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REVIEW

Identification and preoperative optimization of risk factors to prevent periprosthetic joint infection

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Abstract

Despite significant improvements over the past several decades in diagnosis, treatment and prevention of periprosthetic joint infection (PJI), it still remains a major challenge following total joint arthroplasty. Given the devastating nature and accelerated incidence of PJI, prevention is the most important strategy to deal with this challenging problem and should start from identifying risk factors. Understanding and well-organized optimization of these risk factors in individuals before elective arthroplasty are essential to the ultimate success in reducing the incidence of PJI. Even though some risk factors such as demographic characteristics are seldom changeable, they allow more accurate expectation regarding individual risks of PJI and thus, make proper counseling for shared preoperative decision-making possible. Others that increase the risk of PJI, but are potentially modifiable should be optimized prior to elective arthroplasty. Although remarkable advances have been achieved in past decades, many questions regarding standardized practice to prevent this catastrophic complication remain unanswered. The current study provide a comprehensive knowledge regarding risk factors based on general principles to control surgical site infection by the review of current literature and also share own practice at our institution to provide practical and better understandings.

Key words: Total joint arthroplasty; Periprosthetic joint infection; Prevention; Risk factors; Preoperative optimization

Core tip: Despite general success in joint arthroplasty, periprosthetic joint infection remains a serious challenge. With the accelerated incidence and increased charges, PJIs are expected to impose substantial medical and socioeconomic burden in the future. There is no debate that the prevention is the first and the best strategy to minimize this catastrophic complication and the specific strategies for prevention should be integrated into and be in accordance with the general principles to control surgical site infection. Thus, we provide a comprehensive approach based on these general principles as well as own specific practice at our institution for better understandings.

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INTRODUCTION

Although significant improvements have reduced the rate of periprosthetic joint infection (PJI) in the past decades[1-3], PJI still remains the leading cause of revision after total knee arthroplasty (TKA) ranging from 0.4% to 4.0%, and it is the third most common complication afflicting 0.3% to 2.2% following total hip arthroplasty

(THA)[4-7]. A study performed in the United States using the Nationwide Inpatient Sample database estimated that the number of primary TKA and THA would increase by 673% and 174%, respectively from 2005 to 2030[8]. With increasing number of arthroplasties performed every year, the corresponding increase in the number of PJIs is also expected. The authors predicted that the burden of PJI would increase from 1.4% to 6.5% after THA and from 1.4% to 6.8% after TKA, respectively during same period.

Prevention is the first and best strategy to minimize this catastrophic complication. With the recent emerging interests in prevention, several reviews have described the strategies, but most of them put emphasis on intra- or post-operative measures[3,9-19]. Although each reviews provided invaluable information, the strategies to minimize PJI should start from identifying and optimizing preexisting risk factors. The understanding of these risk factors can help identifying patients at high risk and proper screening for prior medical conditions is essential to develop appropriate interventions for those patients. Moreover, those interventions should be integrated into and be in accordance with the general principles for surgical site infection (SSI). Therefore, the purpose of this article is to provide comprehensive knowledge on identifying and optimizing risk factors to minimize PJI based on recommendations on such as a guideline for prevention of SSI by the US Centers for Disease Control and Prevention (CDC) (Table 1)[20]. Also we will provide individualized practice at our institution for practical and thus, effective understanding.

Demographic characteristics such as gender are seldom changeable and will be explored first. Others that increase the risk of PJI, but are potentially modifiable should be optimized prior to elective arthroplasty. In the following sections, demographic characteristics that increase the risk of PJI, will be presented and followed by preexisting comorbidities potentially modifiable

DEMOGRAPHIC CHARACTERISTICS

Specific demographic characteristics such as male gender[4,21,22] and low socioeconomic status[4,22,23] are associated with increased risk of PJI. Female had a significantly lower risk of PJI by 17% after THA[4] and 24% after TKA[22]. The first year following THA, the annual incidence was relatively stable up to 10 years follow-up at 0.3% for female and 0.4% for male[4]. Patients receiving public assistance for Medicare premium, a national social insurance program employed in United States, were at elevated risk for developing PJI by 34% after THA[4] and 27% after TKA[22]. A hypothesis explaining these increased risk is that low socioeconomic status may reflect the level of nutrition, smoking status or preexisting comorbidities, all of which would contribute to the risk of PJI[4] or other complications such as mortality[24] and poor functional outcome[25].

PREEXISTING COMORBIDITIES

Controversies remain regarding some of these risk factors due to lack of prospective studies of high quality as well as low incidence of PJI. Studies using Medicare administrative claims data providing up to 10 years of follow-up identified the following independent risk factors for PJI (in decreasing order of significance): congestive heart failure, chronic pulmonary disease, preoperative anemia, diabetes, depression, renal disease, pulmonary circulation disorders, obesity, rheumatologic disease, psychoses, metastatic tumor, peripheral vascular disease, valvular disease in THA[26] and rheumatologic disease, obesity, coagulopathy and preoperative anemia in TKA[27]. Among retrospective studies with fewer subjects from a single institution, Keats[28] reported higher American Society of Anesthesiologists (ASA) score, morbid obesity, bilateral arthroplasty, knee arthroplasty, allogeneic transfusion, postoperative atrial fibrillation, myocardial infarction, urinary tract infection and longer hospitalization as risk factors for developing PJI within the first year after TJA[5]. ASA score ranks patients for risk of adverse events during an operative procedure and this classification is usually used as a surrogate for underlying severity of illness[29]. Lai *et al*[30] also reported that diabetes, absence of prophylactic antibiotics, previous operations, remote infection and total number of medical comorbidities including cardiovascular, respiratory, gastrointestinal, genitourinary, metabolic/endocrine, neurologic and hematologic conditions had a cumulative effect on the likelihood of developing PJI and each medical comorbidity increased the risk of PJI by 35%. In the following sections, risk factors that are commonly encountered will be discussed separately:

Cardiac disorder

The adjusted hazard ratio (HR) after TKA in patients with congestive heart failure is 1.28, for valvular disease 1.15, and pulmonary circulation disorders 1.42[26]. Patients with cardiac disorders have a higher chance of receiving aggressive anticoagulation, an independent risk factor for developing PJI due to post-operative hematoma[31]. Patients with serious cardiac disorder are generally more sick and older and have slower wound healing resulting in later infection[5]. Thus, the patients at higher risk should be referred to a cardiologist for a pre-operative evaluation. We currently give no aggressive anticoagulation to these patients.

Preoperative anemia

Patients with preoperative anemia are at increased risk for developing PJI, HR of 1.36 after THA[27] and HR of 1.26 after TKA[26]. Patients with preoperative anemia undergoing arthroplasty are more likely to receive allogeneic blood transfusions[32], increasing the risk of postoperative infection[33]. Preoperative prescription of medication such as recombinant human erythropoietin can decrease the need for transfusion, lessening the risk of PJI[34]. Because of high cost, however, we currently do not prescribe preoperative erythropoietin, but instead, evaluate any possible causes of anemia such as poor nutrition, another risk factor for developing PJI[27]. We don't withhold nec-

Table 1 Risk factors for periprosthetic joint infection

Risk factors	Grade of recommendation by CDC[20]
Demographic characteristics	
Gender	-
Socioeconomic states	-
Preexistent comorbidities	
Cardiac disorder	-
Preoperative anemia	-
Obesity	-
Diabetes	Category Ⅰ B
Smoking	Category Ⅰ B
Malnutrition[1]	No recommendation. Unresolved issue
Rheumatologic disease and	No recommendation. Unresolved issue
Cessation of Steroid use[2]	
Coagulopathy	-
Malignancy	-
Depression and Psychosis	-
Treat remote or coexistent infection prior to operation	Category Ⅰ A

[1]Enhance nutritional support for surgical patients solely as a means to prevent infection; [2]Taper or discontinue systemic steroid use (when medically permissible) before elective operation. CDC: Centers for Disease Control and Prevention. Category Ⅰ A: Strongly recommended for implementation and supported by well-designed experimental, clinical, or epidemiological studies; Category Ⅰ B: Strongly recommended for implementation and supported by some experimental, clinical, or epidemiological studies and strong theoretical rationale; Category Ⅱ: Suggested for implementation and supported by suggestive clinical or epidemiological studies or theoretical rationale. No recommendation. Unresolved issue. Practices which insufficient evidence or no consensus regarding efficacy exists.

essary blood products from surgical patients as a means to prevent infection

Obesity

Obese patients are at higher risk of PJI after THA (HR of 1.73) than after TKA (HR of 1.22)[26]. The attributed risk of obesity for PJI has been reported at 2.7% after THA[27]. Patients with a BMI more than 20% of their ideal weight are also at increased risk of developing an infection due to "paradoxical malnutrition"[35,36]. Although obesity is frequently difficult to modify, weight reduction prior to elective arthroplasty should be recommended to minimize PJI. Even when patients are considering surgical management for weight reduction such as gastric bypass, this counsel should come first to pursue the benefit of weight reduction. Although morbid obesity is rare in Asians, obese patients are routinely counseled for weight reduction prior to elective arthroplasty and surgical procedures for weight reduction are rarely performed at our institution.

Diabetes

According to the study using Medicare administrative claims data, 22% of patients undergoing TKA had diabetes and those with diabetes were at increased risk with HR of 1.19 for developing infection after TKA[26]. Currently, our policy is that we do not perform elective arthroplasty in patients with uncontrolled glucose levels and hemoglobin A1C levels that reflect long-term glucose control should be normalized (under 6.9%) in diabetic patients, especially when combined with anemia.

Peripheral vascular disease and smoking

Vascular insufficiencies are at increased risk of PJI, especially after TKA with HR of 1.13[26]. Also, smoking is associated with a higher rate of developing infection after TKA[37]. Smoking has deleterious effects including decreased tissue oxygenation, impaired neutrophil defense and resultant retardation of wound healing[38-40]. Following CDC guidelines, we currently enroll smokers in a smoking cessation program and instruct them to abstain for at least 30 d before elective arthroplasty. Working with patients and an appropriate consultant together is often beneficial to optimize this risk factor and reduce the risk of PJI.

Malnutrition

Although theoretical arguments can be made for a belief that preoperative malnutrition should increase the risk of PJI, the CDC reported that benefits of preoperative nutritional repletion of malnourished patients in reducing SSI risk were unproven and concluded that randomized clinical trials would be necessary to determine if nutritional support alters SSI risk in specific patient-operation combinations (Table 1)[41]. The diagnosis of malnutrition can be made if serum transferrin levels are less than 200 mg/dL, serum albumin less than 3.4 g/dL, and total lymphocyte count less than 1500 cells/mm^3[42]. Greene *et al*[35] reported that preoperative lymphocyte count of less than 1500 cells/mm^3 was associated with a five times greater frequency of developing a major wound complication and an albumin level of less than 3.5 g/dL had a seven times greater risk. At our institution, the level of serum albumin and total lymphocyte count can be easily obtained from routine blood test and elective arthroplasty is delayed in any patients in whom malnutrition is diagnosed until nutritional status improves and medical underlying conditions are optimized.

Rheumatologic disease and immunosuppressant

Patients with rheumatoid arthritis are at increased risk of developing PJI[4,26,27] and the independent attributable risk for developing PJI has been reported up to 5.5% with HR of 1.71 after THA[27] and HR of 1.18 after TKA[26]. The increased risk seems mainly due to the immunosuppressive disease modifying drugs and use of systemic steroids for extended periods[30,36,37]. The CDC reported that data supporting this relationship were contradictory (Table 1)[41], but these controversies may originate from imbalance between suppressive effect of inflammatory disease process and deleterious effect of immune suppression by long-term use of immunosuppressive agents. We currently taper or discontinue systemic steroid use when medically permissible or unless flare is apparent.

Coagulopathy

Coagulopathy including high international normalized ra-

tio (INR), can lead to a higher chance of intra-operative bleeding and subsequent hematoma formation[21,31,36,43] and is an independent risk factor with an attributable risk of 2.7% as well as HR of 1.58 after THA[27]. Recently, increased compliance for venous thromboembolism (VTE) prophylaxis has led to unintended bleeding and increased infections after THA[44]. We routinely use intermittent pneumatic compression device, but reserve chemoprophylaxis against VTE for selective patients with positive ultrasonographic findings because the prevalence of VTE in Korean patients without thromboprophylaxis is reported to be low[45].

Malignancy

Berbari *et al*[46] suggested that the presence of a malignancy is associated with an increased risk of PJI in a matched case-control study and Bozic *et al*[26] reported metastatic tumor as a risk factor with HR of 1.59 as well. At our institution, optimization after evaluating immune function as well as nutritional status are important steps in these patients in whom elective arthroplasty is scheduled.

Depression and psychosis

Depression and psychosis are risk factors of developing PJI after TKA with HR of 1.28 for depression and with HR of 1.26 for psychosis[26]. Depression may be associated with poor nutritional status, an important risk factor for the development of PJI[47]. At our institution, evaluation of coexisting depression is integrated with the initial medical screening and often, management of depressive mood itself improves the clinical symptoms of osteoarthritis. Consequently, we can avoid unnecessary arthroplasty in early stage[47]. Also, we rarely perform elective arthroplasty in patients with psychosis.

Remote or coexistent infection

It is critical to make sure that the patient has no other remote or concurrent infections such as a urinary tract infection and those with remote infections should be optimized by eradication of the infection prior to elective arthroplasty with appropriate antibiotic therapy[5,20]. Human immunodeficiency virus (HIV) is a risk factor for developing PJI and those with HIV should be placed on regimens to maintain the viral load under detectable level[48,49]. In our institution, these infections should be eradicated via appropriate antibiotic therapy prior to elective arthroplasty except hemiarthroplasty for patients with femur neck fracture. We don't have an experience of arthroplasty in those with HIV because of low prevalence in our country.

Other comorbidities

Patients with chronic renal insufficiency should have normal creatinine value before the elective arthroplasty[50]. Although the creatinine values may be optimized, patients with chronic renal failure are still at high risk of mortality and morbidity including PJI (HR of 1.38 after TKA)[26,51,52]. General skeletal abnormalities and combined multiple comorbidities in these patients may explain the increased risk for developing PJI. However, among 32 THAs performed in 18 patients with chronic renal failure (five patients received kidney transplantation later) at our institution, two patients (4 hips) died at two and four years after THA. At the average follow-up of 147 mo, there were two cup revisions due to aseptic loosening, and the remaining 14 patients who have survived have no infection or no revision yet.

Prior history of infection or steroid injection at the same joint was reported as a risk factor for developing PJI that is seldom modifiable[53,54]. We routinely delay TKA in patients with a history of recent injection into the knee joint within 4 weeks and use antibiotic-impregnated cement when performing TKA in these patients.

INTEGRATION OF MULTIPLE RISK FACTORS AND MEDICAL CLEARANCE

The risk factors mentioned above are all important for developing PJI. Measures like the modified Charlson Comorbidity Index[55] or ASA score are of value to quantify overall health of the patient. Patients with an ASA score more than 2[5] or 3[23] are at significantly higher risk for developing infection following THA. Also, those with a Charlson index score greater than 4 are at 157% increased risk of infection after THA and 116% after TKA compared to those with a score of 0[4,22,23]. While these measures help imagine overall pictures of the patients, they are often of limited value at the time of counseling with evaluating the individual-specific risks for developing PJI[27]. An easily accessible electronic risk calculator has recently been developed to provide the individualized risk for PJI after THA integrating interactions between and synergistic effect of these risk factors, especially in patients who have multiple comorbidities[56].

We currently start preoperative medical screening with questionnaires regarding individual background medical history and preoperative routine tests including electrocardiography, chest radiography, blood test and urinalysis. In addition to history taking and laboratory test, we conduct a thorough clinical evaluation with observation of clinical signs or symptoms and physical examination. This is especially important in Asian countries, where acupuncture or moxa cautery is in common use. Also, skin ulceration implies vascular insufficiency or neuropathy, and a patient with any skin problems is not an ideal candidate for elective arthroplasty. These patients are referred to a dermatologist and surgery is delayed until the skin lesion improves. Once any medical comorbidity is identified, they are optimized by a medical consultant prior to elective arthroplasty and the consultant continues to follow the patients during postoperative period as well.

CONCLUSION

Thorough understanding of risk factors in individual patients and attentive application of the general principle

for preoperative optimization are paramount to reduce overall incidence of periprosthetic joint infection. Even though some risk factors such as demographic characteristics are seldom changeable, they allow more accurate expectation regarding individual risks of PJI and thus, make proper counseling for shared preoperative decision-making possible. Others that increase the risk of PJI, but are potentially modifiable should be optimized prior to elective arthroplasty. Although remarkable advances have been achieved in past decades, many questions regarding standardized practice to prevent this catastrophic complication remain unanswered. Randomized controlled trials incorporated with general principles for preventing surgical site infection are necessary to determine the best approach.

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