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INTRASPINAL PRESSURE AND SPINAL CORD PERFUSION PRESSURE PREDICT NEUROLOGICAL OUTCOME AFTER TRAUMATIC SPINAL CORD INJURY

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INTRODUCTION

In the U.K., blood pressure management after acute, severe traumatic spinal cord injury (TSCI) is variable [1]. The American Association of Neurological Surgeons (AANS) recommends maintaining mean arterial pressure (MAP) at 85–95 mmHg for a week after injury, but with little supporting evidence [2]. To rationalise blood pressure management, we monitor intraspinal pressure (ISP) and spinal cord perfusion pressure (SCPP=MAP–ISP) from the injury site [3]. Our technique is safe [4] and analogous to monitoring intracranial pressure (ICP) and cerebral perfusion pressure (CPP) in traumatic brain injury (TBI). The data indicate that, after TSCI, ISP rises and SCPP falls [3]. Here we show strong correlation between high ISP or low SCPP and reduced neurological recovery. Our findings raise the possibility that interventions to reduce ISP or increase SCPP after TSCI may improve neurological outcome.

METHODS

Patient recruitment Approval for this observational cohort study was granted by the National Research Ethics Service London–St Giles Committee. Inclusion criteria are: 1. Severe TSCI defined as American spinal injuries association Impairment Scale (AIS) grade A, B or C; 2. Age 18–70 years; 3. Timing between TSCI and surgery within 72 hours. Exclusion criteria are: 1. Patient unable to consent; 2. Other major injuries or co-morbidities; 3 Penetrating TSCI. Surgery and early management took place at St. George's Hospital. Consent was obtained by each patient.

Surgery Following bony realignment and posterior fixation, the ISP probe (Codman, Depuy Synthes, Leeds, UK) was tunnelled through skin into the wound cavity. Under the operating microscope, the dura was opened one level below the injury. The ISP probe was inserted through the durotomy and placed on the spinal cord surface (Fig. 1A). The dural opening was

sutured and supplemented with fibrin glue (Tisseel®, Baxter, UK). The ISP probe was secured to the skin with silk sutures. Details are given elsewhere [3].

ISP and SCPP monitoring The ISP probe was connected to a Codman ICP box linked via a ML221 amplifier to a PowerLab running LabChart v.7.3.5 (AD Instruments, Oxford, UK). Arterial blood pressure was recorded from a radial artery catheter connected to the Philips Intellivue MX800 bedside monitoring system (Philips, Guildford, UK) in turn connected to the PowerLab system. The ISP and arterial blood pressure signals were sampled for up to seven days. LabChart was used to analyse the signals and compute SCPP. Neurointensivists were blinded to the ISP reading. MAP was treated with noradrenaline according to the neurointensivists' preferences.

Data collection Neurological examinations were done pre-operatively (day of injury) and at 9–12 months. Whole spine CT and MRI were done on admission and another CT within 48 hours of surgery to check probe and screw position. We collected the following: patient age, AIS grade pre-operatively and at 9–12 months, level of injury, ISP and SCPP.

Statistics Data were analysed using exact asymptotic logistic regression (LogXact 11, Cytel, Cambridge MA, USA). Neurological outcome was AIS grade at follow-up *vs.* pre-operative, binarised as improved *vs.* non-improved. We first assessed each factor individually. A forward stepwise method was then used to construct multi-variate models.

RESULTS

There were 45 patients with average age 41 years (range 19–70) and male:female ratio 4:1. 53% patients had cervical (C2–C7), 22% upper thoracic (T1–T6), 7% lower thoracic (T7–T10) and 18% conus medullaris (T11–L2) injuries. Pre-operative AIS grade was A in 67% patients, B in 20 % and C in 13%. For details see Supplementary Table 1. In univariate analysis, AIS grade on admission ($P<0.05$), advanced patient age ($P<0.005$) and upper

thoracic level of injury ($P<0.05$) correlated with reduced chance of AIS improvement by at least one grade at 9–12 months. Patient sex, duroplasty or laminectomy did not predict neurological outcome. For each patient, we computed mean ISP, mean SCPP and mean MAP during the monitoring period. In univariate analysis, ISP (negative correlation, $P<0.05$) and SCPP (positive correlation, $P<0.05$), but not MAP correlated with AIS grade improvement at 9–12 months (Figs. 1B-D). For details see Supplementary Table 2.

Multivariate analysis was used to determine whether AIS grade on admission, injury level, patient age, mean ISP and mean SCPP are independent predictors of improvement by at least one AIS grade. We produced two models. In one model, age, AIS grade on admission and ISP were independent predictors of AIS improvement ($P<0.05$). Increase in ISP by 10 mmHg reduced the chance of AIS grade improvement about five times. In the other model, age, AIS grade on admission and SCPP were independent predictors of AIS improvement ($P<0.05$). Increase in SCPP by 10mmHg increased the chance of AIS grade improvement about 2.7 times. Due to collinearity, ISP and SCPP were not predictors in the same model. For details see Supplementary Table 3.

DISCUSSION

Our key finding is that injury site ISP and SCPP, monitored during the first few days after TSCI, predict neurological improvement at 9–12 months. Mean ISP <10 mmHg and mean SCPP >90 mmHg are associated with the best recovery. In multivariate analysis, elevated ISP or low SCPP is a significant risk factor independent of AIS grade on admission and patient age. Limitations of the study include the small number of patients and use of the AIS as the only outcome measure.

Our findings for TSCI are analogous to the corresponding relationships between ICP, CPP and recovery after TBI. Spinal cord microdialysis indicates that high ISP and low SCPP

are associated with injury site ischaemia [5], which likely causes secondary damage. Because only one patient had mean SCPP>100mmHg, it is impossible to determine what happens to neurological outcome when mean SCPP is >90–100 mmHg. There was no correlation between the AANS MAP guideline of 85–95 mmHg and recovery. In our view, MAP-targeted management does not make physiological sense because patients with the same MAP have different SCPP; our patients with MAP 85–95 mmHg had SCPP 50–90 mmHg. Ultimately, a randomised, controlled trial is required to determine whether interventions that reduce ISP or increase SCPP improve neurological outcome after TSCI.

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FIGURE LEGEND

Fig. 1. Relationship between monitored physiological parameters and neurological outcome. A. Schematic of ISP monitoring technique. % patients with AIS grade improvement at 9 – 12 months *vs.* **B.** mean ISP, **C.** mean SCPP, and **D.** mean MAP. Black bars show improvement by at least one AIS grade. White bars show improvement by at least 2 AIS grades. 85 – 95 mmHg MAP is the AANS recommendation.

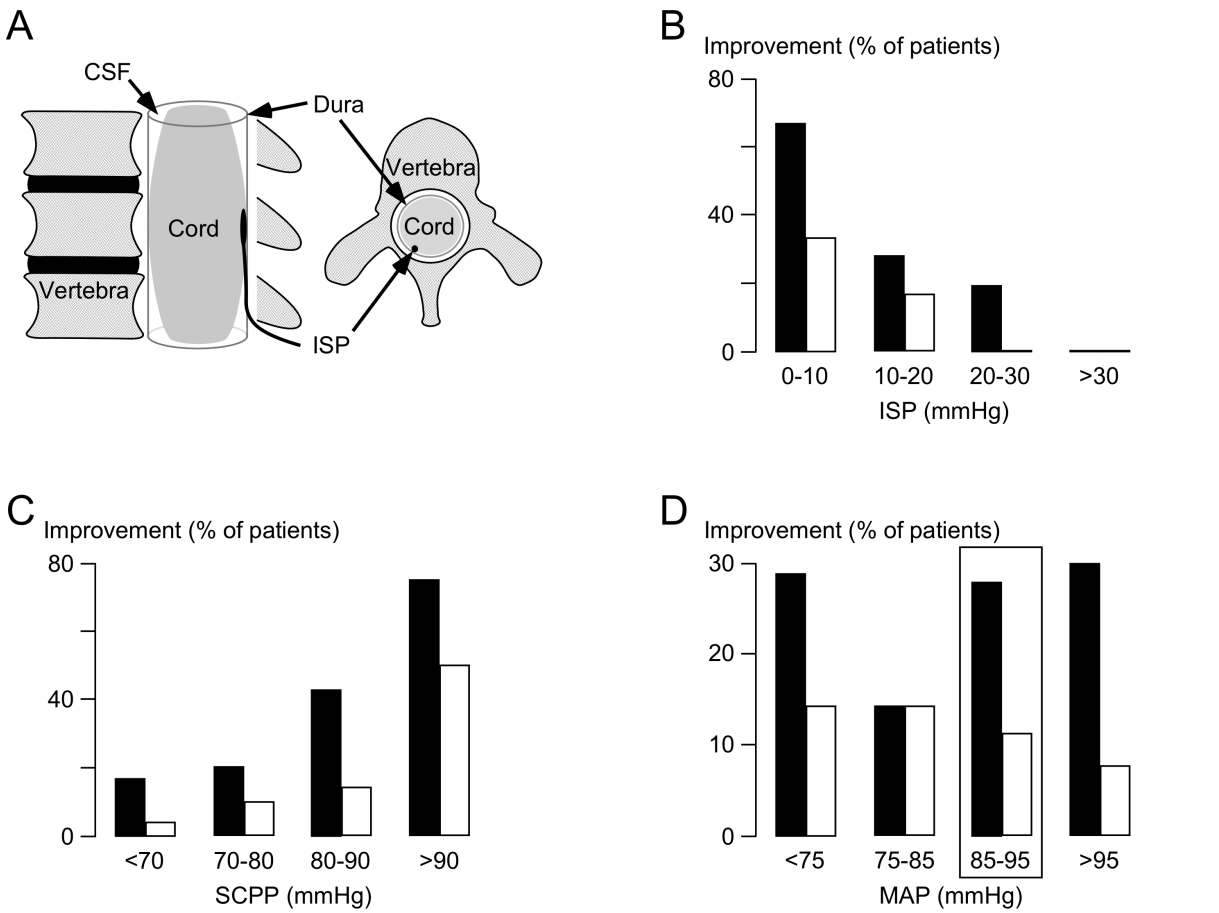
A
CSF
Dura
Vertebra
Cord
Cord
Vertebra
ISP
B
Improvement (% of patients)
80
40
0
0-10
10-20
20-30
>30
ISP (mmHg)
C
Improvement (% of patients)
80
40
0
<70
70-80
80-90
>90
SCPP (mmHg)
D
Improvement (% of patients)
30
20
10
0
<75
75-85
85-95
>95
MAP (mmHg)

Figure 1

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SUPPL Table 1. Demographic details of patients included in this study.

AGE, mean (range)	41 (19-70)
SEX, m:f patients	36:9
ADMISSION AIS GRADE, no. of patients	30 A, 9 B, 6 C
FOLLOW-UP AIS GRADE, no. of patients	26 A, 6 B, 3 C, 8 D, 1 E, 1 ?
INJURY LEVEL, no. of patients	24 C2-7, 10 T1-6, 3 T7-10, 8 T11-L2
*EXTENT OF DECOMPRESSION, no. of patients	11 R, 24 R/L, 10 R/L/D
TIME INJURY TO SURGERY, mean (range)	37 hours (9-72)

** All patients had posterior surgery. For cervical spine, we used lateral mass screws with rods and for thoraco-lumbar spine pedicle screws with rods. We restored the normal alignment of the fractured spine (R). Some patients also had laminectomies spanning the injury (R/L) and some had laminectomy plus duroplasty (R/L/D).*

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SUPPL Table 2. Factors tested in univariate analysis. Outcome was improvement in AIS grade at 9-12 months compared with AIS grade on admission.

FACTOR	P < 0.05?
Age	YES
Sex	NO
Level of injury	YES
Extent of decompression (R, R/L, R/L/D)	NO
AIS grade on admission	YES
Mean ISP	YES
Mean SCPP	YES
Mean MAP	NO

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SUPPL Table 3. Details of the two exact logistic regression models, using AIS improvement by at least one grade at 9 – 12 months as neurological outcome. We first listed the predictors that were statistically significant in univariate analysis at $P<0.05$ i.e. patient age, AIS on admission, level of injury, ISP and SCPP. Though commonly $P<0.25$ is used, for each of our predictors P was either <0.05 or > 0.25. To produce the multi-variate model, we started with no predictors and proceeded forward according to the following algorithm: 1) Add to the multivariate model the predictor with the lowest P-value (from univariate analysis). 2) Re-calculate P-values for each predictor in multivariate model. 3) Remove predictor from multivariate model with $P>0.05$. 4) Stop if adding a predictor to multivariate model causes P-value of that predictor to >0.05.

PREDICTOR	P-VALUE	BETA	BETA SE	ODDS RATIO
[†]MODEL 1				
[*]Age	0.006	-1.179	0.495	3.3
Admission AIS grade	0.015	1.156	0.678	4.8
[♯]ISP	0.016	-1.608	0.727	5.0
[§]MODEL 2				
[*]Age	0.004	-1.225	0.499	3.4
Admission AIS grade	0.027	1.446	0.654	4.3
[♯]SCPP	0.026	0.995	0.454	2.7

[*]In decades, [♯]In intervals of 10 mmHg, [†]P-values are 0.892 (deviance), 10^{-6} (likelihood ratio) and 0.646 (Hosmer-Lemeshow), [§]P-values are 0.422 (deviance), 2×10^{-6} (likelihood ratio) and 0.779 (Hosmer-Lemeshow), SE = standard error.