Clinical Efficacy of Three Surgical Approaches for the Treatment of Cervicothoracic Tuberculosis: A Multicenter Retrospective Study

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Objective: To evaluate the efficacy of three surgical approaches for the treatment of cervicothoracic tuberculosis.

Methods: This is a multicenter retrospective study. We analyzed 74 patients with cervicothoracic tuberculosis who were treated in six institutions between January 2000 and January 2015. There were 37 male and 37 female patients, with an average age of 24 years (range, 5–62 years). The operative method was selected according to the indications. A total of 33 patients underwent one-stage anterior surgery (group A); 16 underwent a combined anterior and posterior surgery (group B) and 25 underwent one-stage posterior surgery (group C). Clinical outcomes, laboratory indexes, and radiological results were analyzed.

Results: All cases were followed up for approximately 36–96 months post-surgery (average, 39 months). At the last follow-up, patients in all three groups had achieved bone fusion, with pain relief and neurological recovery. No major vessel and nerve injuries were found during the operation. There were significant differences before and after treatment for visual analogue scale (VAS), neck disability index (NDI), and Japanese Orthopedic Association (JOA) score (P < 0.001). Three surgical strategies significantly improved kyphosis (P < 0.001).

Conclusion: The choice of operation for cervicothoracic tuberculosis should be selected based on the pathological changes, scope, and general physical condition of the patient. The indication for a posterior approach is narrow and it should be used selectively. The combined anterior and posterior approach involved a longer operating time, larger blood loss, and greater trauma, and also required a higher level of surgical skill. Therefore, the indications for this approach should be strictly controlled. Anterior approach surgery for the treatment of cervicothoracic tuberculosis showed excellent efficacy and fewer complications.

Key words: Anterior approach; Cervicothoracic; Combined approach; Posterior approach; Spinal tuberculosis

Introduction

The term cervicothoracic usually refers to the C6–T3 spinal segment. Because of the deep location and the complicated anatomy, it is difficult for surgeons to expose lesions in this region. At the same time, the diameter of the thoracic spinal cord is small, the buffer space is restricted, and the spinal cord is close to the anterior surface of the body, so compression from the front may cause severe spinal cord injury. In addition, blood supply to the upper thoracic cord is poor, and the circulation can be greatly affected in the advent of compression. Therefore, the disability rate is high, making surgical treatment an important therapy. Even so, there is still no consensus on the correct approach to treatment.

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In recent years, with the development of cervicothoracic anatomy and spinal instrumentation, operations for cervicothoracic tuberculosis have become more diverse, including anterior approach, posterior approach, and combined anterior and posterior approach surgery. The anterior technique includes the classic lower cervical, the trans-sternal, the subcapsular anterolateral, and the median sternotomy approaches. To clarify the indications and treatment effects of different surgical methods, we retrospectively analyzed 74 cases treated in six hospitals from 2000 to 2015. By observing clinical manifestations, and laboratory and radiographic results, we evaluated the clinical effect and complications of the different surgical techniques. This analysis was designed to improve the level of diagnosis and treatment for cervicothoracic tuberculosis, and to provide a reference for decision-making regarding treatment.

Methods

General Information
This is a multicenter retrospective research. Between January 2000 and January 2015, 91 consecutive patients with cervicothoracic tuberculosis were hospitalized in six hospitals; 17 were excluded because of conservative therapy, complicated spinal tumor, active pulmonary tuberculosis, and poor tolerance or compliance. The remaining 74 patients were included in the study, and were all confirmed to have spinal tuberculosis by bacterial culture and/or histopathology or gene chip. All underwent surgical treatment, with decisions regarding surgical approach and instrumentation selection being made by individual surgeons. The selection of the surgical approach was related to the degree of vertebral destruction, position, abscess size, and the characteristics of kyphosis. Clinical outcomes, laboratory indexes, and radiological results of patients with different surgical methods were analyzed. None of the patients in our study were HIV positive. There were 37 men and 37 women, with an mean age of 24 years (range, 5–62). Thirty-three patients underwent anterior surgery (group A), 16 patients underwent combined anterior and posterior surgery (group B), and 25 patients underwent posterior surgery (group C). According to the American Spinal Injury Association (ASIA) classification, 22 cases showed neurological deficit: in group A, 4 patients were grade A, and 5 cases were grade D; in group B, 6 cases were grade D; and in group C, 1 case was grade C, and 6 cases were grade D.

Preoperative Procedure
For at least 2 weeks before surgery, all patients underwent chemotherapy HREZ: H, 6 mg/kg isoniazid, maximum 300 mg/day; R, 15 mg/kg rifampicin, maximum, 600 mg/day; E, 25 mg/kg ethambutol, maximum 750 mg/day; and Z, 25 mg/kg pyrazinamide, maximum 750mg/day. Patients were simultaneously given liver protection treatment and nutrition support, and hepatic and renal functions were assessed, along with electrolytes. In general, preoperative blood sedimentation was <40 mm/1 h, while hemoglobin (Hb) was >100 g/L.

Surgical Procedure
The operations at each center were performed by the same surgical team. All patients had anesthetic administered via tracheal intubation, and an appropriate position was used according to the surgical approach.

One-Stage Anterior Surgery
Surgical indications mainly included: the damaged portion of the vertebra located in the anterior and middle columns of the spine; the abscess or sequestrum invading the spinal canal and causing spinal cord compression; kyphosis deformity; laminectomy had been performed and posterior bone graft fusion was not able to be performed; and the number of damaged vertebrae was <3. For one-stage anterior surgery an improved anterior approach was performed with the patient in a supine position. We utilized an anterolateral oblique skin incision along the anterior border of the sternocleidomastoid, extending to the sternal notch and continuing along the anterior aspect of the sternum distal to the manubriosternal junction. After incising the sternohyoid superficially, the sternothyroid muscles were dissected to access the sternal notch. The surgeon then used blunt finger dissection of the retrobaryngeal space to expose the prevertebral fascia and continued this process retrosternally. The abscess wall was then cut and the pus drained, with complete debridement. Correction of kyphosis was then performed to restore the height of the intervertebral space. Appropriately sized cortical autologous iliac bones, allograft or titanium meshes were placed in the space, followed by installation of an anterior titanium plate with screws. Finally, anti-tuberculosis (TB) drugs were administered locally, and the incision was closed (Fig. 1).

Combined Anterior and Posterior Surgery
Surgical indications mainly included: severely damaged or collapsed vertebral bodies, with ≥3 vertebral bodies involved; unstable spine after debridement; the abscess or sequestrum invading the spinal canal and causing spinal cord compression; severe kyphosis deformity that would be hard to correct using the anterior or posterior approach, accompanied by a massive paravertebral abscess, psoas abscess, or migrating abscess; skipped multi-segmental spinal TB; and severe spinal instability. The surgery was performed with the patient in a prone position. With a median incision, the lamina and articular process was exposed, with pedicle screw implantation; two titanium rods were pre-bent to a lordosis angle and then placed to facilitate vertebral body anterior column height recovery and kyphosis correction. After interspinous or posterolateral bone grafts, the incision was closed. Then, the patient was placed in a supine position, and the classic lower cervical vertebra approach was performed (Fig. 2).
One-Stage Posterior Surgery
Surgical indications mainly included: lesions confined to <3 adjacent segments, or if multiple segments were involved, only 1–2 vertebra needed to be addressed surgically; there was normal bone as a tunnel for internal fixation; patients had experienced anterior surgery and the structure was not clear; complete debridement could be performed through the posterior-only approach; and long segment bone was not needed to restore the anterior and middle column heights after debridement. The surgery is performed on a patient in a prone position, and a linear midline skin incision of the back was made. The posterior spinal elements, including lamina, facet joints, and transverse processes were exposed. Transpedicular screws were implanted. Then, the articular processes were partially removed to expose the intervertebral space. The necrotic bone, granulation tissue, caseous necrosis, and paravertebral abscesses were completely debrided. A suitable iliac bone (autograft or allograft) or titanium mesh was transplanted based on the bone defect size. Rods were then tightened and the kyphosis corrected with the help of the compression and stretch of the internal fixation instrument (Fig. 3).

Postoperative Care
A drainage tube was placed in all patients, and was removed 2 to 3 days later. A postoperative routine was instigated for 3 days to prevent infection and dehydration, and patients also received neurotrophic treatment. All patients received anti-TB chemotherapy with HRZE for at least 18 months. If drug sensitivity results indicated resistant tuberculosis, the chemotherapy regimen was adjusted according to the drug sensitivity test.

Evaluation Index
All patients were followed-up 1, 3, 6, 9, 12, and 18 months after their operation, and then once a year thereafter. The clinical and radiologic evidence of successful bone fusion was defined as an absence of local pain and tenderness over the site of fusion, normal motion, no correction loss or instrumentation failure, and the presence of trabecular bone bridging the grafts and the vertebrae.
Radiologic Outcome Evaluation

X-ray Examination
Static and extension–flexion radiographs of the lumbar spine were performed for all the patients at each interval.

CT Scan
CT scan and reformatted coronal and sagittal images were obtained at 12 and 18-month follow-up.

Clinical Outcome Evaluation
Clinical symptoms, signs, and nerve function improvements were observed. In addition, the erythrocyte sedimentation rate (ESR), and liver and kidney functions were monitored.

Spinal Cord Function
The Japanese Orthopedic Association (JOA) score was used to assess spinal cord function. The JOA score scale (range from 0 to 29) was as follows: less than 10 = bad; 10–15 = medium; 16–24 = good; 25–29 = excellent. The lower the JOA score, the more severe the dysfunction.

Pain
The visual analog scale (VAS) was used to evaluate the degree of pain. The VAS score scale (range from 0 to 10) was as follows: 0 = no pain; less than 3 = the patient can tolerate mild pain; 4–6 = patients have pain, but can sleep, pain can be tolerated; 7–10 = severe pain, unbearable pain.

Dysfunction Improvement
The clinical remission was assessed using the neck disability index (NDI). The scale includes pain level, personal care, pickup, reading, headache, concentration, work, driving, sleep, and entertainment, a total of 10 aspects. NDI (%) = (total score of each project/number of projects completed by subjects × 5) × 100%: 0%–20% = mild dysfunction; 20%–40% = moderate dysfunction; 40%–60% = severe functional impairment; 60%–80% = very severe functional impairment; and 80%–100% = complete dysfunction.

Neurological Status
The ASIA impairment scale was used to assess the level of spinal cord injury. Damage grade: A = complete injury, no sensory or motor function was retained in the sacral segment (S4–S5); B = incomplete injury, sensory function was found below the nerve plane, including the sacral segment S4–S5 but no motor function was observed; C = incomplete injury, motor function was retained below the nerve plane, and more than half of the key muscle strength was less than grade 3; D = incomplete injury, motor function was retained below the nerve plane, and more than half of the key muscles had muscle strength ≥grade 3; and E = normal, normal sensory and motor function.

Statistical Analysis
All analyses were performed using the SPSS statistical software package, version 14.0 (SPSS, Chicago, IL, USA). Preoperative, postoperative, and final follow-up data was used to compare the outcomes for each group, including operative times, blood tests, kyphotic angles, and JOA, VAS and NDI scores. Comparisons were made by analysis of variance between groups, and with the least significant difference (LSD) t-test or Dunnett’s T3 test to compare each group. Gender and age in the three groups was statistically analyzed using the χ²-test and variance analysis, respectively. Values of $P < 0.05$ were considered significantly different.

### TABLE 1 General information for 74 cervicothoracic tuberculosis patients

|                         | Group A (n = 33) | Group B (n = 16) | Group C (n = 25) | Statistical values |
|-------------------------|------------------|------------------|------------------|--------------------|
| Gender (M: F)           | 14:19            | 7:9              | 13:12            | $\chi^2 = 3.0614, P = 0.2164$ |
| Age (years)             | 23.85 ± 14.92    | 24.06 ± 13.43    | 23.32 ± 11.59    | $t_1 = 0.0477, P_1 = 0.9622$ |
|                         |                  |                  |                  | $t_2 = 0.1471, P_2 = 0.8836$ |
|                         |                  |                  |                  | $t_3 = 0.1875, P_3 = 0.8523$ |
| Hospital stay (days)    | 27.06 ± 10.71    | 27.69 ± 9.39     | 28.10 ± 9.15     | $t_1 = 0.2007, P_1 = 0.8418$ |
|                         |                  |                  |                  | $t_2 = 0.3895, P_2 = 0.6984$ |
|                         |                  |                  |                  | $t_3 = 0.1386, P_3 = 0.8905$ |
| Follow-up (months)      | 37.71 ± 1.25     | 37.31 ± 1.39     | 37.28 ± 1.32     | $t_1 = 1.0129, P_1 = 0.3163$ |
|                         |                  |                  |                  | $t_2 = 1.2665, P_2 = 0.2106$ |
|                         |                  |                  |                  | $t_3 = 0.0695, P_3 = 0.9449$ |
| Surgery duration (min)  | 220.33 ± 61.41   | 357.31 ± 63.74   | 236.96 ± 66.50   | $t_1 = 7.2334, P_1 = 0.0000$ |
|                         |                  |                  |                  | $t_2 = 0.9855, P_2 = 0.3286$ |
|                         |                  |                  |                  | $t_3 = 5.7433, P_3 = 0.0000$ |
| Blood loss (mL)         | 193.03 ± 114.88  | 693.75 ± 135.85  | 223.20 ± 127.63  | $t_1 = 13.4766, P_1 = 0.0000$ |
|                         |                  |                  |                  | $t_2 = 0.9442, P_2 = 0.3491$ |
|                         |                  |                  |                  | $t_3 = 11.2321, P_3 = 0.0000$ |

P1: A vs B; P2: A vs C; P3: B vs C.
Results

General Case
There was no significant difference in age and sex between the three groups ($P > 0.05$). All patients were followed for at least 36 months postoperation, with an average of 39 months (range, 36–96 months). Group B showed the largest blood loss and the longest operating time ($P < 0.05$); however, there was no significant difference between groups A and C. In addition, there was no significant difference in length of hospital stay between the three groups (Table 1).

Function Scores
Patients with neurological deficits showed different degrees of recovery after the operation. A total of 4 cases with grade A deficits recovered, with 1 patient recovering to grade C after surgery, and 3 patients recovering to grade D. One patient with grade C deficits recovered to grade D after surgery, and 17 cases of preoperative grade D patients were all restored to grade E by the last follow-up visit (Table 2). VAS and NDI scores of three groups were significantly decreased postoperatively and by the last follow-up, indicating that the three surgical methods could significantly improve pain and dysfunction for the patients. JOA scores significantly increased postoperatively and by the last follow-up visit, compared with preoperative values, indicating that the three surgical methods could significantly improve spinal cord function (Figs. 4–6).

| TABLE 2 Neurologic recovery according to the American Spinal Injury Association classification |
|-----------------------------------------------|
| Groups | A | B | C | Total |
|-------|---|---|---|------|
| Preoperative | | | | |
| A     | 4 | 0 | 0 | 4 |
| B     | 0 | 0 | 0 | 0 |
| C     | 0 | 0 | 1 | 1 |
| D     | 5 | 6 | 6 | 17 |
| E     | 24 | 10 | 18 | 52 |
| Postoperative | | | | |
| A     | 0 | 0 | 0 | 0 |
| B     | 0 | 0 | 0 | 0 |
| C     | 3 | 0 | 0 | 3 |
| D     | 1 | 0 | 1 | 2 |
| E     | 29 | 16 | 24 | 69 |
| Final follow-up | | | | |
| A     | 0 | 0 | 0 | 0 |
| B     | 0 | 0 | 0 | 0 |
| C     | 1 | 0 | 0 | 1 |
| D     | 3 | 0 | 1 | 4 |
| E     | 29 | 16 | 24 | 69 |

Fig. 4 The graph shows Japanese Orthopedic Association (JOA) scores. JOA scores significantly increased postoperatively and by the last follow-up visit, compared with preoperative values in the three groups.

Fig. 5 The graph shows visual analogue scale (VAS) values. VAS scores were significantly decreased postoperatively and by the last follow-up in the three groups.

Fig. 6 The graph shows neck disability index (NDI) scores. NDI scores were significantly decreased postoperatively and by the last follow-up in the three groups.
Radionuclide Evaluation
Postoperatively and at the last follow-up visit, the average Cobb angle was: 7.16° ± 2.37° and 8.15° ± 2.40° in group A, with a correction of 1.01° ± 0.67°; 8.78° ± 2.36° and 9.59° ± 2.19° in group B, with a correction of 0.81° ± 0.82°; and 10.66° ± 3.14° and 11.82° ± 3.37° in group C, with a correction of 1.16° ± 0.74°. Comparing preoperative postoperative and last follow-up data showed that the Cobb angle had significantly improved (P < 0.001). This indicated that the three surgical approaches could significantly correct kyphosis and had marked therapeutic effects. There was no significant difference between the three groups in correction loss at the last follow-up visit (P > 0.05; Table 3). All patients achieved bone fusion within 6–12 months of surgery (Figs. 7–9).

Laboratory Evaluation
At 3 months post-surgery and at the last follow-up, ESR was: 8.91 ± 3.05 mm/1 h and 7.24 ± 3.51 mm/h, in group A; 9.88 ± 2.94 mm/1 h and 8.13 ± 3.03 mm/1 h in group B; and 7.28 ± 2.46 mm/1 h and 5.96 ± 2.64 mm/1 h in group C. ESR returned to normal in all 3 groups at 3 months post-operation, and no obvious abnormality was seen at the last follow-up visit.

Complications
There were 2 cases of postoperative dysphagia in group A, and 3 patients with pain in the iliac donor region. There was 1 case of pain in the iliac donor region, 2 cases of cerebrospinal fluid leakage, 2 patients with electrolyte disturbances, and 1 case of postoperative pectoralgia in group B. In group C, there were 4 cases of cerebrospinal fluid leakage, and 1 patient with paralysis in the left lower limb. All complications were relieved after symptomatic treatment.

Discussion
At present, there is no uniform standard of surgical approach for cervicothoracic tuberculosis, and this issue has engendered some controversy. Each operative procedure has its advantages and disadvantages. In clinical practice, different surgical approaches should be selected according to the characteristics of the lesion, the technical level of the surgeon and the imaging findings.

Anterior Approach for Cervicothoracic Tuberculosis
The main advantage of this approach was not only operating under direct vision, with debridement and decompression being complete but also the convenience of bone grafts, correcting kyphosis, and reconstructing spinal stability. Furthermore, this approach only partially split the sternum, and did not require access to the thoracic cavity, so it had little effect on the respiratory and circulatory systems. Zhang et al. used an improved anterior approach on six patients with cervicothoracic tuberculosis. They found that all patients obtained bone fusion, no patient relapsed, kyphosis was obviously corrected, and there was no marked loss at the last follow-up. Our research suggested that postoperative kyphosis was significantly corrected, symptoms disappeared, JOA, VAS and NDI scores obviously improved, and all patients acquired bone graft fusion, with no complications of internal fixation being reported. However, there were also some shortcomings of this approach in clinical practice. First, due to obstruction of the upper mediastinum, the operation field was still limited; the distal end showed the T4 vertebral body, in general; however, short necked patients could only be exposed to the T3 vertebral body and embedding the implant was difficult. In this study, because of the difficulty in implant placement, 1 patient undergoing anterior approach surgery was converted to a combined anterior and posterior approach during surgery. We considered the main indications for one-stage anterior surgery to include: the damaged portion of the vertebra being located in the anterior and middle columns of the spine; the presence of vast abscess or sequestrum; spinal cord compression causing neurological deficit, or even paralysis; and the presence of kyphosis and spinal instability.
Combined Anterior and Posterior Approach

For patients with short necks and T3 vertebral lesion, the anterior manubrium splitting approach could achieve debridement and decompression; however, the implant was hard to fix, and required full sternotomy, making the surgery difficult, traumatic and, not conducive to postoperative recovery. If the decision is made to remove the manubrium–clavicle section, patients may experience postoperative shoulder joint dysfunction\textsuperscript{6,17}. To reduce the risk associated with the operation, some reports have suggested a combined anterior and posterior surgery to treat cervicothoracic tuberculosis\textsuperscript{2,18}. This approach separates the debridement area from the area of internal fixation to decrease the spread of TB, while allowing direct debridement of the abscess and neural decompression. In addition, the strong internal fixation system can provide satisfactory outcomes for deformity.
correction, promote bone graft fusion, and maintain the long-term stability of the spine. However, this approach does not avoid complications related to exposure from an anterior approach, and adds another incision posteriorly. In addition, combined surgery leads to longer operating times, increased blood loss, greater trauma, and higher complication rates. Our research also found the disadvantages described above.

We considered the main surgical indications for the combined anterior and posterior approach to include: when vertebral bodies were severely damaged or collapsed, and when the total number involved was >3, with accompanying paraplegia or severe nerve root irritation; when both anterior and posterior columns were destroyed, accompanied by an obvious anterior abscess; old tuberculosis, when the kyphosis

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**Fig. 8** The graph shows a case using one-stage posterior debridement, bone grafting, and instrumentation. As illustration, 39-year-old woman with cervicothoracic tuberculosis: (A, B) preoperative anteroposterior and lateral X-ray films; (C, D) preoperative CT scan; (E, F) preoperative magnetic resonance imaging (MRI); (G, H) X-ray film 6 months after operation; (I, J) CT scan 6 months after operation; (K, L) X-ray film 21 months after operation; (M, N) CT scan 21 months after operation.
deformity was severe; and when the anterior approach did not allow placement of internal fixation, requiring complete sternal splitting or cutting off a manubrium–clavicle section, especially for T3 spinal tuberculosis.

**One-Stage Posterior Surgery**

Some surgeons have used the posterior approach to treat cervicothoracic tuberculosis, achieving satisfactory therapeutic effects. Zhang et al. used this technique to treat children with cervicothoracic tuberculosis combined with kyphosis. The results showed remarkable correction of kyphosis and symptoms are obviously improved. Zeng et al. compared three surgical methods to treat cervicothoracic tuberculosis, and found that neurological function was significantly improved with the posterior-only approach, that kyphosis correction was remarkable, clinical symptoms were obviously alleviated, and there were fewer complications than for the other two approaches. However, spinal tuberculosis lesions are often located in front of vertebral bodies, such that posterior approach surgery cannot completely debride and adequately decompress the area, and posterior column destruction may cause spinal instability and affect bone fusion. We believe the posterior approach indications were relatively narrow, and should be mainly applied to adnexal tuberculosis, where the lesion was confined to the posterior column, or could be debrided by a posterior approach, when the general condition of the patient was poor and they could not tolerate complicated procedures, and for those with previous history of anterior surgery.

Although satisfactory outcomes were obtained in this study, several limitations still existed. First, the study was a retrospective study with a short follow-up time; long-term efficacy remains to be examined. Second, the study took place in six hospitals, which inherently created variation in patients’ treatment and in surgical skills. To reduce this variation, the institutions chosen were comprehensive teaching hospitals, and surgeries were performed by the same surgical team in the individual hospitals. Even so, the advantage of posterior surgery found in this study might be caused by bias resulting from patients’ individual status at the time of surgery and the proficiency of surgeons, leading to the decision for this particular approach.

**Conclusion**

Through this multicenter retrospective study, we propose that the choice of operation for cervicothoracic tuberculosis should be selected according to pathological changes, scope, and general physical condition of the patient. A reasonable chemotherapy regimen was essential for the treatment of cervicothoracic tuberculosis, and also guaranteed the success of the operation. A one-stage anterior surgical approach for the treatment of cervicothoracic tuberculosis showed excellent efficacy and fewer complications, so it was the recommended surgical method. Indications for a posterior approach are narrow and should be used selectively. In addition, the combined anterior and posterior approach had a longer operating time, larger blood loss, and greater trauma, and required advanced technical skills in the surgeon.
Consequently, the indications for using this approach should be highly specific.

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