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Intraoperative physiological ranges associated with improved outcomes after major spine surgery: an observational study

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ABSTRACT

Objective There is inadequate information about the values of many intraoperative physiological measurements that are associated with improved outcomes after surgery. The purpose of this observational study is to investigate the optimal physiological ranges during major spine surgery.

Setting A teaching hospital in the USA.

Participants A convenience sample of 102 patients receiving major posterior spine surgery with multilevel spinal fusion in a prone position.

Methods Physiological variables, including but not limited to mean arterial pressure (MAP) and cerebral and somatic tissue oxygen saturation ($SctO_2$/$SstO_2$), were recorded. The results of these measurements were associated with length of hospital stay and composite complication data and were analysed based on thresholds (ie, a cut-off value for optimal and suboptimal physiology) and the area under the curve (AUC) values. The AUC values were measured as the area enclosed by the actual tracing and the threshold. The outcomes were dichotomised into above-average and below-average (ie, improved) categories.

Results Analyses based on thresholds identified the following variables associated with above-average outcomes: MAP <60 mm Hg, temperature <35°C, heart rate >90 beats per minute (bpm), $SctO_2$ <60% and $SstO_2$ >80%. Analyses based on AUC values identified the following as associated with above-average outcomes: MAP <70 and >100 mm Hg, temperature <36°C, heart rate >90 bpm, tidal volume (based on ideal body weight)<6 mL/kg, tidal volume (based on actual body weight) >10 mL/kg and peak airway pressure <15 cmH_2O.

Conclusion The following physiological ranges are associated with improved outcomes (ie, shorter hospitalisation and fewer complications) during major spine surgery: MAP of 70–100 mm Hg, temperature ≥36°C, heart rate <90 bpm, tidal volume based on ideal body weight >6 mL/kg, $SctO_2$ >60% and $SstO_2$ <80%.

Strengths and limitations of this study

- This is the first study to systematically explore the optimal ranges of the physiological measurements performed during major surgery.
- The optimal physiological ranges were defined based on both threshold analysis and area under the curve analysis.
- The optimal physiological ranges suggested by this study need to be validated by randomised controlled trials.
- The study used a convenient sample size, not a sample size that is powered to a specific end point.

INTRODUCTION

During anaesthesia and surgery, multiple physiological variables, including blood pressure (BP), heart rate (HR), pulse haemoglobin oxygen saturation (SpO_2), end-tidal carbon dioxide ($EtCO_2$) and temperature, are continuously monitored (https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring). Recent technological innovations based on near-infrared spectroscopy (NIRS) have enabled the monitoring of cerebral and somatic tissue oxygen saturation ($SctO_2$/$SstO_2$), which is an assessment of the balance between local tissue oxygen consumption and supply.[1] The goal of intraoperative monitoring is to assure patient safety and improve clinical outcome through the timely correction of unwarranted physiological changes.

The first step in maintaining optimal physiological status is to establish the optimal range of the physiological variable being monitored, that is, the range of values beyond which corrective measures are warranted. The common practice is to assign thresholds, defining values for optimal and suboptimal physiology, for a physiological variable whose measurement has a range of distribution due to intraindividual and interindividual variability. BP management is a typical example. Some practitioners use a mean arterial pressure (MAP) of 65 mm Hg as the threshold below which measures will be instituted to

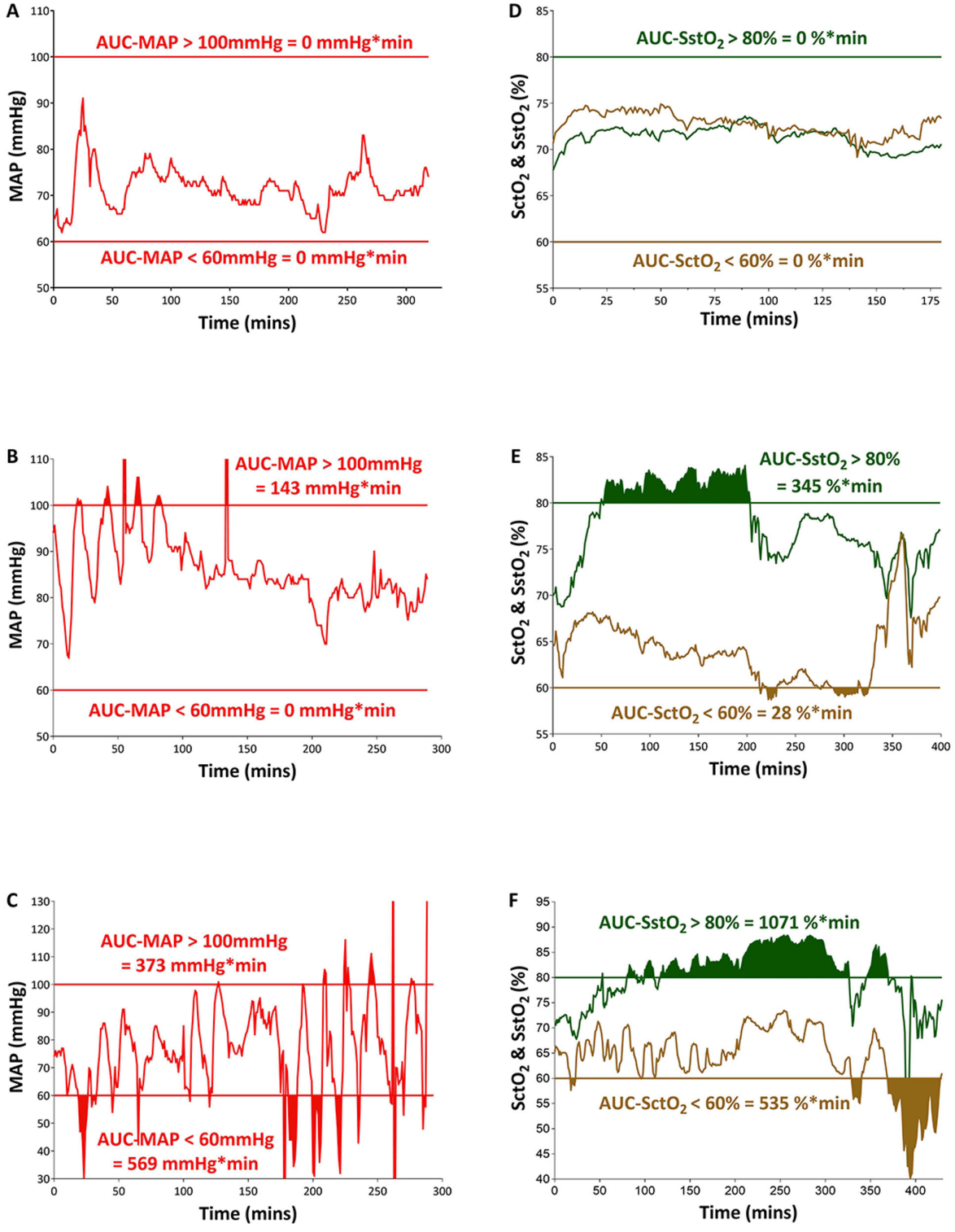

Figure 1 The actual tracing (fluctuating line), threshold (straight line) and area under the curve (shaded area) of mean arterial pressure (MAP, red line) (A–C), cerebral tissue oxygen saturation ($SctO_2$, brown line) and somatic tissue oxygen saturation ($SstO_2$, green line) (D–F) in six patients. The MAP in the patient in A did not pass the thresholds (A). The MAP in the patient in B passed the threshold of 100 mm Hg, not 60 mm Hg (B). The MAP in the patient in C passed the thresholds of both 100 and 60 mm Hg (C). The area under the curve (AUC) based on the threshold of 100 mm Hg was larger in the patient in C (373 mm Hg*min) than that in B (143 mm Hg*min). $SctO_2$ and $SstO_2$ in the patient in D did not pass the thresholds (D); however, both the patient in E and the patient in F passed the respective thresholds. The AUC based on the $SctO_2$ threshold of 60 mm Hg was larger in the patient in F (535%*min) than that in E (28%*min). The AUC based on the $SstO_2$ threshold of 80 mm Hg was larger in the patient in F (1071%*min) than that in E (345%*min).

Table 1 Thresholds used for different physiological parameters

Parameters	Lower thresholds	Upper thresholds
MAP (mm Hg)	<50, <60, <70	>100, >110, >120
HR (bpm)	<40, <50, <60	>90, >100, >110
SpO_2 (%)	<90, <95	None
$EtCO_2$ (mm Hg)	<25, <30	>40, >45
FiO_2	<0.35, <0.45	>0.75, >0.85
Temp (°C)	<35, <35.5, <36	>37, >37.5, >38
iVt (mL/kg)	<5, <6	>8, >9, >10
aVt (mL/kg)	<5, <6	>8, >9, >10
Ppeak (cmH_2O)	<10, <15	>25, >30, >35
PEEP (cmH_2O)	<3	>7, >10
PI	<0.5, <1	>6, >10
$SctO_2$ (%)	<50, <55, <60	>75, >80, >85, >90
$SstO_2$ (%)	<50, <55, <60	>75, >80, >85, >90

aVt, tidal volume based on actual body weight; bpm, beat per minute; $EtCO_2$, end-tidal carbon dioxide; FiO_2, inspired oxygen fraction; HR, heart rate; iVt, tidal volume based on ideal body weight; MAP, mean arterial pressure; PEEP, positive end-expiratory pressure; PI, perfusion index; Ppeak, peak airway pressure; $SctO_2$, cerebral tissue oxygen saturation; SpO_2, pulse oxygen saturation; $SstO_2$, somatic tissue oxygen saturation; Temp, temperature.

increase BP.[2] One of the limitations in the use of thresholds to define suboptimal physiological change is a failure to consider the impact of the duration of the change on outcomes. The adverse impact of a physiological disturbance on outcome is likely determined by not only the magnitude of the deviation but also the duration of the deviation. While a severe disturbance, although brief, can be injurious, so can a minor but prolonged abnormality. This presumption is corroborated by studies which showed that the odds of acute myocardial and kidney injury after noncardiac surgeries are associated with both the degree and the duration of hypotension.[3 4] This two-dimensional consideration can be quantified by the area under the curve (AUC) enclosed by the actual physiological tracing and the chosen threshold (figure 1).[5]

We hypothesise that for each physiological variable monitored intraoperatively there is an optimal range of the measurement, which is associated with improved outcomes. We test this hypothesis via a proof-of-concept study conducted in patients undergoing major posterior spine surgery. All the variables monitored intraoperatively, including both the conventional ones (eg, BP and HR) and the emerging ones (ie, $SctO_2$ and $SstO_2$), are analysed in this study.

METHODS

This observational study was approved by the Institutional Review Board for Clinical Investigations at the University of California San Francisco, San Francisco, California, USA. It was conducted at the University of California, San Francisco - Parnassus Medical Center, from June 2014 to December 2015. Verbal and written informed consents for study participation were obtained from all patients before surgery.

Patient and public involvement

The study was designed to understand the association between intraoperative physiology and postoperative outcome in major spine surgery. However, patients were not included in the design of the study, recruitment or conduct of the study. The study results are available to patients on patient's own request.

Patient selection

The inclusion criteria of this study were as follows: (1) age ≥18 years, (2) lumbar or thoracolumbar spine surgery, (3) elective procedure, (4) prone position, (5) multisegmental fusion, (6) potential of osteotomy and (7) American Society of Anesthesiologists (ASA) physical status ≤III. The exclusion criteria were as follows: (1) patient refusal, (2) emergency or urgent surgery, (3) age <18 years, (4) ASA physical status score >III and (5) fragile skin incompatible with an adhesive tissue oximetry probe.

Anaesthetic care

The anaesthesia team administered routine preoperative medications, including midazolam, fentanyl, gabapentin and oxycodone. On their arrival in the operating room, patients were monitored with electrocardiography, BP and pulse oximetry and were preoxygenated via face mask. Anaesthesia was induced using lidocaine, fentanyl and propofol. Endotracheal intubation was facilitated by the administration of either succinylcholine or rocuronium. All patients were mechanically ventilated with anaesthesia maintained using intravenous propofol, fentanyl, lidocaine and ketamine infusions, with or without a volatile anaesthetic agent at low minimum alveolar concentrations. BP was supported using a phenylephrine infusion. Some patients received tranexamic acid when a large volume of blood loss was anticipated. A blood salvage machine was routinely available. Patients were positioned prone for surgery, with the head supported by a foam frame. Most patients were extubated at the end of surgery; if not, they were admitted to the intensive care unit instead of the postanaesthesia care unit.

Physiological monitoring

BP was monitored via an intra-arterial catheter placed in the radial artery. Temperature was monitored using a nasopharyngeal probe, while inspired oxygen fraction (FiO_2) and $EtCO_2$ were monitored by a gas analyser. Tidal volume (Vt), peak airway pressure (Ppeak) and positive end-expiratory pressure (PEEP) were monitored using spirometry. All these monitoring modalities were incorporated in the anaesthesia workstation (Aisys CS2, GE Healthcare, Chicago, Illinois, USA). SpO_2, HR and perfusion index (PI) were monitored using a pulse oximetry (Radical-7,

Table 2 Risks of having above-average outcomes after major spine surgery based on the analysis between threshold and outcome (n=102)

		Length of hospital stay ≤6 days (n=61) vs length of hospital stay >6 days (n=41)		Composite complications ≤3 (n=70) vs composite complications >3 (n=32)	
Parameters and thresholds	**Beyond threshold (n, total)**	**Beyond threshold (n vs n)**	**RR (95% CI)**	**Beyond threshold (n vs n)**	**RR (95% CI)**
MAP <50 mm Hg†	37	14 vs 23	2.04 (1.29 to 3.23)**	20 vs 17	1.81 (1.03 to 3.16)*
MAP <60 mm Hg	61	29 vs 32	2.04 (1.11 to 3.76)*	35 vs 26	2.49 (1.13 to 5.45)*
MAP <70 mm Hg	85	44 vs 41	NE	54 vs 31	4.01 (0.61 to 26.55)
MAP >100 mm Hg	90	51 vs 39	1.30 (0.41 to 4.13)	60 vs 30	1.00 (0.31 to 3.22)
MAP >110 mm Hg	77	41 vs 36	1.78 (0.81 to 3.91)	49 vs 28	1.73 (0.69 to 4.33)
MAP >120 mm Hg	69	36 vs 33	1.61 (0.86 to 3.03)	43 vs 26	1.70 (0.79 to 3.66)
Temp <35°C	44	22 vs 22	1.53 (0.95 to 2.45)	21 vs 23	3.37 (1.73 to 6.54)***
Temp <35.5°C	70	40 vs 30	1.25 (0.72 to 2.16)	44 vs 26	1.98 (0.91 to 4.33)
Temp <36°C	85	50 vs 35	1.17 (0.58 to 2.33)	57 vs 28	1.40 (0.56 to 3.47)
Temp >37°C	29	14 vs 15	1.45 (0.91 to 2.32)	20 vs 9	0.99 (0.52 to 1.87)
Temp >37.5°C	8	4 vs 4	NE	6 vs 2	NE
Temp >38°C	1	1 vs 0	NE	1 vs 0	NE
SpO_2<90%	10	5 vs 5	1.28 (0.65 to 2.50)	7 vs 3	0.95 (0.35 to 2.57)
SpO_2 <95%	16	7 vs 9	1.51 (0.91 to 2.52)	11 vs 5	1.00 (0.45 to 2.20)
HR <40 bpm	2	0 vs 2	NE	0 vs 2	NE
HR <50 bpm	24	15 vs 9	0.91 (0.51 to 1.63)	16 vs 8	1.08 (0.56 to 2.09)
HR <60 bpm	53	35 vs 18	0.72 (0.45 to 1.17)	33 vs 20	1.54 (0.84 to 2.81)
HR >90 bpm	23	9 vs 14	1.78 (1.14 to 2.79)*	16 vs 7	0.96 (0.48 to 1.93)
HR >100 bpm	18	7 vs 11	1.71 (1.07 to 2.73)*	13 vs 5	0.86 (0.39 to 1.94)
HR >110 bpm	14	6 vs 8	1.52 (0.90 to 2.58)	10 vs 4	0.90 (0.37 to 2.17)
PI <0.5	40	19 vs 21	1.63 (1.02 to 2.59)*	27 vs 13	1.06 (0.59 to 1.90)
PI <1	65	38 vs 27	1.10 (0.66 to 1.82)	47 vs 18	0.73 (0.41 to 1.29)
PI >6	25	14 vs 11	1.13 (0.67 to 1.91)	15 vs 10	1.40 (0.77 to 2.54)
PI >10	3	3 vs 0	NE	0 vs 3	NE
iVt <5 mL/kg	101	61 vs 40	NE	69 vs 32	NE
iVt <6 mL/kg	101	61 vs 40	NE	69 vs 32	NE
iVt >8 mL/kg	1	0 vs 1	NE	1 vs 0	NE
iVt >9 mL/kg	1	0 vs 1	NE	1 vs 0	NE
iVt >10 mL/kg	0	0 vs 0	NE	0 vs 0	NE
aVt <5 mL/kg	79	45 vs 34	1.41 (0.73 to 2.76)	52 vs 27	1.57 (0.68 to 3.62)
aVt <6 mL/kg	94	55 vs 39	NE	64 vs 30	NE
aVt >8 mL/kg	32	18 vs 14	1.13 (0.69 to 1.85)	20 vs 12	1.31 (0.73 to 2.35)
aVt >9 mL/kg	19	10 vs 9	1.23 (0.71 to 2.12)	12 vs 7	1.22 (0.62 to 2.40)
aVt >10 mL/kg	11	8 vs 3	0.65 (0.24 to 1.77)	7 vs 4	1.18 (0.51 to 2.73)
Ppeak <10 cmH_2O	46	27 vs 19	1.05 (0.65 to 1.69)	28 vs 18	1.57 (0.88 to 2.79)
Ppeak <15 cmH_2O	68	39 vs 29	1.21 (0.71 to 2.06)	46 vs 22	1.10 (0.59 to 2.05)
Ppeak >25 cmH_2O	32	20 vs 12	0.91 (0.53 to 1.53)	24 vs 8	0.73 (0.37 to 1.44)
Ppeak >30 cmH_2O	12	8 vs 4	0.81 (0.35 to 1.87)	8 vs 4	1.07 (0.45 to 2.52)
Ppeak >35 cmH_2O	4	1 vs 3	NE	2 vs 2	NE
PEEP <3 cmH_2O	53	32 vs 21	0.97 (0.60 to 1.56)	33 vs 20	1.54 (0.84 to 2.81)
PEEP >7 cmH_2O	17	11 vs 6	0.86 (0.43 to 1.71)	14 vs 3	0.52 (0.18 to 1.50)

Continued

Table 2 Continued

Parameters and thresholds	Beyond threshold (n, total)	Length of hospital stay ≤6 days (n=61) vs length of hospital stay >6 days (n=41)		Composite complications ≤3 (n=70) vs composite complications >3 (n=32)	
		Beyond threshold (n vs n)	RR (95% CI)	Beyond threshold (n vs n)	RR (95% CI)
PEEP >10 cmH_2O	6	3 vs 3	NE	5 vs 1	NE
$EtCO_2$ >25 mm Hg	39	22 vs 17	1.14 (0.71 to 1.84)	26 vs 13	1.11 (0.62 to 1.98)
$EtCO_2$ >30 mm Hg	62	34 vs 28	1.39 (0.82 to 2.35)	39 vs 23	1.65 (0.85 to 3.19)
$EtCO_2$ >40 mm Hg	63	39 vs 24	0.87 (0.54 to 1.41)	44 vs 19	0.90 (0.51 to 1.62)
$EtCO_2$ >45 mm Hg	34	21 vs 13	0.93 (0.56 to 1.55)	23 vs 11	1.05 (0.57 to 1.91)
FiO_2 <0.35	6	3 vs 3	NE	4 vs 2	NE
FiO_2 <0.45	21	13 vs 8	0.94 (0.51 to 1.17)	12 vs 9	1.51 (0.83 to 2.76)
FiO_2 >0.75	96	57 vs 39	1.22 (0.38 to 3.88)	65 vs 31	1.94 (0.32 to 11.87)
FiO_2 >0.85	86	52 vs 34	0.90 (0.49 to 1.67)	58 vs 28	1.30 (0.53 to 3.21)
$SctO_2$ <50%	6	1 vs 5	NE	3 vs 3	NE
$SctO_2$ <55%	13	4 vs 9	1.93 (1.22 to 3.04)*	6 vs 7	1.92 (1.05 to 3.50)
$SctO_2$ <60%	27	11 vs 16	1.78 (1.14 to 2.78)*	15 vs 12	1.67 (0.95 to 2.93)
$SctO_2$ >75%	68	45 vs 23	0.64 (0.40 to 1.01)	48 vs 20	0.83 (0.46 to 1.50)
$SctO_2$ >80%	37	24 vs 13	0.82 (0.49 to 1.37)	25 vs 12	1.05 (0.58 to 1.90)
$SctO_2$ >85%	8	4 vs 4	NE	5 vs 3	NE
$SctO_2$ >90%	2	0 vs 2	NE	1 vs 1	NE
$SstO_2$ <50%	16	8 vs 8	1.30 (0.75 to 2.28)	10 vs 6	1.24 (0.61 to 2.52)
$SstO_2$ <55%	22	11 vs 11	1.33 (0.80 to 2.21)	14 vs 8	1.21 (0.64 to 2.31)
$SstO_2$ <60%	32	15 vs 17	1.55 (0.98 to 2.45)	22 vs 10	0.99 (0.54 to 1.85)
$SstO_2$ >75%	87	50 vs 37	1.59 (0.67 to 3.82)	56 vs 31	5.34 (0.79 to 36.26)
$SstO_2$ >80%	71	40 vs 31	1.35 (0.76 to 2.40)	44 vs 27	2.36 (1.00 to 5.55)*
$SstO_2$ >85%	45	23 vs 22	1.47 (0.91 to 2.35)	26 vs 19	1.85 (1.02 to 3.33)*
$SstO_2$ >90%	9	5 vs 4	1.12 (0.52 to 2.42)	5 vs 4	1.48 (0.67 to 3.26)

The physiological parameters were dichotomised based on whether the intraoperative measurements were beyond or not beyond the thresholds. The adverse outcome was defined as either length of hospital stay >6 days or composite complications >3.
*P<0.05; **P<0.01; ***P<0.001.
†n=96 for MAP due to missing invasive arterial blood pressure measurements.
aVt, tidal volume based on actual body weight; bpm, beats per minute; $EtCO_2$, end- tidal carbon dioxide; FiO_2, inspired oxygen fraction; HR, heart rate; iVt, tidal volume based on ideal body weight; MAP, mean arterial pressure; PEEP, positive end-expiratory pressure; PI, perfusion index; Ppeak, peak airway pressure; $SctO_2$, cerebral tissue oxygen saturation; SpO_2, pulse oxygen saturation; $SstO_2$, somatic tissue oxygen saturation; RR, relative risk ; Temp, temperature; NE, not estimable.

Masimo, Irvine, California, USA). $SctO_2$ and $SstO_2$ were monitored using a NIRS-based tissue oximeter (FORE-SIGHT ELITE, CASMED, Branford, Connecticut, USA), with two probes placed on the left and right upper forehead to monitor $SctO_2$ and another two probes on the left and right lower legs (over the tibialis anterior muscle) to monitor $SstO_2$.

Data recording and analysis

Different monitors had different data output rates. The anaesthesia workstation generated a new data point every 5 s, while both pulse and tissue oximeters reported every 2 s. All data were captured by a research computer synchronously and continuously. The left and right $SctO_2$ and $SstO_2$ measurements were averaged for analysis. There were typically 12 or 30 data points for each minute depending on the data output frequency. The median values of the measurements within each minute were used in the analysis. The AUC (unit*min) was calculated as the sum of the differences between the median values and the chosen threshold whenever the median value was beyond the threshold. The variables and the relevant thresholds used in the analyses are detailed in table 1.

Postoperative outcomes

The outcome measures were length of hospital stay (LOS) in days and composite complications as counted after surgery and throughout patient's hospitalisation. The primary postoperative complications were hypotension requiring volume replacement and/or vasopressor

Table 3 Correlations between area under curves (AUCs) and outcomes based on Spearman's rank correlation coefficient analysis

Parameters and thresholds	AUC>0 (n) *	Length of hospital stay		Composite complication	
		R value	P value	R value	P value
MAP <50 mm Hg	37	0.3	0.1	0.3	0.07
MAP <60 mm Hg	61	0.3	0.03	0.3	0.02
MAP <70 mm Hg	85	0.2	0.05	0.2	0.04
MAP >100 mm Hg	90	0.2	0.06	0.3	0.001
MAP >110 mm Hg	77	0.2	0.1	0.3	0.01
MAP >120 mm Hg	69	0.2	0.06	0.2	0.08
Temp <35°C	44	−0.06	0.7	0.1	0.4
Temp <35.5°C	70	0.06	0.6	0.2	0.06
Temp <36°C	85	0.04	0.7	0.1	0.2
Temp >37°C	29	0.3	0.2	0.2	0.4
Temp >37.5°C	8	NE	NE	NE	NE
Temp >38°C	1	NE	NE	NE	NE
SpO_2 <90%	10	0.3	0.4	0.3	0.4
SpO_2 <95%	16	−0.2	0.5	0.3	0.3
HR <40 bpm	2	NE	NE	NE	NE
HR <50 bpm	24	0.2	0.5	0.3	0.2
HR <60 bpm	53	−0.05	0.7	−0.1	0.5
HR >90 bpm	23	0.6	0.005	0.4	0.07
HR >100 bpm	18	0.4	0.1	0.4	0.1
HR >110 bpm	14	−0.02	0.9	−0.4	0.2
PI <0.5	40	−0.03	0.8	−0.2	0.3
PI <1	65	0.2	0.07	0.08	0.5
PI >6	25	−0.08	0.7	0.3	0.2
PI >10	3	NE	NE	NE	NE
iVt <5 mL/kg	101	0.4	0.0002	0.4	0.0003
iVt <6 mL/kg	101	0.4	0.0001	0.4	0.0001
iVt >8 mL/kg	1	NE	NE	NE	NE
iVt >9 mL/kg	1	NE	NE	NE	NE
iVt >10 mL/kg	0	NE	NE	NE	NE
aVt <5 mL/kg	79	0.007	1.0	0.2	0.1
aVt <6 mL/kg	94	−0.01	0.9	0.02	0.9
aVt >8 mL/kg	32	0.2	0.3	0.1	0.5
aVt >9 mL/kg	19	−0.2	0.3	0.09	0.7
aVt >10 mL/kg	11	0.3	0.3	0.1	0.7
Ppeak <10 cmH_2O	46	0.1	0.5	0.3	0.06
Ppeak <15 cmH_2O	68	0.04	0.8	0.2	0.2
Ppeak >25 cmH_2O	32	0.01	0.9	0.01	0.9
Ppeak >30 cmH_2O	12	0.08	0.8	−0.2	0.5
Ppeak >35 cmH_2O	4	NE	NE	NE	NE
PEEP <3 cmH_2O	53	−0.1	0.5	−0.06	0.7
PEEP >7 cmH_2O	17	0.2	0.6	0.3	0.3
PEEP >10 cmH_2O	6	NE	NE	NE	NE
$EtCO_2$ >25 mm Hg	39	−0.1	0.5	−0.05	0.8

Continued

Table 3 Continued

Parameters and thresholds	AUC>0 (n) *	Length of hospital stay		Composite complication	
		R value	P value	R value	P value
$EtCO_2$ >30 mm Hg	62	0.1	0.3	0.06	0.7
$EtCO_2$ >40 mm Hg	63	0.05	0.7	0.09	0.5
$EtCO_2$ >45 mm Hg	34	0.2	0.4	−0.02	0.9
FiO_2 <0.35	6	NE	NE	NE	NE
FiO_2 <0.45	21	−0.2	0.3	−0.2	0.4
FiO_2 >0.75	96	0.1	0.2	0.2	0.05
FiO_2 >0.85	86	0.2	0.1	0.2	0.07
$SctO_2$ <50%	6	NE	NE	NE	NE
$SctO_2$ <55%	13	−0.1	0.7	−0.3	0.4
$SctO_2$ <60%	27	−0.2	0.2	0.09	0.6
$SctO_2$ >75%	68	0.2	0.1	0.2	0.1
$SctO_2$ >80%	37	0.04	0.8	0.03	0.9
$SctO_2$ >85%	8	NE	NE	NE	NE
$SctO_2$ >90%	2	NE	NE	NE	NE
$SstO_2$ <50%	16	0.1	0.6	−0.1	0.7
$SstO_2$ <55%	22	−0.1	0.5	−0.3	0.3
$SstO_2$ <60%	32	−0.2	0.3	−0.2	0.2
$SstO_2$ >75%	87	0.03	0.8	0.1	0.2
$SstO_2$ >80%	71	0.1	0.4	0.09	0.4
$SstO_2$ >85%	45	0.04	0.8	−0.09	0.6
$SstO_2$ >90%	9	0.6	0.06	0.3	0.5

*Analysis was not attempted if the number of patients whose measurements were beyond a given threshold was ≤8. Only patients whose AUCs were >0 were included in analysis.
NE, not estimable.

infusion, new-onset arrhythmia, intubation >24 hours, acute lung injury or acute respiratory distress syndrome, neurocognitive change, constipation, postoperative nausea and vomiting, urinary infection, creatinine elevation, thrombocytopenia, coagulopathy, red blood cell transfusion requirement, wound infection and wound dehiscence.

Statistical analysis

This preliminary study was based on a convenience sample of 102 patients. It was not powered to a specific end point. The data were expressed in mean ± SD unless specified otherwise.

We first analysed the associations between thresholds and outcomes, that is, if patients whose physiological measurements passed a specific threshold, compared with those did not, had a higher risk of prolonged hospitalisation or more complications. The goal was to find a threshold value that could discriminate between patients with different outcomes. Outcomes were dichotomised into below-average or above-average categories based on the average values. The outcome was regarded as improved outcome if it was below the average value, that is, shorter hospitalization or fewer complications. Analysis was not attempted if the number of patients beyond or not beyond a given threshold was ≤8. Relative risk (RR), 95% CI and p value were reported.

We then analysed the association between AUCs and outcomes. The question was to determine if different AUCs are significantly associated with different outcomes. Because some AUC values were large and there was no standard metric, we calculated correlations between AUCs and outcomes using Spearman's rank correlation with the original values substituted by their ranks. Correlation coefficients and p values were reported. We additionally performed two-sample t-tests to compare the log-transformed AUCs between patients with different outcomes. The medians and p values were reported. Only patients whose AUCs were >0 were included in these analyses.

For statistical calculations, we used R (https://cran.r-project.org) and SAS V9.2 (SAS Institute Inc). Nominal p values <0.05 were regarded as statistically significant.

RESULTS

Data from 102 patients (male=43; female=59) were included in this analysis, with an average age of 63±9 years,

Table 4 Comparisons of area under curves (AUCs) between patients with length of hospital stay (LOS) ≤6 and >6 days, respectively, based on two-sample t-test

Parameters and thresholds	LOS ≤6 days (n=61)		LOS >6 days (n=41)		
	AUC >0 (n)	AUC median (Q1–Q3) (unit*min)	AUC >0 (n)	AUC median (Q1–Q3) (unit*min)	P value
MAP <50 mm Hg	14	11 (5–25)	23	26 (9–53)	0.4
MAP <60 mm Hg	29	15 (4–36)	32	43 (23–144)	0.2
MAP <70 mm Hg	44	83 (34–227)	41	291 (130–441)	0.06
MAP >100 mm Hg	51	200 (42–517)	39	324 (100–656)	0.2
MAP >110 mm Hg	41	123 (56–265)	36	154 (82–501)	0.08
MAP >120 mm Hg	36	82 (29–171)	33	113 (52–338)	0.047
Temp <35°C	22	43 (6–94)	22	34 (16–46)	0.5
Temp <35.5°C	40	51 (9–144)	30	63 (17–129)	0.3
Temp <36°C	50	106 (42–184)	35	118 (55–245)	0.2
Temp >37°C	14	17 (6–31)	15	37 (6–54)	0.6
Temp >37.5°C	4	21 (9–32)	4	4 (2–5)	0.05
Temp >38°C	1	NA	0	NA	NA
SpO_2 <90%	5	8 (2–53)	5	32 (32–928)	0.3
SpO_2 <95%	7	16 (2–94)	9	41 (1–45)	0.3
HR <40 bpm	0	NA	2	1452 (1–2904)	NA
HR <50 bpm	15	35 (1–100)	9	21 (11–518)	0.2
HR <60 bpm	35	211 (32–1107)	18	313 (22–1180)	0.5
HR >90 bpm	9	128 (18–264)	14	351 (210–508)	0.2
HR >100 bpm	7	90 (7–189)	11	142 (39–164)	0.3
HR >110 bpm	6	49 (15–58)	8	36 (8–65)	0.8
PI <0.5	19	6 (1–10)	21	4 (0.3–23)	0.6
PI <1	38	14 (3–76)	27	40 (8–130)	0.1
PI >6	14	5 (0.3–35)	11	3 (1–22)	0.1
PI >10	3	97 (0.2–217)	0	NA	NA
iVt <5 mL/kg	61	421 (340–552)	40	566 (443–816)	0.0001
iVt <6 mL/kg	61	666 (535–904)	40	868 (732–1241)	0.0003
iVt >8 mL/kg	0	NA	1	NA	NA
iVt >9 mL/kg	0	NA	1	NA	NA
iVt >10 mL/kg	0	NA	0	NA	NA
aVt <5 mL/kg	45	8 (3–44)	34	11 (5–72)	0.4
aVt <6 mL/kg	55	98 (8–213)	39	116 (15–335)	0.3
aVt >8 mL/kg	18	1 (1–3)	14	3 (1–24)	0.2
aVt >9 mL/kg	10	1 (0.3–4)	9	0.1 (0.04–7)	0.3
aVt >10 mL/kg	8	0.07 (0.03–4)	3	53 (2–59)	0.01
Ppeak <10 cmH_2O	27	5 (1–10)	19	8 (3–14)	0.3
Ppeak <15 cmH_2O	39	17 (5–55)	29	19 (7–152)	0.2
Ppeak >25 cmH_2O	20	12 (2–161)	12	28 (3–177)	0.5
Ppeak >30 cmH_2O	8	10 (2–51)	4	71 (23–106)	0.8
Ppeak >35 cmH_2O	1	NA	3	8 (2–18)	0.3
PEEP <3 cmH_2O	32	5 (2–74)	21	3 (1–9)	0.6
PEEP >7 cmH_2O	11	5 (1–59)	6	31 (12–295)	0.1
PEEP >10 cmH_2O	3	9 (0.1–31)	3	2 (1–3)	0.3

Continued

Table 4 Continued

Parameters and thresholds	LOS ≤6 days (n=61) AUC >0 (n)	LOS ≤6 days (n=61) AUC median (Q1–Q3) (unit*min)	LOS >6 days (n=41) AUC >0 (n)	LOS >6 days (n=41) AUC median (Q1–Q3) (unit*min)	P value
$EtCO_2$ >25 mm Hg	22	16 (7–36)	17	11 (8–27)	0.5
$EtCO_2$ >30 mm Hg	34	21 (5–29)	28	25 (12–57)	0.3
$EtCO_2$ >40 mm Hg	39	50 (10–212)	24	81 (13–349)	0.9
$EtCO_2$ >45 mm Hg	21	12 (3–153)	13	52 (18–138)	0.6
FiO_2 <0.35	3	4 (0.2–245)	3	1524 (11–2532)	0.2
FiO_2 <0.45	13	78 (60–157)	8	52 (12–1674)	0.1
FiO_2 >0.75	57	1189 (242–3539)	39	1715 (672–4212)	0.8
FiO_2 >0.85	52	460 (89–2206)	34	706 (411–2431)	0.8
$SctO_2$ <50%	1	NA	5	74 (74–213)	0.7
$SctO_2$ <55%	4	26 (6–260)	9	32 (16–232)	0.5
$SctO_2$ <60%	11	161 (28–246)	16	69 (20–492)	0.5
$SctO_2$ >75%	45	92 (7–235)	23	202 (46–505)	0.1
$SctO_2$ >80%	24	19 (6–46)	13	11 (2–88)	0.3
$SctO_2$ >85%	4	21 (6–36)	4	59 (13–140)	0.2
$SctO_2$ >90%	0	NA	2	3 (2–5)	NA
$SstO_2$ <50%	8	59 (1–2632)	8	90 (12–1186)	0.4
$SstO_2$ <55%	11	130 (29–2328)	11	23 (16–1682)	0.4
$SstO_2$ <60%	15	213 (54–1388)	17	41 (18–675)	0.3
$SstO_2$ >75%	50	926 (198–1903)	37	1130 (343–2297)	0.7
$SstO_2$ >80%	40	337 (95–971)	31	595 (97–1071)	0.5
$SstO_2$ >85%	23	109 (11–463)	22	191 (20–478)	0.7
$SstO_2$ >90%	5	4 (1–5)	4	25 (15–65)	0.1

Only patients whose AUCs were >0 were included in analysis.
NA, not assessable; Q1, first quantile; Q3, third quantile.

weight 79±20 kg and height 168±12 cm. Spinal fusion was performed in 89 patients. The number of segments fused was 7±5 and the surgical time 5±2 hours. The LOS was 6±3 days and the composite complication count 3±2. The data specific to tissue oxygenation monitoring were previously published.[6]

Threshold and outcome

The risks of having above-average outcomes (ie, the opposite of improved outcomes) in patients whose physiological measurements crossed the specified thresholds are summarised in table 2. The variables and thresholds that were associated with significant risks were MAP <50 and <60 mm Hg, temperature <35°C, HR >90 and >100 beats per minute (bpm), PI <0.5, $SctO_2$ <55% and <60% and $SstO_2$ >80% and >85%.

AUC and outcome

The correlations between AUCs and outcomes are summarised in table 3. The comparisons of the AUCs between patients with different outcomes are summarised in table 4 (outcome=LOS) and table 5 (outcome=composite complication). Overall, the AUCs that had significant associations with above-average outcomes (ie, the opposite of improved outcomes) were based on the following variables and thresholds: MAP <60, <70, >100, >110, >120 mm Hg, temperature <36°C, HR >90 bpm, PI >6, iVt <5 and <6 mL/kg (ideal body weight), aVt >10 mL/kg (actual body weight) and Ppeak <15 cmH_2O.

DISCUSSION

Our study demonstrated the following intraoperative physiological ranges that are associated with improved outcomes (ie, below-average LOS and composite complication) after major spine surgery: MAP 70–100 mm Hg, temperature ≥36°C, HR <90 bpm, Vt based on ideal body weight >6 mL/kg, $SctO_2$ >60% and $SstO_2$ <80%. It suggests that the optimal physiological ranges during surgery can be defined based on analyses associating thresholds and AUCs with different outcomes.

Multiple physiological variables are monitored in anaesthetised patients during surgery. The goal of monitoring is to timely institute a corrective measure when the

Table 5 Comparisons of area under curves (AUCs) between patients with composite complication ≤3 and >3, respectively, based on two-sample t-test

Parameters and thresholds	Composite complication ≤3 (n=70)		Composite complication >3 (n=32)		P value
	AUC >0 (n)	AUC median (Q1–Q3) (unit*min)	AUC >0 (n)	AUC median (Q1–Q3) (unit*min)	
MAP <50 mm Hg	20	12 (1–30)	17	27 (10–53)	0.3
MAP <60 mm Hg	35	29 (7–60)	26	43 (9–142)	0.2
MAP <70 mm Hg	54	110 (50–331)	31	254 (94–441)	0.08
MAP >100 mm Hg	60	157 (40–373)	30	482 (152–714)	0.045
MAP >110 mm Hg	49	109 (48–206)	28	241 (88–504)	0.05
MAP >120 mm Hg	43	82 (34–150)	26	174 (52–338)	0.04
Temp <35°C	21	28 (6–79)	23	36 (16–77)	0.4
Temp <35.5°C	44	35 (9–90)	26	113 (52–172)	0.057
Temp <36°C	57	97 (44–146)	28	217 (88–305)	0.008
Temp >37°C	20	24 (6–52)	9	23 (7–37)	1.0
Temp >37.5°C	6	9 (4–30)	2	3 (1–5)	0.3
Temp >38°C	1	NA	0	NA	NA
SpO_2 <90%	7	23 (2–53)	3	928 (32–6561)	0.08
SpO_2 <95%	11	16 (1–45)	5	41 (23–1255)	0.08
HR <40 bpm	0	NA	2	1452 (1–2904)	NA
HR <50 bpm	16	19 (1–58)	8	209 (16–521)	0.09
HR <60 bpm	33	360 (46–1000)	20	161 (21–1966)	0.1
HR >90 bpm	16	234 (81–426)	7	350 (84–860)	0.9
HR >100 bpm	13	90 (20–146)	5	164 (75–215)	0.8
HR >110 bpm	10	51 (15–77)	4	26 (8–42)	0.3
PI <0.5	27	7 (1–21)	13	4 (0.3–15)	1.0
PI <1	47	30 (4–101)	18	28 (7–72)	0.8
PI >6	15	2 (0.3–10)	10	26 (1–210)	0.03
PI >10	0	NA	3	97 (0.2–217)	NA
iVt <5 mL/kg	69	447 (340–565)	32	606 (432–751)	0.007
iVt <6 mL/kg	69	689 (581–860)	32	986 (725–1168)	0.004
iVt >8 mL/kg	1	NA	0	NA	NA
iVt >9 mL/kg	1	NA	0	NA	NA
iVt >10 mL/kg	0	NA	0	NA	NA
aVt <5 mL/kg	52	8 (3–44)	27	18 (5–107)	0.2
aVt <6 mL/kg	64	107 (11–296)	30	78 (11–335)	0.4
aVt >8 mL/kg	20	2 (1–13)	12	1 (1–11)	0.5
aVt >9 mL/kg	12	1 (0.1–10)	7	0.3 (0.1–7)	1.0
aVt >10 mL/kg	7	1 (0.03–23)	4	1 (0.02–31)	0.8
Ppeak <10 cmH_2O	28	4 (2–9)	18	8 (3–22)	0.3
Ppeak <15 cmH_2O	46	14 (5–55)	22	29 (7–59)	0.049
Ppeak >25 cmH_2O	24	12 (2–153)	8	76 (7–177)	0.8
Ppeak >30 cmH_2O	8	24 (2–89)	4	23 (5–71)	0.6
Ppeak >35 cmH_2O	2	20 (18–22)	2	5 (2–8)	0.05
PEEP <3 cmH_2O	33	4 (1–57)	20	3 (1–9)	0.5
PEEP >7 cmH_2O	14	12 (2–59)	3	49 (2–295)	0.4
PEEP >10 cmH_2O	5	2 (1–9)	1	NA	NA

Continued

Table 5 Continued

Parameters and thresholds	Composite complication ≤3 (n=70) AUC >0 (n)	Composite complication ≤3 (n=70) AUC median (Q1–Q3) (unit*min)	Composite complication >3 (n=32) AUC >0 (n)	Composite complication >3 (n=32) AUC median (Q1–Q3) (unit*min)	P value
$EtCO_2$ >25 mm Hg	26	16 (8–30)	13	11 (8–27)	0.3
$EtCO_2$ >30 mm Hg	39	22 (5–45)	23	15 (7–69)	0.3
$EtCO_2$ >40 mm Hg	44	58 (15–208)	19	58 (11–339)	1.0
$EtCO_2$ >45 mm Hg	23	29 (5–198)	11	25 (3–153)	0.4
FiO_2 <0.35	4	124 (2–884)	2	1272 (11–2532)	0.4
FiO_2 <0.45	12	99 (59–190)	9	67 (36–223)	0.9
FiO_2 >0.75	65	1183 (248–4216)	31	1395 (672–3336)	0.9
FiO_2 >0.85	58	521 (111–2698)	28	672 (317–1851)	0.7
$SctO_2$ <50%	3	152 (74–213)	3	74 (17–3643)	0.4
$SctO_2$ <55%	6	136 (12–481)	7	21 (8–232)	0.6
$SctO_2$ <60%	15	72 (8–331)	12	112 (40–345)	0.8
$SctO_2$ >75%	48	135 (5–248)	20	155 (55–515)	0.5
$SctO_2$ >80%	25	21 (6–58)	12	11 (2–96)	0.7
$SctO_2$ >85%	5	31 (0.3–40)	3	25 (11–93)	0.9
$SctO_2$ >90%	1	NA	1	NA	NA
$SstO_2$ <50%	10	368 (1–1664)	6	86 (15–100)	0.4
$SstO_2$ <55%	14	113 (23–2328)	8	130 (17–394)	0.4
$SstO_2$ <60%	22	116 (23–1388)	10	64 (18–954)	0.4
$SstO_2$ >75%	56	874 (203–1827)	31	1419 (283–2382)	0.1
$SstO_2$ >80%	44	316 (93–1069)	27	523 (103–1071)	0.4
$SstO_2$ >85%	26	162 (13–543)	19	125 (20–463)	0.6
$SstO_2$ >90%	5	10 (4–17)	4	12 (3–25)	0.6

Only patients whose AUCs were >0 were included in analysis.
NA, not assessable; Q1, first quantile; Q3, third quantile.

measurement of the physiological variable is beyond the optimal range. In order to do so, the optimal range of the physiological variable being monitored needs to be first defined. However, the optimal ranges of most physiological variables monitored during surgery remain unknown or controversial. This is exemplified by the routine monitoring of BP during anaesthesia, even though there is a lack of firm consensus on the targeted range.[2]

It was suggested in our study that the optimal MAP range in the patient population studied may be between 70 (lower threshold) and 100 mm Hg (upper threshold) based on the threshold and AUC analyses combined. Our study also suggested that intraoperative tachycardia (HR >90 bmp) may be unwarranted. However, haemodynamics is a complicated physiology and we did not assess haemodynamic parameters such as the stroke volume and cardiac output, which may also be relevant and may be even more so compared with MAP and HR, to patient outcomes.[2 7 8]

Previous studies examined the association between intraoperative cerebral desaturation based on tissue NIRS monitoring and postoperative outcomes.[9–11] All these studies were performed in cardiac surgical patients and based on $SctO_2$ monitoring only. In contrast, our study was done in a noncardiac population and examined the association between $SstO_2$, in addition to $SctO_2$, and outcomes. Our analysis suggested that maintaining $SctO_2$ above 60% and $SstO_2$ below 80% during surgery may be warranted. Whether there is an upper limit for $SctO_2$ and a lower limit for $SstO_2$ in the patient population studied deserves future investigation. Whether the results of this study can be extrapolated into other patient populations remains to be determined. Importantly, these thresholds should be validated by randomised controlled trials in the future.

Our study showed that a temperature ≥36°C was associated with improved outcomes. This finding is in accordance with the current guideline and the available evidence.[12] Our study suggested that maintaining the Vt less than 5–6 mL/kg based on ideal, not actual, body weight is associated with prolonged hospitalisation and more complications. This seems contradictory to the

current 'small Vt' recommendation in mechanically ventilated patients with a normal lung.[13] The disparity between our finding and previous studies needs to be reconciled, but may indicate that the PEEP applied in our patient population was inadequate to offset the promotion of atelectasis by low Vt.

Our study showed that, although both threshold and AUC can be used to explore optimal versus suboptimal physiological ranges, they do not consistently agree with each other. The approach using a threshold value to define physiology reduces the physiology to a binary variable. In contrast, AUC, as the product of the magnitude and duration of a physiological change, quantifies physiology as a continuous variable. Threshold can be regarded as a method of categorisation, while AUC is a method of quantification. Our study suggested that methods of threshold and AUC can be used together to explore the optimal physiological ranges during surgery.

Our study has limitations. First, we did not evaluate the threshold and AUC based on relative changes (ie, by referring to an individual patient's awake baseline measurements) because the data recording started after anaesthesia induction. This is an important consideration because there is an *interindividual* variability for many physiological variables. The use of absolute values can miss this variability. Second, the sample size of this study is small. Third, this study was performed in patients in prone position; therefore, the extrapolation of our findings in patients in a non-prone position should be cautioned because different positioning may exert different impacts on physiology.[14] Lastly, we used nominal p values to examine associations and did not adjust for multiple comparisons in this analysis.

In summary, the optimal ranges of the physiological variables monitored during surgery should be determined. Analyses based on threshold and AUC can be used together to explore the optimal physiological ranges associated with improved outcomes. The physiological ranges defined by a single-cohort observational study should be validated by randomised controlled trials. As such, our work should be regarded as a proof-of-concept rather than definitive study.

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Contributors GL, LL and LM helped in conception and design of the work. GL, LL and JX contributed to acquisition of the data. GL, LL, JX, SR, PB and LM analysed and interpreted the data, drafted and critically revised the manuscript for important intellectual content, are accountable for all aspects of the work and approved the final manuscript.

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Competing interests LM is a consultant to CAS Medical Systems, Inc. The other authors declare no competing interests.

Patient consent for publication Obtained.

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