

- 2 Kivipelto M, Mangialasche F, Ngandu T. Lifestyle interventions to prevent cognitive impairment, dementia and Alzheimer disease. *Nat Rev Neurol* 2018; **14**: 653–66.
- 3 Burns DK, Alexander RC, Welsh-Bohmer AK et al. Safety and efficacy of pioglitazone for delay of mild cognitive impairment and prognosis of risk of developing mild cognitive impairment due to Alzheimer's disease: a phase 3, randomised, double-blind, placebo-controlled trial. *Lancet Neurol* 2021; **20**: 537–47.
- 4 Heneka MT, Fink A, Doblhammer G. Effect of pioglitazone medication on the incidence of dementia. *Ann Neurol* 2015; **78**: 284–94.
- 5 Jiang Q, Heneka M, Landreth GE. The role of peroxisome proliferator-activated receptor-gamma (PPARGgamma) in Alzheimer's disease: therapeutic implications. *CNS Drugs* 2008; **22**: 1–14.
- 6 Ito K, Romero K. Placebo effect in subjects with cognitive impairment. *Int Rev Neurobiol* 2020; **153**: 213–30.
- 7 Jacobs DM, Ard MC, Salmon DP, et al. Potential implications of practice effects in Alzheimer's disease prevention trials. *Alzheimers Dement* 2017; **3**: 531–35.



Real-world appraisal of intracranial pressure monitoring

See **Articles** page 548

For the **Brain Trauma Foundation** guidelines see <https://braintrauma.org/guidelines/guidelines-for-the-management-of-severe-tbi-4th-ed#/>

The management of elevated intracranial pressure (ICP) is an essential component of modern neurocritical care for acute brain injury. Direct and continuous monitoring of ICP has generally been considered the most reliable evaluation of ICP and is an important aspect of care for patients with severe brain injury. ICP monitoring is recommended in the Brain Trauma Foundation guidelines and its use is well established in managing severe traumatic brain injury (TBI).¹ The deterioration of patients with intracerebral haemorrhage² or subarachnoid haemorrhage³ might also be associated with increased ICP, indicating the importance of ICP monitoring in these patients.

In *The Lancet Neurology*, Chiara Robba and colleagues report the results of the SYNAPSE-ICU study,⁴ involving 2395 patients from 146 sites in 42 countries. For the first time, a large, prospective, international collection of data has been gathered, representing real-world clinical practice, to assess the use of ICP monitoring in individuals with TBI, intracerebral haemorrhage, and subarachnoid haemorrhage, paving the way for an update in the recognition of ICP monitoring in this field.

Continuous ICP monitoring is increasingly used in patients with severe TBI (ie, a Glasgow coma scale score of 3–8) worldwide. A specific ICP-guided management protocol⁵ was made available in 2019 to assist the clinical treatment of patients with TBI through ICP monitoring. However, the beneficial effects of this approach are still uncertain. The Brain Trauma Foundation recommends the use of ICP monitoring as a central issue to ICP management, however the recommendation is only level IIB (ie, based on what was considered a low-quality body of evidence). Chesnut and colleagues⁶ have completed, to the best of our knowledge, the only randomised controlled trial to show no benefits of ICP monitoring in reducing mortality when compared

with using radiographic and clinical examination in ICP management. By contrast, two randomised trials⁸ directly evaluating ICP monitoring have contributed substantially to progress in TBI management. For example, by use of ICP monitoring, the mortality of patients with TBI and refractory elevated ICP (>25 mm Hg) decreased after decompressive craniectomy.⁷ A study published in 2021⁸ showed that hypothermic treatment significantly increased favourable outcomes in patients with severe TBI and refractory intracranial hypertension (initial ICP \geq 30 mm Hg). Considering the differing findings, a real-world view of ICP monitoring in patients with acute brain injury, including current use, indications, therapeutic intensity level, and possible association with prognosis, has been eagerly expected.

The SYNAPSE-ICU study⁴ provides timely insight into the contemporary landscape of ICP monitoring in patients with TBI, intracerebral haemorrhage, and subarachnoid haemorrhage who were admitted to an intensive care unit. The overriding finding of the study is that, in patients with more severe acute brain injury (at least one unreactive pupil), ICP monitoring was associated with a more intensive therapeutic approach, lower 6-month mortality, and better 6-month Extended Glasgow Outcome Scale (GOSE) compared with no ICP monitoring. Furthermore, similar findings were noted when a sub-analysis was done on patients stratified by diagnosis with TBI, intracerebral haemorrhage, and subarachnoid haemorrhage. Additionally, the study showed that ICP monitoring was used more widely in patients from high-income countries (1185 [61%] of 1954) than in those from low-income and middle-income countries (147 [33%] of 441), which is comparable with findings from two large-scale collaborative studies of TBI (table).^{9,10}

The SYNAPSE-ICU findings support the use of ICP monitoring for patients with acute brain injury. However,

	SYNAPSE-ICU ¹	CENTER-TBI European core study ¹⁰	CENTER-TBI China registry ⁹
Enrolment period	2018–19	2014–17	2014–17
Number of enrolled patients	2395 with ABI in ICU (1287 TBI)	4509 with TBI	13 138 with TBI
ICP monitoring rate	1332/2395 (56%) with ABI (710/1287 [55%] TBI)	924/2159 (43%)	1509/13 138 (11%)
ICP monitoring in patients with severe TBI in ICU	1068/1973 (54%)	591/958 (62%)	725/2015 (36%)
HICs	1185/1954 (61%)*	591/958 (62%)†	NA
LMICs	147/441 (33%)*	NA	725/2015 (36%)‡
ICP monitoring and mortality	ICP monitoring was associated with significantly lower 6-month mortality in patients with ABI and at least one unreactive pupil	NA	ICP monitoring decreased mortality in patients with severe TBI and absent pupillary light reflex

ABI=acute brain injury. TBI=traumatic brain injury. ICU=intensive care unit. ICP=intracranial pressure. HICs=high-income countries. LMICs=low-income and middle-income countries. NA=not available. *Data are from all patients in ICU, with or without severe TBI. †17 of 18 of the participating centres in CENTER-TBI are located in HICs and one centre is in a LMIC (Serbia). ‡China is considered an upper-middle-income country, included in the LMICs category.

Table: Clinical prevalence of intracranial pressure monitoring in prospective observational studies

there are some limitations and implications of the study that should be discussed. In patients who did not have ICP monitoring, ICP management was not described in detail. Furthermore, causal inferences cannot be drawn from observational research, as Robba and colleagues discuss. With the advantage of the continuous and digitised value of ICP monitoring, further clinical examination combined with a cranial CT scan when necessary, hypertonic dehydration, decompressive craniectomy, and hypothermic intervention are treatments for managing elevated ICP that might lead to lower mortality. Also, based on ICP monitoring, the derived parameters in multimodal monitoring—pressure reactivity index, pulse amplitude index, and the correlation coefficient between pulse amplitude of ICP and cerebral perfusion pressure—can be used to evaluate the state of cerebrovascular reactivity and estimate optimal cerebral perfusion pressure for patients. These indicators are of great value in ICP management and are highly anticipated for future clinical practice.

The international SYNAPSE-ICU study⁴ and the European¹⁰ and Chinese⁹ CENTER-TBI studies show that global collaboration in the field of acute brain injury is feasible. Further research should focus on the comparative effectiveness of treatment across countries and continents. Investigation into the large variability in high-quality randomised controlled trials will eventually lead to a breakthrough in the understanding

of ICP monitoring and guide policy makers and clinicians to focus on advanced ICP management for acute brain injury.

We declare no competing interests.

Junfeng Feng, Chun Yang, *Jiyao Jiang
jiyaojiang@126.com

Brain Injury Center, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200127, China (JF, CY, JJ); Shanghai Institute of Head Trauma, Shanghai, China (JF, CY, JJ)

- Kolias AG, Rubiano AM, Figaji A, Servadei F, Hutchinson PJ. Traumatic brain injury: global collaboration for a global challenge. *Lancet Neurol* 2019; **18**: 136–37.
- Cordonnier C, Demchuk A, Ziai W, Anderson CS. Intracerebral haemorrhage: current approaches to acute management. *Lancet* 2018; **392**: 1257–68.
- Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. *Nat Rev Neurol* 2014; **10**: 44–58.
- Robba C, Graziano F, Rebora P, et al. Intracranial pressure monitoring in the intensive care unit (SYNAPSE-ICU): an international, prospective observational cohort study. *Lancet Neurol* 2018; **20**: 548–58.
- Hawryluk GWJ, Aguilera S, Buki A, et al. A management algorithm for patients with intracranial pressure monitoring: the Seattle International Severe Traumatic Brain Injury Consensus Conference (SIBICC). *Intensive Care Med* 2019; **45**: 1783–94.
- Chesnut RM, Temkin N, Carney N, et al. A trial of intracranial-pressure monitoring in traumatic brain injury. *N Engl J Med* 2012; **367**: 2471–81.
- Hutchinson PJ, Kolias AG, Timofeev IS, et al. Trial of decompressive craniectomy for traumatic intracranial hypertension. *N Engl J Med* 2016; **375**: 1119–30.
- Hui J, Feng J, Tu Y, et al. Safety and efficacy of long-term mild hypothermia for severe traumatic brain injury with refractory intracranial hypertension (LTH-1): a multicenter randomized controlled trial. *EClinicalMedicine* 2021; **32**: 100732.
- Gao G, Wu X, Feng J, et al. Clinical characteristics and outcomes in patients with traumatic brain injury in China: a prospective, multicentre, longitudinal, observational study. *Lancet Neurol* 2020; **19**: 670–77.
- Steyerberg EW, Wieggers E, Sewalt C, et al. Case-mix, care pathways, and outcomes in patients with traumatic brain injury in CENTER-TBI: a European prospective, multicentre, longitudinal, cohort study. *Lancet Neurol* 2019; **18**: 923–34.