

Effect of arterial oxygen partial pressure on cerebral oxygenation in critically ill patients with acute brain injury

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Abstract

Jugular venous oxygen saturation (SjvO_2) is used in multimodal monitoring to assess cerebral oxygen delivery–consumption balance after acute brain injury (ABI). We evaluated whether arterial oxygen tension (PaO_2) influences SjvO_2 and may mask elevated cerebral oxygen extraction (CEO_2). In this retrospective study, paired arterial and jugular venous blood gases obtained within 30 minutes were analyzed in patients with ABI undergoing multimodal monitoring between 2015 and 2023. SjvO_2 was categorized as low ($< 60\%$), normal ($60\text{--}75\%$), or high ($> 75\%$), and $\text{CEO}_2 \geq 40\%$ was considered elevated. Critical perfusion despite reassuring SjvO_2 was defined as $\text{SjvO}_2 \geq 60\%$ with elevated CEO_2 . Overall, 138 patients contributed 3,090 paired measurements. SjvO_2 increased nonlinearly with PaO_2 . Compared with $\text{PaO}_2 < 100$ mmHg, the odds of preserved SjvO_2 increased progressively across higher PaO_2 categories, whereas PaO_2 was not significantly associated with preserved CEO_2 . Among 3,042 measurements, 29 met criteria for critical perfusion despite reassuring SjvO_2 and had higher PaO_2 values (174 [153–291] vs. 118 [95–174] mmHg). PaO_2 identified these measurements with an AUC of 0.78 (95% CI, 0.73–0.83); 129 mmHg provided 100% sensitivity and 59% specificity. Elevated PaO_2 may therefore produce falsely reassuring SjvO_2 values and should be considered when interpreting cerebral oxygenation in ABI.

Full Text

Multimodal monitoring (MMM) combines cerebral and systemic monitoring modalities to characterize brain physiology and guide individualized management in patients with acute brain injury (ABI) [1]. Because cerebral ischemia and impaired oxygen delivery (DO_2) are major mechanisms of secondary brain injury [2], current guidelines and consensus statements recommend integrating cerebral oxygenation monitoring into MMM [1,3].

Jugular venous oxygen saturation (SjvO_2) provides a global estimation of the balance between cerebral oxygen delivery and oxygen consumption and has been associated with ischemic brain volume [4]. SjvO_2 monitoring is therefore used to identify inadequate cerebral oxygenation and guide hemodynamic optimization in patients with ABI [5,6]. Physiologically, SjvO_2 depends on the interaction between cerebral blood flow, arterial oxygen content (CaO_2), and cerebral oxygen consumption. CaO_2 is determined predominantly by hemoglobin concentration and arterial oxygen saturation, whereas the contribution of dissolved oxygen, determined by the arterial partial pressure of oxygen (PaO_2), is generally considered negligible because of its low solubility in plasma. Consequently, PaO_2 is often overlooked when interpreting SjvO_2 .

However, experimental and clinical data have shown that large increases in PaO_2 induced by changes in inspired oxygen fraction (FiO_2) can substantially increase SjvO_2 , largely through the contribution of dissolved oxygen, even in the absence of changes in cardiac output or hemoglobin concentration [7]. Thus, changes in SjvO_2 across different PaO_2 levels may not necessarily reflect changes in cerebral oxygen extraction (CEO_2). Whether PaO_2 influences the relationship between SjvO_2 and CEO_2 in patients with ABI remains unclear. To study the influence of PaO_2 on SjvO_2 , we first examined the association

between PaO_2 and SjvO_2 and then identified MMM parameters associated with preserved SjvO_2 despite elevated CEO_2 , a pattern suggestive of critical perfusion despite reassuring SjvO_2 .

We conducted a retrospective study of patients with acute brain injury (ABI) admitted to the intensive care unit (ICU) of Hôpital Lariboisière (Paris, France) between 2015 and 2023. The study was approved by the institutional ethics committee (Institutional Review Board no. 00006477, HUPNVS, Paris 7 University, AP-HP). Data were derived from a previously described cohort [5,6] of patients with ABI undergoing MMM. Patients were eligible if they were mechanically ventilated and had at least one paired arterial and jugular venous blood gas measurement during the ICU stay. Samples collected within 30 minutes were considered paired; when several samples met this criterion, the closest in time were selected. Blood gas data were extracted from the analyzer electronic database. ABI included traumatic brain injury (TBI), subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), and ischemic stroke.

SjvO_2 was classified as low ($<60\%$) [4,5], normal ($60\text{--}75\%$), or high ($>75\%$) [8]. CEO_2 was calculated as the arteriojugular oxygen content difference divided by arterial oxygen content (CaO_2), with $\text{CEO}_2 \geq 40\%$ considered elevated [9]. Critical perfusion despite reassuring SjvO_2 was defined as preserved SjvO_2 ($\geq 60\%$) in the presence of elevated CEO_2 ($\geq 40\%$). Measurements with the opposite pattern ($\text{SjvO}_2 < 60\%$ and $\text{CEO}_2 < 40\%$) were excluded from the analysis.

The primary objective was to characterize the association between PaO_2 and SjvO_2 . Secondary objectives were to compare MMM parameters according to the presence or absence of critical perfusion despite reassuring SjvO_2 and to assess the ability of PaO_2 to identify measurements meeting this definition.

The PaO_2 – SjvO_2 relationship was assessed using polynomial regression. The distribution of low, normal, and high SjvO_2 values, as well as low and high CEO_2 values, was then examined across predefined PaO_2 categories (<100 , $100\text{--}200$, $201\text{--}300$, and >300 mmHg). The probability of preserved SjvO_2 and CEO_2 across PaO_2 categories was assessed using logistic regression, with $\text{PaO}_2 < 100$ mmHg as the reference category. MMM parameters were compared according to the presence or absence of critical perfusion despite reassuring SjvO_2 using the Wilcoxon rank-sum test. The ability of PaO_2 to identify measurements meeting this definition was assessed using receiver operating characteristic (ROC) analysis, with calculation of the area under the curve (AUC), sensitivity, and specificity. The PaO_2 threshold yielding 100% sensitivity was selected to minimize false-negative classifications. Analyses were performed using R version 4.4.3 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria); ROC analyses used the pROC package version 1.18.5. All tests were two-sided, with $p < 0.05$ considered statistically significant.

During the study period, 138 patients with ABI underwent MMM and had at least one paired arterial and jugular venous blood gas measurement, yielding 3,090 paired measurements, (median of 19 [IQR 11–30] per patient). Median age was 39 [IQR 30–52] years. The main ABI etiologies were TBI (41%), ICH (23%), and SAH (23%), predominantly high-grade. Median admission Glasgow Coma Scale score was 6 [IQR 4–

9], and all patients were mechanically ventilated. Median ICU length of stay was 19 [IQR 13–32] days, and ICU mortality was 18%.

Among 3,084 measurements with available PaO₂, PaO₂ was <100 mmHg in 967 (31.4%) measurements, 100–200 mmHg in 1,444 (46.8%), 201–300 mmHg in 232 (7.5%), and >300 mmHg in 441 (14.3%). The relationship between SjvO₂ and PaO₂ is illustrated in **Figure 1**. SjvO₂ showed a nonlinear association with PaO₂, with higher SjvO₂ values observed as PaO₂ increased, particularly at higher PaO₂ levels. The distribution of low, normal, and high SjvO₂ values across predefined PaO₂ categories is shown in **Figure 2**. The proportion of measurements with high SjvO₂ increased across PaO₂ categories, from 30.6% at PaO₂ <100 mmHg, 37.4% at 100–200 mmHg to 67.7% at 201–300 mmHg and 79.1% at >300 mmHg. The association between PaO₂ categories with preserved SjvO₂ and CEO₂, together with OR and 95% confidence intervals for each category relative to PaO₂ <100 mmHg, is reported in **Table 1**. Compared with PaO₂ <100 mmHg, the odds of preserved SjvO₂ were higher for PaO₂ 100–200 mmHg (OR, 1.59; 95% CI, 1.13–2.22; p=0.007), and increased markedly at higher PaO₂ levels, with ORs of 3.85 (95% CI, 1.59–9.31; p=0.003) for PaO₂ 201–300 mmHg and 4.91 (95% CI, 2.36–10.21; p<0.001) for PaO₂ >300 mmHg. In contrast, no significant association was observed between PaO₂ categories and preserved CEO₂ (overall p=0.132).

Table 1 – Association between PaO₂ categories with SjvO₂ and CEO₂

PaO ₂ category	OR for preserved SjvO ₂ with 95% CI	P value	OR for preserved CEO ₂ with 95% CI	P value
Overall association	–	<0.001		0.132
<100 mmHg	1.00 (reference)	–	1.00 (reference)	–
100–200 mmHg	1.59 [1.13–2.22]	0.007	0.86 [0.57–1.30]	0.481
201–300 mmHg	3.85 [1.59–9.31]	0.003	1.43 [0.53–3.87]	0.481
>300 mmHg	4.91 [2.36–10.21]	<0.001	2.31 [0.87–6.12]	0.092

Preserved SjvO₂: SjvO₂ ≥60%; preserved CEO₂: CEO₂ ≥40%.

OR: odds ratio; CEO₂: cerebral oxygen extraction fraction, PaO₂: arterial partial pressure of oxygen.

CEO₂ could be calculated in 3,062 measurements. After exclusion of 20 measurements showing the opposite pattern (SjvO₂ <60% and CEO₂ <40%), 3,042 measurements were included in the analysis of critical perfusion (CEO₂ ≥40%) despite reassuring SjvO₂ (SjvO₂ ≥60%). Of these, 29 measurements from 21 patients met this definition. Neurological monitoring parameters were similar between groups. Measurements meeting the definition of critical perfusion despite reassuring SjvO₂ were characterized by higher PaO₂ (174 [153–291] vs. 118 [95–174] mmHg) and SaO₂, together with lower PaCO₂ (39 [36–

42] vs. 41 [39–44] mmHg). PaO_2 identified these measurements with an AUC of 0.78 (95% CI, 0.73–0.83). In the study cohort, a PaO_2 threshold of 129 mmHg yielded 100% sensitivity and 59% specificity (95% CI, 58–61%) for identifying measurements with preserved SjvO_2 despite elevated CEO_2 .

Our findings show an association between PaO_2 and SjvO_2 in patients with ABI. Higher PaO_2 was associated with higher SjvO_2 . As a result, preserved SjvO_2 , defined as $\text{SjvO}_2 \geq 60\%$, may occur despite an imbalance between cerebral oxygen delivery and demand, reflected by increased CEO_2 , defined as $\text{CEO}_2 \geq 40\%$, a pattern consistent with critical cerebral perfusion. Our results are consistent with a previous prospective observational study [7], in which increasing FiO_2 increased SjvO_2 in association with the concomitant rise in PaO_2 .

In our cohort, lower PaCO_2 was associated with discordant measurements. This finding may partly be related to the higher FiO_2 used at the time of blood gas sampling in this subgroup. Higher FiO_2 may reduce ventilation–perfusion mismatch and alveolar dead space, thereby improving CO_2 clearance and contributing to lower PaCO_2 [10].

To our knowledge, this is the first study to investigate the relationship between PaO_2 and SjvO_2 in patients with ABI undergoing MMM. Several limitations should be acknowledged.

First, only 29 measurements met our predefined definition of critical perfusion despite reassuring SjvO_2 , limiting the robustness and precision of our findings. Second, SjvO_2 and CEO_2 were derived from the same monitoring modality and are therefore not fully independent measures of cerebral oxygenation. Ideally, these findings should be confirmed using a more direct and independent assessment of cerebral oxygen extraction, such as oxygen-15 positron-emission tomography. Third, arterial and jugular venous blood gases were considered paired when obtained within 30 minutes, and we cannot exclude that PaO_2 differed between the two sampling times. In our clinical practice, a 30-minute interval was usually performed after changes in FiO_2 before subsequent blood gas sampling. Previous studies in mechanically ventilated, clinically stable patients have shown that approximately 90% of PaO_2 equilibration occurs within 15 minutes after a change in FiO_2 [11], although equilibration may be slower in less stable critically ill patients.

Taken together, our findings suggest that PaO_2 should be considered when interpreting SjvO_2 in patients with ABI, as apparently reassuring SjvO_2 values may coexist with elevated CEO_2 , reflecting critical cerebral perfusion. In our cohort, the probability of this pattern increased at PaO_2 levels above 129 mmHg. These findings support obtaining simultaneous arterial and jugular venous blood samples under stable FiO_2 conditions, with FiO_2 adjusted to maintain normoxemia.

Declarations

The manuscript complies with all instructions to authors.

The authorship requirements have been met, and the final manuscript was approved by all authors.

This manuscript has not been published elsewhere and is not under consideration by another journal.

Artificial intelligence statement

No generative artificial intelligence was used to generate, analyze, or interpret the study data.

Availability of data and materials

The datasets used and/or analysed complain the current study are available from the corresponding author on reasonable request.

Authors' contributions

T.A. and R.B. designed the study. T.A. collected the data. T.A. and R.B. performed the analyses. T.A. and R.B. wrote the manuscript. All co-authors have reviewed and approved the manuscript.

Ethical approval and consent to participate

The study was approved by an institutional ethics committee (Institutional Review Board–n°00006477–of HUPNVS, Paris 7 University, AP-HP) which waived the need for written informed consent.

Competing interests

RB reports non-financial support from Vygon, Getinge France, and Edwards Lifesciences. BGC received fees as a member of an advisory board from Roche Diagnostics. The other authors declare no competing interests.

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Checklist

No checklist was used.

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Figures

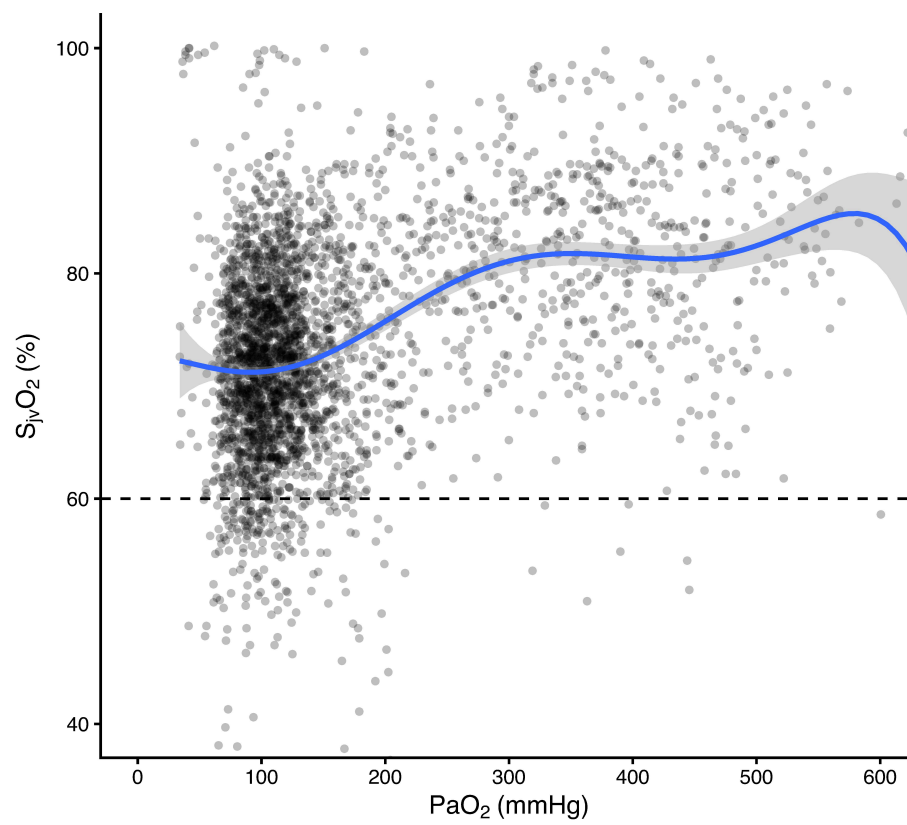


Figure 1

Legend not included with this version.

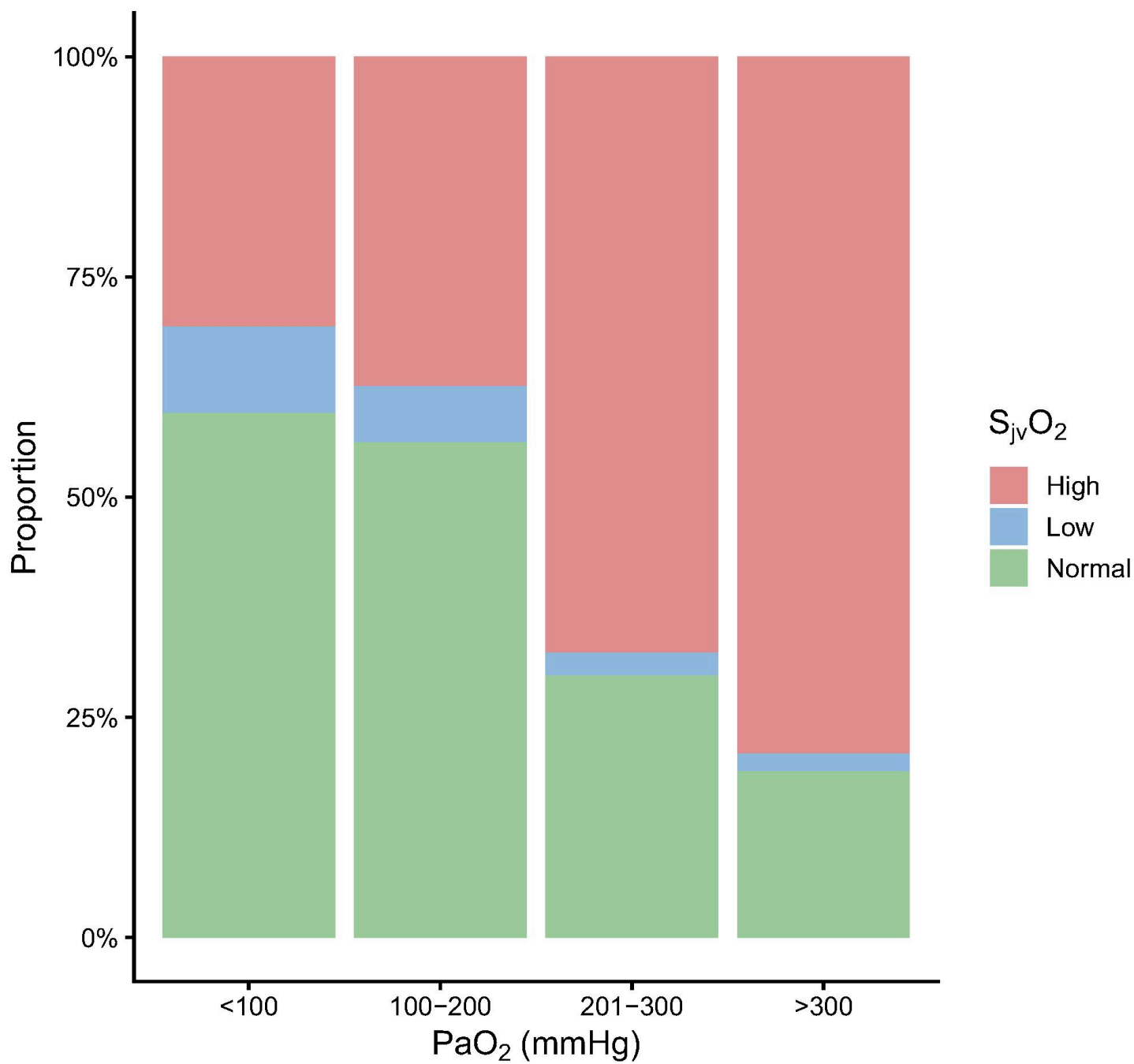


Figure 2

Legend not included with this version.