ICU
MANAGEMENT & PRACTICE

Oxygen Reactivity Index in Traumatic Brain Injury

Moderate-to-severe traumatic brain injury (TBI) often results in impaired cerebral autoregulation (CA), making patients vulnerable to both ischaemia and hyperaemia. The capacity for CA varies between patients and can change over time, complicating the determination of an optimal cerebral perfusion pressure (CPP) target. The pressure reactivity index (PRx), a measure of CA based on the correlation between changes in arterial blood pressure (ABP) and intracranial pressure (ICP), is commonly used in neurocritical care. A high PRx indicates impaired cerebrovascular reactivity and is associated with poor outcomes. The optimal CPP (CPPopt) corresponds to the CPP that results in the lowest PRx.

Another CA metric, the oxygen reactivity index (ORx), correlates changes in CPP with brain tissue oxygen (pbtO2). A positive ORx suggests impaired CA, while a value close to zero indicates intact CA. Elevated ORx has been linked to higher PRx and worse outcomes, though these findings are not consistently replicated. The validity of ORx has been questioned, as it may not accurately reflect ABP slow waves and focuses on localised brain tissue oxygen measurements, which may not represent the global brain state due to variations in injury and physiological disturbances in TBI.

There are only a few small cohort studies on the use of ORx in TBI, making it difficult to draw definitive conclusions about its potential and limitations. However, in other acute brain injuries, such as aneurysmal subarachnoid haemorrhage (aSAH), ORx has been shown to be a strong predictor of clinical outcomes, like the risk of delayed cerebral ischaemia or worse functional recovery.

A recent study investigated how ORx correlates with other cerebral physiological variables, including the PRx. It also explored its relationship with outcomes, particularly in the context of concurrent disturbances in other cerebral variables. The study hypothesised that ORx will be sensitive to ischaemia, characterised by high intracranial pressure (ICP), low CPP, and impaired autoregulation, but not to hyperaemia, since pbtO2 may become saturated at high CPP and cerebral blood flow (CBF). It was also hypothesised that higher ORx will be associated with worse outcomes, especially in combination with high ICP, low CPP, high PRx, CPP below optimal levels (CPPopt), and low pbtO2.

The study included 425 TBI patients at Addenbrooke's Hospital, Cambridge, UK, who were monitored for ICP and pbtO2 for at least 12 hours. The researchers used generalised additive models (GAMs) to assess the associations between the ORx and variables such as ICP, PRx, CPP, ΔCPPopt (the difference between actual CPP and PRx-based optimal CPP), and pbtO2. The relationship between ORx and patient outcomes was also observed.

GAMs showed that ORx increased with higher ICP, PRx above +0.30, CPP below 60–70 mmHg, and negative ΔCPPopt. Unlike PRx, ORx did not increase at higher CPP levels. Outcome heatmaps revealed that when ORx exceeded +0.50, particularly over longer durations, there was a transition to a more unfavourable outcome, especially when combined with high ICP, high PRx, low CPP, negative ΔCPPopt, and low pbtO2. Higher ORx was also found to be associated with increased mortality.

ORx increased with higher ICP, higher PRx, lower CPP, and negative ΔCPPopt, but only slightly with positive ΔCPPopt and not with higher CPP. These results suggest that ORx is primarily sensitive to the lower limit of autoregulation, unlike PRx, which is sensitive to both the lower and upper limits. The combination of high ORx with elevated ICP, high PRx, low CPP, negative ΔCPPopt, and low pbtO2 was particularly linked to worse outcomes compared to any of these factors alone. Therefore, ORx may help identify safe and dangerous perfusion target intervals and could complement the global autoregulatory metric PRx.

GAMs showed that ORx worsened with higher ICP, CPP below 60–70 mmHg, and negative ΔCPPopt. This suggests that ORx is sensitive to the lower limit of cerebral autoregulation (CA), as CPP and pbtO2 change in the same direction in such cases. ORx remained stable and low when CPP was above 60 mmHg, the estimated lower limit of CA. A small increase in ORx was observed for slightly positive ΔCPPopt, but it

decreased for more extreme ΔCPPopt values. Overall, ORx was sensitive to the lower but not the upper limit of CA. The moderate association between ORx and PRx may be due to the fact that pbtO2 and ORx are also influenced by factors like arterial oxygen content and focal energy metabolism, which requires further investigation in future studies.

The study found that when the ORx exceeded +0.50, particularly during longer episodes, there was a clear shift towards worse outcomes. Worse outcomes were also observed in patients with combined physiological disturbances, including elevated ORx, high ICP above 20 mmHg, PRx above +0.30, CPP below 60–70 mmHg, negative ΔCPPopt, and low pbtO2. These findings suggest that ORx provides important prognostic information, indicating a greater burden of ischaemic brain injury as the lower limit of CA is exceeded. ORx could potentially help fine-tune safe and dangerous perfusion pressure and pbtO2 targets.

The combination of ORx and PRx showed an additive or synergistic effect when both were elevated, likely because PRx has a low signal-to-noise ratio. Adding ORx, a complementary variable to PRx based on different input variables, could help clarify the true physiological signal. ORx reflects slow changes in CPP and static CA, while PRx represents dynamic CA, and their combined analysis may improve understanding of brain injury. Moreover, while PRx is a global measure of vascular reactivity, ORx is focused on CBF and oxygen diffusion, making ORx useful for detecting early ischaemia and hypoxia, particularly when PRx is still low.

In terms of focal versus global monitoring, ORx is based on focal pbtO2 measurements, making it more relevant for small, specific brain areas, while PRx is a global metric. Combining both types of measurements may offer added value in analysing brain disturbances. The study also noted that ORx has been useful in predicting outcomes in aneurysmal subarachnoid haemorrhage (aSAH), where it helps identify the risk of delayed cerebral ischaemia. However, PRx may be more effective for TBI patients who experience both ischaemic and hyperaemic insults.

Overall, ORx was found to be sensitive to the lower limit of CA, unlike PRx, which is sensitive to both the lower and upper limits. The combination of high ORx with elevated ICP, high PRx, low cerebral perfusion pressure (CPP), negative ΔCPPopt, and low pbtO2 was strongly associated with worse outcomes. This suggests that pbtO2-monitoring with the corresponding ORx metric could be valuable in neurocritical care for TBI, helping to identify safe and dangerous perfusion target intervals. ORx may also provide complementary information to the global CA metric PRx.

Source: Critical Care

Image Credit: iStock

Published on : Tue, 14 Jan 2025