INVITED COMMENTARY

Critical ICP in Subarachnoid Hemorrhage: How High and How Long?

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There are numerous reasons why intracranial pressure (ICP) may be elevated in patients with aneurysmal subarachnoid hemorrhage (SAH):

- When an aneurysm ruptures, it precipitates a cascade of events that may result in global cerebral edema. Contributing factors include diffuse ischemic injury and sequelae of blood degradation products in the subarachnoid space, including inflammation, oxidative stress, and blood–brain barrier disruption [1]. Global edema is more likely to occur in the presence of high-grade SAH and larger volumes of cisternal blood and is strongly associated with poor outcomes [2].
- SAH is often complicated by acute hydrocephalus.
- Intracerebral hemorrhage, extra-axial hematomas, and infarcts may function as space-occupying lesions.
- Impaired cerebral blood flow (CBF) autoregulation makes patients vulnerable to both ischemia and relative hyperemia [3].

Observational studies demonstrate that raised ICP (conventionally, but somewhat arbitrarily, defined as ≥ 20 mmHg) is relatively common, especially among patients with high-grade SAH [4–8]. In most studies, raised ICP was strongly associated with poor outcomes, although this relationship usually did not persist in multivariable analyses [8]. Thus, it remains unresolved to what degree raised ICP is truly injurious rather than simply an epiphenomenon of more severe brain injury.

Nevertheless, studies do suggest that incrementally higher ICP is more strongly associated with poor outcomes and that failure to respond to therapy is particularly ominous [4, 6, 7].

Existing international guidelines do not provide specific recommendations regarding ICP monitoring and treatment in SAH [9–11]. However, there are multiple reasons to measure ICP in selected patients:

- Placement of an external ventricular drain (EVD) may be needed to treat hydrocephalus, irrespective of ICP. Attachment of the EVD to a transducer makes intermittent ICP measurements readily available.
- Measurement of ICP serves as a surrogate for intracranial volume. Increasing cerebral edema and mass effect is reflected by a rising pressure, influenced by the degree of intracranial compliance.
- Cerebral perfusion pressure (CPP) is defined by the difference between mean arterial pressure (MAP) and ICP (surrogate for venous pressure). Knowing ICP is necessary for clinicians to ensure that CPP levels exceed lower limits of CBF autoregulation (≥ 50 – 60 mmHg), thereby protecting against ischemia.
- Measuring ICP offers more than a number. The relationship between MAP and ICP enables calculation of the pressure reactivity index (PRx) and assessment of CBF autoregulation. Patients with impaired autoregulation may require higher than usual CPP levels [3, 7, 12]. The morphology and amplitude of the waveform and its association with mean ICP (RAP Index) provide information about intracranial compliance. These derived measures may predict outcome more accurately than ICP alone [8]. A small randomized controlled trial suggested benefit to treatment aimed at limiting ICP wave amplitude [13].

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Given the heterogeneous pathophysiology of raised ICP in SAH, optimal treatment may differ from one patient to another. Although clinicians often manage intracranial hypertension similarly to traumatic brain injury (TBI), it remains unclear whether the same therapeutic thresholds are appropriate [14].

In TBI, a number of recent observational studies have used two-dimensional color plots to better characterize the relationship between ICP or CPP (*x*-axis), time (*y*-axis), and outcomes (color intensity) [15–17]. These studies demonstrate that it is not just the magnitude of ICP or CPP derangements that are important, but also the duration and clinical context (depending especially on intracranial compliance and CBF autoregulation). Thus, there is a strong rationale for approaches to ICP management that are more nuanced than simply applying a single treatment threshold in all cases.

In this edition of *Neurocritical Care*, Carra and colleagues have applied this same graphical method of assessing the relationship between ICP-time burden and outcomes in an SAH population [18]. There were 98 patients, almost all of whom had high-grade SAH, managed at two European centers with relatively similar management protocols. ICP was measured using intraparenchymal monitors, while a concomitantly placed EVD was kept open, continuously draining cerebrospinal fluid (CSF). The proportion of time with ICP > 20 mmHg was not associated with 12-month neurological outcomes. In contrast, there was a strong relationship between pressure–time burden and outcome, thereby showing that ICP “dose” is likely more important than a particular ICP threshold.

An unusual aspect of this study was the surprisingly low ICP level that was apparently associated with poor outcomes, especially at one of the two centers (ICP > 7–8 mmHg). This finding highlights that poor outcomes following SAH occur from sequelae of early brain injury that do not always culminate in markedly increased ICP. Also, the proportion of time where the ICP was elevated was low ($\approx$ 2% of time with ICP > 20 mmHg), which is likely due, in part, to the practice of measuring ICP during continuous CSF drainage. Although not affected by an open system to the same degree as EVD measurements, parenchymal ICP readings do vary based on whether a concomitantly placed EVD is open or closed [19].

For now, no definitive, universal ICP treatment threshold, or critical duration above that level, can be recommended based on a high level of evidence. Given that multiple studies have reported ICP $\geq$ 20 mmHg to be associated with mortality and poor neurologic recovery, this remains a reasonable trigger for treatment, as in TBI. However, further research, applying similar methodology

to that of Carra and colleagues in larger multi-center cohorts, is needed to better define critical pressure–time limits and explore whether a lower ICP treatment threshold should be utilized in SAH patients. Such studies will need to consider the modifying impact of autoregulatory status. It is also likely that optimal ICP and CPP thresholds vary depending on timing in relation to the ictus: Cerebral edema and raised ICP are greater concerns during the first few days after aneurysm rupture, while a lower CPP may become more deleterious if and when vasospasm and delayed cerebral ischemia develop later in the clinical course [7].

EVDs are problematic for continuous assessment of ICP and pressure regulation because they must be kept open at least some of the time to treat hydrocephalus, which provides a rationale for concomitant use of a parenchymal monitor [20]. Conversely, some authors have suggested that PRx can reliably be calculated even with an open EVD, particularly when the most proximal EVD side port is used to transduce pressure, but data are conflicting and this work requires greater confirmation [20–22].

Even when critical thresholds for ICP magnitude and duration are better defined, this will still only indicate an epidemiological association with poor outcomes, rather than implicating ICP itself as a causative factor. Such research will help achieve greater consensus for ICP management specifically in SAH. Ultimately, however, prospective randomized controlled trials would be needed to determine whether tightly controlling ICP improves outcomes. In the meantime, clinicians will continue to extrapolate some of their ICP management strategies from recommendations in the setting of TBI [14].

Conflict of interest

The author has no conflict of interest.

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