

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

Incidence, risk factors and airway management of postoperative hematoma following anterior cervical spine surgery: a retrospective nested case-control study

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-090547
Article Type:	Original research
Date Submitted by the Author:	27-Jun-2024
Complete List of Authors:	Tian, Yang; Peking University Third Hospital, Department of Anesthesiology Li, Jiao; Peking University Third Hospital, Department of Anesthesiology Zhou, Guangjin; Peking University Third Hospital, Department of Radiology Wang, Mingya; Peking University Third Hospital, Department of Anesthesiology Qu, Yinyin; Peking University Third Hospital, Department of Anesthesiology Li, Min; Peking University Third Hospital, Department of Anesthesiology Wang, Jun; Peking University Third Hospital, Department of Anesthesiology Xu, Mao; Peking University Third Hospital, Department of Anesthesiology Wang, Shenglin; Peking University Third Hospital, Department of Anesthesiology Wang, Shenglin; Peking University Third Hospital, Department of Orthopaedics Guo, Xiangyang; Peking University Third Hospital, Department of Anesthesiology Han, Yongzheng; Peking University Third Hospital, Department of Anesthesiology
Keywords:	Anaesthesia in neurology < ANAESTHETICS, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Neurosurgery < SURGERY
	·





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Incidence, risk factors and airway management of postoperative hematoma following anterior cervical spine surgery: a retrospective nested case–control study

Yang Tian^{1#}, Jiao Li^{1#}, Guangjin Zhou^{2#}, Mingya Wang¹, Yinyin Qu¹, Min Li¹, Jun Wang¹, Mao Xu¹, Shenglin Wang³, Xiangyang Guo^{1*} and Yongzheng Han^{1*}

1 Department of Anesthesiology, Peking University Third Hospital, Beijing 100191, China

2 Department of Radiology, Peking University Third Hospital, Beijing 100191, China

3 Department of Orthopaedics, Peking University Third Hospital, Beijing 100191, China

[#] Yang Tian, Jiao Li and Guangjin Zhou contributed equally to this study

* Corresponding Author:

Xiangyang Guo, puthmzk@163.com; Tel.: 086-010- 82267272; No. 49, North Garden Street, Haidian District, Beijing, 100191 China

Yongzheng Han, hanyongzheng@bjmu.edu.cn; Tel.: 086-010- 82267260; No. 49, North Garden Street, Haidian District, Beijing, 100191 China

BMJ Open

Objective: The aim of this study was to investigate the incidence, risk factors and airway management of postoperative hematoma (HT) following anterior cervical spine surgery (ACSS). **Design**: A retrospective nested case–control study.

Setting: A tertiary hospital in China.

Participants: A total of 13,523 patients within a single center longitudinal ACSS cohort were identified from March 2013 to February 2022. Patients with postoperative HT after ACSS were enrolled as the HT group, and others in the cohort without HT were randomly selected as the non-HT group by individually matching with the same operator, same gender, same surgery year, and similar age (±5 years) at a ratio of 4:1. Subsequently, patients with HT were included in a subgroup for analysis.

Primary outcome measures: Postoperative HT and difficult intubation (DI) during HT evacuation. **Results**: The incidence of postoperative HT out of all ACSS was 0.4% (55/13,523). A total of 275 patients were enrolled in the study, including 55 patients in the HT group and 220 patients in the non-HT group. Anterior cervical corpectomy and fusion (ACCF) (odds ratio [OR], 2.459; 95% confidence interval [CI], 1.302-4.642; P=0.006) and the maximum mean arterial pressure (MAP) during recovery (OR, 1.030; 95% CI, 1.003-1.058; P=0.028) were identified as independent risk factors for HT. In the subgroup analysis, a significant correlation was identified between retropharyngeal hematoma (RH) and the incidence of DI (OR, 10.435; 95% CI, 1.249-87.144; P=0.030). Patients with HT had longer hospitalization duration (P<0.001) and greater costs (P<0.001).

Conclusion: ACCF and elevated maximum MAP during the recovery period were independent risk factors for postoperative HT following ACSS. High-risk patients should be closely monitored during the perioperative period. Adequate preparation for managing difficult airways must be ensured as part of the clinical protocol, especially for RH patients. Postoperative HT was associated with longer hospitalization duration and greater costs.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Keywords: anterior cervical spine surgery, hematoma, risk factors

Trial registration number: China Clinical Trial Registry: ChiCTR2400086263.

Strengths and limitations of this study

This investigation represents one of the largest series to examine the incidence, risk factors, and clinical outcomes associated with hematoma following anterior cervical spine surgery within a single, tertiary, academic medical center.

This study may represent the pioneering effort in investigating the management of difficult airways in patients with hematoma.

A multicenter, prospective study with a more detailed assessment of risk factors might provide a more comprehensive understanding of the variables associated with postoperative hematoma.

INTRODUCTION

Hematoma (HT) after anterior cervical spine surgery (ACSS) is a rare complication in clinical practice, with an incidence of 0.4% to 1.2% reported in the literature.^{1,2} The location of HT occurrence determines its type, which can be divided into three categories: wound HT, retropharyngeal hematoma (RH), and spinal epidural hematoma (SEH).³ Wound HT typically manifests as localized swelling and ecchymosis at the injury site. RH often presents with respiratory symptoms and can potentially progress to acute airway obstruction, a critical and life-threatening condition.⁴ SEH typically presents with progressive neurological deficits. Severe cases of HT may potentially result in severe morbidity or mortality.

Timely evacuation of HT is an efficacious intervention, notably beneficial for RH and SEH.⁵ In the management of airways during HT evacuation surgery, particular attention must be paid to the occurrence of difficult airways to prevent a "can't intubate, can't ventilate" situation.⁶ Given the infrequency of HT and the potential for severe outcomes, it is imperative to conduct early and systematic assessments of risk factors of HT. This study contributed a thorough retrospective nested case-control analysis to investigate the incidence and risk factors of postoperative HT following ACSS. Furthermore, the study extended its scope to explore the intricacies of airway management in patients presenting with HT, emphasizing the importance of a meticulous approach in clinical practice.

METHODS

Study population and study design

Patients who underwent ACSS in Peking University Third Hospital from March 2013 to February 2022 were selected. Inclusion criteria were as follows: 1) cervical spondylosis; 2) ACSS; 3) elective surgery. Exclusion criteria were as follows: 1) combined anterior and posterior cervical surgery; 2) trans-oral approach to C1-C2; 3) cervical spine tumors; 4) cervical spine fractures; 5) incomplete medical records. In the present study, the definition of postoperative HT following ACSS was symptomatic HT, characterized by respiratory distress, neurological deficits, and other HT-related symptoms, which was confirmed by surgical evacuation. Patients with postoperative HT after ACSS were enrolled as the HT group, and others in the cohort without HT were randomly selected as the non-HT group by individually matching with the same operator, same gender, same surgery year, and similar age (±5 years) at a ratio of 4:1.

Variables

The general characteristics of the two groups were collected, including age, gender, body mass index (BMI), medical comorbidities, smoking history, anticoagulant or antiplatelet therapy, preoperative coagulation function tests, and platelet counts. Disease-related factors encompassed the classification of cervical spondylosis types, such as myelopathy type, radiculopathy type, or other types, as well as preoperative Modified Japanese Orthopaedic Association (m-JOA) scores and Neck Disability Index (NDI) scores. Surgical factors included surgical segments, ossification of the posterior longitudinal ligament (OPLL) within the surgical segments, anterior cervical corpectomy and fusion (ACCF), duration of surgery, estimated blood loss (EBL), and postoperative drainage volume. Anesthetic factors involved the American Society of Anesthesiologists (ASA) physical status classifications and mean arterial pressure (MAP) during both preoperative and postoperative recovery phases. Data on hospitalization duration and costs were also gathered.

Anticoagulant therapy indicated a history of using warfarin or low-molecular weight heparin. Antiplatelet therapy indicated a history of using aspirin or clopidogrel. Preoperative coagulation

BMJ Open

function tests included prothrombin time (PT), International Normalized Ratio (INR), fibrinogen levels (Fib), activated partial thromboplastin time (APTT), and thrombin time (TT). The preoperative mean arterial pressure (MAP) was routinely assessed upon the patient's admission to the ward, and the maximum MAP recorded during the recovery period was obtained from anesthesia records.

We conducted a subgroup analysis of HT patients, with a focus on airway management. Patients were stratified based on the occurrence of difficult intubation (DI) during HT evacuation surgery. A comparative analysis was performed on various parameters between the groups, including sex, age, BMI, hypertension, C3 or C4 involvement, type of HT, the interval from symptom onset to airway intervention, time of presentation of HT, and ASA physical status classifications to assess correlations and statistical differences associated with DI. DI was defined as a clinical scenario requiring more than three attempts by an experienced anesthesiologist to achieve endotracheal intubation.⁷

Statistical analysis

For continuous data that were normally distributed, descriptive statistics were presented as mean \pm standard deviation. Data that were not normally distributed were described using median and interquartile range. Differences between the two groups for continuous variables were analyzed using an independent samples t-test (for data with a normal distribution) or a Mann-Whitney U test (for data without a normal distribution). Categorical data were expressed as percentages and analyzed for differences using the chi-square test or Fisher's exact test. A binary logistic regression model was applied to identify multivariate variables, utilizing the Backward-Wald method for variable selection. Odds ratios (OR) and 95% confidence intervals (CI) were used to quantify the strength of associations. The accuracy of diagnostic tests was assessed using receiver operating characteristic curves and the area under the curve (AUC). Statistical analyses were performed using SPSS version 26.0, with all tests being two-tailed, and P < 0.05 indicating statistical significance of differences.

The number of postoperative HT cases identified during the study period dictated the overall sample size. In subgroup analyses, the count of DI cases similarly determined the subgroup sample size. According to the principle that the number of events per variable should be no less than five, which means the number of outcome events corresponding to each independent factor must meet this threshold, an appropriate number of independent variables were included to satisfy the sample size criterion based on the actual occurrences of outcome events.

RESULTS

Incidence and time of presentation of postoperative HT

From March 2013 to February 2022, a total of 13,523 patients undergoing ACSS met the inclusion criteria. Of these, 55 patients developed postoperative HT, resulting in an incidence rate of 0.4%, with RH occurring at a rate of 0.28% and SEH at 0.12%. Patients without HT were randomly selected as the control group, individually matched for the same surgeon, gender, surgery year, and age within a 5-year range, at a ratio of 4:1. Consequently, the HT group comprised 55 cases, while the control group included 220 cases (Figure 1). The onset of HT varied significantly among patients, with the earliest cases presenting as soon as 0.5 hours postoperatively and the latest occurring up to 7 days after surgery. Notably, four of these patients exhibited symptoms shortly after the removal of drainage tubes (Figure 2).

Difference between the HT group and the non-HT group

BMJ Open

The comparative analysis revealed no statistically significant differences between the two groups in demographic characteristics, including gender, age, and BMI. Furthermore, there were no significant differences in hypertension, smoking, anticoagulant or antiplatelet therapy. In the context of surgical and anesthetic parameters, no discernible statistical differences were observed in the classification of cervical spondylosis, preoperative m-JOA and NDI scales, surgical segments, OPLL within the surgical segments, surgery duration, EBL, drain volume, preoperative MAP, and ASA physical status classifications.

The two groups exhibited statistically significant differences in ACCF (P=0.011) and the maximum MAP during the recovery period (P=0.031). Patients in the HT group had longer hospitalization duration (P<0.001) and incurred greater costs (P<0.001) (Table 1). Analysis of the preoperative blood tests between the two groups showed no differences between the two groups in preoperative PT, INR, Fib levels, TT, and platelet counts. In contrast, there was a statistically significant difference in APTT (P=0.011). In clinical practice, an extension of PT by 3 seconds and APTT by 10 seconds is deemed to have clinical significance. However, in the present study, the mean values of PT and APTT for both the HT group and the non-HT group were within the normal range. Consequently, PT and APTT were not included in the binary logistic regression analysis. Instead, other factors with a p-value less than 0.1 were incorporated into the model. Binary logistic regression analysis revealed that ACCF (OR, 2.459; 95% CI, 1.302-4.642; P=0.006) and the maximum MAP during the recovery period (OR, 1.030; 95% CI, 1.003-1.058; P=0.028) were independent risk factors for HT, as detailed in Table 2. The AUC for the maximum MAP during the recovery period was calculated to be 0.594 (95% CI, 0.510-0.679; P=0.031), whereas for ACCF, the AUC was 0.586 (95% CI, 0.499-0.673; P=0.048).

Subgroup analysis of airway management in HT patients

All 55 cases of HT patients underwent HT evacuation surgery under tracheal intubation and general anesthesia, among which 16 cases developed DI, including 4 cases that failed tracheal intubation and underwent tracheotomy (Figure 1). In the comparison between DI patients and non-DI patients, there were statistically significant differences in RH, the interval between symptom onset and airway intervention, and hospitalization duration (Table 3). Binary logistic regression analysis revealed that RH (OR, 10.435; 95% CI, 1.249-87.144; P=0.030) was independent risk factor for DI. The AUC for RH was calculated to be 0.674 (95% CI, 0.529-0.819; P=0.044).

DISCUSSION

Incidence and time of presentation of postoperative HT

Postoperative HT following ACSS is a rare but potentially high-risk complication. Bovonratwet et al. reported that out of a total of 37,261 patients who underwent anterior cervical discectomy and fusion, 148 (0.40%) developed HT requiring reoperation.¹ In a single-surgeon case series of ACSS, Wang et al. documented a 1.0% incidence of postoperative HT, affecting 11 individuals out of a total of 1,150 patients. Notably, among these HT cases, 10 were specifically classified as RH.⁸ Miao et al. presented a cohort of 1,258 patients who underwent ACSS, revealing an incidence of postoperative HT totaling 1.2%. Specifically, they observed seven cases (0.5%) of RH and eight cases (0.6%) of SEH.² Boudissa et al. reported that 13 out of 2,319 patients (0.56%) undergoing ACSS required reintervention within 72 hours postoperatively, with a distribution of five cases (0.2%) of RH and seven cases (0.3%) of SEH.⁹ O'Neill et al. reported on a series of 2,375 ACSS procedures, documenting 17 occurrences of RH, which corresponded to an incidence of 0.7%.⁵ In the present study, the overall incidence of HT was 0.4%, with RH occurring at a rate of Page 7 of 16

BMJ Open

0.28% and SEH at 0.12%, which is consistent with previous literature reports.

The common clinical assumption is that the risk of HT is most pronounced in the initial hours following surgery. Nevertheless, O'Neill et al. noted that approximately 35% of cases presented with a delayed onset, with an average time frame of 6 days postoperatively.⁵ In the present study, 31 cases exhibited symptoms within the first 6 hours postoperatively, with the earliest symptom onset occurring immediately after awakening from anesthesia. Additionally, 8 cases presented symptoms beyond 24 hours postoperatively, with the longest interval being 7 days.

Risk factors for postoperative HT

Risk factors of HT included male sex, age older than 65, smoking, medical comorbidities, multilevel procedures, OPLL within the surgical segments, therapeutic heparin use, lower BMI and ASA physical status classification grades of III or greater.^{1,2,5,8,10-13} In the present study, no significant differences were observed for the aforementioned risk factors. The type of cervical spondylosis, as well as preoperative scores on the m-JOA and NDI scales, did not influence the occurrence of postoperative HT.

In previous studies, prolonged TT values and INR greater than 1.2 were identified as independent risk factors of HT.^{1,8} Prolonged APTT was associated with an increased risk of HT formation after surgery.¹⁴ In clinical practice, an extension of APTT by 10 seconds is considered to have clinical significance. In the present study, however, the mean values of APTT in both HT group and non-HT group were within the normal range. Therefore, despite the statistically significant difference in APTT between the two groups, the prolonged APTT in the present study should not be construed as a risk factor for HT development.

ACCF surgery exposes at least three vertebral bodies, resecting two intervertebral discs, while also performing partial vertebral body resection, which leads to greater exposure of the epidural space and extensive damage to the venous plexus within the spinal canal, resulting in increased blood loss. Hao et al. reported that among a total of 551 patients who underwent anterior cervical discectomy and fusion or ACCF for 2-level cervical spondylotic myelopathy, a significant difference was observed between the two groups in terms of blood loss.¹⁵ In the current study, logistic regression analysis suggested that ACCF was an independent risk factor for postoperative HT. During the ACCF surgery, special attention should be paid to potential bleeding, including vessels, muscles, and exposed cancellous bone.

Hypertension is recognized as a significant risk factor for postoperative HT, although the underlying mechanisms are not fully defined.¹⁶ Liu et al. suggest that arterial bleeding was predominantly the cause of such hematomas.¹⁷ However, Yin et al. present an alternative view, contending that arterial bleeding is an unlikely major source of hematomas due to its detectability during surgical procedures.¹⁸ During the initial intraoperative period under anesthesia, the MAP is low, making small vessel bleeding potentially undetected and inadequately managed with bipolar coagulation. As patients emerge from anesthesia, the stimulation of the tracheal tube and postoperative pain may precipitate a rise in blood pressure. These small vessels, which have not achieved effective hemostasis, may resume bleeding, leading to the development of HT. In the present study, the MAP at admission showed no significant difference between the two groups, yet a statistically significant difference was observed in the maximum MAP during the recovery period. HT commonly occurs within the first few hours postoperatively. Hemodynamic fluctuations, particularly the surge in blood pressure during the anesthetic recovery period, may play a critical role in the development of HT, and thus, close monitoring and management of blood pressure during

this period could be essential in reducing the risk of postoperative HT.

Optimal timing for evacuation and airway management in HT Patients

For patients with SEH accompanied by severe neurological deficits, emergent surgical evacuation of the hematoma is the most appropriate therapeutic approach. The severity of symptoms prior to surgery may significantly impact postoperative recovery. According to the study by Yin et al., there was a significant statistical difference in the degree of neurological recovery based on whether the SEH was evacuated within 24 hours.⁹ The research by Hohenberger et al. indicated that the key factors influencing recovery were the degree of neurological deficit and the interval between the onset of symptoms and surgery.¹⁰ Similarly, Epstein et al. advocated for aggressive treatment of postoperative SEH.¹⁹ In the present study, all 17 patients with SEH underwent evacuation surgery, and all patients' symptoms were partially or completely relieved after the procedure.

Song et al. reported that patients with RH could be treated with close observation or evacuation surgery, depending on changes in respiratory status, surgical site conditions, and patient behavior.⁴ However, O'Neill et al. believed that whenever a patient presented with an airway complication, the decision was made to reoperate rather than treat the patient with observation and steroids.⁵ In the management of RH, it was crucial to acknowledge the potential risk of difficult airways.²⁰ In the current study, among the 55 cases of HT evacuation, 16 patients encountered DI conditions, with 4 ultimately requiring a tracheostomy. In the subgroup analysis, a significant correlation was identified between RH and the incidence of DI. Of the 16 DI cases, 15 were attributed to patients with RH. In the present study, 37 cases of RH were successfully treated, and the patients were subsequently discharged from the hospital. Regrettably, one patient died due to complications 24 days following the evacuation surgery. Adequate preparation for managing difficult airways must be ensured as part of the clinical protocol, especially for RH patients.

This study presents a substantial clinical series dedicated to investigating HT following ACSS and introduces a novel finding by identifying, for the first time, ACCF and maximum MAP during recovery as independent risk factors associated with postoperative HT. In this retrospective nested case-control study, matching criteria such as the same surgeon, same year of surgery, same gender, and similar age (\pm 5 years) were applied to ensure a high degree of homogeneity and minimize bias. Despite these efforts, this study has its limitations. Firstly, as with any retrospective study, there is an inherent risk of selection and reporting bias. Secondly, due to the low incidence of HT, the sample size is limited. A multicenter, prospective study with a more detailed assessment of risk factors might provide a more comprehensive understanding of the variables associated with postoperative HT following ACSS.

CONCLUSION

ACCF and elevated maximum MAP during the recovery period were independent risk factors for postoperative HT following ACSS. High-risk patients should be closely monitored during the perioperative period. Adequate preparation for managing difficult airways must be ensured as part of the clinical protocol, especially for RH patients. Postoperative HT was associated with longer hospitalization duration and greater costs. Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Contributors: YT, JL and GZ contributed equally to this paper. MX, ML, JW, SW and XG designed and coordinated the study. YT, GZ and YQ collected the data. YT, MW and YH drafted the manuscript. YT and JL analysed the data and performed the statistical analysis. All authors have read and approved the manuscript.

Fundings: This study was funded by grants from Wu Jieping Medical Foundation (320.6750.2023-08-5), Key Clinical Projects of Peking University Third Hospital (BYSYZD2021013) and Capital's Funds for Health Improvement and Research (2024-2-40912).

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Competing interests: None declared

Data availability statement: The data underlying this article are available in [Mendeley Data Repository], at <u>https://data.mendeley.com/datasets/6rx5wgp75p/1</u>

Ethics approval: This study was approved by Medical Scientific Research Ethics Committee of Peking University Third Hospital. IRB number: IRB00006761-M2024464, 2022.06.05

Participants consent statement: Not applicable. This manuscript does not contain personal and/or medical information about an identifiable individual.

REFERENCE

1. Bovonratwet P, Fu MC, Tyagi V, et al. Incidence, Risk Factors, and Clinical Implications of Postoperative Hematoma Requiring Reoperation Following Anterior Cervical Discectomy and Fusion. *Spine (Phila Pa 1976)*. 2019;44:543-549.

2. Miao W, Ma X, Liang D, et al. Treatment of hematomas after anterior cervical spine surgery: A retrospective study of 15 cases. *Neurochirurgie*. 2018;64:166-170.

3. Epstein N. Frequency, recognition, and management of postoperative hematomas following anterior cervical spine surgery: A review. *Surg Neurol Int.* 2020;11:356.

4. Song KJ, Choi BW, Lee DH, et al. Acute airway obstruction due to postoperative retropharyngeal hematoma after anterior cervical fusion: a retrospective analysis. *J Orthop Surg Res*. 2017;12:19.

5. O'Neill KR, Neuman B, Peters C, et al. Risk factors for postoperative retropharyngeal hematoma after anterior cervical spine surgery. *Spine (Phila Pa 1976)*. 2014;39:E246-52.

6. Apfelbaum JL, Hagberg CA, Connis RT, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. *Anesthesiology*. 2022;136:31-81.

7. Shah PN and Sundaram V. Incidence and predictors of difficult mask ventilation and intubation. *J Anaesthesiol Clin Pharmacol*. 2012;28:451-5.

8. Wang H, Yu H, Zhang N, et al. Incidence, Risk Factors, and Management of Postoperative Hematoma Following Anterior Cervical Decompression and Fusion for Degenerative Cervical Diseases. *Neurospine*. 2023;20:525-535.

9. Boudissa M, Lebecque J, Boissière L, et al. Early reintervention after anterior cervical spine surgery: Epidemiology and risk factors: A case-control study. *Orthop Traumatol Surg Res.* 2016;102:485-8.

10. Hohenberger C, Zeman F, Höhne J, et al. Symptomatic Postoperative Spinal Epidural Hematoma after Spinal Decompression Surgery: Prevalence, Risk Factors, and Functional Outcome. *J Neurol Surg A Cent Eur Neurosurg*. 2020;81:290-296.

11. Saitta BH, Shultz P, Hanson K, et al. Post-Operative Spinal Epidural Hematoma: Are We Discontinuing Aspirin Early Enough? *Global Spine J.* 2023;13:2255-2261.

12. Xia T, Zhou F, Chu H, et al. Incidence and risk factors of postoperative symptomatic spinal epidural hematoma in cervical spine surgery: a single center, retrospective study of 18,220 patients. *Eur Spine J.* 2022;31:2753-2760.

13. Chen Q, Zhong X, Liu W, et al. Incidence of postoperative symptomatic spinal epidural hematoma requiring surgical evacuation: a systematic review and meta-analysis. *Eur Spine J*. 2022;31:3274-3285.

14. Liu N, Luo S, Hang C, et al. Changes in coagulation functions and hemorheological parameters may predict hematoma formation after total knee arthroplasty. *J Orthop Surg Res.* 2016;11:35.

15. Hao Q, Ding Q, Yang H, et al. Symptomatic postoperative spinal epidural hematoma preferentially occurs after anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion: a retrospective study. *Ann Palliat Med*. 2022;11:2025-2032.

16. Liao Y, Tian Y, Ye R, et al. Risk and treatment of symptomatic epidural hematoma after anterior cervical spine surgery: A retrospective clinical study. *Medicine (Baltimore)*. 2020;99:e18711.

17. Liu Z, Jiao Q, Xu J, et al. Spontaneous spinal epidural hematoma: analysis of 23 cases. *Surg Neurol*. 2008;69:253-60; discussion 260.

18. Yin G and Ni B. Acute postoperative cervical spinal epidural hematoma. *Acta Orthop Traumatol Turc*. 2014;48:437-42.

19. Epstein NE and Agulnick MA. Perspective: Postoperative spinal epidural hematomas (pSEH) should be treated, not ignored. Surg Neurol Int. 2023;14:363.

20. Debkowska MP, Butterworth JF, Moore JE, et al. Acute post-operative airway complications following anterior cervical spine surgery and the role for cricothyrotomy. J Spine Surg. 2019;5:142-154.

r. 202 xe JE, et a y and the role fo

Table 1 Comparison between HT group and non-HT group
--

Characteristic	HT group N=55	non-HT group N=220	$\chi^2/Z/t$	P value
Gender		~	χ ² =0.000	1.000
Male	39(70.91%)	156(70.91%)		
Female	16(29.09%)	16(29.09%)		
Age/(years)	55(16)	53(15)	Z=0.316	0.752
$BMI/(kg \cdot m^{-2})$	26.15±3.20	24.92±3.76	t=-1.239	0.219
Hypertension	13(23.63%)	66(30.00%)	χ ² =0.870	0.351
Smoking history	15(27.30%)	47(21.40%)	$\chi^2 = 0.880$	0.348
Anticoagulant or antiplatelet therapy	1(1.81%)	13(5.90%)	<i>,</i> ,,	0.315#
Preoperative blood index	()			
PT/(s)	10.95(0.78)	10.60(0.78)	Z=1.960	0.050
INR	1.03(0.07)	0.99(0.10)	Z=1.834	0.067
FIB/ (g/L)	2.89±0.59	2.94±0.50	t=0.702	0.483
APTT/(s)	33.25±4.09	32.03±3.60	t=2.557	0.011
TT/(s)	13.95(1.58)	13.70(1.10)	Z=0.992	0.321
Platelet count/ $(10^{9}/L)$	228(80.50)	220(76.00)	Z=1.711	0.087
Classification of cervical spondylosis		× ,		0.060
CSM	35(63.64%)	115(52.27%)		
CSR	6(10.91%)	57(25.91%)		
Other types	14(25.45%)	48(21.82%)		
Preoperative m-JOA score	14.00(4.10)	14.50(3.10)	Z=-1.623	0.104
Preoperative NDI score	12.00(15.30)	11.00(18.00)	Z=-0.726	0.468
Surgical segments /(Levels)	2(1)	2(1)	Z=1.411	0.158
OPLL within the surgical segments	18(32.70%)	67(30.50%)	χ ² =0.106	0.744
ACCF	23(41.80%)	54(24.45%)	χ²=6.512	0.011
Surgery duration/ (minutes)	86(38)	76(44)	Z=0.939	0.348
EBL/ (mL)	30(48)	20(40)	Z=1.754	0.079
Drain volume/(mL)	30.00(48.75)	30.00 (35.00)	Z=0.560	0.576
Preoperative MAP/ (mm Hg)	96.30(15.05)	97.00(12.60)	Z=0.369	0.712
Maximum MAP during recovery/(mm Hg)	110.00(15.50)	108.30(17.88)	Z=2.159	0.031
ASA physical status classification				1.000#
I - II	55(100%)	216(98.60%)		
≥ Ⅲ	0(0%)	3(1.40%)		0.001
Hospitalization duration /(days)	7(7)	4(2)	Z=7.395	< 0.001
Cost/ (RMB) Data are presented as n (%) or Median (IQR) of	68387 (25340)	57533 (20853)	Z=4.876	< 0.001

HT, hematoma; BMI, body mass index; PT, preoperative prothrombin time; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time; TT, thrombin time; CSM, cervical spondylotic myelopathy; CSR, cervical spondylotic radiculopathy; m-JOA, modified Japanese Orthopaedic Association; NDI, neck disability index; OPLL, ossification of posterior longitudinal ligament; ACCF, anterior cervical corpectomy and fusion; EBL, estimated blood loss; MAP, mean arterial pressure; ASA, American society of Aneshesiologists. #Fisher exact test

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

able 2 Binary multivariate logistic regression (Backward-Wald) analysis of the risk factors for T						
Variable	В	SE	P value	OR	95%CI	
Maximum MAP during recovery	0.030	0.014	0.028	1.030	1.003-1.058	
ACCF	0.900	0.324	0.006	2.459	1.302-4.642	
Constant	-4.914	1.514	0.001	0.007		

HT, hematoma; SE, standard error; OR, odds ratio; CI, confidence interval; MAP, mean arterial pressure; ACCF, anterior cervical corpectomy and fusion.

to beet terien only

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Table 3 Comparison between DI group and non-DI group in the HT patients

Characteristic	DI group	non-DI group	2/72/4	D 1	
Characteristic	N=16	N=39	$\chi^2/Z/t$	P value	
Gender				0.754#	
Male	12(75.00%)	27(69.23%)			
Female	4(25.00%)	12(30.77%)			
Age/(years)	54.56±9.62	53.21±8.71	t=-0.509	0.613	
BMI/ (kg·m ⁻²)	24.95(2.00)	25.50(4.00)	Z=-1.122	0.262	
Hypertension	5(31.25%)	8(20.51%)		0.489#	
C3 or C4 involvement	11(68.75%)	19(48.72%)		0.237#	
Type of HT				0.012#	
RH	15(93.75%)	23(58.97%)			
SEH	1(6.25%)	16(41.03%)			
Interval between symptom onset and airway intervention/ (hours)	2.00(2.90)	1.00(2.50)	Z=2.418	0.016	
Time of presentation of HT/ (hours)	8.50(16.00)	4.00(10.00)	Z=0.688	0.492	
ASA physical status classification			χ²=0.773	0.379	
I	6(37.50%)	10(25.64%)			
≥Ⅱ	10(62.50%)	29(174.36%)			
Hospitalization duration /(days)	12(7)	7(5)	Z=3.094	0.002	
Cost/ (RMB)	68387 (26122)	68329 (23578)	Z=0.474	0.636	

Data are presented as n (%) or Median (IQR) or means \pm standard deviation.

DI, difficult intubation; HT, hematoma; BMI, body mass index; RH, retropharyngeal hematoma;

SEH, spinal epidural hematoma; ASA, American society of Aneshesiologists.

#Fisher exact test



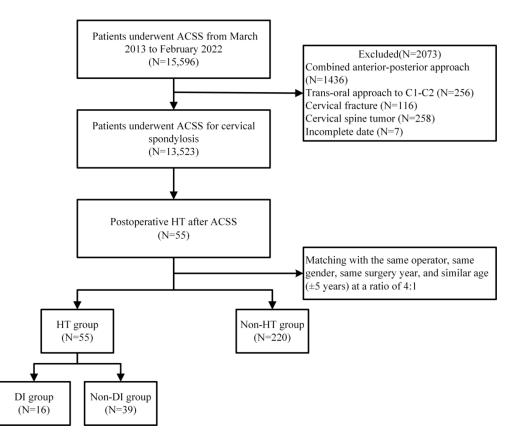


Figure 1: Flow diagram outlining the selection of the study population. ACSS, anterior cervical spine surgery; HT, hematoma; DI, difficult intubation.

172x140mm (300 x 300 DPI)

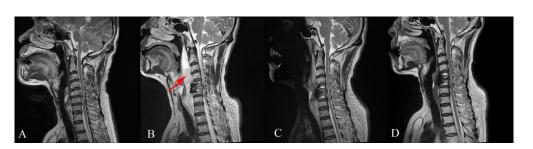


Figure 2: A 67-year-old man developed postoperative RH after C5/6 ACDF. (A) Preoperative sagittal T2weighted MRI showed a disc herniation at C5/6 with spinal cord compression. (B) Sagittal T2-weighted MRI at 24h postoperatively showed RH extending from C2 to T1 (arrow head). (C) Sagittal T2-weighted MRI at 3 days postoperatively showed RH apparently eliminated after hematoma evacuation. (D) Sagittal T2weighted MRI at 3 months postoperatively showed the recovery of prevertebral soft tissues to a normal state. RH, retropharyngeal hematoma; ACDF, anterior cervical discectomy and fusion; MRI, magnetic resonance imaging.

135x34mm (300 x 300 DPI)

BMJ Open

Incidence, risk factors and airway management of postoperative hematoma following anterior cervical spine surgery: a retrospective nested case-control study

Manuscript ID	bmjopen-2024-090547.R1
Article Type:	Original research
Date Submitted by the Author:	14-Mar-2025
Complete List of Authors:	Tian, Yang; Peking University Third Hospital, Department of Anesthesiology Li, Jiao; Peking University Third Hospital, Department of Anesthesiology Zhou, Guangjin; Peking University Third Hospital, Department of Radiology Wang, Mingya; Peking University Third Hospital, Department of Anesthesiology Qu, Yinyin; Peking University Third Hospital, Department of Anesthesiology Li, Min; Peking University Third Hospital, Department of Anesthesiology Wang, Jun; Peking University Third Hospital, Department of Anesthesiology Xu, Mao; Peking University Third Hospital, Department of Anesthesiology Wang, Shenglin; Peking University Third Hospital, Department of Anesthesiology Wang, Shenglin; Peking University Third Hospital, Department of Orthopaedics Guo, Xiangyang; Peking University Third Hospital, Department of Anesthesiology Han, Yongzheng; Peking University Third Hospital, Department of Anesthesiology
Primary Subject Heading :	Surgery
Secondary Subject Heading:	Anaesthesia
Keywords:	Anaesthesia in neurology < ANAESTHETICS, Spine < ORTHOPAEDIC & TRAUMA SURGERY, Neurosurgery < SURGERY





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Incidence, risk factors and airway management of postoperative hematoma following anterior cervical spine surgery: a retrospective nested case–control study

Yang Tian^{1#}, Jiao Li^{1#}, Guangjin Zhou^{2#}, Mingya Wang¹, Yinyin Qu¹, Min Li¹, Jun Wang¹, Mao Xu¹, Shenglin Wang³, Xiangyang Guo^{1*} and Yongzheng Han^{1*}

1 Department of Anesthesiology, Peking University Third Hospital, Beijing 100191, China

2 Department of Radiology, Peking University Third Hospital, Beijing 100191, China

3 Department of Orthopaedics, Peking University Third Hospital, Beijing 100191, China

[#] Yang Tian, Jiao Li and Guangjin Zhou contributed equally to this study

* Corresponding Author:

Xiangyang Guo, puthmzk@163.com; Tel.: 086-010- 82267272; No. 49, North Garden Street, Haidian District, Beijing, 100191 China

Yongzheng Han, hanyongzheng@bjmu.edu.cn; Tel.: 086-010- 82267260; No. 49, North Garden Street, Haidian District, Beijing, 100191 China

BMJ Open

 Objective: The aim of this study was to investigate the incidence, risk factors and airway management of postoperative hematoma following anterior cervical spine surgery (ACSS).

Design: A retrospective nested case–control study.

Setting: A tertiary hospital in China.

Participants: A total of 13,523 patients within a single center longitudinal ACSS cohort were identified from March 2013 to February 2022. Patients with postoperative hematoma after ACSS were enrolled as the hematoma group, and others in the cohort without hematoma were randomly selected as the non-hematoma group by individually matching with the same operator, same gender, same surgery year, and similar age (\pm 5 years) at a ratio of 4:1. Subsequently, patients with hematoma were included in a subgroup for analysis.

Primary outcome measures: Postoperative hematoma and difficult intubation prior to hematoma evacuation.

Results: The incidence of postoperative hematoma out of all ACSS was 0.4% (55/13,523). A total of 275 patients were enrolled in the study, including 55 patients in the hematoma group and 220 patients in the non-hematoma group. Anterior cervical corpectomy and fusion (ACCF) (odds ratio [OR], 2.459; 95% confidence interval [CI], 1.302-4.642; P=0.006) and the maximum mean arterial pressure (MAP) during recovery (OR, 1.030; 95% CI, 1.003-1.058; P=0.028) were identified as independent risk factors for hematoma. In the subgroup analysis, 29% of patients with hematoma experienced difficult intubation, and retropharyngeal hematoma (OR, 10.435; 95% CI, 1.249–87.144; P = 0.030) was identified as an independent risk factor for difficult intubation. Patients with hematoma had longer hospitalization duration (P<0.001) and greater costs associated with their stay (P<0.001).

Conclusion: ACCF and elevated maximum MAP during the recovery period were independent risk factors for postoperative hematoma following ACSS. Patients with post-ACSS hematoma are at high risk of a difficult airway, with retropharyngeal hematoma being strongly associated with challenging airway management. Postoperative hematoma was associated with longer hospitalization duration and greater costs.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

Keywords: anterior cervical spine surgery, hematoma, risk factors

Trial registration number: China Clinical Trial Registry: ChiCTR2400086263.

Strengths and limitations of this study

- This study's large sample size (13,523 patients) strengthened result reliability through a retrospective nested case-control design that controlled confounders via matching.
- The single-center longitudinal cohort ensured consistent data collection while analyzing both postoperative hematoma risks and intubation difficulties comprehensively.
- The retrospective design may introduce selection bias and limits the ability to establish causal relationships.
- The low postoperative hematoma incidence (0.4%) may limit statistical power for detecting rare risk factors.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

INTRODUCTION

Hematoma after anterior cervical spine surgery (ACSS) is a rare complication in clinical practice, with an incidence of 0.4% to 1.2% reported in the literature.^{1,2} The location of hematoma occurrence determines its type, which can be divided into three categories: wound hematoma, retropharyngeal hematoma, and spinal epidural hematoma.³ Wound hematoma typically manifests as localized swelling and ecchymosis at the injury site. Retropharyngeal hematoma often presents with respiratory symptoms and can potentially progress to acute airway obstruction, a critical and life-threatening condition.⁴ Spinal epidural hematoma typically presents with progressive neurological deficits. Severe cases of hematoma may potentially result in severe morbidity or mortality.

Timely evacuation of hematoma is an efficacious intervention, notably beneficial for retropharyngeal hematoma and spinal epidural hematoma.⁵ In the management of airways prior to hematoma evacuation surgery, particular attention must be paid to the occurrence of difficult airways to prevent a "can't intubate, can't ventilate" situation.⁶ Given the infrequency of hematoma and the potential for severe outcomes, it is imperative to conduct early and systematic assessments of risk factors of hematoma. We report the findings of a retrospective nested case-control study aiming to investigate the incidence and risk factors of postoperative hematoma following ACSS.

METHODS

Study population and study design

The present study enrolled patients who underwent ACSS at Peking University Third Hospital between March 2013 and February 2022. The selection of this study period was based on the comprehensive implementation of electronic health records system in the hospital, which ensured the availability of complete and reliable data. Inclusion criteria were as follows: 1) cervical spondylosis; 2) ACSS; 3) elective surgery. Exclusion criteria were as follows: 1) combined anterior and posterior cervical surgery; 2) trans-oral approach to C1-C2; 3) cervical spine tumors; 4) cervical spine fractures; 5) incomplete medical records. In the present study, postoperative hematoma following ACSS was defined as a symptomatic hematoma characterized by respiratory distress, neurological deficits, or other hematoma-related symptoms, confirmed by imaging findings or surgical evacuation. Patients with postoperative hematoma after ACSS were enrolled as the hematoma group, and others in the cohort without hematoma were randomly selected as the nonhematoma group by individually matching with the same operator, same gender, same surgery year, and similar age (±5 years) at a ratio of 4:1.

Variables

The general characteristics of the two groups were collected, including age, gender, body mass index (BMI), medical comorbidities, smoking history, anticoagulant or antiplatelet therapy, preoperative coagulation function tests, and platelet counts. Disease-related factors encompassed the classification of cervical spondylosis types, such as myelopathy type, radiculopathy type, or other types, as well as preoperative Modified Japanese Orthopaedic Association (m-JOA) scores and Neck Disability Index (NDI) scores. Surgical factors included surgical segments, ossification of the posterior longitudinal ligament (OPLL) within the surgical segments, anterior cervical corpectomy and fusion (ACCF), duration of surgery, estimated blood loss (EBL), and postoperative drainage volume. Anesthetic factors involved the American Society of Anesthesiologists (ASA) physical status classifications and mean arterial pressure (MAP) during both preoperative and postoperative recovery phases. Data on hospitalization duration and costs were also gathered.

BMJ Open

Anticoagulant therapy was defined as a history of using anticoagulant agents such as warfarin or low-molecular weight heparin. Antiplatelet therapy was defined as a history of using antiplatelet agents such as aspirin or clopidogrel. Preoperative coagulation function tests included prothrombin time (PT), International Normalized Ratio (INR), fibrinogen levels, activated partial thromboplastin time (APTT), and thrombin time (TT). The preoperative mean arterial pressure (MAP) was routinely assessed upon the patient's admission to the ward, and the maximum MAP recorded during the recovery period was obtained from anesthesia records.

We conducted a subgroup analysis of hematoma patients, with a focus on airway management. Patients were stratified based on the occurrence of difficult intubation prior to hematoma evacuation surgery. A comparative analysis was performed on various parameters between the groups, including sex, age, BMI, hypertension, C3 or C4 involvement, type of hematoma, the interval from symptom onset to airway intervention, time of presentation of hematoma, and ASA physical status classifications to assess correlations and statistical differences associated with difficult intubation. Additionally, the occurrence of difficult intubation prior to the initial surgical procedure was systematically assessed. Difficult intubation was defined as a clinical scenario requiring more than three attempts by an experienced anesthesiologist to achieve endotracheal intubation.⁷

For continuous data that were normally distributed, descriptive statistics were presented as mean \pm standard deviation. Data that were not normally distributed were described using median and interquartile range. Differences between the two groups for continuous variables were analyzed using an independent samples t-test (for data with a normal distribution) or a Mann-Whitney U test (for data without a normal distribution). Categorical data were expressed as percentages and analyzed for differences using the chi-square test or Fisher's exact test. A binary logistic regression model was applied to identify multivariate variables, utilizing the backward Wald method for variable selection. Odds ratios (OR) and 95% confidence intervals (CI) were used to quantify the strength of associations. The accuracy of diagnostic tests was assessed using receiver operating characteristic curves and the area under the curve (AUC). Statistical analyses were performed using SPSS version 26.0, with all tests being two-tailed, and P < 0.05 indicating statistical significance of differences.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

The number of postoperative hematoma cases identified during the study period dictated the overall sample size. In subgroup analyses, the count of difficult intubation cases similarly determined the subgroup sample size. According to the principle that the number of events per variable should be no less than five, which means the number of outcome events corresponding to each independent factor must meet this threshold, an appropriate number of independent variables were included to satisfy the sample size criterion based on the actual occurrences of outcome events. **RESULTS**

LOULIS

Incidence and time of presentation of postoperative hematoma

From March 2013 to February 2022, a total of 13,523 patients undergoing ACSS met the inclusion criteria. Of these, 55 patients developed postoperative hematoma, resulting in an incidence rate of 0.4%, with retropharyngeal hematoma occurring at a rate of 0.28% and spinal epidural hematoma at 0.12%. Patients without hematoma were randomly selected as the control group, individually matched for the same surgeon, gender, surgery year, and age within a 5-year range, at a ratio of 4:1. Consequently, the hematoma group comprised 55 cases, while the control group included 220 cases (Figure). The onset of hematoma varied significantly among patients, with the

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

earliest cases presenting as soon as 0.5 hours postoperatively and the latest occurring up to 7 days after surgery. Notably, four of these patients exhibited symptoms shortly after the removal of drainage tubes.

Difference between the hematoma group and the non-hematoma group

The comparative analysis revealed no statistically significant differences between the two groups in demographic characteristics, anticoagulant or antiplatelet therapy, the classification of cervical spondylosis, surgical segments, OPLL within the surgical segments, surgery duration, EBL, drain volume, or ASA physical status classifications, as shown in Table 1.

The two groups exhibited statistically significant differences in ACCF (P=0.011) and the maximum MAP during the recovery period (P=0.031). Patients in the hematoma group had longer hospitalization duration (P<0.001) and incurred greater costs (P<0.001) (Table 1). Analysis of the preoperative blood tests between the two groups showed statistically significant differences in APTT (P=0.011) and PT (P=0.05). In clinical practice, an extension of PT by 3 seconds and APTT by 10 seconds is deemed to have clinical significance. However, in the present study, the mean values of PT and APTT for both the hematoma group and the non-hematoma group were within the normal range. Consequently, PT and APTT were not included in the binary logistic regression analysis. Instead, other factors with a p-value less than 0.1 were incorporated into the model. Binary logistic regression analysis revealed that ACCF (OR, 2.459; 95% CI, 1.302-4.642; P=0.006) and the maximum MAP during the recovery period (OR, 1.030; 95% CI, 1.003-1.058; P=0.028) were independent risk factors for hematoma, as detailed in Table 2. The AUC for the maximum MAP during the recovery period to be 0.594 (95% CI, 0.510-0.679; P=0.031), whereas for

ACCF, the AUC was 0.586 (95% CI, 0.499-0.673; P=0.048). According to the highest Youden's

index, the cut-off value of the maximum MAP during the recovery period was set to 106 mmHg, with the sensitivity and specificity was 0.727 and 0.473, respectively.

Subgroup analysis of airway management in hematoma patients

Prior to the initial surgery, only one case of difficult intubation was observed among 55 patients. All 55 cases of hematoma patients underwent hematoma evacuation surgery following general anesthesia and tracheal intubation, among which 16 cases exhibited a difficult airway, including four cases where tracheal intubation was not possible requiring urgent tracheostomy (Figure). In the present study, 54 cases of hematoma were successfully treated, and the patients were subsequently discharged from the hospital. Regrettably, one patient died due to complications 24 days following the evacuation surgery.

In the comparison between difficult intubation patients and non-difficult intubation patients, there were statistically significant differences in retropharyngeal hematoma, the interval between symptom onset and airway intervention, and hospitalization duration (Table 3). Binary logistic regression analysis revealed that retropharyngeal hematoma (OR, 10.435; 95% CI, 1.249-87.144; P=0.030) was an independent risk factor for difficult intubation. The AUC for retropharyngeal hematoma was calculated to be 0.674 (95% CI, 0.529-0.819; P=0.044). To evaluate the strength of the association between retropharyngeal hematoma and difficult intubation, the phi coefficient was utilized. The analysis revealed a phi value of 0.342 (indicating a moderate positive correlation, as values between 0.3 and 0.5 are generally considered moderate), with a p-value of 0.011.

DISCUSSION

Incidence and time of presentation of postoperative hematoma

BMJ Open

Postoperative hematoma following ACSS is a rare but potentially high-risk complication. Bovonratwet et al. reported that out of a total of 37,261 patients who underwent anterior cervical discectomy and fusion, 148 (0.40%) developed hematoma requiring reoperation.¹ In a singlesurgeon case series of ACSS, Wang et al. documented a 1.0% incidence of postoperative hematoma, affecting 11 individuals out of a total of 1,150 patients. Notably, among these hematoma cases, 10 were specifically classified as retropharyngeal hematoma.⁸ Miao et al. presented a cohort of 1,258 patients who underwent ACSS, revealing an incidence of postoperative hematoma totaling 1.2%. Specifically, they observed seven cases (0.5%) of retropharyngeal hematoma and eight cases (0.6%) of spinal epidural hematoma.² Boudissa et al. reported that 13 out of 2,319 patients (0.56%) undergoing ACSS required reintervention within 72 hours postoperatively, with a distribution of five cases (0.2%) of retropharyngeal hematoma and seven cases (0.3%) of spinal epidural hematoma.⁹ O'Neill et al. reported on a series of 2,375 ACSS procedures, documenting 17 occurrences of retropharyngeal hematoma, which corresponded to an incidence of 0.7%.⁵ In the present study, the overall incidence of hematoma was 0.4%, with retropharyngeal hematoma occurring at a rate of 0.28% and spinal epidural hematoma at 0.12%, which is consistent with previous literature reports.

The common clinical assumption is that the risk of hematoma is most pronounced in the initial hours following surgery. Nevertheless, O'Neill et al. noted that approximately 35% of cases presented with a delayed onset, with an average time frame of 6 days postoperatively.⁵ In the present study, 31 cases exhibited symptoms within the first 6 hours postoperatively, with the earliest symptom onset occurring immediately after awakening from anesthesia. Additionally, 8 cases presented symptoms beyond 24 hours postoperatively, with the longest interval being 7 days.

Risk factors for postoperative hematoma

Previously described risk factors for hematoma, including male sex, age older than 65, smoking, medical comorbidities, multilevel procedures, OPLL within the surgical segments, therapeutic heparin use, lower BMI and ASA physical status classification grades of III or greater, ^{1,2,5,8,10-13} were not found to show strong associations in our study. The type of cervical spondylosis, as well as preoperative scores on the m-JOA and NDI scales, did not influence the occurrence of postoperative hematoma.

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

In previous studies, prolonged TT values and INR greater than 1.2 were identified as independent risk factors of hematoma.^{1,8} Prolonged APTT was associated with an increased risk of hematoma formation after surgery.¹⁴ In clinical practice, an extension of APTT by 10 seconds is considered to have clinical significance. In the present study, however, the mean values of APTT in both hematoma group and non-hematoma group were within the normal range. Therefore, despite the statistically significant difference in APTT between the two groups, the prolonged APTT in the present study should not be construed as a risk factor for hematoma development.

ACCF surgery exposes at least three vertebral bodies, resecting two intervertebral discs, while also performing partial vertebral body resection, which leads to greater exposure of the epidural space and extensive damage to the venous plexus within the spinal canal, resulting in increased blood loss. Hao et al. reported that among a total of 551 patients who underwent anterior cervical discectomy and fusion or ACCF for 2-level cervical spondylotic myelopathy, a significant difference was observed between the two groups in terms of blood loss.¹⁵ In the current study, logistic regression analysis suggested that ACCF was an independent risk factor for postoperative hematoma. During the ACCF surgery, special attention should be paid to potential bleeding,

Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

including vessels, muscles, and exposed cancellous bone.

Hypertension is recognized as a significant risk factor for postoperative hematoma, although the underlying mechanisms are not fully defined.¹⁶ Liu et al. suggest that arterial bleeding was predominantly the cause of such hematomas.¹⁷ However, Yin et al. present an alternative view, contending that arterial bleeding is an unlikely major source of hematomas due to its detectability during surgical procedures.¹⁸ During the initial intraoperative period under anesthesia, the MAP is low, making small vessel bleeding potentially undetected and inadequately managed with bipolar coagulation. As patients emerge from anesthesia, the stimulation of the tracheal tube and postoperative pain may precipitate a rise in blood pressure. These small vessels, which have not achieved effective hemostasis, may resume bleeding, leading to the development of hematoma. In the present study, the MAP at admission showed no significant difference between the two groups, yet a statistically significant difference was observed in the maximum MAP during the recovery period. Hematoma commonly occurs within the first few hours postoperatively. Hemodynamic fluctuations, particularly the surge in blood pressure during the anesthetic recovery period, may play a critical role in the development of hematoma, and thus, close monitoring and management of blood pressure during this period could be essential in reducing the risk of postoperative hematoma. Optimal timing for evacuation and airway management in hematoma patients

For patients with spinal epidural hematoma accompanied by severe neurological deficits, emergent surgical evacuation of the hematoma is the most appropriate therapeutic approach. The severity of symptoms prior to surgery may significantly impact postoperative recovery. According to the study by Yin et al., there was a significant statistical difference in the degree of neurological recovery based on whether the spinal epidural hematoma was evacuated within 24 hours.¹⁸ The research by Hohenberger et al. indicated that the key factors influencing recovery were the degree of neurological deficit and the interval between the onset of symptoms and surgery.¹⁰ Similarly, Epstein et al. advocated for aggressive treatment of postoperative spinal epidural hematoma.¹⁹ In the present study, all 17 patients with spinal epidural hematoma underwent evacuation surgery, and all patients' symptoms were partially or completely relieved after the procedure.

Song et al. reported that patients with retropharyngeal hematoma could be treated with close observation or evacuation surgery, depending on changes in respiratory status, surgical site conditions, and patient behavior.⁴ However, O'Neill et al. believed that whenever a patient presented with an airway complication, the decision was made to reoperate rather than treat the patient with observation and steroids.⁵ In the management of retropharyngeal hematoma, it was crucial to acknowledge the potential risk of difficult airways.²⁰ In the current study, among the 55 cases of hematoma evacuation, 16 patients encountered difficult intubation conditions, with 4 ultimately requiring a tracheostomy. In the subgroup analysis, retropharyngeal hematoma was identified as an independent risk factor for difficult intubation. Of the 16 difficult intubation cases, 15 were attributed to patients with retropharyngeal hematoma. The thyroid hematoma management guidelines emphasized the importance of anticipating difficult airway scenarios in patients with cervical hematomas²¹. In our study, 29% of hematoma patients experienced difficult intubation, irrespective of the hematoma's location. Therefore, in the airway management of these patients, anesthesiologists should adhere to the ASA practice guidelines for management of the difficult airway⁶, and the following measures should be considered: (1) awake intubation, (2) use of video laryngoscopy for the first intubation attempt, (3) limitation of tracheal intubation attempts, and (4) preparation for emergency front-of-neck airway.

This study presents a substantial clinical series dedicated to investigating hematoma following ACSS and introduces a novel finding by identifying, for the first time, ACCF and maximum MAP during recovery as independent risk factors associated with postoperative hematoma. In this retrospective nested case-control study, matching criteria such as the same surgeon, same year of surgery, same gender, and similar age (\pm 5 years) were applied to ensure a high degree of homogeneity and minimize bias. Despite these efforts, this study has its limitations. Firstly, as with any retrospective study, there is an inherent risk of selection and reporting bias. Secondly, due to the low incidence of hematoma, the sample size is limited. A multicenter, prospective study with a more detailed assessment of risk factors might provide a more comprehensive understanding of the variables associated with postoperative hematoma following ACSS.

CONCLUSION

ACCF and elevated maximum MAP during the recovery period were independent risk factors for postoperative hematoma following ACSS. Patients with post-ACSS hematoma are at high risk of a difficult airway, with retropharyngeal hematoma being strongly associated with challenging airway management. Postoperative hematoma was associated with longer hospitalization duration and greater costs. Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Contributors:

YT, JL and GZ contributed equally to this paper.

The corresponding authors are XG (puthmzk@163.com) and YH (hanyongzheng@bjmu.edu.cn). MX, ML, JW, SW and XG designed and coordinated the study. YT, GZ and YQ collected the data. YT, MW and YH drafted the manuscript. YT and JL analysed the data and performed the statistical analysis. All authors have read and approved the manuscript.

YT is the guarantor of this study and takes responsibility for the overall content and integrity of the work.

Fundings: This study was funded by grants from Wu Jieping Medical Foundation (320.6750.2023-08-5), Capital's Funds for Health Improvement and Research (2024-2-40912), and Peking University Third Hospital Innovation and Transformation Fund (BYSYZHKC2022103).

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Competing interests: The authors declare that they have no competing interests. The funders had no role in the study design; the collection, analysis, and interpretation of data; the writing of the report; or the decision to submit the paper for publication.

Data availability statement: The data underlying this article are available in [Mendeley Data Repository], at <u>https://data.mendeley.com/datasets/6rx5wgp75p/1</u>

Ethics approval: This study was approved by Medical Scientific Research Ethics Committee of Peking University Third Hospital. IRB number: IRB00006761-M2024464, 2022.06.05

Participants consent statement: Not applicable. This manuscript does not contain personal and/or medical information about an identifiable individual.

REFERENCE

[dataset] 1. Bovonratwet P, Fu MC, Tyagi V, et al. Incidence, Risk Factors, and Clinical Implications of Postoperative Hematoma Requiring Reoperation Following Anterior Cervical Discectomy and Fusion. *Spine (Phila Pa 1976)*. 2019;44:543-549. https://doi.org/10.1097/brs.00000000002885

[dataset] 2. Miao W, Ma X, Liang D, et al. Treatment of hematomas after anterior cervical spine surgery: A retrospective study of 15 cases. *Neurochirurgie*. 2018;64:166-170. https://doi.org/10.1016/j.neuchi.2017.12.002

3. Epstein N. Frequency, recognition, and management of postoperative hematomas following anterior cervical spine surgery: A review. *Surg Neurol Int.* 2020;11:356. https://doi.org/10.25259/sni_669_2020

4. Song KJ, Choi BW, Lee DH, et al. Acute airway obstruction due to postoperative retropharyngeal hematoma after anterior cervical fusion: a retrospective analysis. *J Orthop Surg Res.* 2017;12:19. https://doi.org/10.1186/s13018-017-0517-z

[dataset] 5. O'Neill KR, Neuman B, Peters C, et al. Risk factors for postoperative retropharyngeal hematoma after anterior cervical spine surgery. *Spine (Phila Pa 1976)*. 2014;39:E246-52. https://doi.org/10.1097/brs.00000000000139

6. Apfelbaum JL, Hagberg CA, Connis RT, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. *Anesthesiology*. 2022;136:31-81. https://doi.org/10.1097/aln.000000000004002

7. Shah PN and Sundaram V. Incidence and predictors of difficult mask ventilation and intubation. *J Anaesthesiol Clin Pharmacol*. 2012;28:451-5. https://doi.org/10.4103/0970-9185.101901

[dataset] 8. Wang H, Yu H, Zhang N, et al. Incidence, Risk Factors, and Management of Postoperative Hematoma Following Anterior Cervical Decompression and Fusion for Degenerative Cervical Diseases. *Neurospine*. 2023;20:525-535. https://doi.org/10.14245/ns.2245066.533

[dataset] 9. Boudissa M, Lebecque J, Boissière L, et al. Early reintervention after anterior cervical spine surgery: Epidemiology and risk factors: A case-control study. *Orthop Traumatol Surg Res.* 2016;102:485-8. https://doi.org/10.1016/j.otsr.2016.02.003

10. Hohenberger C, Zeman F, Höhne J, et al. Symptomatic Postoperative Spinal Epidural Hematoma after Spinal Decompression Surgery: Prevalence, Risk Factors, and Functional Outcome. *J Neurol Surg A Cent Eur Neurosurg*. 2020;81:290-296. https://doi.org/10.1055/s-0039-1697024

11. Saitta BH, Shultz P, Hanson K, et al. Post-Operative Spinal Epidural Hematoma: Are We Discontinuing Aspirin Early Enough? *Global Spine J.* 2023;13:2255-2261. https://doi.org/10.1177/21925682221079259

12. Xia T, Zhou F, Chu H, et al. Incidence and risk factors of postoperative symptomatic spinal epidural hematoma in cervical spine surgery: a single center, retrospective study of 18,220 patients. *Eur Spine J.* 2022;31:2753-2760. https://doi.org/10.1007/s00586-022-07301-z

13. Chen Q, Zhong X, Liu W, et al. Incidence of postoperative symptomatic spinal epidural hematoma requiring surgical evacuation: a systematic review and meta-analysis. *Eur Spine J*. 2022;31:3274-3285. https://doi.org/10.1007/s00586-022-07421-6

14. Liu N, Luo S, Hang C, et al. Changes in coagulation functions and hemorheological parameters may predict hematoma formation after total knee arthroplasty. *J Orthop Surg Res.* 2016;11:35. https://doi.org/10.1186/s13018-016-0370-5

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

[dataset] 15. Hao Q, Ding Q, Yang H, et al. Symptomatic postoperative spinal epidural hematoma preferentially occurs after anterior cervical discectomy and fusion versus anterior cervical corpectomy and fusion: a retrospective study. *Ann Palliat Med.* 2022;11:2025-2032. https://doi.org/10.21037/apm-22-488

16. Liao Y, Tian Y, Ye R, et al. Risk and treatment of symptomatic epidural hematoma after anterior cervical spine surgery: A retrospective clinical study. *Medicine (Baltimore)*. 2020;99:e18711. https://doi.org/10.1097/md.00000000018711

17. Liu Z, Jiao Q, Xu J, et al. Spontaneous spinal epidural hematoma: analysis of 23 cases. *Surg Neurol*. 2008;69:253-60; discussion 260. https://doi.org/10.1016/j.surneu.2007.02.019

18. Yin G and Ni B. Acute postoperative cervical spinal epidural hematoma. *Acta Orthop Traumatol Turc*. 2014;48:437-42. https://doi.org/10.3944/aott.2014.13.0133

19. Epstein NE and Agulnick MA. Perspective: Postoperative spinal epidural hematomas (pSEH) should be treated, not ignored. *Surg Neurol Int.* 2023;14:363. https://doi.org/10.25259/sni 772 2023

20. Debkowska MP, Butterworth JF, Moore JE, et al. Acute post-operative airway complications following anterior cervical spine surgery and the role for cricothyrotomy. *J Spine Surg*. 2019;5:142-154. https://doi.org/10.21037/jss.2019.03.01

21. Iliff HA, El-Boghdadly K, Ahmad I, et al. Management of haematoma after thyroid surgery: systematic review and multidisciplinary consensus guidelines from the Difficult Airway Society, the British Association of Endocrine and Thyroid Surgeons and the British Association of Otorhinolaryngology, Head and Neck Surgery. *Anaesthesia*. 2022;77(1):82-95. https://doi.org/10.1111/anae.15585

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

Characteristic	Hematoma group N=55	Non-hematoma group N=220	$\chi^2/Z/t$	P value
Gender	1, 00	1, 220	χ²=0.000	1.000
Male	39(70.91%)	156(70.91%)	<i>,</i> ,	
Female	16(29.09%)	64(29.09%)		
Age/(years)	55(16)	53(15)	Z=0.316	0.752
$BMI/(kg \cdot m^{-2})$	26.15±3.20	24.92±3.76	t=-1.239	0.219
Hypertension	13(23.63%)	66(30.00%)	χ²=0.870	0.351
Smoking history	15(27.30%)	47(21.40%)	χ ² =0.880	0.348
Anticoagulant or antiplatelet therapy	1(1.81%)	13(5.90%)		0.315#
Preoperative blood index				
PT/(s)	10.95(0.78)	10.60(0.78)	Z=1.960	0.050
INR	1.03(0.07)	0.99(0.10)	Z=1.834	0.067
FIB/ (g/L)	2.89±0.59	2.94±0.50	t=0.702	0.483
APTT/(s)	33.25±4.09	32.03±3.60	t=2.557	0.011
TT/(s)	13.95(1.58)	13.70(1.10)	Z=0.992	0.321
Platelet count/ (10 ^{^9} /L)	228(80.50)	220(76.00)	Z=1.711	0.087
Classification of cervical spondylosis				0.060
CSM	35(63.64%)	115(52.27%)		
CSR	6(10.91%)	57(25.91%)		
Other types	14(25.45%)	48(21.82%)		
Preoperative m-JOA score	14.00(4.10)	14.50(3.10)	Z=-1.623	0.104
Preoperative NDI score	12.00(15.30)	11.00(18.00)	Z=-0.726	0.468
Surgical segments /(Levels)	2(1)	2(1)	Z=1.411	0.158
OPLL within the surgical segments	18(32.70%)	67(30.50%)	χ ² =0.106	0.744
ACCF	23(41.80%)	54(24.45%)	χ²=6.512	0.011
Surgery duration/ (minutes)	86(38)	76(44)	Z=0.939	0.348
EBL/ (mL)	30(48)	20(40)	Z=1.754	0.079
Drain volume/(mL)	30.00(48.75)	30.00 (35.00)	Z=0.560	0.576
Preoperative MAP/ (mm Hg)	96.30(15.05)	97.00(12.60)	Z=0.369	0.712
Maximum MAP during recovery/(mm Hg)	110.00(15.50)	108.30(17.88)	Z=2.159	0.031
ASA physical status classification				1.000#
Ι-Π	55(100%)	216(98.60%)		
≥ Ⅲ	0(0%)	3(1.40%)		
Hospitalization duration /(days)	7(7)	4(2)	Z=7.395	< 0.001
Cost/ (RMB)	68387 (25340)	57533 (20853)	Z=4.876	< 0.001

Data are presented as n (%) or Median (IQR) or means \pm standard deviation.

BMI, body mass index; PT, preoperative prothrombin time; INR, international normalized ratio; FIB, fibrinogen; APTT, activated partial thromboplastin time; TT, thrombin time; CSM, cervical spondylotic myelopathy; CSR, cervical spondylotic radiculopathy; m-JOA, modified Japanese Orthopaedic Association; NDI, neck disability index; OPLL, ossification of posterior longitudinal ligament; ACCF, anterior cervical corpectomy and fusion; EBL, estimated blood loss; MAP, mean Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

1 2	
3	
4 5	
6	
7 8	
9	
10 11	
12	
13 14	
15	
16 17	
18	
19 20	
20 21 22	
22 23	
24	
25 26	
26 27	
28 29	
30	
31 32	
33	
34 35	
36	
37 38	
39	
40 41	
42	
43 44	
45	
46 47	
48	
49 50	
51	
52 53	
54	
55 56	
57	
58 59	
60	

60

1

arterial pressure; ASA, American society of Aneshesiologists.

[#]Fisher exact test

Table 2 Binary multivariate logistic regression (backward Wald) analysis of the risk factors for hematoma

Variable	В	SE	P value	OR	95%CI
Maximum MAP during recovery	0.030	0.014	0.028	1.030	1.003-1.058
ACCF	0.900	0.324	0.006	2.459	1.302-4.642
Constant	-4.914	1.514	0.001	0.007	

; CI, et J fusion. SE, standard error; OR, odds ratio; CI, confidence interval; MAP, mean arterial pressure; ACCF, anterior cervical corpectomy and fusion.

Characteristic	Difficult intubation group N=16	Non-difficult intubation group N=39	$\chi^2/Z/t$	P value
Gender	N-10	N-39		0.754#
Male	12(75.00%)	27(69.23%)		
Female	4(25.00%)	12(30.77%)		
Age/(years)	54.56±9.62	53.21±8.71	t=-0.509	0.613
BMI/ (kg·m ⁻²)	24.95(2.00)	25.50(4.00)	Z=-1.122	0.262
Hypertension	5(31.25%)	8(20.51%)		0.489#
Difficult intubation prior to the initial surgery	1(6.25%)	0(0)		0.291#
C3 or C4 involvement	11(68.75%)	19(48.72%)		0.237#
ACCF	6(37.50%)	15(38.46%)	χ ² =0.004	0.947
Type of hematoma				0.012#
retropharyngeal hematoma	15(93.75%)	23(58.97%)		
spinal epidural hematoma	1(6.25%)	16(41.03%)		
Interval between symptom onset and airway intervention/ (hours)	2.00(2.90)	1.00(2.50)	Z=2.418	0.016
Time of presentation of hematoma/ (hours)	8.50(16.00)	4.00(10.00)	Z=0.688	0.492
ASA physical status classification			χ ² =0.773	0.379
I	6(37.50%)	10(25.64%)		
\geq II	10(62.50%)	29(174.36%)		
Hospitalization duration /(days)	12(7)	7(5)	Z=3.094	0.002
Cost/ (RMB)	68387 (26122)	68329 (23578)	Z=0.474	0.636

Table 3 Comparison between difficult intubation group and non-difficult intubation group in the

Data are presented as n (%) or Median (IQR) or means \pm standard deviation.

BMI, body mass index; ACCF, anterior cervical corpectomy and fusion; ASA, American society of

Aneshesiologists.

#Fisher exact test

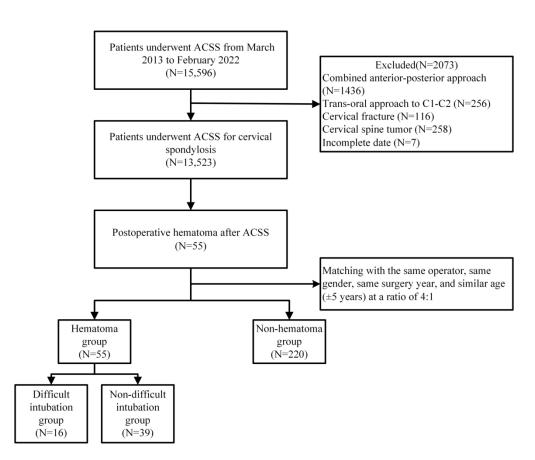
Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies.

Figure legend

Figure: Flow diagram outlining the selection of the study population. ACSS, anterior cervical spine surgery.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



Flow diagram outlining the selection of the study population. ACSS, anterior cervical spine surgery.

172x143mm (300 x 300 DPI)