


ORIGINAL WORK



The Effects of Head Elevation on Intracranial Pressure, Cerebral Perfusion Pressure, and Cerebral Oxygenation Among Patients with Acute Brain Injury: A Systematic Review and Meta-Analysis

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Abstract

Background: Head elevation is recommended as a tier zero measure to decrease high intracranial pressure (ICP) in neurocritical patients. However, its quantitative effects on cerebral perfusion pressure (CPP), jugular bulb oxygen saturation (SjvO₂), brain tissue partial pressure of oxygen (PbtO₂), and arteriovenous difference of oxygen (AVDO₂) are uncertain. Our objective was to evaluate the effects of head elevation on ICP, CPP, SjvO₂, PbtO₂, and AVDO₂ among patients with acute brain injury.

Methods: We conducted a systematic review and meta-analysis on PubMed, Scopus, and Cochrane Library of studies comparing the effects of different degrees of head elevation on ICP, CPP, SjvO₂, PbtO₂, and AVDO₂.

Results: A total of 25 articles were included in the systematic review. Of these, 16 provided quantitative data regarding outcomes of interest and underwent meta-analyses. The mean ICP of patients with acute brain injury was lower in group with 30° of head elevation than in the supine position group (mean difference [MD] – 5.58 mm Hg; 95% confidence interval [CI] – 6.74 to – 4.41 mm Hg; $p < 0.00001$). The only comparison in which a greater degree of head elevation did not significantly reduce the ICP was 45° vs. 30°. The mean CPP remained similar between 30° of head elevation and supine position (MD – 2.48 mm Hg; 95% CI – 5.69 to 0.73 mm Hg; $p = 0.13$). Similar findings were observed in all other comparisons. The mean SjvO₂ was similar between the 30° of head elevation and supine position groups (MD 0.32%; 95% CI – 1.67% to 2.32%; $p = 0.75$), as was the mean PbtO₂ (MD – 1.50 mm Hg; 95% CI – 4.62 to 1.62 mm Hg; $p = 0.36$), and the mean AVDO₂ (MD 0.06 μmol/L; 95% CI – 0.20 to 0.32 μmol/L; $p = 0.65$). The mean ICP of patients with traumatic brain injury was also lower with 30° of head elevation when compared to the supine position. There was no difference in the mean values of mean arterial pressure, CPP, SjvO₂, and PbtO₂ between these groups.

Conclusions: Increasing degrees of head elevation were associated, in general, with a lower ICP, whereas CPP and brain oxygenation parameters remained unchanged. The severe traumatic brain injury subanalysis found similar results.

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Keywords: Head-of-bed, Head elevation, Head position, Cerebral hemodynamics, Intracranial pressure, Cerebral perfusion pressure, Jugular bulb oxygen saturation, Brain tissue partial pressure of oxygen, Arteriovenous difference of oxygen, Brain oxygenation, Meta-analysis, Systematic review

Introduction

Historically, studies have focused on intracranial pressure (ICP) and cerebral perfusion pressure (CPP) as targets in the management of patients with acute brain injury. In general, the treatment thresholds in the setting of intracranial hypertension are mainly derived from traumatic brain injury (TBI) guidelines because targets for non-traumatic etiologies were not adequately studied [1–3]. The fourth edition of Guidelines for the Management of Severe TBI [1], published by the Brain Trauma Foundation, recommends treating an ICP >22 mm Hg and targeting a CPP between 60 and 70 mm Hg, values that are associated with favorable outcomes [4].

By considering only ICP and CPP, important data regarding the physiologic and metabolic state of the brain are overlooked, and significant parenchymal hypoxia may occur even when ICP and CPP are normal [5, 6]. Data regarding cerebral oxygenation can be mainly assessed by jugular bulb oxygen saturation (SjvO₂) or by brain tissue partial pressure of oxygen (PbtO₂). Moreover, the arteriovenous difference of oxygen (AVDO₂) can also be determined by calculating the difference between the arterial oxygen saturation and SjvO₂ [7]. The last severe TBI guidelines [1] recommend that the use of SjvO₂ or AVDO₂ as a source of information for management decisions may be considered to reduce mortality and improve outcomes at 3 and 6 months post injury [1, 8–10]. This guideline provides no recommendations regarding the PbtO₂ for such purposes, although there is increasing interest in this parameter and ongoing phase III clinical trials evaluating whether its use is associated with better functional outcomes [11–13].

A variety of measures may be adopted to reduce ICP of patients with acute brain injury, including pharmacological and nonpharmacological interventions as well as emergent surgery [3]. Head elevation is generally recommended as a tier zero measure [3, 14, 15] in this setting and was demonstrated as an effective measure to reduce ICP in a previous meta-analysis [16]. However, by simultaneously decreasing mean arterial pressure (MAP), head elevation may theoretically reduce CPP and/or cerebral oxygenation [17]. The repercussions of head elevation on these parameters on CPP, as well as on cerebral oxygenation, are uncertain. In fact, we are unaware of meta-analyses addressing such parameters. Therefore, we aim to analyze the effects of different degrees of head elevation

on ICP, CPP, SjvO₂, PbtO₂, and AVDO₂ among patients with acute brain injury through a systematic review and meta-analysis.

Methods

This systematic review and meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement guidelines. The protocol was registered and made publicly available on the PROSPERO database (CRD42023391072) on January 22, 2023. This article complies with ethical standards, and institutional review board approval was not required.

Search Strategy and Selection Process

We systematically searched for studies on PubMed, Scopus, and Cochrane Library from inception to January 17, 2023. The exact search string is presented in Supplementary Table 1. Two independent reviewers analyzed all titles and abstracts for eligibility criteria. Articles were included if they assessed the effect of head elevation on any of the main outcomes in the setting of acute brain injury, defined as the life threatening acute neurological condition requiring the use of an invasive ICP measurement device. The main outcomes were ICP (direct measurements), CPP, SjvO₂, PbtO₂, and AVDO₂. Articles were excluded (1) if they were editorials, letters, book chapters, brief reports, or protocols and (2) if they were not available in the English language. When necessary, the full articles were also analyzed. Discrepancies were resolved by consensus between the reviewers.

Risk of Bias and Publication Bias Assessment

We used the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool for risk of bias assessment. The risk of bias was evaluated by two independent reviewers. Discrepancies were resolved by consensus between the reviewers. Publication bias was assessed through funnel plots.

Data Retrieval

The following main outcomes were collected and analyzed from each report: (1) ICP, (2) CPP, (3) SjvO₂, (4) PbtO₂, and (5) AVDO₂. Other data were also retrieved: (1) number of patients, (2) invasive ICP monitoring type, (3) age distribution, (4) degree of head elevation, (5) type

of brain injury, (6) mean invasive MAP value before and after intervention, (7) site of insertion of MAP catheter (e.g., radial artery or femoral artery), (8) level of MAP transducer (e.g., foramen of Monro or right atrium), (9) timing of intervention, and (10) timing of measurement of main outcomes after head positioning. Patients who underwent the intervention served as their own controls, with different degrees of elevation. When studies reported multiple timings of outcome measurements, we considered the first measurement. When studies reported more than one MAP transducer level, we considered the one measured at the level of Monro foramen.

Statistical Analysis

We used Cochrane's Review Manager version 5.4 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) for statistical analysis. Weighted mean differences (MDs) were used to pool continuous outcomes that appeared in two or more studies. Heterogeneity was evaluated with the Cochran Q test and the I^2 statistic. A $p < 0.10$ and an I^2 statistic $> 25\%$ were considered as heterogeneous. Overall estimates of effect and 95% confidence intervals (CIs) were calculated using a random-effects model and inverse variance weighting. When outcomes were present only on charts and did not show the exact values, we used an online resource to predict the values (<https://apps.automeris.io/wpd/>). When articles reported median and interquartile range, we estimated means and standard deviations (SDs) according to the methodology described by Luo et al. [18] and Wan et al. [19].

Subgroup and Sensitivity Analyses

We performed a subanalysis of studies that included only patients with TBI. When both the Cochran Q test p value and the I^2 statistic indicated heterogeneity, we performed sensitivity analyses. This consisted of (1) leaving individual studies out of the analysis (leave-one-out analysis) and (2) performing a meta-analysis of studies in which the baseline mean ICP (i.e., the ICP in the supine position) plus 1 SD reached the value of at least 22 mm Hg (higher ICP analysis).

Results

Study Selection, Baseline Characteristics, and Qualitative Analysis

The initial search yielded 1,610 results (Fig. 1). After the removal of duplicates and applications of eligibility criteria, 25 articles were included in the systematic review. Of these, 16 provided quantitative data regarding outcomes of interest, allowing for meta-analysis (quantitative analysis) [20–35]. Each outcome was analyzed in each comparison of 15° increments of head elevation when there

were two or more included studies (Fig. 1). Baseline characteristics of the nine studies [36–44] included in the qualitative analysis are shown in Supplementary Table 2, and their main findings are presented in Supplementary Table 3. These studies lacked sufficient information to undergo a meta-analysis, such as those that underwent the quantitative analysis. The baseline characteristics of studies included in the quantitative analysis are shown in Table 1. All included studies were prospective cohort studies.

ICP, MAP, and CPP

The mean ICP of patients with acute brain injury was lower at 30° of head elevation than in the supine position (MD – 5.58 mm Hg; 95% CI – 6.74 to – 4.41 mm Hg; $p < 0.00001$; Fig. 2a). The only comparison in which a greater degree of head elevation did not significantly reduce the ICP was 45° vs. 30°. In all other comparisons, increments of $\geq 15^\circ$ resulted in significantly lower ICP values (Supplementary Figs. 1–5). Increments of $\geq 15^\circ$ also resulted in lower MAP values, except for the 45° vs. 30° comparison (Fig. 2b and Supplementary Figs. 1–5). The mean CPP remained similar between 30° of head elevation and the supine position (MD – 2.48 mm Hg; 95% CI – 5.69 to 0.73 mm Hg; $p = 0.13$; Fig. 2c). Similar findings were observed in all other comparisons (Supplementary Figs. 1–5).

Brain Oxygenation

The mean S_{jv}O₂ was similar between the 30° of head elevation and supine position groups. There was no statistically significant difference between groups (MD 0.32%; 95% CI – 1.67% to 2.32%; $p = 0.75$; Fig. 3a). The mean P_{bt}O₂ was similar between the 30° of head elevation and supine position groups (MD – 1.50 mm Hg; 95% CI – 4.62 to 1.62 mm Hg; $p = 0.36$; Fig. 3b), as well as between the 30° and 15° of head elevation groups (MD – 0.99 mm Hg; 95% CI – 5.02 to 3.05 mm Hg; $p = 0.63$; Supplementary Fig. 3). The mean AVDO₂ was also similar between the 30° of head elevation and supine position groups (MD 0.06 $\mu\text{mol/L}$; 95% CI – 0.20 to 0.32 $\mu\text{mol/L}$; $p = 0.65$; Fig. 3c).

Severe TBI Subanalysis

A total of five articles provided quantitative data regarding outcomes of interest among patients with severe TBI, allowing for meta-analysis. This subanalysis was only possible in the 30° of head elevation group because outcomes were not present in ≥ 2 studies for other comparisons. The mean ICP of patients with TBI was lower with 30° of head elevation when compared with the supine position (MD – 4.78 mm Hg; 95% CI – 6.21 to – 3.36 mm Hg; $p < 0.00001$; Fig. 4a). There was no difference in the

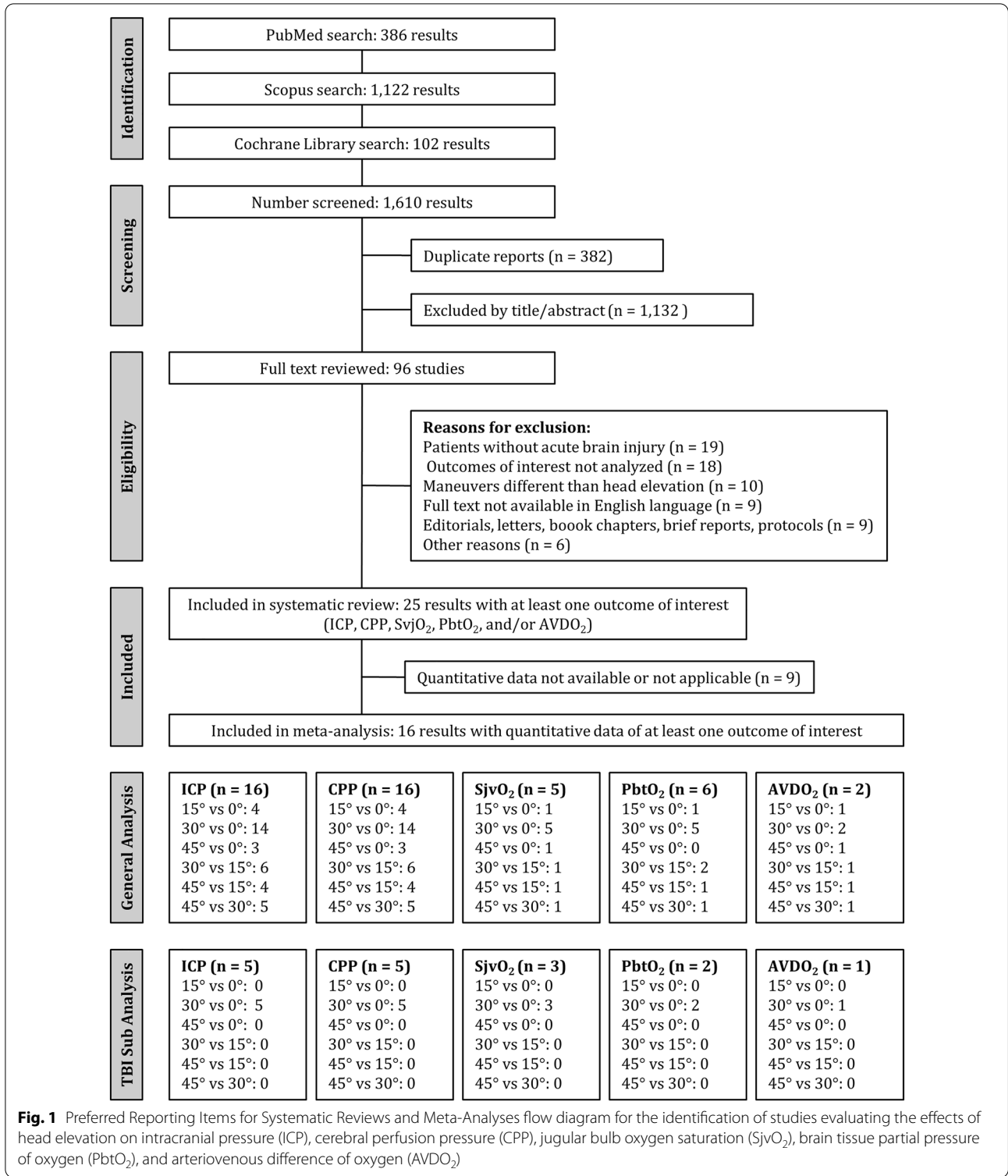


Table 1 Baseline characteristics of studies included in the quantitative analyses

Author, year	N	Mean age in years \pm SD (range)	Type of acute brain injury	Degrees of head elevation	Outcomes of interest measured	Timing of head positioning and assessment	Timing of evaluation after head elevation	Invasive ICP measurement method	Level of MAP transducer ^a	Site (artery) of MAP catheter placement
Brimouille et al. [22]	30	41 \pm N/A (3–78)	TBI, ICH, SAH	30, 45	ICP, CPP	N/A	N/A	Intraventricular	Foramen of Monro	N/A
Burnol et al. [21]	23	39.1 \pm 12.6 (N/A)	TBI, vascular, or other injury	0, 15, 30	ICP, CPP, PbtO ₂	Within 24 h, 48 h and 72 h after patient admission to the ICU	10 min	Intraparenchymal	Foramen of Monro	N/A
Dagod et al. [23]	24	39 \pm 16 (N/A)	TBI	0, 30	ICP, CPP, SjvO ₂	Daily during first 7 days of admission	30 min	Intraparenchymal	Foramen of Monro	Radial or femoral
Feldman et al. [20]	22	35 \pm N/A (18–75)	TBI	0, 30	ICP, CPP, SjvO ₂ , AVDO ₂	Within 72 h post injury	45 min	Intraventricular	Foramen of Monro	N/A
Kierning et al. [24]	18	N/A	TBI, ICH	0, 30	ICP, CPP, SjvO ₂ , PbtO ₂	Started on post injury day persisting to a varying number of days	15 min	Intraparenchymal	N/A	N/A
Kim et al. [25]	10	46 \pm 14.2 (18–62)	TBI, SAH	0, 30	ICP, CPP, PbtO ₂	Varied from post injury day 2 to 12	5 min	Intraparenchymal or intraventricular	Right atrium	Radial
Ledwith et al. [26]	33	48.3 \pm 16.6 (N/A)	TBI, SAH	15, 30, 45	ICP, CPP, PbtO ₂	N/A	15 min	Intraparenchymal	N/A	Radial
Mahfoud et al. [27]	33	54 \pm N/A (16–84)	SAH, ICH, TBI, tumor, AIS	0, 30, 60	ICP, CPP	N/A	5 min	Intraparenchymal or intraventricular	Foramen of Monro	Radial
Meixensberger et al. [28]	22	37 \pm 18.3 (17–71)	TBI	0, 30	ICP, CPP, PbtO ₂	Varied from post injury day 0–12, mostly on day 1 to 4	10–15 min	Intraparenchymal	Foramen of Monro	N/A
Moraine et al. [29]	37	52 \pm 16.8 (18–81)	TBI, SAH, ICH, tumor, hydrocephalus, encephalitis, thrombosis	0, 15, 30, 45	ICP, CPP, SjvO ₂ , ^b AVDO ₂	Varied from post injury day 1 to 36	10 min	Intraventricular	Foramen of Monro	N/A
Ng et al. [30]	38	34.0 \pm 16.0 (18–80)	TBI	0, 30	ICP, CPP, SjvO ₂ , PbtO ₂	Within 24 h after injury	15 min	Intraparenchymal	Foramen of Monro	N/A
Park et al. [31]	34	< 20y/o: 10 patients; 20–69y/o: 24 patients	TBI	0, 30	ICP, CPP, AVDO ₂ , ^c	Started in the first 12 h	240 min	Intraparenchymal	N/A	N/A

Table 1 (continued)

Author, year	N	Mean age in years \pm SD (range)	Type of acute brain injury	Degrees of head elevation	Outcomes of interest measured	Timing of head positioning and assessment	Timing of evaluation after head elevation	Invasive ICP measurement method	Level of MAP transducer ^a	Site (artery) of MAP catheter placement
Rosner et al. [32]	18	36.3 \pm 18.8 (12–83)	TBI, hydrocephalus, ICH, Reye's syndrome, tumor	0, 10, 20, 30, 40, 50	ICP, CPP	N/A	N/A	Intraventricular	Foramen of Monro	N/A
Schneider et al. [33]	25	48 \pm 15 (20–79)	TBI, SAH, ICH	0, 15, 30, 45	ICP, CPP, SjvO ₂	Within 72 h after admission	20 min	Intraventricular, intraparenchymal, or epidural	N/A	Radial
Schwarz et al. [34]	18	61 \pm 9.3 (N/A)	AIS	0, 15, 30	ICP, CPP	Within 6 days after injury	5 min	Intraparenchymal	Foramen of Monro	Radial or femoral
Ugras et al. [35]	30	52.8 \pm 17.0 (22–84)	TBI, tumor, SAH	15, 30, 45	ICP, CPP	N/A	15 min	Intraventricular	Right atrium	Radial

N refers to the number of patients in both the intervention and control groups (patients were their own controls before and after intervention)

AIS, acute ischemic stroke; AVDO₂, arteriovenous difference of oxygen; AVM, arteriovenous malformation; CPP, cerebral perfusion pressure; ICH, intracerebral hemorrhage; ICP, intracranial pressure; MAP, mean arterial pressure; N/A, not available; PbtO₂, brain tissue partial pressure of oxygen; SAH, subarachnoid hemorrhage; SD, standard deviation; SjvO₂, jugular bulb oxygen saturation; TBI, traumatic brain injury

^a Right atrium refers to the phlebostatic axis. Foramen of Monro refers to the level of the tragus of the ear. When both were reported, we considered the measurement at the level of the foramen of Monro

^b SjvO₂ values were obtained but not compared between 30° of head elevation and supine position

^c AVDO₂ values were obtained but not compared between 30° of head elevation and supine position

mean values of MAP, CPP, SjvO₂, and PbtO₂ between these groups (Fig. 4b–e). Other studies that included patients with TBI as part of their sample did not provide data particularly for this condition.

Risk of Bias and Publication Bias

The overall risk of bias was low in 24% ($n=6$ of 25), moderate in 48% ($n=12$ of 25), serious in 28% ($n=7$ of 25), and critical in zero studies. The analysis of each study is presented in Supplementary Table 4. Funnel plots for each publication bias analysis are shown in Supplementary Figs. 6–11.

Heterogeneity

For the main outcomes, there was high heterogeneity (demonstrated by both the Cochran Q test p value and the I^2 statistic) in the analysis of ICP and CPP between 30° of head elevation and the supine position (Fig. 2a, c, respectively). In the TBI subanalysis, there was also high heterogeneity in the analysis of CPP between 30° of head elevation and the supine position (Fig. 4c).

Sensitivity Analysis

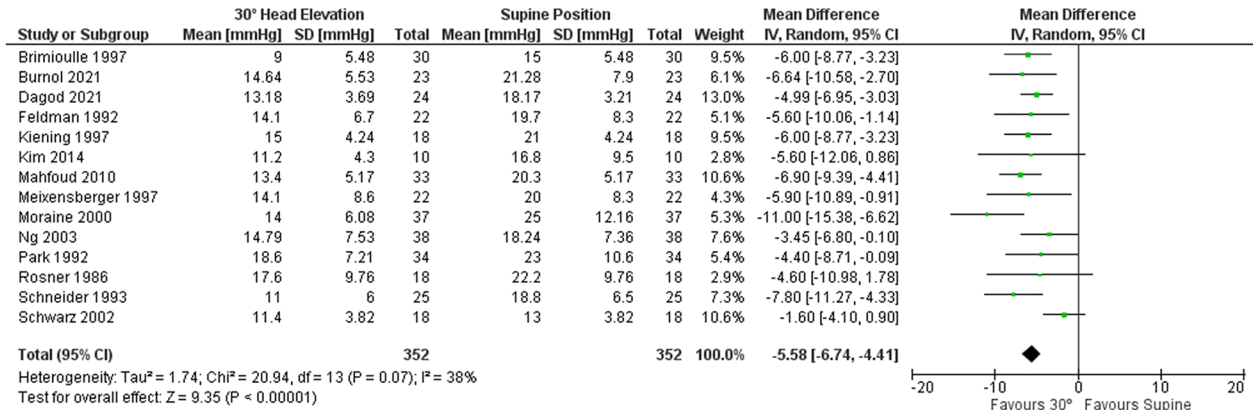
Leave-one-out Analysis

When removing the study by Schwarz et al. [34] from the ICP analysis between 30° and the supine position, the I^2 statistic dropped to 0% and the Cochran Q test p value increased to 0.56, meaning low heterogeneity. The removal of the study by Moraine et al. [29] also reduced in a lesser degree the heterogeneity, with an I^2 statistic of 17% and a Cochran Q test p value of 0.27. In the CPP analysis between 30° and the supine position, the study by Schwarz et al. [34] was the only study that, when removed, reduced the heterogeneity significantly, with an I^2 statistic of 27% and a Cochran Q test p value of 0.18. In the CPP analysis of the TBI subanalysis between 30° and the supine position, the removal of the study by Dagod et al. [23] significantly reduced the heterogeneity, with an I^2 statistic of 0% and a p value of 0.87.

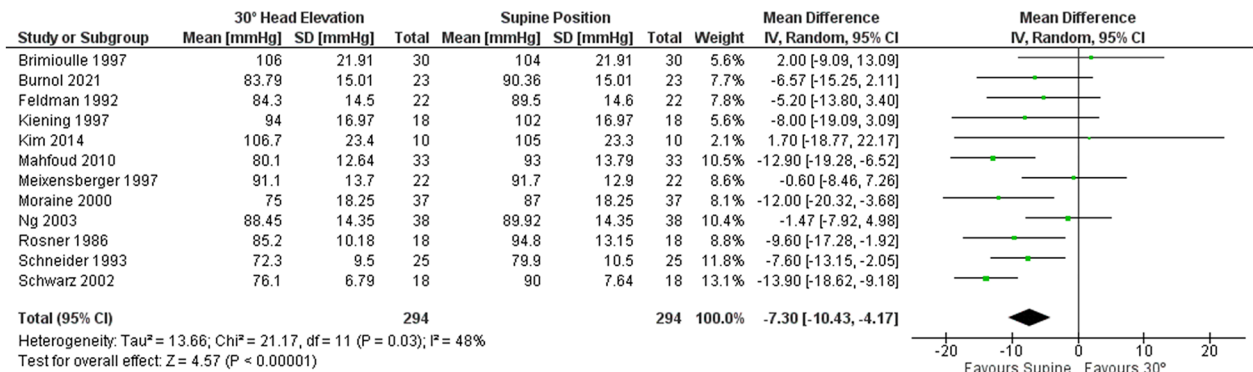
Higher ICP Analysis

For this approach, we removed studies with a lower mean ICP from analyses with a high heterogeneity (the studies by Brimiouille et al. [22], Dagod et al. [23], and Schwarz et al. [34]). The heterogeneity of the ICP analysis between 30° and the supine position reduced substantially (the I^2 statistic dropped to 0%, and the Cochran Q test p value increased to 0.49). The analysis of CPP between 30° and the supine position found similar results (the I^2 statistic dropped to 0%, and the Cochran

A Intracranial Pressure



B Mean Arterial Pressure



C Cerebral Perfusion Pressure

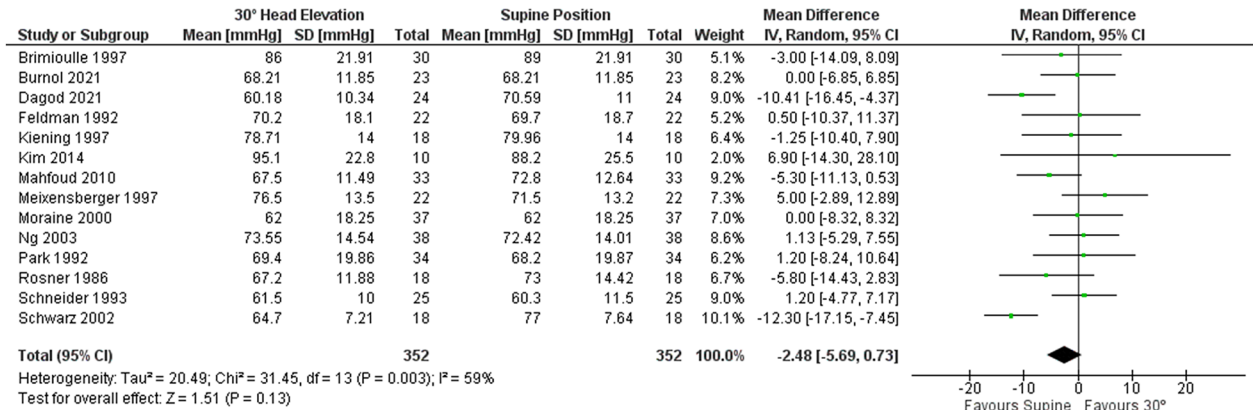
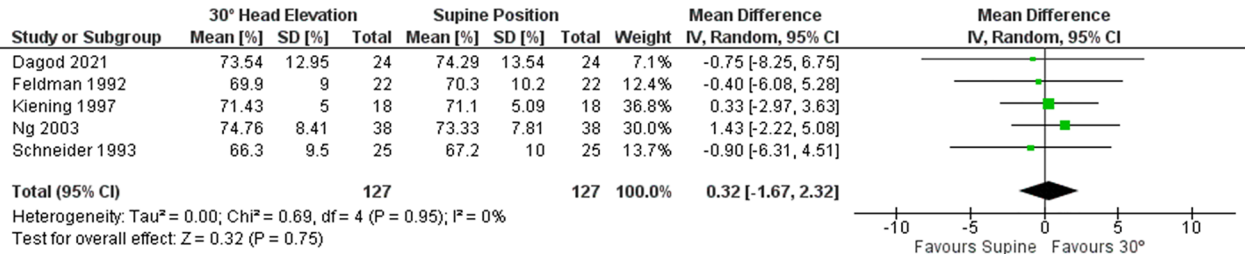


Fig. 2 Forest plots showing the mean differences between 30° of head elevation and supine positions in the setting of acute brain injury on intracranial pressure (ICP) (a), mean arterial pressure (MAP) (b), and cerebral perfusion pressure (CPP) (c). CI confidence interval, IV inverse variance, SD standard deviation

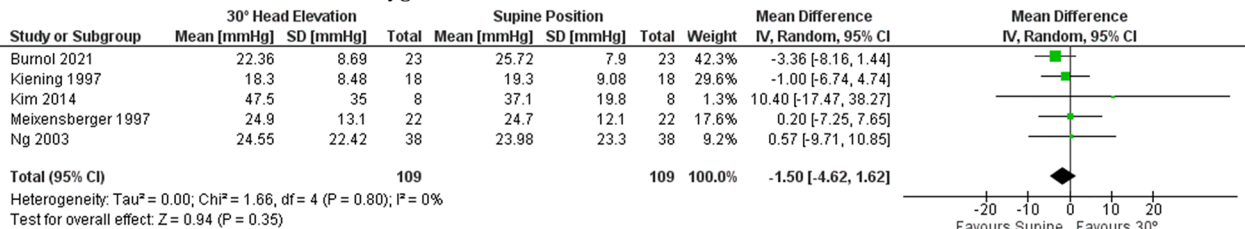
Q test *p* value increased to 0.71). In the severe TBI subanalysis, we removed the study by Dagod et al. [23], and the heterogeneity of the CPP analysis between 30° and

the supine position decreased significantly (the *I*² statistic dropped to 0%, and the Cochran Q test *p* value increased to 0.87).

A Jugular Bulb Oxygen Saturation



B Brain Tissue Partial Pressure of Oxygen



C Arteriovenous Difference of Oxygen

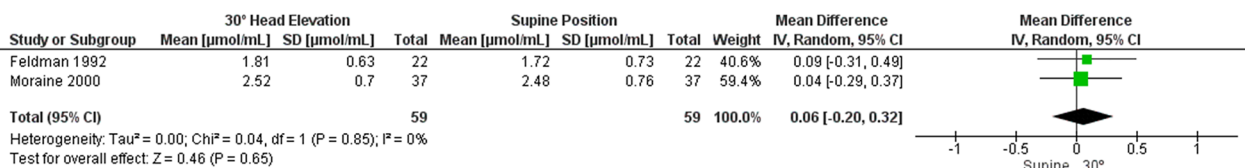


Fig. 3 Forest plots showing the mean differences between 30° of head elevation and supine positions in the setting of acute brain injury on jugular bulb oxygen saturation (SjvO₂) (a), brain tissue partial pressure of oxygen (PbtO₂) (b), and arteriovenous difference of oxygen (AVDO₂) (c). CI confidence interval, IV inverse variance, SD standard deviation

Discussion

Main Findings

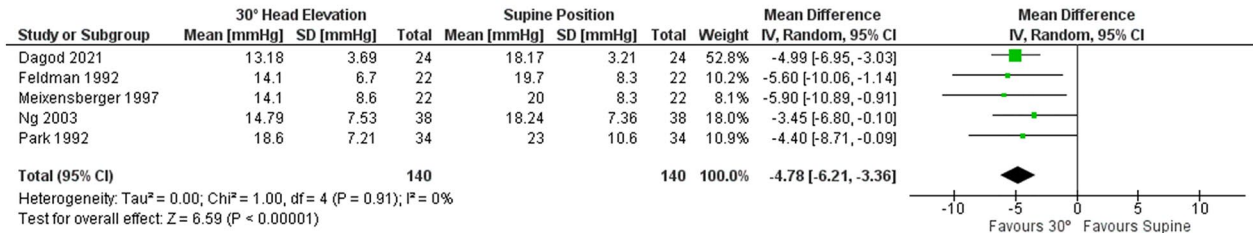
We conducted a systematic review and meta-analysis regarding the effect of head elevation on ICP, CPP, and brain oxygenation in the acute brain injury setting. Increasing degrees of head elevation was associated, in general, with a lower ICP, whereas CPP and brain oxygenation parameters remained unchanged. The severe TBI subanalysis found similar results.

ICP and CPP

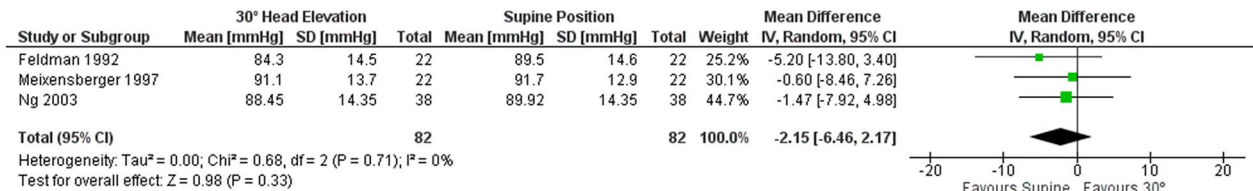
Our results demonstrated that increasing degrees of head elevation decreases ICP in patients with acute brain injury (Fig. 2a and Supplementary Figs. 1–5). This fact was also demonstrated by the severe TBI subanalysis (Fig. 4a). The exception was the comparison between 45° and 30° of head elevation, in which no statistical difference was found in the MD between groups. The CPP remained unchanged in all analyses (Figs. 2c and 4c and Supplementary Figs. 1–5). The MAP values decreased or tended to decrease with head elevation.

Of note, absolute CPP measurements may be affected by some MAP monitoring details, such as site of catheter insertion and level of measurements, which are not consistent across studies and sometimes are not even reported (Supplementary Table 2 and Table 1). In fact, measurements through the radial artery may underestimate MAP when compared to measurements through the femoral artery [45]. However, the differences in CPP measurements according to different degrees of head elevation should not be affected, regardless of the site of insertion. In addition, an MAP transducer at the level of the Monro foramen (approximately at the level of the tragus) tends to generate lower values than an MAP transducer placed at the level of right atrium when the head is elevated. Therefore, when an MAP transducer is placed at the level of right atrium, CPP values may be overestimated during head elevation. For purposes of accurate CPP calculations, councils by the Neuroanaesthesia and Critical Care Society of Great Britain and Ireland and the Society of British Neurological Surgeons endorse positioning (leveling)

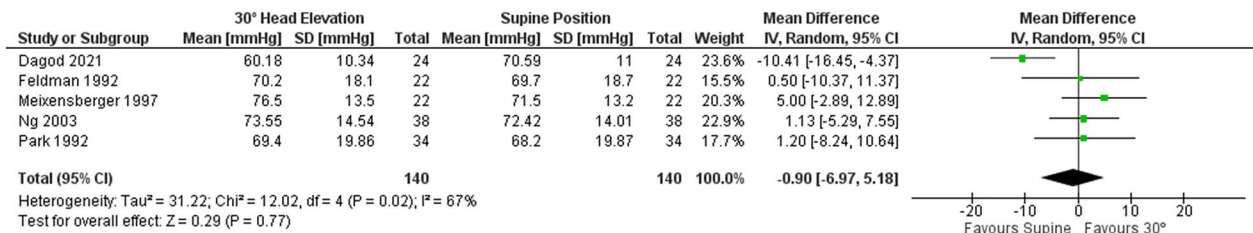
A Intracranial Pressure



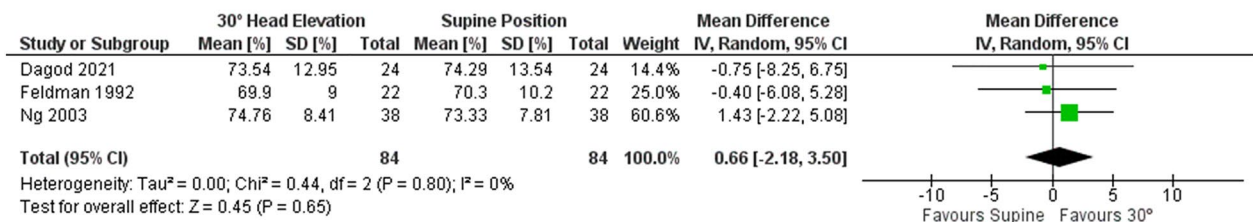
B Mean Arterial Pressure



C Cerebral Perfusion Pressure



D Jugular Bulb Oxygen Saturation



E Brain Tissue Partial Pressure of Oxygen

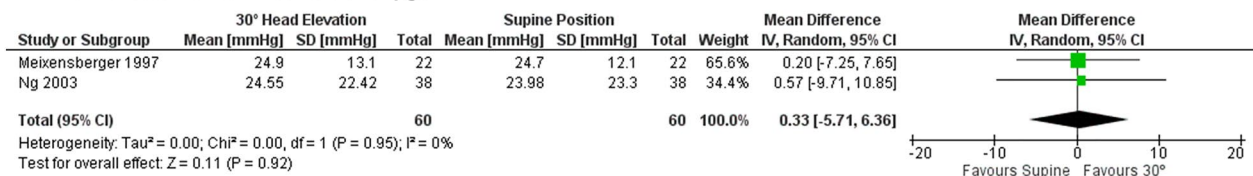


Fig. 4 Forest plots showing the mean differences between 30° of head elevation and supine positions in the subanalysis of severe traumatic brain injury (TBI) on intracranial pressure (ICP) (a), mean arterial pressure (MAP) (b), cerebral perfusion pressure (CPP) (c), jugular bulb oxygen saturation (SjvO₂) (d), brain tissue partial pressure of oxygen (PbtO₂) (e), and arteriovenous difference of oxygen (AVDO₂) (f). CI confidence interval, IV inverse variance, SD standard deviation

the arterial transducer at the level of the middle cranial fossa, which can be approximated to the tragus of the ear [46]. Moreover, we included studies of patients with different conditions and, hence, with different pathophysiology. For instance, the study by Schwarz

et al. [34] notably increased heterogeneity in the analysis of ICP and CPP between 30° of head elevation and the supine position by showing no effect on ICP and impairment on CPP (Fig. 2a, c). Interestingly, this was the only study that included exclusively patients with

hemispheric ischemic stroke. In other articles, patients with ischemic stroke represented a small portion of the sample. In addition, the study by Schwarz et al. [34] was the one in which patients presented the lowest mean ICP in the supine position. Possibly, these factors were the most responsible for these discrepancies, and additional caution should be taken when extrapolating our results to the ischemic stroke population. Indeed, a prior meta-analysis [17] demonstrated that the middle cerebral artery mean flow velocity among patients with acute ischemic stroke increased significantly in the side affected but not in the unaffected side when they were positioned in a lying-flat head position at the supine position or at 15° of head elevation in comparison with 30° of head elevation.

In the severe TBI analysis between 30° of head elevation and the supine position, the study by Dagod et al. [23] increased the heterogeneity of the CPP results by showing a deleterious effect. Conversely, other severe TBI studies showed no significant effect of head elevation on CPP (Fig. 4c). We did not find a specific reason for these discrepancies because we did not detect patient characteristics, measurement methods, or interventional approaches that were exclusive to this specific study.

Brain Oxygenation

There are various types of brain oxygenation monitoring. The most used are the S_{iv}O₂ and the PbtO₂. The S_{iv}O₂ can be used for the indirect measurement of oxygen supply to the brain as a whole and its consumption. It also allows for the calculation of the AVDO₂, whose alterations may reflect changes in cerebral blood flow. S_{iv}O₂ and the AVDO₂ monitoring can be considered to reduce mortality and improve outcomes at 3 and 6 months after severe TBI [1, 8–10].

The PbtO₂ values reflect a regional oxygenation of the brain tissue, and there is increasing research interest in such a parameter. In fact, three phase III clinical trials are underway to study the benefits of PbtO₂ monitoring in the setting of severe TBI: the BOOST-3 trial [12] (NCT03754114), the OXY-TC trial [11] (NCT02754063), and the BONANZA trial [13] (ACTRN12619001328167). In our study, we did not find a statistically significant difference of brain oxygenation parameters (S_{iv}O₂, PbtO₂, and AVDO₂) in all comparisons that we made across different degrees of head elevation (Fig. 3 and Supplementary Fig. 3d). The severe TBI analysis also showed no difference in S_{iv}O₂ and PbtO₂ parameters (Fig. 4d, e) between 30° of head elevation and the supine position.

The Timing Factor

Although the timing of head elevation since acute brain injury or since patient admission may play an important role in the findings, many studies did not mention it or did not detail it adequately. Among studies that mentioned it, this timing varied substantially (Supplementary Table 2 and Table 1). It is not clear whether the outcomes of interest remain steady during the first days after injury [21, 23]. Also, the timing of parameter measurement after intervention varied widely across studies (Supplementary Table 2 and Table 1), which may also influence the results.

ICP Measurement Methods

The most common methods of ICP monitoring were intraparenchymal and intraventricular probes (Supplementary Table 2 and Table 1). The intraventricular measurement is considered the gold standard because of its accuracy [47, 48]. In addition, it also allows the simultaneous drainage of cerebrospinal fluid. Intraparenchymal probes tend to reflect a local cerebral pressure rather than the ventricular pressure. However, its placement is generally easier and faster, especially in patients with small ventricles or severe brain edema [47, 48]. The included studies did not provide comparisons of outcomes according to different types of ICP monitoring.

Strengths and Limitations

This study presents limitations. First, we analyzed patients with acute brain injuries due to pathologies with different pathophysiology altogether, although many included studies also used this approach. We performed a subanalysis of patients with severe TBI to minimize heterogeneity. Subanalyses of other conditions were not possible because of the low or inexistent number of articles analyzing only patients with specific pathologies. Second, we only assessed invasive methods of neuromonitoring and did not perform comparisons among them. Methods such as transcranial Doppler, optic nerve sheath diameter, near-infrared spectroscopy, pupillometry, and skull elasticity-based measurements were beyond the scope of this article. Third, we did not assess clinical outcomes, such as mortality or disability. However, measuring the effect of head elevation on values of brain monitoring is clinically relevant because it allows us to avoid values associated with increased mortality and/or disability, for instance. To the authors' best knowledge, only one randomized trial (HeadPoST trial [49]) assessed the clinical effects of head elevation among neurocritically ill patients. This study found no difference on disability outcomes between patients with acute ischemic stroke assigned to a lying-flat position for 24 h and patients assigned to a sitting-up

position with the head elevated to at least 30° for 24 h. Fourth, we included only English-language studies. This was probably the only exclusion criterion for some articles. Fifth, several aspects may influence our findings and were not quantitatively assessed, such as additional therapies (e.g., hyperosmolar therapy, temperature management, vasoactive drugs, ventilatory parameters, PaCO₂, PaO₂, sedation, decompressive craniectomy) as well as the timing of measurements and interventions. Decompressive craniectomy may heavily affect brain hemodynamics [50] and was only assessed by Burnol et al. [21] and Schwarz et al. [34], whose findings demonstrated no effect of this therapy on postural induced ICP changes. Other studies that included patients who underwent decompressive craniectomy did not perform analysis in this subgroup [24, 32, 34, 36, 38]. Sixth, only 7 of the 25 included studies described how the degrees of head elevation was obtained (by using a goniometer or a protractor). Other studies did not mention the method.

Recommendations for Future Studies

Future studies on head elevation in the setting of acute brain injury should include a more homogeneous sample. For instance, articles should include only patients with a specific condition (e.g., subarachnoid hemorrhage, TBI, or intracerebral hemorrhage) instead of analyzing them together. When more than one pathology is included, subanalyses of each condition or individual patient data reporting would be reasonable approaches. Even within a same pathology, however, important characteristics should be clearly described (e.g., isolated TBI and TBI with concomitant polytrauma) because they may potentially affect the analysis of outcomes. A clear and detailed methodology is essential. Information such as the site of MAP insertion, the level where the MAP transducer was placed, the type of ICP monitoring, the timing of parameter measurement since patient admission, and the timing of parameter measurement after head positioning is imperative.

Conclusions

Our results suggest that head elevation is an effective measure to reduce ICP, without significant effect on CPP and brain oxygenation parameters. We are unaware of previous meta-analyses addressing all these parameters. In the severe TBI subanalysis, we also found similar results. Regarding general clinical practice, head elevation also decreases the rates of ventilator-associated pneumonia [51]. However, studies analyzing the effects of head elevation on brain hemodynamics and oxygenation with other specific conditions (e.g., subarachnoid hemorrhage, intracerebral hemorrhage, and stroke) are scarce. Therefore, additional caution is important when performing

head elevation in these scenarios, with the purpose of improving brain hemodynamics and oxygenation.

Supplementary Information

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Declarations

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval/informed consent

This article complies with ethical standards, and institutional review board approval was not required.

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