

Preventing Deep Infection in Total Knee Replacement

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ABSTRACT

BACKGROUND: The rate of infection following primary total knee replacement (TKR) ranges between 1 and 2%. The medical community has implemented many practices with the intention of preventing infection after TKR.

QUESTION: What are the prevention measures to reduce infection risk after TKR?

METHODS: A PubMed (MEDLINE) search and a Cochrane Library search were performed until 31 March 2014. Six hundred and fifty-seven articles were found but only 42 were finally analysed. The main criteria for selection were that the articles addressed the aforementioned question.

RESULTS: Rheumatoid arthritis, diabetes mellitus, immunosuppression treatment, psoriasis, and previous infections in the knee are the risk factors most clearly related with TKR infection. Appropriate patient selection is fundamental. *Staphylococcus Aureus* is the most common organism in infected TKRs. Systematic preoperative screening by swab is very important. Prevention of MRSA-positive cases by means of nasal decontamination (mupirocin 3 days) is advisable. Preoperative antibiotic prophylaxis has shown to be an efficient method to lower infection rates. Appropriate surgeon's preparation and clean air in the operating room (OR) also seem to be important. Many authors have used ORs equipped with laminar air flow (LAF) although some authors have recently found that the incidence of infection decreased after abandoning the LAF in ORs. Adequate skin preparation and dressings also

appear to be very important. Prolonged operative time seems to correlate with increased infection rate after TKR. The correlation between antibiotic-loaded cement and the risk of infection is still controversial.

CONCLUSIONS: Prevention measures could help diminish the infection rate in patients undergoing TKR but the efficacy of some preventive practices is still controversial.

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Key words: Total knee replacement; Postoperative infection; Prevention

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INTRODUCTION

Total knee replacement (TKR) is a safe and effective procedure that achieves excellent functional results in the treatment of knee osteoarthritis. Nevertheless, as in any major surgical procedure, and in spite of the continuous advances and improvements in the field of instrumentation and surgical techniques, deep infection may occur. Deep infection is among the most severe complications in TKR; infection rate ranges between 1 and 2%^[1-6].

The substantial increase in the number of TKRs performed and the extension of its indications to a younger and more active population seem to presage a significant increase in the infection rates in TKR procedures in the future. Since infection is a severe complication, we should do our best to reduce its incidence. It is vital to have an in-depth knowledge of the risk factors that may be involved so as to be able to correctly prevent the problem.

Despite the many scientific discoveries, infection following TKR continues to be a problem that haunts orthopaedic surgeons and inflicts suffering on patients. The medical community has implemented many practices with the intention of preventing infection^[7]. This paper summarises what it is known on prevention of infection following TKR in the orthopaedic literature.

METHODS

PubMed articles (MEDLINE) in English related to infected TKR were searched until 31 March 2014. The key words used were TKR and infection, and TKA and infection. Six hundred and fifty-seven articles were found but only 42 were finally analysed. The main criteria for selection were that the articles addressed the prevention of infection in patients undergoing TKR.

RESULTS

A number of factors have been identified that may help to prevent the risk of infection following TKR (Table 1).

Table 1 Practices that can help to prevent infection following total knee replacement.

Appropriate patient selection (patient-related factors)
Systematic preoperative dental clearance
Systematic preoperative screening by swab
Preoperative antibiotic prophylaxis
Adequate surgeon's preparation and air in the operating theatre
Antibiotic-loaded cement
Wound closing culture samples and good wound healing
Appropriate skin preparation and dressings
Diminishing duration of surgery

Patient-related factors

Appropriate patient selection and a correct preoperative assessment are fundamental to determine whether the benefits of the surgery may be outweighed by its risks. Rheumatoid arthritis, diabetes mellitus, immunosuppression treatment, psoriasis, and previous infections in the knee are the risk factors most clearly related with TKR infection^[1-6].

Recent HIV therapies have improved life expectancy in HIV positive patients. Habermann *et al*^[8] analyzed the results of total joint replacement in HIV positive patients. A coherency between the infection rate and the CD4+ count was not seen in their study. In a level II study, women had a lower risk of infection than men. Comorbidities also increased TKR infection risk^[9].

In another report, the main factors distinctly associated with infection after TKR were body mass index (BMI), diabetes mellitus, hypertension, steroid therapy, and rheumatoid arthritis^[10]. However, it had no sufficient evidences to reveal that gender could lead to infection after TKR. Osteoarthritis appeared to have a moderately protective effect. There was no correlation between urinary tract infection, fixation method, ASA (American Society of Anesthetics), bilateral operation, age, transfusion, antibiotics, bone graft, and infection.

According to Syahrizal *et al*, the factor that was significantly associated with superficial wound infection was diabetes mellitus. There was no significant difference between duration of surgery, and the mean age among patients with and without wound infections^[11]. Patients with rheumatoid arthritis are at higher risk of infection following TKR relative to those with degenerative osteoarthritis^[12]. Reported independent risk factors for perioperative surgical site infection include male gender, minority race, a diagnosis for cancer, liver disease, coagulopathies, fluid and electrolyte disorders, congestive heart failure, and pulmonary circulatory disease^[13]. Injecting knees with corticosteroids prior to TKR does not increase the incidence of postoperative wound infection^[14].

Systematic preoperative dental clearance

Obtaining dental clearance prior to elective TKR is a common practice; however, little published data exist to justify this requirement. Lampley *et al*^[15] has reported that the perceived need for routine preoperative dental screening for all TKR patients should be reassessed. Patients over 80 years of age have not shown a higher risk of infection following TKR than patients below 80 years of age^[16].

Systematic preoperative screening by swab

Investigation of MRSA risk factors (recent history of surgery, chronic skin lesion) is paramount. Systematic preoperative screening by swab [nose and any skin lesion(s) during the month preceding surgery] is very important.

Van Rijen *et al* tried to determine whether the use of mupirocin nasal ointment in patients with identified *Staphylococcus Aureus* nasal carriage reduced *Staphylococcus Aureus* infection rates^[17]. Randomised controlled trials (RCTs) comparing nasal mupirocin with no treatment or placebo or alternative nasal treatment in the prevention of *Staphylococcus Aureus* infections in nasal *Staphylococcus Aureus* carriers were included. The main conclusion was that in people who are nasal carriers of *Staphylococcus Aureus*, the use of mupirocin ointment results in a statistically significant reduction in *Staphylococcus Aureus* infections. Prevention of MRSA-positive cases by means of nasal decontamination (mupirocin 3 days) is advisable.

Courville *et al*^[18] performed a cost-effectiveness analysis to evaluate preoperative use of mupirocin in patients with total joint replacement. The main conclusion was that empirical treatment with mupirocin ointment or use of a screen-and-treat strategy before TKR is a simple, safe, and cost-effective intervention that can reduce the risk of surgical site infection.

According to Haenle *et al*^[19] bacteriology swabs during primary TKR is not an adequate measure to predict subsequent periprosthetic infections, even if augmented with a tissue sample.

Preoperative antibiotic prophylaxis

Preoperative antibiotic prophylaxis has shown itself to be an efficient method to lower infection rates. *Staphylococcus Aureus* is the most common organism in infected total knee replacements^[1-6]. Regarding antibiotic prophylaxis, Cefazolin 2 g preoperative is recommended, then 1 g/8 h 24-48 h. In the case of beta-lactamin allergy or proven MRSA colonization: vancomycin 15 mg/kg preoperative, then 10 mg/kg par 8 h 24-48 h IV antibiotic at induction of anaesthesia or within the hour preceding surgery.

It is unclear which antibiotic regimen provides the best prophylaxis against deep infection in patients undergoing TKR. Therefore, Sewick *et al*^[20] determined whether dual antibiotic prophylaxis reduced the rate of periprosthetic infection after TKR compared to single antibiotic prophylaxis and altered the microbiology of surgical site infection. The infection rates for dual antibiotic prophylaxis compared to a single antibiotic regimen were 1.1% and 1.4%, respectively. The main conclusion of this level III therapeutic study was that the addition of vancomycin as a prophylactic antibiotic agent apparently did not reduce the rate of surgical site infection compared to cefazolin alone.

Regional administration of teicoplanin (injection of teicoplanin into a foot vein of the leg to be operated on after occlusion of the systemic circulation by inflating the tourniquet) has been reported to be a safe and valuable prophylactic technique; however, in patients at risk of infection a prophylactic regimen which is also active against gram-negative bacteria should be considered^[21].

Staphylococci account for approximately 70% of postoperative

infections in orthopedic prosthetic surgery, with the leading organism being *Staphylococcus epidermidis*^[22]. Therefore, the antibiotics most widely used for prophylaxis are cefazolin, cefamandole and cefuroxime, by virtue of their excellent activity against these pathogens. However, methicillin-resistant coagulase-positive and -negative staphylococci are increasingly being reported as the causative agents of postoperative infection in clean prosthetic surgery, therefore prompting the use of glycopeptide antibiotics (vancomycin and teicoplanin) in the prophylaxis for TKR, particularly in hospitals in which there is high methicillin-resistance among these pathogens. However the routine prophylaxis with vancomycin and teicoplanin may have adverse effects, particularly the engendering of vancomycin and teicoplanin resistant stems^[20,23-25].

According to de Craxford *et al* gentamicin with flucloxacillin is comparable with cefuroxime in rates of surgical site infection and return to OR for infection but is associated with a significant increase in acute kidney injury. Acute kidney injury is associated with additional morbidity and mortality. This association should be considered when choosing a suitable prophylactic regime^[26].

Surgeon's preparation and air in the operating room (OR)

The surgical team must wear sterile robes, masks and double gloves. Hand disinfection must be done by rubbing with a hydro-alcoholic solution. Surgery rooms ideally should be equipped with laminar air flow (LAF). Operating theatre maintenance should comprise floor bio-cleansing and flat-surface spraying with detergent-disinfectant at the start of the surgical program and between operations. Ultraclean air (UCA) in ORs is defined as <10 colony-forming units (cfu)/m³. The current European standards for surgical gowns are contained in EN13795 but these do not include containment of bacterial dispersal as a standard test.

Gulihar *et al*^[27] have compared bacterial air counts using Rotecno gowns with a new type of occlusive gown made from Gore liquid-proof fabric, which were superior to the Rotecno gowns on standard EN13795 laboratory testing. The new gowns were superior in standard laboratory tests but not superior at preventing airborne bacterial dispersal. Rotecno gowns, although many years old, were still effective. ORs ideally should be equipped with LAF. Theatre maintenance should comprise floor bio-cleansing and flat-surface spraying with detergent-disinfectant at the start of the surgical program and between operations. Both LAF and ultraviolet light (UVL) reduce periprosthetic joint infection^[28]. The historically high price of LAF has decreased substantially. Only LAF has been standardized by several European countries. The Centers for Disease Control and Prevention (CDC) recommends further study of LAF but recommends UVL not to be used secondary to documented potential health risks to personnel.

An investigation performed by Babkin *et al*^[29] of the OR revealed three problems: there was significant traffic through the door on the left of the patient; a nonstandard horizontal-flow air conditioner had been installed above that door; a tool-washing sink was in use on the other side of that door. Infection control guidelines were rehearsed: the sink was removed, the air conditioner was disconnected, and the door was locked. In a prospective survey performed 2 years later only 2.2% undergoing TKR developed a superficial surgical site infection. Correction of independent risk factors for infection following TKR led to a decrease in surgical site infection rate^[29]. The main reason for high infection rates and the simplest to treat is excessive traffic in the OR. Panahi *et al*^[30] have tried to define the incidence of door opening during primary and revision total joint arthroplasty, providing a comparison between the two types of procedures, and identify the

causes of door opening in order to develop a strategy to reduce traffic in the operating room. Surgeries (80 primary total joint arthroplasty and 23 revision arthroplasties) were performed under vertical, LAF. The average operating time for primary and revision procedures was 92 and 161 minutes, respectively. Average door openings were 60 in primary cases and 135 in revisions, yielding per minute rates of 0.65 and 0.84, respectively. The circulating nurse and surgical implant representatives constituted the majority of OR traffic. Traffic in the OR is a major concern during TKR. Revision cases demonstrated a particularly high rate of traffic. Implementation of strategies, such as storage of instruments and components in the OR and education of OR personnel, is required to reduce door openings in the OR^[30].

A questionnaire was reported by Miner *et al*^[31] on clean air practices. Two hundred ninety-five (73%) of 405 eligible hospitals that performed 18,374 primary and revision TKR procedures responded to the questionnaire. Among responding hospitals, 30% reported regular use (for >75% of procedures) of LAF, 42% reported regular use of body exhaust, and 5% reported regular use of ultraviolet lights. Among hospitals providing complete data, 150 (58%) performing 66% of procedures reported regular use of at least one of these techniques. On regression analyses, laminar airflow was used more often by hospitals with a TKR volume greater than 25 procedures per year and orthopedic residency programs, but its use was not significantly related to hospital setting or ownership status. Although these clean air practices are not recommended by any U.S. governmental or professional organization, they are used in nearly two-thirds of TKR procedures. Better information about their impact on current practice and more explicit guidelines may aid decisions about the use of these resource-intensive infection control practices^[31].

Antibiotic-loaded cement

In patients whom surgeons considered higher risk for infection, antibiotic-loaded bone cement did not appear to reduce TKR infection rates^[32]. Early findings reported by Hansen *et al*^[33] suggest that routine prophylactic use of antibiotic-loaded bone cement has not led to changes in infecting pathogen profile, nor has led to the emergence of antimicrobial resistance at our institution. Very recently it has been reported that the absolute rate of infection increased when tobramycin-loaded cement was used in TKR^[34].

Wound closing culture samples and wound healing

It is unknown whether intraoperative subcutaneous wound closing culture samples (WCCS) are useful to predict periprosthetic joint infection (PJI). Frank *et al*^[35] prospectively followed 167 out of a total of 175 consecutive patients with primary total hip (THR) or knee replacement (TKR) for a mean follow-up period of 5 years; of those patients, 96.8% underwent WCCS. The results showed a positive WCCS in 5.8%. Nine patients developed postoperative wound complication and required revision surgery. Two patients developed signs of a deep periprosthetic infection; however, only one out of nine patients had initial positive WCCS. These results thus indicate that WCCS during primary joint replacement is not an appropriate predictive method to identify patients at risk for periprosthetic joint infections^[35].

According to Jones *et al*^[36] local factors that influence wound healing include multiple previous incisions, extensive scarring, lymphoedema, and poor vascular perfusion. Systemic factors include diabetes mellitus, inflammatory arthropathy, renal or liver disease, immune compromise, corticosteroid therapy, smoking, and poor nutrition. Modifications in the surgical technique are necessary in

selected cases to minimise potential wound complications. According to Jones *et al*^[36] prompt and systematic intervention is necessary to address any wound healing problems to reduce the risks of infection and other potential complications. However, what is the prompt time to intervention (5 days, 7 days, 10 days?) still is an open question.

Skin preparation and dressings

In the ward, the patient must take a shower the eve of surgery with hibiscrub[®]. There is controversy regarding whether on the day of surgery the patient must be depilated and shaved. It seems that depilating with lotions could be favourable^[37], although shaving is much more controversial. The use of depilatory creams has been shown to be effective, atraumatic, non-toxic and could be self-administered. Depilatory creams could be used safely on granulating wounds and did not give rise to bacterial growth. Their use is associated with a significant reduction in skin-surface bacteria and is cheaper compared with shaving. The best practice is to refrain from hair removal unless it interferes with the surgical procedure or wound closure. If hair has to be removed, it should be done using a depilatory cream^[37].

In the OR the following measures are recommended: cleaning (hibiscrub[®]), sterile water rinse, sterile band drying, antiseptic (hibitane drape[®]), sterile compresses, 2-coat application, and drying before drape application^[1-6]. Microbial sealant is a liquid applied to the skin immediately before surgery. It is thought to contribute to reducing infections following TKR by sealing in the skin flora to prevent contamination and infection of the surgical site.

Lipp *et al*^[38] assessed the effects of the preoperative application of microbial sealants (compared with no microbial sealant) on the rates of surgical site infection in people undergoing clean surgery. The main conclusion was that there is currently insufficient evidence as to whether the use of microbial sealants reduces the risk of periprosthetic knee infection in people undergoing clean surgery and further rigorous randomised clinical trials (RCTs) are required.

In a level III study Farber *et al*^[39] found that introduction of 2% chlorhexidine gluconate (CHG)-impregnated wipes in the presurgical setting was not associated with a reduced surgical site infection incidence. This report suggests that CHG wipes in TKR are unnecessary as an adjunct skin antiseptic.

Duration of surgery

Risk stratification has proven to be a useful tool in surgical site infection prevention. The duration of the surgical procedure has been recommended for use in surgical site infection risk stratification. A retrospective analysis of patients who underwent TKR assessed the association between the duration of the surgical procedure and the risk of postoperative infection^[40]. Patients without infections had surgery durations of 94 +/- 28 min, and patients with infection had durations of 127 +/- 45 min. Operation time has positive correlations with weight, body mass index, and the total number of co-morbidities. These results confirm that the duration of the surgical procedure can be used as a risk predictor for surgical site infection in TKR^[40].

DISCUSSION

In this article the author has analysed the prevention measures to reduce infection risk after TKR. In recent reviews, the incidence of TKR infection was 0.4% in primary surgeries and 1% in prosthetic revisions^[1-3]. Prevention is key to successfully managing TKR

infections. It is vital to have an in-depth knowledge of the risk factors that may be involved so as to be able to correctly prevent and, if needed, manage the condition.

Levent *et al*^[41] assessed the incidence deep infection at one year following TKR and adherence to skin preparation, antibiotic prophylaxis, screening and prevention in case of methicillin-resistant *Staphylococcus Aureus* (MRSA). The incidence of infection was 1.4%. Antibiotic prophylaxis was implemented correctly in 99% of cases, with skin preparation scores of 8.75 in 61% of cases and of 10 in 39%. Among the patients, 2.5% were MRSA-positive, none of whom developed infection. Infection prevention measures were applied in only half of the MRSA-positive cases. No MRSA-positive patients developed surgical site infection. Periprosthetic knee infection incidence in Levent's series was low, but certainly underestimated. Assessment found good implementation of infection prevention protocols, with surgical site infection occurring randomly with regard to adherence parameters (antibiotic prophylaxis, skin preparation, MRSA status).

Blom *et al*^[42] found infection rates of 4.4% after primary TKRs and 15% after revision TKRs at a mean follow-up of 2.8 years. Later on they introduced stringent 2 antibiotic prophylaxis, and the routine use of occlusive clothing within vertical LAF ORs and 0.05% chlorhexidine lavage during arthroplasty surgery. One percent of the patients who underwent primary TKR, and 5.8% of those who underwent revision TKR developed deep infection. 22.2% who developed infection after primary TKR were successfully treated without further surgery. Although infection rates have declined with the introduction of prophylactic measures, and more patients are undergoing TKR, the outcome of infected TKR has improved very little.

Despite the many scientific discoveries and technological advances, such as the advent of antibiotics and the use of sterile techniques, infection continues to be a problem that haunts orthopaedic surgeons and inflicts suffering on patients. The medical community has implemented many practices with the intention of preventing infection and treating it effectively when it occurs. Although high-level evidence may support some of these practices, many are based on little to no scientific foundation. Thus, around the world, there is great variation in practices for the prevention and management of infection following primary TKR^[7].

In conclusion, the most important infection risk prevention measures appear to be patient selection, skin preparation, antibiotic prophylaxis, screening and management for MRSA, and adequate preparation of the surgical team and OR. Implementing the aforementioned preventive measures could help diminish the rate of infection following TKR.

CONFLICT OF INTERESTS

There are no conflicts of interest with regard to the present study.

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