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SINGLE-STAGE POSTERIOR RECONSTRUCTION FOR VERTEBRAL TUBERCULOSIS: KYPHOSIS CORRECTION AND FUNCTIONAL OUTCOMES

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ABSTRACT

Objective: Single-stage posterior reconstruction is used for spinal tuberculosis, but outcome data vary. To report outcomes after single-stage posterior debridement/decompression, titanium mesh cage fusion, and posterior instrumentation.

Materials and Methods: Retrospective series of 18 patients (2014-2019) treated with a posterior single-stage approach and ≥22 months' follow-up. Indications included neurological deficit; instability, progressive collapse, or deformity; compressive epidural or paravertebral abscess; and/or failure of anti-tuberculosis therapy. Outcomes included regional kyphosis/lordosis, visual analog scale (VAS), Frankel grade, Oswestry disability index (ODI) at final follow-up, and C-reactive protein (CRP)/erythrocyte sedimentation rate (ESR).

Results: Mean age was 36.3±11.7 years; mean follow-up 37.9±20.1 months. Involvement was thoracolumbar in 10 cases, thoracic in 4, and lumbar in 4. In thoracic/thoracolumbar cases (n=14), kyphosis improved from approximately 30° to 15.2° (p=0.005); lumbar lordosis showed no significant change (p=0.655). VAS decreased from 7.81 to 3.15 (p<0.002). Frankel increased from 4.75±0.52 to 4.92±0.28 (p>0.05); two patients improved (D→E) with no deterioration. Final ODI was 27.33±17.40 (median 22; 10-64). CRP rose early and returned toward baseline by ~3 months; ESR showed no significant change at ~3 months.

Conclusion: Posterior single-stage reconstruction was associated with maintained regional kyphosis correction and significant pain reduction; functional improvement could not be quantified without baseline ODI.

Keywords: Kyphosis correction, spinal tuberculosis, regional kyphosis correction, titanium mesh cage, single-stage posterior surgery

INTRODUCTION

Pott disease is a granulomatous infection by *Mycobacterium tuberculosis* that primarily involves the vertebral bodies, spreads subligamentously across discs, and can lead to collapse, kyphosis, and neurologic deficit[1]. Extrapulmonary involvement accounts for ~15-20% of all tuberculosis (TB) cases in recent cohorts; half of these involve the spine, and 10-45% develop neurological deficits and vertebral damage[2-5]. The spine is the most frequently affected skeletal site and the one most prone to serious complications[2-5]. Pathological fractures and dislocations produce mechanical instability, while compression from bony fragments or abscesses leads to neurological compromise-scenarios that often render surgery unavoidable[6,7].

Surgical goals in spinal TB are to eradicate infection, restore spinal stability, and address neurological dysfunction. To this end, a spectrum of procedures has been described: abscess drainage[8], anterior[9] and posterior[6,7] debridement, postero-lateral[10,11] approaches, anterior or posterior grafting[12] and kyphosis correction with preservation of fusion to prevent late deformity[7,13]. Because anterior and postero-lateral strategies can demand broader multidisciplinary resources and may carry higher complication profiles, single-stage posterior surgery is increasingly favored. In this study, we evaluate outcomes of single-stage posterior transpedicular debridement and decompression with titanium mesh cage fusion and posterior instrumentation, and we outline its advantages and limitations relative to alternative methods.

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MATERIALS AND METHODS

Between 2014 and 2019, 18 patients (12 females, 6 males) with vertebral TB, who underwent single-stage posterior debridement, decompression, fusion and instrumentation, were included in the study. The mean age was 36.3±11.7 years (range: 18-72). Eligible patients were those with vertebral TB treated with single-stage posterior debridement, decompression, titanium mesh cage fusion, and posterior instrumentation, with a minimum follow-up of 22 months. Patients with follow-up <22 months and/or incomplete clinical-radiographic data were excluded. Surgical indications included neurological deficit due to compression, mechanical instability/progressive collapse or deformity, compressive epidural/paravertebral abscess, and/or failure of appropriate anti-TB chemotherapy with clinical or radiological progression. The level of involvement at presentation was thoracolumbar (TL) in 10, thoracic (T) in 4, and lumbar (L) in 4 patients. Ethical approval was obtained from the University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital Ethics Committee for Non-Interventional Studies (approval no: 694, date: 07.11.2025). In addition, a written informed voluntary consent form was obtained from all patients participating in the study. For final follow-up assessment, patients were contacted by phone/e-mail and invited for clinical and radiographic evaluation. Demographic data, medical history, treatment modalities, physical examination findings, functional outcomes, and laboratory results were evaluated. Imaging studies, including plain radiographs, magnetic resonance imaging, and computed tomography, were also reviewed. In addition, preoperative and postoperative physical examination, laboratory, and radiography findings of the patients were retrieved via the hospital information system. Neurological status was graded preoperatively and at final follow-up using the Frankel classification (A-E)[14]. Pain intensity was assessed preoperatively and postoperatively using the visual analog scale (VAS)[15]. Functional status was evaluated at final follow-up using the Oswestry disability index (ODI)[16], with higher scores indicating greater disability.

Surgical Procedure

A midline incision was performed, hemostasis was achieved, and the paraspinal muscles were subperiosteally elevated to allow pedicle screw placement. Depending on the level of involvement, laminectomy was performed to expose the spinal cord, and tuberculous debris was circumferentially debrided with specimens sent for microbiology and pathology. The cleaned cavity was irrigated and filled with an appropriately sized titanium cage, and rods were contoured for kyphosis/lordosis correction and fixed. Facet and pedicle sites were grafted and vancomycin powder was applied, a Hemovac drain was placed, and the wound was closed in layers (Figure 1A-G). Postoperative management included thoracolumbosacral orthosis measurement on the first postoperative day; if there was no contraindication, the patient was mobilized and instructed to wear the corset during mobilization. Corset use for 6-12 months was recommended depending on the level of involvement. Anti-TB chemotherapy was initiated postoperatively under infectious disease supervision using a daily 4-drug regimen (isoniazid, rifampicin, pyrazinamide, and ethambutol) for 2 months, followed by daily isoniazid plus rifampicin for 10 months with weight-based dosing. Microbiological specimens were routinely submitted for smear/culture and drug-resistance assessment (drug-susceptibility testing when culture yielded growth and rapid molecular testing when available), and the regimen was modified according to susceptibility results and tolerability. A 12-month duration was selected for this spinal osteoarticular TB cohort treated with instrumentation, consistent with expert recommendations and contemporary World Health Organization/national guidance that commonly allow extended treatment durations for bone/joint (including spinal) disease[17,18]. Routine controls were scheduled at post-op 2 weeks, 6 weeks, 3 months, 6 months, and annually thereafter. Radiological fusion was defined as trabecular bridging across the cage/graft-endplate interfaces without progressive radiolucency or hardware failure. Loss of correction was defined as ⩾5° deterioration in regional kyphosis/lordosis versus immediate postoperative values. Implant loosening was defined as progressive ⩾1-mm peri-screw radiolucency and/or hardware migration/breakage, and cage subsidence as ⩾3-mm loss of segmental height or cage sinking compared with immediate postoperative films. Infection recurrence was defined as renewed disease activity after initial improvement, supported by rising erythrocyte sedimentation rate (ESR)/C-reactive protein (CRP) and radiological progression (progressive abscess or bone destruction). Regional kyphosis/lordosis angles were measured by specialist surgeons in our clinic and were re-evaluated by a senior surgeon; measurements were revised when necessary after repeat assessment.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 21.0. Continuous variables are presented as mean ± standard deviation and categorical variables as n (%). Normality was assessed with Kolmogorov-Smirnov/Shapiro-Wilk tests. Paired comparisons used the paired t-test or Wilcoxon signed-ranks test, as appropriate. All tests were two-tailed; p⩽0.05 was considered significant.

RESULTS

Eighteen patients (12 female, 6 male) were analyzed. Mean age was 36.3±11.7 years (range: 18-72). Mean hospital stay was 8.25±3.41 days and mean follow-up was 37.92±20.1 months (range: 22-94). The involved levels were TL (n=10), T (n=4), and L (n=4) (Table 1). In the L subgroup (n=4), lordosis showed no significant change (preoperative mean 27.5°; p=0.655). Pain decreased from a mean VAS of 7.81 preoperatively to 3.15 postoperatively (p<0.002) (Figure 2). In the T/TL subgroup

(n=14), regional kyphosis improved from approximately 30° preoperatively to approximately 15.2° at final follow-up (p=0.005) (Figure 3). Mean Frankel grade increased from 4.75±0.52 (median 5; range: 4-5) preoperatively to 4.92±0.28 (median 5; range: 4-5) at final follow-up (p>0.05). Two patients improved from Frankel D to E, and no neurological deterioration occurred. At final follow-up, functional status was assessed using the ODI. The mean ODI was 27.33±17.40 (median 22; range: 10-64), as summarized in Table 1. Regarding inflammatory markers, CRP increased in the early postoperative period (1.39→13.49 mg/L) and returned toward baseline by 3 months (2.08 mg/L), while ESR showed no significant change at 3 months (32.83→30.08 mm/h). No recurrence or loss of correction was observed during follow-up according to the predefined criteria.

DISCUSSION

Defining a single, universally applicable treatment algorithm for spinal TB is challenging because acceptable outcomes can be achieved with different surgical strategies. That said, contemporary implants and posterior techniques have made single-stage posterior surgery a commonly preferred option in many centers, as it can provide decompression/debridement, regional deformity correction, and stable reconstruction through one approach with less soft-tissue morbidity than combined procedures. Anterior or combined anterior-posterior approaches may still be appropriate in selected scenarios (e.g., extensive anterior column destruction, specific abscess patterns, or cases requiring anterior structural support), but our study was not designed to compare strategies and therefore does not support claims of superiority.

Pain reduction in our cohort was comparable to prior posterior-only series, where VAS reductions of approximately 4-6 points have been reported[9,10,13]. In this study, mean VAS decreased from 7.81 to 3.15 (p<0.002), indicating a clinically relevant reduction in pain after single-stage posterior reconstruction.

Neurological change in our cohort was modest. Although neurological improvement after posterior surgery is frequently reported[11,13], only two patients improved (Frankel D→E) and the overall change was not statistically significant. Mean Frankel grade increased from 4.75±0.52 (median 5; range: 4-5) preoperatively to 4.92±0.28 (median 5; range: 4-5) at final follow-up (p>0.05), with no neurological deterioration. This likely reflects the small sample size and the relatively preserved baseline neurological status, limiting the ability to detect measurable neurological improvement.

Radiographic findings in our study should be interpreted as regional correction rather than global sagittal realignment. Prior posterior-only series have reported meaningful reductions in T kyphosis after debridement, instrumentation, and fusion[11,19]. In our T/TL subgroup, kyphosis decreased from approximately 30° preoperatively to 15.2° at final follow-up, indicating maintained regional correction. In contrast, L lordosis did not change significantly, and this neutral finding is reported separately.

Table 1. Posterior single-stage surgery outcomes in spinal TB

No	Gender	Age (year)	Follow-up (month)	VAS (preoperative)	VAS (postoperative)	Angle (preoperative/final)	Level	Oswestry (0-100)
1	Female	18	22.0	8.06	2.79	Preop: 26°	L	22.0
2	Female	72	94.0	7.41	3.78	Preop: 30°/final: 14.8°	TL	37.0
3	Female	23	22.0	7.41	2.94	Preop: 30°/final: 15.2°	TL	22.0
4	Female	25	23.9	7.98	2.64	Preop: 30°/final: 14.8°	TL	29.4
5	Female	27	22.1	8.28	3.50	Preop: 35°/final: 15.2°	T	22.0
6	Female	29	34.7	8.23	3.12	Preop: 30°/final: 14.8°	TL	24.3
7	Female	31	81.6	7.90	3.52	Preop: 25°	L	25.6
8	Female	32	33.3	8.21	2.72	Preop: 30°	L	26.4
9	Female	34	27.1	7.59	2.91	Preop: 29°/final: 15.2°	TL	22.0
10	Female	36	30.3	8.20	3.48	Preop: 29°/final: 18.0°	T	26.7
11	Female	37	28.9	7.86	2.93	Preop: 29°/final: 15.2°	TL	24.7
12	Female	38	36.3	7.80	3.30	Preop: 30°/final: 14.8°	TL	30.0
13	Male	38	38.7	7.43	3.41	Preop: 30°/final: 14.0°	TL	22.0
14	Male	40	22.0	7.47	3.10	Preop: 30°/final: 15.2°	T	31.6
15	Male	41	37.9	7.24	3.25	Preop: 30°/final: 15.2°	TL	22.0
16	Male	42	36.6	8.06	3.14	Preop: 30°/final: 15.2°	T	29.4
17	Male	44	54.4	7.81	3.41	Preop: 29°	L	24.8
18	Male	46	37.0	7.64	2.76	Preop: 28°/final: 15.2°	TL	29.7

TB: Tuberculosis, VAS: Visual analog scale, TL: Thoracolumbar, T: Thoracic, L: Lumbar

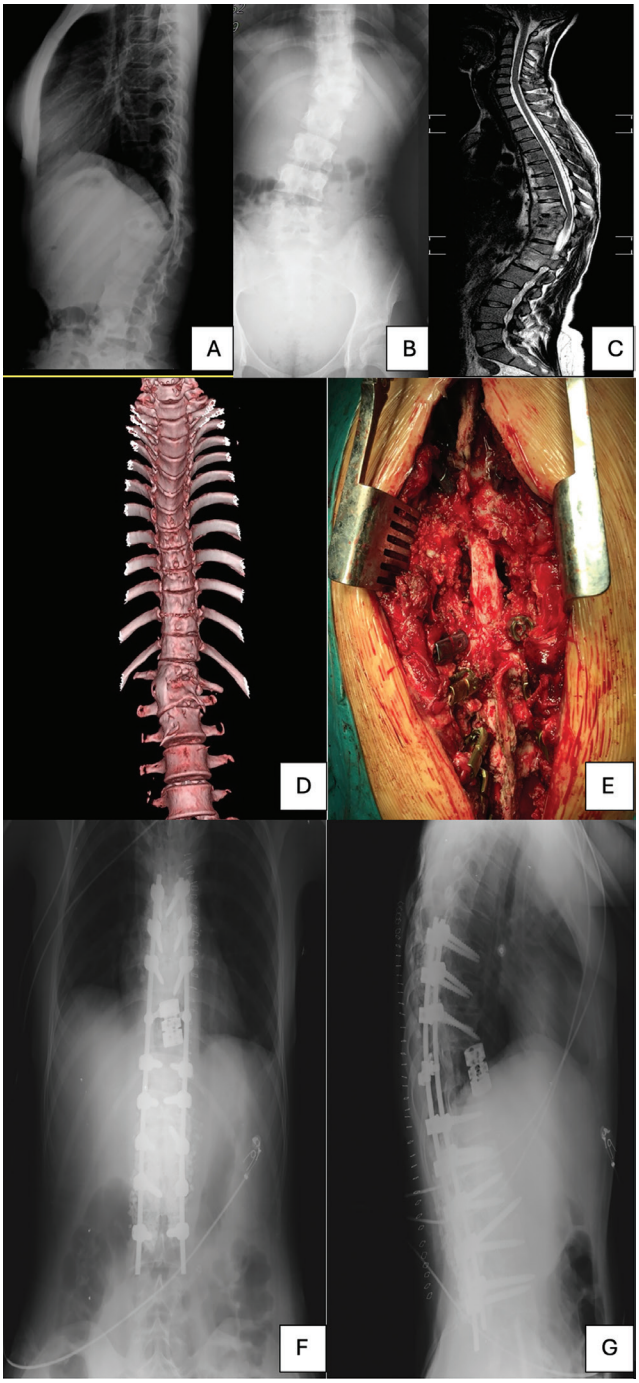


Figure 1. Panels (**A-G**) illustrate the preoperative imaging, intraoperative steps, and early postoperative radiographs in a representative patient with thoracolumbar Pott disease (**A,B**). Preoperative anteroposterior and lateral radiographs demonstrating thoracolumbar involvement (T12-L2) (**C**). Sagittal MRI showing the extent of vertebral destruction and compression (**D**). CT image detailing bony collapse and deformity (**E**). Intraoperative view during posterior debridement and long-segment pedicle screw instrumentation (**F,G**). Early postoperative anteroposterior and lateral radiographs demonstrating titanium cage reconstruction and pedicle screw instrumentation with improved regional alignment. MRI: Magnetic resonance imaging, CT: Computed tomography

Overall, these data are consistent with posterior single-stage reconstruction providing durable regional kyphosis correction in T/TL disease, while effects on L alignment appear limited in this small cohort.

In our cohort, T/TL involvement predominated and patients were relatively young (mean age 36.3 years), consistent with other published series. The mean length of hospital stay was 8.25±3.41 days, which lies at the lower end of ranges reported in prior posterior-only and combined approach cohorts (reported ~10-18 days)[20]. This comparison should be interpreted cautiously because length of stay is strongly influenced by local healthcare systems, perioperative pathways, and discharge practices.

Inflammatory markers showed a postoperative pattern that is commonly observed after major spinal procedures. CRP increased early postoperatively and returned toward baseline by approximately 3 months in our cohort, whereas ESR demonstrated a slower and less specific trajectory, as reported in prior studies[21,22]. Given that CRP/ESR were obtained at limited time points, these measures should be interpreted as supportive laboratory trends rather than standalone indicators of TB control or recurrence.

Functional interpretation is limited by measurement design. ODI was available only at final follow-up (mean 27.33±17.40; median 22; range: 10-64), and baseline ODI was not recorded; therefore, functional improvement cannot be quantified in this series. Accordingly, ODI is reported strictly as final functional status rather than pre-post change. Final ODI values were broadly comparable to those reported in prior posterior-only cohorts[23].

Study Limitations

This study is limited by its retrospective design, small and heterogeneous sample (n=18), absence of a comparator group, and limited power for subgroup analyses, particularly for L disease. Follow-up imaging was not fully standardized, and radiographic assessment was restricted to regional kyphosis/lordosis angles; global sagittal alignment and pelvic parameters were not evaluated, precluding conclusions regarding global alignment. Patient-reported outcomes were limited to VAS and ODI, with ODI available only at final follow-up and without broader health-related quality of life instruments, which restricts comparability and prevents robust assessment of functional change. CRP/ESR measurements were obtained at limited time points, and rehabilitation adherence and provider-related variability were not systematically captured. Finally, formal interobserver reliability statistics were not calculated. These limitations reduce generalizability and underscore the need for prospective comparative studies with standardized PROMs, comprehensive alignment assessment, and predefined reliability analysis.

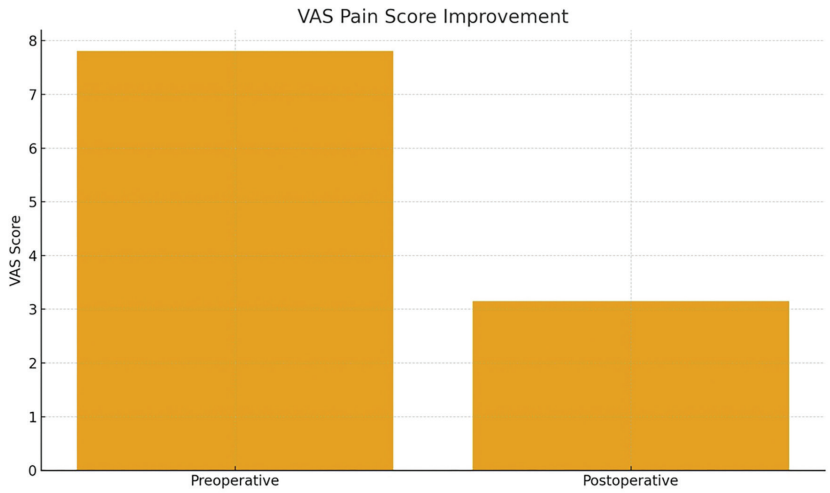


Figure 2. Mean VAS pain scores decreased from preoperative to postoperative assessment (0-10 scale). VAS: Visual analog scale

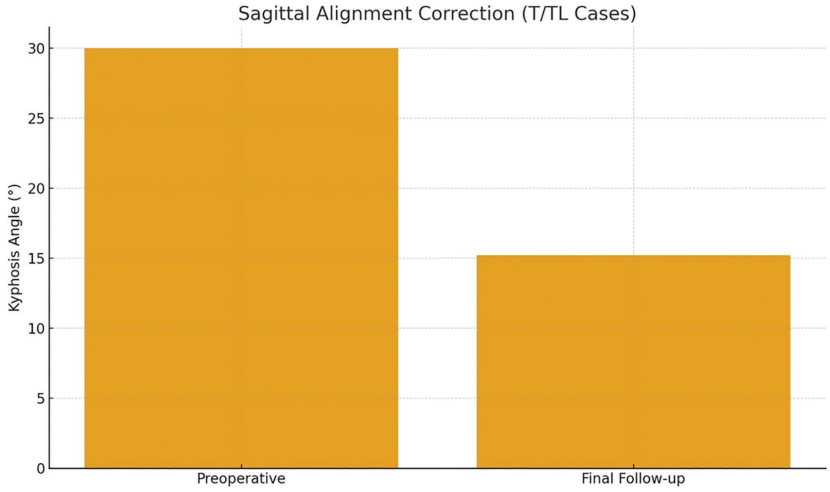


Figure 3. Change in regional kyphosis angle from preoperative to final follow-up in thoracic/thoracolumbar cases. T: Thoracic, TL: Thoracolumbar

CONCLUSION

In this small retrospective series, single-stage posterior debridement/decompression with titanium mesh cage-assisted fusion and posterior instrumentation was associated with durable regional kyphosis correction in T/TL disease and significant postoperative pain reduction. Final functional status was favorable (mean ODI 27.33±17.40; median 22; range: 10-64); however, functional improvement cannot be quantified because baseline ODI was unavailable. No recurrence or loss of correction was observed during follow-up according to the predefined radiological criteria.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the University of Health Sciences Türkiye, Gazi Yaşargil Training and Research Hospital Ethics Committee for Non-Interventional Studies (approval no: 694, date: 07.11.2025).

Informed Consent: Written informed voluntary consent form was obtained from all patients participating in the study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: A.Y., R.A., Concept: A.Y., R.A., Design: A.Y., R.A., C.A., A.A., Data Collection or Processing: A.Y., R.A., C.A., A.A., Analysis or Interpretation: A.Y., R.A., A.A., Literature Search: A.Y., R.A., C.A., Writing: A.Y., R.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Jain AK, Rajasekaran S, Jaggi KR, Myneedu VP. Tuberculosis of the spine. J Bone Joint Surg Am. 2020;102:617-28.
2. Klingmüller A, Feldmann M, Rohr S, Helmhold L, Junker L, Scherer M, et al. Clinical heterogeneity and treatment outcomes of extrapulmonary tuberculosis in a low-incidence setting: insights from a prospective cohort study. Infection. 2025;53:1809-18.
3. VidyaRaj CK, Vadakunnel MJ, Mani BR, Anbazhagi M, Pradhabane G, Venkateswari R, et al. Prevalence of extrapulmonary tuberculosis and factors influencing successful treatment outcomes among notified cases in South India. Sci Rep. 2025;15:8290.
4. Guillet-Caruba C, Bénet C, Jmel H, Doucet-Populaire F, Bourgeois-Nicolaos N. Accelerating extrapulmonary tuberculosis diagnosis with a rapid molecular assay. Microbiol Spectr. 2025;13:e0010425.
5. Wolinsky E. Tuberculosis. In: Goldman L, Bennett JC (eds). Cecil textbook of medicine. WB Saunders, Philadelphia 2001:1620-30.
6. Levine MJ, Heller JG. Spinal infection. In: Garfin SR, Vaccaro AR (eds). Orthopaedic knowledge update: spine. American Academy of Surgeons, Rosemont 1997:261-3.
7. Shanmuganathan R, Ramachandran K, Shetty AP, Kanna RM. Active tuberculosis of spine: current updates. N Am Spine Soc J. 2023;16:100267.
8. Li J, Li XL, Zhou XG, Zhou J, Dong J. Surgical treatment for spinal tuberculosis with bilateral paraspinal abscess or bilateral psoas abscess: one-stage surgery. J Spinal Disord Tech. 2014;27:e309-14.
9. Hodgson AR, Stock FE. Anterior spine fusion for the treatment of tuberculosis of the spine. Journal of Bone & Joint Surgery. 1960;42A:295-310.
10. Zeng Y, Wu W, Lyu J, Liu X, Tan J, Li Z, et al. Single-stage posterior debridement, decompression and transpedicular screw fixation for the treatment of thoracolumbar junction (T12-L1) tuberculosis with associated neurological deficit: a multicentre retrospective study. BMC Musculoskelet Disord. 2019;20:95.
11. Zhang H, Sheng B, Tang M, Guo C, Liu S, Huang S, et al. One-stage surgical treatment for upper thoracic spinal tuberculosis by internal fixation, debridement, and combined interbody and posterior fusion via posterior-only approach. Eur Spine J. 2013;22:616-23.
12. Pang X, Shen X, Wu P, Luo C, Xu Z, Wang X. Thoracolumbar spinal tuberculosis with psoas abscesses treated by one-stage posterior transforaminal lumbar debridement, interbody fusion, posterior instrumentation, and postural drainage. Arch Orthop Trauma Surg. 2013;133:765-72.
13. Zhang H, Zeng K, Yin X, Huang J, Tang M, Guo C. Debridement, internal fixation, and reconstruction using titanium mesh for the surgical treatment of thoracic and lumbar spinal tuberculosis via a posterior-only approach: a 4-year follow-up of 28 patients. J Orthop Surg Res. 2015;10:150.
14. Frankel HL, Hancock DO, Hyslop G, Melzak J, Michaelis LS, Ungar GH, et al. The value of postural reduction in the initial management of closed injuries of the spine with paraplegia and tetraplegia. I. Paraplegia. 1969;7:179-92.
15. Huskisson EC. Measurement of pain. Lancet. 1974;2:1127-31.
16. Fairbank JC, Pynsent PB. The Oswestry disability index. Spine (Phila Pa 1976). 2000;25:2940-52; discussion 2952.
17. World Health Organization. Treatment of extrapulmonary TB. Composition and duration of the regimen [Internet]. TB Knowledge Sharing Platform. Last accessed date: 18 February 2026. Available from: https://tbksp.who.int/en/node/3024
18. World Health Organization. WHO operational handbook on tuberculosis. Module 3: diagnosis. Rapid diagnostics for tuberculosis detection [Internet]. Last accessed date: 18 February 2026. Available from: from:https://www.paho.org/sites/default/files/2024-04/2024-cde-who-consolidated-handbook-tb-module-3-rapid-tx-web-annex-c.pdf
19. Wu P, Luo C, Pang X, Xu Z, Zeng H, Wang X. 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.
20. Wang X, Pang X, Wu P, Luo C, Shen X. One-stage anterior debridement, bone grafting and posterior instrumentation vs. single posterior debridement, bone grafting, and instrumentation for the treatment of thoracic and lumbar spinal tuberculosis. Eur Spine J. 2014;23:830-7.
21. Liu Z, Zhang P, Zeng H, Xu Z, Wang X. A comparative study of single-stage transpedicular debridement, fusion, and posterior long-segment versus short-segment fixation for the treatment of thoracolumbar spinal tuberculosis in adults: minimum five year follow-up outcomes. Int Orthop. 2018;23:830-7.
22. Zhang HQ, Li M, Wang YX, Tang MX, Guo CF, Liu SH, et al. Minimum 5-year follow-up outcomes for comparison between titanium mesh cage and allogeneic bone graft to reconstruct anterior column through posterior approach for the surgical treatment of thoracolumbar spinal tuberculosis with kyphosis. World Neurosurg. 2019;127:e407-15.
23. Yin XH, Liu ZK, He BR, Hao DJ. Single posterior surgical management for lumbosacral tuberculosis: titanium mesh versus iliac bone graft: a retrospective case-control study. Medicine (Baltimore). 2017;96:e9449.