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Review Article

Methicillin-resistant Infection After Hip and Knee Replacement: Reason to Change Practice?

髖關節及膝關節置換術後的抗甲氧西林感染：是改變臨床治療手段的原因嗎？

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ABSTRACT

Infection after a primary total-joint replacement can be devastating. If the infecting organism is methicillin resistant, the chance of successful eradication of the infection is considerably decreased. What is more concerning is that these organisms are becoming increasingly common in periprosthetic joint infection. We have reviewed the literature and have outlined the effectiveness of single- and two-stage treatment regimens for this difficult problem. We have also looked at the screening and decolonisation methods that have been implemented in an attempt to decrease the risk of surgical site infections. Lastly, we outline our recommendations on how we should tackle this emerging and difficult problem that is affecting the orthopaedic world.

中 文 摘 要

全關節置換術後的感染之破壞性極大。若果感染的細菌為抗甲氧西林時，成功根絕感染的機會是相當之低，更使人擔心的是這類型的細菌在關節假體周圍的感染愈來愈普遍。對於這種難題，我們重新探討文獻並概述I和II期翻修術的治療方案，也仔細檢查篩選法和去细菌定植法的實施，在減少手術處感染風險之效用。最後，我們概述一些建議，應該怎樣去處理這些正在影響矯型骨科界新出現的難題。

Introduction and Background

Infections after total-joint replacement have always posed a difficult problem for the treating orthopaedic surgeons and the multidisciplinary team. Incidence rates of infection after primary total-joint replacement have historically ranged between 1% and 2%, whereas for revision procedures, they range from 3% to 4%.[1] When an infection occurs, the resulting costs can exceed three to four times the cost of a primary total-joint replacement resulting in a large financial burden to both the patient and the health care system.[2] The most common offending organisms are typically *Staphylococcus* species, namely, *Staphylococcus aureus* or *Staphylococcus epidermidis*. Decades earlier, most of these organisms were sensitive to first-line antibiotics; however, more recently, there has been an alarming trend of higher rates of methicillin-resistant infective organisms causing periprosthetic infections.

Parvizi et al[3] reported a steady increase in the prevalence of infections caused by methicillin-resistant organisms, most prominently *Staphylococcus* species. Methicillin-resistant *S aureus* (MRSA) infections were noted to increase from 16% in 1999 to 37% in 2006, and methicillin-resistant *S epidermidis* infections showed a similar increase from 11% to 25% from 1999 to 2006. They also noted that methicillin-resistant organisms became the most dominant infecting organisms within the final 3 years of the study, with the incidence of methicillin-resistant cases outnumbering the infections caused by methicillin-sensitive species. This trend is indeed worrisome.

Many reasons have been advanced to explain this increase in methicillin-resistant infections; the most common one is the liberal use of antibiotics by the medical community as a whole for the past half century. Other reasons include the increased use of invasive haemodynamic monitoring devices and the rise in the number of surviving immunocompromised patients secondary to advances in modern medical technology. We are also seeing an increase in the colonisation of methicillin-resistant organisms in the general population as well as among physicians and health care workers.

In a recently published article by Schwarzkopf et al,[4] the authors examined the prevalence of the colonisation of methicillin-sensitive and resistant *S aureus* species in the nares of orthopaedic surgeons and residents. They obtained nasal swabs from 74

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orthopaedic surgeons and 61 orthopaedic residents from a university hospital in New York and compared the colonisation rates with those of their patient population. They demonstrated similar colonisation rates among the orthopaedic surgeons, residents, and the high-risk patient population. The colonisation rates for methicillin-sensitive *S aureus* (MSSA) were 23.3% across the orthopaedic surgeons, 59.0% among the orthopaedic residents, and 18% in the sampled patient population. As for the colonisation rates of MRSA, the results showed a 2.7% prevalence rate across the orthopaedic surgeons, a similar 2.17% rate seen in the patient population, and no MRSA colonisation among the sampled orthopaedic residents. This article demonstrates the relatively high prevalence of carrier status of MSSA and MRSA among orthopaedic surgeons and residents in a typical university hospital setting, thus highlighting the importance of health care professionals to practise proper hand hygiene and other precautionary measures to minimise the risk of surgical site infection (SSI). In addition, this article shows a gradual increase in colonisation in orthopaedic surgeons as they progress from residency to practice, presumably because of more frequent exposure to patients who are carriers.

Single-stage Treatment

Completely eradicating deep periprosthetic infections remains a challenging problem faced by orthopaedic surgeons, especially in the face of increasing rates of methicillin-resistant infections. In the past, for acute periprosthetic total-joint infections, open irrigation and debridement and component retention achieved a reliable rate of infection eradication if the timing from the onset of infection to surgery was within the first few weeks.[5] However, these data largely dealt with infections caused by methicillin-sensitive organisms. The more recent literature suggests a higher rate of failure using a single-stage approach when dealing with methicillin-resistant organisms. Bradbury et al[6] looked at 19 cases of acute periprosthetic MRSA total-knee infections managed by open debridement and component retention with a minimum of 4 weeks of postoperative intravenous vancomycin therapy. At 2-year follow-up, 16 of the 19 cases (84%) had failed and become reinfected, with 13 patients requiring a subsequent two-stage exchange procedure. In a much larger study, Parvizi et al[7] compared the effectiveness of open debridement and component retention with that of two-stage exchange arthroplasty in treating periprosthetic infection caused by methicillin-resistant staphylococcal species. They reviewed 127 patients, of whom 35 underwent open debridement and retention of the prosthesis and 92 underwent a full two-stage component exchange. At a minimum of 2 years' follow-up, debridement alone was successful in only 37%, whereas two-stage exchange arthroplasty had success rates of 60% for total knee replacement (TKA) and 75% for total hip replacement (THA). These findings suggest that there may be evidence for a shift in the treatment algorithm for acute periprosthetic total-joint infections to favour immediate removal of the prosthesis and subsequent two-stage component exchange when the offending organism is found to be methicillin resistant or for only using debridement and irrigation within the first few days of symptom onset as opposed to the first few weeks.

Two-stage Treatment

Two-stage component exchange arthroplasty with intervening culture-specific intravenous antibiotic-directed treatment remains the gold standard for any type of periprosthetic joint infection. In today's landscape of increasing methicillin-resistant infections, it remains the best treatment for affected patients. Even so, the failure rate of this treatment strategy, as it applies to methicillin-specific infections, is emerging as a significant cause for concern. Table 1[7–13,15] outlines numerous two-stage component exchange studies over the past 10 years that have demonstrated less-than-optimal results for the treatment of methicillin-resistant organisms compared with the historical results of infections caused by sensitive organisms.

The experience at our institution is summarised in the final row of Table 1, Leung et al.[9] We elect to use the PROSTALAC (DePuy, Warsaw, IN, USA) articulated cement spacers for our periprosthetic infections. We adhere to strict surgical procedure protocols and postoperative monitoring. The first stage consists of removal of infected implants, hardware, and cement followed by meticulous debridement of all the infected tissue. We send a minimum of three specimens for culture and sensitivity evaluation. The operative field is then thoroughly irrigated with 3 L of normal saline. In most of our cases, the exact antibiotic composition of the articulated spacer consisted of a combination of a minimum of 1.5 g vancomycin and 3.6 g tobramycin. All patients receive intravenous antibiotic therapy or a combination of intravenous and oral antibiotics for a minimum of 6 weeks, under the supervision of an Infectious Disease specialist. The exact antibiotics prescribed for this therapy is at the discretion of the Infectious Disease specialist depending on the final intraoperative culture and sensitivity results. Most cases involve intravenous vancomycin therapy with or without another antibiotic agent, most commonly oral rifampin. Our standard protocol after that is to delay the second stage for another 6 weeks, and often longer, and to not proceed unless the local physical findings are quiescent and the standard laboratory markers (erythrocyte sedimentation rate (ESR) and C reactive protein (CRP)) are declining towards normal or are already at that point. If there is any doubt that the infection is controlled, then joint aspiration and further monitoring are considered. We are prepared to repeat the wound debridement and reinsert a new antibiotic-loaded articulating spacer if necessary, but these have been required in less than 10% of the overall cases. We do not routinely perform joint aspirations, preferring instead to use the clinical examination and blood test to guide our decision making. At the second stage, we remove the PROSTALAC articulated cement spacer and reconstruct the joint with the appropriate revision implants. We do not elect to perform a frozen section at the time of the second-stage procedure unless we encounter a cause for concern. We, however, send routine intraoperative cultures and continue the intravenous antibiotics until the final intraoperative culture results are available, typically at 5 days postoperatively. In our study, all 38 patients had negative intraoperative cultures during the second-stage procedure.[9]

Infection Prevention and Decolonisation Techniques

Despite our best-known treatment strategy (i.e. two-stage exchange arthroplasty), the recent literature suggests that we are still left with a 20–40% failure rate when dealing with methicillin-resistant periprosthetic infections (Table 1). Thus, we feel that the focus must include a more concerted effort in the prevention of these problematic methicillin-resistant organism infections. In a recent article by Kim et al,[14] the authors instituted a screening and eradication programme for MRSA in patients undergoing elective orthopaedic surgery at the New England Baptist Hospital in Boston. The theory behind instituting such a programme was based on the multiple previous studies, which have shown that *S aureus* is the most common causative organism in infections after orthopaedic operations, and the fact that this organism can be often found in the nasal passages of patients. The authors wished to investigate the feasibility and efficacy of instituting a hospital-wide programme for identifying carriers and reducing the nasal bacterial load of these patients before elective orthopaedic operations. They screened more than 7000 patients for both MRSA and MSSA with

Table 1
Literature review of two-stage surgical management for methicillin-resistant periprosthetic joint infections

Study	Infecting organism	Joint affected	No. of patients	Treatment protocol	Successful control of infection (%)	Follow-up interval (mo)
Lim et al[8]	MRSA (14/24), MRCNS (10/24)	THA	24	2-Stage arthroplasty with Stage 1 consisting of resection arthroplasty + cement beads (5/24), cement spacer (9/24), autoclaved prosthesis reimplanted with antibiotic-impregnated cement (10/24)	67 (16/24)	56 ± 31 (24–117)
Volin et al[13]	MRSA (1/6), MRCNS (5/6)	THA	6	2-Stage arthroplasty with Stage 1 consisting of resection arthroplasty	100 (6/6)	48 (24–120)
Kilgus et al[15]	MRSA (11/19), MRSE (8/19)	THA	19	Irrigation + debridement + polyethylene exchange (3/19); 2-stage arthroplasty (details of Stage 1 not provided) (6/19); excision arthroplasty (10/19)	48 (9/19)	27
Salgado et al[11]	MRSA	THA (8), TKA (4)	12	Debridement and retention of prosthesis (3/12); 1-stage revision arthroplasty (3/12); 2-stage revision arthroplasty with Stage 1 consisting of resection arthroplasty + cement spacer (4/12); resection arthroplasty (2/12)	50 (6/12)	190 days (4–2279 days)
Mittal et al[10]	MRSA (25/37), MRSE (12/37)	TKA	37	2-Stage arthroplasty with Stage 1 consisting of resection arthroplasty + antibiotic-impregnated cement spacer	76 (28/37)	51 (24–111)
Toulson et al[12]	MRSE (12/21), MRSA (7/21), VRE (2/21)	THA	21	2-Stage arthroplasty with Stage 1 consisting of an antibiotic-impregnated cement spacer	100 (21/21)	64.8 (24–203.5)
Parvizi et al[7]	MRSA (54/127), MRSE (53/127)	THA (66), TKA (61)	127	Irrigation + debridement + polyethylene exchange (35/127); 2-stage arthroplasty with Stage 1 consisting of resection arthroplasty + antibiotic-impregnated cement spacer (92/127)	I + D 37% (13/35), 2-stage 75% THA and 60% TKA	Minimum 2 y
Leung et al[9]	MRSA (10/38), MRSE (26/38), MRSA and MRSE (2/38)	THA	39	2-Stage arthroplasty with Stage 1 consisting of resection arthroplasty + antibiotic-impregnated articulated cement spacer	79 (30/38)	58 (24–123)

I + D = I&D (incision and drainage); MRSA = methicillin-resistant *Staphylococcus aureus*; MRSE = methicillin-resistant *Staphylococcus epidermidis*; VRE = vancomycin resistant enterococcus.

a remarkable screening rate of 95.7%. They identified 1588 patients (22.6%) as positive carriers for MSSA and 309 patients (4.4%) as positive carriers for MRSA. Patients who were screened as carriers for both types of organisms underwent an eradication protocol consisting of intranasal mupirocin (Bactroban; GlaxoSmithKline, Middlesex, UK) and chlorhexidine showers. Their main outcome measure was the rate of SSI in carriers versus noncarriers as well as before and after implementing the prescreening programme. They found that the rate of SSI among MRSA carriers was significantly higher (0.97%) compared with the SSI rate in noncarriers (0.14%). They also demonstrated more than 50% reduction in the SSI rate after implementing the screening and eradication protocol (reduction from 0.45% before the protocol *vs.* 0.19% once the screening programme began). The reduction in infection rate was also relatively greater for MRSA-associated SSI than that for MSSA-associated infections. This article highlights the importance of a screening and eradication programme for MRSA carrier status among patients undergoing elective orthopaedic surgery as it can lead to statistically significant reductions in postoperative rates of SSI.

At our centre, we are approaching this in a different way. A comprehensive bacterial decolonisation programme to reduce the risk of SSI in orthopaedic and other high-risk surgical patients has just commenced. The decolonisation strategy will combine two separate elements: (1) chlorhexidine gluconate–impregnated wash cloths for skin decolonisation below the neck in the 24 hours preceding surgery and (2) specific decolonisation of the anterior nasal passages, the primary anatomical colonisation site for *S aureus* in humans. The nasal decolonisation element proposed in this quality-improvement project consists of the use of antimicrobial photodynamic therapy to rapidly reduce the microbiological burden in the nares immediately before surgery and uses light energy to activate a topically applied photoactive agent. It represents technology that has been in use for some time in dental patients. It is being evaluated prospectively in a multidisciplinary surgical setting, with expected results on its effectiveness within 2 years.

Conclusions

Based on the evidence presented, we feel we can make the following conclusions regarding methicillin-resistant periprosthetic joint infections:

- Methicillin-resistant periprosthetic joint infections are occurring with increasing frequency, and the failure rates are higher than that reported in the literature after treatment of nonresistant organisms.
- Single-stage treatment consisting of irrigation, debridement, and component retention will have a high likelihood of failure when dealing with a methicillin-resistant organism, and the treating surgeon should seriously consider performing a definitive procedure (i.e. two stage) in the face of a methicillin-resistant periprosthetic infection, unless the infection is truly acute and debridement can be instituted within a few days of symptoms. Certainly, if a patient presents with an acute infection with cementless implants before bone ingrowth, it is probably preferable to remove the implants rather than debride the joint.
- Two-stage reconstruction using an antibiotic-impregnated cement spacer as part of the first-stage procedure is our treatment of choice for periprosthetic infections involving resistant organisms. However, the treating surgeons must be aware that the failure rate still ranges from 20% to 40% if dealing with a methicillin-resistant organism. For that reason,

new treatment strategies are being explored in collaboration with infectious disease specialists and basic scientists.

- It is imperative to work to prevent periprosthetic joint infections by methicillin-resistant organisms. Effective decolonisation methods have been shown in the literature to decrease the risk of SSIs, and widespread implementation of such prevention and decolonisation protocols is to be recommended if we are going to halt the increasing incidence of this difficult problem.

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