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Visualising the pressure-time burden of elevated intracranial pressure after severe traumatic brain injury: a retrospective confirmatory study

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Editor—Elevated intracranial pressure (ICP) after severe traumatic brain injury (TBI) is an important cause of secondary brain injury, either by hypoperfusion because of decreased cerebral perfusion pressure (CPP), or by mechanical distortion leading to brain herniation.¹ The thresholds to treat elevated ICP in severe TBI (20 or 22 mm Hg) are based on epidemiological studies,^{2,3} however, early application of aggressive measures to treat brief episodes of ICP elevations above 20 mm Hg have shown harm.⁴ Moreover, the association between elevated ICP and outcome is not merely attributable to crossing a threshold, but depends upon the magnitude and the duration of intracranial hypertension. This has been demonstrated in a multicentre prospective European dataset ($n=261$) by Güiza and colleagues.⁵ Using a three-dimensional visualisation technique, they showed that worse outcomes (taken at 6 months) could be explained by the interaction between the level of ICP elevation and the duration of the hypertensive episode, confirming a clinically intuitive concept. For instance, insults of high ICP, >30 mm Hg, seemed to be only tolerated for a short time (<8 min), whereas ICP>20 mm Hg leads, on average, to a poor outcome if sustained over 37 min. The ability to tolerate elevated ICP was decreased in children, when cerebrovascular autoregulation was absent, and when CPP was inadequate. To date, this visualisation technique has not been replicated outside of the prospective European dataset.⁵

We sought to confirm these findings by applying the same visualisation method on an independent patient cohort of 1112 severe TBI patients from Addenbrooke's Hospital

(Cambridge, UK) collected between 1991 and 2017. Patient characteristics and management protocols have been described.⁶ Because all data were extracted from the hospital records and fully anonymised, no data on patient identifiers were available, and therefore formal patient or proxy consent and institutional ethics approval were not required.

From minute-by-minute resolution data (time-averaged), ICP hypertensive episodes were defined as being above a given intensity threshold I , for at least a given duration D . For each pair of intensity and duration thresholds $\langle I, D \rangle$, the average number of corresponding episodes per patient was calculated, separately in each 6-month Glasgow outcome scale (GOS) group.⁵ Thereafter, the Pearson correlation between the average number of ICP episodes and GOS was calculated for each $\langle I, D \rangle$, and colour-coded according to a predefined colour map (Fig. 1). In this way, a single time point with elevated ICP can contribute to multiple insults on the colour contour plot. For example, an ICP of 12.5 mm Hg for 5 min will contribute to the episode-outcome Pearson correlation for the ICP>10, 11, and 12 mm Hg intensity category, and for the >1, 2, 3, 4, and 5 min duration category. Multivariable logistic regression was used to study the effect of the amount of time in the red zone of these plots, with patient outcome (mortality and unfavourable outcome) after adjustment for age and initial Glasgow Coma Scale.

From the 1112 patients, 34 million ICP insults were identified. By plotting the relationship between the insult count for each $\langle I, D \rangle$ pair and the outcome, a three-dimensional colour-coded contour plot was obtained, similar to that of Güiza and

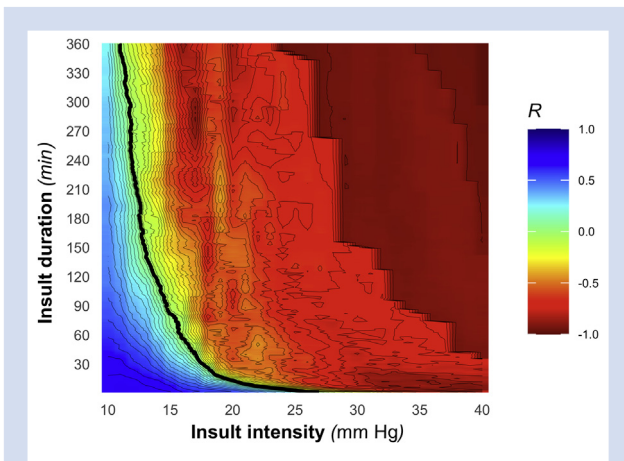


Fig 1. Visualizing the relationship between the number of ICP insults and Glasgow outcome scale across different intensities and durations ($n=1112$, 34 million episodes). Each coordinate $\langle I, D \rangle$ in the figure refers to a hypertensive ICP episode of at least a certain intensity (magnitude) I (x -axis), for at least a certain duration D (y -axis). The colour coding indicates the univariate correlation between the average number of episodes $\langle I, D \rangle$ per patient and GOS; a blue colour indicates association with better outcome whereas a red colour indicates association with worse outcome (i.e. more ICP insults related to worse outcome). The black line marks the transition zone between a positive and negative correlation. The current data are qualitatively and quantitatively similar to those previously published by Güiza and colleagues.⁵ GOS, Glasgow outcome scale; R, Pearson correlation coefficient.

colleagues⁵ (Fig. 1). The contour of zero correlation (i.e. the transition curve between the good and bad outcome associations) occurred at similar, but not identical values. For example, the current data indicate that an ICP insult of at least 20 mm Hg starts to be associated with poor outcome once longer than 13 min, compared with 37 min from the multi-centre European cohort.⁵ Differences in patient population or patient management likely contribute to these quantitative differences in the transition curve and should be investigated in appropriately designed studies that include detailed patient descriptors. Unfortunately, a detailed description of patient ICP therapies is not available in the current cohort. Nevertheless, the striking qualitative similarity of contour plots indicates that the concept of intensity-duration burden of ICP insults is important after TBI. Maintaining CPP > 70 mm Hg allowed longer and more intense ICP insults to be tolerated without worse outcome (Supplementary Fig. S1). Preserved pressure reactivity index (PRx) during ICP insults was also protective (Supplementary Fig. S2). On multivariable analysis, after adjusting for age and initial Glasgow coma scale, the fraction of time spent in the red zone ($r > 0$) was significantly related to mortality (odds ratio 6.87, confidence interval 4.2–11.3, $P < 0.001$) and unfavourable outcome (odds ratio 2.85, confidence interval 1.9–4.3, $P < 0.001$).

Prospective studies of this visualisation technique at the bedside can begin taking into account information on therapeutic intensity and other important prognostic variables. This will require international concerted efforts in high-

fidelity brain monitoring data coupled with detailed clinical contextual information. With increasing size of datasets, important subanalyses may be performed to answer questions such as: are males more sensitive to increases in ICP; are ICP increases more harmful in diffuse injuries; or should ICP management in older patients be different to younger patients? After elucidation of the aforementioned issues, overlaying of a particular patient's current ICP over the colour-coded ICP burden plot could assist in ICP interpretation and patient management.

Whilst elevated ICP after TBI is an intuitive example of physiologic insult burden visualisation, it is likely that this technique could be applied to other secondary injuries such as autonomic dysfunction, hyperthermia, brain hypoxia, or neuro-metabolic dysfunction. Furthermore, the technique could be applied to monitoring physiologic insults in anaesthetic or intensive care contexts outside of TBI.

Despite modern ICP and multimodal brain monitoring over the past 25 yr, patient mortality remains relatively static.⁶ This underlines an urgent need for innovative and reproducible techniques to allow meaningful interpretation of bedside signals. While unlikely to be a panacea, intensity-duration contour plots are a promising tool that may allow more nuanced interpretation of secondary brain injury.

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Declaration of interests

PS and MC have a financial interest in a part of the licencing fee for ICM+ software (www.icmplplus.neurosurg.cam.ac.uk) used for recording data. The remaining authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bja.2020.09.018>.

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Overfatigue amongst Chinese anaesthesiologists from 2017 to 2019

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Editor—Chinese anaesthesiologists are currently suffering from work overload, and sudden death is increasing dramatically. Between 1966 and 2015, 29 Chinese physicians suffered cardiac arrest caused by a heavy workload; 14 of these physicians were anaesthesiologists, with the average age of 35 yr.¹ Of six anaesthesiologists dying from overfatigue in the first half of 2017, most were young adults. Three studies conducted between 2012 and 2015^{2–4} focused on the occupational status of anaesthesiologists in China. They found that Chinese anaesthesiologists were facing increased physical and mental health issues, with staff shortages as the main contributor of physician burnout. In August 2018, seven Chinese ministries and commissions jointly issued a notice of strengthening and perfecting anaesthesia medical services, referred to as Document 21.⁵ We investigated whether there was any improvement in the physical and mental well-being of Chinese anaesthesiologists before and after the issuance of Document 21.

In August 2017 and September 2019, our team conducted electronic cross-sectional questionnaire surveys with the help of the New Youth Anaesthesia Forum, the Chinese Society of Anesthesiology, and the Chinese Association of Anesthesiologists (Supplementary file). Unlike previous studies, whose participants were individual anaesthesiologists, the participants for this survey were directors of anaesthesiology departments, aiming to investigate a wide range of problems with a small sample size. In August 2017, before the issuance of Document 21, 810 questionnaires were collected from directors of anaesthesiology, amongst which 626 were complete (77.2%; Exclusion criteria: 1) Age \leq 35 years; 2) Answer time \leq 2 minutes; 3) The IP address is a foreign website; 4) Lack of important data). In September 2019, after the first anniversary of the issuance of Document 21, 867 questionnaires were

collected from directors of anaesthesiology, amongst which 752 were effective (efficacy rate: 86.7%).

In 2017, 93.5% of directors of anaesthesiology reported varying rates of excessive fatigue in their department, and 65.2% reported a shortage of medical staff (Fig. 1a). These conditions have not been improved in 2019. There was no statistical significant difference in caseload per day, prevalence of overfatigue and human resource allocation status between 2017 and 2019. There were some improvements in heavy workload, high medical risk, research work and promotion pressure, and doctor–patient relationship, whilst other criteria were worsening, including low income, poor working condition, and pressure to increase income. In both 2017 and 2019, the first three main root causes of employee turnover were low income, heavy workload, and high medical risk (Fig. 1b), and the greatest pressure on directors of anaesthesiology came from clinical anaesthesia risk, medical quality and safety (Fig. 1c). Our findings show that Chinese anaesthesiologists were still experiencing severe physical overfatigue, high mental stress and low job satisfaction in 2019.

A study in 2018 showed that China only had 53 000 anaesthesiologists and residents along with 6700 anaesthesiologist assistants to serve a total population of 1.3 billion people.⁴ According to American and European standards of 2.4 anaesthesia providers per 10 000 people, China should have about 300 000 anaesthesiologists. In other words, China has a shortage of over 200 000 anaesthesiologists. Staff shortages resulted in frequent increased overtime work.⁴ China is now trying to expand anaesthesiology recruitment and increase the number of anaesthesiologists in standardised training, but because the training cycle of anaesthesiologists is very long, increasing the number of staff is not a task that can be