

# BMJ Open Association between tissue oxygenation and myocardial injury in patients undergoing major spine surgery: a prospective cohort study

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## ABSTRACT

**Objective** To describe the association between intraoperative tissue oxygenation and postoperative troponin elevation in patients undergoing major spine surgery. We hypothesised that a decrease in intraoperative skeletal muscle tissue oxygenation (SmO<sub>2</sub>) was associated with the peak postoperative cardiac troponin value.

**Design** This is a prospective cohort study.

**Setting** Single-centre, University of California San Francisco Medical Center.

**Participants** Seventy adult patients undergoing major elective spine surgery.

**Primary and secondary outcome measures** High-sensitivity troponin T (hsTnT) was measured in plasma preoperatively and on the first and second day after surgery to assess the primary outcome of peak postoperative hsTnT. Secondary outcomes included MINS and intensive care unit (ICU) admission within 30 days. Skeletal cerebral tissue oxygenation and SmO<sub>2</sub> was measured continuously with near-infrared spectroscopy during surgery. The primary exposure variable was time-weighted area under the curve (TW AUC) for SmO<sub>2</sub>.

**Results** Mean age was 65 (33–85) years and 59% were female. No significant association was found between TW AUC for SmO<sub>2</sub> and peak hsTnT (Spearman's correlation, r<sub>s</sub>=0.17, p=0.16). A total of 28 (40%) patients had MINS. ICU admission occurred in 14 (40%) in lower vs 25 (71%) in upper half of patients based on TW AUC for SmO<sub>2</sub>, p=0.008.

**Conclusions** Decrease in SmO<sub>2</sub> was not a statistically significant predictor for peak troponin value following major spine surgery but is a potential predictor for other postoperative complications.

**Trial registration number** NCT03518372.

## INTRODUCTION

Major non-cardiac surgery is associated with significant risks of postoperative complications which are sometimes asymptomatic such as covert stroke<sup>1</sup> and myocardial infarction and injury.<sup>2</sup> Cardiovascular events are the leading cause of morbidity and mortality<sup>3</sup> with myocardial injury after non-cardiac surgery (MINS) being a major contributor to further postoperative complications.<sup>4–7</sup> MINS

## Strengths and limitations of this study

- Prospective observational study including 70 patients undergoing major spine surgery.
- Contributing knowledge to potential predictors for myocardial injury and clinical implications of tissue oxygenation monitoring.
- Applying skeletal muscle tissue oxygenation as primary predictor, decreasing risk of cerebral autoregulation modification of outcomes.
- There is no clinical consensus of absolute threshold for tissue hypoxaemia, thus, population median for skeletal muscle tissue oxygenation was used as cut-off in this study.

is frequently caused by ischaemia and can be diagnosed from elevated postoperative high-sensitivity cardiac troponin, in the absence of non-ischaemic factors for troponin elevation.<sup>8</sup> The 30-day mortality is increased up to eightfold in patients with covert stroke compared with matched controls<sup>9</sup> and stroke occurs in 9% of patients with MINS, making it a substantial public health problem.<sup>10</sup> Peak postoperative cardiac troponin has a linear association with 30-day mortality.<sup>7</sup> Each year, 8 million surgical patients worldwide suffer from MINS but there is sparse knowledge about triggering causes and contributing factors to the magnitude of peak postoperative cardiac troponin.<sup>5 11</sup>

Intraoperative tissue oxygen desaturation is common in patients undergoing major spine surgery<sup>12</sup> probably because of the substantial blood loss and haemodynamic changes that occur in this type of operation. Tissue oxygenation (StO<sub>2</sub>) can be measured non-invasively with near-infrared spectroscopy (NIRS). Previous studies found that a decrease in intraoperative StO<sub>2</sub> was associated with wound infection, stroke and renal failure,<sup>13</sup> and that decrease in skeletal muscle tissue oxygenation (SmO<sub>2</sub>) was a stronger

predictor for these complications than cerebral tissue oxygenation ( $\text{ScO}_2$ ) in spine surgery.<sup>12</sup> However, current knowledge of how  $\text{StO}_2$  affects other important clinical outcomes, including MINS, is lacking. In this prospective cohort study, we hypothesised that a decrease in  $\text{SmO}_2$  was associated with higher peak postoperative high-sensitivity troponin T (hsTnT). The primary exposure variable was time-weighted area under the curve (TW AUC) for  $\text{SmO}_2$  and the primary outcome was peak postoperative hsTnT. This study was conducted with the aim of examining the association between intraoperative  $\text{StO}_2$  and postoperative troponin elevation in patients undergoing major spine surgery.

## METHODS

This prospective cohort study was conducted at the University of California, San Francisco (UCSF). This manuscript adheres to the applicable Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

### Patients

The patients were adults ( $\geq 18$  years) undergoing elective spine surgery at UCSF from January to May 2018. The surgeries selected were scheduled to last for more than 2 hours and included instrumentation. Exclusion criteria were: American Society of Anesthesiologists Physical Status Classification System score  $>IV$ , surgery for tumour or infection, emergent or urgent surgery.

### Data collection

Patient characteristics, comorbidities, preoperative physical status and postoperative complications were extracted from the electronic medical record (KFB). Data were collected at two time points: prior to surgery and 30 days after surgery. A follow-up phone call to the patient was made 30 days after surgery to verify postoperative outcomes. Baseline values were defined as the preincision value. Intraoperative values were defined as data from incision to end of procedure when last suture was placed. Study data were managed using the REDCap (Research Electronic Data Capture) tools hosted at UCSF.

### Tissue oximetry

$\text{StO}_2$  was monitored using a tissue oximeter based on NIRS (FORE-SIGHT Elite, CASMED, Branford, Connecticut, USA). Cerebral and leg skeletal muscle oxygenation was monitored via two cables connected to adhesive probes provided by the manufacturer. Probes were placed after tracheal intubation and a baseline was measured from placing of probe to incision. One probe was placed on the left side on the upper forehead to monitor one-sided frontal cortex  $\text{ScO}_2$ . The second probe was placed on the left tibialis anterior muscle, four fingers below the tibial tuberosity and two fingers lateral to the anterior edge of the tibial shaft, to monitor the  $\text{SmO}_2$  of the lower leg muscle. The oximeter generated a data point every 2 seconds. The anaesthesia team was blinded to

the oximeter. Data from the oximeter were used for  $\text{StO}_2$  indices derivation. Indices were maximum, minimum, median and TW AUC for  $\text{SmO}_2$  and  $\text{ScO}_2$ , respectively. The primary exposure variable was TW AUC for  $\text{SmO}_2$ . TW AUC was calculated for each participant as the area below the intraoperative median for the study population and divided by length of surgery. This was chosen because there is no international consensus on a universal baseline level or normal range for  $\text{StO}_2$ .

### Troponin measurements

A total of three blood samples for hsTnT were drawn. First sample was drawn by the anaesthesiologist in the operating room after placement of the arterial line prior to surgery. Second and third sample were drawn by a phlebotomist or nurse the first and second day after surgery, respectively. After the blood was drawn, the sample was centrifuged immediately and the plasma was divided into two cryo collecting tubes and placed in a  $-80^\circ\text{C}$  freezer for storage. All plasma samples were sent to a specialised laboratory at Hennepin Medical Center (Minneapolis, Minnesota, USA) to be analysed for the Roche fifth generation, Elecsys hsTnT assay after the study was completed. The data collector was blinded to the results of hsTnT and laboratory personnel analysing the blood samples were blinded to patient data. Medical records and perioperative information (eg, ECG, laboratory values) were reviewed for patients with troponin elevation, to exclude a non-ischaeamic aetiology.<sup>8</sup>

### Outcomes

The primary outcome was defined as postoperative peak high-sensitivity cardiac troponin T (hsTnT). A secondary related outcome was MINS, initially defined as  $\text{hsTnT} \geq 14\text{ ng/L}$ <sup>14</sup> with factors for non-ischaeamic aetiology excluded (eg, sepsis, kidney failure, heart failure). This MINS definition was registered at ClinicalTrials.gov, but during the course of the study and prior to hsTnT analysis of the blood samples, new data were published, where MINS was defined as an elevated postoperative hsTnT (ie, 20 to  $<65\text{ ng/L}$  with an absolute change  $\geq 5\text{ ng/L}$  or a single  $\text{hsTnT} \geq 65\text{ ng/L}$ ) with factors for non-ischaeamic aetiology excluded (eg, sepsis, kidney failure, heart failure).<sup>8</sup> We, therefore, updated the protocol to the latter and current MINS definition. Other secondary outcomes were myocardial infarction, non-fatal cardiac arrest, new-onset arrhythmia (defined as new atrial fibrillation or other treatment requiring arrhythmia), heart failure, transient cerebral ischaemia, symptomatic stroke, sepsis, surgical site infection, pulmonary complications (including pulmonary infection, pneumothorax, atelectasis, pulmonary embolus and other pulmonary complication), creatinine elevation ( $>1.3\text{ mg/dL}$  for men and  $>1.1\text{ mg/dL}$  for women), intensive care unit (ICU) admission, length of hospital stay and mortality, all within 30 days after surgery. In addition, we analysed a composite outcome that consisted of all above mentioned postoperative complications.

## Sample size

Sample size calculations were based on clinical data and previous studies investigating  $StO_2$  as an outcome for postoperative complications.<sup>12 13</sup> These studies evaluated all types of complications as primary outcome. Mean (SD) TW AUC for  $SmO_2$  was  $1.59\% \times \text{min} \times \text{h}^{-1}$  (2.35).<sup>12</sup> We estimated a minimal clinically relevant difference to be a 36% increase in TW AUC for  $SmO_2$  for participants with high peak hsTnT (with a cut-off of 14 ng/L based on the 99th percentile of a healthy population)<sup>15</sup> compared with participants with low peak hsTnT. Using a power of 80% and a significance level of 0.05, a sample size of 68 participants for this study was needed. We anticipated a low number of drop-outs, as the study design was observational, resulting in a total sample size of 70 participants.

## Statistical analysis

Results are presented as mean  $\pm$  SD and median (IQR) when appropriate. Revised Cardiac Risk Index (RCRI) and corresponding risk of cardiac complications at 30 days after surgery were computed according to current criteria.<sup>16</sup> Postoperative outcomes were compared stratifying the study population in two groups by median TW AUC for  $SmO_2$ . Comparison between groups were based on  $\chi^2$  tests for categorical variables, analysis of variance and Wilcoxon rank-sum test.

The primary analysis of the association between TW AUC for  $SmO_2$  and peak hsTnT was tested by Spearman correlation analysis. Univariable and multivariable logistic regression models were used in secondary analyses to examine the associations of baseline characteristics, intraoperative variables and  $StO_2$  indices with higher peak hsTnT which was dichotomised in high/low categories using median peak hsTnT in the study population as cut-off. Univariable and multivariable logistic regression was used to test the association between  $StO_2$  indices and MINS and the adjusted prediction for TW AUC for  $SmO_2$  and MINS was calculated. Variables for adjustment in the multivariable analyses were age, sex, body mass index, smoking, diabetes, hypertension, previous stroke, chronic lung disease, arrhythmia, valvular disease, chronic kidney disease, length of surgery, osteotomy performed, estimated blood loss, mean arterial blood pressure and mean heart rate.

Stata Statistical Software (release V.15; StataCorp) was used for all analyses.

## Patient and public involvement

Patients or the public were not involved in the design, conduct, reporting or dissemination plans of this study.

## RESULTS

A total of 70 patients undergoing spine surgery was included in this prospective cohort study. Mean age was 65 (33; 85) years and 41 (59%) participants were female. Mean (95% CI) risk of cardiac complications at 30 days after surgery, calculated according to RCRI was 7.7 (7.0

to 8.3) %. The median percentage estimated blood loss of estimated blood volume was 17 (IQR 8–31) %. A summary of patient characteristics, medical history, surgical information and values for  $StO_2$  are found in table 1.

## Incidence of MINS and major outcomes

The median peak hsTnT was 19 (IQR 10–30) ng/L and based on a hsTnT of 20 to <65 ng/L with an absolute change  $\geq 5$  ng/L or a single hsTnT  $\geq 65$  ng/L, 28 (40%) participants had MINS (table 2). The number of participants with any postoperative complications were 41 (59%) and when MINS was included as a complication, 52 (74%) of participants had one or more postoperative complications (table 2). Estimated blood loss and length of surgery was associated with MINS (OR (95% CI): 1.001 (1.000 to 1.002),  $p=0.002$  and 1.007 (1.002 to 1.011),  $p=0.004$ , respectively).

## Relationships of $StO_2$ to MINS and other outcomes

In the univariable correlation analysis of TW AUC for  $SmO_2$  and peak hsTnT, no significant association was found ( $r_s=0.17$ ,  $p=0.16$ , figure 1). There was a statistically significant association between higher TW AUC for  $SmO_2$  and the composite outcome of postoperative complications (participants in lower half: 21 (60%) vs participants in upper half: 31 (89%),  $p=0.006$ , table 2) but when logistic regression was performed, this association was not significant. Furthermore, a statistically significant association between higher TW AUC for  $SmO_2$  and ICU admission was found (participants in lower half: 14 (40%) vs participants in upper half: 25 (71%),  $p=0.008$ , table 2). There were no other statistically significant differences in outcomes between the two groups based on median TW AUC for  $SmO_2$ . When testing the  $StO_2$  indices as predictors for higher peak hsTnT by logistic regression, the univariable analysis found that for every 1% increase in median and maximum  $SmO_2$ , the odds of having high peak hsTnT decreased (OR (95% CI): 0.93 (0.87 to 0.996),  $p=0.039$  and 0.92 (0.85 to 0.99),  $p=0.025$ , respectively, table 3). After multivariable adjustment for baseline and clinical variables, median and maximum  $SmO_2$  were not independent predictors for higher peak hsTnT (table 3). None of the  $StO_2$  indices were found to be significant predictors for MINS (table 3). Adjusted predicted probability was calculated based on univariable logistic regression and showed increasing probability for MINS with increasing TW AUC for  $SmO_2$  (figure 2) although this was not statistically significant (OR (95% CI): 1.00 (0.99 to 1.01),  $p=0.74$ ). Although this was not systematically assessed for the purpose of this study, only one participant presented with ischaemic symptoms on the first two postoperative days according to medical records. This patient was not diagnosed with clinical myocardial infarction after examination, although hsTnT was 31 ng/L.

**Table 1** Participant characteristics and intraoperative data

Variables	Participants n=70
<b>Demographics</b>	
Age, years	65 (33; 85)
Sex, female	41 (59%)
BMI, kg/m <sup>2</sup>	28.8 (24.4; 32.9)
<b>ASA</b>	
I	1 (1%)
II	37 (53%)
III	31 (44%)
IV	1 (1%)
<b>Smoking</b>	
Never	37 (53%)
Current	3 (4%)
Former	30 (43%)
<b>Medical history</b>	
Stroke	5 (7%)
TCl	3 (4%)
Hypertension	36 (51%)
Diabetes mellitus	8 (11%)
Chronic lung disease*	15 (21%)
Sleep apnoea	16 (23%)
Arrhythmia	11 (16%)
Valvular disease	6 (9%)
Coronary artery disease	8 (11%)
Creatinine elevation	2 (3%)
<b>RCRI class</b>	
I	49 (70%)
II	15 (21%)
III	6 (9%)
IV	0
<b>Surgical information</b>	
Length of surgery, minutes	264 (201; 405)
Osteotomy performed	35 (50%)
Estimated blood loss, mL	753 (400; 1400)
Mean arterial pressure, mmHg	83±9
Heart rate, bpm	69±11
<b>Tissue oximetry</b>	
SmO <sub>2</sub> median, %	75 (70; 79)
SmO <sub>2</sub> minimum, %	66 (61; 70)
SmO <sub>2</sub> maximum, %	84 (78; 88)
TW AUC for SmO <sub>2</sub> , %×min/hour	98 (9; 298)
ScO <sub>2</sub> median, %	66 (62; 71)
ScO <sub>2</sub> minimum, %	60 (56; 65)
ScO <sub>2</sub> maximum, %	77 (72; 82)
TW AUC for ScO <sub>2</sub> , %*min*h <sup>-1</sup>	33 (0.06; 131)

Continued

**Table 1** Continued

Variables	Participants n=70
Data are mean±SD for normally distributed variables and median (IQR) for variables with skewed distributions.	
*Includes asthma and chronic obstructive pulmonary disease.	
ASA, American society of Anesthesiologists; BMI, body mass index; RCRI, Revised Cardiac Risk Index; ScO <sub>2</sub> , cerebral tissue oxygenation; SmO <sub>2</sub> , skeletal muscle tissue oxygenation; TCl, transient cerebral ischaemia; TW AUC, time-weighted area under the curve.	
<b>DISCUSSION</b>	
In a prospective cohort study of 70 participants, we investigated intraoperative StO <sub>2</sub> as predictor for myocardial injury after spine surgery. We found that SmO <sub>2</sub> and ScO <sub>2</sub> were not independent predictors for elevated hsTnT or MINS. However, in exploratory analyses, some other indices for SmO <sub>2</sub> were associated with higher peak hsTnT, whereas ScO <sub>2</sub> indices were not.	
StO <sub>2</sub> is a result of the oxygen supply and demand of the specific tissue and is determined by multiple physiological factors including oxygen saturation, haemoglobin (Hgb) concentration and cardiac output. <sup>17</sup> Measurement of StO <sub>2</sub> with NIRS has been investigated in previous studies as predictor for a number of different outcomes. Several studies have examined cerebral oxygenation in patients undergoing cardiac surgery, whereas few studies have investigated SmO <sub>2</sub> as predictor for clinical outcomes. In patients undergoing cardiac surgery, ScO <sub>2</sub> was found to be associated with stroke, cognitive decline, length of hospital stay and mortality. <sup>18 19</sup> One study found that decrease in ScO <sub>2</sub> was not a predictor for delirium in elderly patients. <sup>20</sup> A recent meta-analysis of 10 trials with a total of 1466 patients, found that NIRS-based algorithms for ScO <sub>2</sub> did not reduce mortality or organ injury affecting the heart, brain or kidneys. <sup>21</sup> Despite the lack of evident benefit for ScO <sub>2</sub> -guided clinical algorithms, ScO <sub>2</sub> monitoring is routinely used in cardiac surgery.	
Cerebral and skeletal muscle tissue have different physiological characteristics. Meng <i>et al</i> <sup>12</sup> found that SmO <sub>2</sub> was a stronger predictor than ScO <sub>2</sub> for composite post-operative outcomes, including myocardial injury, stroke, pulmonary complications and creatinine elevation. Although findings in the current study were statistically insignificant, the exploratory analyses yielded a stronger association between SmO <sub>2</sub> and outcomes as compared with ScO <sub>2</sub> . This aligns with the theory that SmO <sub>2</sub> is a leading indicator for global desaturation due to low autoregulation in skeletal muscle tissue compared with the higher level of autoregulation in cerebral tissue. <sup>22</sup> Of note, skeletal and myocardial autoregulation may not be the same and it is possible that myocardial autoregulation shows similar patterns to cerebral autoregulation in some physiological instances. The importance of preserved cerebral autoregulation is substantial. Brain tissue is more sensitive to hypoxia than skeletal muscle. <sup>17</sup> One study showed that impaired cerebrovascular autoregulation was	

**Table 2** Summary of postoperative outcomes within 30 days after spinal surgery

Postoperative complications	Lower half TW AUC for SmO <sub>2</sub> , N=35	Upper half TW AUC for SmO <sub>2</sub> , N=35	P value
TW AUC for SmO <sub>2</sub> , (%×min×h <sup>-1</sup> )	9 (1; 53)	298 (189; 586)	<0.001
Peak hsTnT, ng/L	17 (9; 26)	24 (10; 33)	0.15
MINS	12 (34%)	16 (46%)	0.33
Myocardial infarction	0	0	–
Non-fatal cardiac arrest	0	0	–
New-onset arrhythmia	1 (3%)	2 (6%)	0.56
Heart failure	0	0	–
TCI	0	0	–
Stroke	0	0	–
Sepsis	1 (3%)	1 (3%)	1.00
Surgical site infection	2 (6%)	2 (6%)	1.00
Pulmonary complications	4 (11%)	3 (9%)	0.69
Creatinine elevation	1 (3%)	1 (3%)	1.00
ICU admission	14 (40%)	25 (71%)	0.008
Length of postoperative hospitalisation	6 (4; 7)	6 (6; 8)	0.056
Mortality	0	0	–
Composite outcome	21 (60%)	31 (89%)	0.006

Data are mean±SD for normally distributed variables and median (IQR) for variables with skewed distributions). P values are based on  $\chi^2$ -tests, ANOVA and Wilcoxon rank-sum tests.

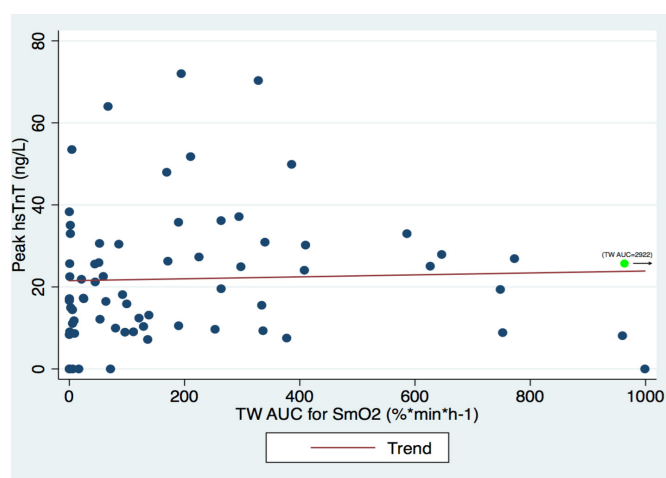
ANOVA, analysis of variance; hsTnT, high-sensitivity troponin T; ICU, intensive care unit; MINS, myocardial injury after non-cardiac surgery; SmO<sub>2</sub>, skeletal muscle tissue oxygenation; TCI, transient cerebral ischaemia; TW AUC, time-weighted area under the curve.

associated with increased morbidity and mortality within 30 days from surgery in patients undergoing major non-cardiac surgery.<sup>23</sup> A study in healthy subjects suggested SmO<sub>2</sub> to be an early indicator for impending cardiovascular collapse and showed that SmO<sub>2</sub> declined in parallel with stroke volume.<sup>24</sup> Perfusion of skeletal muscle tissue follows the same linearity in decline with decreasing cardiac output whereas cerebral tissue perfusion only

decreases approximately one-third of cardiac output.<sup>25</sup> This study found TW AUC for SmO<sub>2</sub> to be almost three times larger than TW AUC for ScO<sub>2</sub> (98% vs 33%×min/hour) indicating autoregulation in brain tissue. Of note, spine surgery patients at UCSF almost all receive anaesthetics that include very low amounts of inhalational anaesthetics, probably preserving brain autoregulation of blood flow. Despite these findings, the clinical implications of SmO<sub>2</sub> monitoring is still yet to be determined. TW AUC for SmO<sub>2</sub> was chosen as a predictor in this study as it maximises sensitivity by including all available data for the specific parameter (magnitude and duration of desaturation as well as covering the entire duration of surgery). Furthermore, it minimises the effect of potential error measurements on the StO<sub>2</sub> value but because TW AUC for SmO<sub>2</sub> is a calculated value it currently has limitations in regards of clinical utility.

StO<sub>2</sub> was not statistically significant associated with MINS in the current study but other indicators of supply-demand mismatch, that is, estimated blood loss and length of surgery, were significantly associated with MINS and peak hsTnT. These are established predictors for MINS<sup>26</sup> and contributes to the understanding of the pathophysiology for elevated troponin.<sup>27</sup>

In general, the majority of MINS are undetected (80%) as patients do not have ischaemic symptoms.<sup>4 10</sup> In this study, only one participant presented with ischaemic symptoms. The type of surgery the participants underwent



**Figure 1** Relationship between time-weighted area under the curve (TW AUC) for skeletal muscle tissue oxygenation (SmO<sub>2</sub>) and peak value of high-sensitivity troponin T (hsTnT) measured within the first 2 days after surgery.

**Table 3** StO<sub>2</sub> measures as predictors for higher peak hsTnT and MINS

StO <sub>2</sub> indices	High peak hsTnT versus low peak hsTnT				MINS versus no MINS	
	Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	P value	Univariable OR (95% CI)	P value
Median SmO <sub>2</sub> , %	0.93 (0.87 to 0.996)	0.039	0.92 (0.82 to 1.04)	0.18	0.96 (0.76 to 1.21)	0.75
Minimum SmO <sub>2</sub> , %	0.97 (0.92 to 1.01)	0.16	0.94 (0.86 to 1.03)	0.20	0.95 (0.75 to 1.22)	0.70
Maximum SmO <sub>2</sub> , %	0.92 (0.85 to 0.99)	0.025	0.90 (0.80 to 1.02)	0.11	0.90 (0.70 to 1.15)	0.41
TW AUC SmO <sub>2</sub> , %×min×h <sup>-1</sup>	1.00 (1.00 to 1.00)	0.15	1.00 (1.00 to 1.01)	0.22	1.00 (0.99 to 1.01)	0.74
Median ScO <sub>2</sub> , %	0.99 (0.91 to 1.06)	0.70	0.92 (0.79 to 1.06)	0.24	0.79 (0.59 to 1.07)	0.13
Minimum ScO <sub>2</sub> , %	0.96 (0.91 to 1.03)	0.26	0.83 (0.69 to 0.98)	0.030	0.10 (0.00 to 5.34)	0.26
Maximum ScO <sub>2</sub> , %	0.97 (0.90 to 1.05)	0.47	0.99 (0.94 to 1.05)	0.82	1.01 (0.96 to 1.06)	0.76
TW AUC ScO <sub>2</sub> , %×min×h <sup>-1</sup>	1.00 (1.00 to 1.01)	0.32	1.00 (1.00 to 1.01)	0.33	1.00 (1.00 to 1.01)	0.32

This table shows the odds of having an outcome (high peak hsTnT or MINS, respectively) for every 1%/one unit increase in the specific StO<sub>2</sub> variable. Multivariable analysis is adjusted for age, sex, BMI, smoking, diabetes, hypertension, previous stroke, chronic lung disease, arrhythmia, valvular disease, chronic kidney disease, length of surgery, osteotomy performed, estimated blood loss, mean arterial blood pressure and mean heart rate.

BMI, body mass index; hsTnT, high-sensitivity troponin T; MINS, myocardial injury after non-cardiac surgery; ScO<sub>2</sub>, cerebral tissue oxygenation; SmO<sub>2</sub>, skeletal muscle tissue oxygenation; StO<sub>2</sub>, tissue oxygenation; TW AUC, time-weighted area under the curve.

was comprehensive and many participants were treated with strong analgesics postoperatively which could be a contributing factor to the lack of ischaemic symptoms in the participants with MINS. The incidence of MINS among the participants in this study was 40%. In comparison the general incidence of MINS in patients undergoing non-cardiac surgery is 8%<sup>4</sup> but this is not restricted to major surgery only and the incidence depends on the cut-off for troponin elevation used. Other groups found similar high incidence of MINS.<sup>28</sup>

### Study limitations

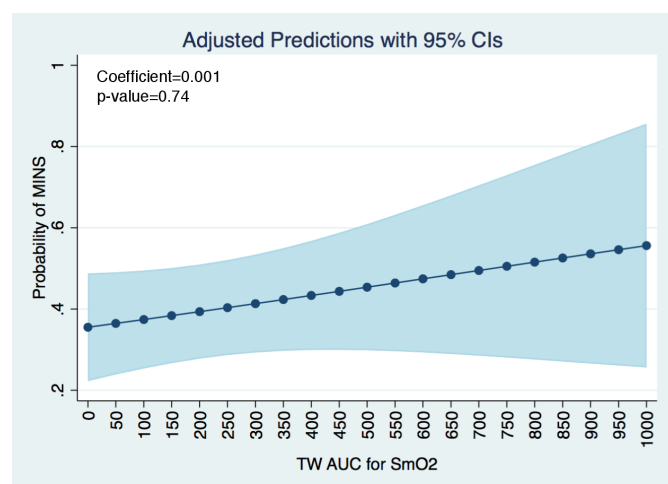
As this was an observational cohort study it was not designed to determine causality between StO<sub>2</sub> and post-operative myocardial injury. The study was not powered for all secondary outcomes, as we based the power

calculation on a study with the outcome composite post-operative complications that included less severe complications (constipation, oliguria, etc).<sup>12</sup>

We found a high incidence of MINS in this study but the number of serious outcome events (eg, death, stroke, non-fatal cardiac, myocardial infarction) were sparse in the 30-day follow-up period. The participants underwent spine surgery which was not emergent, conducted as cancer treatment/tumour resection or indicated by any life-threatening condition. Thus, it is possible that participants were in a better physical condition when scheduled for this type of elective surgery than for other major non-cardiac surgical procedures. Changes in blood pressure and heart rate may trigger MINS. Extensive analyses of associations between these parameters and MINS were not possible in this study.

The NIRS method is non-invasive and tracks StO<sub>2</sub> continuously. However, limitations in regard to the technology has been presented and includes bias regarding skin pigmentation, gender and assumed mixture of venous and arterial blood.<sup>29</sup> With the equipment used in this study it was not possible to obtain data on different Hgb fractions (total Hgb, oxy-Hgb and deoxy-Hgb), which could potentially have qualified the analysis even further. Total blood loss was included in the predefined model to predict MINS but relative changes in Hgb concentrations, including those caused by transfusions, was not accounted for. Interindividual differences in saturation contributes to the difficulty of determining an absolute threshold for tissue hypoxia. In the calculation of the primary predictor of TW AUC for SmO<sub>2</sub> we used the population median for intraoperative SmO<sub>2</sub> as cut-off. The choice of cut-off should be considered when interpreting results of studies investigating the impact of StO<sub>2</sub>.

In summary, in this study StO<sub>2</sub> was not a statistically significant predictor for peak postoperative hsTnT but



**Figure 2** Adjusted prediction curve for time-weighted area under the curve (TW AUC) for skeletal muscle tissue oxygenation (SmO<sub>2</sub>) as predictor for myocardial injury after non-cardiac surgery (MINS).

is a potential predictor for other postoperative complications. Future studies should focus on determining a threshold for StO<sub>2</sub> taking interindividual factors into account and apply NIRS technology with the ability of detecting different Hgb fractions. The frequency of MINS was high (40%) and related to blood loss, suggesting supply-demand mismatch aetiology in spine surgery. StO<sub>2</sub> did not have the power to predict myocardial injury but other intraoperative indicators for supply-demand mismatch should be considered as potential predictors for MINS in future studies.

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