

# Is Intraoperative Blood Loss Volume in Elderly Cervical Spine Injury Surgery Greater in Patients with Ankylosis? A Multicenter Survey

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**Abstract:**

**Introduction:** Preoperative estimations of blood loss are important when planning surgery for cervical spine injuries in older adults. The association between ankylosis and blood loss in perioperative management is of particular interest. This multicenter database review aimed to evaluate the impact of ankylosis on surgical blood loss volume in elderly patients with cervical spine injury.

**Methods:** The case histories of 1512 patients with cervical spine injury at among 33 institutions were reviewed. After the exclusion of patients without surgery or whose blood loss or ankylosis status was unclear, 793 participants were available for analysis. Differences in blood loss volume were compared between the Ankylosis (+) group with ankylosis at the cervical level and the Ankylosis (–) group without by the inverse probability of treatment weighting (IPTW) method using a propensity score.

**Results:** Of the 779 patients (mean age: 75.0±6.3 years) eligible for IPTW calculation, 257 (32.4%) had ankylosis at the cervical level. The mean blood loss volume was higher in Ankylosis (+) patients than in Ankylosis (–) patients ( $P<0.001$ ). This difference did not reach statistical significance when weighted by background factors, with mean blood loss of 244 mL and 188 mL, respectively, after adjustment.

**Conclusions:** This study revealed that ankylosis was significantly associated with increased blood loss volume when unadjusted by surgical time. Elderly patients with cervical spine injury accompanied by ankylosis appear predisposed to higher bleeding and severe hemorrhage, both as a result of the condition and their particular demographic characteristics.

**Keywords:**

cervical spine injury, elderly patients, blood loss volume, ossification of the posterior longitudinal ligament, ossification of the ligamentum flavum, diffuse idiopathic skeletal hyperostosis

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## Introduction

Recent increases in life expectancy have led to a greater number of elderly patients with cervical spinal cord injuries<sup>1-5</sup>. The elderly also more frequently suffer ankylosis-related diseases, such as ossification of the posterior longitudinal ligament (OPLL), ossification of the ligamentum flavum (OLF), and diffuse idiopathic skeletal hyperostosis (DISH)<sup>6-8</sup>. Therefore, OPLL, OLF, and DISH are often associated with cervical spinal cord injury in this population. We regularly encounter cases of unexpectedly large blood loss due to a bleeding tendency in patients with ankylosis in the spine. Previous studies have also reported that the propensity for bleeding was greater in OPLL than in cervical spondylotic myelopathy<sup>9-11</sup>. Since elderly patients are at an elevated risk of complications from heavy bleeding, it is important to preoperatively estimate blood loss when planning surgery for cervical spine injury. The association between ankylosis and blood loss during perioperative management is of particular interest.

This multicenter database review aimed to evaluate the impact of the presence of OPLL, OLF, and DISH on surgical blood loss in elderly patients with cervical spine injury.

## Materials and Methods

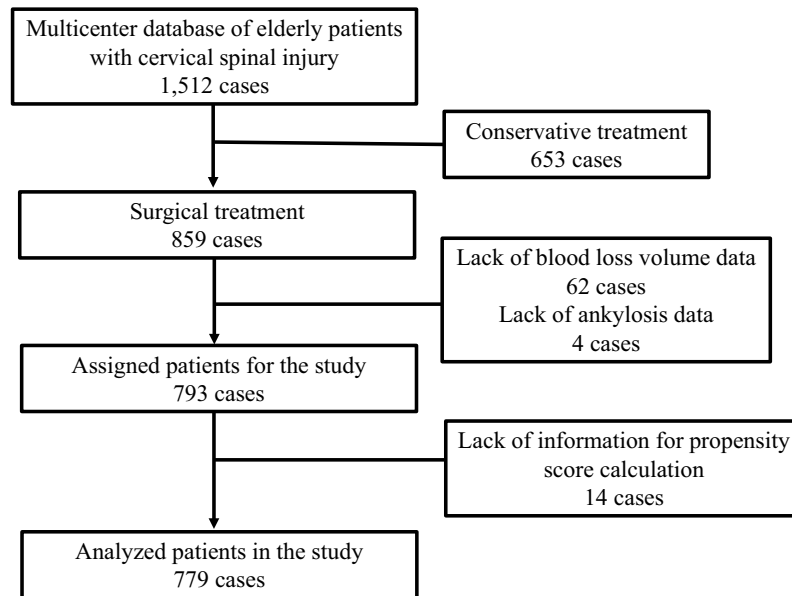
Our institutional review board (no. 4824) and those of all participating institutions approved the study protocol. The Japan Association of Spine Surgeons with Ambition undertook this examination as part of a multicenter joint study<sup>12-17</sup>.

### Cohort construction

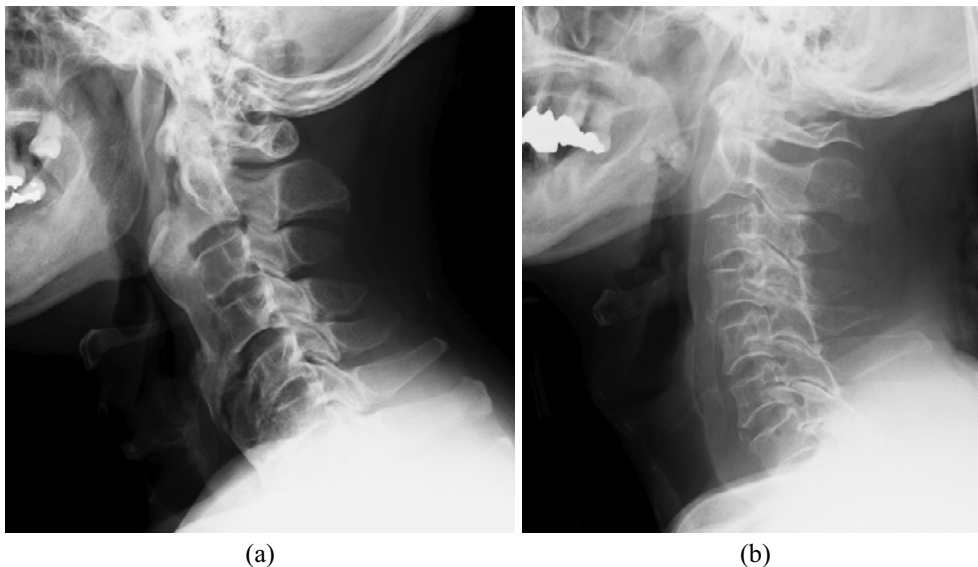
The subject selection process in this study has been previously reported<sup>12-17</sup>. All subjects were aged 65 years or older, which has been generally defined as elderly<sup>18</sup>. We retrospectively reviewed the case histories of 1512 patients with cervical spine injury recorded between 2010 and 2020 at among 33 institutions across Japan (Fig. 1). Of the 859 patients who underwent surgical treatment, 62 and 4 patients with uncertain data on blood loss or OPLL, OLF, or DISH status, respectively, were excluded, leaving 793 participants available for analysis. Each institute used an opt-out system for informed consent; patients refusing to participate were omitted. The study was conducted in accordance with the Declaration of Helsinki.

### Evaluations

We recorded data on blood loss; existence of ankylosis such as OPLL, OLF, and DISH; age; gender; blood test findings; pre-injury activities of daily living (ADL); prior medical conditions; medications used; complications other than cervical spine injury; trauma characteristics (presence of fracture, presence of dislocation, and location of fracture); American Spinal Cord Injury Association (ASIA) classification; and facility at which the medical record was collected. Blood volume loss was the main outcome of interest. Total blood loss was treated as the amount of blood loss in cases of two-stage surgery. Blood loss records described as “slight” without a quantitative measurement were counted as 10 mL. We compared the differences in blood loss volume



**Figure 1.** Patient flowchart.



**Figure 2.** Representative cervical spine radiographs.  
(a) Ankylosis (+), (b) Ankylosis (-).

between the Ankylosis (+) group with OPLL, OLF, or DISH at the cervical level and the Ankylosis (-) group (Fig. 2).

### **Statistical analysis**

Since the background factors of Ankylosis (+) and Ankylosis (-) patients were different, statistical analysis was performed by the inverse probability of treatment weighting (IPTW) method by calculating a propensity score and weighting it by its inverse. Candidate factors for inclusion in the propensity score were items that could be extracted from the database, which are as follows: age, gender, total protein, albumin, hemoglobin, pre-injury ADL, medical history (cerebrovascular disease, cognitive impairment, Parkinson's disease, diabetes mellitus, rheumatoid arthritis, osteoporosis,

hypertension, heart disease, respiratory disease, renal disease, surgery for musculoskeletal disease, among others), medications used prior to injury (number of medications, anticoagulants, antiplatelets, antipsychotics, antianxiety medication, sleeping medication, vitamin D, bisphosphonates, other osteoporosis medication, neurotrophin, non-steroidal anti-inflammatory drugs, pregabalin/mirogabalin, serotonin noradrenaline reuptake inhibitors, tramadol, other analgesics, antihypertensive medication, antiarrhythmic medication, steroids, diabetes medication, and other medication), presence of complications (head, chest, abdomen, upper extremity, lower extremity, pelvis, thoracolumbar spine, and other), injury type (existence of fracture, existence of dislocation, and vertebral fracture level), number of surgical waiting days,

surgical technique (posterior fixation, posterior decompression, posterior decompression and fixation, anterior decompression, anterior fixation, anterior-posterior fixation, and posterior-anterior fixation), operative time, presence of intraoperative complications, presence of dural tear, ASIA score (sum of manual muscle testing of key muscles; 0-100), and enrollment site. Logistic regression analysis was performed with the above factors as explanatory variables and ankylosis status as the response variable. The optimal model was selected using a stepwise method based on the Akaike information criterion. Ultimately, gender, history of rheumatoid arthritis or respiratory disease, osteoporosis medication, vitamin D, lower extremity trauma complications, cervical fracture, cervical dislocation, axial fracture, surgical waiting days, operative technique, operative time, and ASIA score were adopted in the IPTW analysis. Fourteen patients with missing items were excluded from the propensity score calculation; thus, the final number of patients included in the analysis is 779 patients (Fig. 1). The C-statistic indicating the fit of the propensity score was good at 0.776. Before the IPTW-weighted test, unweighted *t*-testing was also performed on those patients.

All statistical analyses were conducted using the statistical package R, version 4.1.0 (available at: <http://www.r-project.org>). The level of significance was set at  $P < 0.05$ .

## Results

A total of 779 patients (534 [68.5%] males, 245 [31.5%] females; mean age:  $75.0 \pm 6.3$  years) were suitable for IPTW calculation. Table 1 provides a summary of the characteristics of the Ankylosis (+) and Ankylosis (-) patients. We observed 257 (32.4%) cases of OPLL, OLF, or DISH at the cervical level. The mean surgical time was 177 min and 159 min in the Ankylosis (+) and Ankylosis (-) groups, respectively. The mean bleeding volume was 279 mL and 171 mL in the Ankylosis (+) and Ankylosis (-) groups, respectively. We first examined for an unweighted difference in the amount of blood loss with and without ankylosis. The surgical blood loss volume was higher in the Ankylosis (+) group than in the Ankylosis (-) group ( $P < 0.001$ ) (Table 2). However, when weighted by background factors, this difference did not reach statistical significance, with calculated mean volumes of 244 mL and 188 mL, respectively.

Since ankylosis was positively associated with a longer operative time (Ankylosis (+): 177 min, Ankylosis (-): 159 min;  $P = 0.002$ , Welch's *t*-test), we reperformed the IPTW analysis to investigate the possibility that this factor was responsible for the increased blood loss by excluding operative time from the propensity score calculation. The C-statistic for this model was good at 0.739. The estimated blood loss volume was significantly higher under this condition, with mean volumes of 333 mL and 170 mL in the Ankylosis (+) and Ankylosis (-) groups, respectively (Table 3).

Lastly, we analyzed the proportion of patients who lost

more than 1000 mL of blood. The Ankylosis (+) group displayed severe hemorrhage in 11 of 257 cases (4.3%), while the Ankylosis (-) group showed severe hemorrhage in 7 of 522 cases (1.3%) ( $P = 0.01$ , Fisher's exact test). Table 4 summarizes the details of the 11 ankylosing spine cases with massive bleeding. One of the four cases displaying surgical blood loss exceeding 2000 mL resulted in intraoperative cardiac arrest (Case 2).

## Discussion

This study evaluated the impact of ankylosis in the spine, such as OPLL, OLF, and DISH, on intraoperative blood loss volume in elderly patients with cervical spine injury by means of a multicenter database. We revealed that the presence of ankylosis was significantly associated with increased blood loss volume when surgical time was excluded from IPTW calculations, with the rate of severe bleeding also higher in Ankylosis (+) patients.

In recent years, the number of cervical spine injuries in the elderly has been increasing, with a correspondingly higher demand for surgery. Surgical complications are more common in older adults as both operating time and blood loss increase<sup>19,20</sup>. Therefore, forecasting the amount of blood loss before surgery may assist in operation planning. Several other studies have developed sliding scales that indicate the risk of complications, showing that hemorrhage should be minimized in older patients<sup>20,21</sup>.

Elderly patients with cervical spine injuries are frequently complicated by OPLL and DISH, and we often encounter massive bleeding during surgery in such cases with accompanying ankylosis. Several reports have demonstrated increased bleeding in OPLL, OLF, and DISH complicated with ankylosis. Kato et al. examined the distribution of intraoperative bleeding in laminoplasty for OPLL and revealed that 8.3% of patients experienced major bleeding of 500 g or more, with an occupancy rate of more than 60% as the only clear risk factor for major intraoperative hemorrhage<sup>9</sup>. Kishiya et al. compared blood loss for OPLL and cervical spondylotic myelopathy in cervical spine surgery and witnessed significantly higher values in OPLL<sup>10</sup>. Meng et al. reported that OPLL was an independent risk factor for significant intraoperative blood loss during cervical laminoplasty by multivariable logistic regression analysis<sup>22</sup>. A single-center study of surgical outcomes for thoracic myelopathy showed that patients with OPLL or OLF had greater blood loss than those without those ossifications and bleeding was significantly higher in patients with both<sup>11</sup>. In an investigation of spine fracture patients, blood loss tended to be greater in ankylosing spine and DISH patients than in controls<sup>23</sup>. Okada et al. found that the amount of hemorrhage in open surgery for thoracolumbar fracture patients with DISH was approximately 500 mL, with one patient each succumbing to hypovolemic shock, respiratory failure, or pneumonia<sup>24</sup>. In this study, the presence of OPLL, OLF, and DISH resulted in more blood loss, but this difference was not sig-

**Table 1.** Study Population Characteristics.

	Ankylosis (-) (n=522)	Ankylosis (+) (n=257)
Age, years	74.9±6.3 (65–94)	75.2±6.3 (65–91)
Sex, male/female	326:196	208:49
Preoperative laboratory data		
Total protein, g/dL	6.5±0.7 (2.9–8.8)	6.5±0.6 (4.5–8.1)
Albumin, g/dL	3.7±0.6 (1.7–11.7)	3.6±0.5 (1.7–4.7)
Hemoglobin, g/dL	12.6±1.9 (3.1–18.7)	12.7±1.9 (6.0–16.9)
Pre-injury ADL		
Independence of walking, n (%)	474 (90.8)	226 (87.9)
Cane use, n (%)	27 (5.1)	21 (8.1)
Walker or caregiving, n (%)	16 (30.6)	9 (3.5)
Standing and transferable, n (%)	2 (0.3)	1 (0.3)
Sitting, n (%)	3 (0.5)	0 (0)
Comorbidities, n (%)	426 (81.6)	218 (84.8)
Medication, n (%)	391 (74.9)	63 (24.5)
Combined injury, n (%)	135 (25.8)	42 (16.3)
Cervical spine findings		
OPLL, n (%)	0 (0)	197 (76.6)
OLF, n (%)	0 (0)	14 (5.4)
DISH, n (%)	0 (0)	123 (47.8)
Cervical fracture, n (%)	336 (64.3)	112 (43.5)
Cervical dislocation, n (%)	145 (27.7)	35 (13.6)
Preoperative ASIA motor score	74±32 (0–100)	64±34 (0–100)
Days between injury and operation	30.6±108 (0–1435)	21.8±44.7 (0–403)
Surgical procedure		
Anterior		
Fusion, n (%)	37 (7.1)	2 (0.8)
Decompression and fusion, n (%)	15 (2.9)	2 (0.8)
Posterior		
Decompression, n (%)	132 (25.3)	116 (45.1)
Fusion, n (%)	212 (40.6)	68 (26.5)
Decompression and fusion, n (%)	106 (20.3)	67 (26.1)
Anterior and posterior combined, n (%)	20 (3.8)	2 (0.8)
Surgical time, min	159±71 (32–583)	177±80 (66–554)
Blood loss volume, mL	171±254 (5–2574)	279±467 (5–4327)

Note: Values are expressed as the mean±standard deviation (range) or patient number (%).

ADL, activities of daily living; OPLL, ossification of the posterior longitudinal ligament; OLF, ossification of the ligamentum flavum; DISH, diffuse idiopathic skeletal hyperostosis; ASIA, American Spinal Cord Injury Association

**Table 2.** Blood Loss Estimates and Differences between Patients with and without Ankylosis by the IPTW Method.

	Blood loss (mL) Ankylosis (-)	Ankylosis (+)	Difference	P-value
Crude	171 (150–193)	279 (222–336)	108 (46–169)	<0.001
Weighted (IPTW)	188 (156–219)	244 (180–308)	57 (-15–128)	0.12

Notes: Values are expressed as the estimated mean (95% confidence interval). Crude values were estimated by unweighted *t*-tests. Weighted values were estimated by IPTW *t*-tests.

IPTW, inverse probability of treatment weighting

nificant after adjusting for ambient conditions, and so we could not conclusively state that blood loss was higher due to ankylosis. However, analysis without adjusting for the imbalance in operative time showed that blood loss was sig-

nificantly higher in Ankylosis (+) patients than in Ankylosis (-) patients.

Several papers have addressed the mechanism of increased intraoperative blood loss in OPLL, OLF, and DISH.

**Table 3.** Blood Loss Estimates and Differences between Patients with and without Ankylosis by the IPTW Method after Removal of Surgical Time as an Adjustment Factor.

	Blood loss (mL) Ankylosis (-)	Ankylosis (+)	Difference	P-value
Weighted (IPTW)	170 (147–192)	333 (210–457)	163 (38–289)	0.01

Notes: Values are expressed as the estimated mean (95% confidence interval). Weighted values were estimated by IPTW *t*-tests.

IPTW, inverse probability of treatment weighting

**Table 4.** Details of the Ankylosing Spine Cases with Massive Bleeding of More than 1000 mL.

Case	Age (years)	Sex	Surgical procedure	Decompression level	Fusion level	Surgical time (min)	Blood loss (mL)
1	91	Male	Anterior decompression and fusion	C7-T1	C7-T1	475	3357
2	84	Male	Posterior decompression and fusion	C2-7	C3-7	350	4327
3	76	Male	Posterior decompression and fusion	C5-6	C2-T2	212	2242
4	73	Male	Posterior decompression and fusion	C4-6	C4-T2	295	1258
5	71	Male	Posterior fusion	N/A	C5-T3	190	1066
6	81	Male	Posterior fusion	N/A	C4-T2	178	1250
7	66	Male	Posterior fusion	N/A	C2-T3	209	1044
8	82	Female	Posterior fusion	N/A	C2-T1	270	1100
9	77	Female	Posterior fusion	N/A	C4-7	210	1600
10	70	Male	Posterior decompression	C3-7	N/A	196	1310
11	89	Male	Posterior fusion	C7-T1	C3-T2	306	2780

N/A, not available

Kakiuchi performed intraoperative pressure measurements in the first thoracic vertebra and found that the amount of bleeding in cervical vertebroplasty was related to vertebral interosseous pressure, and not arterial pressure<sup>25</sup>. The higher bleeding in the K-line (-) OPLL group in Li et al.'s study demonstrated that narrowing of the jugular canal resulted in increased blood pressure in the regional veins, decreased venous return in the jugular canal, and overdistribution to the epidural veins, resulting in more hemorrhage<sup>26</sup>. In a report comparing lumbar spinal surgery outcomes with and without DISH, lumbar canal stenosis patients with DISH were more frequently obese than those without, which might have led to higher blood loss volume and longer surgery time<sup>27</sup>. In our study, testing unadjusted for operative time showed significantly more blood loss in Ankylosis (+) patients and a greater proportion of massive bleeding of 1000 mL or more, suggesting that ankylosis contributed at least in part to more bleeding. However, when background factors were taken into account, ankylosis did not necessarily appear to cause significantly more bleeding despite higher mean values. As our estimates changed depending if operative time was included as an adjustment factor, hemorrhage might be related to longer operative time in Ankylosis (+) cases. In the univariate analysis, the Ankylosis (-) group exhibited a higher percentage of fractures and dislocations and a greater proportion of fusion cases or decompression and fusion cases in terms of surgical technique, which indicated a difference in instability between the patient groups. Both the type of

trauma and surgical technique were included in the multivariate analysis. Thus, while the results accounted for those factors, an effect of trauma type due to ankylosis remained possible, and ankylosis itself could have been a bleeding risk. Blood pressure control may be effective for mitigating blood loss in ankylosing cases. To clarify whether there is more bleeding due to longer operative time or vice versa, the cause-and-effect relationship of our findings requires further study.

This investigation had some limitations. First, it was a retrospective case series. Second, the participating medical institutions were primarily tertiary care centers and might have had treatment biases contributing to the population's heterogeneity; the patients' history and general health were also unavoidably taken into account when choosing the course of treatment. Third, age, gender, medications, type of fracture, and surgical technique are some of the variables that can affect blood loss<sup>28,29</sup>. Fourth, intraoperative blood pressure data were not available in our study despite a previous report showing this factor to significantly influence surgical bleeding<sup>30</sup>. Nevertheless, the multicenter design of this study enabled a high number of surgical cases of cervical spine injury. Since this cohort is the largest of its kind on elderly cervical spine injuries, it was possible to evaluate the relationship between ankylosis and blood loss while considering numerous parameters.

## Conclusion

This study addressed the question of whether ankylosis, including OPLL, OLF, and DISH, impacted the amount of bleeding in surgery for elderly patients with cervical spinal cord trauma using a multicenter database. The existence of ankylosis was significantly associated with increased blood loss volume when unadjusted for surgical time. Increased blood loss, the potential for massive bleeding, and prolonged operative time are generally expected in patients with ankylosis. There remains a need for better blood loss management, such as advance risk assessment, transfusion preparation, technique selection, and hemostatic measures.

**Disclaimer:** Nakajima and Okada are the Editors of Spine Surgery and Related Research and on the journal's Editorial Committee. They were not involved in the editorial evaluation or decision to accept this article for publication at all.

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**Ethical Approval:** The ethics committee of Shinshu University School of Medicine, approved the study (no. 4824).

**Informed Consent:** Informed consent for publication was obtained from all participants in this study.

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