

# Patient-related medical risk factors for periprosthetic joint infection of the hip and knee

Aleeson Eka, Antonia F. Chen

Rothman Institute, Department of Orthopaedic Surgery, Thomas Jefferson University, Philadelphia, PA 19107, USA

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*Correspondence to:* Antonia F. Chen, MD, MBA. 925 Chestnut Street, Philadelphia, PA 19107, USA. Email: Antonia.chen@rothmaninstitute.com.

**Abstract:** Despite advancements and improvements in methods for preventing infection, periprosthetic joint infection (PJI) is a significant complication following total joint arthroplasty (TJA). Prevention is the most important strategy to deal with this disabling complication, and prevention should begin with identifying patient-related risk factors. Medical risk factors, such as morbid obesity, malnutrition, hyperglycemia, uncontrolled diabetes mellitus, rheumatoid arthritis (RA), preoperative anemia, cardiovascular disorders, chronic renal failure, smoking, alcohol abuse and depression, should be evaluated and optimized prior to surgery. Treating patients to get laboratory values under a specified threshold or cessation of certain modifiable risk factors can decrease the risk of PJI. Although significant advances have been made in past decades to identify these risk factors, there remains some uncertainty regarding the risk factors predisposing TJA patients to PJI. Through a review of the current literature, this paper aims to comprehensively evaluate and provide a better understanding of known medical risk factors for PJI after TJA.

**Keywords:** Total joint arthroplasty (TJA); periprosthetic joint infection (PJA); prevention; risk factors; preoperative optimization

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## Introduction

Total joint arthroplasty (TJA) is a surgical procedure that provides pain relief and restores function for patients suffering from debilitating arthritis (1). The number of TJAs performed annually has risen in recent years and is expected to reach 572,000 for total hip arthroplasty (THA) and 3.48 million for total knee arthroplasty (TKA) by 2030 (2,3). Despite the overall success of the procedure, periprosthetic joint infection (PJI) is a rare but devastating complication that is a major cause of failure after TJA (4,5). As the number of TJAs increases with time, the number of PJIs is also expected to increase, leaving more patients with the burden of compromised function and reduced quality of life (1). Despite established perioperative methods of preventing infection, there are multiple medical risk factors that predispose patients to infection.

Medical conditions, such as obesity, diabetes and

rheumatologic disease, have been reported as consistent risk factors for PJI (5-7). However, a great deal of variability exists in the literature with regards to other medical conditions that have been reported as risk factors for infection, including coagulopathy, preoperative anemia, congestive heart failure, chronic pulmonary disease, depression, renal disease, pulmonary circulation disorders, psychoses, metastatic tumor, peripheral vascular disease, and valvular disease (7-11). Strategies to reduce the rate of PJI in TJA patients should begin with addressing these modifiable, patient-related, medical risk factors. It is imperative that orthopaedic surgeons understand and identify these risk factors prior to TJA so that they can develop interventions to optimize patients and minimize their risk of developing a postoperative infection. Therefore, the purpose of this review is to describe the risk factors associated with PJI and current strategies for preventing infection.

### Morbid obesity

Obesity is a major health concern in the United States, as being obese is associated with increased risk for other comorbid conditions, such as diabetes mellitus, ischemic heart disease, hypertension, poor nutritional status and early mortality (12). Obese patients are more likely to undergo TJA (12), but these patients have a higher incidence of perioperative complications (10,13-15). Obese patients have an increased risk of PJI after THA [adjusted hazard ratio (HR) =1.73] and after TKA (HR =1.22) (5,8). The risk of PJI has been shown to increase exponentially with body mass index (BMI), as BMI >40 kg/m<sup>2</sup> (obese) increased the risk of infection by 3.3 times, while a BMI >50 kg/m<sup>2</sup> (morbidly obese) increased the risk of infection by 21 times (15,16). Likewise, Jämsen *et al.* evaluated 7,181 primary TJAs and reported that the infection rate increased from 0.37% in patients with normal BMI to 4.66% in morbidly obese patients (17). Thus, morbid obesity has frequently been implicated as an independent risk factor for PJI in several studies.

Obese patients may be at increased risk of PJI due to prolonged operative time, increased need for allogeneic blood transfusion, and the presence of other medical comorbidities (18-20). This patient population is also at an increased risk of wound dehiscence due to increased surface tension at the surgical site, as well as postoperative surgical wound complications such as hematoma formation and prolonged wound drainage that may increase the risk of PJI (21,22). Obese patients undergoing TJA are also at increased risk of developing an infection due to “paradoxical malnutrition”, as these patients are often malnourished despite their obesity (5). Interestingly, studies have shown that the effects of obesity on the risk of PJI decline with time. Bozic *et al.* reported that the risk of PJI associated with obesity was 19% lower (P=0.025) 1 year after TJA (7).

Preoperative weight reduction should be recommended to minimize the risk of PJI in morbidly obese patients undergoing elective TJA (5). While an absolute cutoff with respect to BMI has yet to be established, orthopaedic surgeons should attempt to optimize obese and morbidly obese patients to BMI below 40 kg/m<sup>2</sup> preoperatively while maintaining overall nutritional status (23).

### Malnutrition

While several underlying conditions, such as age and obesity, can potentially contribute to the poor nutritional state in malnourished patients, malnutrition independently

increases the risk of PJI in patients undergoing TJA (5,22,24,25). Malnutrition can be defined as a serum albumin level <3.5 g/dL, serum transferrin levels <200 mg/dL, serum prealbumin <15 gm/dL and total lymphocyte count (TLC) <1,500 cells/mm<sup>3</sup> (22,26). Green *et al.* reviewed the records of 217 patients undergoing primary TJA and found that there was 5 times greater risk of PJI in patients with preoperative TLC <1,500 cells/mm<sup>3</sup> and a 7 times greater risk of infection in patients with albumin levels <3.5 g/dL (25). For revision TJA, Yi *et al.* prospectively evaluated 600 patients and reported a high infection rate of 7% in patients that had one or more parameters positive for malnutrition compared to 1% in patients without malnutrition (P=0.003) (27). Malnutrition has been shown to interfere with optimal synthesis of collagen and proteoglycan, resulting in disruptions in the wound healing process that can lead to persistent wound drainage and increased risk of infection (22,28,29).

The current definitions of malnutrition are effective for identifying protein deficiency, however, they fail to indicate other aspects of malnutrition including caloric or vitamin deficiency (22,30). For example, Maier *et al.* reported a higher prevalence of vitamin D deficiency in PJI patients compared to non-infected patients (4). This indicates a need for more comprehensive parameters for defining malnutrition and also suggests a need for screening and treating hypovitaminosis D before orthopaedic surgery.

Thus, the data suggests that poor nutrition increases the risk of postoperative PJI in patients undergoing TJA. It may be beneficial to comprehensively assess the nutritional status of suspected malnourished patients prior to elective TJA (22,25). Though the optimal method for addressing malnutrition has yet to be determined, treatment options include administration of high protein supplements, vitamin and mineral supplementation and increased caloric intake (26,31,32).

### Hyperglycemia and uncontrolled diabetes mellitus

Diabetes mellitus is one of the most common disorders worldwide and the prevalence of diabetes has increased in the past few decades. Globally, 382 million people had diabetes in 2013 and that number is expected to rise to 592 million by 2035 (33). The number of diabetic patients undergoing TJA has also increased yearly, as diabetes significantly increases the risk of developing severe osteoarthritis (34,35). Yang *et al.* has reported that the

prevalence of diabetes among TKA patients was 12.2% (34).

Diabetes mellitus is a known, independent risk factor for developing PJI (8,9,34). Jämsen *et al.* reported that PJI occurred in 1.59% of THA and 2.19% of TKA patients with diabetes, compared to infection rates of 0.66% and 0.48%, respectively, in non-diabetic patients (17). The level of glycemic control has also been reported to influence the risk of PJI (22). Uncontrolled diabetes is defined as blood glucose levels greater than 200 mg/L or hemoglobin (Hgb) A1c levels greater than 7% (11). Marchant *et al.* compared uncontrolled diabetes, controlled diabetes, and non-diabetic patients and found that there was a significantly increased risk of developing a postoperative wound infection when diabetes was inadequately controlled [adjusted odds ratio (OR) =2.28; 95% confidence interval (CI), 1.36-3.81; P=0.002] (36).

Perioperative hyperglycemia is also a risk factor for PJI in arthroplasty patients, as blood glucose values greater than 200 mg/dL double the risk of PJI (37). Mraovic *et al.* reported that even patients without a diagnosis of diabetes were 3 times more likely to develop PJI if their postoperative day (POD) 1 blood glucose values were >140 mg/dL. PJI patients had significantly higher perioperative blood glucose values (PJI 112±36 mg/dL; non-PJI 105±31 mg/dL; P=0.043) and higher POD 1 blood glucose values (PJI 154±37 mg/dL; non-PJI 138±31 mg/dL; P<0.001). Additionally, there were significantly more diabetic patients in the infected group (22%) than the non-infected group (9%, P<0.001) (37). These results indicate that diabetes mellitus and perioperative blood glucose levels are predictors for PJI following TJA.

This increased risk of PJI in diabetics and hyperglycemic patients may be due to impaired defenses against bacteria, including reduced vascular permeability, oxygen delivery and redox reactions, neutrophil adherence, chemotaxis and phagocytosis of immune cells, functionality of antibody responses and complement proteins, and intracellular bactericidal activity (38). This can impair wound healing (39,40), as 1.2-12% of diabetic patients experience wound related complications following TJA (22). Likewise, elevated glucose levels may increase biofilm formation (41).

The role of HgbA1c in predicting the development of PJI has not yet been definitively confirmed and the literature for a HgbA1c cut off is controversial. Iorio *et al.* failed to report an association between HgbA1c values and susceptibility to infection, and concluded that HbA1c values may not be effective predictors for postoperative infection (42). Likewise, Kremers *et al.* reported that poor

glycemic control, as assessed by HgbA1c levels, was not a good predictor of PJI risk (43). More recently, Chrastil *et al.* reported no increased risk of PJI associated with elevated HgbA1c (HR =0.86, P=0.23) (44).

However, several studies have indicated a specific cutoff value above which risk of postoperative infection increases significantly. The reported values vary between studies, but preoperative HgbA1c values of 7% (38), 7.5% (45), and 8% (46) have been suggested as cutoffs. Harris *et al.* also reported that preoperative HgbA1c ≥7% increased risk of postoperative complications. However, they suggest that this value of 7% should not be designated as a discrete threshold; optimizing a patient from 8.5% to 7.2% will reduce complication risk more than a reduction from 7.2% to 6.9% (47). Furthermore, enforcing a strict cutoff HgbA1c values above which elective surgery is delayed, especially if this value is too low, can postpone surgery for a number of patients who may not have otherwise experienced a postoperative complication (47). Giori *et al.* reported that 41% of diabetic patients whose surgery was delayed pending reduction of HgbA1c to ≤7% were unable to cross this threshold (48). A HgbA1c value of 8% may be a more realistic threshold value necessitating preoperative optimization for diabetic patients. While it is critical to optimize patients before elective TJA, increased risk of postoperative infection in patients with uncontrolled diabetes and perioperative hyperglycemia must be balanced against the fact that access to TJA could significantly improve their quality of life. Orthopaedic surgeons must work with their diabetic and hyperglycemic patients to decide how to balance these factors.

### Rheumatoid arthritis (RA)

Nearly 5% of TJA patients have RA (24). Several studies have reported RA as an independent risk factor for PJI, with infection rates being higher in RA patients compared to patients without RA (HR =1.71 after THA and HR =1.18 after TKA) (7,8,17,49). The underlying mechanism causing this increased risk of infection has yet to be defined. However, reports suggest that the disease itself, associated comorbid conditions, and immunosuppressive therapies collectively contribute to increased PJI susceptibility (50).

Immunosuppressive therapies involving corticosteroids, such as prednisone, and disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate, that inhibit tumor necrosis factor alpha (TNF- $\alpha$ ) or interleukin 6 (IL-6) production place TJA patients with RA at greater risk

for postoperative infection (51-53). Decreased immunity with these medications increases the incidence of surgical wound complications like wound dehiscence, which may lead to PJI (54). Likewise, continued use of methotrexate therapy during the perioperative period has been shown to increase the rate of postoperative infection. Postoperative investigations by Carpenter *et al.* demonstrated that discontinuation of methotrexate one week before and after surgery significantly decreased the risk of PJI in RA patients undergoing elective TJA (55). However, there is some controversy surrounding this association, as some studies have reported no increase in the incidence of PJI, regardless of whether these treatments are discontinued perioperatively (56). Grennan *et al.* studied patients with RA undergoing elective orthopaedic surgery and reported that patients undergoing continued methotrexate treatment showed a significantly reduced infection rate compared to patients who discontinued methotrexate two weeks before and after surgery, suggesting that methotrexate treatment should not be stopped in RA patients before elective surgery (57).

Although there is a lack of consensus in the literature regarding the discontinuance of anti-rheumatic therapy before elective TJA, expert opinion seems to suggest the importance of cessation to reduce PJI risk. The American College of Rheumatology and the British Society for Rheumatology recommends withholding TNF- $\alpha$  inhibitors around the time of TJA (58-60). Likewise, the International Consensus Group (ICG) on Periprosthetic Joint Infection recommended stopping DMARDs prior to elective joint arthroplasty and developed a cessation schedule for different immunosuppressive agents (*Table 1*).

### Preoperative anemia

Preoperative anemia, defined as hemoglobin level less than 12 g/dL in women and less than 13 g/dL in men, frequently occurs in 15% to 33% of patients undergoing elective TJA (61). Patients with preoperative anemia are at greater risk for developing PJI (HR =1.36 after THA and HR =1.26 after TKA) (7,8). Out of 15,722 elective TJA patients, PJI occurred more frequently in anemic patients (4.3%) compared to non-anemic patients (2%,  $P<0.01$ ). Multivariate analysis showed that the risk of PJI was higher in anemic patients than in non-anemic patients, identifying preoperative anemia as an independent risk factor for PJI (61).

The literature describing the pathophysiologic association

**Table 1** Recommendation for cessation of anti-inflammatory agents prior to total joint arthroplasty

Recommendation	Half life	Medication
Continue therapy up to and including the surgery day	1-2 months	Hydroxychloroquine
Hold for at least 1.5 weeks prior to surgery	4.3 days	Etanercept
Hold for 3 weeks prior to surgery	8-10 days	Infliximab
Hold for 1 month prior to surgery	12-14 days	Abatacept; adalimumab; certolizumab; golimumab; tocilizumab
Hold for 6 weeks prior	~2 weeks	Leflunomide
Hold for 2 months prior	21 days	Rituximab
Discontinue 1 week prior to surgery	2-17 h	NSAIDs*
	1-2 h	Allopurinol
	26-32 h	Colchicine
	26-32 h	Probenecid
	5 h	Sulfasalazine
	7.6 h	Azathioprine
	0.7-5.8 h	Methotrexate <sup>a*</sup>

Adapted from Aggarwal *et al.* and Rezapoor *et al.* (26,58).  
<sup>a</sup>, continue therapy 2 weeks after surgery, for patients with renal dysfunction, hold 2 weeks prior to surgery; \*, controversial stop time.

between preoperative anemia and increased risk for PJI is limited. However, reports indicate that patients with preoperative anemia are more likely to receive perioperative allogeneic blood transfusions, which is associated with increased postoperative infection (62,63). Though it is costly, preoperatively prescribing recombinant human erythropoietin can decrease the perioperative need for transfusion, lowering the risk of subsequent joint infection (5,64). Conversely, orthopedists can preoperatively evaluate any other possible causes for anemia, such as iron deficiency, in order to minimize the risk of PJI (5,65,66).

### Cardiovascular disorders

Several studies have indicated that cardiovascular disorders predispose arthroplasty patients to PJI (8,10,37). Bozic *et al.* reported that the following specific cardiovascular diseases can significantly predispose patients to PJI: congestive heart failure (HR =1.28), peripheral valvular disease (HR =1.13),

valvular disease (HR =1.15) and pulmonary circulation disorders (HR =1.42) (8). Pulido *et al.* reported that atrial fibrillation and myocardial infarction are independent comorbid factors associated with higher risks of infection, as well (10). These authors suggested that this increased risk of infection could be due to the fact that patients with cardiac disorders are more likely to receive aggressive anticoagulation (10).

For example, in patients with atrial fibrillation, the American College of Chest Physicians (ACCP) recommends high-dose aspirin or warfarin anticoagulation therapy. Warfarin therapy typically keeps the international normalized ratio (INR) in the range of 2.0-3.0, which significantly increases the risk of bleeding events after TJA. In a retrospective study examining atrial fibrillation and chronic anticoagulation therapy, Aggarwal *et al.* reported that patients with atrial fibrillation had a significantly higher prevalence of PJI (5.6% *vs.* 0.62%;  $P=0.02$ ) (67).

To minimize the risk of PJI, patients with cardiovascular disorders should work with cardiologists to halt anticoagulation therapy and normalize INR levels (67). Patients with serious cardiovascular disorders tend to be older and may have increased problems with wound healing (10). These patients are at higher risk of infection and should be referred to a cardiologist for preoperative evaluation (8,10).

### Chronic renal failure

Chronic renal failure is a growing problem worldwide. Patients suffering from chronic renal failure are initially treated with medications, though many ultimately require hemodialysis or renal transplantation (68). Long-term hemodialysis patients often develop  $\beta$ 2-microglobulin amyloid deposition in and around joints, which invades the synovium, capsule, and cartilage and causes effusive arthropathy (68,69). Likewise, renal transplant patients receive life-long corticosteroid and immunosuppressive therapy, and are at greater risk of developing avascular necrosis of the femoral head (70-72). Thus, a significant number of patients with chronic renal failure develop degenerative joint disease and many eventually require TJA for erosive osteoarthritis, osteonecrosis, or following femoral neck fractures (69,73). In fact, these patients are 5 to 6 times more likely to require TJA than the general population (70,71).

Reports suggest that patients with chronic renal failure are also at a greater risk of developing PJI (HR

=1.38 after TKA) (8,68,70,74). Interestingly, the risk of infection seems to be higher in hemodialysis patients than immunosuppressed transplant patients. Lieu *et al.* reported that hemodialysis patients had approximately twice the infection rate and higher rates of mortality than renal transplant patients (70). Likewise, Shrader *et al.* found that the PJI rate was 22% in hemodialysis patients and 8% in renal transplant patients (75). Notably, studies have shown that both groups showed increased rates of PJI compared to patients without chronic renal failure (70,75). Though several studies have reported that this increased infection rate is seen in both hemodialysis and renal transplant patients undergoing TJA, some studies suggest the opposite, reporting that there was no increased risk of infection in renal transplant patients following TJA (71,76-78). However, from the available data, it appears that chronic renal failure patients in both groups are at greater risk of developing PJI.

The exact cause of this increased risk of has yet to be determined, but it is likely multifactorial. Multiple combined comorbidities in these patients may collectively contribute to an increased infection rate (5,70). Additionally, the immunosuppressive nature of therapies associated with renal transplantation and hemodialysis could increase susceptibility to infection (70,74). Regardless of the pathophysiological association between chronic renal failure and PJI, it is imperative that in patients with renal failure, prophylaxis and treatment of infection is strictly monitored due to the potential nephrotoxicity from antibiotics (68).

### Smoking

Smoking is known to be associated with increased postoperative morbidity and mortality (79). In arthroplasty patients, smoking reduces blood flow to the healing tissue and impairs delivery of humoral and cellular mechanisms of immunity to the surgical site (80,81). Nicotine in cigarettes releases catecholamines that lead to vasoconstriction and hypoperfusion and also increases local platelet aggregation and thrombi formation, which may further limit soft-tissue perfusion (82). Additionally, studies have demonstrated that nicotine in cigarettes has immunomodulatory effects, disrupting immune cell function and placing TJA patients at increased risk of developing a postoperative infection (83,84). Wound hypoxia associated with smoking also disturbs neutrophil defense mechanisms against pathogens and disrupts tissue repair (80,85). Tissue hypoxia can occur not only from vasoconstriction but also from inhaled carbon

monoxide in cigarette smoke (86). Carbon monoxide binds strongly to hemoglobin and forms carboxyhemoglobin, which has a high affinity for oxygen and significantly decreases oxygen delivery to healing tissues (87,88). As adequate oxygenation is essential for effective tissue repair, smoking significantly impairs soft tissue repair and wound healing, increasing susceptibility to infection (80).

Current smokers undergoing TJA showed significantly increased rates of surgical site infection (SSI) compared to nonsmokers (OR =1.41; 95% CI, 1.16-1.72) (89), and current smokers were more likely to experience wound complications than former smokers and nonsmokers (1.8% compared to 1.3% and 1.1%, respectively;  $P < 0.001$ ) (90). Current smoker status was also identified as a significant risk factor for wound infection, as current smokers had approximately twice the rate of deep wound infection compared with former smokers or nonsmokers (91). These findings support reports that current smoking at the time of elective TJA is associated with increased rates of postoperative wound infection (79,92-94).

While smoking increases the risk of infection, discontinuing smoking prior to surgery has been shown to reduce the risk of postoperative complications [relative risk (RR) =0.76; 95% CI, 0.69-0.84], especially complications related to poor wound healing (95). Although an optimal period of preoperative smoking cessation has yet to be established, most reports suggest a period of 4 to 8 weeks is effective (93,94,96-98). Tønnesen *et al.* reported that, in smokers, immune function is restored after 4-6 weeks of abstinence and wound healing capability is restored after 3-4 weeks (99). Longer periods of preoperative smoking cessation, however, have also been associated with lower rates of postoperative infection and preoperative cessation periods of up to 6 months have also been suggested (83,100). Abrupt reduction in cigarette consumption is rarely permanently successful in terms of smoking cessation. However, individual counseling, self-help groups, nicotine-replacement therapy and physician advising are proven techniques that promote prolonged cessation (97,100). Tobacco use and history of smoking should be preoperatively evaluated and smoking cessation should be highly encouraged in order to optimize the patient prior to TJA and lower the risk of SSI and PJI.

### Alcohol abuse

Excessive alcohol consumption (greater than 40 units per week) increases the risk of postoperative complications,

including episodes of excessive bleeding and infection (99,101). Bradley *et al.* evaluated 9,176 male United States veterans who underwent major, non-cardiac surgery and reported that excessive alcohol consumption significantly increased the risk of developing infection (102). Postoperative complications associated with alcohol abuse are the result of alcohol-induced disruptions of the immune response and the metabolic stress response that augment the physiological stress from the surgical procedure (99). Consuming 2-3 drinks daily disrupts the function of the immune response, manifested as significantly suppressed delayed type hypersensitivity (DTH) (103,104).

Although alcohol cessation has not been demonstrated to reduce the risk of PJI prior to elective TJA, several studies have reported reduced morbidity after a period of abstinence (103,105). DTH is significantly improved after a 2-week period of abstinence and restored to normal after 8 weeks. In alcoholics, immune competence is recovered after 2-6 weeks of alcohol cessation (106) and wound-healing capability is restored after 3-4 weeks of cessation (107). Furthermore, Tønnesen *et al.* reported that alcohol cessation 4 weeks prior to surgery significantly reduced postoperative morbidity in alcohol abusers (99).

A history of alcohol consumption should be preoperatively evaluated and a cessation period of at least 4 weeks prior to surgery should be recommended for alcoholic arthroplasty patients in order to reverse physiological abnormalities associated with excessive alcohol consumption that increase the risk of PJI (58,105).

### Depression

Bozic *et al.* identified depression as an independent risk factor for PJI (HR =1.28) (8). Though the pathophysiology of this association is unknown, physiologic depression and psychosis may be associated with malnutrition and subsequent need for allogeneic blood transfusion, which are separate risk factors for PJI (8,108). Furthermore, depression has a direct effect on the immune system, leaving patients more susceptible to infection (58). Because depression places patients at a greater risk for developing PJI, it may be beneficial to integrate evaluation of depression into the initial medical screening before elective TJA and to delay the elective procedure until depression is well managed (58,109).

### Conclusions

There are many medical risk factors associated with the

**Table 2** Patient-related medical risk factors for periprosthetic joint infection

Risk factor	Link to PJI	Intervention	Goal
Morbid obesity	Prolonged operative time, increased risk of poor wound healing, paradoxical malnutrition, presence of other medical comorbidities	Diet and exercise, bariatric surgery	BMI $\leq 40$ kg/m <sup>2</sup>
Malnutrition	Poor wound healing and persistent wound drainage	Administration of protein, vitamin and mineral supplementation; increased caloric intake	Serum albumin levels $\geq 3.5$ g/dL; Serum transferrin levels $\geq 200$ mg/dL; Serum prealbumin levels $\geq 15$ mg/dL; TLC $\geq 1,500$ cells/mm <sup>3</sup>
Hyperglycemia and uncontrolled diabetes mellitus	Advanced glycation end products, decreased bacterial defenses	Diet and exercise, insulin	HgbA1c $\leq 8\%$ , blood glucose $\leq 200$ mg/dL
Rheumatoid arthritis	Immunosuppressive therapies (corticosteroids and DMARDs), increased rate of surgical wound complications, presence of other medical comorbidities	Perioperative cessation of immunosuppressive therapies	
Preoperative anemia	Increased need for allogeneic blood transfusions	Preoperatively screen for other possible causes of anemia (i.e. iron deficiency), preoperative administration of recombinant human erythropoietin	Hgb $\geq 12$ g/dL in women and 13 g/dL in men
Cardiovascular disorder	Chronic anticoagulation therapy and increased INR; increased risk of wound related complications and poor wound healing	Perioperative cessation of anticoagulation therapy, preoperative evaluation by cardiologist	INR level $\leq 2$
Chronic renal failure	Presence of other medical comorbidities, immunosuppressive nature of therapy (hemodialysis and renal transplantation)	Preoperative evaluation of patient by nephrologist, postoperative management of renal function	
Smoking	Hypoperfusion, platelet aggregation and formation of thrombi, wound hypoxia, poor wound healing, decreased immune defenses	Preoperative evaluation of smoking history, perioperative smoking cessation, individual counseling, physician advising, NTR	
Alcohol abuse	Protein deficiency and malnutrition, diminished host immunity, impaired wound healing	Preoperative evaluation of alcohol history, perioperative alcohol cessation	
Depression	Presence of other medical comorbidities (i.e., malnutrition and need for allogeneic blood transfusion); immunomodulatory effects	Evaluation of depression during preoperative medical screening, treatment of depression prior to surgery	

PJI, periprosthetic joint infection; BMI, body mass index; DMARD, disease-modifying anti-rheumatic drugs; Hgb, hemoglobin; INR, international normalized ratio; TLC, total lymphocyte count; NTR, nicotine replacement therapy.

development of PJI following TJA. Since TJA is an elective surgery, this allows orthopaedic surgeons to medically optimize patients prior to surgery to minimize their risk of developing a postoperative infection (*Table 2*). Although a number of risk factors for PJI have been identified in the literature, the evidence is too limited for many of these risk factors to be able to determine their full association with PJI after TJA. There is a need for further, high-quality research studies to strengthen this limited evidence so that high-risk patients can be more effectively counseled and optimized

preoperatively. It is important to remember that no TJA patient is free of risk, and there are certain risk factors for PJI that have yet to be identified; however, knowledge and understanding of these known risk factors can help orthopaedic surgeons to minimize such risks in order to reduce the incidence of infection.

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## Footnote

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