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Hip Tuberculosis at Stage IV: Outcomes and Some Conditions for Total Hip Replacement

Do Dang Hoan[1,2], Dao Xuan Thanh[2,3], Nguyen Khac Trang[1], Ngo Van Toan[2,4]

[1]Department of General Surgery, National Lung Hospital, Hanoi, Vietam
[2]Hanoi Medical University, Hanoi, Vietam
[3]Department of Orthopaedic, Hanoi Medical University Hospital, Hanoi, Vietam
[4]Hanoi Medical University Hospital, Hanoi, Vietam
Email: dodanghoan@gmail.com

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Abstract

Background: Treatment of hip disorders during active hip tuberculosis has long been a controversial issue. Some authors have reported performing hip replacement with different strategies with very good outcomes. This study aimed to describe the surgical outcomes and necessary conditions for total hip replacement in active hip tuberculosis. **Methods:** We conducted a quasi-experimental study. The study enrolled 40 patients with 42 active tuberculosis hips at stage IV treated by total hip replacement from October 2016 to December 2019 at the National Lung Hospital. We followed up with the patients for at least 12 months, evaluated surgical outcomes, and investigated the factors associated with these outcomes by logistic regression analysis. **Results:** Surgical outcomes showed that 37 patients (88.1%) had excellent hip function, no abscesses, and no sinus tract formation. Four cases (9.5%) had sinus tract formations. One case (2.4%) had good hip function. Binary logistic regression models revealed that sinus tract formation was associated with preoperative tuberculosis infection syndrome. The average time to obtain antituberculosis drug treatment preoperatively was 4.6 weeks. **Conclusion:** Total hip replacement for active hip tuberculosis is a practical and promising treatment method. Surgeons should consider improving patients' conditions before performing total hip replacement, administering antitubercular drugs, and arthrotomy to eliminate all abscesses, and decrease the risk of tuberculosis infection syndrome and the inflammatory response.

Keywords

Active Hip Tuberculosis, Stage IV, Total Hip Replacement

1. Introduction

Hip tuberculosis constitutes approximately 15% - 20% of all osteoarticular tuberculosis cases [1] and is the second most common site of osteoarticular involvement after the spine.

According to Babhulkar *et al.* and Saraf *et al.* [1] [2], early diagnosis and effective chemotherapy are vital to saving the joint. Procedures for diagnosis include diagnostic imaging, histopathology and mycobacteria tuberculosis detection from hip necrotic tissues [1] [2] [3].

Treatment of patients with advanced tuberculous arthritis of the hip is controversial. The surgical options include excision arthroplasty, arthrodesis, and total hip replacement (THR). Although THR remains controversial, it shows the best outcome in treating patients with stage IV hip tuberculosis [2] [4] [5].

There have been several studies discussing total hip replacement in hip tuberculosis. Some authors advocate hip replacement during the healed stage [6] [7] [8], while others believe that THR should be performed in active hip tuberculosis [9]-[19]. Bi *et al.* (2014) presented a study of 12 active advanced hip TB patients who had radical debridement and total hip replacement in one stage with a good result, no prosthesis shift, prosthesis loosening, or sinus tract formation [17]. Li *et al.* (2016) studied nine active advanced hip TB replacements and suggested performing an extensive, two-stage total hip replacement for patients with sinus tract formation or hip destruction, which features the difficulty of thorough debridement in one operation [19].

The remaining considerations of THR in active hip tuberculosis are prosthetic joint infection and unstable prosthetic joints due to gross bone loss leading to hip dysfunction after THR. Choosing between one- and two-stage replacement is still debatable. We assumed that THR should be performed in the active phase of hip tuberculosis, but the proper conditions need to be prepared. This study aimed to determine the outcomes and necessary conditions for total hip replacement in active hip tuberculosis.

2. Subjects and Methods

Design: A quasi-experimental study was applied for this study.

Subjects: We enrolled 40 patients with 42 active tuberculosis hips at stage IV. They were treated by the total hip replacement strategy between October 2016 and December 2019 at the National Lung Hospital, Vietnam. The study included thirty-five males and five females. The criteria of hip tuberculosis were based on clinical features, image diagnosis, and laboratory tests. The disease was confirmed postoperatively by histological examination, mycobacteria indicator tube culture (MGIT, Bactec), and molecular line probe assay to detect resistance to isoniazid and rifampicin (LPA, Hain Life Science, Germany).

The following characteristics were recorded for each patient: age, sex, diabetes mellitus, rheumatoid arthritis, corticoid dependence, pulmonary tuberculosis, tuberculosis infection syndrome, serum CRP (C-reactive protein) level, intra-ar-

ticular abscess (checked on MRI), para-articular abscess (checked on MRI), tuberculosis osteomyelitis in the acetabulum (checked on MRI), tuberculosis osteomyelitis in the neck of the femur (checked on MRI), roof destruction of the acetabulum (checked on X-rays), acetabular protrusion (checked on X-rays), neck fracture of the femur (checked on X-rays), and Harris hip score.

Tuberculosis infection syndrome is defined as signs of a patient's overall condition that the consequence of tuberculosis infection. The signs include weight loss greater than 10%, hypoalbuminemia with a serum albumin level less than 3.5 g/dl, and anemia with hemoglobin less than 13 g/dl (males) or 12 g/dl (females).

Shortly after the diagnosis of hip TB was made, patients received anti-tubercular treatment with a combination of antituberculosis drugs following the formula 2RHZE/10RHE. Rifampicin, isoniazid, pyrazinamide, and ethambutol were administered daily for the first two months, and then rifampicin, isoniazid, and ethambutol were administered daily for an additional ten months. If drug-resistant tuberculosis was detected in patients, they were treated with an individual formula with second-line antituberculosis drugs. In this study, *hip tuberculosis* at stage IV was defined as advanced tuberculosis arthritis with subluxation/dislocation. Features on radiology included gross bone destruction, joint space reduction, and wandering acetabulum [1].

There were two groups of patients (**Figure 1**): Group I: patients with intra-articular and/or para-articular abscesses (**Figure 2**). Group II: patients without abscesses in the area of tuberculosis hips. There were some differences between the 2 groups on admission: serum CRP was elevated sharply between 30 - 150 mg/dl, and tuberculosis infection syndrome was clearly revealed in Group I, while we could see a mild increase in CRP between 12 - 35 mg/dl and insufficient tuberculosis infection syndrome in Group II. Surgical procedures were different between the two groups.

3. Methods

In Group I, we performed 2-stage surgery after the patient was given antituberculosis drugs. Stage I involved arthrotomy with the Smith-Petersen approach, removal of all pus and necrotic tissues. Stage II involved total hip replacement with a posterior approach at least two weeks after stage I when sonography revealed no recurrent abscess and the serum CRP had decreased to less than 20 mg/dl (**Figure 1**).

In Group II, we performed total hip replacement in 1 stage with the posterior approach after patients had taken antituberculosis drugs for at least two weeks and the serum CRP had decreased to less than 20 mg/dl (**Figure 1**).

The patients were followed up and examined every three months to assess hip function and were checked for recurrent abscess and sinus tract formation. The final results were confirmed at least one year after the hip replacement. The Harris hip score was used to evaluate the outcomes of hip replacement. The

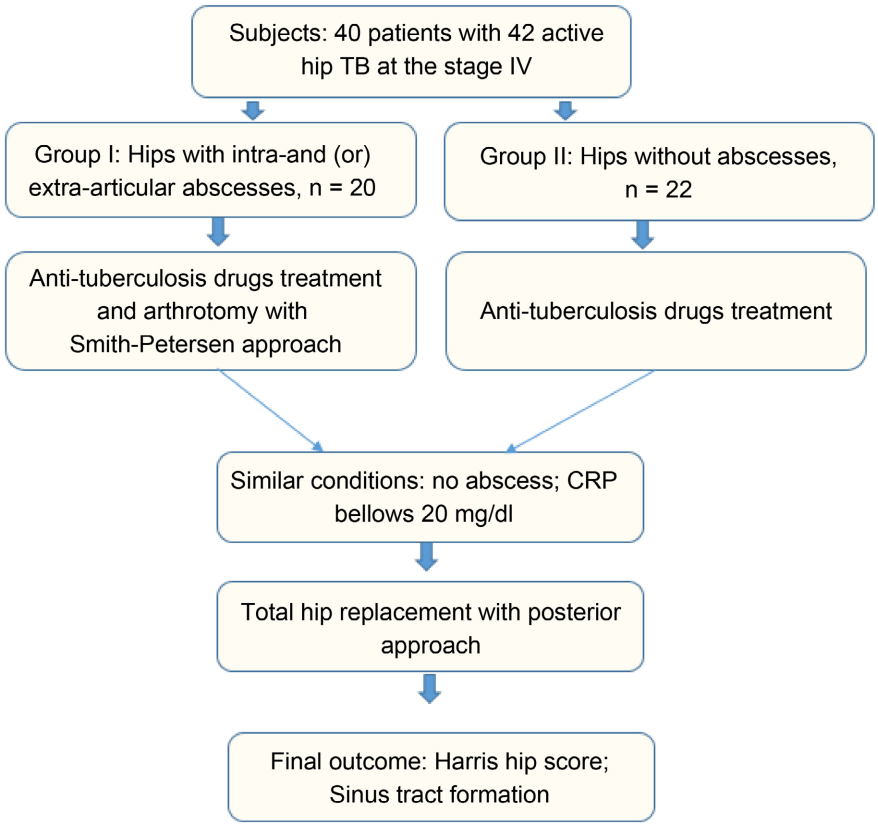

Figure 1. Process of stage IV hip tuberculosis replacement study.

Figure 2. MRI showing an abscess in the left hip; CT showing destruction in the acetabulum' medium wall and femur' head. Male, 28 years old, code: 36.

Harris hip score was measured by the Harris hip scale with ten items covering four domains, with scores ranging from 0 - 100 [20].

3.1. Main Variables and Measurements

The main outcome of our study included four levels as follows: Excellent: patients with very good hip function, Harris hip score over 90, no recurrent abscess and no sinus tract formation; Good: patients with good hip function, Harris hip score between 81 - 90, no recurrent abscess, no sinus tract or patient with hip function varied from good to very good, Harris hip score over 80, sinus tract formed but the patient did not have to undergo additional orthopedic surgery; Fair: patients with fair hip function, Harris hip score between 71 - 80 with or without sinus tract formation; Bad: patients with bad hip function, Harris hip

score under 70, recurrent abscess or fistula created, need to remove prosthetic join and have to do further orthopedic surgery.

The preoperative patient's conditions included time from tuberculosis treatment to hip replacement (weeks); inflammatory response detected by CRP, tuberculosis infection syndrome, pulmonary tuberculosis, acetabular osteomyelitis, transtrochanteric osteomyelitis, history of diabetes, rheumatoid arthritis, and corticosteroid dependence.

3.2. Statistical Analysis

Data were managed and analyzed using IBM SPSS statistics 22.0 (IBM Corp., Armonk, NY, USA). Descriptive analysis was used to estimate means and proportions. We used independent sample t-tests (two-tailed) and chi-square tests (two-tailed) to compare means and proportions. Binary logistic regression was applied to analyze the associations between sinus tract formation and other factors, including preoperative tuberculosis infection syndrome, pulmonary tuberculosis, acetabular osteomyelitis, trans-trochanteric osteomyelitis, history of diabetes, rheumatoid arthritis, and corticosteroid dependence.

3.3. Ethical Consideration

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The trial was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The patients were informed in detail about the study, and written informed consent was obtained. The study proposal was submitted to and approved by the IRB (No. 69/GCN/HĐĐĐNCYSH-ĐHYHN, dated: March 17, 2020) of Hanoi Medical University.

4. Results

There were 40 patients with 42 tuberculosis hips, with an average follow-up of 30 months (range, 14 - 50 months). Among the 42 tuberculosis hips, 20 cases had hip joint abscesses (45.2%) eradicated by arthrotomy. All patients were treated with antituberculosis drugs until the inflammatory response detected by CRP decreased below 20 mg/dl (average 9.2 ± 4.8 mg/dl) (**Table 1**).

The mean time of the total hip replacement surgery was 120 minutes. All synovial membrane was debrided. Three patients with acetabular protrusion underwent total hip replacement with an anti-protrusion cage, and the others underwent total hip replacement with a dual mobile hip supplied by Evolutis India Company (Mulund West, Mumbai, India).

The final examination showed four out of 42 cases (9.5%) had sinus tract formations, but hip function was still excellent following the Harris hip score (HHS) classification. In microbiological testing, we did not detect tuberculosis reactivation; instead, we found 3 cases of *Staphylococcus aureus* infection and

Table 1. The differences in preoperative patient characteristics between the two groups.

Preoperative characteristics	Group I	Group II	Total	P value
Number of cases	20	22	42	NA[a]
Abscess (%)	100	0	47.6	NA
Average ages (years)	48.3 ± 15.4	53.2 ± 14.1	50.9 ± 14.8	0.29*
Male proportion, n (%)	17/20 (85)	19/22 (86.4)	36/42 (85.7)	0.59**
Average CRP[b] on admission (mg/dl)	69.8 ± 35.7	19.7 ± 9.8	43.6 ± 35.8	<0.01*
Average CRP just before THR (mg/dl)	9.9 ± 4.8	8.7 ± 4.9	9.2 ± 4.8	0.44*
TB[c] infection syndromeon admission, n (%)	17/20 (85)	10/22 (45.5)	27/42 (64.3)	<0.01**
TB[c] Infection syndrome[2] just before THR[d], n (%)	4/20 (20)	5/22 (22.8)	9/42 (21.4)	0.83**
Acetabular infection n (%)	2/20 (10)	6/22 (27.3)	8/42 (19.1)	0.08**
Trans-trochanter Infection, n (%)	1/20 (5)	4/22 (18.2)	5/42 (11.9)	0.2**
Average preoperation HHS[e] (scores)	31 ± 7.4	31 ± 5.9	31 ± 6.6	0.98**
Femur neck fracture, n (%)	1/20 (5)	1/22 (4.6)	2/42 (4.8)	NA
Protrusion, n (%)	2/20 (10)	1/22 (4.6)	3/42 (7.1)	NA
THR timing[f] (weeks)	6.8 ± 5.6	2.7 ± 0.8	4.6 ± 4.4	<0.01*
Drug-resistance (n)	2 (1R[g], 1H[h])	0	2	NA

Note: [a]NA: not applicable; [b]CRP: C-reactive protein; [c]TB: tuberculosis; [d]THR: total hip replacement; [e]HHS: Harris hip score; [f]THR timing: time from taking antituberculosis drugs to total hip replacement in weeks; [g]R: Rifampicin; [h]H: Isoniazid; *Independent sample T-test, two tailed; **Chi square test, two tailed.

one case of *Enterococcus* infection (Table 2).

The binary logistic regression model revealed that chronic fistula formation was associated with preoperative tuberculosis infection syndrome but not with pulmonary tuberculosis, acetabular osteomyelitis, transtrochanteric osteomyelitis, a history of diabetes, rheumatoid arthritis, or corticosteroid dependence (Table 3).

5. Discussion

Total hip replacement was previously performed in the healed stage of hip tuberculosis, at least ten years after active tuberculosis [1]. However, when performing hip replacement in this stage, the surgeon will face many difficulties due to anatomical changes of the hip, gross destruction of the acetabulum and joint capsule, and tendon contracture. These changes are consequences of tuberculosis

Table 2. Final outcomes of hip replacement in both groups (n = 42).

Final outcomes	Total of cases (%)	Sinus tract formation	Average Harris hip score
Excellent	37 (88.1)	0	96.0 ± 2.8
Good	5 (11.9)	4	91.4 ± 3.4
Fair	0	0	NA
Bad	0	0	NA
Total	42 (100)	4	NA

Table 3. Association between sinus formation and some patient conditions (binary logistic regression analysis).

Variables	Sinus tract (cases)		P value
	Yes	No	
Total	4	38	
Diabetes mellitus	1	8	0.99
Rheumatoid arthritis	0	3	0.99
Corticoid dependence	1	7	0.26
Pulmonary tuberculosis	2	7	0.17
Tuberculosis infection syndrome before THR*	3	6	**<0.05***
Abscesses on admission	3	17	0.3
Acetabular infection before THR	0	8	0.99
Trans-trochanter infection before THR	0	5	0.99
Acetabular protrusion before THR	0	3	0.99

THR: total hip replacement. We do not present OR indices because of some limitations of this research (see limitations part below).

damage and prolonged hip dislocation. Moreover, it is difficult for patients to accept pain and loss of hip joint function for such a long interval.

Our study focused on total hip replacement in active hip tuberculosis at stage IV among 42 cases. Recently, several studies (*in vitro* and *in vivo*) proved that TB bacteria could not form biofilm materials that adhered to the surfaces of porcelain, metal, and hydroxyapatite [21] [22]. Therefore, hip replacement during active tuberculosis did not affect the antituberculosis drug's ability to kill *Mycobacteria tuberculosis*. Thus, we can place a prosthetic hip in an active tuberculosis joint. Many surgeons have performed hip replacement in the active stage with promising results [9]-[19]. However, there were a small number of cases in each study compared to our study.

There are some issues related to hip replacement in active tuberculosis to be considered. *Mycobacterium tuberculosis* causes infection of the synovial membrane, the neck of the femur, the trochanteric area, and the acetabulum. These invasions can lead to hip replacement failure. Moreover, tuberculosis synovitis

can cause ossification. If the transtrochanteric area is overspread with caseous necrosis, femoral stem loosening may occur. Acetabular infection may cause malpositioning of cup prostheses postoperatively, resulting in dislocations. According to Tiwari's systematic review [4], among the 135 hip replacement cases during the active tuberculosis period, there were four heterotrophic ossifications and two dislocations. In our study, we found that these problems could be solved. Our experience showed that it is necessary to debride synovial membranes radically to eliminate *mycobacterium* residence and avoid heterotrophic ossification. Transtrochanteric area necrosis needs to be removed by curettage. In acetabular infection cases, it is advisable to increase the cup size by 1 - 2 mm, making the cup more robust.

Attention should be given to the gross bone devastation caused by the tuberculosis bacillus, especially in the acetabulum, as it can cause failed prostheses. According to Telleria M. [23], if there is a bone loss of more than 50% of the acetabulum, an allograft or a specially designed cup will be necessary. In our study, three cases of acetabular protrusion required total hip replacement using an anti-protrusion cage (**Figure 3**). In the remaining cases, We used dual mobile hip to minimize the possibility of joint dislocation due to acetabular defect (**Figure 4**).

Findings related to *Mycobacteria tuberculosis* reactivation from Tiwari's systematic review showed that 6/135 cases had reactive tuberculosis bacteria [4]. We believe that these operations do not reactivate tuberculosis, but the bacteria that reside in the abscess are hardly killed by antituberculosis drugs and are still present. Thus, before replacing the joint, it is necessary to ensure that there is no abscess. Some authors advocate single-stage replacement with extensive debridement, removing all abscesses and caseous necrosis [17]. This idea is not

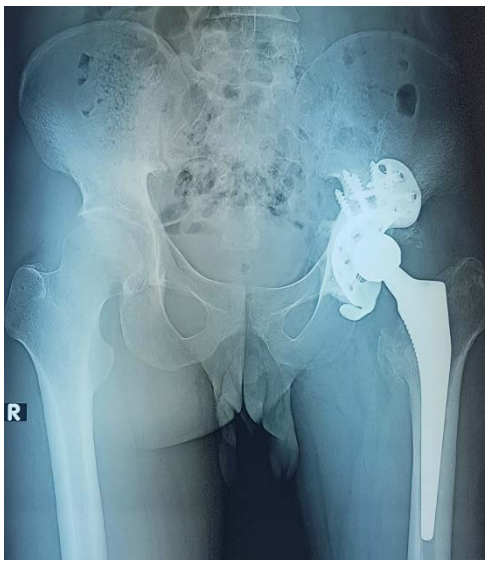

Figure 3. X-ray showing total hip replacement using an anti-protrusion cage. Male, 28 years old, code: 36.

feasible because the abscesses may not be removed in one operation.

Our study showed that 88.1% of the hip replacement cases had excellent hip function (average Harris hip score 96 ± 2.8 points, no abscess or fistula formation); 9.5% had sinus tract formations (Figure 5), and 2.4% had good hip function (HHS = 86 points) without sinus tract formation (Table 2). Compared to other studies in Tiwari's systematic review, among 135 cases of hip replacement during active tuberculosis, eight patients (5.9%) had a chronic fistula [4].

In our study, although total hip replacements were performed in conditions of no abscess, inflammatory reactions were reduced significantly, four patients still had chronic fistulas (Table 3). Bacterial culture results showed no reactivation of tuberculosis, but three samples were positive for *Staphylococcus aureus*, and one sample was positive for *Enterococcus faecalis*. The binary logistic regression model revealed that patients with chronic fistula were associated with preoperative

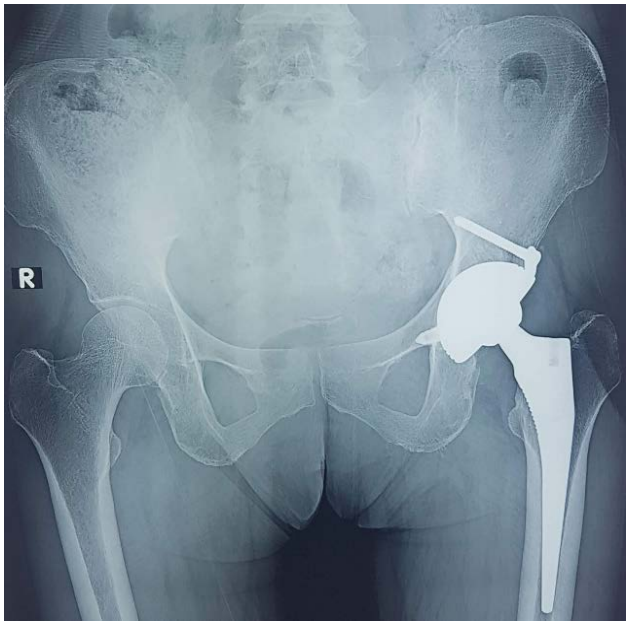

Figure 4. X-ray showing total hip replacement with a dual mobile hip. Female, 56 years old, code: 22.

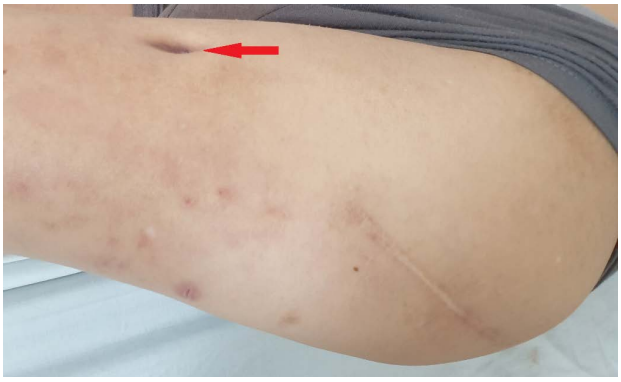

Figure 5. Fistula after total hip replacement (red arrow). Male, 46 years old, code: 08.

tuberculosis infection syndrome but not with pulmonary tuberculosis, acetabular osteomyelitis, transtrochanteric osteomyelitis, a history of diabetes, rheumatoid arthritis, or corticosteroid dependence (Table 3). These results may be explained by tuberculosis infection impairing the patient's immune system, affecting the ability to fight other bacteria, meaning that cross-infection can easily occur postoperatively. Thus, in addition to ensuring the patient's condition (*i.e.*, no abscesses and low inflammatory reaction), it is necessary to confirm that the patient overcomes the tuberculosis infection syndrome, as evidenced by weight gain, no hypoalbuminemia, and no anemia before a total hip replacement.

In this study, the mean time from receiving antituberculosis treatment to total hip replacement was 4.6 ± 4.4 weeks. That time was significantly longer in Group I (patients with hip joint abscess) than in Group II (patients without abscess) (6.8 ± 5.6 weeks and 2.7 ± 0.8 weeks, respectively). The delay in hip replacement is intended to wait for a reduced inflammatory response and to prevent abscess due to TB infection syndrome from recurring before a joint replacement.

Our findings indicated that the most critical hip replacement issues for active tuberculosis were preoperative conditions such as no abscess, antituberculosis drug treatment to reduce CRP <20 mg/dl and no tuberculosis infection syndrome.

6. Limitations

In our study, the sample size was large enough for a quasi-experimental study compared to other studies to determine the outcomes of hip replacement. However, the data were not strong enough for a logistic regression analysis. Moreover, there was no one with fair or bad results due to the small sample size; therefore, the study should be continued with a larger scale.

Our follow-up period was still short, between 14 and 50 months (average 30 months). That time is not sufficient to thoroughly assess TB infection's effects on hip replacement outcomes, so additional studies with longer follow-up times are needed.

7. Conclusion

Total hip replacement for active hip tuberculosis is a practical and promising treatment method. Surgeons should consider improving the patient's condition before performing total hip replacement, administering antitubercular drugs and arthrotomy to eliminate all abscesses, decrease the risk of tuberculosis infection syndrome, and improve the inflammatory response.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

CRP: C-reactive Protein

CT: Computed Tomography

HHS: Harris Hip Score

MRI: Magnetic Resonance Image

TB: Tuberculosis

THR: Total Hip Replacement