Prevention of Periprosthetic Joint Infection

Subjects: Biology

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Periprosthetic joint infections (PJI) represent one of the worst complications following total joint arthroplasty (TJA) in general, and total knee arthroplasty (TKA) in particular. The clinical impact on patients is dramatic: the 5-year mortality rate following PJI equals the one of oncologic patients. On the other side, hospital readmission rates following explants already double those of many cardiac and oncologic procedures, leading to a significant burden on healthcare systems. At current times, the combination of increasing antibiotic resistance and the growth in the number of culture-negative PJI makes preventing infection a key aspect of adult reconstruction practices in order to avoid an epidemic escalation of PJI and musculoskeletal infections in general.

TKA PJI periprosthetic joint infections knee hip infection prevention

1. Introduction

Unfortunately, effective prevention strategies to reduce the burden of this complication have not been fully determined. Decisions on patient selection and evaluation criteria, comorbidity detection, quantification of the perioperative risk, and application of countermeasures are often left on the shoulders of the treating physician, and not many standardized protocols for the prevention of PJI have been established [1].

This study aimed to review the current literature and multiple recommendations from well-recognized international scientific societies on preventive PJI measures with the objective to produce a clear, innovative, multimodal, perioperative protocol for TKA PJI prevention in high-risk patients. To achieve this goal, the European Knee Associates (EKA) formed a transatlantic panel of experts with a special interest in PJI and PJI prevention: the current authors first analyzed multiple modifiable patient-related and perioperative PJI risk factors, and secondarily produced guidelines for each of the three phases (preoperative, intraoperative, and postoperative) of the TKA procedure. The protocol presented here, despite representing the opinion of several EKA members, does not represent a consensus document from EKA.

2. Preoperative Factors Increasing PJI Risk

2.1. Obesity

The American Academy of Orthopaedic Surgeons' (AAOS) clinical practice guidelines [2] defined obesity as a moderate-strength criteria for increased risk. It has been described that patients with a body mass index (BMI) of 35 or greater have a two- to six-fold increased risk of PJI [3][4]. Consensus opinion from the American Association of

Hip and Knee Surgeons (AAHKS) suggests that consideration should be given to delaying total joint arthroplasty in a patient with a BMI > 40, especially when associated with other comorbidities, such as poorly controlled diabetes or malnutrition [5].

2.2. Malnutrition

Since paradoxical malnutrition in patients having a high caloric but nutritionally poor diet is present in 42.9% of obese patients [6], malnutrition has been associated with a five to seven times greater risk of developing a major wound complication [7], ultimately leading to a PJI. Therefore, to cope with postoperative catabolic demands, nutritional supplementation has been strongly recommended to minimize PJI risk [8].

2.3. Diabetes Mellitus

Diabetes is a well-known risk factor for complications following TJA [9]. Historically, patients with uncontrolled diabetes have been found to have a 2.8 times increased risk of infection after TJA [10][11]. More recently, the critical role of acute glycemic control in patients undergoing TJA has been determined since multiple studies have shown patients with peri-operative hyperglycemia, not simply diabetes alone, have a significantly higher risk for complications [12][13]. Blood glucose levels between 110 and 180 mg/dL, a non-fasting glucose value less than 200 mg/dL, and a hemoglobin A1c value less than 7.5–8% have all been reported as ideal for elective TKA [11][12][13].

2.4. Smoking

Tobacco use and smoking are substantial risk factors for poor wound healing and infection. There is strong evidence that previous smokers had a similar risk profile to non-smokers: a few reports indicated that four weeks of cessation are required before elective surgery to attenuate the risk of surgical complications [14][15]. The normal value of serum cotinine assay has been reported as ≤ 10 ng/dl [16].

2.5. Skin Decolonization Prior to Surgery

Recent studies suggest the use of preoperative chlorhexidine cloth skin decolonization to reduce PJI after TJA because of its superiority compared to regular soap for preoperative cleansing of the skin—this has been demonstrated particularly in reducing infections related to MRSA [17][18]. The use of octenidine-palmitate (OL 11) has also been shown to reduce SSIs [19].

2.6. Nasal Decolonization

Since *S. aureus* nasal colonization correlates with increased risk for surgical site infections (SSIs) [20] and a few reports showed that an institutional decolonization protocol helped to decrease overall infection rate [21], the AAOS workgroup [2] suggested preoperative nasal mupirocin decolonization in all patients who are MRSA carriers because of its minimal potential risk of nasal irritation and its relatively low cost.

3. Intraoperative and Perioperative Factors Increasing PJI Risk

3.1. Surgical Site Hair Removal

Kowalski et al. [22] recommended that hair removal should be considered in all patients undergoing elective joint arthroplasty, and should be performed by clippers before arrival in the operating room.

3.2. Perioperative Antibiotics

Since the increasing number of MRSA and gram-negative PJIs [23], the classical single antibiotic prophylaxis prior to TJA has been recently challenged [24]. On the other side, Sewick et al. [25] demonstrated that the addition of vancomycin did not significantly reduce the rate of SSI when compared with cefazolin alone, but reduced the overall incidence of MRSA infections; because of this, it has been suggested by the same authors that only patients who are proven or potential carriers of MRSA, or those with a cephalosporin allergy, may benefit from vancomycin prophylaxis. This therapeutic strategy has also been shown to minimize the development of vancomycin-resistant *Enterococcus* [24][25].

3.3. Perioperative Antibiotics Timing

Although the Centers for Disease Control and Prevention (CDC) guidelines recommend a single preoperative dose in the case of TJA, there is a surprisingly limited amount of literature to support this recommendation [26][27]. It has been shown that a single perioperative dose of antibiotics does not increase the SSI/PJI rates if compared to multiple doses [26]. Interestingly, Inabathula et al. [28] reported that extended postoperative antibiotic prophylaxis up to seven days led to a statistically significant and clinically meaningful reduction in the 90-day infection rate in a selected group of high-risk patients. Claret et al. [29] also demonstrated a reduction in PJI when a prolonged post-operative antibiotic treatment was applied to total joint arthroplasty revisions.

3.4. Surgical Site Skin Decolonization

Chlorhexidine-gluconate (CHG) has been recommended as the most efficient intra-operative surgical site preparation agent [8]; dual skin preparation, before and after draping and adding alcohol in a secondary scrubbing phase, has also shown favorable outcomes [18][30] as a preventive PJI measure.

3.5. Intraarticular Irrigation

Various intraoperative irrigation solutions have been recently studied. The World Health Organization (WHO), CDC, and International Consensus Meeting Clinical Practice Guidelines advocate for the use of diluted povidone-iodine (PID) irrigation during surgical procedures [27][31][32]; interestingly, cytotoxicity studies have shown that the bactericidal effect occurs even before individual human cells are affected [33]. Multiple studies have been performed in order to determine the optimal PID dilution in normal saline [34][35][36] prior to irrigation. Cichos et al. [36] evaluated the minimal inhibitory concentration (MIC) and time to bacterial death for 1% PID, 0.05% CHG, and 5 µg/mL

vancomycin against multiple bacteria: those authors reported that PID, with a MIC of 0.63%, killed all tested micro-organisms immediately after contact, concluding that PID-accurate intra-articular diffusion was more important than extended exposure time. A recent in vitro study by Schmidt et al. [37] suggested that chlorhexidine may be a more effective irrigation solution for *S. epidermidis* eradication in biofilm than other commonly used solutions, such as povidone-iodine, Dakin's solution, and triple antibiotic solution.

3.6. Fibrinolytic Agents

Since postoperative hematoma represents a well-known risk factor for PJI and SSI, the use of tranexamic acid (TXA) was recently introduced in many multimodal TKA protocols, since its use was strongly associated with reduced blood loss and decreased transfusion rates without an increase in thromboembolic complications [38].

3.7. Wound Closure

It has been reported that prolonged wound drainage (> 5 days) increases the risk of PJI by 13 times [39]: because of this, proper wound closing and postoperative wound monitoring represent key factors to avoid bacteria invading the joint space [39]. Recently, the use of a barbed monofilament suture was shown to provide a more watertight seal requiring no knots and allow for quick and cosmetic wound closure [40][41]. Interestingly, results from several meta-analysis studies showed that the incidence of SSI or wound infections decreased after using triclosan-coated sutures [42][43]. Since a moist environment protects the incision area from contamination, the use of silver-impregnated hydrofiber dressings have shown to decrease wound complications, the number of required re-dressings, and the rate of PJI by 4.6-fold [44][45]. In high-risk patients, wound checks and possible dressing changes should be performed on a daily basis—in the case of postoperative drainage, vacuum-assisted incisional dressing (iVAC) or negative-pressure wound therapy (NPWT) may play a role in reducing PJI risk [46].

3.8. Implant Surfaces

Since bacterial adhesion to the implant surface represents a key step of biofilm formation, several studies have focused on the relationship between prosthetic biomaterials and the increased risk of PJI [47][48][49]. Material and surface engineering led to the development of bactericidal/bacteriostatic modification of implant surfaces, such as chemical immobilization of antimicrobials, coatings with a broad range of antibacterial compounds (Gentamycin polymer, DAC hydrogel, silver-coated and iodine-coated implants), micro-textured surfaces, or anti-adhesion topographies: nevertheless, no method seems ideal, different results are reported, and no consensus exists on the use of a specific bactericidal surface [26].

3.9. Local Antibiotic Delivery

During an acute or chronic PJI, bacterial infiltration is mainly identified in the joint space which is poorly vascularized and more tolerant to bacteria proliferation before a local immune response can be stimulated. Because of this, a strategy to prevent bacterial colonization and biofilm formation may be needed to support a delayed and compromised immune response. Localized delivery of antibiotics is able to provide high concentrations of antibiotics that cannot be achieved systemically. Current evidence on the efficacy of Antibiotic-

Impregnated Bone Cement (AIBC) in primary TKA is inconclusive [8][19][50]. Recently, calcium-sulphate antibiotic-added resorbable beads have received much attention, particularly due to their faster and longer elution compared to AIBC and poly-methyl-methacrylate (PMMA) beads. Unlike PMMA beads, calcium sulphate beads (CSB) do not need removal from the joint space and there is no risk of acting as a potential foreign body for bacterial colonization [51][52]. In vitro studies reported that calcium sulphate beads were capable of bacterial growth inhibition, preventing early bacterial colonization and biofilm formation by MRSA, *S. epidermidis,* and gram-negative bacteria by reaching localized antibiotic levels above the minimum inhibitory concentration (MIC) up to 39 days. However, various complications have been described when a higher volume of beads has been used—these include transient hypercalcemia, wound drainage, and heterotopic ossification [53][54].

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