Prediction of prolonged mechanical ventilation in critically ill obstetric patients: Ten years of data from a tertiary teaching hospital in mainland China

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Abstract

Background

Maternal admission to the intensive care unit (ICU) during pregnancy or in the postpartum period is a marker of severe acute maternal morbidity. Mechanical ventilation is an important and basic method of maintaining life support in the ICU, but prolonged mechanical ventilation (PMV) is associated with a prolonged length of hospital stay and other adverse outcomes. Therefore, we conducted this retrospective study to describe morbidity and further try to identify the risk factors for PMV in critically ill obstetric women.

Methods

The clinical data were obtained from a single-centre retrospective comparative study of 143 critically ill obstetric patients at a tertiary teaching hospital in mainland China between January 1, 2009, and December 31, 2019. Clinical and obstetric parameters were collected to analyse the risk factors for PMV. Patients were separated into groups with and without PMV. Potential risk factors were identified by univariate testing. Multivariate logistic regression was used to evaluate independent predictors of PMV.

Results

Out of 29,236 hospital deliveries, 265 critically ill obstetric patients entered the ICU. One hundred forty-five (54.7%) of them were treated with mechanical ventilation. Two were excluded because of death within 24 hours. Sixty-five critically ill obstetric patients (45.5%) underwent PMV. The independent risk factors for PMV included estimated blood loss (odds ratio (OR) = 1.296, P = 0.029), acute kidney injury (AKI) (OR = 4.305, P = 0.013), myocardial injury (OR = 4.586, P = 0.012), and PaO_2/FiO_2 (OR = 0.989, P < 0.001). The area under the receiver operating characteristic (ROC) curve based on the predicted probability of the logistic regression was 0.934.

Conclusions

Estimated blood loss, AKI, myocardial injury, and PaO_2/FiO_2 were independent risk factors for PMV in critically ill obstetric patients.

Background

Although maternal deaths in China have decreased substantially in recent decades, the incidence of severe acute maternal morbidity (SAMM) is still high [1, 2]. Due to the implementation of the two-child policy in China, since 2016, the number of pregnant women with an older maternal age and history of caesarean section has increased, which has further increased the incidence of gestational diabetes mellitus, dangerous placenta previa, placental implantation, and severe postpartum haemorrhage [3–5]. Maternal admission to the intensive care unit (ICU) during pregnancy or in the postpartum period is a marker of SAMM [2, 6–11]. ICU admission of pregnant and postpartum women presents significant

challenges to ICU clinicians because of altered maternal physiology, foetal considerations and medical emergencies associated with pregnancy [12, 13]. Mechanical ventilation is an important and basic manner of maintaining life support in the ICU, but prolonged mechanical ventilation (PMV) increases the risk of a prolonged length of hospital stay, increased hospitalization costs, and other adverse outcomes [14, 15]. Therefore, exploring the risk factors for prolonged mechanical ventilation in critically ill pregnant and postpartum women is important for quality and prognosis improvement. However, little is known about the proportion and risk factors for PMV in critically ill obstetric patients. Therefore, we conducted this retrospective study to describe morbidity and further try to identify the risk factors for PMV in critically ill obstetric women.

Methods

Participants

The clinical data were obtained from a single-centre retrospective comparative study of 143 critically ill obstetric patients at a tertiary teaching hospital in mainland China between January 1, 2009, and December 31, 2019. This study was approved by the institutional review board following the Declaration of Helsinki principles.

The inclusion criteria for this study were obstetric patients (i.e., those who were pregnant or up to 42 days postpartum) with the following conditions: (1) entered the intensive care unit (ICU) and (2) treated with mechanical ventilation (MV). The exclusion criteria were as follows: (1) age < 18 years; (2) those who gave up therapy; and (3) death within 24 hours after MV.

Clinical and obstetric parameters

The baseline clinical and obstetric patient characteristics were collected within the first 24 hours after mechanical ventilation (the worst results within the first 24 hours were chosen) (see Table 1). Clinical parameters included age, sex, causes of ICU admission, Acute Physiology and Chronic Health Evaluation (APACHE) II score, body mass index (BMI), acute kidney injury (AKI), myocardial injury (defined as an increase in blood cardiac troponin I [16]), total bilirubin (TBIL), albumin, brain natriuretic peptide (BNP), white blood cell (WBC) count, platelets arterial blood pH, arterial partial pressure of carbon dioxide ($PaCO_2$), the ratio of the arterial partial pressure of oxygen and the fraction of inspired oxygen (PaO_2/FiO_2), and lactate.

Obstetric parameters included gestational weeks, obstetric causes of ICU admission, and the estimated blood loss volume during delivery.

Outcomes

The outcomes of the critically ill obstetric patients in our study included the length of ICU stay, length of hospital stay, length of mechanical ventilation, and hospital mortality.

Prolonged mechanical ventilation

Previous studies used predefined values of mechanical ventilation time, ranging from 24 hours to 72 hours, and even to 21 days, to define critically ill patients as having PMV [17]. In this study, PMV was defined as a mechanical ventilation length of more than 24 hours. This definition was based on the median length of mechanical ventilation of this study. According to PMV status, patients were divided into two groups: the PMV group and the non-PMV group.

Statistical analysis

All the analyses were performed with Stata software, version 15.1 (Stata Corp). Continuous data were expressed as means with standard deviations or as medians with interquartile ranges, depending on their normality. Categorical variables are shown as proportions. In the univariate testing, continuous variables were examined using Kruskal-Wallis equality-of-populations rank tests. Categorical variables were examined using Pearson chi-square tests or Fisher exact tests where appropriate. Predictors with a P value of <0.05 on univariate analysis were identified as risk factors for PMV. The variance inflation factor (VIF) and tolerance were used to test the multicollinearity of the risk factors. A VIF > 10 or tolerance < 0.1 was identified as significant multicollinearity. Binary logistic regression was used to determine independent risk factors for PMV. The Hosmer-Lemeshow test was used to estimate the goodness of fit for the logistic regression mode. We generated a receiver operating characteristic (ROC) curve using predicted probability values from the logistic regression. The coefplot module was used to plot the regression coefficients. We used a nomogram to demonstrate the risk points and probability of independent risk factors for predicting PMV. A P value of < 0.05 in 2-sided tests was statistically significant.

Results

Participants

Out of 29,236 hospital deliveries, 265 critically ill obstetric patients entered the ICU between January 1, 2009, and December 31, 2019, in our hospital. One hundred forty-five (54.7%) of them were treated with mechanical ventilation. Two were excluded because of death within 24 hours after mechanical ventilation. Finally, one hundred forty-three patients were enrolled in this study (see Fig. 1).

The median age was 31 years, and the median gestational week was 34.9 weeks. Obstetric causes made up the majority of the causes of ICU admission (60.8%). The main obstetric cause was postpartum haemorrhage (35%). Other obstetric causes included eclampsia or pre-eclampsia (18.9%), puerperal infection (5.6%), and others (1.4%). Nonobstetric causes included haematological diseases (11.2%), autoimmune diseases (5.6%), cardiovascular disease (2.1%), neuropsychiatric diseases (4.2%), acute fatty liver of pregnancy (AFLP) (2.1%), acute pancreatitis (3.5%), gastrointestinal perforation (3.5%) and others (7.0%). The median length of mechanical ventilation was 19 hours. The median length of ICU

stay and hospital stay were 72 hours and 13 days, respectively. Four obstetric patients died in the hospital (2.8%) (see Table 1).

Prolonged mechanical ventilation and outcomes

Sixty-five critically ill obstetric patients (45.5%) underwent PMV. The length of ICU stay (P<0.001) and hospital stay (P<0.001) were both significantly longer in the PMV group than in the non-PMV group. The mortality was very low, and there was no significant difference between the two groups (P=0.229).

Univariate analysis

Compared with non-PMV patients, PMV patients had a higher APACHE II score (P=0.008) and a larger amount of estimated blood loss during delivery (P<0.001). The incidence of AKI (P<0.001) and myocardial injury (P<0.001) was significantly higher in the PMV group than in the non-PMV group. PMV patients had significantly higher blood TBIL (P<0.001), BNP (P<0.001), $PaCO_2$ (P=0.012), and lactate (P=0.002) levels. The blood platelet count (P=0.026) and the arterial blood PaO_2/FiO_2 (P<0.001) were significantly lower in the PMV group. No significant difference in age, BMI, gestational weeks, causes of ICU admission, blood WBC count, blood albumin level, arterial blood pH, or bicarbonate was observed.

Multivariate analysis

Variables with a P value of <0.05 in the univariate analysis mentioned above were identified as risk factors for PMV. We tested the multicollinearity of all the risk factors. The results showed that the largest VIF was 1.66 and the smallest tolerance was 0.60 (see Additional file 1). Therefore, we included all 10 chosen risk factors in the logistic regression model, and we found that estimated blood loss (odds ratio (OR) =1.296, P=0.029), AKI (OR=4.305, P=0.013), myocardial injury (OR=4.586, P=0.012), and PaO_2/FiO_2 (OR=0.989, P<0.001) were independent risk factors for PMV in critically ill obstetric patients (see Table 4). The Hosmer-Lemeshow test showed that the fit for the logistic regression model was good (P=0.097, chi2=153.56). The ROC curve based on the predicted probability of the logistic regression is shown in Fig. 2, and the area under the curve was 0.934 (95% CI, 0.895 to 0.974). The plot of the regression coefficients is shown in Fig. 3.

Nomogram

Through the logistic regression model, we built a prognostic nomogram incorporating the above independent prognostic factors for visualization and facilitation of clinical practice, as shown in Fig. 4. In this model, we transferred PaO_2/FiO_2 into four classes based on the Berlin definition of acute respiratory distress syndrome (ARDS) to simplify clinical practice [18].

Discussion

Early extubation for critically ill obstetric patients is important, as it may lead to more rapid recovery, a shorter length of ICU stay, and lower hospitalization costs. To our knowledge, this is the first study to

identify the characteristics of mechanical ventilation and the risk factors for PMV in critically ill pregnant and postpartum patients. In our study, the incidence of mechanical ventilation was 54.7% among obstetric patients admitted to the ICU. Estimated blood loss, AKI, myocardial injury, and PaO_2/FiO_2 were independent risk factors for PMV in critically ill obstetric patients.

In our study, the incidence of mechanical ventilation was 54.7% in obstetric ICU patients, and 45.5% of the patients who received mechanical ventilation had a ventilation time of more than 24 hours. These results are similar to those of another multicentre report. Zhao et al. enrolled 491 obstetric patients with ICU admissions from three tertiary hospitals in China. They found that 40% of the patients underwent intubation and mechanical ventilation, and the median length of mechanical ventilation was one day [2].

Our study showed that estimated blood loss was an independent risk factor for the development of PMV. Several studies have shown that the most common cause of pregnancy-related admission to the ICU is obstetric haemorrhage [2, 12]. A multicentre study in China found that postpartum haemorrhage (170/491; 34.62%) was the main reason for ICU admission [2]. Chantry et al. determined the reasons for pregnancy-related ICU admissions from all ICUs in France from 2006 to 2009. They enrolled 11,824 pregnancy-related ICU admissions and showed that the leading cause of transfer to ICUs was obstetric haemorrhage (4,043; 34.2%) [12]. We also found that postpartum haemorrhage was the main reason for ICU admission (87/143; 35%). Possible reasons for the association of estimated blood loss and PMV included the following: massive obstetric haemorrhage that induced hypovolemic shock and tissue hypoperfusion and further caused lung injury; an independent, dose-dependent relationship between blood transfusion and the subsequent development of acute lung injury; and massive haemorrhage and subsequent resuscitation leading to fluid overload, which is associated with pulmonary oedema and ventilator dependence [19, 20]. Therefore, timely treatment of postpartum haemorrhage could prevent lung injury and reduce the length of mechanical ventilation.

In our study, obstetric patients with an AKI were more likely to have PMV than those without an AKI. Ghauri et al. systematically reviewed the predictors of the need for PMV in adult patients admitted to ICUs for medical and surgical needs. They found that kidney dysfunction was one of the most significant independent predictors of the need for PMV [17]. Clark et al. retrospectively assessed 130 ICU patients and showed that serum creatinine levels greater than 2.0 mg/dL were independently associated with PMV. They further validated their findings in a prospective trial. Acute kidney injury is one of the manifestations of insufficient organ perfusion [21]. On the other hand, kidney dysfunction can cause fluid accumulation and tissue oedema. Therefore, it is very important to monitor renal function and treat potential causes in critically ill obstetric patients in a timely manner.

Our results demonstrated that myocardial injury was an independent risk factor for the development of PMV. We defined myocardial injury as an increase in blood cardiac troponin I [16]. Myocardial injury may be caused by hypoperfusion, hypoxia, global ischaemia, surgery, and sepsis in noncardiac patients. Previous studies showed that myocardial injury was associated with mortality among patients undergoing noncardiac surgery [16, 22–24]. A prospective cohort study recruited 21,842 patients who

underwent noncardiac surgery at 23 centres in 13 countries. This study demonstrated that peak postoperative troponin during the first 3 days after surgery was significantly associated with 30-day mortality, even in patients without an ischaemic feature [24]. Our previous study retrospectively enrolled 381 critically ill patients who underwent major abdominal surgery. We found that myocardial injury is an independent risk factor for weaning failure from mechanical ventilation [25]. Abdalla et al. also demonstrated that troponin elevation was associated with a longer duration of mechanical ventilation in patients who were admitted to the ICU with sepsis [22].

According to our logistic regression analysis, PaO_2/FiO_2 is an independent risk factor for the development of PMV. PaO_2/FiO_2 is an important variable for evaluating lung injury, and it is the basis for the Berlin definition of ARDS risk stratification [18]. PaO_2/FiO_2 is also an important indicator for evaluating mechanical ventilation weaning [26]. Therefore, we need to monitor PaO_2/FiO_2 to evaluate the lung function of critically ill obstetric patients and improve PaO_2/FiO_2 through mechanical ventilation and other aetiological treatments.

This study has several limitations. First, the data were retrospectively collected. We could not control for some variables, which may have resulted in data bias. Second, the study was a single-centre study, and most obstetric patients were admitted to the ICU based on local criteria and local practice. Third, we derived four independent risk factors for prolonged mechanical ventilation and built a nomogram for visualization and facilitation of clinical practice. However, we did not validate the nomogram with a new database. A prospective, multicentre study is needed to address these issues and validate our findings.

Conclusions

We conclude that it is important to predict prolonged mechanical ventilation (PMV) in critically ill obstetric patients. Logistic regression analysis shows that the independent risk factors for PMV in critically ill obstetric patients are estimated blood loss, AKI, myocardial injury, and PaO_2/FiO_2.

Abbreviations

SAMM: Severe acute maternal morbidity; ICU: Intensive care unit; PMV: Prolonged mechanical ventilation; MV: mechanical ventilation; APACHE: Acute physiology and chronic health evaluation; BMI: Body mass index; AKI: Acute kidney injury; TBIL: Total bilirubin (TBIL); BNP: Brain natriuretic peptide; WBC: Blood white blood cell; $PaCO_2$: Arterial partial pressure of carbon dioxide; PaO_2/FiO_2: Ratio of arterial partial pressure of oxygen and fraction of inspired oxygen; VIF: Variance inflation factor; ROC: Receiver operating characteristic; AFLP: Acute fatty liver of pregnancy; ARDS: acute respiratory distress syndrome.

Declarations

Ethical Approval and Consent to participate

The study was approved by Ethics Committee of Peking University People's Hospital. This study was in accordance with the ethical standards of the institutional research committee, the 1964 Helsinki declaration, and its later amendments. For this type of study formal consent is not required.

Consent for publication

Not applicable.

Availability of data and materials

The authors declare that all data supporting the findings of this study are available within the article and its additional Files.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HZ conceived of and designed the study, collected the data, performed the statistical analysis, interpreted the results, and drafted the manuscript. GW collected the data and helped in drafting the manuscript. JL participated in data collecting and manuscript revising. XZ participated in the study design and manuscript revising. YA participated in study design and coordination, and revised the manuscript. All authors read and approved of the final manuscript for publication.

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Tables

Table 1 Baseline characteristics of critically ill obstetric patients

Variables	Results
Age, year	31(28 - 36)
BMI, kg/m^2	27.8(24.3 – 30.1)
Gestational weeks, weeks	34.9(30.4 - 38)
APACHE II score	15(14 -18)
Causes of the admission of ICU	
Obstetric causes, no. (%)	87(60.8%)
Postpartum haemorrhage, no. (%)	50(35.0%)
Eclampsia/pre-eclampsia, no. (%)	27(18.9%)
Puerperal infection, no. (%)	8(5.6%)
Others, no. (%)	2(1.4%)
Non-obstetric causes, no. (%)	56(39.2%)
Haematological diseases, no. (%)	16(11.2%)
Autoimmune diseases, no. (%)	8(5.6%)
Cardiovascular disease, no. (%)	3(2.1%)
Neuropsychiatric diseases, no. (%)	6(4.2%)
AFLP, no. (%)	3(2.1%)
Acute pancreatitis, no. (%)	5(3.5%)
Gastrointestinal perforation, no. (%)	5(3.5%)
Others, no. (%)	10(7.0%)
Length of MV, hours	19(5 - 73)
Length of ICU stay, hours	72(27 - 168)
Length of hospital stay, days	13(9 - 20)
Mortality, no. (%)	3(2.1%)

Values are expressed as the median (interquartile range) or number (percentage).

Abbreviations: BMI body mass index, APACHE acute physiology and chronic health evaluation, ICU intensive care unit, AFLP acute fatty liver of pregnancy, no. number, MV mechanical ventilation.

Table 2 Comparison of outcomes for the prolonged mechanical ventilation group and the non-prolonged mechanical ventilation group

Outcomes	PMV group	Non-PMV group	*P* value
Number	65	78	
Length of ICU stay, hours	168(99 - 312)	31(23 - 67)	<0.001
Length of hospital stay, days	15(12 - 26)	11(8 - 16)	<0.001
Mortality, no. (%)	3(4.6%)	1(1.3%)	0.229

Abbreviation: ICU intensive care unit, PMV prolonged mechanical ventilation.

Table 3 Comparison of the clinical characteristics of the prolonged mechanical ventilation group and the non-prolongedmechanical ventilation group

Variables	Overall	PMV group	Non-PMV group	*P* value
Number	143	65	78	
Age, years	31(28 - 36)	31(28 – 34)	31.5(28 – 36)	0.226
BMI, kg/m^2	27.8(24.3 – 30.1)	27.0(23.9 – 29.4)	28.3(25.4 – 30.4)	0.178
Gestational weeks, weeks	34.9(30.4 - 38)	34.2(29.2 – 37.2)	35(32 – 38)	0.157
APACHE II score	15(14 -18)	16(14 – 20)	15(13 – 18)	0.008
Causes of the admission of ICU, Obstetric causes, no. (%)	87(60.8%)	45(69.2%)	42(53.9%)	0.061
Estimated blood loss, L	1.1(0.4 – 3.9)	2.8(0.7 – 6.3)	0.7(0.3 – 2.4)	<0.001
AKI, no. (%)	63(44.1%)	48(73.9%)	15(19.2%)	<0.001
Myocardial injury, no. (%)	61(42.7%)	47(72.3%)	14(18.0%)	<0.001
TBIL, μmol/L	14.8(9.5 – 27.4)	20.2(11.1 – 39.2)	12.4(8.3 – 22.6)	<0.001
Albumin, g/L	26.3(23 – 29.3)	25.3(22.6 – 28.8)	26.7(23.8 – 29.9)	0.121
BNP, pg/mL	368(135 - 631)	539(368 – 820)	194(91 – 397)	<0.001
WBC, $\times 10^9/L$	13.6(10.1 – 16.2)	13.2(9.7 – 16.1)	13.7(10.7 – 16.2)	0.557
Platelet, $\times 10^{12}/L$	74(40 - 119)	66(37 – 97)	88.5(53.1 – 138)	0.026
PH	7.4(7.4 – 7.5)	7.4(7.4 – 7.5)	7.4(7.4 – 7.5)	0.406
$PaCO_2$, mmHg	31.9(27.4 - 35)	33.3(28.6 – 36.8)	30.6(27 – 34)	0.008
Bicarbonate, mmol/L	22.3(19.7 – 24.1)	23.1(20.7 – 25.2)	21.2(19.2 – 24.1)	0.071
PaO_2/FiO_2, mmHg	322.3(223.5 - 441)	240(173.3 – 318.3)	403.4(319.8 – 501.5)	<0.001
Lactate	1.4(0.9 – 2.6)	1.8(1.1 – 3.4)	1.2(0.8 – 1.9)	0.002

Abbreviations: PMV prolonged mechanical ventilation, BMI body mass index, APACHE acute physiology and chronic health evaluation, ICU intensive care unit, AKI acute kidney injury, BNP brain natriuretic peptide, WBC white blood cell, TBIL total bilirubin, no. Number, $PaCO_2$ arterial partial pressure of carbon dioxide, PaO_2/FiO_2 the ratio of the arterial partial pressure of oxygen and the fraction of inspired oxygen.

Table 4 Logistic regression of prolonged mechanical ventilation and clinical variables

Variables	OR	*P*value	95% CI
Estimated blood loss, L	1.296	0.029	1.028 - 1.634
Myocardial injury	4.596	0.012	1.394 – 15.159
AKI	4.305	0.013	1.361 – 13.617
PaO_2/FiO_2, mmHg	0.989	<0.001	0.984 – 0.995

Abbreviations: AKI acute kidney injury, PaO_2/FiO_2 the ratio of the arterial partial pressure of oxygen and the fraction of inspired oxygen.

Figures

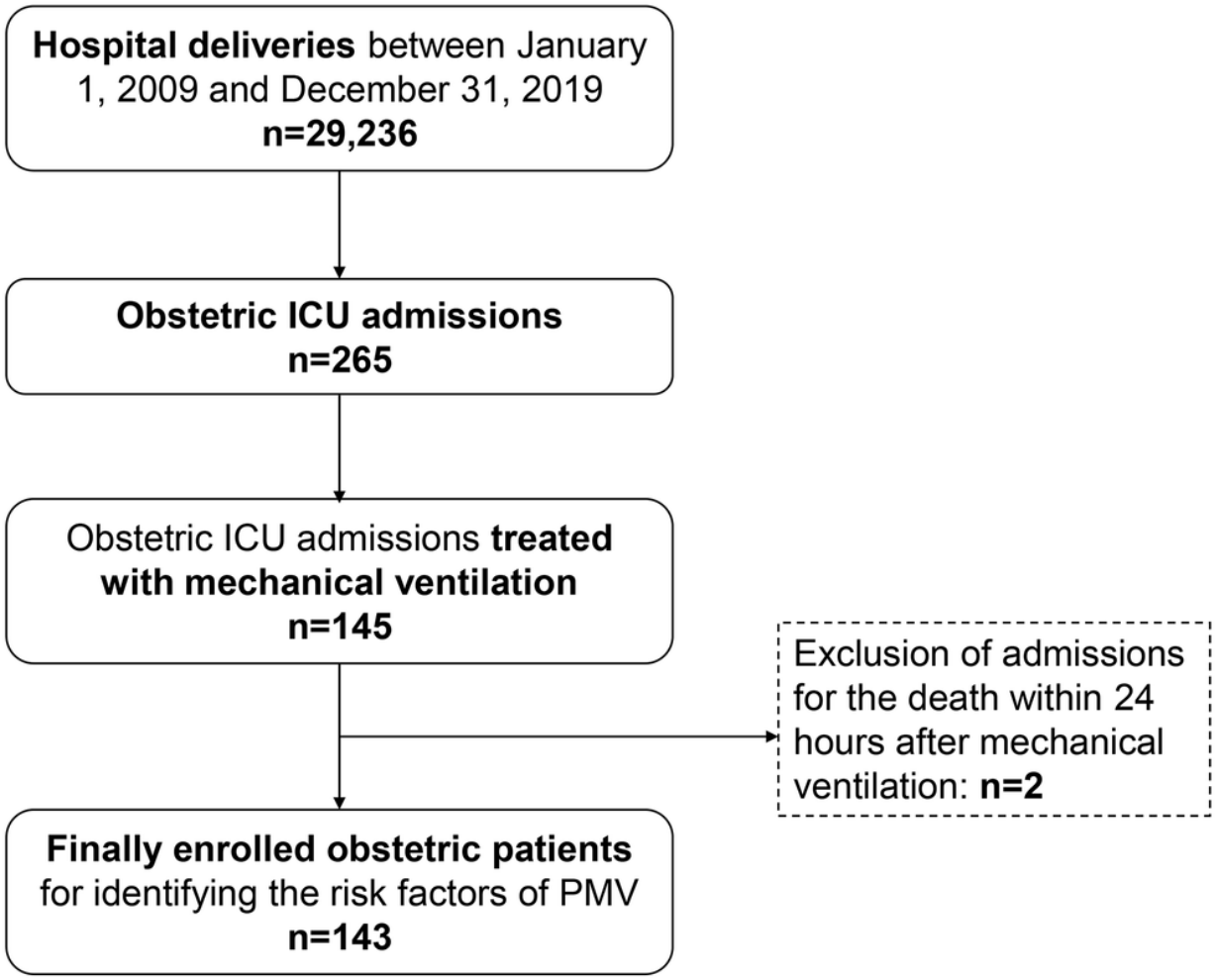

Figure 1

Algorithm for selection of critically ill obstetric patients with mechanical ventilation.

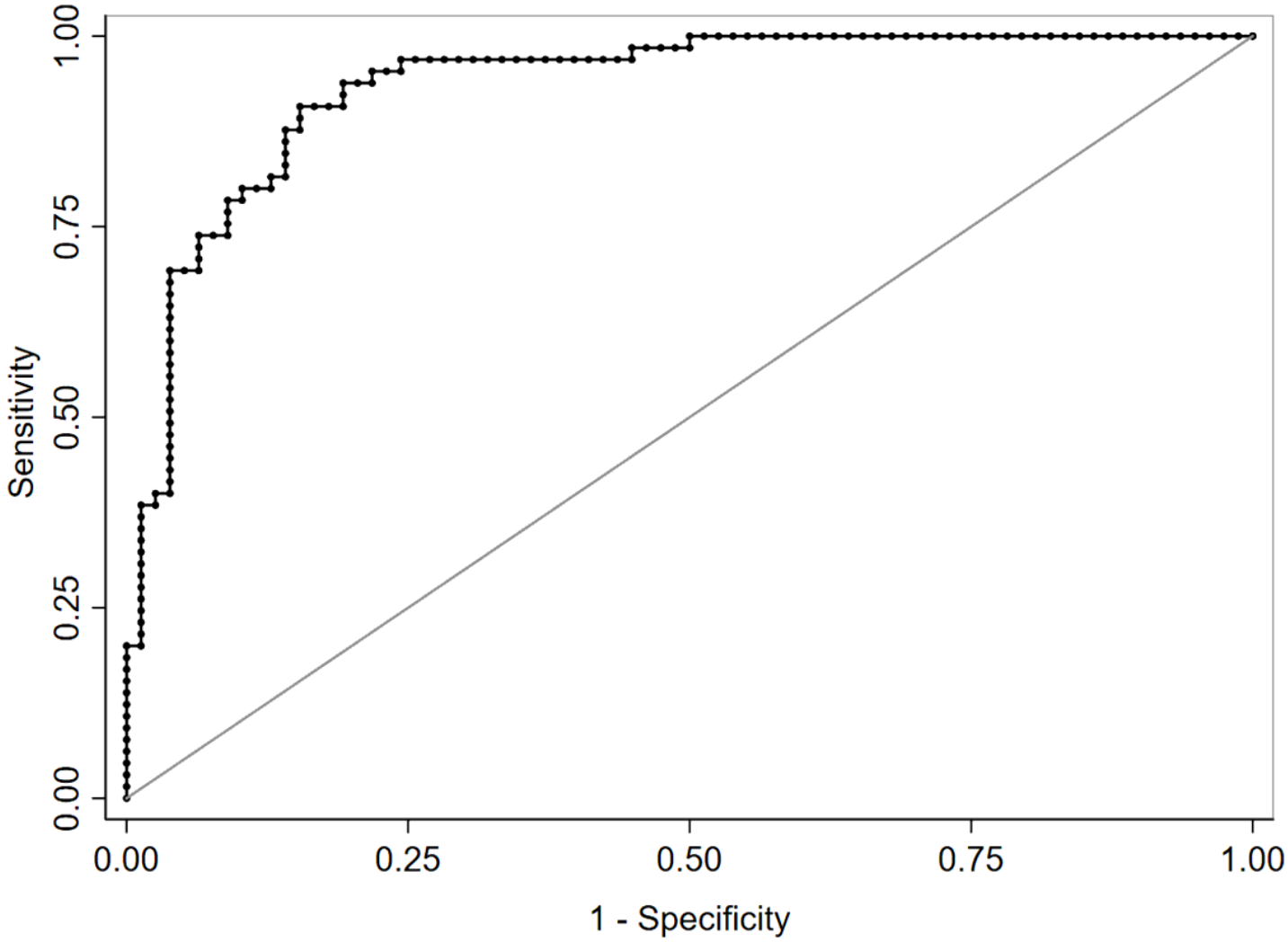

Figure 2

The ROC curve using predicted probability values from the logistic regression.

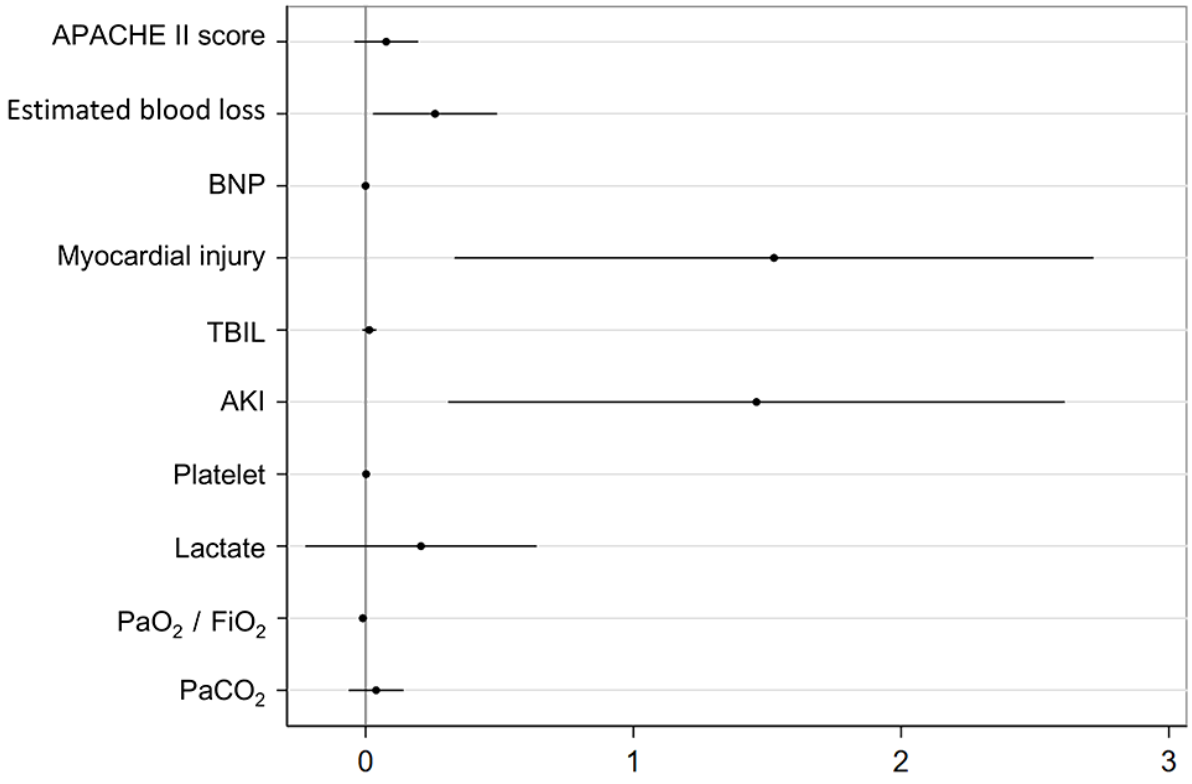

Figure 3

Coefplot of the Logistic regression coefficient.

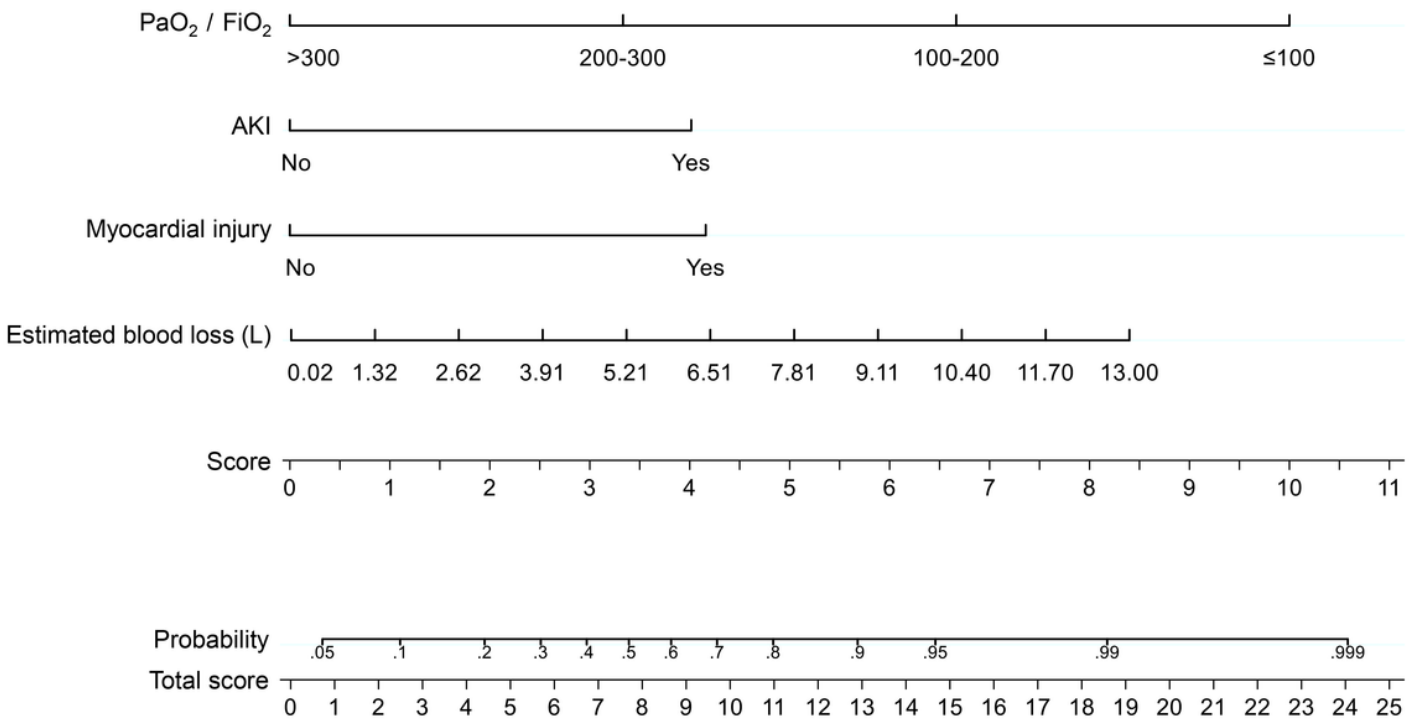

Figure 4

Nomogram for prolonged mechanical ventilation using the independent prognostic factors critically ill obstetric patients.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.docx