Original Article
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Does Preoperative Radiation Therapy Performed for Metastatic Spine Cancer at the Cervical Spine Increase Perioperative Complications of Anterior Cervical Surgery?

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Background: Radiation therapy (RT) performed before anterior cervical spine surgery (ACSS) may cause fascial plane fibrosis, decreased soft-tissue vascularity, and vertebral body weakness, which could increase the risk of esophageal and major vessel injuries, wound complications, and construct subsidence. Therefore, this study aimed to evaluate whether preoperative RT performed for metastatic spine cancer (MSC) at the cervical spine increases perioperative morbidity for ACSS.

Methods: Forty-nine patients who underwent ACSS for treatment of MSC at the cervical spine were retrospectively reviewed. All the patients underwent anterior cervical corpectomy via the anterior approach. Patient demographics, surgical factors, operative factors, and complications were recorded. Results of patients who were initially treated with RT before ACSS (RT group) were compared with those who did not receive RT before ACSS (non-RT group).

Results: Eighteen patients (36.7%) were included in the RT group, while the remaining 31 (63.3%) were included in the non-RT group. Surgery-related factors, including operation time (p = 0.109), estimated blood loss (p = 0.246), amount of postoperative drainage (p = 0.604), number of levels operated (p = 0.207), and number of patients who underwent combined posterior fusion (p = 0.768), did not significantly differ between the 2 groups. Complication rates, including esophageal injury, dural tear, infection, wound dehiscence, and mechanical failure, did not significantly differ between the RT and non-RT groups. Early subsidence was significantly greater in the non-RT group compared to that in the RT group (p = 0.012).

Conclusions: RT performed before surgery for MSC does not increase the risk of wound complication, mechanical failure, or vital structure injury during ACSS. The surgical procedural approach was not complicated by previous RT history. Therefore, surgeons can safely choose the anterior approach when the number of levels or location of MSC favors anterior surgery, and performing a posterior surgery is unnecessary due to a concern that previous RT may increase complication rates of ACSS.

Keywords: *Metastatic spine cancer, Cervical spine, Radiation therapy, Anterior cervical corpectomy and fusion, Complications*

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Metastatic spine cancer (MSC) causes severe pain, neurologic compromise, or spinal column instability and often requires local treatment, including surgery and radiation therapy (RT).[1-3] Although surgery could provide instant stability and effective cord decompression, it is accompanied by risk for patients prone to complications due to multiple comorbidities.[4] Therefore, RT is often chosen as an initial management for MSC because it does not cause surgical damage to patients.[2,3,5] However, when symptoms or instability progresses, despite previous RT, surgery is required again.[4]

It has been suggested that preoperative RT increases surgical complication risks.[6-8] RT reduces neovascularization and causes tissue fibrosis that could impede wound healing.[9] Furthermore, the vertebral body within the radiation field is weakened, which could occasionally result in a compression fracture.[7,10] Previous studies have demonstrated that preoperative RT is associated with increased wound dehiscence, infection, and risk of compression fracture after surgery.[6,7,9,10] However, these studies have mainly focused on the thoracolumbar spine, and studies regarding the association between anterior cervical spine surgery (ACSS) and complication risk due to preoperative RT are lacking.

There are theological specifics for ACSS that might affect complication risk due to preoperative RT.[11,12] First, surgery is performed on fascial layers passing between the esophagus and neurovascular structures.[11] Preoperative RT could cause fibrosis of the fascial plane, which could complicate a surgical approach.[8] Such a complicated surgical approach due to fibrosis might increase the risk of esophageal injury, hoarseness, or dysphagia postoperatively.[8,13,14] Second, corpectomy is usually performed using an anterior approach, which is prone to subsidence or mechanical failure.[15,16] Since RT weakens the vertebral body within a radiation field, thereby causing vertebral body fracture, the risk of subsidence could further increase when RT is performed before surgery.[7] Finally, dehiscence or infection might increase due to skin fibrosis and decreased vascularization (Fig. 1).[8,9] In contrast, since the cervical spine has a great blood supply, which promotes wound healing, an increased risk of wound complication due to preoperative RT demonstrated in the thoracolumbar spine may not apply to the cervical spine.[17]

Despite such specifics of ACSS, the association between preoperative RT and perioperative complication risk of ACSS remains unknown. Therefore, the present study evaluated whether preoperative RT performed for MSC at the cervical spine increases perioperative morbidity for ACSS.

METHODS

Study Design and Patient Characteristics

This retrospective cohort study was approved by the Institutional Review Board of Asan Medical Center (No. 2024-0038). Informed consent was waived due to the retrospective nature of the study. Fifty-seven patients who underwent ACSS owing to MSC of the cervical spine between March 2016 and December 2019 were retrospectively reviewed. Patients who were followed up for less than 3 months or had previous cervical spine surgery were excluded; this was because they might not address perioperative complications appropriately. Patients who underwent a combined cervical posterior approach were included in the study because the current study mainly focuses on perioperative complications of ACSS rather than clinical outcomes. Surgeries were performed by 4 surgeons (JWC, JWP, JHP, and SHP) in a single institute.

A decision to perform RT or surgery was discussed by a medical oncologist, spine surgeon, and radiation oncologist, with a consideration of patient life expectancy, performance, symptoms, future treatment plan, and instability of the spine.[5] For patients who were initially sched-

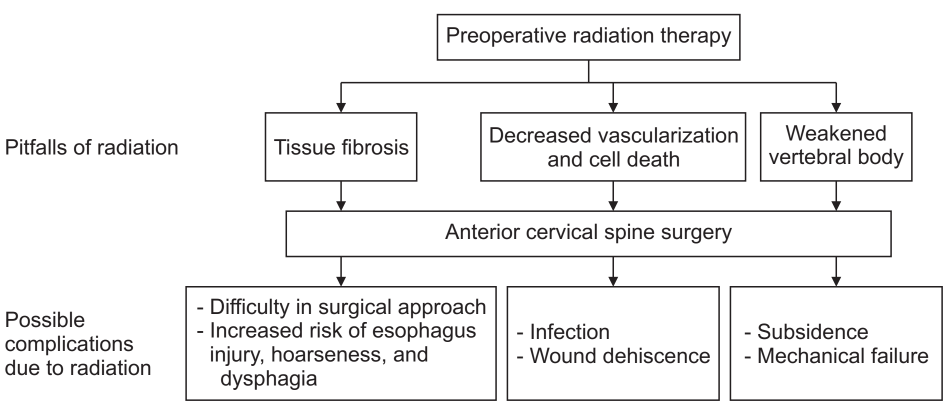

Fig. 1. Theologically possible increased complications due to radiation therapy before anterior cervical spine surgery.

uled to receive RT, the surgery option was considered when the patients' symptoms were aggravated or failed to improve. A decision for surgery after RT was again discussed during a multi-panel discussion. Patients who underwent RT before ACSS were included in an RT group, while those who did not undergo RT before surgery were classified as a non-RT group. Results were compared between the RT and non-RT groups.

Surgical Procedures

The standard Smith-Robinson approach was performed for index level. After placing the Casper self-retractors for visualization, discectomy and corpectomy were performed in a standard fashion. Decompression was performed until cord decompression was confirmed with direct visualization. After careful endplate preparation, a titanium mesh cage or fibular allograft was inserted for reconstruction. An anterior cervical plate was added for stability. Combined posterior fixation was performed when ≥ 2-level corpectomy was required.[15,18] Neck collar was worn for 3 months after the surgery.

Variables

Patient demographic factors, Bilsky grades, spine neoplastic instability score, number of levels operated, and preoperative and postoperative motor power assessment using the American Spinal Injury Association scale were recorded. Surgical factors, including operation time, estimated blood loss (EBL), and postoperative drainage, were assessed. For patients who had RT before surgery, radiation dosage per time, number of fractions, total dosage, and the time interval between RT and surgery were also recorded. Complications, including esophageal injury, dural tear, major vessel injury, dysphagia, hoarseness, infection, wound dehiscence, mechanical failure, and early mortality defined as death within a 6-month postoperative period, were assessed based on electronic medical records.

To assess early postoperative subsidence, total interbody height (TIH) determined by the distance between the midpoint of the uppermost vertebral upper endplate and the lowermost vertebral lower endplate in a lateral cervical spine radiograph in the neutral position was measured.[19,20] Early subsidence was defined as the difference between the TIH measured at an immediate postoperative period and 3 months postoperatively. Assessment of subsidence was performed only for patients who underwent one-level corpectomy and those who did not undergo combined posterior fixation.

Statistical Analysis

All continuous variables were tested for normality using the Shapiro-Wilk test. Continuous variables were analyzed using the Student *t*-test, while categorical variables were analyzed using the chi-square test. All data management and analyses were performed using IBM SPSS ver. 24.0 software (IBM Corp.), and $p < 0.05$ was considered significant.

RESULTS

Forty-nine patients met the inclusion criteria and were included in the study. Thirty-one patients did not receive RT preoperatively and were included in the non-RT group (age, 59.7 ± 18.1 years; 18 men [58.1%]). The remaining 18 patients underwent RT before surgery for the management of MSC and were included in the RT group (age, 59.7 ± 7.0 years; 13 men [72.2%]). The preoperative motor grade was significantly higher in the non-RT group preoperatively ($p = 0.004$), and the RT group had a significantly greater incidence of diabetes mellitus ($p = 0.010$). Otherwise, there were no significant differences in patient characteristics in the 2 groups (Table 1). Hepatocellular carcinoma was the most common primary origin of MSC in both the non-RT

Table 1. Patient Characteristics

Variable	Non-RT group (n = 31)	RT group (n = 18)	*p*-value
Age (yr)	59.7 ± 18.1	59.7 ± 7.0	0.993
Sex (male : female)	18 : 13	13 : 5	0.372
Body mass index (kg/m^2)	22.6 ± 3.7	21.9 ± 2.7	0.489
Hypertension	9 (29.0)	6 (33.3)	0.780
Diabetes mellitus	6 (19.4)	10 (55.6)	0.010*
Smoking	7 (22.6)	5 (27.8)	0.730
Bilsky grade	1.8 ± 1.0	1.8 ± 0.9	0.937
Pathologic fracture	27 (87.1)	10 (55.6)	0.125
SINS	10.8 ± 2.1	11.6 ± 3.2	0.348
Preoperative AIS motor grade	4.7 ± 0.4	4.2 ± 0.7	0.004*
Postoperative AIS motor grade	4.9 ± 0.4	4.7 ± 0.5	0.109
Postoperative RT	18 (58.1)	14 (77.8)	0.081
Survival period (mo)	19.6 ± 23.8	15.3 ± 10.0	0.651

Values are presented as mean ± standard deviation or number (%).
RT: radiation therapy, SINS: spine instability neoplastic score, AIS: American Spinal Injury Association impairment scale.
*$p < 0.05$.

Table 2. Primary Pathology of Metastatic Spine Cancer

Variable	Non-RT group	RT group	*p*-value
HCC	6 (19.4)	8 (44.4)	0.057
Breast	6 (19.4)	0	
Prostate	1 (3.2)	2 (11.1)	
Other gastric origin	1 (3.2)	1 (5.6)	
Hematologic	4 (12.9)	0	
Others	13 (41.9)	7 (38.9)	

Values are presented as number (%). Comparison was performed using a chi-square test.
RT: radiation therapy, HCC: hepatocellular carcinoma.

(6 patients, 19.4%) and RT (8 patients, 44.4%) groups. The distribution of the primary origin of MSC was not significantly different between the 2 groups (p = 0.057) (Table 2). Among 18 patients included in the RT group, 15 patients (83.3%) underwent surgery due to persistent or aggravating neck or arm pain, while the other 3 patients (16.7%) had surgery due to new onset neurological deficits. Three patients (16.7%) in the RT group demonstrated aggravation of pathologic compression fracture.

Surgery-related factors, including operation time (p = 0.109), EBL (p = 0.246), amount of postoperative drainage (p = 0.604), number of levels operated (p = 0.207), and number of patients who underwent combined posterior fusion (p = 0.768), did not significantly differ between

Table 3. Treatment-Related Factors

Variable	Non-RT group	RT group	*p*-value
Operative factor			
Operation time (min)	291.2 ± 165.7	225.6 ± 58.4	0.109
EBL (mL)	250.0 ± 198.7	183.3 ±141.4	0.246
Postoperative drainage (mL)	76.7 ± 48.6	66.33 ± 45.7	0.604
Number of levels operated	1.3 ± 0.6	1.1 ± 0.3	0.207
Combined posterior fusion	22 (71.0)	10 (55.6)	0.768
Radiation therapy factor			-
Dosage per time (Gy)	-	52.0 ± 35.7	
Number of fractions	-	8.9 ± 2.4	
Total dosage	-	425.1 ± 204.1	
Time interval from RT to surgery (mo)	-	2.6 ± 1.1	

Values are presented as mean ± standard deviation or number (%). All analyses were performed using Student *t*-test.
RT: radiation therapy, EBL: estimated blood loss.

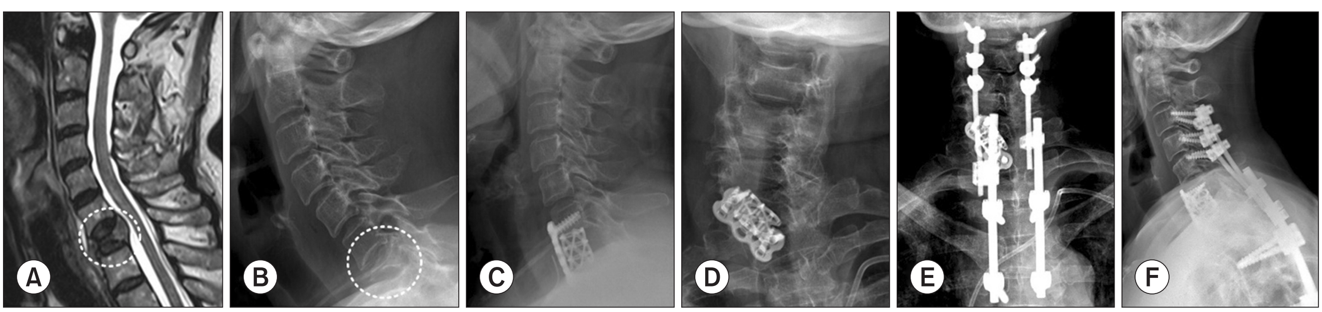

Fig. 2. Illustrative case 1. A 61-year-old woman with a previous history of breast cancer presented with intractable neck pain. The preoperative sagittal magnetic resonance imaging (A) and lateral radiograph (B) show a pathological fracture of the C7 vertebral body (dashed circles). (C) Anterior cervical corpectomy and fusion using a mesh cage and anterior cervical plate was performed. (D) However, the neck pain recurred 6 months after the surgery. Mechanical failure with cage dislodgement was observed in the radiograph. (E, F) Revision posterior fusion of C3–T5 was performed for reconstruction.

Table 4. Perioperative Complications

Variable	Non-RT group	RT group	*p*-value
Complication			
Esophageal injury	0	0	NA
Dural tear	0	1 (5.6)	0.340
Major vessel injury	0	0	NA
Dysphagia	11 (35.5)	4 (22.2)	0.539
Hoarseness	7 (22.6)	2 (11.1)	0.701
Infection	2 (6.4)	0	0.329
Wound dehiscence	0	0	NA
Mechanical failure	0	1 (5.6)	0.340
Early mortality	1 (3.2)	0	1.000
Subsidence			
Immediate postoperative TIH	55.0 ± 12.7	48.6 ± 10.6	0.213
Three months postoperative TIH	48.0 ± 14.3	46.8 ± 10.2	0.824
Subsidence	4.7 ± 3.1	1.8 ± 1.4	0.012*

Values are presented as number (%) or mean ± standard deviation. Complications were analyzed using the chi-square test, and TIH and subsidence were analyzed using the Student *t*-test.
RT: radiation therapy, TIH: total interbody height.
*$p < 0.05$.

the 2 groups. All the patients included in the RT group received conventional external beam RT. The total dosage of radiation performed was 425.1 ± 204.1 Gy. The interval between RT and surgery was 2.6 ± 1.1 months (Table 3).

One patient (5.6%) included in the RT group had a dural tear, which was managed conservatively using a lumbar drain and bed rest for 3 days. Two patients (6.4%) had an infection in the non-RT group, while there was no infection in the RT group. There were no patients with esophageal injury, major vessel injury, and wound dehiscence in both groups. The incidence of complications did not significantly differ between the 2 groups. In the non-RT group, mechanical failure of cage dislodgement occurred in 1 patient (5.6%) (Fig. 2), and there were no instrument-related complications in the RT group ($p = 0.340$) (Table 4). One patient (5.6%) in the RT group underwent surgery that was assisted by an ear, nose and throat (ENT) surgeon. However, this was preoperatively planned due to the extensiveness of the tumor, and not due to the complicated approach of an orthopedic or neurosurgeon (Fig. 3). Otherwise, there were no patient records of difficult surgical procedure.

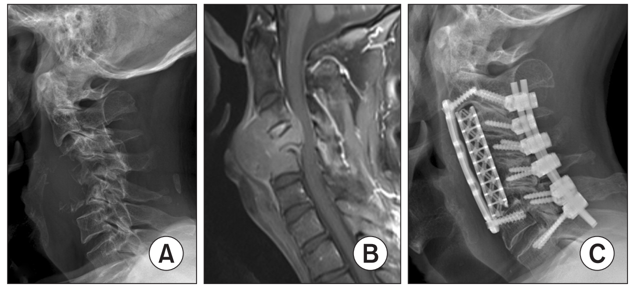

Fig. 3. Illustrative case 2. A 65-year-old man who was being followed up for hepatocellular carcinoma presented with severe neck pain. His neurological status was intact. (A) The preoperative lateral cervical spine radiograph demonstrated osteolysis of the C3–5 vertebral bodies with kyphotic deformity. (B) Sagittal T1 gadolinium-enhanced magnetic resonance imaging shows metastatic mass compressing the spinal cord and protruding anteriorly of the vertebral body. Due to the extensiveness of the metastatic mass, an ear, nose and throat (ENT) surgeon was consulted preoperatively for the surgical procedure. With the help of the ENT surgeon, the surgical procedure was performed without complication. (C) C3–5 corpectomy and C2–7 posterior fusion were performed. The patient experienced no neck pain without neurological complications for 3 years of follow-up.

The TIH measured immediately after the surgery ($p = 0.213$) and at 3 months postoperatively ($p = 0.824$) did not demonstrate significant intergroup differences between the RT and non-RT groups. However, early subsidence was significantly greater in the non-RT group compared to that in the RT group ($p = 0.012$) (Table 4).

DISCUSSION

Anterior and posterior approaches to the cervical spine have their own advantages and limitations; however, carefully selecting an appropriate surgical approach that considers the specifics of pathology is of great importance to achieving optimal outcomes.[5] Furthermore, since surgery for MSC is often extensive for patients who are prone to complications, the significance of selecting a surgical strategy should be further emphasized.[4] Moreover, if RT performed preoperatively as an initial treatment modality for MSC increases the complication rates of ACSS, surgeons should consider performing the posterior approach instead for patients who underwent preoperative RT. A posterior approach of the cervical spine is rather a simple procedure than an anterior approach, which requires fascial plane dissection between vital structures.[11] Previous studies have demonstrated that RT performed for head and neck cancers increases the risk of fibrosis, osteonecrosis, and infection of the radiation field, which could be applied equally for MSC of the cervical spine.[13] Therefore, the current study was conducted to elucidate whether preoperative RT performed for MSC increases the surgical complications of MSC and identify whether this would be a critical factor when deciding a surgical method.

Previous reports suggest that radiation-induced fibrosis could occur with RT.[8)] Radiation injury triggers excessive collagen production and remodels normal tissue. If radiation injury triggered fibrosis of the fascial plane utilized during the ACSS, a surgical approach would be difficult with an increased risk of vital structure injury, including the esophagus or major vessel injury.[8)] Furthermore, radiation is known to cause mucosal injury and muscle shortening, as well as atrophy, which might change the esophageal wall structure prone to injury.[8,13)] Difficulty in an approach owing to fibrosis might increase the incidence of hoarseness or dysphagia, which are related to recurrent laryngeal nerve injury and excessive soft-tissue traction. However, the current study showed that the surgical approach is not complicated by RT performed before surgery. Although 1 patient underwent the surgical approach with the help of an ENT surgeon (Fig. 3), this was due to the extensivity of MSC, and not by previous RT history or a complicated approach. The surgery time did not increase owing to previous RT history, and RT did not cause injuries to structures that are nearby and in the approach pathway. Furthermore, the incidence of dysphagia and hoarseness were similar between the 2 groups. Therefore, previous RT history does not seem to complicate surgical procedures of the standard Smith-Robinson approach.

The wound dehiscence or infection rate of MSC surgery has been reported to be higher (9.5%–42.0%) compared to surgeries for other degenerative causes.[6,9,21-23)] RT also has theological specifics that could increase the risk of surgical site infection and wound dehiscence.[8)] Radiation induces decreased vascularity and cell death in soft tissues, which raises concerns about wound healing.[8)] Previous studies have demonstrated conflicting results regarding the association between wound complication and RT.[9,22)] Schilling et al.[9)] reported that preoperative RT is a risk factor for wound-related complications after surgery in an MSC cohort. However, Vargas et al.[6)] suggested that the rate of wound complication did not significantly differ between the RT and non-RT cohorts. In the current study, wound dehiscence or infection did not occur in the RT group, and wound complication rates were not significantly different compared to those of the non-RT group. The wound complication rate of ACSS is reported to be significantly lower (0.2%–0.49%) compared to that of the thoracolumbar spine, which may apply equally for MSC surgery.[17)] Furthermore, studies reporting increased wound complication rates with preoperative RT for MSC were mostly reported before 2000, and the literature has had very few studies in nearly 20 years since 2001 that addressed the association between wound complication and preoperative RT for MSC.[6)] Modern surgical environments and RT techniques could have possibly decreased the wound complication rate for MSC.[6)]

RT weakens the vertebral body included in the radiation field, which could occasionally cause compression fracture.[7,10)] Jawad et al.[10)] reported that the compression fracture rate after stereotactic body RT for MSC was 3%, and solitary metastasis was a risk factor owing to a more aggressive treatment approach. Vargas et al.[7)] also suggested that the compression fracture rate after stereotactic body RT for MSC was 22.2% during a 5-year follow-up. The results of these studies raise concern for subsidence or mechanical failure following surgery for MSC after RT. Construction of corpectomy is inherently prone to subsidence compared to anterior cervical discectomy and fusion since it has a longer lever arm and fewer fixation points.[15,18,24)] However, the present study demonstrated that RT was not associated with an increased risk of subsidence or mechanical failure. There were no cases of mechanical failure in the RT group, and the amount of subsidence after 3 months of follow-up was significantly less in the RT group.

Type of RT and dosage are factors that could affect complication rates.[2,3,7)] It has been reported that the vertebral compression fracture rate is higher in the stereotactic body RT compared to that of an external beam RT.[7)] Increased dosage and hypofractionation also increase the likelihood of complications.[8)] However, the current study was unable to clarify the association between RT type/dosage and complications, since all the patients underwent conventional external beam radiation and the number of patients with complications was small. Further studies with larger cohorts should be conducted to clarify this manner.

The majority of patients in the RT group (15/18, 83.3%) underwent surgery after RT due to persistent neck pain or arm pain, and not many patients suffered from new onset neurological deficits (3/18, 16.7%). However, we cannot provide a success rate of initial RT to control pain due to MSC of the cervical spine since the current study was conducted with patients who had operations. Therefore, the current study has limited capacity to provide information regarding indications to perform RT or surgery at an initial stage. Further evaluation would be needed to clarify how the initial treatment modality (RT or surgery) could be selected for patients with MSC at the cervical spine.

The current study has a few limitations. First, the study was conducted with a limited sample size. Therefore, although the current study suggests that preoperative RT may not increase the complication rates of ACSS, the results should be further clarified with a larger cohort. Second, radiographic measurement of TIH was performed with only radiography and not with computed tomography or magnetic resonance imaging since we did not routinely obtain these images postoperatively. Certain errors of measurement could have occurred since the magnification of radiography may be different.[25] Third, as previously mentioned, the current study has limitations in identifying whether different radiation types or dosages could affect surgical complications. Fourth, patients who underwent a combined posterior approach were also included. Ideally, including patients who had anterior surgery only would be more appropriate. However, patients with a combined posterior approach were included due to the limited number of patients who underwent anterior only surgery, and the current study focused mainly on perioperative complications and not efficacy or radiographic findings of the operation. Finally, the study is not free from inherent bias, as it is a retrospective study.

In conclusion, RT performed before surgery for MSC does not increase the risk of wound complication, mechanical failure, or vital structure injury during ACSS. Procedure of the surgical approach was not complicated by a previous RT history. Therefore, surgeons can safely choose an anterior approach when the number of levels or MSC location favors anterior surgery, and there would be no need to perform a posterior surgery due to a concern that previous RT may increase the complication rates of ACSS. These results would need verification with a larger cohort.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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