A Review Paper

Historical Perspective on Two-Stage Reimplantation for Infection After Total Hip Arthroplasty at Hospital for Special Surgery, New York City

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Abstract

In this article, we report on our use of a 2-stage exchange in managing infected total hip arthroplasties (THAs) at the Hospital for Special Surgery in New York City. This protocol involves resection arthroplasty, 6 weeks of intravenous antibiotics to obtain a minimum "postpeak" serum bactericidal titer (SBT) of 1:8, and reimplantation.

Over the past 20 years, we have conducted several studies showing the effectiveness of this treatment. Since our previous report was published in 1994, prevalence of multidrug-resistant (MDR) organisms has increased significantly. In 2008, we set out to determine if 2-stage exchange remains an effective treatment for newer pathogens, many of which are MDR.

The overall eradication rate was 95% (80/84 hips). All 21 MDR pathogens implicated in the infected THAs were eradicated. We conclude that 2-stage exchange with a standard 1:8 minimum SBT remains an effective treatment even when resistant infections are involved.

Infection, a devastating complication of total hip arthroplasty (THA), not only is a problem for patients but also poses challenges for orthopedic surgeons. In this article, we report on our long-term experience in preventing and managing post-THA infection at the Hospital for Special Surgery (HSS) in New York City. We describe our successes and failures and what we believe are key factors in complete eradication of periprosthetic infection, particularly in the light of increasing antibiotic resistance.

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Early Experience With Infected THAs

The first THA was performed at HSS in August 1967. At that time, a lateral, transtrochanteric approach was used; the surgical technique was crude, instrumentation was primitive, and prosthetic components were very limited in number, shape, and size. There was no experience in use of acrylic cement. Each operation lasted an entire morning, and only 1 case was performed in a day (seldom 2), which meant an entire day of surgery. Only patients with extreme pain and disability were considered for THA, and they were carefully informed of the very limited experience with this operation, which was considered experimental.

The surgical team wore washable, reusable linen head covers, masks, gowns, and drapes. The surgery was performed in conventional operating rooms and antibiotic prophylaxis was not used. The infection rate for the first 100 McKee-Farrar THAs (August 1967–August 1969) was 11%.[1]

That rate decreased to 2% for the first 100 Charnley THAs (October 1968–October 1980).[2] Both infections occurred when antibiotic prophylaxis was not used (first 13 cases). Given this high infection rate, we instituted a policy of routine administration of perioperative antibiotics beginning in December 1969.[3]

In the 1960s, Charnley[4] pioneered performing THA in an enclosure having a vertical flow of ultraclean air. The surgical team wore "space suits" with impervious exhaust gowns. Instruments were divided and placed in trays that were to be opened sequentially, only as they became needed during the operation, to minimize environmental exposure and bacterial contamination. Taking these measures, and without administering perioperative antibiotics, Charnley reduced the deep infection rate in the Hip Center at Wrightington Hospital, Wigan, England, from between 7% and 9% to less than 1%.[5,6]

Diagnosis and Management of Infected THAs

Dr. Salvati was in charge of the Hip Clinic at HSS in the early years of THA. Experience with many

early infections generated a large amount of clinical information on diagnosing and managing deep infection after THA. Although some infections were obvious (systemic symptoms, wound inflammation, wound drainage, abnormal laboratory tests, positive cultures), others were subacute and difficult to diagnose. Aside from persistent hip pain, no features suggested infection.

At that time, the accepted treatment for deep infection after THA was removal of prosthetic components, acrylic cement, and trochanteric wires; excision of inflamed and devitalized tissues; and wound closure, primary or secondary depending on degree of inflammation. Bed rest and skeletal traction were continued for 3 weeks, until the hip was adequately scarred. Walker ambulation then began, which progressed to ambulation with crutches and weight-bearing as tolerated. This resection arthroplasty, or Girdlestone procedure, resulted in mild to moderate hip pain, fair motion, poor muscle power, shortening by 2 inches, abductor lurch, and overall functional disability.[7,8] For patients who underwent resection arthroplasty, oxygen use during ambulation was similar to that of patients who underwent above-knee amputation.[9] Although some patients accepted this outcome, many were unhappy and demanded additional surgery to address their disability.

In 1970 in Hamburg, Germany, Buchholz and Engelbrecht[10] pioneered use of antibiotic-impregnated cement in 1-stage reimplantation of THA after infection. They found that antibiotics eluted from cement in therapeutic amounts (high local concentrations). In 1981, Buchholz and colleagues[11] reported on their extensive experience in performing 1-stage reimplantation.

Their early experience encouraged us to take a similar approach with patients who were unwilling to accept resection arthroplasty, although at the time there was worldwide consensus that reimplantation after infected THA was contraindicated. In 1974, we reported on experience with our first 19 cases; we reimplanted 14 of these in 1-stage and 5 in 2-stages.[12] After a minimum follow-up of 2 years, 17 cases had no evidence of infection, and the outcomes of these 17 cases were superior to those of resection arthroplasty. Perioperative intravenous (IV) antibiotic therapy was administered for several days to a few weeks and then oral antibiotics for a mean of 3 months (range, 1 week–15 months). Of the pair of infections that recurred, 1 was caused by *Pseudomonas aeruginosa* and the other by *Staphylococcus epidermidis*.

In 1976, we were the first to report on hematogenous seeding of infections in THA after dental procedures.[13] This breakthrough idea was received with skepticism but, after several years, became widely accepted, and routine administration of prophylactic antibiotics before dental work became a standard of care.

During our early experience with infected THAs, antibiotic therapy was not standardized or monitored by an infectious diseases specialist. In addition, recommendations made in the literature were conflicting.[14] In 1975, we recruited an infectious diseases specialist to consult on all deep infections after total joint arthroplasty. This consultant standardized antibiotic therapy according to the quantitative sensitivities of the infecting bacteria.

Under the leadership of this physician, and drawing on our experience in managing other deep-tissue infections, such as bacterial endocarditis, we applied the basic tenets of orthopedic surgery and infectious diseases to the design of an innovative protocol for managing infected joint prostheses. This regimen, which we have been using for more than 30 years now, has 4 essential elements: (1) prosthesis removal with meticulous debridement of foreign materials and nonviable tissues, (2) 6-week course of antibiotic therapy after prosthesis removal and before reimplantation, (3) bactericidal antibacterial therapy (if possible), and (4) quantitated, standardized antimicrobial therapy potency (antimicrobial therapy quantitated to provide minimum 8-fold bactericidal potency and standardized so that a broad spectrum of pathogens would be managed with an equally potent minimum standard of effective therapy even though the sensitivity/resistance patterns of the pathogens differed). Using this approach, we have achieved remarkably consistent good outcomes for THAs (90%-95% cure rates) and total knee arthroplasties (95%-97% cure rates) in patients with both sensitive and relatively resistant pathogens, methicillin-resistant *Staphylococcus aureus* (MRSA) in particular.[15-20]

Four Essential Elements

1. Prosthesis Removal. Meticulous debridement should be performed to remove the prosthesis and any polymethylmethacrylate (PMMA) cement. As prosthesis retention and a finite course of systemic antibiotic therapy were reported to fail as a regimen in more than 80% of cases,[21] we remove the prosthesis. In addition, though in most cases tissue-adherent PMMA cannot be entirely removed, we think the highly focused attempt to remove as much cement as possible may play a major role in eliminating any biofilms. Removing all foreign bodies, including joint prosthesis and PMMA, is important in creating a tissue environment that is optimal for eradicating pathogens. Comprehensive debridement should result in any biofilms being extensively disrupted, if not substantially removed. Biofilms create an environment that protects pathogens; therefore, removal of these materials (membranes, mucous layers, other matrix substances) increases the likelihood that an invading microorganism will be eradicated.

2. 6-Week Course of Antibiotic Therapy. A course of 6 weeks' duration was based on the success of antibiotic regimens used for osteomyelitis and bacterial endocarditis. This duration may be critical for the efficacy of therapy. In similar approaches, antibiotics are administered for only 2 weeks before reimplantation. With this shorter protocol, however, the pathogen was eradicated in only 79% of cases, and only 35% of patients obtained good function with the new prosthesis.[22]

3. Bactericidal Antibacterial Therapy. The rationale for preferentially designing bactericidal antibiotic therapy was based on success rates for management of infections with characteristics similar to those of our patients with joint prostheses. Osseous tissues have a paucity of resident polymorphonuclear leukocytes, and often neutrophils are not high in number even in the presence of a fulminant bone infection. In clinical situations in which infected tissues have few or no polymorphonuclear leukocytes, bactericidal antibiotic therapy is preferred. The reasoning is that therapy is needed to kill the pathogen directly instead of only inhibiting the growth of the microbe and "relying" on the patient's neutrophils and other phagocytes to kill the damaged but still viable organism. Infected cardiac valvular vegetations have very few neutrophils, and neutropenic patients often have no demonstrable circulating neutrophils to combat their bacteremias. Bactericidal antibiotic therapy has higher success rates and better outcomes in patients with bacterial endocarditis and in patients with severe neutropenia and bacteremia. We should expect the same advantage in treating our patients with prosthetic joints and bone infections.

4. Quantitated and Standardized Antimicrobial Therapy Potency. Systemic antibiotic potency against an infecting pathogen should be tested using a quantitative serum bactericidal test. Quantitating the potency of the therapies we design is a reasonable and sensible response to managing infections in an environment of steadily increasing microbial resistance to the medications we use. The serum bactericidal titer (SBT), the Schlichter test, provides a specific standard of potency for all aerobic bacterial pathogens. The test is labor-intensive and costly. For several decades, SBT reproducibility was not uniform, but the methods are now standardized.[23] SBT represents an attempt to standardize the effective potency of antibiotic therapy. We empirically chose an SBT of 1:8, drawn at a point 25% into the time interval between antibiotic doses, a "postpeak" time, in an attempt to have 1 blood study represent the potency of the entire time interval between antibiotic doses. This quantitation was designed to mimic the SBT of 1:8, which was used to confirm adequate potency of continuous drip IV penicillin G during the initial decades of successful management of streptococcal endocarditis.

Postpeak time points are 1 hour after dosing a medication that is given every 4 hours; 1.5 hours after dosing a medication given every 6 hours; 2 hours after dosing a medication given every 8 hours; 3 hours after dosing a medication given every 12 hours; and 6 hours after dosing a medication given every 24 hours. With SBT, the goal is to obtain a minimum 1:8 titer against all infecting aerobic bacteria, in which case both gram-positive bacteria, including MRSA and enterococci, and gram-negative bacilli, including *P aeruginosa,* may be eliminated if the specific sensitivity of each isolate allows eradication. As we achieved good outcomes with a high percentage of infections using the postpeak SBT of 1:8, we never studied success rates with lower SBTs (1:4 or 1:2). Therefore, we cannot be certain that a 1:8 titer is the only effective potency level. It is possible that lesser titers could be effective, but this possibility has not been evaluated.

As a testament to its success, the 2-stage removal/reimplantation protocol has remained virtually unchanged since 1976, except for the addition of antibiotic-loaded PMMA when cemented prostheses are used for reimplantation.[17]

When we established our new protocol, there was no consensus about the significance of positive cultures of low virulent bacteria obtained by hip aspiration. Some orthopedic surgeons thought that low virulent bacteria, such as *S epidermidis* and *Propionibacterium acnes,* could not cause deep periprosthetic infection (personal communication, F. Stinchfield, closed meeting of Hip Society, 1979, New York, NY). In contrast, other orthopedic surgeons started to report success in reimplantation after deep periprosthetic infections in which laboratory growths from operative specimens were caused by cultural contamination and not true infection. Thus, in the late 1970s, we designed a classification system that can help in diagnosing prosthetic joint infections. In this system, points are assigned on the basis of presence of clinical symptoms and signs, wound status, radiology and hematology results, bacteriology, histopathology, and intraoperative findings regarding tissue status.[24]

Recent Experience With Infected THAs

In 1994, we reported on our experience in performing 2-stage reimplantation to manage infected THAs.[17] We evaluated 46 hips in 44 patients. All patients were treated with resection arthroplasty and a 6-week course of IV antibiotics in doses sufficient to obtain postpeak SBT of at least 1:8. An infectious diseases consultant chose antibiotics on the basis of type and sensitivity of infecting organism. After reimplantation, patients received IV antibiotics until intraopera-

tive cultures were reported negative. Of the 46 hips, 32 (69.6%) underwent successful reimplantation.

By the minimum follow-up of 2 years, 3 infections (9.4%) recurred in the reimplanted group. One patient was treated with oral suppressive antibiotics (clinical results were poor), 1 was treated with IV antibiotics and oral suppressive antibiotics (good clinical results), and 1 was treated with debridement and antibiotics suppression (good clinical results). In all 3 cases, infection recurred less than 1 year after reimplantation. A minimum postpeak SBT of 1:8 was obtained in 28 of the 32 reimplanted hips. Infection recurred in only 1 of these 28 hips. In contrast, 2 of 4 hips with inadequate postpeak SBT had an infection recur. The difference was statistically significant (P = .035). We did not find that delayed reimplantation prevented infection from recurring.

Causes for not reimplanting were severe acetabular bone loss, recurrent local infection, poor wound healing with prolonged postoperative drainage, limited duration of antibiotic therapy secondary to diarrhea, inadequate antibiotic levels, femoral fracture that required femoral intramedullary rodding, 3 sacral decubitus ulcers, and limited rehabilitation expectations. The 1 patient (7%) who became reinfected despite resection arthroplasty was treated with IV antibiotic therapy. Two years later, this patient received antibiotic suppression for a recurrent infection.

In recent years, multidrug-resistant (MDR) organisms have become significantly more prevalent.[25] In 2009, we reported on our experience in managing MDR infections in an effort to determine whether 2-stage reimplantation remains effective treatment for these new infections.[19] Of 104 patients with a minimum follow-up of 2 years, 87 entered the protocol, and 82 (94.3%) of these underwent successful reimplantation surgery without recurrence of infection. The higher reimplantation rate may be the result of improved cemented and cementless reconstruction techniques and advances in use of allograft bone and augments.

After implant removal, patients were given IV antibiotics for 6 weeks in doses sufficient to obtain postpeak SBT of at least 1:8. Infection was eradicated in 78 of the 82 patients (80/84 hips; 95.2% success rate) who completed the 2-stage protocol. Total proportion of MDR organisms was 25.0% (21/84). All 21 hips (100%) with MDR infections were successfully managed, including 12 methicillin/oxacillin-resistant strains of *S epidermidis,* 7 methicillin/oxacillin-resistant strains of *S aureus,* and 2 vancomycin-resistant strains of *Enterococci bacteria*. There was no significant difference in infecting organism (P = .92) or medication resistance (P = .57) between patients whose infections were and were not eradicated. Our study results support efficacy of a 2-stage reimplantation protocol with a standardized 1:8 minimum antibiotic SBT for managing periprosthetic infections of the hip, including MDR infections.

Conclusion

Over the past 40 years, prevention and management of infected THAs have changed significantly. Innovations, such as routinely administering perioperative antibiotics, performing THAs with ultraclean air vertically flowing in the operating room, using "space suits" with impervious exhaust gowns, and dividing instruments in trays to be opened when needed during the operation, have reduced rate of infection from 11% to less than 1%. In addition, the change from resection arthroplasty to 1-stage reimplantation to 2-stage reimplantation has significantly improved our ability to manage deep infections.

An important aspect of our 2-stage reimplantation protocol is its focus on obtaining a minimum postpeak SBT of 1:8. Using this antimicrobial potency standardization, we and others using this protocol have had equally high rates of successful outcomes with methicillin-resistant and methicillin-susceptible staphylococcal prosthetic hip infections.[19,26] Those using different approaches have had substantially lower rates of success in managing methicillin-resistant staphylococci compared with methicillin-sensitive staphylococci in this setting.[27,28]

Using a postpeak SBT of 1:8, we have been providing consistently successful treatment regimens for prosthetic joint infections despite the emergence of progressively less sensitive bacterial pathogens.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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