

REVIEW

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Effect of blood pressure threshold on adverse outcomes in patients with acute spinal cord injury: a systematic review and meta-analysis

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Abstract

Background Inadequate spinal perfusion in acute spinal cord injury (SCI) can exacerbate secondary injury. While current guidelines recommend maintaining mean arterial pressure (MAP) ≥ 75 –80 mmHg post-injury, no quantitative analysis on effects of blood pressure on neurological outcomes exists. We aim to address this gap and evaluate the impact of blood pressure thresholds on adverse outcomes in acute traumatic and non-traumatic SCI to inform current guidelines.

Methods The project adhered to PRISMA and MOOSE guidelines and was registered in PROSPERO (CRD42024550044). We searched seven databases: MEDLINE, Embase, Cochrane Central, Cochrane Reviews, CINAHL, Scopus, and Web of Science. We included studies involving patients ≥ 16 yrs with acute SCI, randomized control trials, prospective cohorts, and retrospective (case-control, cohort) studies. Excluded were chronic SCI and studies mentioning induced hypotension. The main outcome was the relationship between blood pressure thresholds and adverse functional outcome at up to one-year post-injury. Outcomes (unadjusted odds ratios (uOR) and adjusted odds ratios (aOR)) were calculated using a random-effect model with 95% confidence intervals (CI). Quality was assessed using the Newcastle-Ottawa Scale and Cochrane Risk of Bias Tool.

Results Of 16,366 identified articles, 38 ($n = 7,167$, 73% male) were included in the qualitative and 14 ($n = 2,553$, 76% male) in the quantitative analysis. Pooled analysis found an increase in adverse functional outcomes in patients with below threshold blood pressures (uOR, 3.28; 95% CI, 2.39–4.50; aOR, 1.04; 95% CI, 1.03–1.05). Subgroup analyses consistently showed that lower blood pressure thresholds were associated with worse outcomes across all subgroups. Risk of bias was low to moderate in most studies. Heterogeneity was moderate to high (I^2 : 69.88%).

Conclusion Lower blood pressure thresholds were consistently associated with worse functional outcomes in patients with acute SCI. While these findings support the rationale for MAP augmentation, they should be interpreted cautiously due to the observational nature of the data and high heterogeneity. High-quality prospective studies are needed to determine optimal blood pressure targets.

Keywords Spinal cord injury, Functional recovery, Blood pressure, Mean arterial pressure, Vasopressors, Meta-analysis

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Background

Spinal cord injury (SCI) is a prevalent issue worldwide, with the World Health Organization (WHO) estimating around 15.4 million people living with SCI in 2021 [1]. Hypotension, a common complication in patients with SCI, has been found to precipitate secondary injury, due to ischemia and hypoxia, leading to worse clinical outcomes [2]. The 2024 AO Spine & Praxis guidelines recommend maintaining mean arterial pressure (MAP) of at least 75–80 mmHg for the first 3–7 days to optimize spinal cord perfusion in acute traumatic SCI [3]. However, the quality of evidence supporting this recommendation is very low, and the strength of the recommendation is weak. Moreover, there is an unmet need for quantitative analyses examining the effect of blood pressure (BP) thresholds on outcomes for patients sustaining SCI. Our study aimed to address this gap by reviewing relevant literature and presenting the first meta-analysis pertaining to the impact of low BP thresholds on adverse functional outcomes in patients with SCI.

Methods

This review is registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024550044) and follows the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) [4] and Meta-analysis of Observational Studies in Epidemiology (MOOSE) [5] (Supplement eTables 11–12) reporting guidelines.

Data sources

The search strategy was developed in collaboration with an institutional librarian. Literature searches were conducted from inception until June 10, 2024, across the following databases: (1) MEDLINE, (2) Embase, (3) Cochrane Central Register of Controlled Trials, (4) Cochrane Database of Systematic Reviews, (5) Cumulative Index to Nursing & Allied Health Literature (CINAHL), (6) Web of Science, and (7) Scopus. The MEDLINE search strategy is provided in Supplement eTable 1.

Study selection

Initial title and abstract screening was performed by multiple independent reviewers (AT, AAR, WW, HA). Full text for titles that passed initial screening were retrieved and screened for eligibility. Disagreements were resolved by consensus or by consulting a senior author (TC). Inter-reviewer reliability was assessed using Cohen's Kappa, which measures the degree of agreement between reviewers. The selection process was conducted using the Covidence software [6].

The inclusion criteria were: (1) original research articles investigating BP thresholds in patients with SCI;

(2) population: patients ≥ 16 years presenting with acute traumatic or non-traumatic SCI; (3) intervention: any type of BP threshold; (4) study design: primary research articles including randomized control trials (RCTs), prospective cohorts, and retrospective (case-control, cohort) studies. Exclusion criteria were: (1) abstracts, case series, case reports, reviews, letters, post hoc analyses, editorials; (2) articles discussing controlled or induced hypotension. No language restriction was applied. Only studies reporting odds ratios (ORs) or allowing calculation of ORs from study data were included in the meta-analysis.

Data extraction and synthesis

Summary data was extracted by four authors (AT, AAR, WW, HA) using a standardized data collection spreadsheet, including study characteristics, patient characteristics (age, sex, injury severity and mechanism), sample size, spinal level, BP threshold, functional outcomes, and study quality. All data was extracted from published reports, and study authors were contacted if additional information was required.

The primary outcome of interest was the functional outcome at up to one year post injury, defined as either neuromotor recovery (measured by the American Spinal Injury Association Scale (ASIA) grade recovery) or visceral organ function (defined as internal organ function, such as bladder, bowel, and respiratory function). We focused on functional outcomes as these were most often reported across studies and therefore most suitable for a meta-analysis. Secondary outcomes included vasopressor usage. We extracted ORs reported for the relationship between BP thresholds and functional outcomes. If an OR was not provided, we calculated it using the study's exposure (patients above or below the BP threshold) and adverse outcome (binary) if possible. Among studies reporting only correlation coefficients, we estimated the corresponding OR as described previously in the literature [7, 8].

Quality assessments of all included studies were performed by two reviewers (AAR, HA) using the Newcastle-Ottawa Scale (NOS) for cohort studies. The quality of studies was based on total points, with 7–9 points for good quality studies, 4–6 points for moderate quality, and 1–3 points for poor quality [9]. The Cochrane Risk of Bias Assessment was applied for RCTs [10]. We evaluated the certainty of evidence using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [11] framework approach, which considers several factors: risk of bias, indirectness, imprecision, inconsistency, and potential publication bias.

Statistical analysis

Meta-analysis was performed using Stata software version 18.0 (Stata Corporation, College Station, Texas).

The measures of effect of interest were unadjusted OR (uOR) and adjusted OR (aOR) with 95% confidence intervals (CI). Adjusted effect estimates, when available, were extracted as reported by the individual studies, which includes adjustment for covariates including age, injury severity, sex, and comorbidities (Supplement eTable 3). Subgroup analyses were conducted to explore potential sources of heterogeneity. The statistical heterogeneity between and within groups was assessed using Cochran's Q statistic. A p -value < 0.05 was considered statistically significant. We calculated pooled estimates and CIs assuming a random-effects model. Sensitivity analysis was performed using a leave-one-out analysis. Publication bias was investigated both visually by using a funnel plot and statistically with Egger's bias test, which

measures the degree of funnel plot asymmetry. $P < 0.1$ was considered to be representative of statistically significant publication bias.

Results

Search results and study characteristics

The search identified 28,396 studies. After removing duplicates, 16,366 were screened for title and abstracts, of which 127 were included for full text screening. Of these, 92 were excluded, with reasons listed in Fig. 1 and Supplement eTable 9. The Cohen's Kappa value for full text screening was 0.97, indicating excellent agreement between reviewers. Three additional articles were identified from citation searching, resulting in a total of 38 articles included for qualitative analysis [12–49]. Of these,

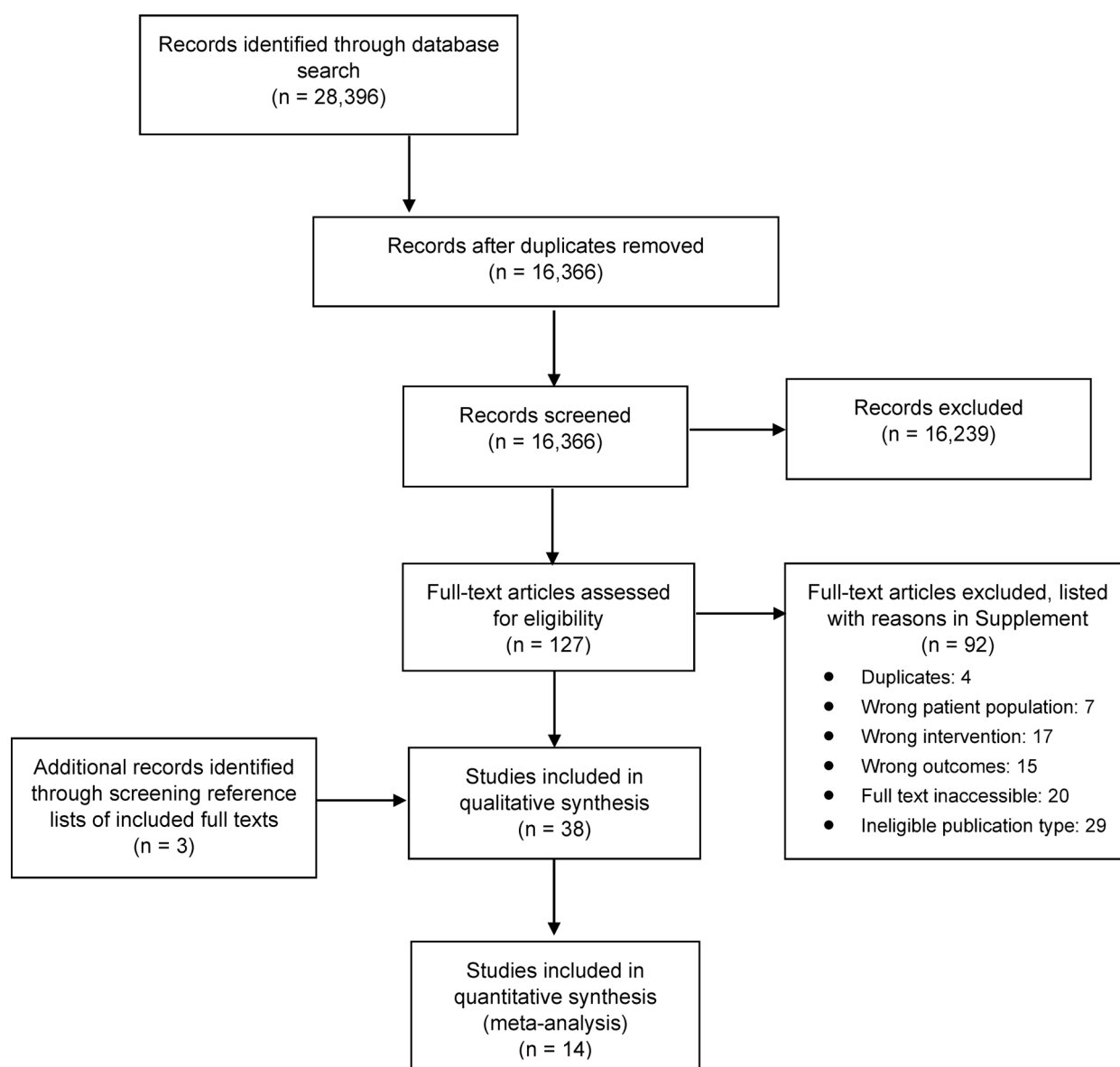


Fig. 1 PRISMA flow diagram of study selection

14 were eligible for quantitative meta-analysis [13, 20, 21, 25, 26, 29–32, 41, 43, 44, 46, 47] as they either reported ORs directly or provided sufficient data to allow OR calculation as outlined in the methods section.

The demographics and study characteristics of the 38 included studies are summarized in Table 1. A total number of 7,167 participants [mean age (std) 48.17 (14), 73% male] from 38 studies were included. Twelve studies (31%) were prospective cohort [18, 23, 27–29, 33, 35, 42, 43, 45, 46, 48], 22 (58%) were retrospective cohort [12, 13, 15–17, 19–22, 24–26, 31, 32, 34, 36–40, 44, 47], 3 (8%) were retrospective case control [14, 30, 49], and one (3%) was an RCT [41].

Meta-analysis of 14 studies (2,553 patients) revealed that lower BP thresholds (as defined in the individual study, based on the 2013 American Association of Neurological Surgeons (AANS) guidelines) was associated with increased adverse functional outcomes (uOR: 3.28, 95% CI: 2.39–4.50, $p < 0.0001$; aOR: 1.04, 95% CI: 1.03–1.05, $p < 0.0001$) (Supplement eFigure 1).

Subgroup analyses assessing MAP and SBP thresholds found that studies reporting both MAP and SBP thresholds showed an association between lower BP and adverse functional outcomes. The uORs for MAP and SBP thresholds were 3.83 (95% CI: 2.65–5.54, $p < 0.0001$) and 2.00 (95% CI: 1.41–2.84, $p < 0.0001$), respectively. The aORs were 1.88 (95% CI: 1.22–2.90, $p < 0.0001$) and 1.04 (95% CI: 1.02–1.06, $p < 0.0001$), respectively (Fig. 2).

In a subgroup analysis comparing MAP thresholds, patients whose MAP fell below 85 mmHg had higher odds of adverse functional outcome as compared to those whose MAP was maintained at or above 85 mmHg. This directionality was noted for both uOR [4.86 (95% CI: 2.73–8.64, $p < 0.0001$) vs. 2.85 (95% CI: 2.26–3.60, $p < 0.0001$)] and aOR [1.54 (95% CI: 0.94–2.52, $p = 0.09$) vs. 1.15 (95% CI: 0.99–1.34, $p = 0.06$)] (Supplement eFigure 3).

To assess the association between BP thresholds and adverse functional outcomes based on severity of SCI, as measured by the ASIA Impairment Scale, studies were grouped into two categories: complete motor complete injury (ASIA A and B) in 1) $\geq 50\%$ of patients and 2) $< 50\%$ of patients. Pooled uOR for the two groups was 7.27 (95% CI: 2.35–22.48, $p < 0.0001$) and 2.01 (95% CI: 1.18–3.43, $p = 0.01$), respectively (Supplement eFigure 4).

The effects of lower BP thresholds were further analyzed based on the level of SCI. For both cervical (uOR: 2.71, 95% CI: 2.13–3.47, $p < 0.0001$) and thoracolumbar SCI (uOR: 3.00, 95% CI: 1.72–5.22, $p < 0.0001$), lower BP thresholds had higher odds of adverse functional outcome (Supplement eFigure 5).

Subgroup analysis for studies reporting only isolated SCI and studies reporting both isolated and polytraumatic SCI showed an uOR of 3.15 (95% CI: 2.23–4.46,

$p < 0.0001$) and aOR of 1.04 (95% CI: 1.03–1.05, $p < 0.0001$) for isolated only injuries and an uOR of 3.89 (95% CI: 1.83–8.26, $p < 0.0001$) and aOR of 1.22 (95% CI: 1.04–1.42, $p = 0.01$) for both isolated and polytraumatic injuries (Supplement eFigure 6).

Subgroup analysis based on SCI etiology was also conducted, looking at traumatic (blunt or penetrating injury) (uOR 3.43, 95% CI: 2.40–4.89, $p < 0.0001$; aOR: 1.04, 95% CI: 1.03–1.05, $p < 0.0001$) and non-traumatic SCI (i.e. intraoperative ‘trauma’ or myelopathy) (uOR 2.57, 95% CI: 1.58–4.19, $p < 0.0001$; aOR 3.13, 95% CI: 1.78–5.50, $p < 0.0001$) (Supplement eFigure 7).

Subgroup analyses are presented for mean arterial pressure (MAP), systolic blood pressure (SBP), and spinal cord perfusion pressure (SCPP). Overall pooled estimates and heterogeneity (I^2) are shown for each group.

We also separated the functional outcomes into neuro-motor recovery (uOR: 3.61, 95% CI: 2.43–5.38, $p < 0.0001$; aOR: 1.04, 95% CI: 1.03–1.05, $p < 0.0001$) and visceral function (uOR: 2.54, 95% CI: 1.81–3.56, $p < 0.0001$; aOR 1.42, 95% CI: 0.91–2.23, $p = 0.12$) (Supplement eFigure 8).

Across the 38 studies, different vasopressors were used to maintain hemodynamic stability, including norepinephrine (21 studies) [14, 19, 21, 22, 24–28, 31, 32, 35, 37, 39, 40, 42, 43, 45–48], dopamine (13 studies) [12, 14, 16, 20–22, 26, 38–40, 42, 43, 46], phenylephrine (12 studies) [12, 14, 16, 20, 22, 25, 26, 33, 38, 42, 43, 47], ephedrine (2 studies) [19, 22], vasopressin (2 studies) [14, 22], dobutamine (2 studies) [37, 39], and epinephrine (1 study) [14] (Supplement eTable 2).

Dopamine was associated with an increased risk of cardiac complications (e.g., arrhythmias), whereas the risk was lower for norepinephrine and phenylephrine [12, 16, 38]. Two studies noted that vasopressor use in general was linked to cardiac dysrhythmias [18, 26]. One paper found that patients requiring vasopressors experienced a significantly increased risk of acute kidney injury (AKI) [19]. Another reported that vasopressor use was associated with an increased risk of in-hospital complications, such as pneumonia, deep vein thrombosis, unplanned return to the operating room, and unplanned intubation [47]. They also noted that higher cumulative doses of vasopressors did not improve outcomes, and the benefits of MAP augmentation diminished at excessive doses. Few studies reported outcome differences between the various vasopressors. Twelve studies maintained or monitored the BP for seven or more days [13, 18, 20, 27, 28, 36, 39, 42, 43, 45, 46, 48], three studies for five days [14, 21, 26], and five studies for three days or less [16, 17, 34, 44, 47].

The Galbraith plot (Supplement eFigure 10) was examined to assess potential outliers. A leave-one-out analysis was conducted (Supplement eTable 7–8) and did not reveal any studies that disproportionately influenced the

Table 1 Study characteristics of all included studies

Study	Country	Study design	Sample size	Mean age	Male (%)	SCI severity	SCI scale	Type of blood pressure	BP threshold (mmHg)	BP measurement setting	Days followed	Type of SCI
Agarwal [12]	USA	RC	74	51	73	Mod, Sev	AISA	MAP	76	Intraoperative	Discharge	Blunt/ Penetrating tSCI
Alfin [13]	Nigeria	RC	296	35.96	83.3	Mod, Sev	ASIA	MAP	80	Neurosurgical unit	42	Blunt tSCI
Balasubramaniam [14]	Canada	RCC	82	50.6	89	Sev	AISA	MAP	80	Trauma unit	Discharge	tSCI
Blue [15]	USA	RC	910	61.6	48.9	NA	NA	MAP	65	Intraoperative	NA	Intraoperative trauma
Catapano [16]	USA	RC	62	41.6	NA	Sev	ASIA	MAP	85	ICU	40	Blunt/ Penetrating tSCI
Chen [17]	China	RC	105	48.78	68.6	Mod, Sev	ASIA	SBP	NA	On admission, ICU	180	Cervical tSCI
Chen [18]	UK	PC	45	NA	77.8	Sev	ASIA	SCPP	NA	ICU	270–365	Blunt tSCI
Chiang [19]	China	RC	1833	NA	57.4	NA	NA	SBP	80	Intraoperative	NA	Intraoperative trauma
Cohn [20]	USA	RC	17	32.8	82.4	Sev	ASIA	MAP	Variable	In hospital	7	Blunt tSCI
Dakson [21]	Canada	RC	94	47.6	79	Mod, Sev	ASIA	MAP	85	ICU	26.7	Blunt tSCI
Ehsanian [22]	USA	RC	25	42.44	68	Mod, Sev	ASIA	MAP	50	Intraoperative	41.8	Blunt tSCI
Gallagher [23]	UK	PC	12	40	66.7	Sev	ASIA	SCPP	NA	Neurosurgical unit	240	Blunt tSCI
Glassman [24]	USA	RC	539	59.8	42	NA	NA	MAP	65	Intraoperative	30	Intraoperative trauma
Haldrup [25]	Denmark	RC	129	50	81.4	Mod, Sev	ASIA	MAP	80	Pre-Hospital, Intraoperative, ICU	365	Blunt tSCI
Hawryluk [26]	USA	RC	100	NA	75.3	Mod, Sev	ASIA	MAP	85	ICU	30	Blunt/Penetrating tSCI
Hogg [27]	UK	PC	14	47.4	92.9	Sev	ASIA	SCPP	60	ICU	243	Blunt tSCI
Hogg [28]	UK	PC	13	47.1	92.3	Sev	ASIA	SCPP	60	ICU	365	Blunt tSCI
Jiang [29]	Canada	PC	798	44.6	78	Mod, Sev	AISA	MAP, SBP	85, 90	On admission	365	Blunt/Penetrating tSCI
Kamel [30]	USA	RCC	152	53	53	Mod, Sev	NA	MAP	55	Intraoperative	NA	Intraoperative trauma
Långsjö [31]	Finland	RC	51	54.9	84	Mod, Sev	ASIA	MAP	85	ICU	110, 69	Cervical tSCI
LaRiccia [32]	USA	RC	96	52.74	77	Mod, Sev	ASIA	MAP	85	Trauma unit	NA	Blunt tSCI
Li [33]	China	PC	102	63	42.2	NA	ASIA	MAP	Variable	Intraoperative	NA	Intraoperative trauma
Martin [34]	USA	RC	105	49.53	70.5	Mod, Sev	AMS	MAP	85	ICU	Discharge	Blunt/Penetrating tSCI
Müller [35]	Germany	PC	99	72.2	50.5	NA	NA	SBP	NA	Intraoperative	365	Intraoperative trauma
Mushlin [36]	USA	RC	193	43	82	Sev	ASIA	MAP	85	Neurosurgical unit	180	Cervical tSCI
Rask [37]	Sweden	RC	52	53	73	Mod, Sev	ASIA	MAP	85	ICU	90	Blunt tSCI
Readdy [38]	USA	RC	36	39.39	77.8	Sev	ASIA	MAP	85	ICU	Discharge	Penetrating tSCI
Reikh [39]	Russia	RC	104	34.3	82.7	Mod, Sev	ASIA	MAP	85	ICU	120–180	Blunt tSCI
Santos [40]	Brazil	RC	49	34.7	89.8	Mod, Sev	ASIA	SBP	90	Trauma unit	Discharge	Blunt/Penetrating tSCI
Sharma [41]	India	RCT	60	55.45	NA	NA	NA	MAP	NA	Intraoperative	365	Intraoperative trauma
Squair [42]	Canada	PC	92	43	78.3	Sev	ASIA	MAP, SCPP	80, 60	ICU	180	NA
Squair [43]	Canada	PC	92	43	78.3	Sev	ASIA	MAP, SCPP	80, 50	ICU	180	NA
Tee [44]	Australia	RC	570	49.2	71.9	Mod, Sev	ISS	SBP	100	Trauma unit	365	Blunt tSCI
Visagan [45]	UK	PC	13	44.17	76.9	Sev	ASIA	MAP	85	ICU	237	Cervical tSCI

Table 1 (continued)

Study	Country	Study design	Sample size	Mean age	Male (%)	SCI severity	SCI scale	Type of blood pressure	BP threshold (mmHg)	BP measurement setting	Days followed	Type of SCI
Vale [46]	USA	PC	64	NA	84	Mod, Sev	ASIA	MAP	85	ICU	365	Blunt tSCI
Weinberg [47]	USA	RC	136	52	75	Mod, Sev	ASIA	MAP	85	Trauma unit	NA	Blunt tSCI
Wernle [48]	UK	PC	18	45.16	61.2	Sev	ASIA	SCPP	60	ICU	7	Blunt tSCI
Zhang [49]	China	RCC	40	54.67	67.5	Mod, Sev	ASIA	MAP	70	On admission	365	Cervical tSCI

ASIA = American Spinal Injury Association Scale; BP = Blood Pressure; ICU = Intensive Care Unit; MAP = Mean Arterial Pressure; Mod = Moderate; NA = Not Available; PC = Prospective Cohort; RCC = Retrospective Cohort; RC = Randomized Control Trial; SBP = Systolic Blood Pressure; SCI = Spinal Cord Injury; SCPP = Spinal Cord Perfusion Pressure; Sev = Severe; tSCI = Traumatic Spinal Cord Injury

overall results, supporting the robustness of the findings. There was very weak evidence of publication bias as assessed using both visual inspection via funnel plot (Supplement eFigure 9) and quantitatively via Egger's test (z-test statistic of 0.99, $p=0.32$). There was substantial heterogeneity across the included studies, as reflected by an I^2 value of 69.88% (Supplement eFigure 1).

Quality assessment by the NOS (Supplement eTable 4) showed 35 studies were of 'good' quality, while three were 'fair'. Cochrane Risk of Bias Assessment (Supplement eTable 5) for the RCT was found to have a low risk of bias. GRADE classification (Supplement eTable 10) identified the evidence of nine results as 'low' and four as 'moderate'.

Discussion

This meta-analysis encompassing 2,553 patients across 14 studies provides the first quantitative synthesis of the association between BP thresholds and functional outcomes following acute SCI. Our findings show a consistent association between lower BP thresholds (e.g., MAP < 85 mmHg) and worse functional recovery. This directionality was consistent across all subgroups. However, it is important to emphasize that these findings are based on observational data and do not establish causality. Whether actively targeting high MAP improves outcomes remains uncertain.

The discrepancy between the adjusted and unadjusted effect estimates in our meta-analysis is notable and likely reflects the influence of confounding variables in observational studies. Interpretation of this result is challenging due to the substantial heterogeneity across studies and relatively small number of studies reporting adjusted effect estimates. However, the consistent directionality of effect across both measures supports the underlying association between lower BP thresholds and adverse functional outcomes. Future studies with rigorous adjustments for confounders will shed light on the clinical significance of this relationship.

Our findings support the idea that a universal MAP target may offer neurological benefit but also raise questions about whether a single MAP target is appropriate for all patients. For instance, studies with a greater proportion of motor complete injuries (ASIA A-B) showed a stronger association between lower MAP and adverse outcomes. It is possible that patients with more severe injuries are more vulnerable to suboptimal perfusion, potentially due to impaired autoregulatory mechanisms [50]. A systematic review involving animal models found that the rate of axonal degeneration was higher in severe injuries [51], which may increase susceptibility to secondary ischemic damage especially in the setting of suboptimal perfusion. However, this observation needs to be validated in controlled prospective studies.

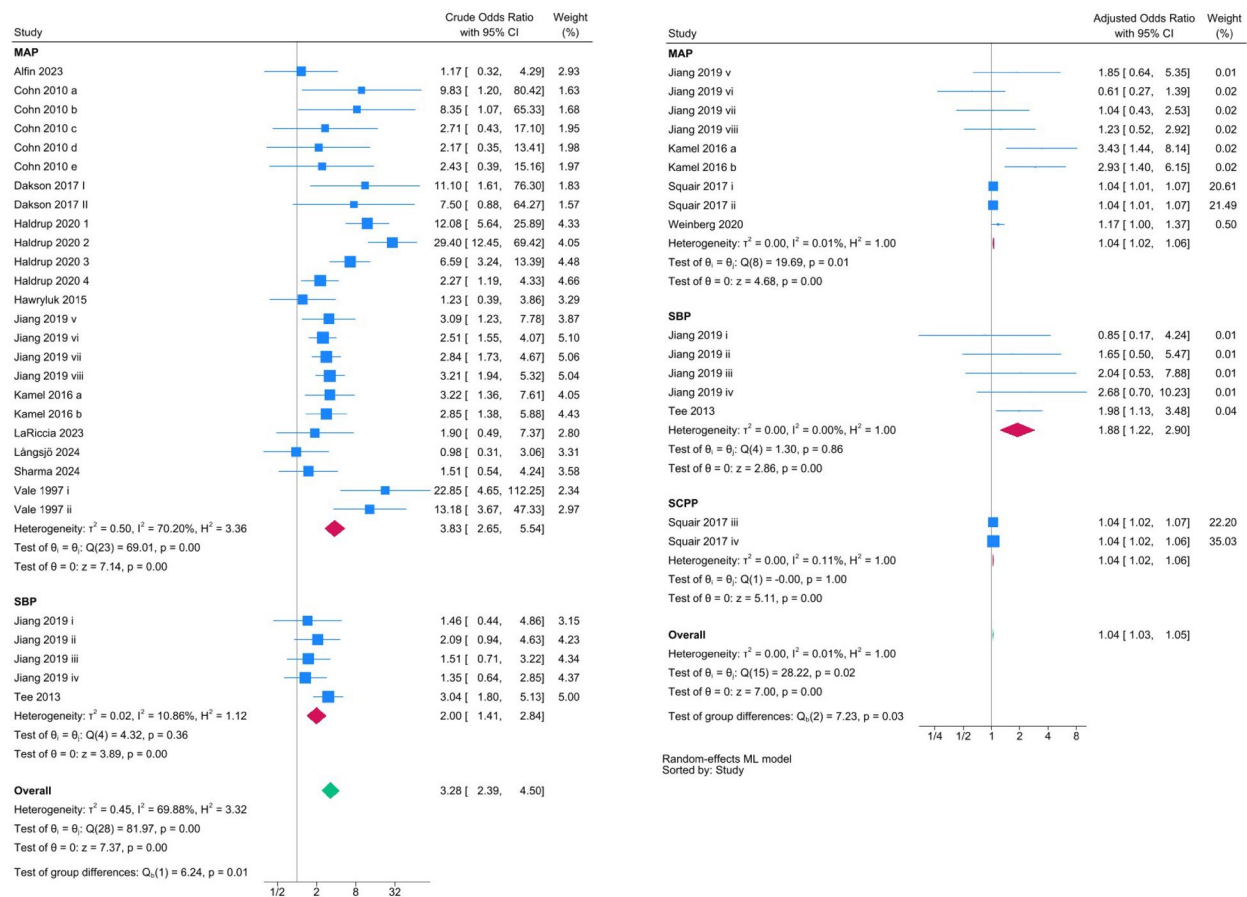


Fig. 2 Forest plot summarizing the unadjusted (left) and adjusted (right) odds ratios for adverse outcomes associated with blood pressure thresholds in acute SCI

Moreover, the widespread reliance on vasopressors to augment MAP introduces clinical issues. Cumulative vasopressor exposure was reported to increase adverse complications, such as AKI and respiratory complications [18, 47]. Notably, some studies in our review observed diminishing returns or even harm with aggressive augmentation strategies. These findings pose an important question as to when vasopressor therapy becomes detrimental rather than beneficial. Determining this inflection point is essential to ensuring that interventions intended to preserve spinal cord perfusion do not inadvertently contribute to secondary morbidity. Additionally, the overall impact of vasopressors on long-term neurological recovery remains unclear. Future studies should investigate whether specific vasopressor agents contribute to improved functional outcomes or introduce additional risks. Future studies should also investigate optimal agent, dosing, and upper hemodynamic target limits for vasopressor use.

These results are consistent with results of prior reviews exploring hemodynamic management in SCI. Qualitative analyses done by Evaniew et al. [52] identified a positive association between SCPP and neurological

outcomes, and Lee et al. [53] found that MAP > 85 mmHg improved outcomes. Our study builds upon prior reviews by incorporating a larger sample size and conducting extensive meta-analysis to produce an estimate of effect size. Across all reviews, limitations such as low-quality evidence, absence of meta-analyses, and study heterogeneity highlight the need for robust, prospective research to establish evidence-based protocols. These prior reviews are summarized in Table 2.

Our findings are also consistent with broader neurocritical care evidence, such as in traumatic brain injury, where hypotension has also been linked to worsened outcomes [54]. These parallels highlight the susceptibility of both the brain and spinal cord to ischemic insults and support the principle that maintaining perfusion may mitigate secondary injury and improve outcomes.

Our study also aligns with evidence that early physiologic optimization in the acute phase of SCI is associated with improved neurological outcomes. A recent meta-analysis looking at surgical decompression to restore spinal cord blood flow reported that early decompression significantly improved recovery compared to delayed surgery [55]. The report reinforces the critical nature of

Table 2 Comparison of existing reviews on blood pressure management and outcomes in spinal cord injury

	No. of Studies	Sample Size	Main Findings	Strengths	Limitations
Evaniew et al. [52]	• 28 studies (1 RCT, 11 cohort, 15 case series, 1 case report)	• 1433 patients	• Increased SCPP may be associated with improved neurological outcomes	• Systematic approach (PRISMA guidelines) • Recent studies included	• Heterogenous studies • Low quality evidence • No meta-analysis*
Lee et al. [53]	• 8 studies (5 prospective, 3 retrospective)	• 431 patients	• MAP > 85 mmHg benefits outcomes, but requires vasopressors, which have complications • SCPP also critical to consider	• Comprehensive review of MAP and SCPP • Vasopressors analyzed	• Single database search • No systematic review/meta-analysis*
Bertram-Ralph & Horner [56]	• 12 studies	• Unknown	• High MAP helps early SCI stages, but induced HTN is not best practice due to risks	• Discussed 2 systematic reviews with high-quality evidence	• No systematic approach (shortcut review) • No qualitative synthesis of included articles • No meta-analysis*
Sabit et al. [57]	• 9 cohort studies (2 prospective, 7 retrospective)	• 632 patients	• Objective outcomes related to MAP documented, but no clear conclusions	• Systematic approach (PRISMA guidelines) • Comprehensive database search & manual reference checks	• Small, mostly retrospective studies • Heterogenous studies • No meta-analysis*
Saadeh et al. [58]	• 11 cohort studies (2 prospective, 9 retrospective)	• 788 patients	• MAP 85–90 mmHg for 5–7 days suggested for acute SCI	• Systematic approach (PRISMA guidelines) • Vasopressors analyzed	• Lack of high-quality data • Reliance on retrospective studies • No meta-analysis*
Ploumis et al. [59]	• 7 human studies	• 906 patients	• Complete cervical SCI requires vasopressors more than other SCI • No single vasopressor proven superior	• Systematic approach (PRISMA guidelines) • Animal & human studies • Vasopressors analyzed	• Outdated (2010) • Limited database search • Low quality evidence • No meta-analysis*

*Prior reviews did not include a meta-analysis, highlighting a key distinction between these reviews and the present study, which is the first to perform a meta-analysis on this topic

the early post-injury window and highlights the importance of restoring and maintaining spinal cord perfusion in neurological recovery.

A key strength of our review is its robust methodology, including a comprehensive search strategy across multiple major databases without any language restrictions. Furthermore, our study is the first to include a quantitative analysis on the relationship between BP thresholds and functional outcomes, providing a unique insight into managing SCI. We also report extensive subgroup analyses, stratifying by BP type and magnitude, spinal level, polytrauma injuries, and mechanism of injury.

Despite the strengths, there are several limitations in our study that must be acknowledged. First, the substantial heterogeneity of the included studies poses a challenge in interpreting the results. Differences in study design, patient populations, and BP management protocols may have contributed to variations in reporting outcomes, limiting the generalizability of our findings. However, the consistency in the direction of effect across all subgroup analyses lends support to the overall findings.

Second, we did not have access to individual patient data, and pooling and adjusting was done at the study level. This may increase uncertainty around effect estimates. Individual level data would allow for more accurate adjustment of confounders and stratified analyses across a broader range of variables.

Third, although we conducted subgroup analyses based on ASIA grade groupings (i.e. proportion of patients with motor complete ASIA A and B injuries), we were unable to analyze the impact of BP thresholds on each individual ASIA grade (A through E) due to limited available data. Ideally, such stratification would provide more precise insights into how injury severity changes the effect of hemodynamic management.

Finally, reliance on observational studies means that causal relationships between BP thresholds and functional outcomes cannot be definitively established. The majority of the studies in our review were retrospective in nature, which introduces the potential for confounding, selection and reporting biases, although most included studies were rated as ‘good’ based on the NOS scale. Only one included study was an RCT [41], however, its findings were broadly consistent with the overall direction observed in the observational studies, suggesting an association between higher MAP targets and improved functional outcomes.

While our study reports the first meta-analysis of the effect of BP thresholds in SCI, several research gaps remain. Future research should aim to address the limitations identified in our review by conducting well designed prospective studies to more definitively establish optimal BP targets for patients with SCI.

Conclusion

Taken together, the evidence presented in this meta-analysis suggests a consistent association between lower BP thresholds and worse functional outcomes in patients with acute SCI. While these findings reinforce the rationale behind current guidelines recommending MAP augmentation, they should be interpreted with caution due to the observational nature of the data. Causality cannot be inferred, and it remains unclear whether targeting higher MAP values through interventions such as vasopressors would definitively improve outcomes. Given the potential risks associated with vasopressor use, future RCTs are essential to evaluate the safety and efficacy of specific hemodynamic targets in this population. Ultimately, these findings can be used to shape future investigations aimed at optimizing hemodynamic management in SCI.

Abbreviations

AKI	Acute kidney injury
aOR	adjusted Odds ratio
ASIA	American Spinal Injury Association Scale
BP	Blood pressure
CI	Confidence interval
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
MAP	Mean arterial pressure
NOS	New Castle Ottawa
OR	Odds ratio
RCT	Randomized control trial
SBP	Systolic blood pressure
SCI	Spinal cord injury
SCPP	Spinal cord perfusion pressure
uOR	unadjusted Odds ratio
WHO	World Health Organization

Supplementary Information

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Additional file 1. Supplementary Appendix: Contains all supplementary information and data as referenced in manuscript.

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Acquisition, analysis, and interpretation of data: AT, AAR, WW, HA, HS, HL, PM, TC.

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Data availability

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

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

FAZ currently has provisional patents (63/659, 989; provisional filed June 14, 2024 and 63/652,106; provisional filed May 27, 2024) and software copyrights (Canada IP Office Registration #: 1231355 and 1231080) held in relation to advanced brain monitoring devices and physiologic metric algorithms. All of this is unrelated to the content of this manuscript.

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