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Monitoring Spinal Cord Tissue Oxygen in Patients with Acute, Severe Traumatic Spinal Cord Injuries

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Study location

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None declared.

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ABSTRACT

OBJECTIVE: To determine the feasibility of monitoring tissue oxygen partial pressure from the injury site in patients with acute, severe traumatic spinal cord injuries.

DESIGN: During surgery to fix the fractured spine, we inserted intradurally at the injury site a pressure probe, a microdialysis catheter and an oxygen electrode to monitor for up to a week intraspinal pressure, spinal cord perfusion pressure, tissue glucose, lactate/pyruvate ratio and oxygen. We analysed 2,213 hours of such data. Follow-up was 6–28 months post-injury.

SETTING: Single-center Neurosurgical and Neurocritical Care units.

SUBJECTS: 26 patients with traumatic spinal cord injuries, American spinal injury association Impairment Scale grades A–C, who had surgery within 72 hours of injury.

INTERVENTIONS: Insertion of subdural oxygen electrode (Licox), pressure probe and microdialysis catheter

MEASUREMENTS AND MAIN RESULTS: The tissue oxygen signal was pulsatile with prominent cardiac frequency component. Increasing the fraction of inspired oxygen by 0.44 caused increase in cord tissue oxygen by 71.8% above baseline within 8.4 minutes. The following were associated with low cord tissue oxygen: high intraspinal pressure (>10mmHg), low spinal cord perfusion pressure (<90mmHg), low tissue glucose (<8mM/L), high tissue lactate/pyruvate ratio (>20) and fever (cord temperature >39^0C *versus* 37–38). Tissue hypoxia also occurred independent of these factors. In patients with motor-incomplete injuries, fluctuations in cord tissue oxygen strongly correlated with fluctuations in limb motor score. Compared with patients who had motor-incomplete outcome at follow-up, in patients with motor-complete outcome, the injured cord spent significantly more hours (1 *vs.* 11%, 30 *vs.* 39%) at low tissue oxygen values (<5, < 20mmHg). Complications were cerebrospinal fluid leak (5/26) and wound infection (1/26).

CONCLUSIONS: Monitoring tissue oxygen after traumatic spinal cord injury is feasible and safe. Our findings support cord tissue oxygen optimization as a novel therapy for spinal cord injury.

INTRODUCTION

Traumatic spinal cord injury is a catastrophic event that affects 0.7–0.8 million new cases annually worldwide (1) and causes disability (paralysis, sensory loss, incontinence, loss of sexual function, hypotension, poikilothermia) (2), morbidity (renal failure, decubitus ulcers, pneumonia, urosepsis) (2) and psychological distress (anxiety, depression, chronic pain) (3). Unlike the management of acute, severe traumatic brain injury, which focuses on reducing secondary damage by monitoring and optimizing intracranial pressure and cerebral perfusion pressure (4), the management of acute, severe traumatic spinal cord injury is limited (5), lacking monitoring techniques to provide physiological information about the injury site.

To facilitate the management of spinal cord injury in the Neurocritical Care Unit, we place a pressure probe intradurally at the injury site to record intraspinal pressure and spinal cord perfusion pressure, analogous to intracranial pressure and cerebral perfusion pressure for traumatic brain injury (6). Intraspinal pressure and spinal cord perfusion pressure are clinically important parameters that correlate with injury site metabolism (6,7) and long-term outcome (8). Interventions to increase spinal cord perfusion pressure improve somatosensory (9) and motor-evoked (10) responses at the injury site, increase limb motor score (7,10), lower the sensory level (11) and improve urinary (12) and anal sphincter (13) functions.

After traumatic brain injury, some units also monitor brain tissue oxygen. Factors other than high intracranial pressure and low cerebral perfusion pressure reduce brain tissue oxygen, e.g. low arterial oxygen, anemia, fever, dysglycemia, hypovolemia, vasospasm and patient transfer (14,15). The benefit of brain tissue oxygen monitoring in brain injured patients is currently being investigated in three randomized trials (BOOST-III (16), OXYTC (17), BONANZA (18)). Unfortunately, the enthusiasm to establish brain tissue oxygen-guided interventions for brain injury has not been mirrored in spinal cord injury where there are no techniques to monitor spinal cord tissue oxygen. Here we demonstrate the feasibility

and safety of monitoring spinal cord tissue oxygen, identify treatable factors associated with cord hypoxia and explore the relation between cord tissue oxygen and neurological outcome.

MATERIALS AND METHODS

Institutional Research Board Approvals. Patients were recruited as part of the Injured Spinal Cord Pressure Evaluation (ISCoPE) study (www.clinicaltrials.gov NCT02721615) at St George's Hospital. Approvals were from the St George's, University of London Joint Research and Enterprise Service and the National Research Ethics Service London–St Giles Committee (10/H0807/23). The study has been performed in accordance with ethical standards, laid down in the 1964 Declaration of Helsinki and its later amendments. Informed consent was obtained from all participants.

Inclusion/exclusion criteria. We included all traumatic spinal cord injury patients recruited into ISCoPE between September 2016 and December 2020. Inclusion criteria are: i) severe traumatic spinal cord injury (American spinal injury association Impairment Scale grade A–C); ii) age 18–70 years; iii) timing between injury and surgery within 72 h. Exclusion criteria are: i) patient unable to consent; ii) other major comorbidities; iii) penetrating injury.

Probe placement. During posterior surgery, a pressure probe (Codman Microsensor Transducer®: Depuy Synthes, Leeds, UK), a microdialysis catheter (CMA61: CMA microdialysis AB, Solna, Sweden) and an oxygen electrode (Licox - CC1P1: Integra, Sophia-Antipolis, France) were inserted under the operating microscope between cord and dura at the site of maximal cord swelling and were secured to the skin using sutures (Fig. 1). For patient management see S-Methods.

Intraspinal pressure and spinal cord perfusion pressure. The pressure probe was connected to a Codman ICP box linked via a ML221 amplifier to a PowerLab data acquisition hardware device, in turn linked to a laptop running the data acquisition and analysis software LabChart v.8 (ADInstruments, Oxford, UK). Blood pressure was recorded from a radial artery catheter connected to the Philips Intellivue MX800 bedside monitor and then to the PowerLab system. Intraspinal pressure and blood pressure signals were sampled at 1 kHz. Spinal cord perfusion pressure was computed as mean arterial pressure minus intraspinal pressure. Intraspinal pressure is the same as intraparenchymal cord pressure at the injury site (19), which differs from cerebrospinal fluid pressure above or below because the swollen cord is compressed against dura thus compartmentalizing the intrathecal space (10,20,21).

Microdialysis. Microdialysis was started postoperatively in the Neurocritical Care Unit as described (22–24). Central nervous system fluid (CMA microdialysis AB) was perfused at 0.3 μL/min using the CMA106 pump (CMA microdialysis AB). Microdialysis vials were changed hourly and analysed using ISCUS Flex (CMA microdialysis AB) for glucose, lactate, and pyruvate. The first two samples from each patient were discarded to allow priming of the microdialysis catheter and stabilization of the metabolite concentrations. 100-fold changes in metabolite concentration, compared with the preceding hour, were excluded from analysis. Our method measures spinal cord surface metabolism at the injury site, which correlates with intraparenchymal injury site metabolism, but differs from metabolites measured from lumbar cerebrospinal fluid (22–24).

Tissue oxygen. The Licox oxygen electrode was connected to a tissue oxygen Monitor (Integra, Integra, Sophia-Antipolis, France), in turn linked to a Philips Intellivue MX800

bedside monitor (Philips, Guildford, UK), which was connected to the PowerLab system. The signal was sampled at 1 kHz. In two patients, a second oxygen electrode was inserted intradurally about 2 cm below the injury site.

Cord tissue oxygen changes. For each ≥5 mmHg change in cord tissue oxygen, the preceding hour was assessed for the following possible causes: change in intraspinal pressure or spinal cord perfusion pressure, spinal cord metabolism, fraction of inspired oxygen, spinal cord temperature or sedation. We assessed whether the change in the putative causative factor could explain the change in cord tissue oxygen.

Cerebrospinal fluid drainage. A lumbar catheter was placed in 11/26 patients at the time of surgery and about 10 mL cerebrospinal fluid was drained on several occasions to evaluate the effect on tissue oxygen. No more than 30 mL of cerebrospinal fluid was drained in a 24-hour period (25).

Limb Motor Score. Patients underwent regular motor limb assessments performed with the patient off sedation or during sedation hold. The motor scores were standardized by subtracting the minimum postoperative motor score for each patient from all motor scores for that patient. Standardized motor scores were compared to cord tissue oxygen values averaged over the hour preceding the neurological assessment.

Statistics. Fourier analysis of the tissue oxygen signal was done using Weka v.3.8.5 (Waikato, New Zealand). www.mycurvefit.com was used to fit linear, exponential, sigmoid and Michaelis-Menten curves with R^2 and P values. The effects of temperature and cerebrospinal fluid drainage on tissue oxygen were evaluated with Student's t-test. The %

hours with tissue oxygen <5 mmHg for different outcomes were compared using χ^2. Data are mean $\pm$ standard error. Statistical tests are noted as not significant (*NS*) or $P < 0.05^{*}$, 0.005^{**}, $0.0005^{\dagger}$, $5 \times 10^{-6\#}$. Figs. 1C, 2 (A, B, D) and S-Figs. 1, 2, 4 use 1 kHz data. Figs. 2C, 3, 4 and S-Fig. 3 use averaged hourly values.

RESULTS

Participants. We recruited 26 patients (Table 1). Most (21/26) are males and most (22/26) are younger than 60 years. There are 14/26 cervical, 10/26 thoracic and 2/26 conus injuries. On admission, 15/26 had grade A, 3/26 grade B and 8/26 grade C injury severity (American spinal injury association Impairment Scale). 22/26 had posterior surgery only, and 4/26 had combined anterior-posterior approach. We analyzed 2,213 hours of monitoring data; on average, each patient was monitored for 85.0 hours (range 3.0–149.0). Patients were followed up at least 6 months (mean 12.9, range 6.0–28.0).

Complications. 5/26 patients had cerebrospinal fluid leak from the probe exit site successfully managed by placing extra skin sutures at the bedside, and 1/26 had wound infection successfully managed with wound washout (S-Table 1). We had no spinal cord damage, hematoma, or meningitis. Non-probe related complications were pneumonia (11/26), urosepsis (2/26), pressure ulcers (3/26), pulmonary embolus (1/26) and dysphagia (1/26).

Cord tissue oxygen signal. The cord tissue oxygen signal has major cardiac and minor respiratory frequency components (S-Fig. 1). Altering the fraction of inspired oxygen influences cord tissue oxygen (Fig. 2A). On average, increasing the fraction of inspired oxygen by 0.48 causes sigmoid rise in cord tissue oxygen to 71.8 % above baseline within 8.4 minutes. Decreasing the fraction of inspired oxygen by 0.44 causes exponential fall in cord

tissue oxygen to 79.0 % below baseline within 6.0 minutes. Increasing the arterial oxygen partial pressure significantly correlated with increase in cord tissue oxygen in a Michaelis-Menten saturation curve relation (Fig. 2C). Increasing the fraction of inspired oxygen also correlated exponentially with increase in cord tissue oxygen. The injury site had lower tissue oxygen than the cord below, with no correlation between the two (Fig. 2D).

Cord tissue oxygen correlates with injury site physiology and metabolism. We observed significant sigmoid correlations between intraspinal pressure, spinal cord perfusion pressure, tissue glucose and tissue lactate/pyruvate ratio *versus* cord tissue oxygen (Fig. 3): As intraspinal pressure rises >5–10 mmHg, cord tissue oxygen falls reaching a minimum at intraspinal pressure 15–20 mmHg. As spinal cord perfusion pressure rises >80–90 mmHg, cord tissue oxygen suddenly rises reaching a maximum at spinal cord perfusion pressure 90–100 mmHg. As tissue glucose increases >4–6 mM/L, cord tissue oxygen progressively rises to a maximum at tissue glucose 8–10 mM. As tissue lactate/pyruvate ratio increases >10–20, cord tissue oxygen progressively falls to a minimum at tissue lactate/pyruvate ratio 40–50. Fever is associated with lower cord tissue oxygen compared with normothermia. Blood transfusion is also associated with significant rise in cord tissue oxygen (6.1$\pm$3.2 mmHg, mean$\pm$standard error), but without significant change in cord metabolism (tissue glucose -0.7$\pm$0.3 mmol/L, tissue lactate/pyruvate ratio -0.6$\pm$2.8) (S-Fig. 2).

Causes of changes in cord tissue oxygen. Rise in intraspinal pressure or drop in spinal cord perfusion pressure was often accompanied by drop in tissue oxygen (S-Fig. 3A): On the left, a transient drop in spinal cord perfusion pressure is followed by a transient drop in tissue oxygen, then rebound hyperoxia. In the middle, a sustained rise in spinal cord perfusion pressure is followed by a sustained rise in tissue oxygen. On the right, a sustained rise in

intraspinal pressure is followed by a sustained drop in tissue oxygen; then, a drop in spinal cord perfusion pressure is followed by a drop in tissue oxygen. We also observed changes in tissue oxygen that are independent of changes in intraspinal pressure and spinal cord perfusion pressure (S-Fig. 3B): a large drop in tissue oxygen is not preceded by change in intraspinal pressure or spinal cord perfusion pressure. Factors that may cause change in tissue oxygen by ≥5 mmHg, ranked in decreasing frequency, are change in cord metabolism, change in intraspinal pressure or spinal cord perfusion pressure, change in the fraction of inspired oxygen, change in sedation, and change in cord temperature (S-Table 2). In more than a third of cases, the cause of tissue oxygen change is unknown.

Effect of lumbar cerebrospinal fluid drainage on cord tissue oxygen. Cerebrospinal fluid drainage had a variable effect on tissue oxygen, ranging from increase by 14.4 mmHg to decrease by -20.8 mmHg (S-Fig. 4). On average, cerebrospinal fluid caused no change in tissue oxygen in 9/11 patients, and caused a significant, but modest, reduction in tissue oxygen in 2/11 patients.

Cord tissue oxygen correlates with neurological status. The injured cord spends significantly more hours at low tissue oxygen values in patients with motor-complete compared with patients with motor-incomplete outcome at follow-up (Fig. 4A). For example, in patients with motor-complete outcome at follow-up, the cord spends 7–21 % hours daily at tissue oxygen <5 mmHg (cord infarction), compared with 0–2 % hours in patients with motor-incomplete outcome. In the eight patients motor-incomplete at presentation, the lower the minimum $p_{sct}O_2$ in the hour preceding the motor examination, the lower the standardized limb motor score (Fig. 4B).

DISCUSSION

We showed that, after spinal cord injury, it is feasible and safe to monitor tissue oxygen from the injury site, analogous to brain tissue oxygen monitoring in brain injury (18,26). Cord tissue oxygen is a key physiological parameter that correlates with injury site physiology, metabolism, and neurological outcome. In our spinal cord injury patients, time spent below tissue oxygen thresholds was strongly associated with outcome, as reported for brain injury (27). The observation that, in patients with motor-incomplete injuries, fluctuations in cord tissue oxygen were accompanied by fluctuations in limb power suggests that cord tissue oxygen may influence spinal cord function. We have also identified factors that influence cord tissue oxygen that may be modified to improve outcome, e.g. increasing the fraction of inspired oxygen or increasing spinal cord perfusion pressure. These are analogous to brain injury, where increasing the fraction of inspired oxygen (28,29) or cerebral perfusion pressure (30,31) augments low brain tissue oxygen. Together, our findings support cord tissue oxygen as a novel therapeutic target for spinal cord injury in Neurocritical Care.

Current management guidelines recommend maintaining mean arterial pressure 85–90 mmHg for the first week after spinal cord injury (5). However, two patients with the same mean arterial pressure, but different intraspinal pressures, will have different spinal cord perfusion pressures. Also, two patients with the same spinal cord perfusion pressure may have different cord tissue oxygen. Multi-modality monitoring overcomes these problems by allowing individualized management (10,22) that may ultimately yield management guidelines for spinal cord injury analogous to brain injury protocols that incorporate both pressure and tissue oxygen monitoring (32,33). Multi-modality monitoring may also be employed to evaluate the impact of therapeutic interventions on the injury site. For example, treating fever in spinal cord injury improves injury site metabolism (assessed using

microdialysis) (24) and cord tissue oxygen (shown here), whereas blood transfusion increases tissue oxygen, but without improving metabolism, in spinal cord (shown here) and brain injury (34).

A limitation of our study is the small numbers of patients (n = 26), though our conclusions are supported by a large dataset (2,213 hours of monitoring, 165 motor examinations) and long follow-up (>6 months). Placing probes at the injury site is safe (35), but requires surgery, which is another limitation. An alternative is to insert probes into the lumbar cerebrospinal fluid, which is technically easy and does not require surgery (36,37). However, there is lack of correlation between intraspinal pressure, spinal cord perfusion pressure and microdialysis values measured at the injury site compared with the lumbar cerebrospinal fluid (25) Draining lumbar cerebrospinal fluid has been proposed as a therapeutic maneuver in spinal cord injury, but it does not effectively reduce intraspinal pressure (25) or improve cord tissue oxygen (shown here) at the injury site probably because the swollen cord is compressed against the dura (38). The effect of durotomy on cord tissue oxygen has not been investigated; however, a randomized, controlled trial termed DISCUS (Duroplasty for Injured Spinal Cord with Uncontrolled Swelling) is underway to evaluate the effect of expansion duroplasty on neurological outcome after spinal cord injury. [https://fundingawards.nihr.ac.uk/award/NIHR130048].

CONCLUSIONS

After spinal cord injury, tissue oxygen monitoring is feasible and safe and allows prompt detection and treatment of injury site hypoxia. We thus propose tissue oxygen-guided treatment as a novel therapy for spinal cord injury.

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FIGURE LEGENDS

Fig. 1. Monitoring technique. 23-year-old male, C5 American spinal injury association grade A (patient no. 89). **A.** Intraoperative photo of exposed dorsal dura at injury site. **B.** Surgical site after wound closure. Drain, wound drain; ISP, intraspinal pressure probe; MD, microdialysis catheter; $p_{sct}O_2$, oxygen probes (at injury site + below); suction, suction tubing. **C.** Multi-modality monitoring from injury site: ISP (intraspinal pressure), SCPP (spinal cord perfusion pressure), $p_{sct}O_2$ (cord tissue oxygen), tissue glucose, LPR (lactate/pyruvate ratio).

Fig. 2. Fraction of inspired oxygen and arterial oxygen *vs.* cord tissue oxygen. A. Effect of oxygen challenge on intraspinal pressure, spinal cord perfusion pressure and cord tissue oxygen in 23-year-old male, C5 American spinal injury association grade A (patient no. 89). **B.** Summary of oxygen challenge data. (*top*) Cord tissue oxygen ($p_{sct}O_2$) *vs.* time after increasing the fraction of inspired oxygen **(**F_iO_2) from 0.38 $\pm$ 0.04 to 0.82 $\pm$ 0.09 (9 repeats, 4 patients) and (*bottom*) decreasing the fraction of inspired oxygen from 0.89 $\pm$ 0.07 to 0.41 $\pm$ 0.04 (8 repeats, 3 patients). **C.** Cord tissue oxygen ($p_{sct}O_2$) *vs.* arterial oxygen (p_aO_2). *Inset:* p_aO_2 *vs.* F_iO_2. **D.** Cord tissue oxygen ($p_{sct}O_2$) *vs.* time. 23-year-old male, C5 American spinal injury association Impairment Scale grade A (patient no. 89). Green, Cord tissue oxygen ($p_{sct}O_2$) at injury site; Black, Cord tissue oxygen ($p_{sct}O_2$) of spinal cord below injury site. *Inset*: $p_{sct}O_2$ at injury site *vs.* $p_{sct}O_2$ below. B, C and D-inset show mean $\pm$ standard error. Regression lines: B-top (sigmoid, $R^2 = 1.00$), B-bottom (exponential decay, $R^2 = 0.99$), C (Michaelis-Menten, $R^2 = 0.83$), C-inset (exponential, $R^2 = 0.98$), D-inset (linear, $R^2 = 0.02$). *NS*, Not significant; $P < 0.005^{**}$, $0.0005^{\dagger}$, $5\times10^{-6\#}$.

Fig. 3. Injury site parameters *vs.* cord tissue oxygen. A. Cord tissue oxygen ($p_{sct}O_2$) *vs.* intraspinal pressure (ISP), $R^2 = 0.94$. **B.** $p_{sct}O_2$ *vs.* spinal cord perfusion pressure (SCPP), $R^2 =$

0.94. **C.** $p_{sct}O_2$ *vs*. tissue glucose, $R^2 = 0.95$. **D.** $p_{sct}O_2$ *vs.* tissue lactate/pyruvate ratio (LPR), $R^2 = 1.00$. Data (A-D) are hourly values, mean$\pm$standard error fitted with sigmoid regression. **E.** $p_{sct}O_2$ readings at spinal cord temperatures 37–38 ^{0}C and $\geq$39 ^{0}C. Individual data points (circles), means (lines). $P < 0.05^*$, $5\times10^{-6\#}$.

Fig. 4. Cord tissue oxygen ($p_{sct}O_2$) correlates with neurological status. A. % of hours with cord tissue oxygen ($p_{sct}O_2$) below threshold *vs.* $p_{sct}O_2$ threshold, for American spinal injury association Impairment Scale (AIS) grade at follow-up (A, B *vs.* C, D) fitted with sigmoid regressions ($R^2 = 1.00$ for both) *Inset*: % of hours with $p_{sct}O_2$ <5 mmHg *vs.* days after injury for AIS at follow-up (A, B *vs.* C, D). **B.** Standardized motor score *vs.* lowest $p_{sct}O_2$ (mmHg) in the hour preceding the motor exam in motor-incomplete patients (AIS grade C) patients. Linear regression, $R^2 = 0.77$. Mean $\pm$ standard error. $P < 0.05^*$, $0.0005^\dagger$, $5\times10^{-6\#}$.

Table 1. Patient details.

Patient No	Age (y)	Sex	TSCI – surgery (h)	Neuro level	AIS (adm)	Surgery	Monitoring (h)	Follow-up (m)	AIS (follow-up)
48	29	M	58.0	C4	A	Post	3	25	B
59	22	M	58.0	T9	A	Post	16	7	A
62	36	F	47.0	T8	B	Post	129	13	C
63	60	M	72.0	T3	B	Post	130	28	C
64	28	F	40.0	C5	A	Post	139	11	A
66	67	M	38.0	C4	C	Post	99	11	C
67	32	M	38.0	C4	C	Post+Ant	147	9	D
68	37	F	23.0	L3	C	Post	87	20	C
69	39	M	39.0	T7	A	Post	114	14	B
70	35	M	39.0	C4	C	Post+Ant	60	11	A
71	27	M	41.0	L1	C	Post	95	6	D
72	50	M	22.0	C5	B	Post	137	19	B
73	47	M	22.0	T8	A	Post	79	12	B
74	57	M	35.0	C4	A	Post	149	8	A
75	66	M	40.0	C4	A	Post	117	7	A
76	46	M	18.0	T12	A	Post	33	19	C
78	26	M	39.0	C6	A	Post+Ant	34	12	B
80	55	M	45.0	T7	A	Post	79	23	B
81	54	M	69.0	C4	C	Post	149	17	D
83	51	M	49.5	T7	A	Post	50	17	A
84	22	M	70.0	C6	C	Post+Ant	67	17	D
85	54	F	38.0	C3	C	Post	58	8	C
86	54	F	45.0	C3	A	Post	15	7	C
87	44	M	24.0	T4	A	Post	43	7	A
88	61	M	48.0	T11	A	Post	54	6	A
89	23	M	15.5	C5	A	Post	130	6	B

Adm, admission; A, anterior; AIS, American spinal injuries association Impairment Scale; F, female; h, hours; m, months; M, male; Neuro, neurological; No, number; P, posterior; y, years

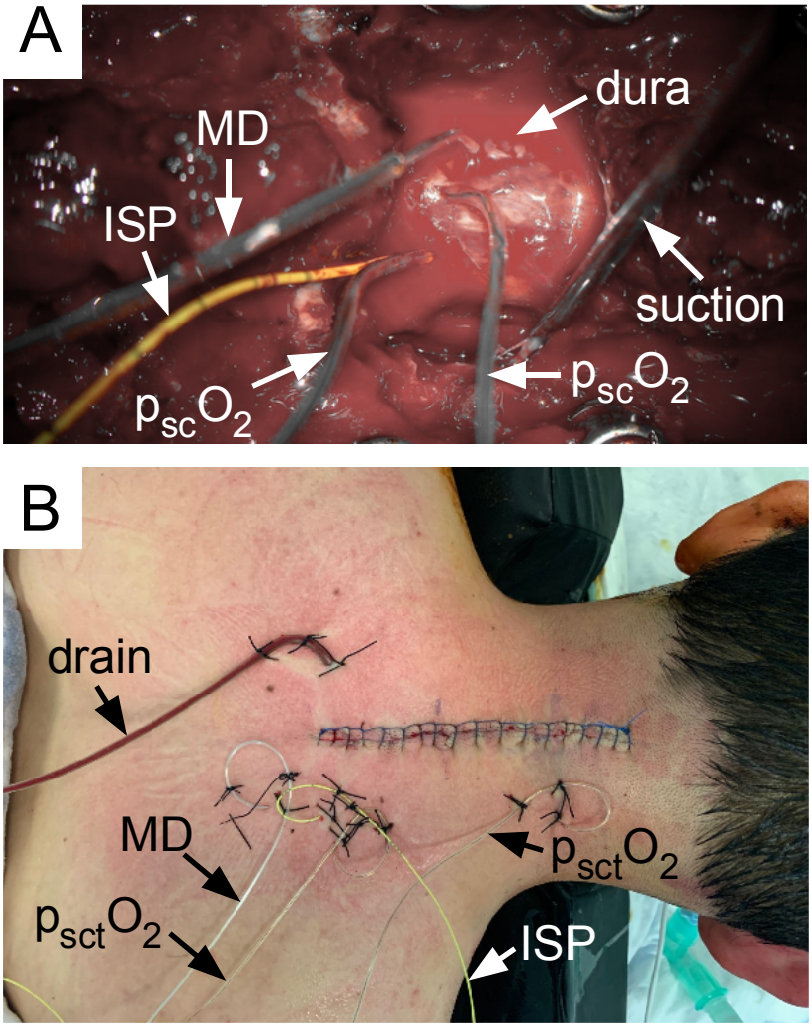

A
dura
MD
ISP
suction
$p_{sc}O_2$
$p_{sc}O_2$
B
drain
MD
$p_{sct}O_2$
$p_{sct}O_2$
ISP
C
ISP (mmHg)
30
10
SCPP (mmHg)
90
50
$p_{sct}O_2$ (mmHg)
60
0
Glucose (mM)
12
4
LPR
60
20
6 h

FIGURE 1

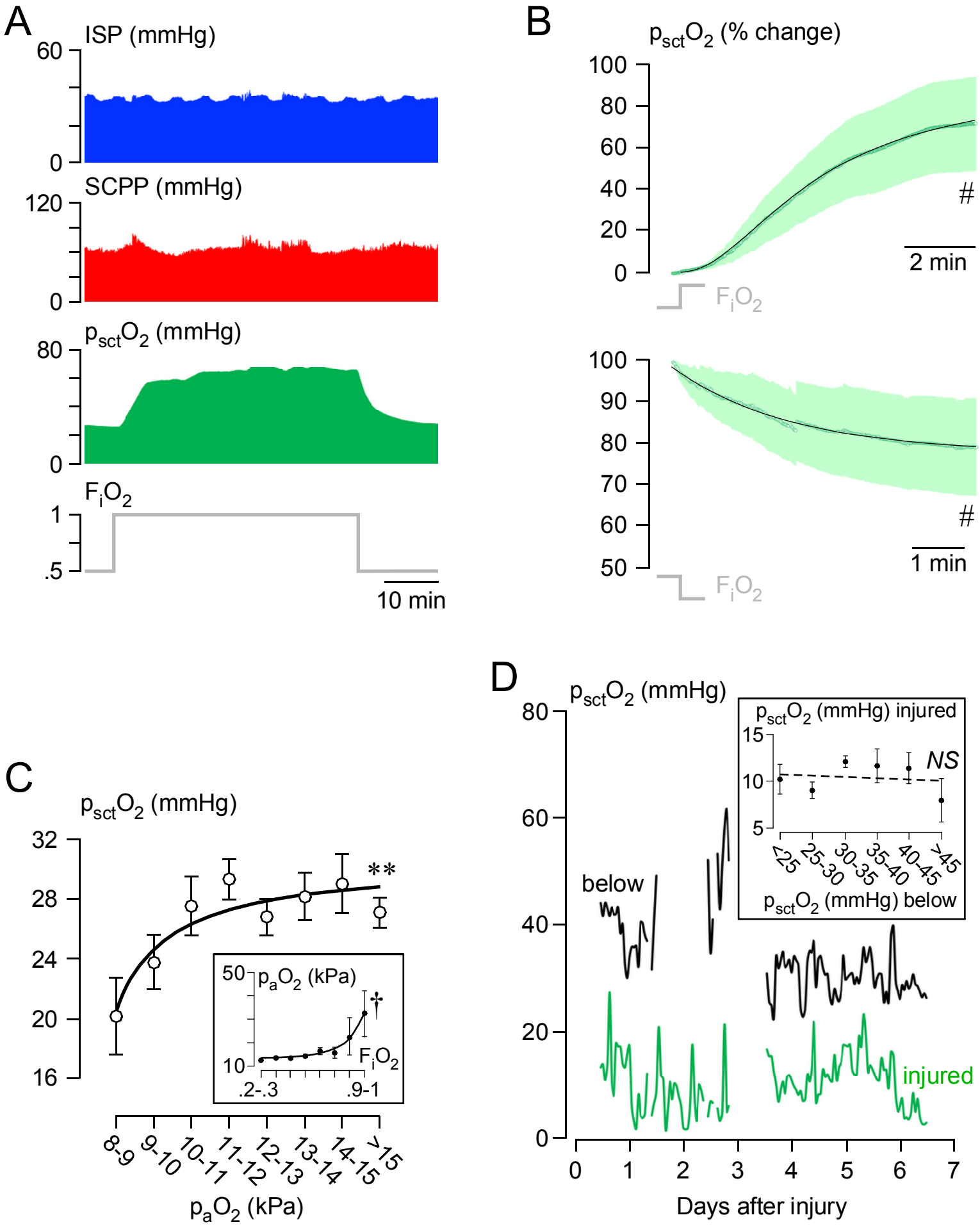

A
ISP (mmHg)
60
0
SCPP (mmHg)
120
0
$p_{sct}O_2$ (mmHg)
80
0
F_iO_2
1
.5
10 min
B
$p_{sct}O_2$ (% change)
100
80
60
40
20
0
#
2 min
F_iO_2
100
90
80
70
60
50
#
1 min
F_iO_2
C
$p_{sct}O_2$ (mmHg)
32
28
24
20
16
**
50
p_aO_2 (kPa)
10
F_iO_2
.2-.3
.9-1
†
8-9
9-10
10-11
11-12
12-13
13-14
14-15
>15
p_aO_2 (kPa)
D
$p_{sct}O_2$ (mmHg)
80
60
40
20
0
below
injured
$p_{sct}O_2$ (mmHg) injured
15
10
5
NS
<25
25-30
30-35
35-40
40-45
>45
$p_{sct}O_2$ (mmHg) below
0
1
2
3
4
5
6
7
Days after injury

FIGURE 2

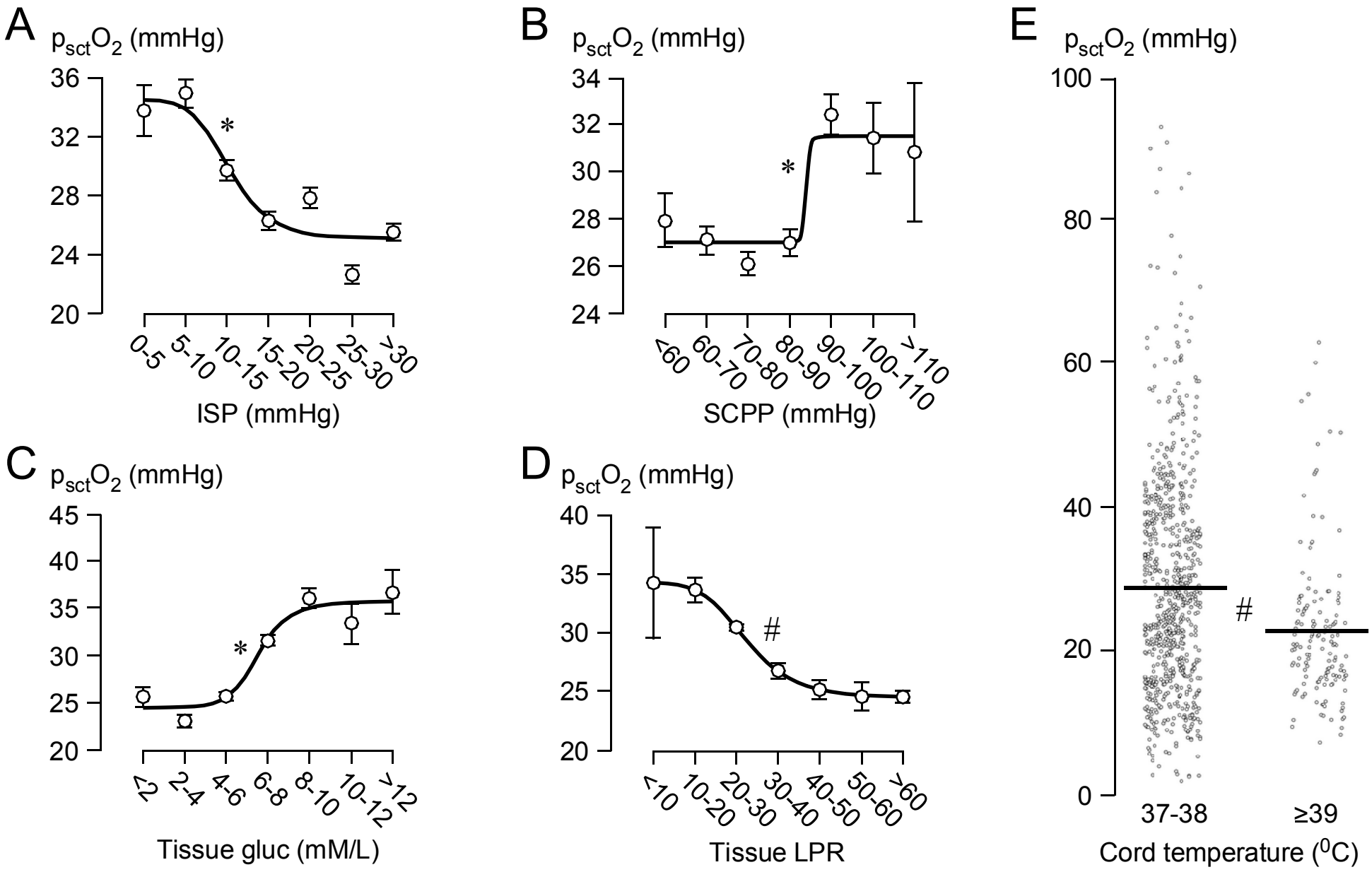
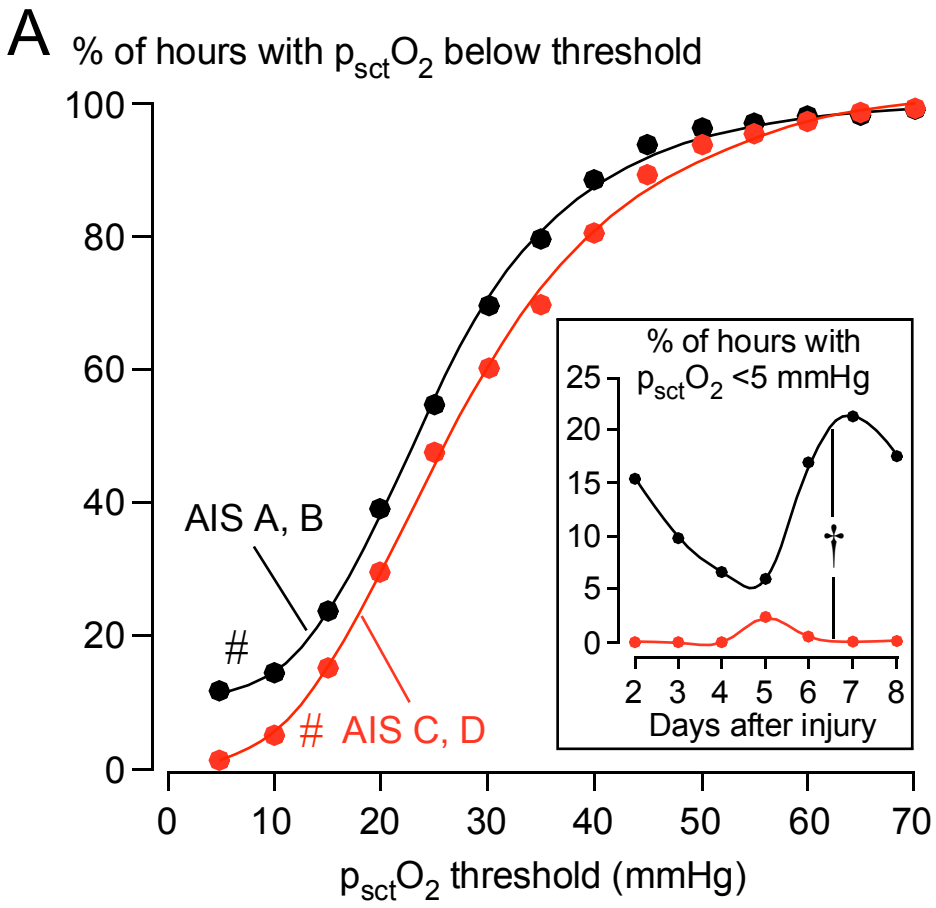

A
$p_{sct}O_2$ (mmHg)
36
32
28
24
20
*
0-5
5-10
10-15
15-20
20-25
25-30
>30
ISP (mmHg)
B
$p_{sct}O_2$ (mmHg)
34
32
30
28
26
24
*
<60
60-70
70-80
80-90
90-100
100-110
>110
SCPP (mmHg)
C
$p_{sct}O_2$ (mmHg)
45
40
35
30
25
20
*
<2
2-4
4-6
6-8
8-10
10-12
>12
Tissue gluc (mM/L)
D
$p_{sct}O_2$ (mmHg)
40
35
30
25
20
#
<10
10-20
20-30
30-40
40-50
50-60
>60
Tissue LPR
E
$p_{sct}O_2$ (mmHg)
100
80
60
40
20
0
#
37-38
≥39
Cord temperature (^{0}C)

FIGURE 3


A
% of hours with $p_{sct}O_2$ below threshold
100
80
60
40
20
0
AIS A, B
#
AIS C, D
0
10
20
30
40
50
60
70
$p_{sct}O_2$ threshold (mmHg)
% of hours with
$p_{sct}O_2$ <5 mmHg
25
20
15
10
5
0
†
2
3
4
5
6
7
8
Days after injury

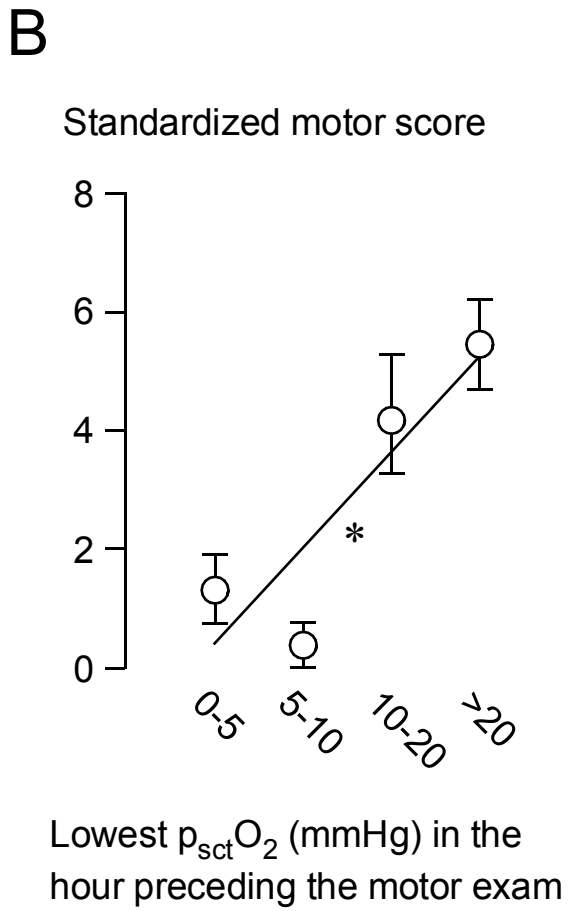

B
Standardized motor score
8
6
4
2
0
*
0-5
5-10
10-20
>20
Lowest $p_{sct}O_2$ (mmHg) in the
hour preceding the motor exam

FIGURE 4

SUPPLEMENTARY METHODS

Neurosurgical management. Patients were admitted to the neurosurgical unit at St. George's Hospital and underwent International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) assessments by a trained neurosurgical resident, which was repeated at follow-up. Surgery was performed by a neurosurgeon. The type of surgery was based on surgeon preference and included posterior approach with lateral mass (cervical) or pedicle (thoracic) screw and rod fixation (Stryker Oasys for cervical, Stryker Xia for thoracic; Stryker, Newbury, Berkshire, England). Patients had CT + MRI of the spine before surgery, CT at 48 hours and MRI at 1 – 2 weeks postoperatively.

NeuroICU management. Post-operatively, patients were admitted to the Neuro Intensive Care Unit and were reviewed daily by the Neuro Intensive Care Unit and Neurosurgery teams. Ventilation was supported as appropriate, including timely extubation post-operatively or early tracheostomy. The wound drain was kept for the duration of monitoring 'on gravity'. Patients was turned in bed to avoid decubitus ulcers and given foot pumps and prophylactic low-molecular weight heparin (commenced at 24 after surgery) to reduce the risk of venous thromboembolism. Mean arterial Pressure management was at the discretion of the Neuro Intensive Care Unit consultant who was blinded to probe values. The probes were removed in the Neuro Intensive Care Unit.

SUPPLEMENTARY TABLES

S-TABLE 1. Complications of monitoring.

Complication	No. of patients (/26)	Patients (%)	Comment
SURGICAL / PROBE RELATED			
CSF leak	5	19.2	Required bedside suture. No one returned to operating theatre
Hematoma / cord damage from probes	0	0.0	
Wound infection	1	3.8	Return to operating theatre for wound washout
Meningitis	0	0.0	
NON-SURGICAL			
Chest infection	11	42.3	One ICU readmission (immunocompromised, DM, stage IV CKD, obesity)
Urine infection	2	7.7	
Pulmonary Embolus	1	3.8	
Pressure Ulcer	3	11.5	Conservatively managed
Dysphagia	1	3.8	FEES confirmed; from TSCI; PEG insertion

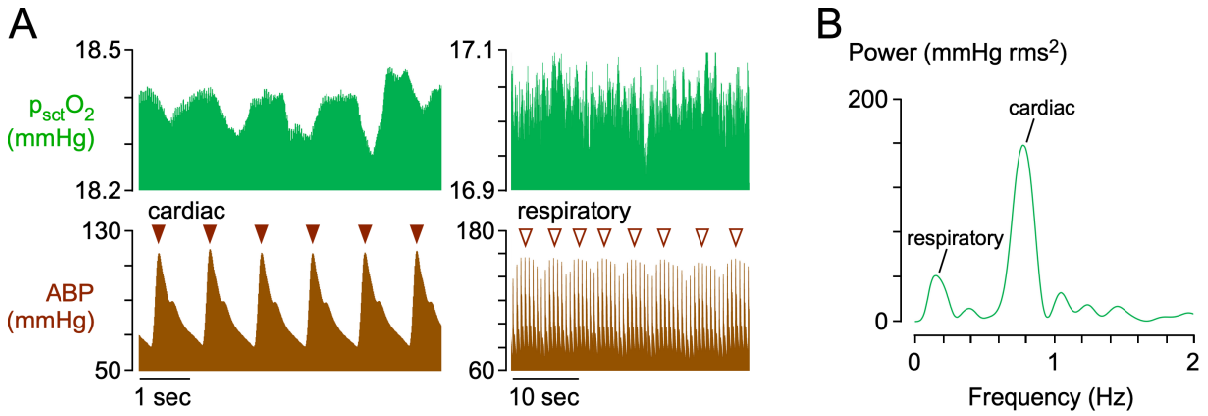
CSF, Cerebro Spinal Fluid; No., number. ICU, Intensive Care Unit; CKD, Chronic Kidney Disease; DM, diabetes mellitus; FEES, Fibre-optic Endoscopic Evaluation of Swallowing; No, number; TSCI, traumatic spinal cord injury; PEG, percutaneous endoscopic gastrostomy

S-TABLE 2. Possible causes of changes in the cord tissue oxygen signal.

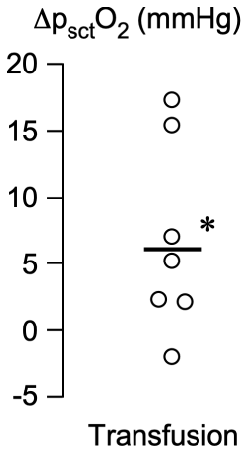
Possible cause	Number	%
Unknown	134	36.7
Change in cord metabolism	83	22.7
Change in ISP and/or SCPP	82	22.5
Change in F_iO_2	36	9.9
Change in sedation	18	4.9
Change in cord temperature	12	3.3
TOTAL	365	100.0

F_iO_2, fraction of inspired oxygen; ISP, Intra Spinal Pressure, SCPP, Spinal Cord Perfusion Pressure

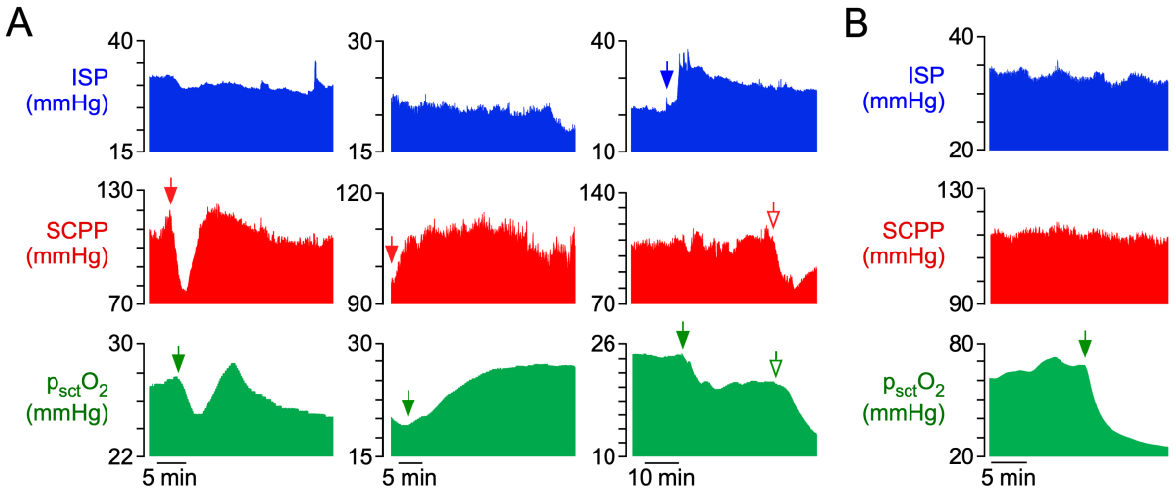
SUPPLEMENTARY FIGURES



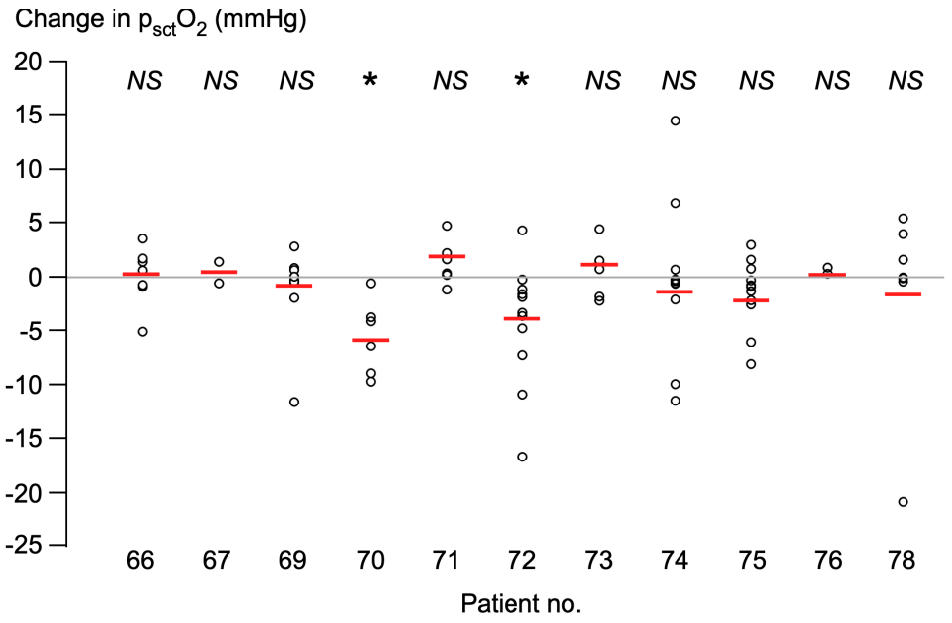
S-FIG. 1. Properties of $p_{sct}O_2$ signal. A. (*top, green*) $p_{sct}O_2$ signal and (*bottom, brown*) corresponding blood pressure signal. Cardiac (closed arrowheads) and respiratory (open arrowheads) pulsations. **B.** Fast Fourier Transform (power *vs.* frequency) of $p_{sct}O_2$ signal with respiratory and cardiac peaks. 50-year-old male, C5 AIS grade B injury (patient 72).



S-FIG. 2. Change in spinal cord tissue oxygen($p_{sct}O_2$) associated with blood transfusion (mean of 2 hours after minus mean of 2 hours before transfusion).



S-FIG. 3. Fluctuations in $p_{sct}O_2$. A. Changes in $p_{sct}O_2$ (green) preceded by changes in ISP (blue) and/or in SCPP (red): (*left*) Fall in SCPP (onset at red arrow) followed by fall in $p_{sct}O_2$ (onset at green arrow). (*middle*) Rise in SCPP (onset at red arrow) followed by rise in $p_{sct}O_2$ (onset at green arrow). (*right*) Rise in ISP (onset at blue closed arrow) followed by fall in $p_{sct}O_2$ (onset at green closed arrow); then, fall in SCPP (onset at red open arrow) followed by fall in $p_{sct}O_2$ (onset at green open arrow). 36-year-old female, T8 AIS grade B injury (patient 62). **B.** Change in $p_{sct}O_2$ (green) not associated with change in ISP (blue) or SCPP (red). Onset of drop in $p_{sct}O_2$ at green arrow. 60-year-old male, T3 AIS grade B injury (patient 63).



S-FIG. 4. Effect of cerebrospinal fluid drainage on cord tissue oxygen. Plot of change in cord tissue oxygen ($p_{sct}O_2$) from draining 10 mL lumbar cerebrospinal fluid (circles are individual values, red lines are means) from 11/26 patients. $P < 0.05^{*}$; *NS*, not significant.