Is Anterior Trans-Intervertebral Space Decompression Important in Treating Cervical Spondylosis with Severe Intervertebral Space Narrowing? A Retrospective Cohort Study

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Objective: To evaluate the clinical efficacy and practicality of anterior trans-intervertebral space decompression and fusion (ATIDF) by comparing radiological and clinical outcomes between ATIDF and traditional anterior cervical corpectomy and fusion (ACCF) in cervical spondylosis patients with severe disc space narrowing.

Methods: Seventy-one cervical spondylosis patients with severe disc space narrowing underwent anterior cervical spine surgery were included in this retrospective study. Thirty-seven patients underwent ATIDF and 34 patients underwent ACCF. The neck disability index (NDI), Japan Orthopaedic Association (JOA) score and the Hirabayashi improvement rate were used to evaluate patient neurological status. Cervical sagittal alignment (C2–C7 Cobb angle), surgical segment sagittal alignment (Cobb angle of surgical segment) and disc space height were also compared between the two groups.

Results: There were 39 males and 32 females; mean age was 63.72 ± 6.36 years (range, 39–81 years). Mean follow-up was 22.4 months (range, 6–45 months). All patients achieved an adequate neurological improvement. There were no significant differences in NDI, JOA scores and Hirabayashi improvement rate between the two groups. The change of C2–7 Cobb angle and surgical segment Cobb angle were both greater in the ATIDF group. The average intervertebral height ratio of the patients in the ATIDF group increased significantly after surgery (0.38 ± 0.17 before surgery to 1.13 ± 0.32 after surgery, \( P < 0.01 \)). The overall complication rate was lower in the ATIDF group than the ACCF group (35.14% and 44.12%). At 6 months follow-up, three patients in the ACCF group presented with subsidence of the titanium mesh cage.

Conclusion: ATIDF is an effective technique for treating cervical spondylosis with severe disc space narrowing; it can achieve adequate decompression and improve sagittal alignment while avoiding and reducing the implant-related complications inherent to traditional ACCF.

Key words: Anterior Trans-Intervertebral Space Decompression and Fusion; Cervical Spondylosis; Severe Disc Space Narrowing

Introduction

Anterior cervical discectomy and fusion (ACDF) is the gold standard for the treatment of cervical degenerative disease.\(^1\) It can directly address anterior compression of the spinal cord, improve sagittal alignment of the cervical spine, and effectively achieve bone graft fusion.\(^2\) Severe degenerative cervical spondylosis patients often have severe intervertebral disc space narrowing with adjacent vertebral...
osteoophyte formation and significant hyperplasia of the Luschka joints. The traditional ACDF procedure is often difficult to perform in patients with severe disc space narrowing, due to the limited visualization during surgery; insufficient spinal cord decompression may result. Anterior cervical corpectomy and fusion (ACCF) is an alternative approach that can provide improved range for removal of osteophytes and ossified disc; however, the incidence of complications is high. Lei et al. reported a technique to remove a focal ossification mass through a single-level discectomy which involves partial wedge-shaped excision of the inferior border of the cephalad and the superior border of the caudal vertebral body to enlarge the disc space, allowing decompression. However, the bony endplate is completely removed, which can increase the incidence of implant-related complications such as collapse of the cage or graft. Therefore, it is particularly important to find a surgical method that does not destroy the vertebral endplate and decompresses through the intervertebral space for the treatment of such patients.

Based on the above considerations, we attempted to use the anterior trans-intervertebral space decompression and fusion (ATIDF) to treat cervical spondylosis patients with severe disc space narrowing. ATIDF can avoid the resection of vertebral body, reduce the complications such as titanium mesh subsidence after ACCF, and reduce intraoperative bleeding. For multiple level patients, segmental distraction can improve cervical curvature. In addition, if there are posterior compressive factors such as the folds of the ligamentum flavum, indirect decompression can also be achieved after distraction of the intervertebral space. The purpose of this study was: (i) to introduce the new type of anterior cervical decompression surgery for the treatment of severe intervertebral space narrowing patients; and (ii) to investigate the clinical effectiveness and practicality of ATIDF by comparing radiological and clinical outcomes and complications between ATIDF and traditional ACCF in patients with cervical spondylosis and severe disc space narrowing.

Material and Methods

Patient Population
From January 2015 to September 2018, 71 cervical spondylosis patients with severe disc space narrowing underwent anterior cervical spine surgery in our department and were included in this study. There were 39 males and 32 females; mean age was 63.72 ± 6.36 years (range, 39–81 years). The inclusion criteria were as follows: (i) patients had typical symptoms, signs, and imaging findings of cervical spondylosis; (ii) patients had severe disc space narrowing of varying degree at various levels; and (iii) at least one efficiency and safety outcome measurement was available. Severe disc space narrowing was defined as surgical level disc space height <50% of the C2/3 intervertebral disc height.

The exclusion criteria included the following: (i) trauma; (ii) cervical spine malformation; (iii) ossification of the posterior longitudinal ligament; (iv) cervical spinal stenosis requiring a posterior approach; (v) infection, tumor and other related diseases; (vi) previous history of cervical spine surgery; and (vii) history of other neurological diseases such as motor neuron disease.

All surgical procedures in this study were performed by a spine surgical team in our department. Surgical decision making was based on clinical symptoms and sagittal and axial magnetic resonance imaging (MRI) studies of the cervical spine. Plain radiographs and MRI of the cervical spine were performed in all patients to clearly define the segments responsible for symptoms. Computed tomography (CT) with three-dimensional reconstruction was also performed preoperatively to evaluate the osteophytes adjacent to the disc space and hyperplasia of the Luschka joints. All study patients underwent anterior cervical spinal decompression and fusion. Thirty-seven patients underwent ATIDF (21 males, 16 females) and 34 patients underwent ACCF (19 males, 15 females).

Surgical Technique

ATIDF Group
Subsequent to anterior disc space osteophyte removal, distraction of the disc space was performed with a deep intervertebral space distractor to achieve uniform expansion from anterior to posterior; this is the most important step of the surgery. Kerrison rongeurs were used to carefully remove the osteophytes and hypertrophic Luschka joints at the posterior margin of the intervertebral space. If necessary, partial resection of the posterior margin of the upper and lower vertebral bodies and Luschka joints was also performed to completely decompress the nerve root exit zone into the foramen. The posterior longitudinal ligament was removed for a complete decompression. Then, a “flask-like” decompression zone was formed in the deep side of intervertebral space (Fig. 1). After adequate treatment of the bony endplate, a suitable intervertebral cage was implanted. Generally, a larger interbody cage was selected to replicate a disc height similar to the C2/3 level. After completing all responsible levels, an anterior cervical titanium plate of appropriate length was selected and fixed to the anterior cervical spine with screws. Postoperative infection prevention and aerosol inhalation were routinely performed and symptomatic support was provided for related complications. All patients were placed in halo immobilization followed by a Philadelphia collar for 6–8 weeks postoperatively.

ACCF Group
Preoperative preparation and surgical approach in the ACCF groups were the same as ATIDF. The anterior disc space osteophytes were removed, portions of the responsible vertebrae were resected, and a titanium mesh cage of appropriate size and length packed with morcellated bone from the vertebral resection was implanted. After the corpectomy was completed, an anterior cervical plate of appropriate length was selected for fixation and fixed to the anterior cervical spine with screws. All postoperative treatments and measures were the same as the ATIDF group.
Clinical Outcomes Evaluation

The Neck Disability Index (NDI)
NDI score was used to evaluate patient neurological function status perioperatively and postoperatively. The NDI self-report measure contains seven items related to activities of daily living, two items related to pain, and one item related to concentration (ability to read). Each item is scaled from 0 to 5, and the total score is expressed as a percentage, with higher scores representing greater levels of disability.

Visual Analogue Scale (VAS)
Postoperative neck and shoulder pain symptoms were recorded and evaluated using the VAS scores. VAS is a common subjective method to measure pain intensity. A score of 0 indicates no pain at all, while 10 indicates the unbearable severe pain.

Japanese Orthopaedic Association (JOA) Score and Hirabayashi Improvement Rate
JOA score was used to evaluate patient neurological status perioperatively and postoperatively. JOA score is a principal outcome measure used in the management of cervical spine disorders, and to assess functional status. The JOA score of the cervical spine includes upper limb motor function (4), lower limb motor function (4), sensory function (6), and bladder function (3), with a total score of 17. The myelopathy severity was defined as mild if the JOA score is larger than 13, as moderate if the JOA score ranges from 9 to 13 and as severe if the JOA score is less than 9. The Hirabayashi improvement rate was also calculated: \( \text{Hirabayashi improvement rate} = \frac{\text{postoperative JOA score} - \text{preoperative JOA score}}{17 - \text{preoperative JOA score}} \times 100\% \).

Blood loss, operation time, and postoperative complications were also recorded. Radiographic fusion was defined as lack of motion across the fusion site on flexion-extension plain radiographs or CT and the presence of bridging bony trabeculae between the endplate and the graft. If the fusion was questionable, sagittal reconstruction of CT imaging was performed.

Radiological Evaluation
Imaging-related indices included cervical sagittal alignment (C2–C7 Cobb angle), surgical segment sagittal alignment (Cobb angle of surgical segment), and disc space height. The disc space measurement method is shown in Fig. 2. Five lines measuring distance between the upper and lower endplates of the disc space were selected, added, then divided by 5; in other words, the intervertebral space height = \( \frac{a + b + c + d + e}{5} \). To eliminate measurement errors caused by magnification differences between radiographs, we used average intervertebral height ratio to evaluate disc space height. The average intervertebral height ratio = measured disc space height/C2/3 disc space height. Sagittal alignment was measured in the neutral and maximal flexion and extension positions. Cervical MRI and CT with three-dimensional reconstruction were used to evaluate spinal cord decompression and implant-related complications, respectively (Fig. 3).

Statistical Analysis
Statistical analysis was performed using SPSS software, version 22.0 (SPSS, Inc., Chicago, IL, USA). Continuous variables are presented as mean values with standard deviation; categorical variables are presented as frequencies and percentages. Preoperative, postoperative, and last follow-up data were compared using the paired t test. Categorical variables between the two groups were compared using the chi-square or Fisher exact test, as appropriate. \( P < 0.05 \) was considered significant.
Results

Patient Characteristics
The patient demographics and clinical data in two groups were demonstrated in Table 1. Mean follow-up was 22.4 months (range, 6–45). There was no significant difference between groups with respect to age, sex, duration of symptoms, and follow-up duration. The average operation time was 97.8 ± 17.3 min in the ATIDF group and 115.3 ± 19.1 min in the ACCF group; the difference was not significant. The average blood loss volume was significantly higher in the ACCF group (65.1 ± 15.3 ml vs. 43.5 ± 11.6 ml; P < 0.01).

Neurological Outcomes
All patients experienced good neurological improvement (Table 2). There was no significant difference in preoperative or postoperative NDI and JOA scores between the two groups. Both groups demonstrated significant improvement in NDI and JOA scores after surgery (P < 0.001). The Hirabayashi improvement rate in the ATIDF and ACCF groups was 64.3% ± 10.4% and 58.8% ± 11.9%, respectively. There was no significant difference in postoperative JOA score or its recovery rate between the groups in any pairwise comparison.

Radiographic Results
Cervical spine sagittal alignment parameters significantly improved in both groups after surgery. In the ATIDF group, the C2–C7 Cobb angle increased from 8.43° ± 5.82° before surgery to 19.14° ± 7.95° at last follow-up (P < 0.01). In the ACCF group, the C2–C7 Cobb angle increased from 7.95° ± 6.03° before surgery to 15.34° ± 8.33° at last follow-up (P < 0.01). The postoperative C2–C7 Cobb angle and its change were both greater in the ATIDF group (Table 3). The average intervertebral height ratio of the patients in the ATIDF group was 64.3% ± 10.4% and 58.8% ± 11.9%, respectively. There was no significant difference in postoperative JOA score or its recovery rate between the groups in any pairwise comparison.

| TABLE 1 Demographics and clinical data |
|----------------------------------------|
| ATIDF | ACCF | t/χ² | P    |
|-------|------|------|------|
| Number of patients | 37    | 34    | 0.65 | 0.63 |
| Age (years) | 62.85 ± 7.04 | 65.12 ± 6.48 | 0.93 | 0.34 |
| Sex        |       |       | 0.10 | 0.75 |
| Male       | 21    | 18    |      |      |
| Female     | 16    | 16    |      |      |
| Duration of symptoms (years) | 2.4 ± 0.8 | 2.0 ± 1.2 | 4.83 | 0.21 |
| Follow-up time (months) | 23.8 ± 6.8 | 21.4 ± 7.4 | 3.97 | 0.48 |
| Surgical segment |       |       |      |      |
| One segment | 13    | 0     |      |      |
| Two segments | 15    | 21    |      |      |
| Three segments | 8     | 13    |      |      |
| Four segments | 1     | 0     |      |      |
| Operation time (min) | 97.8 ± 17.3 | 115.3 ± 19.1 | 5.42 | 0.01 |
| Blood loss (ml) | 43.5 ± 11.6 | 65.1 ± 15.3 | 6.36 | 0.01 |

Abbreviations: ACCF, anterior cervical corpectomy and fusion; ATIDF, anterior trans-intervertebral space decompression and fusion.

| TABLE 2 Comparison of neurological outcomes in two groups |
|-----------------------------------------------------------|
| ATIDF | ACCF | t/χ² | P    |
|-------|------|------|------|
| NDI scores |       |       |      |      |
| Preoperative | 55.4 ± 9.5 | 50.9 ± 10.2 | 0.77 | 0.61 |
| Last follow-up | 30.3 ± 8.2 | 32.8 ± 9.4 | 0.92 | 0.54 |
| t        | 5.42  | 6.03  |      |      |
| p        | <0.01 | <0.01 |      |      |
| JOA scores |       |       |      |      |
| Preoperative | 9.5 ± 8.2 | 8.7 ± 7.5 | 0.83 | 0.48 |
| Last follow-up | 12.8 ± 9.0 | 12.5 ± 8.1 | 0.91 | 0.74 |
| t        | 5.83  | 7.18  |      |      |
| p        | <0.01 | <0.01 |      |      |
| Hirabayashi improvement rate | 64.3% ± 10.4% | 58.8% ± 11.9% | 0.82 | 0.77 |

Abbreviations: ACCF, anterior cervical corpectomy and fusion; ATIDF, anterior trans-intervertebral space decompression and fusion; JOA: Japanese Orthopedic Association scores; NDI, the neck disability index.
performed a retrospective study of
Although the ATIDF procedure requires distraction
signics and local physical therapy, the symptoms were alleviated.
Conservative treatment with oral anti-in
/C6
cenerative neck and shoulder pain was 3.8
/pain; the ATIDF group showed a slightly higher incidence
patients complained of postoperative neck and shoulder
in the ATIDF and ACCF groups was 35.14% and 44.12%,
6 months. In the ACCF group, 8.82% (three of 34) of the
ACCF group presented with subsidence of the titanium mesh
ed dysphagia. All patients
seven patients in the ATIDF group and six in the ACCF
compared with the traditional ACCF method for the treatment
of patients with severe intervertebral space narrowing,
ATIDF can achieve effective decompression through the
intervertebral space, and at the same time, it can improve
the sagittal parameters of the cervical spine.

**Discussion**

Advantages of ATIDF
For patients who cannot tolerate ACCF due to various conditions, trans-intervertebral space decompression techniques are needed. ATIDF uses the anterior cervical approach through the disc space to perform decompression and expansion followed by implantation of a relatively large interbody cage to complete the anterior reconstruction. The key point of the ATIDF procedure is expansion of the disc space before decompression, which increases the field of view, allowing a more thorough decompression with minimal disturbance of the spinal cord and nerve roots. Compared with the traditional ACCF method for the treatment of patients with severe intervertebral space narrowing, ATIDF can achieve effective decompression through the intervertebral space, and at the same time, it can improve the sagittal parameters of the cervical spine.

**Comparison of Clinical Outcomes between ATIDF and ACCF**
Both ATIDF and ACCF can achieve satisfactory neurological improvement. Oh et al. performed a retrospective study of 31 patients with cervical spondylotic myelopathy who underwent single-level ACCF or 2-level ACDF and showed that neurological outcome did not differ between the groups; however, ACCF was associated with significantly longer operative time and greater blood loss. The results of numerous meta-analyses also suggest that ACDF and ACCF have equivalent or similar clinical outcomes but ACDF has less blood loss, shorter operation time, and shorter hospital stay. Although the ATIDF procedure requires distraction and expansion of the disc space and the steps of the operation are more complicated than traditional ACDF, our

group increased significantly from 0.38 ± 0.17 before surgery to 1.13 ± 0.32 after surgery (P < 0.01).

**Complications**
The incidence of complications during the follow-up period in the ATIDF and ACCF groups was 35.14% and 44.12%, respectively. The overall complication rate was lower in the ATIDF group than the ACCF group (Table 4). After surgery, seven patients in the ATIDF group and six in the ACCF group complained dysphagia. All patients’ symptoms improved significantly within 2 weeks with conservative treatment. At 6 months follow-up, three patients in the ACCF group presented with subsidence of the titanium mesh cage; no patient in the ATIDF group experienced this at 6 months. In the ACCF group, 8.82% (three of 34) of the patients complained of postoperative neck and shoulder pain; the ATIDF group showed a slightly higher incidence (13.51%, five of 37), however the difference was not significant (P = 0.53). The VAS score of the patients with postoperative neck and shoulder pain was 3.8 ± 1.7. After conservative treatment with oral anti-inflammatory analgesics and local physical therapy, the symptoms were alleviated. No significant complications such as neck pain were observed at the last follow-up. One patient experienced C5 nerve root palsy in each group and two patients in the ACCF group experienced cerebrospinal fluid leakage. No hardware failure occurred in either group.

| TABLE 3 Comparison of radiographic outcomes in two groups |
|----------------------------------------------------------|
| ATIDF | ACCF | t | P |
| C2-C7 Cobb angle | 8.43° ± 5.82° | 7.95° ± 6.03° | 1.05 | 0.55 |
| Prophylactic | | | | |
| Last follow-up | | | | |
| Alignment change | 10.71° ± 6.31° | 7.39° ± 8.68° | 9.35 | 0.01 |
| Cobb angle of the surgical segment | | | | |
| Preoperative | 3.51° ± 4.04° | 3.97° ± 4.88° | 1.25 | 0.63 |
| Last follow-up | 9.75° ± 6.12° | 6.50° ± 5.93° | 4.84 | 0.04 |
| Alignment change | 6.24° ± 6.01° | 2.53° ± 3.14° | 8.97 | 0.01 |
| Average intervertebral height ratio | | | | |
| Preoperative | 0.38 ± 0.17 | | | |
| Last follow-up | 1.13 ± 0.32 | | | |

Abbreviations: ACCF, anterior cervical corpectomy and fusion; ATIDF, anterior trans-intervertebral space decompression and fusion.

| TABLE 4 Comparison of complications in two groups |
|------------------------------------------------|
| ATIDF (n = 37) | ACCF (n = 34) |
| Dysphagia | 7 (18.92%) | 6 (17.65%) |
| C5 palsy | 1 (2.70%) | 1 (2.94%) |
| Axial symptom | 5 (13.51%) | 3 (8.82%) |
| Cerebral fluid leakage | 0 | 2 (5.88%) |
| Subsidence | 0 | 3 (8.82%) |
| Hardware breakage | 0 | 0 |
| Total | 13 (35.13%) | 15 (44.12%) |

Abbreviations: ACCF, anterior cervical corpectomy and fusion; ATIDF, anterior trans-intervertebral space decompression and fusion.
results were similar to previously published studies: we found significant differences in postoperative JOA score and its recovery rate between the ACCF and ATIDF groups in any pairwise comparison. In addition, the ATIDF group had lower intraoperative blood loss and shorter operation time.

Comparison of Sagittal Alignment between ATIDF and ACCF
A major advantage of anterior cervical surgery is that it can effectively improve the sagittal alignment parameters of the cervical spine. A few studies have reported improvement in
cervical alignment following anterior cervical decompression surgery.\textsuperscript{13,14} ACDF appears to have an advantage over ACCF in improving cervical sagittal alignment. ACDF has been shown to result in greater improvement of cervical lordosis and segmental height.\textsuperscript{15} In addition, Zhang et al.\textsuperscript{16} found that the effect of ACDF on sagittal balance was better. Lin et al.\textsuperscript{17} also observed significant differences in radiographic parameters between ACDF and ACCF in terms of postoperative global lordotic angle. In our study, the postoperative C2–C7 Cobb angle and its change were greater in the ATIDF group than the ACCF group. This may indicate that ATIDF provided a more warranted distraction and more remarkable change in cervical alignment than ACCF. In addition, ATIDF can restore alignment by pulling the fixed vertebral bodies toward the lordotic ventral plate, while the titanium mesh cage may straighten the cervical spinal column.

**Comparison of Complications between ATIDF and ACCF**

The high incidence of complications after ACCF is another factor that needs to be taken into consideration. Puvanesarajah et al.\textsuperscript{18} found that patients treated with ACCF were more likely to need revision surgery than those treated with ACDF. Similar results were seen in a previous study by our team that demonstrated a higher rate of complications in patients who underwent long corpectomy compared to those who underwent ACDF.\textsuperscript{19} In this study, the overall complication rate in the ATIDF group was lower than the ACCF group. In particular, ATIDF appears to avoid ACCF-associated complications such as internal implant collapse. No subsidence of the titanium mesh cage was observed in the ATIDF group, which may be related to preservation of the vertebral endplates.

**Postoperative Axial Symptoms of Patients Underwent ATIDF**

Axial symptoms, such as neck pain, neck stiffness, and shoulder pain, are very common after cervical spine surgery and can seriously affect patient quality of life, particularly after laminoplasty and laminotomy.\textsuperscript{20} The reported incidence of axial symptoms after posterior cervical spine surgery is as high as 60%–80%.\textsuperscript{21} Kawakami et al.\textsuperscript{22} indicated that the incidence of axial symptoms in patients following ACDF is as high as 38.3%. It appears that disc space distraction resulting from surgery may lead to postoperative cervical axial symptoms. Bai et al.\textsuperscript{23} found that the incidence of cervical axial symptoms increased when the disc space height change after ACDF increased by >10%. Distraction of the disc space is an important component of the ATIDF procedure that serves to increase visualization for decompression and restore disc space height. Therefore, we also evaluated the extent of intervertebral space distraction resulting from the ATIDF procedure and incidence of postoperative axial symptoms; 26.5% of patients in the ATIDF group experienced postoperative axial symptoms, which was slightly higher than the ACCF group (13.5%) and similar to previous reports. We speculate that the reasons were as follows: during the process of disc space distraction, the deep intervertebral space distractor was used to evenly distract the intervertebral space without increasing pressure on the posterior facet joints; this may prevent or reduce postoperative facet joint-related neck pain. In addition, before cage implantation, the Caspar distractor was relaxed to prevent over-distra tion. Finally, the size of the implanted cage was determined by the C2/3 disc space height. In our study, the average intervertebral height ratio of the surgical level in the patients of the ATIDF group only increased to approximately 113% of the C2/3 disc space height, indicating that the normal height of the intervertebral space was restored with minimal overdistraction.

**ATIDF for Osteoporosis Patients**

Another concern is patients with osteoporosis. The degree of disc degeneration in patients with cervical spondylosis is directly proportional to age.\textsuperscript{24} Patients with severe disc space narrowing are generally older and have more severe disc degeneration. Similar results were also found in our study. The average patient age was 63.72 ± 6.36 years and 53.5% were older than 60 years at the time of surgery. In elderly patients undergoing ACCF surgery, complications such as titanium mesh cage subsidence are more likely. Ji et al.\textsuperscript{25} found a 42.5% incidence of postoperative subsidence in a retrospective review of 73 consecutive patients who underwent single-level ACCF. Therefore, when performing ATIDF, a gentle touch is required during the alternating process of disc space distraction to avoid causing an endplate fracture. In this study, no endplate fracture occurred in the ATIDF group, probably because we preserved the bony endplate as much as possible; only a small part of the bony endplate was removed. For patients with severe osteoporosis, ATIDF should be avoided. When the disc space is adequately opened, distraction should stop; maximum distraction should not be pursued.

**Strength and Limitations**

This study is limited by its relatively small sample size and short follow-up period. Future multicenter randomized prospective studies with a large number of patients and longer follow-up duration should be performed to confirm our results.

**Conclusions**

In conclusion, ATIDF is an effective technique for treating cervical spondylosis with severe disc space narrowing; transvertebral space decompression can achieve adequate decompression and improve sagittal alignment while avoiding and reducing the implant-related complications inherent to traditional ACCF.

**Author Contributions**

QW, SXL and YW conceived and designed the study. WHQ and SBF contributed to the data collection. CP,
TY and WXD analyzed the data. SBF and LY helped to draft the manuscript. LY and CY carried out the image review. All authors read and approved the final manuscript.

Conflict Of Interest

All authors declared that there are no competing interests.

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Ethics Statement

This retrospective study was approved by the institutional review board of the Naval Medical University, Shanghai, China (IRB number: 130710022105).