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

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OBJECTIVES: To determine the feasibility of monitoring tissue oxygen tension from the injury site ($p_{sct}O_2$) in patients with acute, severe traumatic spinal cord injuries.

DESIGN: We inserted at the injury site a pressure probe, a microdialysis catheter, and an oxygen electrode to monitor for up to a week intraspinal pressure (ISP), spinal cord perfusion pressure (SCPP), tissue glucose, lactate/pyruvate ratio (LPR), and $p_{sct}O_2$. We analyzed 2,213 hours of such data. Follow-up was 6–28 months postinjury.

SETTING: Single-center neurosurgical and neurocritical care units.

SUBJECTS: Twenty-six patients with traumatic spinal cord injuries, American spinal injury association Impairment Scale A–C. Probes were inserted within 72 hours of injury.

INTERVENTIONS: Insertion of subarachnoid oxygen electrode (Licox; Integra LifeSciences, Sophia-Antipolis, France), pressure probe, and microdialysis catheter.

MEASUREMENTS AND MAIN RESULTS: $p_{sct}O_2$ was significantly influenced by ISP ($p_{sct}O_2$ 26.7 ± 0.3 mm Hg at ISP > 10 mmHg vs $p_{sct}O_2$ 22.7 ± 0.8 mm Hg at ISP ≤ 10 mm Hg), SCPP ($p_{sct}O_2$ 26.8 ± 0.3 mm Hg at SCPP < 90 mm Hg vs $p_{sct}O_2$ 32.1 ± 0.7 mm Hg at SCPP ≥ 90 mm Hg), tissue glucose ($p_{sct}O_2$ 26.8 ± 0.4 mm Hg at glucose < 6 mM vs 32.9 ± 0.5 mm Hg at glucose ≥ 6 mM), tissue LPR ($p_{sct}O_2$ 25.3 ± 0.4 mm Hg at LPR > 30 vs $p_{sct}O_2$ 31.3 ± 0.3 mm Hg at LPR ≤ 30), and fever ($p_{sct}O_2$ 28.8 ± 0.5 mm Hg at cord temperature 37–38°C vs $p_{sct}O_2$ 28.7 ± 0.8 mm Hg at cord temperature ≥ 39°C). Tissue hypoxia also occurred independent of these factors. Increasing the F_{IO_2} by 0.48 increases $p_{sct}O_2$ by 71.8% above baseline within 8.4 minutes. In patients with motor-incomplete injuries, fluctuations in $p_{sct}O_2$ correlated with fluctuations in limb motor score. The injured cord spent 11% (39%) hours at $p_{sct}O_2$ less than 5 mm Hg (< 20 mm Hg) in patients with motor-complete outcomes, compared with 1% (30%) hours at $p_{sct}O_2$ less than 5 mm Hg (< 20 mm Hg) in patients with motor-incomplete outcomes. Complications were cerebrospinal fluid leak (5/26) and wound infection (1/26).

CONCLUSIONS: This study lays the foundation for measuring and altering spinal cord oxygen at the injury site. Future studies are required to investigate whether this is an effective new therapy.

KEY WORDS: Licox, microdialysis, monitoring, perfusion pressure, spinal cord injury, tissue oxygen

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, and poikilothermia) (2), morbidity (renal failure, decubitus ulcers, pneumonia, and urosepsis) (2), and psychologic distress (anxiety, depression, and 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

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spinal cord injury is limited (5), lacking monitoring techniques to provide physiologic 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). We use the Codman intracranial pressure (ICP) microsensor (Integra LifeSciences, Sophia-Antipolis, France) that has little (2 mm Hg) drift in 108 hours (7). Intraspinal pressure and spinal cord perfusion pressure are clinically important parameters that correlate with injury site metabolism (8) and long-term outcome (9). Interventions to increase spinal cord perfusion pressure improve somatosensory (10) and motor-evoked (11) responses at the injury site, increase limb motor score (11, 12), lower the sensory level (13), and improve urinary (14) and anal sphincter (15) 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, for example, low arterial oxygen, anemia, fever, dysglycemia, hypovolemia, vasospasm, and patient transfer (16, 17). The benefit of brain tissue oxygen monitoring in brain injured patients is currently being investigated in three randomized trials (Brain Oxygen optimization in Severe Traumatic brain injury, Phase III [BOOST-III [18], Comparison of strategies for monitoring and treating patients at the early phase of severe traumatic brain injury [OXY-TC] [19], and Brain Oxygen Neuromonitoring in Australia and New Zealand Assessment [BONANZA] [20]). 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 used the Licox oxygen probe that has no significant drift for at least 5 days (21). We demonstrate the feasibility of monitoring spinal cord tissue oxygen, identify treatable factors associated with cord hypoxia, and explore the relation between cord tissue oxygen and neurologic 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: 1) severe traumatic spinal cord injury (American spinal injury association Impairment Scale [AIS] grade A–C), 2) age 18–70 years, and 3) timing between injury and surgery within 72 hours. Exclusion criteria are: 1) patient unable to consent, 2) other major comorbidities, and 3) penetrating injury.

Probe Placement

During posterior surgery, a pressure probe (Codman Microsensor Transducer; Depuy Synthes, Leeds, United Kingdom), a microdialysis catheter (CMA61; clinical microdialysis analyzer [CMA] microdialysis AB, Solna, Sweden), and an oxygen electrode (Licox combined oxygen and temperature catheter [CC1P1]; Integra LifeSciences) were inserted under the operating microscope between cord and arachnoid at the site of maximal cord swelling and were secured to the skin using sutures (**Fig. 1**). For patient management, see **Supplemental Methods** (http://links.lww.com/CCM/G947).

Intraspinal Pressure and Spinal Cord Perfusion Pressure

The pressure probe was connected to a Codman ICP box linked via a bridge amplifier (ML221) to a PowerLab data acquisition hardware device (AD Instruments, Oxford, United Kingdom), in turn linked to a laptop running the data acquisition and analysis software LabChart Version 8 (AD Instruments). Blood pressure was recorded from a radial artery catheter connected to a Philips bedside monitor (Intellivue MX800; Philips, Guildford, United Kingdom) and then to the PowerLab system. Intraspinal pressure and blood pressure signals

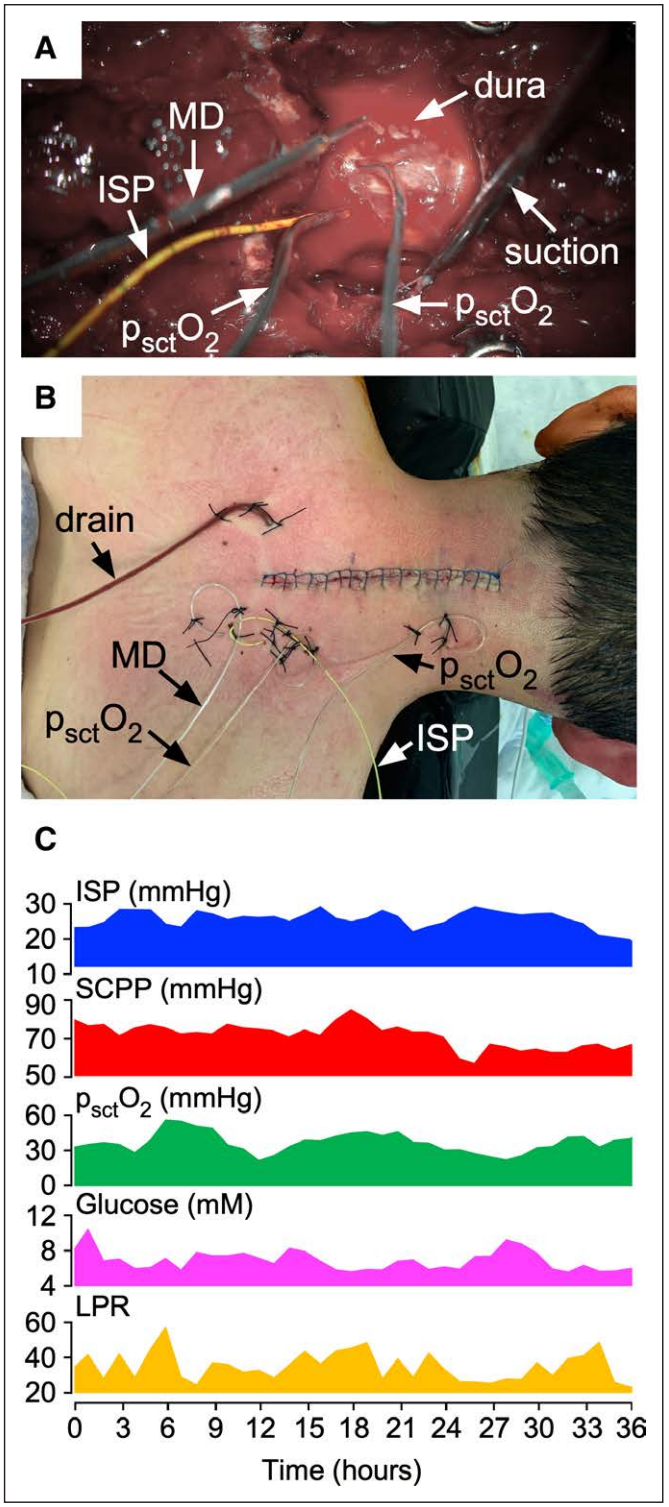

Figure 1. Monitoring technique. A 23-yr-old male, C5 American spinal injury association Impairment Scale grade A (patient no. 89). **A**, Intraoperative photo of exposed dorsal dura at injury site. **B**, Surgical site after wound closure. **C**, Multimodality monitoring from injury site: intraspinal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

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 (22), which differs from cerebrospinal fluid pressure above or below because the swollen cord is compressed against dura, thus compartmentalizing the intrathecal space (11, 22–24).

Microdialysis

Microdialysis was started postoperatively in the Neurocritical Care Unit as described (8, 25, 26). CNS fluid (CMA microdialysis AB) was perfused at 0.3 µL/min using the CMA106 pump (CMA microdialysis AB). Microdialysis vials were changed hourly and analyzed using ISCUSflex microdialysis analyzer (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. Hundred-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 (8, 25, 26).

Tissue Oxygen

The Licox oxygen electrode was connected to a tissue oxygen Monitor (Integra LifeSciences), in turn linked to a Philips Intellivue MX800 bedside monitor, 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 greater than or equal to 5-mm Hg 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, F_{IO_2}, 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 of 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 (27).

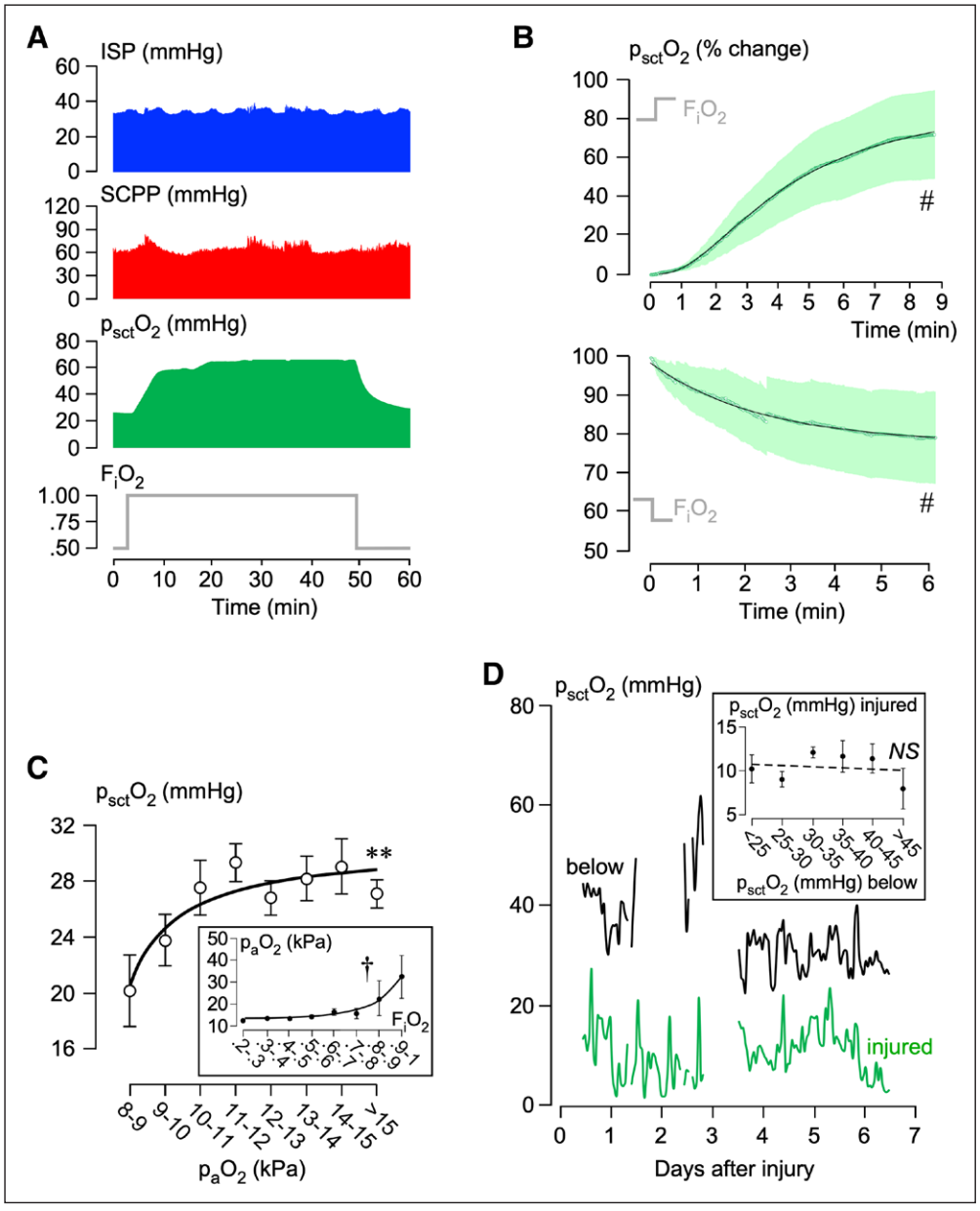

Figure 2. F_{IO_2} and Pa_{O_2} versus cord tissue oxygen ($p_{sct}O_2$). **A**, Effect of oxygen challenge on intraspinal pressure (ISP), spinal cord perfusion pressure (SCPP), and $p_{sct}O_2$ in 23-yr-old male, C5 American spinal injury association Impairment Scale grade A (patient no. 89). **B**, Summary of oxygen challenge data. $p_{sct}O_2$ versus time after (*top*) increasing the F_{IO_2} from 0.38 ± 0.04 to 0.82 ± 0.09 (nine repeats and four patients) and (*bottom*) decreasing the F_{IO_2} from 0.89 ± 0.07 to 0.41 ± 0.04 (eight repeats and three patients). **C**, $p_{sct}O_2$ versus Pa_{O_2}. *Inset:* Pa_{O_2} versus F_{IO_2}. **D**, $p_{sct}O_2$ versus time. Twenty-three-yr-old male, C5 American Spinal Injury Association Impairment Scale grade A (patient no. 89). *Green*: $p_{sct}O_2$ at injury site. *Black*: $p_{sct}O_2$ of spinal cord below injury site. *Inset*: $p_{sct}O_2$ at injury site versus $p_{sct}O_2$ below. **B**–**D** (*inset*): Mean ± SE. 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, $R^2 = 0.98$), and **D** (*inset*) (linear, $R^2 = 0.02$). ¨$p < 0.005$, †0.0005, #5×10^{-6}. NS = not significant.

Limb Motor Score

Patients underwent regular AIS motor limb assessments with the patient off sedation or during sedation hold. Motor scores were compared with cord tissue oxygen values in the hour preceding the neurologic assessment.

Statistics

Fourier analysis of the tissue oxygen signal was done using Weka Version 3.8.5 (Waikato, New Zealand). www.mycurvefit.com was used to fit linear, quadratic, 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 t test. The % hours with tissue oxygen less than 5 mm Hg for different outcomes were compared using chi-square test. Data are mean ± SE. Statistical tests are noted as not significant or $p < 0.05$, 0.005, 0.0005, 5×10^{-6}. **Figures 1*C***, **2*A***, ***B***, and ***D***, and **S-Figures 1, 2**, and **4** (http://links.lww.com/CCM/G947) use 1-kHz data. **Figures 2*C***, **3**, and **4**, and **S-Figure 3** (http://links.lww.com/CCM/G947) use averaged hourly values.

RESULTS

Participants

We recruited 26 patients (**Table 1**). Most are males (21/26) and most are younger than 60 years (22/26). There are 14 of 26 cervical, 10 of 26 thoracic, and two of 26 conus injuries. At admission, 15 of 26 had grade A, three of 26 grade B, and eight of 26 grade C injury severities (AIS). Twenty-two of 26 had posterior surgery only, and four of 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 hr). Patients were followed up at least 6 months (mean, 12.9 mo; range, 6.0–28.0 mo).

Complications

Five of 26 patients had cerebrospinal fluid leak from the probe exit site successfully managed by placing extra skin sutures at the bedside, and one of 26 had wound infection successfully managed with wound washout (**S-Table 1**, http://links.lww.com/CCM/G947). We had no spinal cord damage, hematoma, or meningitis. Nonprobe-related complications were pneumonia

TABLE 1.
Patient Details

Patient No.	Age (yr)	Sex	TSCI – Surgery (hr)	Neuro Level	AIS (Admission)	Surgery	Monitoring (hr)	Follow-Up (mo)	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

AIS = American spinal injuries association Impairment Scale, Ant = anterior, F = female, M = male, Neuro = neurological, Post = posterior.

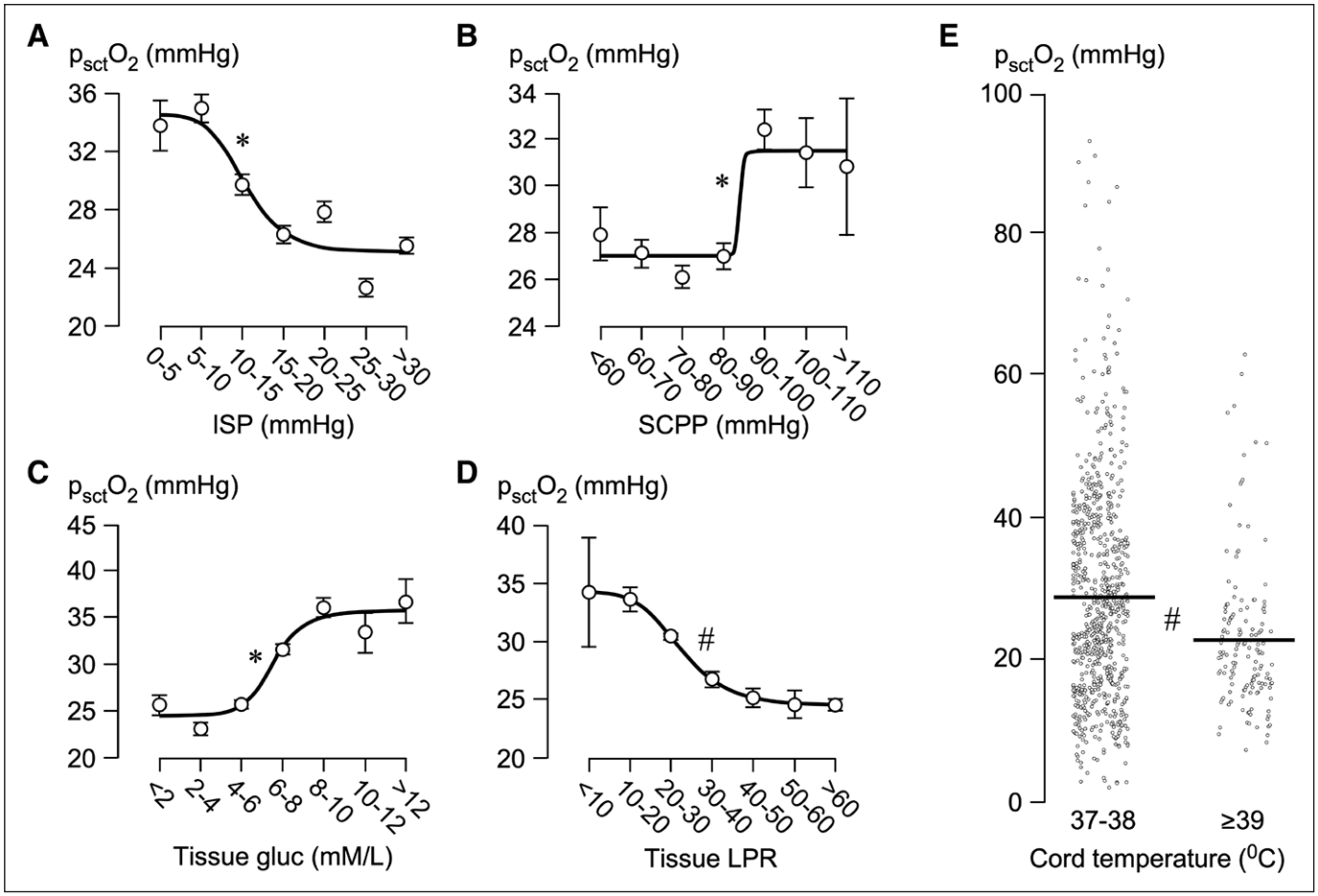

Figure 3. Injury site parameters versus cord tissue oxygen. **A**, Cord tissue oxygen ($p_{sct}O_2$) versus intraspinal pressure (ISP), $R^2 = 0.94$. **B**, $p_{sct}O_2$ versus spinal cord perfusion pressure (SCPP), $R^2 = 0.94$. **C**, $p_{sct}O_2$ versus tissue glucose, $R^2 = 0.95$. **D**, $p_{sct}O_2$ versus tissue lactate/pyruvate ratio (LPR), $R^2 = 1.00$. Data (**A**–**D**) are hourly values, mean ± SE fitted with sigmoid regression. **E**, $p_{sct}O_2$ readings at spinal cord temperatures 37–38°C and greater than or equal to 39°C. Individual data points (*circles*) and means (*lines*). $p < 0.05^*$, $5 \times 10^{-6\#}$.

(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, http://links.lww.com/CCM/G947). Altering the FIO_2 influences cord tissue oxygen (Fig. 2*A*). On average, increasing the FIO_2 by 0.48 causes sigmoid rise in cord tissue oxygen to 71.8% above baseline within 8.4 minutes. Decreasing the FIO_2 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. 2*C*). Increasing the FIO_2 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. 2*D*).

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 greater than 5–10 mm Hg, cord tissue oxygen falls reaching a minimum at intraspinal pressure 15–20 mm Hg. As spinal cord perfusion pressure rises greater than 80–90 mm Hg, cord tissue oxygen suddenly rises reaching a maximum at spinal cord perfusion pressure 90–100 mm Hg. As tissue glucose increases greater than 4–6 mM/L, cord tissue oxygen progressively rises to a maximum at tissue glucose 8–10 mM. As tissue

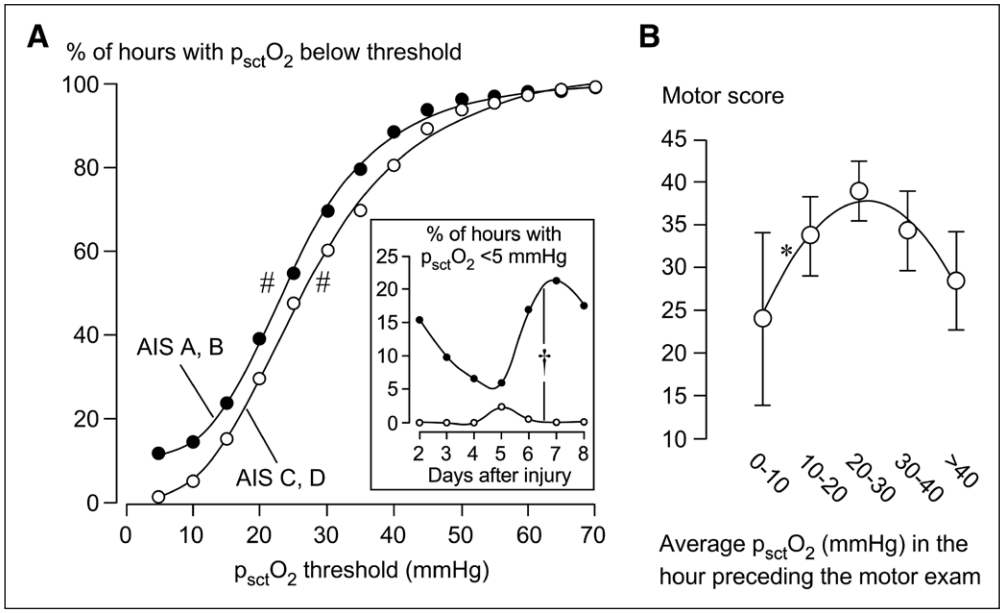

Figure 4. Cord tissue oxygen ($p_{sct}o_2$) correlates with neurologic status. **A**, Percentage of hours with $p_{sct}o_2$ below threshold versus $p_{sct}o_2$ threshold, for American spinal injury association Impairment Scale (AIS) grade at follow-up (**A** and **B** vs **C** and **D**) fitted with sigmoid regressions ($R^2 = 1.00$ for both). *Inset*: Percentage of hours with $p_{sct}o_2$ less than 5 mm Hg versus days after injury for AIS at follow-up (**A** and **B** vs **C** and **D**). **B**, Motor score versus average $p_{sct}o_2$ (mm Hg) in the hour preceding the motor examination in motor-incomplete patients (AIS grade C) patients. Quadratic regression, $R^2 = 0.97$. Mean ± SE. $^{*}p < 0.05$, $^{\dagger}0.0005$, $^{\#}5 \times 10^{-6}$.

lactate/pyruvate ratio increases greater than 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 ± 3.2 mm Hg, mean ± SE), but without significant change in cord metabolism (tissue glucose, –0.7 ± 0.3 mmol/L; tissue lactate/pyruvate ratio, –0.6 ± 2.8) (S-Fig. 2, http://links.lww.com/CCM/G947).

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. We also observed changes in tissue oxygen that are independent of changes in intraspinal pressure and spinal cord perfusion pressure. Examples are shown in S-Figure 3 (http://links.lww.com/CCM/G947). Factors that may cause change in tissue oxygen by greater than or equal to 5 mm Hg, ranked in decreasing frequency, are change in cord metabolism, change in intraspinal pressure or spinal cord perfusion pressure, change in the F_{IO_2}, change in sedation, and change in cord temperature (**S-Table 2**, http://links.lww.com/CCM/G947). 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 mm Hg to decrease by –20.8 mm Hg (S-Fig. 4, http://links.lww.com/CCM/G947). On average, cerebrospinal fluid caused no change in tissue oxygen in nine of 11 patients and caused a significant, but modest, reduction in tissue oxygen in two of 11 patients.

Cord Tissue Oxygen Correlates With Neurologic 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. 4*A***). For example, in patients with motor-complete outcome at follow-up, the cord spends 7–21% hours daily at tissue oxygen less than 5 mm Hg (cord infarction), compared with 0–2% hours in patients with motor-incomplete outcome. In the eight motor-incomplete patients at presentation, we observed an inverted U-shaped relationship between the limb motor score versus the average tissue oxygen tension from the injury site ($p_{sct}o_2$) in the hour preceding each motor examination (Fig. 4*B*).

DISCUSSION

We showed that, after spinal cord injury, it is feasible to monitor tissue oxygen from the injury site, analogous to brain tissue oxygen monitoring in brain injury (20, 28). Cord tissue oxygen is a key physiologic parameter

that correlates with injury site physiology, metabolism, and neurologic outcome. In our spinal cord injury patients, time spent below tissue oxygen thresholds was associated with long-term outcome, as reported for brain injury (28). 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. The inverted U-shaped relationship between motor score and cord tissue oxygen suggests that not only hypoxia but also hyperoxia may impair motor function. We have also identified factors that influence cord tissue oxygen that may be modified to improve outcome, for example, increasing the FIO_2 or increasing spinal cord perfusion pressure. These appear analogous to brain injury, where increasing the FIO_2 (29, 30) or cerebral perfusion pressure (31) augments low brain tissue oxygen.

The Licox oxygen probe tip comprises a cylindrical polyethylene membrane ~18 mm^2 that contains two polarographic electrodes and an electrolyte solution (**S-Fig. 5*A***, http://links.lww.com/CCM/G947). Oxygen diffuses through this membrane to reach the electrodes where it is electrolytically reduced using revoxode technology that is the chemical reaction at the electrode tips is reversible. This means that there is no calibration "drift" with time, ensuring accurate measurement over days. We did not place the oxygen electrode intraparenchymally to avoid causing further spinal cord damage. Studies of other organs indicate that monitoring surface tissue oxygen provides accurate information about tissue perfusion and viability. Such studies include intraoperative monitoring of surface tissue oxygen from human brain during clipping of a middle cerebral artery aneurysm (32), in various brain tumors, in edematous brain, and in arteriovenous malformations (33). Intraoperative surface tissue oxygen monitoring also detects changes in tissue perfusion in liver before and after portacaval shunting, in kidney during nephrectomy, in normal versus gangrenous bowel (32), and in graded ischemic regions of bowel (34). In our study, the injured cord is swollen and compressed against the dura with the oxygen probe sandwiched between cord and dura. Because the dura is largely metabolically inactive, the electrodes primarily detect oxygen that diffuses into the probe from the adjacent cord (**S-Fig. 5*B***, http://links.lww.com/CCM/G947). If the cord is surrounded by cerebrospinal fluid, the oxygen electrode will detect oxygen that diffuses into the probe from the adjacent cord and cerebrospinal fluid (**S-Fig. 5*C***, http://links.lww.com/CCM/G947). Therefore, the surface probe is always sensitive to cord tissue oxygen tension but less sensitive when the cord is not compressed against dura.

Our study aimed to establish the technique of monitoring $p_{sct}O_2$ from the injury site and investigate whether the measurements are meaningful and likely to help clinical management. This is by no means the definitive trial in the field. Though we did intervene for short periods, for example, by increasing FIO_2 to determine its effect on $p_{sct}O_2$, we did not set out to compare neurologic outcome in an interventional arm versus a control arm. Our study provides the basis for future research to determine whether intervention to alter $p_{sct}O_2$ is an effective new therapy. Such studies will require multivariable analysis to define whether any benefit of increasing $p_{sct}O_2$ is independent of other prognostic factors such as severity of injury (35), patient age (36), comorbidities (37), fever burden (26), timing of surgery (38), and spinal cord perfusion pressure (9).

Current management guidelines recommend maintaining mean arterial pressure 85–90 mm Hg 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. In addition, two patients with the same spinal cord perfusion pressure may have different cord tissue oxygen. Multimodality monitoring overcomes these problems by allowing individualized management (8, 11) that may ultimately yield management guidelines for spinal cord injury analogous to brain injury protocols that incorporate both pressure and tissue oxygen monitoring (39, 40). Multimodality 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) (26) and cord tissue oxygen (shown here), whereas blood transfusion increases tissue oxygen, but without improving metabolism, in spinal cord (shown here) and brain injury (41).

A limitation of our study is the small numbers of patients (n = 26), though our conclusions are supported by a large dataset (2,213 hr of monitoring, 165 motor examinations) and long follow-up (> 6 mo). As

shown here and in an earlier study (42), the main complication of injury site monitoring is cerebrospinal fluid leak through the probe skin exit sites. The insertion procedure 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 (43, 44). 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 (27). Draining lumbar cerebrospinal fluid has been proposed as a therapeutic maneuver in spinal cord injury (43, 44), but it does not effectively reduce intraspinal pressure (27) or improve cord tissue oxygen (shown here) at the injury site probably because the swollen cord is compressed against the dura (11, 22–24). The effect of durotomy on cord tissue oxygen has not been investigated; however, a randomized, controlled trial termed Duroplasty for Injured cervical Spinal Cord with Uncontrolled Swelling is underway to evaluate the effect of expansion duroplasty on neurologic outcome after spinal cord injury (https://fundingawards.nihr.ac.uk/award/NIHR130048).

CONCLUSIONS

After spinal cord injury, tissue oxygen monitoring is feasible and allows prompt detection and treatment of injury site hypoxia. Further studies are needed to investigate whether such intervention improves neurologic outcome.

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