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REVIEW ARTICLE

The Prevention of Periprosthetic Joint Infections

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Abstract: Periprosthetic joint infection (PJI) following total joint arthroplasty (TJA) adversely affects patient quality of life and health status, and places a huge financial burden on the health care. The first step in combating this complication is prevention, which may include implementation of strategies during the preoperative, intraoperative, or postoperative period. Optimization of the patient with appreciation of the modifiable and non-modifiable factors is crucial. Preoperative optimization involves medical optimization of patients with comorbidities such as diabetes, anemia, malnutrition and other conditions that may predispose the patient to PJI. Among the intraoperative strategies, administration of appropriate and timely antibiotics, blood conservation, gentle soft tissue handling, and expeditious surgery in an ultra clean operating room are among the most effective strategies. During the postoperative period, all efforts should be made to minimize ingress or proliferation of bacteria at the site of the index arthroplasty from draining the wound and hematoma formation. Although the important role of some preventative measures is known, further research is needed to evaluate the role of unproven measures that are currently employed and to devise further strategies for prevention of this feared complication.

Keywords: Periprosthetic joint infection, Prevention, Total hip arthroplasty, Total knee arthroplasty.

INTRODUCTION

Total joint arthroplasty (TJA) is currently the most successful surgical procedure for improving patient quality of life. However, there are still unsolved problem in TJA, one of the most devastating after TJA is periprosthetic joint infection (PJI). The treatment of PJI often requires multiple surgical procedures and is associated with increased complications and morbidity as well as increased costs. As the volume of primary and revision TJA increases, the burden of treatment is becoming a major economical and public health issue [1].

Therefore, the prevention of PJI through implementation of effective strategies should be a priority. Several modifiable factors may influence the outcome of TJA. Identification of risk factors is important so that resources can be focused more effectively and greater attempts at risk reduction can be pursued [2]. In this review, the current evidence for the optimization of patient and surgery-related modifiable risk factors are assessed in the preoperative, intraoperative and postoperative periods.

BEFORE THE DAY OF SURGERY

Infection Screening

The presence of any local or systemic infection is considered to be a contraindication for elective joint arthroplasty [3]. The infection may exist in the urinary tract, skin, nails as well as the oral cavity [4]. Also the anterior nares can be a site of reservoir for *Staphylococcus aureus*.

The cost effectiveness of routine dental or urinary screening before an arthroplasty has been questioned. Although all infections should be treated before TJA is performed, no relationship has been demonstrated between routine dental clearance and PJI incidence [5, 6]. Due to the lack of evidence regarding dental pathology as a source of PJI, only

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high-risk patients (such as tobacco and narcotic users, and patients who have not had a dental visit within the past 12 months) should be screened preoperatively for dental infection [7]. On the other hand, high-level nasal carriage of *S. aureus* is an important risk factor for subsequent surgical site infection (SSI) [8, 9]. Males, obese patients, a history of a cerebrovascular accident, multiple hospital admissions, and having a pet at home have been associated with nasal carriage of *S. aureus* [10]. Empirical use of mupirocin ointment without screening is shown to be a simple, safe, cost-effective [11] and associated with a decreased incidence of SSI [12, 13]. On the other hand, there are concerns regarding the development of resistance to mupirocin in the setting of routine use [14].

Smoking and Alcohol Use

Patients who smoke were found to have increased postoperative complications compared to non-smokers [15, 16]. In different studies, former and current smokers were found to have a 24% to 43% and 32% to 56% higher risk of postoperative complications after TJA, respectively [17, 18]. Complication rates increased proportionally with the amount of smoking. Although there is no consensus on the definition of heavy smoking, it is stated that smoking more than one pack per day is significantly associated with development of PJI and other postoperative complications [19]. The optimal time for cessation of smoking is not known, but at least 4 to 8 weeks prior to surgery is recommended [20 - 22].

Alcohol consumption is related to increased risks of postoperative morbidity and mortality [23, 24]. Alcohol cessation or a reduction in consumption four weeks prior to surgery is effective in reducing the risk of developing postoperative complications. [2, 25]

Diabetes Mellitus (DM)

Regardless of the diabetes type, patients with uncontrolled DM exhibit a significantly increased risk of postoperative complications following TJA [26]. Thus, preoperative optimization of patients with a fasting glucose level < 200 mg/L and HbA1C levels <7% after arthroplasty is extremely important in minimizing postoperative complications [27]. Stress-induced hyperglycemia is activated by the hypothalamic-pituitary axis in up to two thirds of non-DM patients following surgery and this increases the risk of 30-day mortality in comparison to patients with well-controlled diabetes [28 - 30].

Liver and Kidney Disease

Patients with chronic renal and liver failure (CRF) are at risk of increased postoperative complications [31]. The mortality of patients with chronic liver failure is reported to be 15.8% in patients undergoing total hip arthroplasty (THA) [32, 33]. The risk of mortality was found correlated by the preoperative Child-Turcotte-Pugh score [33, 34]. Advanced stage of disease (Child's B and C), INR >1.6, prolonged PT and concurrent encephalopathy were reported as poor prognostic factors. [7, 32, 33] The hemostatic balance should be corrected before surgery in order to avoid excessive bleeding or perhaps patients with advanced stage of disease should not subjected to elective arthroplasty [35, 36].

There is increased risk of infection in chronic renal failure [37 - 41], particularly high in patients receiving hemodialysis [41 - 45]. Most CRF patients may also be carriers of MRSA and should receive vancomycin as a preoperative prophylactic antibiotic [40]. Because of the higher risk of infection in patients with CRF, some authorities have advocated that femoral component fixation should be performed with antibiotic-impregnated cement. There is no evidence in the current literature to support the use of one mode of implant fixation over another in this population [40, 46, 47]. As a result, TJA in CFR patients may be considered a reliable surgical option if performed within the framework of careful multidisciplinary patient management.

Inflammatory Joint Disease (IJD)

Patients with rheumatoid arthritis (RA), juvenile inflammatory arthritis, and spondylarthropathies, such as ankylosing spondylitis and psoriatic arthritis (PA), have been identified as having a higher baseline risk of infection compared with that of the general population [48].

In addition to the immune modulating effect of the disease itself, most patients who are on disease modifying anti-rheumatic drugs (DMARDs) may be at an additional risk of developing an infection [49]. The most commonly used

medications are synthetic DMARDs such as methotrexate, hydroxychloroquine, and leflunomide; corticosteroids; and biologic agents, including TNF-blocking agents. The SSI rate among RA patients was found to be two to four times higher than in those with osteoarthritis [50].

The main issue in patients with psoriasis is the presence of skin lesions. Colonization of the skin plaques with staphylococcal species and more strikingly enteric Gram-negative organisms and Bacteroides spp. has been confirmed [51]. Because of the increased risk of infection, performing elective arthroplasty in patients with active and aggressive psoriatic arthritis and skin lesions is considered inappropriate. It is agreed that incisions should not be placed through active skin lesions [52].

The appreciation of significantly higher risk of PJI in patients with IJD by using all possible pre- and postoperative prophylactic interventions may help to reduce infection rates in this high-risk group [50]. This includes proper timing of surgery, cessation of DMARDs, proper skin preparation, and antibiotic prophylaxis. The cessation of DMARDS should be performed in consultation with a rheumatologist, which can be arranged based on the specific medication, the individual patient, and the half-life of the particular medication [2]. Although there is no clear evidence, routine use of antibiotic-laden cement for fixation in IJD patients may be justified.

Anemia

Preoperative anemia, usually an underestimated problem, has also been shown to be an independent risk factor for PJI, and reported to be as high as 35% [53, 54]. Efforts should be made to treat the anemia preoperatively in order to prevent postoperative complications with surgical blood loss [55]. There are some treatment options for anemia such as autologous blood donation, iron replacement, and administration of erythropoietin. Autologous blood transfusion has well known disadvantages [56, 57] whereas iron replacement, with or without erythropoietin, was found safe and efficient to reduce the risk of transfusion in patients undergoing TJA [58].

Malnutrition

Patients with a history of extreme weight loss and poor nutritional habits are at particular risk of being malnourished. All forms of malnutrition predispose patients to SSI up to 4 times, therefore patients undergoing elective arthroplasty should be evaluated for the presence of malnutrition [59 - 64]. The WHO has defined the threshold limits for malnourished patient as serum total lymphocyte count <1,500 cells/mm^3, a serum albumin concentration of <3.5 g/dL, low serum prealbumin, and serum transferrin levels <200 mg/dL [63, 65 - 67].

Obesity is considered as paradoxical malnutrition due to carbohydrate rich and protein poor diet [68, 69]. Thus, obese patients should undergo screening for the presence of malnutrition [64] Malnutrition is a modifiable risk factor, postponing the TJA is strongly recommended because patients with a body mass index [BMI] ≥40.0 kg/m^2, significantly increases the risk of PJI [21]. On the other hand, rapid weight loss can result in malnutrition as well and has greater likelihood of developing a deep SSI compared with those who remained the same weight [65, 70].

THE OPERATION DAY

Prophylactic Perioperative Antibiotics

The goal of administering preoperative antibiotics is to allow for adequate tissue concentrations above the minimal inhibitory concentrations before surgical incision [71]. First or second generation cephalosporins are recommended for routine perioperative surgical prophylaxis with the use of vancomycin or clindamycin as secondary options in patients with a penicillin allergy. Vancomycin should be reserved for patients with known colonization or infection with MRSA [72 - 74].

The timing of administration is one of the most important discussions, ranging from 30 minutes to two hours before the incision [75 - 77]. In current literature, most of the authors recommend to use within one hour of surgical incision for cephalosporins and can be extended to two hours for vancomycin and fluoroquinolones [74]. In patients with large blood volume loss (>2000 cc) or high volume of fluid resuscitation (>2000cc), and surgery times that last more than two half-lives of the prophylactic agent, an additional intraoperative dose of antibiotics is necessary [78].

In order to avoid under dosing of the preoperative prophylactic antibiotic dose adjustment for antibiotics is recommended, and in this regard, the routine dose of cefazolin should be doubled in patients more than 80 kg [79 - 82].

Air Quality

There are two main routes for contamination of the wound during TJA:

1. Direct contamination by airborne particles, approximately
2. Indirect contamination

30% and 70% of all contaminations are measured to become by these routes, respectively [85 - 87].

Although laminar flow and space suits are one of the most popular methods, the evidence seems not consistent in the literature. Some registry data does not confirm the reduced infection rates with the use of laminar flow ORs and space suits [88]. Moreover, some studies have shown that the incidence of PJI was higher when the surgery was performed in a laminar flow room or while space suits were worn by personnel [89 - 91]. Therefore, the efficacy of laminar flow in reducing PJI remains unproven.

The use of ultraviolet lighting was found to be correlated with reduced rates of PJI, however, the exposure hazards were 6 to 28 times greater than the recommended limits which also effects the orthopedic operating room personnel [92, 93]. Because of these safety concerns, there are recommendations against the routine use of UV lights in the OR [94 - 96].

One of the most important strategy to improve the air quality is to reduce the room traffic as the number of people in the room increases the air currents and subsequently reduce the quality of the air [87]. Also, a direct correlation between the activity level of OR personnel and bacterial counts in the OR air was shown [97, 98]. Therefore, minimizing the number of personnel in the OR, using a sub-sterile hallway for entry, storing the implants in the room are likely to help improve the air quality in the OR environment.

Skin Preparation

A bath with chlorhexidine soap and to sleep in clean garments and bedding one night before surgery appears to be a simple and cost-effective method to reduce PJI rates [52, 83]. A whole body disinfection was significantly superior compared with local washing or no washing at all [84, 99]. Hair clipping on the morning of surgery as opposed to shaving lowers the rate of SSI because a razor may cause superficial skin abrasions and results an increase in colonization of bacteria at the incision site [100]. Only hair around the incision should be removed [101].

There is no consensus as to use whether chlorhexidine gluconate (CHG) or povidone-iodine provides superior preoperative skin antisepsis [102 - 104]. On the other hand, alcohol-containing products are found to be more effective due to their rapid antimicrobial action [105]. Therefore, whichever agent is chosen, either CHG or iodine-based antiseptics, it is suggested that they should be used in combination with alcohol [52].

Surgical Team

Hospital and surgeon volume are also believed to influence SSI rates. The high-volume surgeons have less SSI rates possibly due to improved surgical skills and a more efficient protocol to minimize the risk of PJI [106]. The type of hospital is also a factor that have influence on revision rates; non-teaching hospitals are found to have a higher risk of SSI [107].

Blood Management

Numerous studies have shown that allogeneic blood transfusion increases the risk of SSI through the mechanism of immunomodulation [108]. Moreover, rates of SSI and lower and upper respiratory tract infections were significantly increased after elective TJA in patients receiving allogeneic blood transfusion compared with patients who did not receive blood transfusion [109]. On the other hand, the role of autologous transfusion in the risk of developing SSI and PJI remains inconclusive. Taken together, much effort should be exercised before the surgery in order to decrease the need for any type of blood product transfusion.

Wound Closure

There are various methods of wound closure including staples, skin adhesives, barbed sutures, however, none of these methods have an overall superiority over another. Livesey *et al.* found closure with staples quicker and less expensive compared with skin adhesives, without significant complications [110, 113]. TKA and THA may differ in

some aspects in regards to closure methods, it was reported that skin adhesives are not appropriate for TKA because of the risk of failure during the early rehabilitation [111, 114]. Although the use of barbed sutures provide advantages in terms of time and cost some studies found increased the frequency and severity of wound complications [112, 113, 115, 116]. The use of monofilament sutures are recommended because they are less susceptible to bacterial growth [114, 117].

There is ample evidence to suggest that routine use of surgical drains during TJA may not be necessary. The tips of the drains are showed to be contaminated in many studies from 41% to 54% [110, 111, 115, 116]. Theoretically, the contamination of drain tips may lead to infection, on the other hand, these results were not correlated with a subsequent PJI rates [117].

After closure of the wound the wound dressing should be placed in the theater under sterile conditions, kept in place for a few days without a need for changes, allow for range of motion without causing skin stretching and blistering, and the dressing should be occlusive which may result in lower rates of SSI [118 - 120].

CONCLUSION

Prevention is the most critical step in decreasing rates of PJI. A patient with high risk factors will ultimately compromise the healing process, allowing bacteria to settle and replicate in the surgical field. Defining the risks preoperatively and optimizing the patient is the most effective strategy for the prevention of PJI. Implementation of a comprehensive, standardized, evidence-based perioperative protocol should be the first step to battle this frustrating and challenging complication. A protocol can be instituted on either an institutional or national basis. Clarification of the most common risk factors for the patient population is critical for taking further steps. Ongoing research for prevention of PJI, such as vaccination or smart implants, is promising; however, further improvements in prevention practices are warranted before these methods can be clinically applied.

DISCLOSURE

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CONFLICT OF INTEREST

JP is an equity owner in CD Diagnostics, a company that is involved in developing molecular biomarker for diagnosis of PJI. JP is also a paid consultant to various companies that are involved in development of novel techniques for management of PJI.

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