Hip tuberculosis at stage IV: Outcomes and some conditions for total hip replacement

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Abstract

Background: Total hip replacement during active hip tuberculosis has been a controversial issue for a long time. Some authors advocate hip replacement during the healed stage, while others believe it should be done in active hip tuberculosis. The purpose of this study was to describe the surgical outcomes, a suitable time and necessary conditions for the 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 strategy between October 2016 and December 2019 at the National Lung Hospital, Vietnam. The patients had been done total hip replacement by either one- or two-stage depending on hip abscesses to assess surgical outcomes and some factors associated with the logistic regression analysis model. The patients were then evaluated based on Harris hip score and sinus tract formation.

Results: The average follow-up was 30 months (range, 14-50 months). Surgical outcomes showed that 37 cases (88.1%) had an excellent hip function and no abscess or sinus tract formation. Four cases (9.5%) had sinus tract formations, but the hip
function was still in the excellent class by Harris hip-score (HHS). One case (2.4%) had a good hip function with a Harris hip score of 86 points, without sinus tract formation. The binary logistic regression models revealed that sinus tract formation was associated with preoperative tuberculosis infection syndrome but not associated with pulmonary tuberculosis, acetabular osteomyelitis, trans-trochanteric osteomyelitis, a history of diabetes, rheumatoid arthritis, or corticosteroid dependence. The average time from patients getting antituberculosis treatment to hip replacement was 4.6 weeks.

**Conclusion:** Total hip replacement for active hip tuberculosis was a practical and promised treatment method (excellent result: 88.1% and good: 11.9%). The surgery should be considered to improve patients' conditions pre-operation in taking antitubercular drugs, eliminating all abscesses, diminishing tuberculosis infection syndrome, inflammatory response, and choosing a suitable time of getting tuberculosis treatment.

**Keywords:** Total hip replacement, Stage IV, Active hip tuberculosis

**Background**

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. Diagnostic procedures include plain X-rays, computed tomography scan of the hips, and hip magnetic resonance imaging; taking out pus and necrotic tissues from the hip joint for tuberculosis histopathology, tuberculosis culture, and mycobacteria tuberculosis gens detection[1, 3]. Because of its insidious onset and nonspecific early findings, hip tuberculosis diagnosis is often
late after excluding other hip infections. The patients may lose the opportunity to receive appropriate treatment earlier[3].

Mycobacterium tuberculosis devastates the hip joint in many ways. They may cause synovitis, start an inflammation reaction chain. They may form intra-articular abscesses, increasing intra-articular pressure, which leads to avascular necrosis later. They may destroy the acetabulum, the femur's head and neck result in joint deformity and joint dislocation[1, 2, 4].

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 it remains controversial, THR still shows the best outcome in the treatment of patients with stage IV of hip tuberculosis[3-5]. There have been several studies discussing total hip replacement in hip tuberculosis. Some authors advocate hip replacement during healed stage[6-8], while others believe that THR should be done 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 replaced in one stage with a good result, no prosthesis shift, prosthesis loosening, or sinus tract[17]. Lee et al. (2016) studied nine active advanced hips TB replacement, suggested doing a two-stage total hip replacement for patients with sinus tract or hip destroyed extensively with the difficulty of thorough debridement at one operation[19].

The remained considers of THR in active hip tuberculosis are prosthetic joint infection, unstable prosthetic joint due to gross bone loss leading to hip dysfunction after THR. The right timing for hip replacement and choosing between one-stage replacement and two-stage replacement is still debatable. We assumed that THR should be done in the active phase of hip tuberculosis, but we need to prepare the proper conditions. This study aimed to determine the outcomes and necessary conditions for the total hip replacement in active hip tuberculosis.
Subjects and Methods

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

Figure 1: Process of stage IV hip tuberculosis replacement

Subjects: We enrolled 40 patients with 42 active tuberculosis hips at stage IV. They were treated by 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. Criteria of hip tuberculosis based on clinical features, images diagnosis, and laboratory tests before surgery. 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 patient's demographic characteristics were recorded: age, sex, diabetes mellitus, rheumatoid arthritis, corticoid dependence, pulmonary tuberculosis, tuberculosis infection syndrome, Serum C-reactive protein lever, intra-articular abscess (checked on MRI), para-articular abscess (checked on MRI), tuberculosis osteomyelitis in the acetabulum (checked on MRI), tuberculosis osteomyelitis in femur's neck (checked on MRI), acetabulum's roof destruction (checked on X-rays), acetabular protrusion (checked on X-rays), femur's neck fracture (checked on X-rays), and Harris hip score.

*Tuberculosis infection syndrome* is defined as signs of a patients' overall condition, which is the consequence of tuberculosis infection. They include weight loss of more than 10% of the patient's average weight, hypoalbuminemia with serum albumin lever under 3.5 g/dl, and anaemia with haemoglobin less than 13g/dl (males) or 12g/dl (females).

Shortly after the diagnosis of hip TB was carried out, patients received antitubercular treatment with a combination of antituberculosis drugs following the formula 2RHZE/10RHE. Rifampicin, Isoniazid, Pyrazinamide, and Ethambutol were taking daily in the first two months, then Rifampicin, Isoniazid, and Ethambutol were taking daily in further ten months. If the patients had been detected drug resistance tuberculosis, they would be treated by 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 include gross bone destruction, joint space reduction, and wandering acetabulum[1].

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

**Methods**

In group I, we performed 2-stage surgery after taking antituberculosis drugs. Stage I: arthrotomy with Smith-Petersen approach, removed all pus, necrotic tissues, assessed quality of mineral density of acetabular and femur's neck. Patients did not need to do Girdstone's excision or filling in a cement spacer. Stage II: total hip replacement with posterior approach after stage I at least two weeks when sonography revealed no recurrent abscess, serum CRP decreased less than 20 mg/dl. In group II, we performed the total hip replacement in 1 stage with the posterior approach; after taking antituberculosis drugs for at least two weeks, serum CRP decreased to under 20 mg/dl.

The patients were followed-up and examined every three months to assess hip function, hip pain, checked for recurrent abscess and sinus tract formation. Final results were confirmed at least one year after replacement. Harris hip-score was used to evaluate outcomes of hip replacement. Harris hip score was measured by the Harris hip scale with ten items covering four domains ranging from 0-100 scores[20].

**Main variables and measurements**
The main outcome of our study included four levels as below: 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 was over 80, sinus tract formed but the patient did not have to undergo additional orthopaedic surgery; Fair: Patients with fair hip function, Harris hip-score was 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 orthopaedic surgery.

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

Statistical analysis
Data were managed and analysed using SPSS software (version 22.0). Descriptive analysis was used to estimate means and proportions. We used Independent Sample T-Test (two-tailed) and Chi-square test (two-tailed) to compare means and proportion. A binary logistic regression was applied to analyse the association between sinus tract formation, and some factors include preoperative tuberculosis infection syndrome, pulmonary tuberculosis, acetabular osteomyelitis, transf trochanteric osteomyelitis, history of diabetes, rheumatoid arthritis, and corticosteroid dependence.

Ethical consideration
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:
3. Results

There were 40 patients with 42 tuberculosis hips, an average follow-up of 30 months (range, 14–50 months). Among 42 tuberculosis hips, there were 20 cases with hip joint abscesses (45.2%) eradicated by arthrotomy; eight cases (19.1%) with acetabular tuberculosis osteomyelitis remained; five cases (11.9%) with trans-trochanteric tuberculosis osteomyelitis remained. All patients were treated with antituberculosis drugs until the inflammatory response detected by CRP decreased below 20 mg/dl (average $9.3\pm4.8$ mg/dl). The number of patients who had tuberculosis infection syndrome decreased from 27 cases (64.3%) on admission to nine cases (21.4%) before total hip replacement. All patients had a poor hip function, with the average Harris hip score was $31\pm6.6$ points (Min 18 points; Max 42 points) (Table 1).

The mean time from patients receiving antitubercular treatment to total hip replacement was $4.6 \pm 4.4$ weeks. That time was significantly longer in group I (patients with hip joint abscess) as compared to group II (patients without abscess) ($6.8 \pm 5.6$ weeks and $2.7 \pm 0.8$ weeks, respectively).

The mean time of total hip replacement surgery was 120 minutes. All synovial membrane was debrided. Three cases with acetabular protrusion had a total hip replacement with an anti-protrusion cage, and the others had a total hip replacement with a dual mobile hip supplied by Evolutis Company, France.

The final examination showed 37 out of 42 cases (88.1%) had excellent hip function, the average Harris hip score $96\pm2.8$ points, no abscess or fistula formation. Four out of 42 cases (9.5%) had sinus tract formations, but the hip function was still excellent
following the Harris hip-score (HHS) classification. Doing microbiological testing, we did not detect tuberculosis's reactivation; instead, we found 3 cases of Staphylococcus aureus infection and one case of Enterococcus infection. One out of 42 cases (2.4%) had good hip function (HHS was 86 points) without sinus tract formation (Table 2). The binary logistic regression model revealed that chronic fistula formation was associated with preoperative tuberculosis infection syndrome but not associated with pulmonary tuberculosis, acetabular osteomyelitis, trans-trochanteric osteomyelitis, a history of diabetes, rheumatoid arthritis, or corticosteroid dependence (Table 3).

Table 1: The differences of pre-operation patient's characteristics between two groups

<table>
<thead>
<tr>
<th>Pre-operation patient’s characteristics</th>
<th>Group I</th>
<th>Group II</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>20</td>
<td>22</td>
<td>42</td>
<td>NA</td>
</tr>
<tr>
<td>Abscess (%)</td>
<td>100</td>
<td>0</td>
<td>47.6</td>
<td>NA</td>
</tr>
<tr>
<td>Average ages (years)</td>
<td>48.3±15.4</td>
<td>53.2±14.1</td>
<td>50.9±14.8</td>
<td>0.29*</td>
</tr>
<tr>
<td>Male proportion, n (%)</td>
<td>17/20 (85)</td>
<td>19/22(86.4)</td>
<td>36/42(85.7)</td>
<td>0.59**</td>
</tr>
<tr>
<td>Average CRP on admission (mg/dl)</td>
<td>69.8±35.7</td>
<td>19.7±9.8</td>
<td>43.6±35.8</td>
<td>&lt; 0.01*</td>
</tr>
<tr>
<td>Average CRP before THR (mg/dl)</td>
<td>9.9±4.8</td>
<td>8.7±4.9</td>
<td>9.2±4.8</td>
<td>0.44*</td>
</tr>
<tr>
<td>TB infection syndrome* on admission, n (%)</td>
<td>17/20 (85)</td>
<td>10/22 (45.5)</td>
<td>27/42 (64.3)</td>
<td>&lt;0.01**</td>
</tr>
<tr>
<td>Condition</td>
<td>20 Cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>----------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB Infection syndrome before THR</td>
<td>4/20 (20)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetabular infection</td>
<td>2/20 (10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trans-trochanter Infection</td>
<td>1/20 (5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Pre-operation HHS (scores)</td>
<td>31±7.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femur neck fracture</td>
<td>1/20 (5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protrusion</td>
<td>2/20 (10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>THR timing (weeks)</td>
<td>6.8±5.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug-resistance</td>
<td>2 (1R, 1H)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note:

NA: Not applicable

1*: Abscesses: including patients who had intra-articular and (or) para-articular abscesses.

2*: TB infection syndrome: patients with tuberculosis infection syndrome.

3*: THR: total hip replacement.

4*: Acetabular infection: patients had acetabular tuberculosis osteomyelitis

5*: Trans-trochanter infection: patients had tuberculosis osteomyelitis in the transtrochanteric area

6*: Pre-operation HHS: Harris hip score pre-operation

7*: Femur neck fracture: patients with femur neck fracture due to hip tuberculosis pre-operation
8*: Protrusion: patients with acetabular protrusion pre-operation
9*: THR timing: time from taking antituberculosis drugs to total hip replacement by weeks
10*: Drugs resistance: patients who had mycobacterium tuberculosis resist at least 1 in 4 antituberculosis drugs include: rifampicin (R), isoniazid (H), pyrazinamide (Z), and ethambutol (E).

*: Independent sample T-test, two tailed
**: Chi square test, two tailed

Table 2: Final outcome of hip replacement in both groups (n=42)

<table>
<thead>
<tr>
<th>Final outcomes</th>
<th>Total of cases (%)</th>
<th>Sinus tract formation</th>
<th>Average Harris hip score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>37 (88.1)</td>
<td>0</td>
<td>96.0±2.8</td>
</tr>
<tr>
<td>Good</td>
<td>5 (11.9)</td>
<td>4</td>
<td>91.4±3.4</td>
</tr>
<tr>
<td>Fair</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Bad</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Total</td>
<td>42 (100)</td>
<td>4</td>
<td>NA</td>
</tr>
</tbody>
</table>

Table 3: The association between sinus formation and some patient’s conditions
(Binary logistic regression analysis)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Sinus tract (cases)</th>
<th>(P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>38</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Corticoid dependence</td>
<td>1</td>
<td>7</td>
</tr>
</tbody>
</table>
### 4. Discussion

According to Babukar et al. (2002), hip tuberculosis is divided into four stages [1], then Tuli et al. (2010) modified Babukar's classification[21]. Thus, *hip tuberculosis* at stage IV is defined as advanced tuberculosis arthritis with subluxation/dislocation. Features on radiology include gross destruction, reduction of joint space, and wandering acetabulum[21].

According to Saraf et al. (2015), a surgical treatment for hip tuberculosis at stage IV includes debridement, arthrodesis, resection arthroplasty, and hip replacement combined with a specific period of antituberculosis therapy[2]. Arthrodesis is no longer popular because of its inconvenience. After arthrodesis, patients could not do some basic movements such as squatting, kneeling, and sitting cross-legged. Besides, it may lead to progressive degeneration of the lumbar spine and adjacent joints[22-24]. In recent years, arthrodesis is considered a temporary treatment for severe hip infection patients, preparing necessary conditions for total hip replacement[25].

The excision arthroplasty provides a mobile, painless hip joint with control of infection and deformity correction[26]. However, a significant shortening of the limb and instability occurred, making patients depend on a crutch.
Total hip replacement was previously performed in the healed stage of hip tuberculosis, at least ten years after active tuberculosis[1]. However, doing hip replacement in this stage, the surgeon will face many difficulties due to anatomical changes of the hip, gross destruction of the acetabulum, joint capsule, and tendons contracture. These changes are consequences of tuberculosis damage and prolonged hip dislocation. On the other hand, the patients can hardly accept pain and loss of hip joint function for too long.

Our study focused on the 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-material for adhering to the surface of porcelain, metal, hydroxyapatite [27, 28]. Therefore, Hip replacement during active tuberculosis did not affect the antituberculosis drug's ability to kill mycobacteria tuberculosis. We can replace the prosthetic hip in the active tuberculosis joint. Many surgeons had performed the hip replacement in the active stage with promising results[11-19]. However, there were a small number of cases in each study as 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, femur's neck, trochanteric area, and acetabulum. These invading can lead to hip replacement failure. Tuberculosis synovitis can cause ossification. If the trans-trochanteric area is overspread with caseous necrosis, femoral stem loosening may occur. Acetabular infection may cause malposition of cup prosthesis postoperatively, which results in dislocations. According to Tiwari's systematic review, among the total of 135 cases of hip replacement during the active tuberculosis period had four heterotrophic ossifications, two dislocations[5]. In our study, we found that these above problems can be solved. Our experience showed that it is necessary to debride radically synovial membrane to eliminate
mycobacterium residence and avoid heterotrophic ossification. Trans-trochanteric area necrosis needs to remove by curettage. In the acetabular infection cases, it is wider to increase the cup size by 1-2 mm, making the cup more robust.

Attention should be paid to the gross bone devastation caused by the tuberculosis bacillus, especially in the acetabulum, as it can cause fail prosthesis. If there is a bone loss of more than 50% acetabulum, it is necessary to have allograft or use a specially designed cup. In our study, three cases of acetabular protrusion had a total hip replaced using an anti-protrusion cage.

Findings related to mycobacteria tuberculosis's reactivation from Tiwari's systematic review showed that 6/135 cases had reactive tuberculosis bacteria[5]. We believed that these are not reactivating tuberculosis, but the bacteria that reside in the abscess are hardly killed by antituberculosis drugs and still exist. 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. That idea is not feasible because abscesses may not be removed in one operation.

Our study showed that 88.1% of the hip replacement cases had excellent hip function (the average Harris hip score 96±2.8 points, no abscess or fistula formation); 9.5% had sinus tract formations, and 2.4% had good hip function (HHS=86 points) without sinus tract formation. As 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[5].

In our study, although total hip replacements had been done in conditions of no abscess, inflammatory reactions reduce significantly, there were still four patients who got chronic fistula. 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 tuberculosis infection syndrome but not associated with pulmonary tuberculosis, acetabular osteomyelitis, trans-trochanteric osteomyelitis, a history of diabetes, rheumatoid arthritis, or corticosteroid dependence. That results may be explained as tuberculosis infection impaired the patient's immune system, affecting the ability to fight other bacteria, so it is easy to have cross-infection postoperatively. Thus, in addition to ensuring the patient's conditions of no abscesses and low inflammation reaction, it is necessary to confirm that the patient comes over the tuberculosis infection syndrome by weight-gained, no hypoalbuminemia, and no anaemia before 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) as compared to 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 reduced inflammatory response and TB infection syndrome as well as not to recur an abscess before a joint replacement.

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

**Limitations:**

In our study, the study subjects included 40 patients with 42 hips with stage IV tuberculosis. The sample size is large enough for a quasi-experimental study as compared to other studies to find out the outcomes of hip replacement [Ref.]. However, it is not strong enough for the logistic regression analysis. On the other hand, there was no one with moderate 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 to 50 months (average 30 months). That time was not enough to thoroughly assess TB infection's effects on hip replacement outcomes, so additional studies with longer follow-up times are needed.

Figure 2: MRI showing Intra-articular abscess (red arrow) and para-articular abscess (yellow arrow) in the left hip. Male, 28-year-old, code: 16.

Figure 3: MRI and CT- scanner showing abscess (yellow arrow) and femur's neck fracture (blue arrow). Male, 67 year-olds, code:09.
Figure 4: X-ray showing total hip replacement using an anti-protrusion cage, long stem in the left hip. M, 39 year-olds, code: 04, protrusion acetabulum, subtrochanteric fracture due to trans-trochanteric osteomyelitis).

Figure 5: X-ray showing total hip replacement with a dual mobile hip. Female, 49 year-olds, code: 35.
Figure 6: Fistula after a total hip replacement (red arrow). Male, 46 year-olds, code: 38.

5. Conclusions

Total hip replacement for active hip tuberculosis was a practical and promised treatment method (excellent result: 88.1% and good: 11.9%). The surgery should be considered to improve the conditions of patients' pre-operation in taking anti-tubercular drugs, eliminating all abscesses, diminishing tuberculosis infection syndrome, inflammatory response, and choosing a suitable time of getting tuberculosis treatment.

Abbreviations

CRP: C-reactive protein

CT: Computed Tomography

HHS: Harris Hip Score

MRI: Magnetic Resonance Image

TB: Tuberculosis

THR: Total Hip Replacement
References


