Postoperative Outcomes of Subaxial Cervical Spine Metastasis: Comparison Among The Anterior, Posterior, and Combined Approaches

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Research Article

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Abstract

Background: Incidence of subaxial spinal metastases is increasing due to longer life expectancy resulting from successful modern treatments of cancer. The three most utilized approaches for surgical treatment include the anterior, posterior, and combined approach. However, despite increasing surgical volume, data on the postoperative complication profiles of different operative approaches for this patient population is scarce.

Methods: The institutional databases of two large referral centers in Thailand were retrospectively reviewed. Patients with subaxial cervical spine metastasis who underwent cervical surgery during 2005 to 2015 were identified and enrolled. Clinical presentations, baseline characteristics, operative approach, perioperative complications, and postoperative outcomes, including pain, neurological recovery, and survival, were compared among the three surgical approaches.

Results: This study included 70 patients (44 anterior approach, 14 posterior approach, 12 combined approach). There were no statistically significant differences in preoperative characteristics, including Charlson Comorbidity Index (CCI), Tomita score, and revised Tokuhashi score, among the three groups. There were also no significant differences among groups for medical complications, surgical complications, neurological recovery, verbal pain score improvement, survival time, or ambulatory status improvement. However, the combined approach did show a significantly higher rate of overall perioperative complications ($p=0.01$), intraoperative blood loss, ($p<0.001$), and operative time ($p<0.001$) compared to the other two approaches.

Conclusions: The results of this study do not reveal any clear superiority among the three main surgical approaches used to treat subaxial cervical spine metastasis. Patients in the combined approach group had the highest rates of perioperative complications. However, although the differences were not statistically significant, patients in the combined group tended to have better clinical outcomes after follow-up, and the longest survival time.

Background

The incidence of cervical spine metastasis ranges from 10%-15%, and it most often occurs in the subaxial cervical region. Most patients present with axial neck pain (from tumor biology and cervical instability) and neurologic deficits – both of which are associated with poor prognosis due to high-level disability. Operative treatment may show benefit in patients who are not responsive to nonoperative treatment, who have intractable pain due to cervical instability, or who have progressive neurological deficits.

Decision-making regarding operative approach depends on multiple factors. In the majority of subaxial cervical spine metastasis cases, the anterior approach is recommended. However, in certain situations, such as multiple consecutive tumor involvement, anterior surgical decompression can result in massive
bleeding, which may make reconstruction difficult. In these types of cases, the posterior approach is more appropriate. Previous studies reported promising results for pain reduction and neurological recovery without serious complications for both the anterior and posterior surgical approach.[2-4, 8, 9] However, to our knowledge, no previous study has directly compared the clinical outcomes and perioperative complications of these two approaches.

Accordingly, the purpose of the current study was to evaluate the perioperative complication profiles and postoperative outcomes of subaxial cervical spine metastasis treatment compared among the anterior, posterior, and combined surgical approaches.

Methods

This retrospective cohort comparison study aims to evaluate postoperative outcomes following anterior, posterior, or combined surgical approach in patients with subaxial cervical spinal metastasis. After receiving Institutional Review Board (IRB) approval to do so, we reviewed the institutional databases of both participating centers for patients who underwent surgery for subaxial cervical metastasis in Faculty of Medicine Siriraj Hospital, Mahidol University during April 2005 to March 2015. The inclusion criteria were patients with spinal metastasis involving the subaxial cervical region (C3-C7), age at surgery from 20-90 years, and pathological report or radiographic study confirming metastatic disease. Exclusion criteria were previous surgery at the same level, loss to follow-up, and incomplete medical records.

Recorded variables included demographic and clinical data (gender, age at operation, comorbidities, and preoperative neurological status), operative data (surgical approach, level of decompression, reconstruction materials, type of instrumented fixation, operative time, and estimated blood loss [EBL]), and postoperative data (postoperative complications, length of hospital stay, neurological outcomes, ambulatory status, reoperation, and survival). Severity of comorbidity was calculated using the Charlson Comorbidity Index (CCI).[10] Neurological status was classified by American Spinal Injury Association (ASIA) grading during the preoperative and postoperative periods.[11] Ambulatory status was classified as ambulator or non-ambulator. Preoperative predicted survival was calculated using the revised Tokuhashi score[12] and Tomita score.[13] Preoperative pain and postoperative pain were evaluated using a verbal numerical scale (VNS) that ranged from 0 (no pain) to 10 (most extreme pain). Pain assessment agreement between the visual analog scale (VAS) for pain and the VNS for pain was reported to be good.[14]

Anterior techniques included corpectomy at the compressive level and reconstruction with autologous bone graft, polymethyl methacrylate (PMMA), or metallic cage, combined with anterior cervical plate fixation (Figure 1). Posterior techniques included laminectomy at the compressive level and stabilization with cervical pedicle screws or lateral mass screws and rod system (Figure 2). Combined surgery could be performed simultaneously or staged (Figure 3).
The primary outcomes were perioperative complications that were classified as medical-related complications (pneumonia, urinary tract infection, myocardial infarction, deep vein thrombosis, and pulmonary embolism) and surgery-related complications (surgical wound infection, implant failure, reoperation). The secondary outcomes were improvement in VNS, neurological recovery, improvement in ambulatory status at discharge date, and median survival time after surgery with the censoring date set as 31 May 2015.

**Statistical analysis**

Descriptive statistics were calculated and reported as mean ± standard deviations or median and range for quantitative data, and as frequency and percentage for categorical data. Chi-square test or Fisher’s exact test were used to analyze categorical variables as appropriate. One-way analysis of variance (ANOVA) was used to analyze verbal pain scale. Survival curves were created using Kaplan-Meier method. Data were compiled and analyzed using SPSS Statistics version 18.0 (SPSS, Inc., Chicago, IL, USA). \( P \)-values of less than 0.05 were considered statistically significant.

**Results**

Seventy-two patients were identified; however, two of those patients were excluded – one for having previous surgery, and the other was lost to follow-up. The remaining 70 patients were enrolled (33 men and 37 women). The average age was 58.3±11.6 years. The mean duration of symptoms before surgery was 55 days. Most patients (57/70, 81.42%) had neurological deficit before surgery. Primary tumors were classified according to Revised Tokuhashi Score, as shown in Table 1.

There were no significant differences in preoperative demographic or clinical characteristics, including gender, duration of symptoms, CCI, revised Tokuhashi score, and Tomita score, among the three surgical approach groups. Additional demographic and comorbidity data are shown in Table 1. Concerning operative data, the combined group had significantly greater intraoperative blood loss, longer operative time, and more perioperative complications (1,235.4±869 mm, 333.42±80.11 minutes, and 58.3%, respectively [all \( p<0.05 \)]) compared to the anterior and posterior approach groups.

**Perioperative complications**

The overall perioperative medical-related complication rate was 22.9%, and the surgery-related complication rate was 17.1%. The overall perioperative mortality rate was 84.28% of 70 people is 59 people. Pneumonia was found in 6 patients (8.6%; 4 anterior approach, 2 posterior approach), and one patient in the posterior group expired due to severe obstructive pneumonia. Urinary tract infection was found in 8 patients (11.4%; 4 anterior, 2 posterior, and 2 combined). One patient in the anterior group died from perioperative ST-elevation myocardial infarction (STEMI) and congestive heart failure. One patient in the combined group had deep vein thrombosis (DVT) and pulmonary embolism (PE) that required anticoagulant therapy. Surgical wound infection was found in 6 patients (1 anterior, 1 posterior, and 4 combined). Implant-related complications were found in 4 patients. Two patients in the anterior group
had cement displacement during the postoperative period after receiving anterior reconstruction using PMMA without anterior plate fixation. Both of those patients underwent revision surgery with anterior cervical plate fixation after the cement from the previous surgery was removed. One patient in the anterior group had implant failure at 2 months after surgery, but did not undergo revision surgery due to progression of disease. One patient in the posterior group had right C7 lateral mass screw malposition and underwent revision surgery. Dysphagia was found in 1 patient, but improvement was observed during follow-up.

**Clinical outcomes**

The average follow-up duration was 17.80±22.86 months. The mean overall preoperative VNS was 5.64, and the average postoperative VNS was 3.14. The mean preoperative VNS was 6.04, 4.28, and 5.75 in the anterior group, posterior group, and combined group, respectively. The mean postoperative VNS in the same groups were 3.43, 2.78, and 2.50, respectively. Improvement in VNS was found in more than 75% of patients in all 3 groups.

Neurological recovery rate and ambulatory status improvement were both poor (22.7-33.3% and 11.4-33.3%, respectively). Neurological improvement was found in only 18 of 70 patients, with the best improvement observed in the combined group, and the least improvement observed in the anterior group. Twelve of 70 patients became ambulatory after treatment (Table 2). These results are also reported in Figure 4.

**Survival**

Thirty-one patients (77.5%) had expired – 2 patients due to postoperative complications, and 29 patients due to disease progression. Analysis of mortality by group revealed that 15 patients were in the anterior group, 12 patients were in posterior group, and 4 patients were in the combined group. Mean and median survival times are shown in Table 2. Kaplan-Meier survival analysis showed the median survival time in the anterior, posterior, and combined approach groups to be 6.03, 6.76, and 27.93 months, respectively (Figure 5).

**Discussion**

Subaxial cervical metastases are known to have a poorer prognosis than metastases to the thoracic or lumbar regions.\(^{[15]}\) Despite the potential complications, operative treatment for subaxial cervical metastasis has been shown to be more effective than nonoperative treatment for relieving pain, and may also reverse neurologic deficits and improve ambulatory function.\(^{[16,17]}\) Operative treatment options in this region include the anterior approach, the posterior approach, or the combined anterior and posterior approach. Fehlings, *et al.* conducted a systematic review and recommended the anterior approach for most subaxial cervical spine metastases, and the posterior approaches for most craniovertebral metastases.\(^{[7]}\) Combined anterior and posterior approach is recommended in circumferential tumor involvement and poor bone quality.\(^{[7]}\) However, data on the perioperative complication profiles of these
three approaches is lacking. Therefore, the purpose of the current study was to compare the clinical results among these three standard approaches. This information may help to guide decision-making for surgical treatment of subaxial cervical spine metastases.

Previous studies reported low complication rates for the anterior surgical approach. Jonsson, et al. reported complications, such as dysphagia, reversible vocal cord paralysis, and a postoperative mortality rate of about 2%. Heidecke, at al. reported complications in 62 patients including reversible vocal cord paralysis (8%), early instrumentation failure (4.8%), thrombosis and embolism (4.8%), wound infection (3.2%), and neurological deterioration (6.5%). Oda, et al. reported results from 32 patients (25 for posterior fixation alone, and 7 for combined approach) and found an overall complications rate of 19% [Radiculopathy from screw malposition (3%), deep wound infection (3%), postoperative hematoma (3%), cerebrospinal leakage (3%), and one patient in combined group (14%) had displacement of an anterior strut and required revision surgery]. In the current study, the overall perioperative complication rate was slightly higher because more types of complications were included in our analysis. For the subgroup analysis, even though there was no difference in preoperative patient characteristics among groups, the perioperative complication rate was highest in the combined approach group (75%). This may be due to the fact that the combined approach is the most extensive surgical approach, and it has the longest operative time and the most blood loss.

There are three main types of pain that are experienced by patients with spinal metastasis. An expanding tumor can cause periosteal 'stretching', which leads to constant localized pain and compression of nerve roots, which in turn leads to radicular pain. Axial pain is associated with pathological vertebral body fractures that can cause spinal instability. Surgical treatment can reduce the tumor size and stabilize the vertebral column, which results in pain reduction. Previous studies reported decreased pain as measured by pain scale after surgical treatment. Cho, et al. analyzed the results of 46 patients treated with surgery for cervical spine metastasis and reported reduced pain in 37 of 44 patients (84.1%). They found that the mean visual analog scale (VAS) for pain decreased from a preoperative 7.86±1.05 points to a postoperative 4.48±2.09 points, which represents a decrease of 3.39±2.14 points (p=0.001). The only factor found to influence pain improvement was neural foramina invasion by preoperative MRI. Rao, et al. reported on a series of 11 patients who underwent surgical treatment for symptomatic cervical spinal metastasis (5 anterior approach, 4 posterior approach and 2 combined approach). All patients experienced reduced axial neck pain according to patient postoperative VAS scores taken at the 1-month follow-up after surgery. The current study found greater than 75% improvement in the VNS in all approaches, with the greatest improvement in pain observed in the combined approach group (87.5%). Due to extensive soft tissue dissection, the combined approach provides more decompression and stability compared to the two other approaches, so this may explain the greater decrease in pain in this group. Gallazzi, et al. reported a case series that treated thirty cervical spinal metastasis patients using posterior-only laminectomy and posterior stabilization. Their results showed a strong significant improvement in pain score (5.5±1.8 to 2.1±1.0, p<0.00001). After average follow up of 13.7±14.8 months,
fifteen (50%) patients died, 2 (6.9%) had surgical-site infection that required reoperation, and there were no mechanical failures reported.\[^{21}\]

Cho, \textit{et al.} reported neurological improvement in 75.7\% (28/37) preoperative neurological deficit patients.\[^{19}\] In the current study, neurological recovery was highest in the combined approach group (33.3\%), which may be explained by more adequate decompression. However, the high rate of neurological recovery in the combined group could have been confounded by preoperative neurological status. Most patients in the combined group were ASIA class D (75\%) compared to 55.6\% in the anterior group, and 42.9\% in the posterior group. The overall neurological recovery rate in our study was quite low when compared to the rate reported by Cho, \textit{et al.;} however, this difference between studies may be due to the fact that our follow-up period was shorter.

Regarding ambulatory status improvement, Denaro, \textit{et al.} reported improvement in 5 of 18 (27.8\%) nonambulatory patients (Frankel B/C) who later became ambulatory (Frankel D) after surgery.\[^{22}\] In the current study, 12 of 70 nonambulatory patients (17.1\%) became ambulatory with the highest rate of improvement in the combined group (33.3\%). This result may be related to the better neurological recovery rate observed in the combined group. Heidecke, \textit{at al.} reported survival after surgery of 58\% and 21\% at 1 year and 2 years, respectively, after surgery.\[^{2}\] Cho, \textit{et al.} found primary tumor growth rate, preoperative Tomita score, radiotherapy (RT), timing of RT, and postoperative adjuvant treatment to be related to longer survival.\[^{19}\] In the current study, despite the statistically similar preoperative Tomita score among the three approaches, the median survival time was longest in the combined group.

\textit{Limitations}

The primary limitation of this study is its retrospective design, which rendered it vulnerable to missing or incomplete data in some cases. Another notable limitation is that our relatively small study population was recruited from only two centers. This could limit the generalizability of our findings to other care setting, and the small sample size may have impeded our ability to statistically reveal all existing differences and associations among the 3 evaluated surgical approaches. Third and last, the relatively short follow-up time could have prevented us from uncovering advantages or disadvantages of one approach over the other that may emerge over time. A prospective multi-center study with a longer follow-up period is warranted to confirm the findings of this study, and to identify additional information that may enhance surgical approach-related decision-making in this patient population.

\textit{Conclusion}

The results of this study do not reveal any clear superiority among the three main surgical approaches used to treat subaxial cervical spine metastasis. Patients in the combined approach group had the highest rates of perioperative complications. However, although the differences were not statistically significant, patients in the combined group tended to have better clinical outcomes, including
neurological recovery and ambulatory improvement, after follow-up, and they also had the longest survival time.

**Abbreviations**

Charlson Comorbidity Index (CCI)

verbal numerical scale (VNS)

visual analog scale (VAS)

polymethyl methacrylate (PMMA)

**Declarations**

**Ethics approval and consent to participate**

This study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. 428/2558(EC2)). All methods were carried out in accordance with relevant guidelines and regulations. And all authors confirmed that informed consent was obtained from all subjects or, if subjects are under 18, from a parent and/or legal guardian.

**Consent for publication**

I, Sirichai Wilartratsami MD hereby declare that I participated in the study and in the development of the manuscript. I have read the final version and give my consent for the article to be published.

**Availability of data and materials**

The datasets generated during and/or analyzed during the current study are available from the corresponding author, Sirichai Wilartratsami MD, on reasonable request.

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This was an unfunded study.

**Conflict of interest declaration**

All authors declare no personal or professional conflicts of interest relating to any aspect of this study.

**Authors contribution**

PL, PR and TC conceived of the presented idea and developed the theoretical formalism, KC and PB planned and carried out the implementation. PL and BS wrote the manuscript in consultation with SW. All authors provide critical feedback and helped shape the research, analysis and manuscript.
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**Tables**

**Table 1.** Demographic and clinical characteristics of the total cohort, and compared among approach groups
| Characteristics                  | Total (N=70) | Anterior (n=44) | Posterior (n=14) | Combined (n=12) | p-value |
|--------------------------------|--------------|----------------|-----------------|----------------|---------|
| Males gender                   |              |                |                 |                |         |
|                                | 33 (47.1%)   | 19 (43.2%)     | 7 (50.0%)       | 7 (58.3%)      | 0.629   |
| Average age (years)            | 58.33±11.56  | 58.82±11.45    | 57.79±13.76     | 57.17±9.95     | 0.894   |
| Average duration of symptom (days) | 55.00±40.26 | 47.68±34.07   | 75.86±49.39     | 57.50±44.40    | 0.119   |
| Average Charlson Comorbidity Index | 8.93±1.77   | 8.91±1.55      | 9.07±2.20       | 8.83±2.23      | 0.868   |
| Average Revised Tokuhashi score | 6.44±2.79    | 6.52±2.44      | 6.71±3.63       | 5.38±3.07      | 0.696   |
| Average Tomita score           | 6.90±2.28    | 6.90±2.00      | 6.85±2.76       | 6.91±2.77      | 0.995   |
| Tumor type                     |              |                |                 |                |         |
| - Lung, osteosarcoma, stomach, bladder, esophagus, pancreas | 17 | 9 | 5 | 3 |
| - Liver, gallbladder, unidentified** | 30 | 24 | 2 | 4 |
| - Others                      | 5            | 3             | 0              | 2              |         |
| - Kidney, uterus              | 0            | 0             | 0              | 0              |         |
| - Rectum                      | 1            | 1             | 0              | 0              |         |
| - Thyroid, breast, prostate, carcinoid tumor | 17 | 7 | 7 | 3 |
| ASA class                     |              |                |                 |                | 0.825   |
| I                             | 3 (4.3%)     | 2 (4.5%)       | 0 (0.0%)        | 1 (8.3%)       |         |
| II                            | 18 (25.7%)   | 11 (25.0%)     | 4 (28.6%)       | 3 (25.0%)      |         |
| III                           | 36 (51.4%)   | 23 (52.3%)     | 6 (42.9%)       | 7 (58.3%)      |         |
| IV                            | 13 (18.6%)   | 8 (18.2%)      | 4 (28.6%)       | 1 (8.3%)       |         |
| V                             | 0            | 0             | 0              | 0              |         |
| Preoperative ASIA grade       |              |                |                 |                |         |
| A                             | 0 (0.0%)     | 0 (0.0%)       | 0 (0.0%)        | 0 (0.0%)       |         |
| B                             | 3 (4.3%)     | 2 (4.5%)       | 0 (0.0%)        | 1 (8.3%)       |         |
| C                             | 17 (24.3%)   | 11 (25.0%)     | 3 (21.4%)       | 3 (25.0%)      |         |
|   | A   | B   | C   | D   | E   |
|---|-----|-----|-----|-----|-----|
|   | 0 (0.0%) | 1 (1.4%) | 9 (12.8%) | 42 (60.0%) | 18 (25.7%) |
|   | 0 (0.0%) | 1 (2.3%) | 5 (11.4%) | 30 (68.2%) | 8 (18.2%) |
|   | 0 (0.0%) | 0 (0.0%) | 3 (21.4%) | 7 (50.0%) | 4 (28.6%) |
|   | 0 (0.0%) | 0 (0.0%) | 1 (8.3%) | 5 (41.7%) | 6 (50.0%) |

Data presented as number and percentage or mean ± standard deviation

A $p$-value < 0.05 indicates statistical significance

**Abbreviations:** ASA, American Society of Anesthesiologists; ASIA, American Spinal Injury Association

**Table 2.** Operative data and clinical outcomes compared among the anterior, posterior, and combined approach groups
### Data and outcomes

| Data and outcomes                          | Anterior (n=44) | Posterior (n=14) | Combined (n=12) | p-value |
|-------------------------------------------|-----------------|------------------|-----------------|---------|
| Number of decompression levels            |                 |                  |                 |         |
| 0                                         | 0 (0.0%)        | 2 (14.3%)        | 0 (0.0%)        | <0.001  |
| 1                                         | 32 (72.7%)      | 1 (7.1%)         | 2 (16.7%)       |         |
| 2                                         | 12 (27.3%)      | 2 (14.3%)        | 4 (33.3%)       |         |
| 3                                         | 0 (0.0%)        | 7 (50.0%)        | 4 (33.3%)       |         |
| 4                                         | 0 (0.0%)        | 2 (14.3%)        | 2 (16.7%)       |         |
| Average blood loss (ml)                   | 287.50±199.56   | 780.00±702.79    | 1,235.40±689.00 | <0.001  |
| Average operative time (minutes)          | 130.41±56.98    | 242.86±62.93     | 333.42±80.11    | <0.001  |

#### Postoperative outcomes

| Postoperative outcomes                          | Anterior | Posterior | Combined | p-value |
|------------------------------------------------|----------|-----------|----------|---------|
| Preoperative verbal pain score                 | 6.04±2.36| 4.28±2.97 | 5.75±1.54| 0.105   |
| Postoperative verbal pain score                | 3.43±1.53| 2.78±2.25 | 2.50±1.56| **0.008**|
| Change in verbal pain score                    |          |           |          | 0.06    |
| Increment                                      | 1 (2.3%) | 3 (21.4%) | 0 (0.0%) |         |
| No change                                      | 3 (6.8%) | 0 (0.0%)  | 1 (8.3%) |         |
| Decrement                                      | 40 (90.9%)| 11 (78.6%)| 11 (91.7%)|         |
| Postoperative ASIA grade                       |          |           |          |         |
| A                                              | 0 (0.0%) | 0 (0.0%)  | 0 (0.0%) |         |
| B                                              | 1 (2.3%) | 0 (0.0%)  | 0 (0.0%) |         |
| C                                              | 5 (11.4%)| 3 (21.4%) | 1 (8.3%) |         |
| D                                              | 30 (68.2%)| 7 (50.0%) | 5 (41.7%)|         |
| E                                              | 8 (18.2%)| 4 (28.6%) | 6 (50.0%)|         |
| Neurological recovery (ASIA improved >1 grade) | 10 (22.7%)| 4 (28.6%) | 4 (33.3%)| 0.73    |
| Ambulatory improvement (non-ambulate to ambulate) | 5 (11.4%)| 3 (21.4%) | 4 (33.3%)| 0.18    |
| Perioperative complications                    | 11 (25%) | 7 (50.0%) | 7 (58.3%)| **0.01**|
| Medical complications                          | 7 (15.9%)| 5 (35.7%) | 4 (33.3%)| 0.328   |
| Urinary tract infection                        | 4 (9.1%) | 2 (14.3%) | 2 (16.7%)|         |
| Condition                                               | Group 1 | Group 2 | Group 3 |
|---------------------------------------------------------|---------|---------|---------|
| Myocardial infarction                                   | 1 (2.3%)| 0 (0.0%)| 0 (0.0%)|
| Pneumonia                                               | 4 (9.1%)| 2 (14.3%)| 0 (0.0%)|
| Deep vein thrombosis / pulmonary embolism              | 0 (0.0%)| 0 (0.0%)| 1 (8.3%)|
| Electrolyte imbalance                                   | 1 (2.3%)| 0 (0.0%)| 1 (8.3%)|
| Surgical complication                                  | 6 (13.6%)| 2 (14.2%)| 4 (33.3%)| 0.177 |
| Wound infection                                          | 1 (2.3%)| 1 (7.1%)| 4 (33.3%)|
| Implant failure                                         | 3 (6.8%)| 1 (7.1%)| 0 (0.0%)|
| Reoperation                                              | 3 (6.8%)| 1 (7.1%)| 0 (0.0%)|
| Neurological deficit                                    | 2 (4.5%)| 0 (0.0%)| 0 (0.0%)|
| Dysphagia                                               | 1 (2.3%)| 0 (0.0%)| 0 (0.0%)|
| Average length of stay (days)                           | 19.7±13.7| 31.8±28.2| 26.2±12.7| <0.001 |
| Median survival (months)                                 | 6.03 | 6.76 | 27.93 | 0.08 |

Data presented as number and percentage, mean ± standard deviation, or median

A *p*-value<0.05 indicates statistical significance

**Abbreviation:** ASIA, American Spinal Injury Association