Therapeutic effect of minimally invasive catheter drainage and local chemotherapy for the lumbosacral tuberculosis without neural symptoms

Tian-qing Li, MM, Zhen-sheng Ma, MD, Yang Zhang, MD, Hui-fa Xu, MM, Wei Lei, MD

Abstract
Increasing number of studies have shown growing incidence of lumbosacral tuberculosis and its complications. However, the treatment options for this disorder are still limited.

To evaluate the long-term therapeutic effect and prognosis of minimally invasive puncture catheter drainage and Isoniazid local chemotherapy for the treatment of lumbosacral tuberculosis without neural symptoms under the guidance of computed tomography (CT).

A total of 45 patients with asymptomatic lumbosacral tuberculosis were treated by minimally invasive catheter drainage under CT guidance. Forty-two cases had been followed up, which included 22 women and 20 men with an average age of 36.45 years old. Isoniazid was injected locally and antituberculosis drugs were administered for postoperative treatment. Oswestry Disability Index (ODI), visual analogue scale (VAS) evaluation and Cobb angle were recorded before and after operation.

Forty-two patients had been followed up and the follow-up term was from 1.2 to 8.5 years (average 60 months). All patients were healed without recurrent cases. The ODI were improved from 14.86 ± 2.02 before operation to 1.48 ± 1.55 after operation. The post-operative (4.19 ± 1.17) VAS score was improved compared to the pre-operative VAS score (5.55 ± 0.55). The post-operative Cobb angle (6.19° ± 3.85°) was also improved relatively to the preoperative Cobb angle (5.90° ± 3.71°).

Minimally invasive puncture catheter drainage combined with Isoniazid local chemotherapy is an effective method for lumbosacral tuberculosis without neural symptom. Meanwhile, it can be applied for the treatment of spinal tuberculosis before open surgery.

Abbreviations: CRP = C-reactive protein, CT = computed tomography, DST = drug susceptibility testing, ESR = erythrocyte sedimentation rate, Frankl E = Frankl evaluation, IUATLD = International Union Against Tuberculosis Lung Diseases, L–J = Lowenstein–Jensen, MRI = magnetic resonance imaging, MTC = M tuberculosis complex, ODI = Oswestry functional disorder index, VAS = visual analogue scale.

Keywords: lumbar spine, minimal invasive surgery, spine, therapeutic effect, tuberculosis
critical to find alternative and adequate treatment options for patients with spinal tuberculosis. Isoniazid has the advantages of strong anti-tuberculosis effect, low toxicity, high efficacy, stable nature, and low price. It is the most important first-line anti-tuberculosis drug in clinical practice.\(^9\) The treatment effect of Isoniazid local chemotherapy in combination with minimally invasive catheter drainage for lumbosacral tuberculosis without neural symptoms has not been evaluated so far. In this study, we aimed to scrutinize the long-term therapeutic effect and prognosis of minimally invasive puncture catheter drainage combined with Isoniazid local chemotherapy in the treatment of the tuberculosis of lumbosacral junction without neural symptoms under the guidance of computed tomography (CT).

2. Materials and methods

2.1. Study population

This study was approved by the Institutional Review Boards of The Fourth Military Medical University (Xi’an, China) and Xijing Hospital (Xi’an, China). All procedures involving human participants were performed in accordance with the ethical standards of the Institutional Review Boards of The Fourth Military Medical University (Xi’an, China) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all individual participants included in the study. A total of 45 patients with asymptomatic lumbosacral tuberculosis were collected from January 2010 to October 2017 in our institution. The subjects underwent minimally invasive puncture therapy and the tuberculous segments of the spinal canal were respectively 5 cases of T12-L1, 8 cases of L1-2, 11 cases of L2-3, 7 cases of L3-4, 13 cases of L4-5 and 9 cases of L5-S1. There were 20 male and 22 female patients with the average age of 36.45 years old (range from 10 to 67 years old). According to the Frankl evaluation (Frankl E), all patients had no neural symptom before operation.

2.2. Isolation of Mycobacterium tuberculosis and drug susceptibility testing

The sputum was harvested and stored at 4°C in a 50mL container. After purification with 4% NaOH, the bacteria were cultured in 2% Kudo medium. Subsequently, the purified colonies of M tuberculosis transferred in Middlebrook 7H9 broth medium (Becton Dickinson, Sparks, MD, USA) for the collection of the bacterial suspension, followed by the detection of the purified bacilli with the Capilia TB (TOUNS, Numazu, Japan) which was employed for identifying M tuberculosis complex (MTC). The drug susceptibility testing (DST) was carried out on Lowenstein–Jensen (L–J) medium containing Isoniazid (0.2μg/mL). Bacilli diluted 100-fold were seeded on drug-free L–J medium as a control. The initial colony count started after 4 weeks and was finally completed at 6 weeks. Resistance was shown if colonies were grown on the drug-containing medium comparatively to the control.

2.3. Pre-operation

The patients were all clinically diagnosed and confirmed with spinal tuberculosis. The X-rays showed no obvious kyphosis and 35 subjects had lumbar spinal stenosis which was caused by lesions of the intervertebral disc. There were 32 cases with destroyed vertebral body and 30 cases with paravertebral abscess and psoas abscess. Thirty-five cases had received magnetic resonance imaging (MRI) and the results showed 23 cases with single intervertebral disc, 9 cases with 2 intervertebral discs and 3 cases with 3 intervertebral discs. Their blood pressure was elevated. The average erythrocyte sedimentation rate (ESR) was 53 ± 18 mm/h and the average C-reactive protein (CRP) was 15 ± 5.2 mol/L. Tspot test was conducted on 36 cases and the results indicated 34 cases of positive reaction.

The systemic chemotherapy was the recommended standard treatment of International Union Against Tuberculosis Lung Diseases (IUATLD) in 1986. The chemotherapy was lasted from 12 to 18 months with average time of 13 ± 3 months. All patients accepted two kinds of treatments based on systemic chemotherapy. There were 35 cases with bigger nidus, paravertebral abscess, and psoas abscess using persistent local chemotherapy simultaneously with local drainage. The other 7 cases with pure tuberculosis of the vertebral body accepted local chemotherapy.

2.4. Surgery methods

Epidural paracentesis, local anesthetic, blade, needle and thread, pathway, and drainage device (initial negative pressure drainage suction) were prepared for surgery (Fig. 1). Operation was conducted under the guidance of CT with local anesthesia. The incision was about 4 cm away from lumbar posterolateral spinous and the direction was oblique into the disc spaces of spines or paravertebral bodied. Inserting needles and the approach direction were confirmed through the CT guidance. After the conventional disinfection and draping of the area, the 20th epidual needle was used for puncture and then a guide wire was inserted. The location of dural outer tube was confirmed in nidus after CT-scan. The first guide wire was conducted to fix the dural outer tube for injecting isoniazid drug into nidus. From the location of needling, we cut a 4 mm incision. Next, the injection point of drainage tube was opened with a 4 mm-length incision and the working casing pipe was inserted into negative drainage tube under the guidance of guide wire. It was clear that the drainage tube was in nidus or abscess through the CT-scan. Finally, the drainage tube was fixed on skin by first wire. The operation picture was depicted in Fig. 2 and the pre-operative image was presented as Fig. 3.

2.5. Post-operation

Isoniazid (5 mg/kg/dose, with a maximum dose of 300 mg){\(^9\)} was used for local chemotherapy once every day and lasted for 3 months from the dural outer tube. Negative pressure drainage tube was used to elicit pus. Pus should be poured out regularly and the bottle of drainage could contain 300 mL pus at most. If there was no way to elicit pus or inject medicine result from the obstructed dural outer tube or the drainage tube, repeated insertion of the tube and changing of medicine could be tried till final cure. In 42 cases, the patients who had a better spinal stability, light pain, and light level of vertebral damage could move around for ordinary activities under the specific stabilizing brace’s protection. The other patients should be required strictly in bed for cure. Oral isoniazid (300 mg/dose), Rifampicin (450 mg/dose), Ethambutol (750 mg/dose), intramuscular injection of Streptomycin (750 mg/dose) were used for combination therapy. After discharging, liver function, ESR, and X-ray scan or CT or MRI should be checked for follow-up for every patient.
2.6. Efficacy evaluation criteria
The standard of clinical curative treatment according to Rasouli’s study was used to evaluate spinal tuberculosis: body presented as good shaping and good condition without fever, normal appetite, and local pain. ESR was in the normal range under repeated examination. The X-ray showed that the vertebral body of the lesion had healed osteologically with clear contour and no abnormal shadow. The normal activity and light work could be done for 3 to 6 months without recurrence. MRI showed that the lesion and their vertebral body had the same signal as surrounding tissue and normal vertebral body. Oswestry functional disorder index (ODI) and visual analogue
scale (VAS) score were used to assess neurological function and pain in patients. Kyphotic deformity was evaluated using Cobb angle measurement. ESR, ODI, VAS, and Cobb angle were recorded pre-operatively and post-operatively.

2.7. Statistical analysis
All analyses were performed using SPSS version 12.0 (IBM Corp., Armonk, NY). Continuous variables were expressed as mean with standard deviations. Categorical variables are presented as
the number and/or frequency. The counting data was tested by the $\chi^2$ test and the measurement data by the $t$-test. $P < .05$ was considered as statistically significant.

3. Results

All patients were healed with no recurrent cases. The DST indicated that about 32% of $M$ tuberculosis isolated from the patient’s sputum were Isoniazid resistant. The preoperative clinical symptoms did not show sinus tract formation and neural symptom. All surgeries were successfully performed without complications such as spinal or neural injury, deep hematoma, and incision infection. Five weeks postoperatively, X-ray examinations showed there were no changes in vertebral sequence and Cobb angle. The duration of local chemotherapy before regression of symptoms, and hematologic and radiological abnormalities ranged from 2 to 9 months (average: 4 months) (Figs. 4 and 5). Forty-two patients had been followed up and the follow-up term was from 1.2 to 8.5 years (average 60 months).

The ODI and VAS scores showed significant differences between pre-operation and post-operation ($P < .05$). The ODI was improved from 14.86 ± 2.02 before operation to 1.48 ± 1.55 after operation. The VAS score was improved postoperatively (0.55 ± 0.55) compared to the pre-operative value (4.19 ± 1.17). No obvious pain symptoms were observed at the last follow-up and the patients could conduct usual activities. ESR levels returned to normal at the final follow-up. A mild increase in Cobb angle was observed after the minimally invasive surgery. The preoperative Cobb angle was $5.90\,{}^\circ \pm 3.71\,{}^\circ$ but improved postoperatively ($6.19\,{}^\circ \pm 3.85\,{}^\circ$). The Cobb angle increased postoperatively in the 2 patients without obvious kyphosis. The patients achieved spinal stabilization with no neurological impairment and no need for a second surgery. There was statistical significance ($P > .05$) between the preoperative Cobb angle and the Cobb angle at final follow-up (Table 1).
4. Discussion

The traditional debridement surgery with bone graft and internal fixation orthopedic correction is accompanied by high cost, more trauma, and post-operative complications.[11] For example, the prevalence of neurologic involvement represents 10% to 47% of those with spinal tuberculosis,[12] which cannot, in some cases, be cured by drug alone. It is imperative to perform surgery which will be more beneficial and safer. In this study, we achieved

Figure 4. The puncture image during treatment for a 23-year-old female patient with paravertebral abscess 1 year was diagnosed as L4-S vertebral tuberculosis. A. The second puncture for the third-month treatment. B. The third puncture for the fifth-month treatment. C. The forth puncture for the sixth-months treatment.
satisfactory outcome with the spinal tuberculosis through minimally invasive catheter drainage combined with local chemotherapy in patients with spinal tuberculosis.

Spinal canal abscess can result in paraplegia, particularly in the thoracic vertebrae. In traditional method of systemic chemotherapy for bone tuberculosis, medicines cannot enter into the core of necrotic liquefied nidus. So, it takes long time to control pathogenetic condition with low rate tuberculosis\textsuperscript{[13–16]} Abscess, sequestrum, and nerve complications constitute the common indication of nidus radical surgery. In 1950s, spinal tuberculosis surgery was proposed and the rate of death was largely reduced. However, there are some problems of indication surgery, which refers to big trauma, high relapse, and high expenses. In our study, local spinal tuberculosis therapy was replaced by minimally invasive tuberculosis puncture catheter drainage and local chemotherapy with minimal incision and extracted pus and mycobacteria locally. This method could augment drug concentration, kill mycobacteria quickly, and restrain malgenic elements of sinus tract formation with the help of local medical chemotherapy, which was the main reason for our cases with no sinus tract formation in drainage part.

Conclusively, perivertebral abscess and lumbar major muscle abscess caused by spinal tuberculosis can be improved by local chemotherapy in long-term application. Thus, radical operation for tuberculosis should no longer be used to cause severe trauma to the patient. The drainage tube effectively removed the abscess and relieved spinal cord compression with little damage to the paravertebral muscle and minimal iatrogenic injury.\textsuperscript{[15]} Moreover, this approach was time-effective. With regard to kyphosis, chemotherapy alone has been reported to result in an average increase in the Cobb angle of 15° and >60° in 3% to 5% of cases. Open drainage is not recommended for tuberculous abscesses due to hard healing for sinus tract formation. In this study, close drainage was applied for the patients to avoid secondary infection or sinus tract. Abscess drainage has a low requirement for the patient’s overall condition and does not require adequate preparation for chemotherapy before treatment. The local abscess drainage abscess can make the patient shrinks rapidly, and the local stimulation caused by the abscess and the symptoms of tuberculosis can be relieved quickly. Additionally, the Cobb angle showed no significant difference during pre- and post-operation, which had slightly increased after operation.

The purpose of spinal tuberculosis therapy is to control active tuberculosis rather than to dislodge necrosis of bone, also known as sequestrum. Indication surgery can dislodge lots of sequestrums with no new bone graft, which is in part the reason for terminal Cobb. In our treatment, we found that the bone density of surrounding vertebrae was elevated after the cure of spinal tuberculosis, but the sclerotin of bone resorption was difficult to be calcified once again. Compared with non-specific spinal infection, the bone bridge surrounding tuberculosis was relatively weak and sequestrum in local tuberculosis could not influence the result of local chemotherapy. Thus, local chemotherapy to clear percutaneous tuberculosis without cleaning sequestrum could provide weight bearing for spine after cure.

The patients with neural symptom or spinal deformity caused by vertebral damage underwent anterior approach or posterior approach to clear tuberculosis for bone graft. The inter-fixation therapy was adopted in the first term or the second term. The anterior approach\textsuperscript{[17]} indicated that tuberculosis nidus is cleared up thoroughly for full earlier bone fusion. However, it has the disadvantages of big trauma, multi-complications, high expense, and long hospitalization.\textsuperscript{[18,19]} The posterior approach\textsuperscript{[20,21]} could destroy posterior spinal structure and be difficult for clearance of tuberculosis. Meanwhile, it also has the disadvantages of the anterior approach.\textsuperscript{[22]} In this study, minimally invasive puncture catheter drainage apparently solves these problems and each indicator was improved after operation. The ODI were improved from 14.86 ± 2.02 before operation to 1.48 ± 1.55 after operation. The VAS score was improved from preoperative 4.19 ± 1.17 to postoperative 0.55 ± 0.55. The Cobb angle was from preoperative 3.90° ± 3.71° to postoperative 6.19° ± 3.85°. Therefore, we concluded that minimally invasive puncture catheter drainage is an effective method for lumbosacral tuberculosis

![Figure 5.](image)

The post-operative image for a 23-year-old female patient with paravertebral abscess 1 year was diagnosed as L4-5 vertebral tuberculosis. A. The post-operative 5 months X-ray image. B. The post-operative 18 months X-ray image. C. The post-operative 36 months X-ray image.

| Table 1 | The indicators compare between pre- and post-operation. |
|---------|----------------------------------------------------------|
|         | Preoperation    | Postoperation     | P    |
| ODI     | 14.86 ± 2.02    | 1.48 ± 1.55       | .05  |
| VAS     | 4.19 ± 1.17     | 0.55 ± 0.55       | .05  |
| Cobb angle | 5.90 ± 3.71   | 6.19 ± 3.85       | .05  |
| ESR     | 51.6 ± 15.5     | 4.41 ± 2.27       | .05  |

ESR = erythrocyte sedimentation rate, ODI = Oswestry functional disorder index, VAS = visual analogue scale.
without neural symptom. Meanwhile, it can be an attempt to treat spinal tuberculosis before open surgery. But minimally invasive surgery could not improve the pressure of inter-vertebrae soft tissues and bony tissues. It cannot correct pathologic changes of neural dysfunction resulted by interior convex kyphosis and posterior kyphosis.

This study had a number of limitations. First, there was no control group with relatively small sample size. Second, the patients who have spinal deformity and neural symptom are not advised to adopt minimally invasive puncture drainage. Third, proper selection criteria should be laid down depending on the type of the disease and more cohort studies are recommended.

In conclusion, minimally invasive puncture catheter drainage is an effective method for lumbosacral tuberculosis without neural symptom. Meanwhile, it can be an attempt to treat spinal tuberculosis before open surgery. However, the clinical benefits of this treatment strategy need further studies with a larger sample size and appropriate controls.

Author contributions
Wei Lei conceived and designed the experiments. Tian-qing Li and Wei Lei wrote the paper. Tian-qing Li, Zhen-sheng Ma, Yang Zhang, and Hui-fa Xu performed the experiments. Tian-qing Li, Zhen-sheng Ma, and Wei Lei analyzed and interpreted the data. All authors contributed equally. All authors read and approved the final manuscript.

Conceptualization: Hui-fa Xu.
Data curation: Tian-qing Li.
Formal analysis: Zhen-sheng Ma.
Investigation: Zhen-sheng Ma, Yang Zhang, Wei Lei.
Methodology: Yang Zhang.
Project administration: Hui-fa Xu.
Writing – original draft: Tian-qing Li.
Writing – review & editing: Wei Lei.
Wei Lei orcid: 0000-0001-5599-6616.

References
[1] Reiche MA, Warner DF, Mizrahi V. Targeting DNA replication and repair for the development of novel therapeutics against tuberculosis. Front Mol Biosci 2017;4:75.
[2] Rothschild BM, Cohn L, Aviza A, et al. Aortic aneurysm producing back pain, bone destruction, and paraplegia. Clin Orthop Relat Res 1982;123–5.
[3] Yang Z, He J, Shi J, et al. Clinical efficacy of posterior intervertebral surgery for treating single-segment thoracolumbar spinal tuberculosis. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2018;43:328–36.
[4] Buyukkubeci O, Seçkiner I, Karslı B, et al. Retroperitoneoscopic drainage of complicated psoas abscesses in patients with tuberculous lumbar spondylitis. Eur Spine J 2012;21:470–3.
[5] Yang H, Hou K, Zhang L, et al. Minimally invasive surgery through the interlaminar approach in the treatment of spinal tuberculosis: a retrospective study of 31 patients. J Clin Neurosci 2016;22:9–13.
[6] Yin XH, Zhang HQ, Hu XK, et al. Treatment of pediatric spinal tuberculosis abscess with percutaneous drainage and low-dose local antituberculous therapy: a preliminary report. Childs Nerv Syst 2015;31:1149–55.
[7] Aryan CE, Brady MS, Siegelbaum RH, et al. Robust antitumor responses result from local chemotherapy and CTLA-4 blockade. Cancer Immunol Res 2018;6:189–200.
[8] Cobelens FG, For whom the bell tolls: isoniazid preventive therapy and tuberculosis drug resistance. Sci Transl Med 2013;5:180ps112.
[9] Zhang X, Lv Y, Xue W, et al. Mycobacterium tuberculosis infection in solid organ transplant recipients: experience from a single center in China. Transplant Proc 2008;40:1382–5.
[10] Rasouli MR, Mirkooohi M, Vaccaro AR, et al. Spinal tuberculosis: diagnosis and management. Asian Spine J 2012;6:294.
[11] Eikinci S, Agilli M, Ersen O, et al. Surgical treatment of tuberculous spondylodiscitis. Eur Rev Med Pharmaco Sci 2015;19:700–1.
[12] Dai LY, Jiang LS, Wang W, et al. Single-stage anterior autogenous bone grafting and instrumentation in the surgical management of spinal tuberculosis. Spine (Phila Pa 1976) 2005;30:2342–9.
[13] Brodkis DS, Dick JC, Kunz DN, et al. Posterior lumbar interbody fusion. A biomechanical comparison, including a new threaded cage. Spine (Phila Pa 1976) 1997;22:26–31.
[14] Centers for Disease Control and Prevention (CDC). Global routine vaccination coverage, 2010. MMWR, Morb Mortal Wkly, Rep. 2011;60:1520–2.
[15] Moon MSSM. Tuli: Severe kyphotic deformity in tuberculosis of the spine. International Orthopaedics (SICOT) (1995) 19:327–331. Int Orthop 1997;21:417.
[16] Tuli SM. Severe kyphotic deformity in tuberculosis of the spine. Int Orthop 1995;19:327–31.
[17] Abulizi Y, Liang WD, Maimaiti M, et al. Smith-Petersen osteotomy combined with anterior debridement and allografting for active thoracic and lumbar spinal tuberculosis with kyphotic deformity in young children: a prospective study and literature review. Medicine 2017;96:e7614.
[18] Rauf F, Chaudhry UR, Atif M, et al. Spinal tuberculosis: our experience and a review of imaging methods. Neuroradiol J 2015;28:498–503.
[19] Singh S, Kumaraswamy V, Sharma N, et al. Evaluation of role of anterior debridement and decompression of spinal cord and instrumentation in treatment of tubercular spondylitis. Asian Spine J 2012;6:183–93.
[20] Wu P, Luo C, Pang X, et al. Surgical treatment of thoracic spinal tuberculosis with adjacent segments lesion via one-stage transpedicular debridement, posterior instrumentation and combined interbody and posterior fusion, a clinical study. Arch Orthop Trauma Surg 2013;133:1341–50.
[21] Zeng Y, Chen Z, Qi Q, et al. Clinical and radiographic evaluation of posterior surgical correction for the treatment of moderate to severe post-tuberculous kyphosis in 36 cases with a minimum 2-year follow-up. J Neurosurg Spine 2012;16:351–8.
[22] Lee SH, Sung JK, Park YM. Single-stage transpedicular decompression and posterior instrumentation in treatment of thoracic and thoracolumbar spinal tuberculosis: a retrospective case series. J Spinal Disord Tech 2006;19:595–602.