HHS Public Access

Author manuscript

Intensive Care Med. Author manuscript; available in PMC 2016 August 15.

Published in final edited form as:

Intensive Care Med. 2012 July ; 38(7): 1184–1190. doi:10.1007/s00134-012-2544-x.

PROSPECTIVE VALIDATION OF THE VASOACTIVE-INOTROPIC SCORE AND CORRELATION TO SHORT TERM OUTCOMES IN NEONATES AND INFANTS AFTER CARDIOTHORACIC SURGERY

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Abstract

Purpose—Prospective validation of vasoactive-inotropic score (VIS) and inotrope score (IS) in infants after cardiovascular surgery

Methods—Prospective observational study of 70 infants (≤90 days of age) undergoing cardiothoracic surgery. VIS and IS were assessed at 24 (VIS24, IS24), 48 (VIS48, IS48), and 72 (VIS72, IS72) hours after surgery. Maximum VIS and IS scores in the first 48 hours were also calculated (VIS48max and IS48max). The primary outcome was length of intubation. Additional outcomes included length of intensive care (ICU) stay and hospitalization, cardiac arrest, mortality, time to negative fluid balance, peak lactate, and change in creatinine.

Results—Based on Receiver Operating Characteristic (ROC) analysis, area under the curve (AUC) was highest for VIS48 to identify prolonged intubation time. AUC for the primary outcome was higher for VIS than IS at all time points assessed. On multivariate analysis VIS48 was independently associated with prolonged intubation (OR 22.3, p=0.002), prolonged ICU stay (OR 8.1, p=0.017), and prolonged hospitalization (OR 11.3, p=0.011). VIS48max, IS48max, and IS48 were also associated with prolonged intubation, but not prolonged ICU or hospital stay. None of the scores were associated with time to negative fluid balance, peak lactate, or change in creatinine.

Conclusion—In neonates and infants, a higher VIS at 48 hours after cardiothoracic surgery is strongly associated with increased length of ventilation, and prolonged ICU and total hospital stay. At all time points assessed, VIS is more predictive of poor short term outcome than IS. VIS may be useful as an independent predictor of outcomes.

Keywords

Congenital; cardiovascular; VIS; children; outcomes; inotrope score

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Introduction

Cardiac surgery for the repair or palliation of congenital heart disease often results in a decrease in cardiac output during the immediate post-operative period. In approximately 25% of infants and young children, low cardiac output develops, and these patients are at higher risk of death in the post-operative period [1,2,4]. The management of these patients relies on multiple strategies intended to mitigate the potential threat of low cardiac output. As part of this management, inotropic and vasoactive agents are routinely employed after cardiac surgery in infants to decrease the risk of low cardiac output.

In 1995, Wernovsky created an inotrope score (IS) as part of a study on post-operative hemodynamics following the arterial switch operation [2]. This score attempted to quantify the amount of inotropic support provided in the post-operative period. Since this initial publication, the inotrope score has been used as a research tool to describe the effects of various treatments on the required amount of hemodynamic support [3-6]. No study has ever shown a correlation between the original IS and clinical outcomes of interest. Also, newer vasoactive-inotropic agents have been introduced to pediatric cardiac intensive care, most notably milrinone and vasopressin [4, 7-9], potentially limiting the accuracy of the inotrope score. More recently, Gaies *et al* published a retrospective study using an updated vasoactive-inotropic score (VIS) [10]. VIS incorporates the original medications from the inotrope score and adds milrinone, vasopressin, and norepinephrine. In their population of infants undergoing cardiac surgery with cardiopulmonary bypass (CPB), higher maximum VIS in the first 48 hours after operation was associated with increased odds of poor short term outcomes.

Our study sought to prospectively validate VIS and IS in a population of infants 90 days of age or less undergoing cardiothoracic surgery. We hypothesized that higher VIS would correlate with worse short term clinical outcomes in both CPB and non-CPB patients and that VIS between 48 and 72 hours would more accurately predict patients at risk for poor short term outcome.

Methods

We conducted a prospective observational study of infants ≤90 days of age undergoing cardiothoracic surgery. Patients were enrolled as part of an Institutional Review Board approved study on the post-operative kinetics of the inflammatory marker procalcitonin (PCT). Analysis of VIS and outcomes was included as a sub-analysis of the parent PCT trial. Seventy patients were enrolled between July 2009 and September 2010. Infants were excluded if they were born at less than 34 weeks estimated gestational age, if informed consent could not be obtained, or if the patient was less than 1200g at the time of surgery due to concerns for excessive blood draw volume in the PCT portion of the study.

Demographic and pre-operative clinical information collected on all patients included gender, ethnicity, gestational age at delivery, age and weight at the time of surgery, anatomic diagnosis, surgical procedure, Aristotle comprehensive complexity score [11-13], use of pre-operative steroids, CPB time, aortic cross-clamp time, and deep hypothermic circulatory

arrest time. Pre-operative laboratory tests included a basic metabolic panel (BMP) as part of the surgical clinical guidelines and PCT and liver function tests as part of the research protocol.

Patients were stratified into three groups based on the following operative characteristics: 1) delayed sternal closure (DSC), 2) CPB without DSC, and 3) no CPB or DSC. Stratification determined the blood draw schedule for the procalcitonin portion of the study and did not affect the VIS portion of the study other than for purposes of statistical analysis. The decision to perform DSC was made by the attending surgeon as a precaution in patients thought to be at high risk for low cardiac output with primary closure. Inotropic and vasoactive medications were initiated in the operating room at the discretion of the attending surgeon and cardiac anesthesiologist. Decisions regarding ongoing titration of vasoactive/inotropic medications were made by the CICU physician team and did not follow a pre-established protocol. Neither the surgical team nor the CICU team was aware of the intention to study vasoactive/inotropic support. Doses of milrinone, dopamine, epinephrine, vasopressin, and norepinephrine were recorded hourly throughout the course of CICU admission. IS was calculated as per Wernovsky *et al* [2] and VIS was calculated as per Gaies *et al* [10] at 24, 48, and 72 hours after admission to the CICU (figure 1): IS[a] = dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + 100 × epinephrine dose (μg/kg/min) VIS[b] = IS + 10 × milrinone dose (μg/kg/min) + 10,000 × vasopressin dose (Units/kg/min) + 100 × norepinephrine dose (μg/kg/min). In addition, maximum VIS and IS during the first 48 hours of the CICU admission were recorded.

Hemodynamic monitoring included invasive arterial pressure monitoring and central venous pressure monitoring in all cases. Additional monitoring was instituted as necessary by the intensivist. All groups had a BMP, arterial blood gas and lactate performed on admission and on post-operative day one. Patients in groups 1 and 2 also had a BMP and lactate drawn at 12 hours after admission and liver function tests on post-operative day one. Additional laboratory testing was performed as directed by the intensivist.

The primary outcome determined *a priori* was time to first extubation in hours. Secondary outcomes included length of CICU stay in days, length of hospital stay, time to negative fluid balance [10], peak lactate, and change in creatinine. Due to the low expected mortality, a combined dichotomous poor outcome variable was utilized, defined as any one of the following: cardiac arrest requiring chest compressions, death within 30 days or at any point prior to discharge, renal replacement therapy, or mechanical circulatory support [10].

Outcomes were classified as upper 25% vs. lower 75% of the measures. The primary outcome was used to determine the best predictors and their cut-offs among the various VIS and IS time points. All time points were modeled as predictor using unconditional logistic regression by Lambert's SAS Macro [14]. The sensitivity, specificity, total accuracy, weighted error ratios and AUC were then calculated and plotted. The score with the largest AUC was chosen as the best predictor of the outcomes. Additional time points were also chosen for modeling to allow more direct comparison to prior studies. The best cut-off was determined by maximizing combined sensitivity, specificity, and accuracy while minimizing weighted error ratio.

For multiple logistic regression modeling, baseline characteristics were assessed exhaustively between groups with appropriate descriptive statistics. Characteristics that differed significantly among groups were then chosen as candidate covariates. Best subset logistic regression model technique was employed to choose the best fit models for each of the outcomes. Group effect and presence of a functional single ventricle were kept in all multivariate models to adjust for clinical differences.

Results

Between July 2009 and September 2010, seventy patients were successfully enrolled. All patients completed the procalcitonin study protocol. Of the 70 patients enrolled, 56 underwent CPB, of which 26 required DSC. One additional patient did not undergo CPB but required DSC due to shunt malfunction and immediate reoperation for shunt revision. No patients underwent sternal opening in the CICU. After completion of trial participation, one patient was found to have an inaccurate date of birth in the medical record and was older than inclusion criteria permitted. This patient was excluded from all subsequent analyses.

Demographic and baseline surgical data are shown in table 1. Overall, the DSC and non-bypass patients were younger than the general CBP patients, and the DSC patients were significantly smaller at the time of operation. The DSC group had higher Aristotle scores, a higher prevalence of single ventricle physiology, and greater use of pre-operative steroids. Median bypass and circulatory arrest times were longer in the DSC group, although aortic cross clamp time was comparable. Median time to sternal closure in the DSC group was 2 days (range 1-5).

Median VIS and IS for each group are also shown in table 1. Patients with DSC had significantly higher VIS and IS at all time points assessed. The remaining CPB patients initially had a higher VIS than the non-bypass patients, but this difference had largely disappeared by 72 hours. Post-operative outcomes are provided in table 2.

ROC analysis was performed for VIS24, VIS48, VIS72, IS24, IS72, IS48, VIS48max, and IS48max. AUC and confidence intervals for each time point are shown in table 3. All time points performed well with an AUC of at least 0.85. AUC was highest for VIS48 (0.93). At similar time points, the AUC was greater for VIS than IS. Scores at 48 and 72 hours had higher AUC than maximum scores in the first 48 hours. None of these differences, however, reached statistical significance.

Given the overall strong performance of VIS and IS at predicting prolonged intubation, we chose to perform multiple logistic regression modeling for several different time points. VIS48 was chosen as the primary score to model due to its high AUC and ease of clinical computation. We also modeled VIS48max to compare to prior studies [10]. In order to offer a comparison between VIS and IS, we added models using IS48 and IS48max. Cutoffs for each predictor variable were chosen to maximize total accuracy and minimized weighted error ratios as described by Lambert *et al* [14]. Based on this technique we chose cut-offs for each score as listed in table 4.

The results of the multivariate logistic regression are presented in table 5. All models were controlled for operative group and presence of single ventricle physiology. Additional covariates including age, weight, bypass time, cross clamp time, circulatory arrest time, and Aristotle score were assessed but did not significantly improve the fit of the model and were not included. High VIS48 was independently associated with greatly increased odds of prolonged intubation (OR 22.3, 95% confidence interval (CI) 3.2-157.7, p value 0.002). High VIS48max, IS48, and IS48max were also associated with increased odds of prolonged intubation [(OR 14.9, 95%CI 2.4-94.1, p=0.004), (OR 18.1, 95%CI 2.4-138.1, p=0.005), and (OR 7.1, 95%CI 1.3-37.6, p=0.021) respectively].

Higher VIS48 was also independently associated with increased odds for prolonged ICU stay (OR 8.1, 95%CI 1.4-45.4, p value=0.017) and hospitalization (OR 11.3, 95%CI 1.7-73.7, p value 0.011). High VIS48max, IS48, and IS48max predicted mildly increased odds of prolonged ICU stay and hospitalization, but none of these associations reached statistical significance. Overall, we did not find any association between VIS or IS and time to negative fluid balance, change in creatinine, or peak lactate.

Only 9 patients met criteria for poor outcome. These small numbers limited the extent of statistical analysis possible, particularly with VIS48 and IS48 where two of the patients died before 48 hours and thus did not receive a 48 hour score. VIS48max and IS48max both showed a moderate association with poor outcome with a trend towards statistical significance when adjusted for group [(OR 6.0, 95%CI 0.8-43.4, p value=0.076), (OR 4.8, 95%CI 0.7-31.1, p value=0.099) respectively].

Discussion

To our knowledge, this study is the first to prospectively validate the use of VIS and IS in infants. Our findings confirm that in this population, VIS, assessed in the first 72 hours after surgery, correlates better with outcomes than does IS. The exact timing of scoring, however, remains unclear. The sentinel study using VIS by Gaies *et al* focused primarily on the intensity of medical cardiovascular support (maximum VIS in the first 48 hours after ICU admission) [10]. In our design, we opted to assess both markers of peak intensity (VIS48max) as well as markers of prolonged high intensity therapy (VIS48). We found a striking association between VIS48 and several important short term outcomes including length of intubation, length of intensive care unit stay, and length of hospital stay. Overall in our study VIS48 outperformed VIS48max, suggesting that duration of intensive cardiovascular support may be more important than maximal intensity of therapy as a predictor of these short term outcomes. We hypothesize that VIS48 may place less emphasis on patients with transient poor function or vasoplegia whose outcomes are likely to be good, while potentially identifying patients with persistent issues such as myocardial injury, poor surgical repair, or capillary leak. VIS48 has the added clinical benefit of ease of calculation, requiring a simple bedside check without review of prior records. Our patient population does differ slightly from the initial VIS publication, focusing on younger infants (0-3 months instead of 0-6 months) and including a small sample of non-bypass patients. This may account for some of the difference in our findings. The odds ratios for maximum VIS,

however, are quite similar in our population as compared to that of Gaies *et al*, suggesting that maximum VIS behaved in a very similar manner as a predictor in both populations [10].

The strong association between VIS and length of intubation makes intuitive sense. Positive pressure ventilation decreases the energy expended by the patient for breathing. In a critically ill post-operative infant who already requires high levels of inotropic and vasoactive support, clinicians are less likely to extubate and thereby transfer the work of breathing exclusively to the patient. So while we agree with the general idea that high VIS is largely a surrogate marker for poor outcomes and VIS should not be targeted as a primary intervention to improve outcomes, it is likely that therapies capable of improving post-operative VIS would directly improve intubation times as well.

The relationship between high VIS48 and prolonged ICU and hospital stay is less obvious. Our very young patient group experiences a wide range of ICU and hospital days. In many cases, this variation is due to factors not immediately associated with VIS such as poor feeding, vocal cord paralysis/paresis, phrenic nerve injury, and chylothorax. However, even in the presence of these other factors, VIS48 showed a strong, independent association with length of ICU and hospital stay. Likely high VIS is simply a marker for poor physiology in the immediate post-operative period. This poor physiology may in turn lead to prolonged therapies, more frequent complications, and borderline cardiac and pulmonary function that impair convalescence, particularly feeding. Conversely, in the face of conflicting data in the literature concerning the risk/benefit of specific medications for cardiovascular support [4, 7-9, 15], our study results do not exclude a true causal relationship between high levels of vasoactive/inotropic support and the need for extended intensive and general hospital care. Our population had too few events in the poor outcome variable to undergo rigorous statistical testing. Trends in our population, however, agree with the findings of the prior study, associating high VIS scores with increased odds of cardiac arrest and death [10]. Contrary to the retrospective study, we did not find an association between high VIS and time to negative fluid balance. This difference may be explained by variable clinical strategies regarding the use of vasoactive medications to stabilize hemodynamics and augment urine output. We also found no association between VIS and biochemical markers such as peak lactate or change in creatinine. In most of our patients, peak lactate was found immediately after arrival in the ICU and for the most part, represents physiology during the operation. Changes in creatinine were small and would require a much larger cohort to detect statistical differences.

We attempted to design our study to minimize issues associated with observational studies. By utilizing prospectively collected data, we hoped to reduce the potential biases inherent in retrospective studies, particularly recording bias in the medical record. We also felt that it was important to control for the effects of DSC on our outcome measures. Not only does DSC account for a very different pre-operative risk profile, we hypothesized that it also represents the culmination of multiple intra-operative issues that might not be captured by specific variables such as bypass or cross clamp time. In addition, following the operation, DSC has direct effects on length of intubation due to the inability to extubate a patient with an open sternum. Failure to account for DSC during multivariate analysis risks introduction of a significant confounding variable in our study. Lastly, the inclusion of non-bypass

patients in the analysis increases the applicability of VIS to the general cardiac intensive care population.

Our study has a number of limitations. It reflects a single institutional experience in a well defined patient population. The sample size is relatively small with significant variability in the outcome measures. Because clinical management was not under protocol, patient progression may have been affected by variations in attending physicians' practices. Finally, VIS is subject to the same inherent weakness of many scoring system: it attributes arbitrary power to the different factors included in the equation without any assessment of the relative importance of the individual components.

Additional research is needed to better refine the potential uses of VIS. Based on the findings of this study and those of Gaies *et al* , VIS should replace IS as the best measure of cardiovascular support available for research involving this patient population. From a clinical perspective, a high VIS at 48 hours should trigger physician awareness that the infant in question continues to be at risk for poor outcome. Use of this scoring system for different age groups and in different disease entities may be warranted but requires further research. Future studies should be multi-centered and adequately powered to detect small differences short term outcomes, particularly cardiac arrest and mortality. They should also address some important unanswered questions such as the relative importance of different vasoactive/inotropic medications and should include a long term follow-up plan to assess neurologic outcome and long term morbidity and mortality.

Conclusion

Vasoactive-inotropic score at 48 hours after cardiac surgery is a simple clinical tool that can provide valuable information regarding likely length of intubation, intensive care unit stay, and hospital stay. VIS at 48 hours performs better than maximum VIS in the first 48 hours after surgery in predicting poor short term outcomes. Within the first 72 hours after surgery, VIS is a stronger predictor of poor short term outcome than inotrope score. Given these findings, we believe that VIS, particularly at 48 hours, should replace the previous inotrope score as the best available measure of cardiovascular support after cardiac surgery in infants.

Acknowledgements

We would like to thank Dr. James Jaggers for his assistance in preparing this manuscript. We would also like to recognize the nurses and staff of the CICU and CTRC at the Children's Hospital of Colorado for their valuable contributions to our project. This study was supported by grant MO1-RR00069, General Clinical Research Centers Program, NCRR, NIH.

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IS[a] = dopamine dose (μg/kg/min) + dobutamine dose (μg/kg/min) + 100 x epinephrine dose (μg/kg/min)

VIS[b] = IS + 10 x milrinone dose (μg/kg/min) + 10,000 x vasopressin dose (Units/kg/min) + 100 x norepinephrine dose (μg/kg/min)

IS, inotrope score; VIS, vasoactive-inotropic score
[a] Wernovsky G, et al (1995) Circulation 92, 2226-2235.
[b] Gaies MG, et al (2010) Pediatr Crit Care Med 11, 234-238.

Figure 1.
Calculation of IS and VIS

Table 1

Demographics, surgical data, and VIS/IS

Characteristic	No CPB n=13	CPB n=29	DSC n=27	P-value No CPB vs. CPB	P-value No CPB vs. DSC	P-value CPB vs. DSC
Male, n(%)	8(62%)	16 (55%)	18 (67%)	0.699	0.75	0.379
Ethnicity, n(%)				0.757	0.61	0.883
White	9 (69%)	18 (62%)	15 (56%)			
Hispanic	4 (31%)	10 (35%)	11 (41%)			
Other	0 (0%)	1 (3%)	1 (3%)			
Age in days, median(range)	8 (2-54)	49 (3-90)	5 (2-81)	<.0001	0.525	0.001
Weight (Kg)	3.3 (2.4-4.2)	3.4 (2.6-5.2)	3.1 (2.3-3.7)	0.162	0.554	0.004
Aristotle Score median(range)	8 (6-13)	10 (6-18)	11 (6.3-17.5)	0.049	<.0001	0.004
Bypass Time (minutes), median(range	N/A	130 (61-213)	168.5 (88-316)	N/A	N/A	0.038
Cross Clamp Time (minutes), median(range)	N/A	86 (28-248)	77 (31-440)	N/A	N/A	0.801
DHCA Time (minutes), median(range)	N/A	0 (0-110)	20 (0-72)	N/A	N/A	0.009
Single Ventricle Physiology	3 (23%)	2 (7%)	12 (44%)	0.134	0.201	0.001
Pre-operative Steroids	1 (8%)	12 (41%)	23 (85%)	0.029	<.0001	0.001
VIS, 24 hrs, median(range)	0 (0, 8)	8 (0, 20)	15 (8.0, 23.5)	0.002	<.0001	<.0001
VIS, 48 hrs, median(range)	0 (0, 8)	3 (0, 16.5)	13 (5, 34)	0.016	<.0001	<.0001
VIS, 48 hrs max, median(range)	0 (0, 13)	10 (0, 24.5)	21 (12, 34)	0.001	<.0001	<.0001
VIS, 72 hrs, median(range)	0 (0, 10)	0 (0, 15)	10.5 (3, 31)	0.202	0.0009	<.0001
IS, 24hrs, median (range)	0 (0, 5)	3 (0, 15)	7 (3, 15.5)	0.084	0.0008	0.0001
IS 48 hrs, median (range)	0 (0, 3)	0 (0, 5)	5 (0, 14)	0.465	<.0001	<.0001
IS 48 hrs max, median (range)	0 (0, 9)	5 (0, 17)	10 (3, 17.5)	0.024	0.0004	0.0004
IS, 72 hrs, median (range)	0 (0, 5)	0 (0, 5)	3 (0, 12)	0.898	0.008	0.0001

VIS, vasoactive-inotropic score; IS, inotrope score; CPB, cardiopulmonary bypass; DSC, delayed sternal closure; DHCA, deep hypothermic circulatory arrest

Table 2

Outcomes

Outcome	No CPB n=13	CPB without DSC n=29	DSC n=27
Intubation, hrs, median(range)	27.5 (8-99)	39.5 (5-148)	117 (50-410)
Time to negative fluid balance, hrs, median(range)	26.5 (14-45)	30.5 (16-79)	28 (13-61)
Length of hospital stay, days median(range)	11.5 (2-81)	9.5 (4-36)	21 (7-106)
Length of ICU stay, days median(range)	3 (1-23)	4 (1-26)	9 (4-70)
Creatinine, Peak, mg/dL median(range)	0.6 (0.3, 4.0)	0.5 (0.3, 1.8)	0.8 (0.3, 2.0)
Lactate, Peak, mmol/L median(range)	2.3 (0.9, 4.8)	3.7 (1.0, 15.3)	7.1 (2.9, 15.1)
Death, n (%)	1 (7.7%)	1 (3.5%)	3 (11.1%)
Poor Outcome[a] n(%)	1 (7.7%)	1 (3.5%)	7 (25.9%)

ICU, intensive care unit; CPB, cardiopulmonary bypass; DSC, delayed sternal closure

[a]Poor Outcome=death, cardiac arrest, renal replacement therapy, or mechanical circulatory support

Table 3

Receiver operating characteristic analysis for the prediction of prolonged intubation

Score and Time Point	ROC AUC	95% CI
VIS24	0.90	(0.81, 0.99)
VIS48	0.93	(0.85, 1.00)
VIS48max	0.88	(0.80, 0.97)
VIS72	0.92	(0.82, 1.00)
IS24	0.86	(0.76,0.97)
IS48	0.88	(0.78, 0.98)
IS48max	0.85	(0.76, 0.95)
IS72	0.85	(0.73,0.96)

ROC, receiver operating characteristic; AUC, area under curve; CI, confidence interval; VIS24, vasoactive-inotropic score 24 hours after surgery; VIS48, vasoactive-inotropic score 48 hours after surgery; VIS48max, maximum vasoactive-inotropic score in the first 48 hours after surgery; VIS72, vasoactive-inotropic score 72 hours after surgery; IS24, inotrope score 24 hours after surgery; IS48, inotrope score 48 hours after surgery; IS48max, maximum inotrope score in the first 48 hours after surgery; IS72, inotrope score 72 hours after surgery

Table 4

Cut-offs for high versus low VIS/IS based on ROC analysis

Score and Time point	Cut-off value
VIS48	10.5
VIS48max	17
IS48	3.9
IS48max	8

ROC, receiver operating characteristic; VIS48, vasoactive-inotropic score 48 hours after surgery; VIS48max, maximum vasoactive-inotropic score in the first 48 hours after surgery; IS48, inotrope score 48 hours after surgery; IS48max, maximum inotrope score in the first 48 hours after surgery

Table 5

Association with outcomes based on multiple logistic regression controlling for CPB/DSC group and the presence of single ventricle physiology

	OR	95% CI	P Value
VIS48			
Prolonged intubation time	22.3	(3.1, 157.7)	0.002
Prolonged time to negative fluid balance	0.5	(0.1, 4.3)	0.557
Prolonged ICU stay	8.1	(1.4, 45.4)	0.017
Prolonged hospital stay	11.3	(1.7, 73.7)	0.011
Peak Creatinine Change	0.6	(0.1, 3.3)	0.574
Peak lactate	0.9	(0.2, 5.2)	0.919
Poor Outcome	n/a		
VIS48max			
Prolonged intubation time	14.9	(2.4, 94.1)	0.004
Prolonged time to negative fluid balance	0.5	(0.1, 3.1)	0.476
Prolonged ICU stay	2.5	(0.6, 11.5)	0.225
Prolonged hospital stay	2.4	(0.5, 11.1)	0.259
Peak Creatinine Change	1.9	(0.4, 7.8)	0.399
Peak lactate	2.5	(0.5, 11.5)	0.245
Poor Outcome	4.6	(0.5, 35.6)	0.165
IS48			
Prolonged intubation time	18.1	(2.4, 138.1)	0.005
Prolonged time to negative fluid balance	0.4	(0.04, 2.8)	0.322
Prolonged ICU stay	2.8	(0.6, 14.4)	0.212
Prolonged hospital stay	2.5	(0.5, 12.4)	0.275
Peak Creatinine Change	1	(0.2, 5.1)	0.964
Peak lactate	1.8	(0.3, 9.4)	0.502
Poor Outcome	n/a		
IS48max			
Prolonged intubation time	7.1	(1.3, 37.6)	0.021
Prolonged time to negative fluid balance	0.8	(0.2, 3.8)	0.802
Prolonged ICU stay	2.4	(0.6, 9.8)	0.222
Prolonged hospital stay	1.4	(0.3, 6.0)	0.690
Peak Creatinine Change	2.2	(0.6, 8.0)	0.255
Peak lactate	2.4	(0.6, 9.8)	0.224
Poor Outcome	4.4	(0.6, 30.7)	0.136

OR, odds ratio; CI, confidence interval; VIS24, VIS48, vasoactive-inotropic score 48 hours after surgery; VIS48max, maximum vasoactive-inotropic score in the first 48 hours after surgery; IS48, inotrope score 48 hours after surgery; IS48max, maximum inotrope score in the first 48 hours after surgery; ICU, intensive care unit