (double lumen cannula)	1 (1.1%)	1(7.7%)	0	0	E0

* % within each BMI group.
** BMI expressed as kg/m^2.
ECD = extracorporeal device; BMI = body-mass index; CRRT = continuous renal replacement therapy; CPR = cardiopulmonary resuscitation; iLA = iLA® Membrane Ventilator (Novalung); VV ECMO = veno-venous extracorporeal membrane oxygenation; DIC = disseminated intravascular coagulation; HIT = heparin-induced thrombocytopenia.

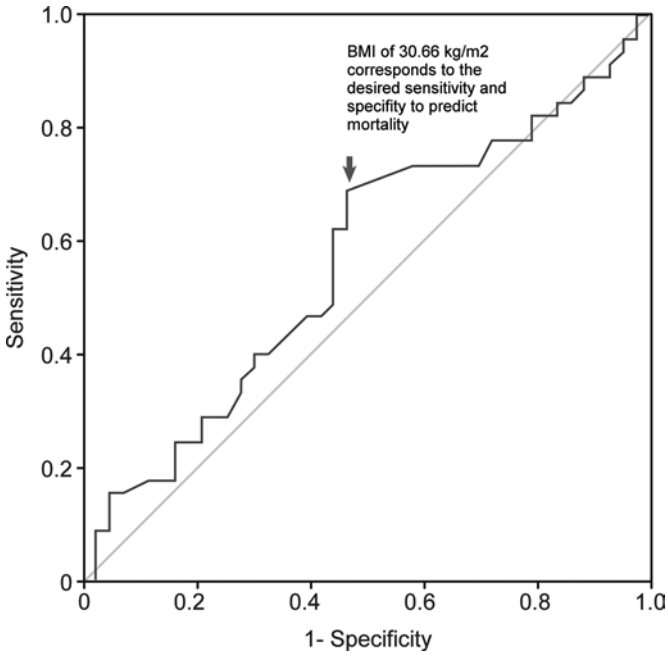

Fig. 1 - ROC curve for determination of the cutoff BMI to predict mortality Arrow: BMI of 30.66 kg/m^2 corresponds to the desired sensitivity and specificity to predict mortality

of the oxygenator. Consequently, VV ECMO may be of limited utility for the management of hypoxia in overweight patients with respiratory failure (24). In the described group of 89 surgical patients, the complications did not vary based on BMI. The results led to the same conclusion as reported by Al-Soufi and the ELSO registry group. Based on the ELSO registry population, there was a lack of association between body weight and mortality in patients on veno-venous extracorporeal membrane oxygenation (24).

Difficulties in interpreting the hemodynamic parameters may contribute to the increased mortality rate in obese patients (27). A severity score adapted to obese patients in the ICU has not been validated in the literature. The scores designed for ICU patients, including the APACHE II, APACHE III, Sequential Organ Failure Assessment and Simplified Acute Physiology Score II, may not be adaptable to obese patients, as BMI is not included in these protocols (28, 29). The excess mortality rate attributed to obesity may be underestimated. For example, the alveolar arterial gradient is increased in both obesity and pulmonary infections (30). This may increase the APACHE II, which is a multifactorial explanation of the syndrome. Consequently, the severity of disease at admission could confound the assessment of actual outcomes in obese patients (29).

Obese patients are recognized as “difficult to intubate, difficult to ventilate, difficult to wean, [and] difficult to move”

(30). For patients with severe hypoxemia, circuit flows that are indexed to either weight or body surface area are generally required to sustain lung rest and recovery.

Bercault et al (9) suggested that obesity is an independent risk factor for ICU death and should be regarded as a severe comorbidity in such units. However, without an analysis of the method of treatment in obese patients, the expectation of a poor outcome for critically ill obese patients may lead to a physician-fulfilling prophecy (31).

Limitations

Our study was a single-center, retrospective study that focused on the association between BMI and outcomes. The population is very specific (a high number of trauma cases), and this explains the low external validity of our findings. Trauma patients are frequently younger and healthier than medical patients or patients with severe abdominal sepsis. Nevertheless, trauma was previously considered to be a contraindication for extracorporeal life support due to the risk of bleeding. It is also evident that trauma was predominant in the low BMI group. This population characteristic has possible effects on the results of the study and is a major limitation. The conditions in the BMI groups vary significantly. When comparing different BMI groups, different conditions leading to indications of extracorporeal therapy were also compared.

The number of patients treated per year is relatively small, which makes it difficult to address mortality as a primary end point. The surgical cohort was heterogeneous, including primarily patients treated with VV ECMO; however, patients treated with pumpless support were also included. The group of pECLA patients is too small to analyze significant differences separately. However, this diversity provides an opportunity to include a larger number of cases.

Treatment with an ECD in obese patients presents unique challenges, including percutaneous cannulation. In this study, obesity was found to be not associated with poorer outcomes. Based on these data, ECD support should not be withheld from obese patients and obesity should not be a general exclusion criterion for ECD therapy.

Disclosures

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Conflict of interest: None of the authors has any financial interest related to this study to disclose.

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