Systemic Hypertension and Postoperative Symptomatic Spinal Epidural Haematoma: A Scoping Review

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Short Title:

Postoperative Spinal Haematoma: A Scoping Review

Conflicts of Interest:

No conflicts of interest to declare.

Abstract:

Postoperative symptomatic spinal epidural haematoma (PSSEH) is a serious complication of spinal surgery and is associated with significant morbidity. Studies suggest that hypertension is a risk factor for developing PSSEH. The purpose of this review is to identify and evaluate the existing literature on the association between hypertension and the incidence of postoperative symptomatic spinal epidural haematoma. A comprehensive literature search was conducted using the databases MEDLINE/PubMed, Embase and Cochrane Library to identify studies that investigated PSSEH and included data on hypertension status or blood pressure values. References were also screened to include as many relevant studies as possible. Eighteen studies were included in the review, which explored the association between blood pressure and PSSEH to some degree. Although most studies did not provide detailed information on blood pressure beyond demographics, some observational data suggested that preoperative uncontrolled and untreated hypertension, blood pressure rise at the time of extubation, and postoperative systolic pressure were all associated with an increased risk of PSSEH. However, the level of certainty was considered very low due to the retrospective nature of the studies, the heterogeneity, incoherence, and lack of precision. Further research is needed to explore the relationship between blood pressure and mild PSSEH. Although the current literature is limited, our findings suggest that preoperative hypertension status and blood pressure monitoring during and after surgery may be factors associated with PSSEH. These findings can inform clinical decision-making, while considering risk factors for PSSEH in spinal surgery.

Keywords:

Hematoma, Epidural, Spinal – Hemostasis, Surgical – Hypertension – Spinal Cord Compression

Introduction:

Postoperative symptomatic spinal epidural haematoma (PSSEH) is a rare but significant complication of spinal surgery that can result in prolonged neurological damage and paralysis if left untreated.[1] In the postoperative period, it can present as severe pain over the operation site, with radiation to the lower extremities, and new onset neurological deficit. If there is sufficient cord compression, patients can also experience autonomic dysfunction in the form of urinary retention and sexual dysfunction.[1] On examination, these patients may experience flaccid hypotonia and hyporeflexia.[2] The distribution of these neurological deficits corresponds to the spinal level of and below the compressive haematoma. The differential diagnosis of a postoperative patient experiencing acute neurological deficit is wide and includes conditions such as direct neural tissue trauma, spinal cord infarction, compression from bony or ligamentous structures and PSSEH, all of which need to be considered rapidly to prevent lasting neurological injury.[3] Investigation for PSSEH is best conducted using MRI, at the region of neurological deficit or operated spinal level. PSSEH can appear as heterogenous hyperintense/isointense signals on T2 weighted images or isointense/ slightly hyperintense signals on T1-weighted images with dural sac compression.[4] To complicate the diagnosis further, PSSEH, most commonly, presents in the early postoperative period however there have been cases of delayed-onset PSSEH (>72 hours post-surgery).[5] This is a time sensitive complication as patient prognosis is positively correlated with timely diagnosis and intervention. One study demonstrated that patients operated within 12 hours of symptom onset had higher average postoperative Frankel grades and a greater rate of complete neurological recovery.[1]

Although bleeding in the epidural space is a common occurrence after spinal surgery, it rarely leads to symptomatic cord compression. Several prospective studies have demonstrated an incidence of

asymptomatic spinal epidural haematoma ranging from 33% to 100% after spinal surgery, as determined by regular MRI scans in the postoperative period.[6-8] However, symptomatic haemorrhage has a documented incidence of 0.5%, according to a recent meta-analysis of 40 studies involving over 160,000 patients who underwent spinal surgery.[9] This meta-analysis identified various risk factors for PSSEH, including spinal level (thoracic > lumbar > cervical), minimally invasive spinal surgery, and posterior approach surgery. However, hypertension was not analysed at different points during the surgical admission as a risk factor.[9]

The mechanism by which PSSEH occurs is unclear and there is debate between authors as to the exact cause. Some studies hypothesise state in their discussions that the dorsal venous plexus can be easily injured in transforaminal lumbar interbody fusion surgery, and this could partially explain the aetiology of the condition.[10-11] Another study expands on this by highlighting that multilevel spinal surgery is a risk factor for development of PSSEH due to increased exposure and risk of trauma to the dorsal venous plexus.[12] The dorsal venous plexus surrounding the spine is also at increased risk when operating on a highly vascular tumour. Angiogenic tumours increase the risk of venous plexus rupture and therefore increase intraoperative blood loss which has been identified, by one study, to increase the risk of PSSEH.[13-14] Alternatively, there has been speculation that some bleeding can be arterial in nature from the epidural arteries. There is potential for this to be missed intraoperatively if the patient is hypotensive and there is inadequate haemostasis.[15] As neither a unique mechanism for PSSEH has been found, then risk factor identification may help stratify patients and guide perioperative management.

While there has been debate regarding whether hypertension is a risk factor for spontaneous spinal epidural haematomas, a review conducted in 1990 analysed case reports and found an association

between hypertension and PSSEH. However, the causation was deemed unlikely due to the percentage of patients who were hypertensive aligning with that of the wider population.[16]

To our knowledge, there has not been a dedicated review exploring the relationship between blood pressure, hypertension, and PSSEH. Therefore, the objective of this review is to identify all literature that analyses the incidence of PSSEH and hypertension as a potential risk factor. We will summarise the existing studies and identify gaps in the literature in order to make recommendations for further research. This will assist future meta-analyses and help inform clinical decision-making.

Methods:

A study protocol was created and uploaded to the Open Science Framework database. A brief summary of the background, methods of data gathering, and data charting is contained in this protocol. Link: https://doi.org/10.17605/OSF.IO/JU6VD

We conducted an inclusive search without restrictions on publication year. Studies were only included in, or translated to, English. We included retrospective studies, prospective studies, case-control studies, systematic reviews, and meta-analyses. We excluded case reports. In order to be eligible for inclusion, studies had to compare preoperative hypertension status or perioperative/postoperative blood pressure values during the surgical admission and perform statistical analysis between groups. We did not contact authors for additional data.

A comprehensive search was conducted using three major databases (Ovid MEDLINE, Embase, and Cochrane Library) using the following search terms: "exp spinal hematoma," "exp Hematoma, Epidural, Spinal/ OR exp Hematoma, Subdural, Spinal," "spinal epidural hematoma" AND "exp Hypertension," and "Hypertension." The University of Aberdeen Library database on Primo and

PubMed were also searched to locate relevant literature. In addition, references were screened (backwards snowballing) to identify studies that were not captured by the electronic searches. The search was not restricted by language or year of publication.

The search process was conducted by a single author (LR), in accordance with the aforementioned methodology. In order to be considered eligible for inclusion, studies had to provide radiological confirmation and/or documentation of return to the operating theatre for PSSEH evacuation. The JBI template for evidence source evaluation was utilized to further exclude studies that did not meet the criteria of this review.

The relevant data points for this review were preoperative hypertension status (with a preference for additional information on medication status or severity of hypertension), blood pressure values recorded throughout the surgical admission, and any statistical analysis conducted between these data points in both the control and effect groups.

Results:

The study flow diagram gives a visual representation of the literature yield from the database search and the characteristics that lead to elimination (Figure 1). After full text reading, we identified 18 studies relevant to the review question. Twelve were case control studies, and 6 were retrospective cohort studies. These studies are presented in a summary table identifying the component of blood pressure investigated with respect to PSSEH (Table 1).

All 18 studies included in this review reported preoperative demographic data on blood pressure.[2,5,10,12-15,17-27] Ten studies found a statistically significant difference in preoperative hypertension status between patients who suffered PSSEH versus their control or "no-complication" group on univariable analysis.[2,5,10,12,14,15,19,22-24] Two studies, Fujiwara et al.[19] and

Park et al.[22], found a significant difference on multivariable analysis. Four studies provided more detail about preoperative hypertension, including mean blood pressure values or subdividing patients into "controlled" versus "uncontrolled" hypertension.[5,12,19,21] Fujiwara et al.[19] found that a significantly greater proportion of patients in the PSSEH group had either "uncontrolled" or "untreated" hypertension ($p=\leq 0.001$). Wang et al.[5] found that preoperative systolic blood pressures were higher in both of the PSSEH groups when compared with the control. This was despite the sample size of the delayed group being less than half of the early group (n=15 versus n=32). The majority of other studies, however, did not comment on the degree of hypertension in their patients.[2,10,13-15,18,20,22-27] Two studies subdivided patients into those who were being treated with anti-hypertensives and those who were not.[5,19] A summary table (Table 2) is given compiling the mean preoperative blood pressure values of studies which included them in their results.

Five studies explored blood pressure rise at extubation and compared this with the incidence of PSSEH.[5,19,24-26] Two of these studies found no significant difference[24,25], while three studies found significant differences.[5,19,26] Soejima et al.[24] included comparison of blood pressure after extubation amongst all patients and those who specifically underwent multilevel procedures. They also included data specifically at the L2/L3 surgical site. Neither of these smaller, specific subdivisions showed significant differences between the PSSEH group and control group.[24] Tsuge et al.[25] did not find a significant difference when comparing blood pressure rise at extubation between groups, however, when they calculated a ratio of systolic blood pressure at extubation/systolic blood pressure at rest, they found a significant difference on multivariant analysis with an odds ratio of 3.9. It is worth noting that Tsuge et al.[25] is not case controlled, and their “control” group is vastly larger than the PSSEH group leading to unreliability in their results. Fujiwara et al.[19] found significant differences in both the number of patients experiencing a

50mmHg rise in SBP at extubation between groups and the mean SBP and DBP at the time of extubation. Wang et al.[5] found significant differences between mean SBP and DBP at extubation; however, the number of patients with an SBP rise of ≥50mmHg was not significant. Contrasting this, Yamada et al.[26] found a significant difference on multivariable analysis in the PSSEH group where patients experienced an SBP rise of ≥50mmHg at extubation. This was clearly defined as a rise from the intraoperative median SBP.

Five studies looked at blood pressure in the immediate postoperative period[5,12,19,24,27] Four of these studies presented mean systolic and diastolic BP values of the PSSEH and control groups whilst Yang et al.[27] omitted these values. Fujita et al.[12] found no significant difference in mean SBP or DBP between groups. In contrast, both Fujiwara et al.[19] and Soejima et al.[24] found a statistically significantly higher mean SBP in the PSSEH group when compared to the control. Wang et al.[5] found that mean postoperative SBP in both their early and delayed onset groups were significantly higher on multivariable analysis when compared to mean SBP in their control group. They elicited an adjusted odds ratio of 1.1. Despite this being a very small increase in relative risk, it was statistically significant. Finally, Yang et al.[27] found that if postoperative SBP was to rise by 10mmHg from a baseline of 120 mmHg, then this significantly increased the incidence of PSSEH on multivariable analysis with an adjusted odds ratio of 1.68. We made a second summary table (Table 3) showing postoperative mean blood pressure values to illustrate the differences between studies.

Quality of Evidence and Risk of Bias:

All the current evidence exploring hypertension in relation to PSSEH is retrospective, with most studies being case-controlled. However, the small number of patients in each group adds variance to the results, affecting their reliability. The inclusion criteria between these control groups differed

between studies, which could add bias to their results. Some studies established their control groups by purely randomizing patients, while others controlled based on the same surgeon in a similar time period.[10,14,15,17,26] Some studies attempted to reduce bias by controlling for already proposed risk factors from previous observational studies. For example, Yamada et al.[27] controlled patients according to matching spinal levels of the PSSEH cases, as multiple studies have suggested that multilevel spinal surgery increases the incidence of PSSEH.[12,14,15,17,21]

Additionally, the low incidence rate of PSSEH leads to large heterogeneity between studies due to the individuality of cases. Hypertension, in the demographics table of most studies, is often poorly defined or not defined at all. In these studies, authors did not focus on blood pressure as a primary outcome and have charted patients that are diagnosed with hypertension but not elaborated on their present condition or treatment status. Therefore, subdividing these patients into more detailed groups is essential when considering their overall cardiovascular risk. Treated patients have significantly lower cardiovascular risk, and combining these patients with untreated ones will lead to inconsistency in results. Fujiwara et al.[19] has the most comprehensive analysis, dividing hypertensive patients into four defined groups, including well- and poorly treated hypertension. Saitta et al.[2] separates patients into uncomplicated and complicated hypertension but does not give criteria of these groups.

Furthermore, there is also inconsistency among studies at how they define PSSEH. All studies, in this review, identified PSSEH on MRI after developing neurological deficit in the postoperative period. Where they differ, is that most studies charted patients as suffering a PSSEH if the haematoma required surgical evacuation.[2,5,10,13-15,17-23,25-27] Soejima et al.[24] investigated a much lower cohort of patients (n=313) and found a disproportionately high incidence rate of 13.1% postoperative symptomatic spinal haematoma's because most patients did not require revision

surgery. Only 7/313 patients (2.24%) underwent surgical revision. Similarly, Fujita et al.'s[12] inclusion criteria did not require patients to have surgical evacuation and found an incidence rate of 3.0% from a cohort of 1007 patients. Since there is a large difference in incidence between mildly and severely symptomatic patients, it would be useful having a study, focussing on preoperative and perioperative blood pressure, which investigated patients who were symptomatic but did not require revision surgery. This may give us a larger sample size to discuss if risk factors differ between the mild and severe haematomas. To our knowledge there has been no study exploring hypertension or blood pressure in the context of mild PSSEH.

The compounding quality of evidence would be graded as low due to the retrospective nature of studies, overarching heterogenicity, inconsistency and the lack of precision related to the low number of PSSEH events.

Discussion:

Only limited data was available regarding the odds ratios for PSSEH and perioperative hypertension in our search. The modestly increased risk of increased mean postoperative blood pressure documented in Wang et al.[5] and Yang et al.[27] are statistically significant although we cannot exclude the existence of confounders, being other risk factors influencing both the risk of hypertension and the risk of PSSEH, like a history of vascular disease. However, a signal clearly appeared allowing us to consider a possible association between hypertension as a risk factor for PSSEH.

The British Hypertension Society has established guidelines for blood pressure targets for elective surgery referrals.[28] According to these guidelines, patients with a blood pressure reading of less than 160/100mmHg in primary care should be able to undergo surgery. However, if no blood

pressure readings are taken in primary care, patients with a preoperative clinic blood pressure reading of 180/110mmHg should be referred to the General Practitioner for further investigation. Interestingly, the quoted blood pressure values, on this guideline, are much higher than the mean preoperative blood pressures found in studies on postoperative symptomatic spinal epidural haematoma (PSSEH) identified in this review.[5,12,19,21] Awareness that postoperative systolic blood pressure above 140mmHg has observational evidence to suggest increased risk of PSSEH, despite being below treatment threshold, is useful information for clinicians when reviewing patients postoperatively.

Four studies in this review have provided a significant link between blood pressure rise at extubation and the incidence of PSSEH.[5,19,25,26] It is worth noting that Tsuge et al.[25] and Yamada et al.[26] both use a method of "hypotensive anaesthesia" (defined as a mean intraoperative systolic blood pressure of ≤100mmHg) when performing spinal surgery to mitigate blood loss and improve surgical exposure. Yamada et al.[26] specifies that this is not performed in patients who have poorly controlled hypertension or ischaemic disease but amounted to almost 90% of cases. Due to this anaesthetic variance, their intraoperative blood pressure results will be subject to bias since some patients will be subjected to different haemodynamic parameters. Despite this, Yamada et al's[26] recommendation is to gradually return to normal blood pressure and wean from anaesthesia gently to prevent these blood pressure spikes.

The primary objective of this study is to focus on symptomatic haematoma, given its severity. Although postoperative asymptomatic haematoma is much more common, it is more challenging to study due to the prospective nature of the study and the need for regular MRI scans to radiologically assess the haematoma in all patients. Therefore, it would be helpful to conduct a study robustly investigating blood pressure as a potential risk factor to substantiate some of the

evidence regarding PSSEH. A study by Modi et al.[29] found that preoperative hypertension was not significant for increasing the risk of asymptomatic haematoma, while another study by Izeki et al.[30] found hypertension to be significant for increasing postoperative asymptomatic subdural bleeding. Investigating hypertension and admission blood pressure in a prospective observational study regarding asymptomatic bleeding would help interpret blood pressure in the much rarer PSSEH.

This study has limitations, mainly due to the nature and characteristics of the included studies. The evidence is of low grade, due to the aforementioned concerns, and therefore hard to draw concrete conclusions from. That being said, this study does have some significant strengths including our large patient cohort from a robust literature search. Included studies originated from 8 different countries across 3 continents. We included 110,403 patients in total with the mean patient number per study being 6,334. This wide cohort increases the generalisability of our findings since the studies are so diverse.

Conclusion:

Several studies have shown an association between preoperative hypertension and the development of postoperative symptomatic spinal epidural haematoma (PSSEH). However, due to the nature and the limitation of these studies, we can only conclude with a very low degree of certainty that uncontrolled and untreated hypertension is a risk factor for PSSEH.

To advance our understanding in the area, future research should stratify patients into categories of treated, poorly treated, and untreated hypertension. Additionally, observational studies on symptomatic, and asymptomatic, patients who do not require surgical evacuation of haematoma could provide valuable insight into potentially modifiable risk factors associated PSSEH.

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Figure Legends:

Figure 1: Study flow diagram showing study selection process and the points at which studies were eliminated.