Knee

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Total knee arthroplasty and infection: how surgeons can reduce the risks

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- Total joint arthroplasty (TJA) is one of the most common orthopaedic procedures. Nevertheless, several complications can lead to implant failure.
- Peri-prosthetic joint infections (PJI) certainly represent a significant challenge in TJA, constituting a major cause of prosthetic revision. The surgeon may have an important role in reducing the PJI rate by limiting the impact of significant risk factors associated to either the patient, the operative environment or the post-operative care.
- In the pre-operative period, several preventive measures may be adopted to manage reversible medical comorbidities. Other recognised pre-operative risk factors are urinary tract infections, intra-articular corticosteroid injections and nasal colonisation with *Staphylococcus (S.) aureus*, particularly the methicillin-resistant strain (MRSA).
- In the intra-operative setting, protective measures for PJI include antibiotic prophylaxis, surgical-site antisepsis and use of pre-admission chlorhexidine washing and pulsed lavage during surgery. In this setting, the use of plastic adhesive drapes and sterile stockinette, as well as using personal protection systems, do not clearly reduce the risk of infection. On the contrary, using sterile theatre light handles and splash basins as well as an increased traffic in the operating room are all associated with an increased risk for PJI.
- In the post-operative period, other infections causing transient bacteraemia, blood transfusion and poor wound care are considered as risk factors for PJI.

Keywords: total knee arthroplasty; infection; risk factors; surgeons

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Introduction

The number of total joint arthroplasties (TJAs) performed has increased steadily in recent years, with projected numbers for the coming years rising further.[1] Consequently, increasing incidence of TJA revision can also be expected.[2] Differing causations hase been reported for TJA failure and revision.[3,4] According to recent data, peri-prosthetic joint infection (PJI) incidence constitutes between approximately 0.3% and 1.7% of all total hip arthroplasties (THA), and between 0.8% and 1.9% of all total knee arthroplasties (TKA).[4,5]

PJI can be classified in intra-operative, early post-operative, acute haematogenous and chronic infections, according to both timing and cause of infection.[6]

The risk factors potentially correlated with acute PJI infection can be divided into pre-operative (usually related to patient comorbidities), peri-operative and post-operative, which are mainly linked to the behaviours of the surgeon and the hospital staff.[7] Conversely, chronic infections are less influenced by the conduct of the surgeon, as they are most often related to haematogenous diffusion of bacteria.[6]

The aim of this paper is to review the recent literature, summarising the most relevant risk factors that the surgeon can modify in order to reduce the incidence of peri-prosthetic joint infection.

Pre-operative factors

Several studies demonstrated that some comorbidity can be associated with an increased risk of PJI.[6,8-10] The American Academy of Orthopaedic Surgeons (AAOS) reported on the different risk factors for PJI and developed a guideline for PJI prevention and treatment.[11]

In 2013 an international group of orthopaedic surgeons gathered in Philadelphia, Pennsylvania to develop a 'consensus' for definition, prevention and management of PJI, as an update to the previous guidelines. The consensus included a list of potential risk factors associated with PJI. (Table 1).[7]

Table 1. Potential risk factors for development of surgical site infection or peri-prosthetic joint infection after elective total joint arthroplasty, according to The International Consensus on Periprosthetic Joint Infection[7]

Comorbidities
Poorly controlled diabetes mellitus (glucose > 200 mg/L or HbA1C >7%)
Poor nutritional state
Morbid obesity (BMI >40 Kg/m2)
Prolonged hospital admission
Severe immunodeficiency
Inflammatory arthropathy (rheumatoid arthritis)
Anaemia
Male sex
Excessive smoking (> one pack per day)
Excessive alcohol consumption (> 40 units per week)
Intravenous drug abuse
Active liver disease
Chronic renal disease
Diagnosis of post-traumatic arthritis
Prior surgical procedure in the affected joint

BMI, body mass index; HbA1c, glycated haemoglobin.

Although the majority of these conditions must be considered as non-modifiable factors, many preventive measures may be adopted to reduce their impact on the development of PJI. Table 2 summarises the modifiable and non-modifiable factors related to PJI, including some preventive measures to manage reversible medical comorbidities, according to the existing literature.[8-10,12-18]

Other potential pre-operative risk factors are intra-articular corticosteroid injections and any infectious disease, particularly urinary tract infection (UTI) and nasal colonisation with *Staphylococcus (S.) aureus*.[19-25]

The relationship between steroid injections and post-operative PJI was evaluated in several studies. Papavasiliou et al[19] reported an incidence of only 2% of infections in a series of 114 TKAs, but all of the infected TKAs had previously been treated with an intra-articular corticosteroid injection within the 11-month period prior to surgery.

Conversely, Desai et al[20] stated that the incidence of infection did not increase in patients with prior steroid injection treatment.

The correlation between post-operative UTIs and PJI has been demonstrated. However, the association between pre-operative bacteriuria and early deep infections remains uncertain.[21,22]

David and Vrahas[23] defined an algorithm for urological evaluation before TJA. The presence of symptoms of a UTI in association with urinary leukocyte counts greater than 1×10^4/mL and a bacterial count greater than 1×10^3/mL should be the only indication for surgical delay. Conversely, in asymptomatic patients it is still possible to proceed with TJA by treating those patients with urine colony counts greater than 1×10^3/mL.[23]

There may be a correlation between nasal colonisation with *S. aureus* and PJI. Different authors confirmed that being a high-level nasal carrier of *S. aureus* is an important and significant independent risk factor for developing SSI with *S. aureus*.[24-26] Nasal application of mupirocin is widely accepted as treatment for nasal carriers of *S. aureus*. In a recent randomised controlled trial (RCT), mupirocin treatment resulted in a simple, safe and cost-effective intervention that can reduce the risk of SSI.[27] However, literature still exists doubting the effectiveness of this treatment in prevention.[28-31]

Intra-operative factors

Different intra-operative components may play an important role as risk factors for developing PJI (Table 3).The first six hours following surgery are the most important regarding infection, as during those hours the numbers of bacteria multiply exponentially. Maintaining a low blood level

Table 2. Pre-operative modifiable and non-modifiable risk factors; measures the surgeon can adopt to reduce impact of risk factors on development of PJI

Non-modifiable risk factor	Conditions favouring PJI	Role of the surgeon
Obesity[13,14]	BMI > 40 Kg/m2	Weight loss Antibiotic adaptation
Anemia[15]	Blood transfusion	Iron supplementation; erythropoietin therapy
Nutritional status[10]	Serum albumin level < 34g/l Low total lymphocyte levels	Correction of abnormal laboratory parameters
Diabetes[16,17]	HbA1c level > 8 Fasting blood glucose level of 200 mg/dL	Accurate peri-operative monitoring of blood glucose
Smoking[11,18]	>1 pack/day or 25 cigarettes	Cessation between four and six weeks before surgery
Oral corticosteroid therapy[12]	Steroid doses over 15 mg/day	Reduction or suspension
Rheumatoid arthritis[19]	Steroid doses over 15 mg/day Other immunosoppressive agents (cyclophosphamide, methotrexate)	Reduction or suspension of immunosoppressive therapy with reumatologist collaboration
Modifiable risk factor	**Correlation with PJI incidence**	**Role of the surgeon**
Urinary tract infection[23-25]	Unclear	Delay surgery when urine leukocytes count > 1 × 10(4)/mL and bacterial count > 1 × 10(3)/mL
Intra-articular corticosteroid injections[20,21]	Unclear	Surgical delay of between six and 12 months
Nasal colonisation with *S. aureus*[26-28]	Influencing, predisposing	Nasal MRSA bonification with mupirocin application (debated efficacy)

PJI, peri-prosthetic joint infections; BMI, body mass index; HbA1c, glycated haemoglobin; MRSA, methicillin-resistant *staphylococcus aureus; S. aureus*, *staphylococcus aureus*

Table 3. Intra-operative factors potentially associated with PJIs

	Correlated to reduced PJI risk	Correlated to increased PJI risk	Unclear factors	Potential sources of infection
Intra-operative factors (surgeon's role)	Antibiotic prophylaxis	Portable devices	Surgical gloves	Sterile stockinette (no foot preparation)
	Pre-admission chlorhexidine cloths	Splash basins	Laminar flow	Personal protection system
	Surgical site antisepsis	Traffic in operating room	Antibiotic-loaded bone cement	Light handle
	Ultraviolet light		Use of plastic adhesive drapes	
	Pulsed lavage			
	Reduced operative time (< 2.5 hours)			

PJI, peri-prosthetic joint infections

of bacteria in this period is critical, and for this reason prophylactic antibiotics are infused to decrease bacterial multiplication and to extend this 'golden' period.[8] The pre-operative dose of antibiotics should be administered within one hour before the surgical incision; this can be extended to two hours for vancomycin and fluoroquinolones. Most authors agree that a single pre-operative prophylactic infusion of cefazolin (1 gr if < 80 Kg; 2 gr if > 80 Kg) is a good choice.[7,8] However, recent studies have demonstrated that targeted use of vancomycin and cefazolin among patients undergoing revision TKA significantly reduced the rate of overall infections, in particular of MRSA.[32] Surgeons should consider additional antibiotic administration if the surgery time is twice the length of the half-life of the antibiotic, or whenever the blood loss exceeds 2000 mL and fluid resuscitation is over 2000 mL.[7] To reduce PJI infection rate, some authors advocate using antibiotic-loaded bone cement (ALBC) for the cementation. However, it was demonstrated that routine use of ALBC does not change the PJI rate, though it may be useful in the reduction of the PJI rate in high-risk patients (for example those with diabetes or immunosuppression).[33,34]

Surgical site preparation also plays a role in reducing PJI rate. Some authors have confirmed the reduction of PJI in patients who underwent pre-admission surgical site preparation using chlorhexidine washing.[35] Different studies have evaluated the best solutions for surgical site preparation to reduce PJI. In a RCT conducted by Darouiche et al, it was demonstrated that a chlorhexidine–alcohol solution was more protective than povidone–iodine against both superficial and deep infections. This is probably due to the more rapid action, persistent activity despite exposure to bodily fluids, and residual effect of chlorexidine compared with povidone.[36]

The preparation of the surgical site often includes using plastic adhesive drapes and sterile stockinette. However, a recent Cochrane review showed no evidence that adhesive drapes reduce surgical site infection rates.[37]

The bactericidal action of incision drapes containing iodine is inferior to conventional skin preparation solutions, so using incision drapes as a substitute for conventional skin preparation is not recommended.[7] Furthermore, Boekel et al[38] concluded that the surgical field for TKA can be contaminated by proximal microbial spread from the unprepared foot with the use of a sterile stockinette drape. So the preparation of the foot is mandatory if combined with stockinette drapes.[38]

The risk of PJI is also directly correlated with the length of the surgery, which should be less than 2.5 hours as a reasonable cut-off point.[8,39,40] Zhu et al, in their meta-analysis, concluded that increased operative time is associated with a higher risk of PJI development (OR = 2.18, CI 95% 1.39-3.42, p = 0.003). However, these data may also be correlated with the high complexity of long procedures.[10] Furthermore, the surgeon's surgical volume may be directly associated with PJI: surgeons with low volumes may have higher rates of infection.[41]

Hand care is another crucial point in reducing PJI infection; hand surgical scrub recommendations were previously published by the Centers for Disease Control and Prevention.[42] In particular, surgeons should remove debris from underneath the fingernails using a nail cleaner under running water, and either an antimicrobial soap or an alcohol-based hand rub should be used persistently for at least five minutes. Different studies evaluated the number of glove changes necessary to reduce the risk of PJI. Of note, Beldame et al[43] recommended :

- renewing outer gloves after draping (before placing a cutaneous adhesive);
- opening the instrumentation secondarily, with a new glove change after handling instruments which may cause perforations;
- renewing outer gloves after each surgical stage.

No strong evidence is available in the literature regarding the appropriate number of glove changes. Different authors recommended double gloving to reduce the risk of inner glove perforation, but no correlation with PJI has been demonstrated.[44,45]

The role of the personal protection system (PPS) in preventing PJI is still debated. Kearns et al demonstrated that the external surface of the PPS cannot be assumed to be sterile after removal from the original packaging, and they suggested the need to change gloves if the PPS is touched or adjusted during the procedure.[46] Other authors agree

with the consideration of PPS as more a personal 'protection' than equipment specifically to reduce PJI.[7,8,39]

The operating room environment is another crucial point in preventing infection. Light handles can be a source of contamination, and surgeons must minimise their handling as far as possible. Furthermore a limited number of portable devices such as mobile telephones and tablet computers in the operating room is recommended, although no evidence in the literature is able to link their use to increased risk.[7]

As airborne pathogens are a potential source of infection, the location and length of time that surgical instruments remain exposed is related to contamination risk. For this reason, all instruments should be opened in operating rooms with clean air systems.[7] Furthermore, during TJA, bloody instruments are commonly washed in 'splash' basins. These basins are repeatedly used during a surgical procedure and should therefore be considered a potential source of contamination.[47] Anto et al demonstrated that 23.8% of specimens from splash basins tested positive for bacterial contamination, and they suggested that surgeons should stop using them.[48]

The use of laminar flow to reduce PJI rate is another controversial topic. A recent systematic review showed no conclusive results regarding the utility of laminar flow in reducing PJI rate.[49] Other authors agree that, despite the number of previous studies demonstrating the efficacy of laminar flow, more recent research has failed to prove this efficacy.[7,8,39] Ultraviolet light seems to be more effective when compared with laminar flow in reducing PJI; however it is characterised by potentially unacceptable health costs to operative personnel.[8,50,51]

Traffic in the operating room is also a potential risk factor for PJI development. A level III study showed that the number of door openings had a role in increased infection rate.[52]

Surgeons may also play a role in reducing the rate of PJI using power-pulsed lavage or wound lavage at surgery. In a level IV study, power-pulsed lavage showed a statistically significant decrease in bacterial contamination.[53]

Post-operative factors

Different post-operative variables may also play a role as risk factors for PJI development.

Antibiotic prophylaxis for other surgical procedures before and after TJA, such as dental care or urological procedures, seems to play a role as a 'protecting' factor towards PJI by reducing the transient bacteraemia.[54] Despite the lack of literature demonstrating the relationship between dental procedures and PJI, the current recommendation of the AAOS is to use antibiotic prophylaxis in patients with a TJA who are undergoing dental procedures, as well as any other invasive procedure.[8,11,55] Furthermore, patients should be aware that any infection is a potential source of haematogenous dissemination. As previously reported by different authors, patients with TJA who have an active infection anywhere in the body are at risk of developing a PJI. For this reason, a prompt diagnosis and management of those infections is a mandatory prevention mechanism.[8,56]

There is still debate regarding the association between blood transfusion and PJI. In a level II study, Pulido et al[57] demonstrated that transfusion with allogenic blood is an independent risk factor for PJI. Patients receiving allogenic transfusions were 2.1 times more likely to develop PJI compared with patients receiving no transfusion. In their study, Innerhofer et al concluded that allogenic filtered transfusion is an independent variable for PJI prediction (OR 23.65; CI 95%, 1.3-422.1; p = 0.01).[58] Furthermore, the Centers for Disease Control and Prevention guidelines defined peri-operative allogeneic transfusion as a potential risk factor for developing PJI, but concluded that the interpretation of the existing literature is difficult due to variations in assessment criteria.[59] However, different measures can be adopted to reduce the need for blood transfusion, such as pre-operative screening for anaemia and its treatment, intra-operative accurate haemostasis, minimisation of surgical time and use of tranexamic acid.[8,59]

Haematoma and persistent wound drainage were also related to an increased PJI rate; these conditions should be treated promptly with antibiotic prophylaxis, a decrease in anticoagulation dose, surgical evacuation of the haematoma, irrigation and debridement and modular component exchange.[7,8]

Wound care plays an important role in PJI prevention. Recently, more advanced surgical bandages such as hydrofibre absorbent dressings were proposed, with the aim of reducing the medication to allow for better wound healing and to prevent bacteria from entering the wound site from the external environment. In a level II study, Cai et al concluded that advanced surgical dressings such as hydrofibre may contribute to a reduction in the incidence of acute PJI.[60]

Conclusions

Infection represents a major challenge in TJA, and is costly and demanding to manage for both surgeons and patients. The main risk factors involved in PJI development are divided into pre-operative, intra-operative and post-operative factors. Pre-operative risk factors are often related to patients' comorbidities. The surgeon can act to reduce the impact of some reversible comorbidities, for example controlling glycaemia in diabetic patients or improving malnutrition. Various intra-operative risk factors such as operating theatre traffic, use of light handles, pulsed lavage or number of glove changes may also be

related to infection. Post-operative risk factors include transient bacteraemia related to dental procedures or other infections, wound care and blood transfusion as well as haematoma, and wound drainage should be controlled with care.

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CONFLICT OF INTEREST

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