CURRENT CONCEPT REVIEW

Prevention of Periprosthetic Joint Infection

Alisina Shahi, MD; Javad Parvizi MD, FRCS

Research performed at the Rothman Institute of Orthopaedics at Thomas Jefferson University, Philadelphia, PA

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Abstract

Prosthetic joint infection (PJI) is a calamitous complication with high morbidity and substantial cost. The reported incidence is low but it is probably underestimated due to the difficulty in diagnosis. PJI has challenged the orthopaedic community for several years and despite all the advances in this field, it is still a real concern with immense impact on patients, and the healthcare system. Eradication of infection can be very difficult. Therefore, prevention remains the ultimate goal. The medical community has executed many practices with the intention to prevent infection and treat it effectively when it encounters. Numerous factors can predispose patients to PJI. Identifying the host risk factors, patients' health modification, proper wound care, and optimizing operative room environment remain some of the core fundamental steps that can help minimizing the overall incidence of infection. In this review we have summarized the effective prevention strategies along with the recommendations of a recent International Consensus Meeting on Surgical Site and Periprosthetic Joint Infection.

Key words: Infection, Prevention, Total Hip Replacement, Total Joint Arthroplasty, Total Knee Replacement

Introduction

Total joint arthroplasty (TJA) is the ultimate treatment for degenerative joint disease. It restores function in the majority of patients and improves quality of life. It is projected that by the year 2030 the total number of primary total knee arthroplasty (TKA) procedures in the United States will reach 3.48 million per year, a 673% increase in comparison with the number of procedures in 2005. Furthermore, the demand for total hip arthroplasty (THA) is projected to grow by 174%, which would be 572,000 procedures per year. That is about 4 million TJAs per year (1).

Similar to all medical interventions, TJA is accompanied by some complications, the most challenging of which is periprosthetic joint infection (PJI). Infection is the leading cause of revision after TKA and the third most common reason for revision THA in the Medicare population. PJI can occur any time after the surgery, and there is no "gold standard" for diagnosis (2–8). PJI has a huge financial impact on the healthcare system. Revision due to infection cost about $320 million in 2001, increased to $566 million in 2009, and is projected to exceed $1.62 billion by 2020 in the United States (9). Prevention of PJI is therefore imperative.

Definition of PJI

Until recently there was no unified definition for PJI. In 2011, in an effort to standardize the definition of PJI, a list of criteria was provided by the Musculoskeletal Infection Society (MSIS) (10).

In addition, in August 2013, the International Consensus Meeting (ICM) on PJI was held in Philadelphia. More than 400 experts from 52 countries and representative from over 130 societies convened. The ICM supported the MSIS definition of PJI and modified it by adding a minor criterion (leukocyte esterase test) and determining the threshold for lab results (11).

According to the modified definition, a definite PJI is present when:

A. There is a sinus tract communicating with the prosthesis, OR
B. A phenotypically identical pathogen is isolated by culture from 2 or more separate tissue or fluid samples obtained from the affected prosthetic joint, OR
C. When three of the following five criteria exist:
   I. Elevated serum erythrocyte sedimentation rate AND serum C-reactive protein concentration
   II. Elevated synovial white blood cell count, OR ++

Corresponding Author: Javad Parvizi, the Rothman Institute, 125 S 9th St. Ste 1000, Philadelphia, PA 19107.
Email: research@rothmaninstitute.com

change on leukocyte esterase test strip
III. Elevated synovial polymorphonuclear percentage
IV. Positive histological analysis of periprosthetic tissue
V. A single positive culture

Note that PJI can exist regardless of the absence of these criteria in some cases, such as low-virulence microorganisms like Propionibacterium acnes.

Classifications of PJI

Based on the pathogenesis or the timing of the clinical manifestation, different classifications are suggested for PJI. As far as pathogenesis is concerned, PJI is either exogenous or hematogenous (12).

PJI can occur any time postoperatively. Based on the time interval between the surgery and the onset of the clinical manifestations, PJI can be divided into four different stages (12–14).

1. Stage one/early: symptoms start within the first 4 to 8 weeks postoperatively.
2. Stage two/delayed: presents 3 to 24 months after the surgery.
3. Stage three/late onset: usually occurs after 2 years postoperatively.
4. Stage four/silent PJI: a condition in which a positive culture is captured at the time of revision in a patient with no symptom of infection.

Early, delayed, and silent infections are often exogenous. Early PJI is usually caused by virulent organisms such as S. aureus. Late PJI has an acute clinical manifestation and is usually hematogenous. Silent PJI mostly caused by low-virulence microorganisms such as coagulase-negative staphylococci or Propionbacterium acnes (14,15). The most common sources of contamination are the patient's skin and soft tissue. Nevertheless, some studies reported seeding from the respiratory, urinary, and gastrointestinal tracts, and dental infections (16). Sendi et al. reported that in 57.5% of hematogenous PJI, there was no sign of primary bacteremia or infection during the clinical manifestation; therefore, it is usually difficult to identify the source of infection (17).

Prevention of PJI

Many different factors are involved in the development of PJI. These elements concern both the host and the environment. Conditions that can increase the risk of infection include (but are not limited to): uncontrolled diabetes, rheumatoid arthritis, renal failure, congestive heart failure, hypercholesterolemia, malnutrition, pulmonary disease, valvular heart disease, preoperative anemia, venous thromboembolism, peripheral vascular disease, metastatic tumor, psychosis, alcohol abuse, and depression (3,18–20).

Patients who undergo elective arthroplasty are typically in suboptimal health. Additionally, the impact of various risk factors is cumulative (21,22). Therefore, it is imperative to identify the risk factors and address them preoperatively to reduce the risk of PJI and other postoperative complications.

Generally strategies to prevent PJI are categorized as preoperative, intraoperative, and postoperative.

Preoperative Period

Medical Optimization of Host

All modifiable conditions should be optimized prior to an elective TJA. Studies have shown that the patient's general health has a direct link with postoperative complications. An American Society of Anesthesiologists score of greater than 2, uncontrolled diabetes, and rheumatoid arthritis, for example, can significantly increase the risk of PJI (18,20,23–25). Furthermore, any other comorbidity accompanied by diabetes is shown to place patients at a cumulatively higher risk for infection (21,26).

Merchant et al. reported that patients with a higher level of hemoglobin A1c are at a higher risk of PJI, with an odds ratio of 2.31 (27). Additionally, not only is the preoperative glucose level an important factor, but Mraovic et al. demonstrated that the postoperative blood glucose level also plays an important role as far as the risk for PJI is concerned (28). The authors stated that patients with sugar levels of greater than 200 mg/dl on postoperative day one were twice more likely to develop PJI. Therefore, evaluating patients in a multidisciplinary clinic prior to performing TJA is crucial in order to identify comorbidities and manage them, if required. These assessments significantly reduce postoperative mortality and pre-admission costs in complex orthopaedic surgeries, including TJA (29).

The ICM Comment

The ICM workgroup stated that certain conditions such as history of previous surgery, uncontrolled diabetes mellitus (glucose levels > 200 mg/L or HbA1C > 7%), malnutrition, morbid obesity (body mass index > 40 kg/m2), chronic renal disease, active liver disease, excessive smoking (> one pack per day), exorbitant alcohol use (> 40 units per week), intravenous drug abuse, extended stay in a rehabilitation facility, recent hospitalization, post-traumatic arthritis, inflammatory arthropathy, previous surgical procedure in the affected joint, male gender, and severe immunodeficiency can increase the risk of developing PJI (30).

Bacterial Decolonization (Preoperative Skin Cleansing)

Prevention guidelines regarding surgical site infections (SSI) published by the Centers for Disease Control (CDC) recommended patients to take a bath with an antiseptic agent at least once on the night before the operation to reduce the load of bacteria (31). Many reports have shown that a whole-body bath with an antiseptic agent reduces the bacterial load in the skin and lowers the risk of developing SSI (32–35). According to the CDC, SSIs are the second most common cause of nosocomial infections and are responsible for more than 25% of hospital-related infections in the United States (36,37). There is still a debate on how to achieve entire-body coverage and maintain adequate concentrations of the solution for effective results. Another issue is the patient's compliance with these protocols (38).

The ICM Comment

The ICM group suggests that a whole-body skin cleansing regimen with chlorhexidine gluconate (CHG) should begin at least one night before the surgery. In case of sensitivity to CHG or when it is not available, antiseptic soap can also be used (39).

Prophylactic Antibiotics

It is believed that prophylactic antibiotics are one of the most important factors in preventing PJI (40–43). One of the sentinel studies in the field of orthopaedic surgery is that of Fogelberg et al., in 1970 (40). They compared two groups of patients; one group was given prophylactic penicillin preoperatively, intraoperatively, and up to 5 days postoperatively; and the other group was not given any antibiotics. The incidence of infection was 1.7% the group receiving antibtiotics versus 8.9% in the group that did not receive antibiotics. The study also demonstrated that methicillin-resistant Staphylococcus aureus (MRSA) infections were increased in the antibiotic group, demonstrating the fine balance between appropriate use of antibiotics and its overuse.

The American Association of Orthopaedic Surgeons (AAOS) published a guideline discussing the choice and dosing of prophylactic antibiotics (22). The optimum time for prophylactic antibiotic administration is within an hour prior to the surgery, in order to reach the minimal inhibitory concentration in the end organs during the operation (44). In certain conditions such as prolonged surgical duration beyond the half-life of the antibiotic or when excessive blood loss occurs during the surgery, a second dose of antibiotic is required.

Indications for Vancomycin

First-generation cephalosporins are adequate for the majority of patients undergoing elective TJA. In some circumstances, however, administration of vancomycin or a teicoplanin is also indicated. Currently the use of vancomycin or teicoplanin is deemed to be appropriate in:

1. Patients who are carriers of MRSA.
2. Patients from dialysis units or centers with an outbreak of MRSA.
3. Healthcare workers.
4. Patients who are allergic to penicillin.

The ICM Comment

A first- or second-generation cephalosporin (cefazolin or cefuroxime) is suggested as routine preoperative surgical prophylaxis, administered within an hour prior to the surgical incision. The timing can be extended up to two hours for vancomycin and fluoroquinolones. No special considerations are required for patients with preexisting prostheses such as heart valves, and the same antibiotics can be used (45).

Intraoperative

Hair Removal

Hair removal at the incision site has become a part of the routine patient preparation for surgery. Interestingly, there is no evidence to support the role of hair removal in reducing the risk of SSI. A review article by the Cochrane group stated that there is no statistical difference in the incidence of SSI when hair, at the surgical site, is removed versus when it is not. The article mentioned that patients whose hair was removed using a razor had even higher rates of infection compared to those on whom clippers were used (46).

The ICM Comment

The consensus group suggested the hair removal be attempted as close to surgery as possible and done with the use of clippers. The ICM group had no comment on the use of depilatory cream for hair removal (39).

Preoperative Skin Preparation

Patients

One of the most common causes of SSI are the native microorganisms of the skin (47,48). In a study by von Eiff et al. it was shown that in more than 80% of nosocomial infections with Staphylococcus aureus, the source of the infection was endogenous based on the genotyping evaluations (49).

According to the CDC's estimation, SSI is the second major cause for nosocomial infections, and is responsible for more than one fourth of the hospital-related infections in the United States (37). Hence, despite new advances in prophylactic antibiotics, skin-decolonizing agents still have crucial importance. Various antiseptic agents are available for surgical skin preparation. The most common ones are: CHG, alcohol-based solutions, and povidone-iodine, all of which have advantages and disadvantages. CHG, for instance, is very popular due to its long-lasting and cumulative effect against Gram-positive and Gram-negative bacteria. Povidone-iodine is very effective on skin flora; however, it becomes relatively ineffective upon contact with blood and has a shorter duration of activity in comparison with CHG (36). Alcohol is a very good antimicrobial agent but the flammability and discontinued effect after drying are the downsides. A meta-analysis by the Cochrane group in 2004 stated that there was no significant difference in the rate of SSI in clean surgeries carried out using different antiseptic agents (50). Recent studies mentioned that alcohol and CHG combination is more successful than alcohol and povidone-iodine in reducing the bacterial load of the skin; however, the rate of SSI was not significantly different (51–53).

The ICM Comment

The ICM workgroup stated that there is no superiority of one skin preparation agent over another. There is some evidence that combinations of antiseptic agents with alcohol may be helpful for skin antisepsis (39).

Surgeons

Antiseptic hand preparation agents are categorized into two main groups: hand scrub and hand rub agents. Hand scrubs are usually solutions of CHG or povidone-iodine and hand rubs are mostly alcohol-based solutions. Most studies reported equivalent efficacy in decreasing

bacterial colony units when comparing povidone-iodine with CHG. Furthermore, the incidence of SSI is not different using either hand scrub solutions or hand rubs (54,55). However, hand rubs require less water consumption and have better surgeon compliance (54).

The ICM Comment

The surgeon and other operating room (OR) personnel should wash their hands with an antiseptic agent for at least two minutes prior to the first case. The ICM group stated no preference for one antiseptic agent over others (39).

Draping

There is a strong support in the literature for the use of plastic adhesive tapes for draping the surgical site. Numerous studies have shown that the rate of SSI is significantly increased when traditional cloth drapes were used (56–60). In one study, plastic adhesive drapes were compared with cloth, and deep wound contamination rates were compared. Cultures were collected right before closing and the result showed 60% of contamination when cloth drapes were used versus 6% with plastic adhesive drapes (57). Ritter et al. presented that iodophor-incorporated drapes can reduce wound contamination but do not decrease the wound infection rate after TJA (61). Plastic adhesive drapes are effective when skin preparation is performed using alcohol-based solutions. DuraPrep (3M Company, St. Paul, MN) is believed to improve the adhesion properties of the drapes (62). However, there are controversies about the effectiveness of adhesive incise drapes for the prevention of bacterial contamination. In 2007, the Cochrane group reviewed about 3,000 patients in five different studies and concluded that there is no evidence to support that the use of adhesive incise drapes (plain or infused with antimicrobials) can reduce the rate of SSI (63).

The ICM Comment

The ICM group identified studies that demonstrated iodine-impregnated skin incise drapes can decrease skin bacterial loads. However, they found no study that would be able to demonstrate a correlation between the use of iodine-impregnated drapes and the incidence of SSI. The ICM has no comment on the use of skin barriers and recommends further studies (64).

Surgical Gloves

Sterile surgical gloves are dual protection barriers; on one side the glove protects the patient from residual bacteria on the surgeon's hands, and on the other side it protects the surgeon from the patient's body fluids.

Double gloving reduces the risk of glove perforation; and in procedures such as orthopaedic surgeries, where sharp edges could be encountered easily, following double gloving protocols is highly recommended (65–67). However, with a double gloving protocol, the inner glove could still be perforated and become contaminated during the course of the procedure. Therefore, some studies have shown that in procedures such as implantation, triple gloving is the protocol of choice (68,69).

Sutton et al. introduced the triple gloving protocol in 1998 (70). The authors used two latex gloves with a cut-resistant layer between them. Results showed a significant decrease in perforation compared with the double gloving protocol. In a study by Pieper et al. different protocols of triple gloving were compared to double gloving in maxillofacial surgeries (71). The authors presented that various techniques of triple gloving are superior to double gloving in terms of protecting inner glove from perforation. However, triple gloving has some disadvantages, such as decreased tactile sensation and surgeon dexterity.

The ICM Comment

The ICM group suggested the use of double gloving. However, they recognized the theoretical advantages of triple gloving (64).

Antibiotics in Cement

There are many reports stating that adding antibiotics to cement can decrease the risk of PJI in THA (72,73). However, there is no consensus on the fact that it is an effective strategy for TKA or not (74,75).

The ICM Comment

The ICM group believes that antibiotic-impregnated polymethylmethacrylate cement can reduce the risk of PJI development and should be considered in patients at high risk for PJI following elective arthroplasty (76).

Blood Conservation

Allogeneic blood transfusion is an independent predictor for PJI and the number of transfused units has a direct link with the likelihood of developing PJI (77). The latter statement can be justified with the modulating effects of transfusion on the immune system (78). This fact endorses the importance of preoperative patient optimization. Correction of preexisting anemia is one of the best ways to minimize the amount of intraoperative transfusion (79). Other preventive strategies include meticulous hemostasis to minimize blood loss, neuraxial anesthesia, and the use of tranexamic acid (80,81).

The ICM Comment

The ICM group believes that allogeneic blood transfusion can increase the risk of developing SSI and/or PJI. Furthermore, management of preoperative anemia with iron, with or without erythropoietin, can decrease the risk of intraoperative transfusion. The ICM group endorses neuraxial anesthesia to reduce the amount of blood loss during TKA and THA (82).

The OR Environment

Laminar Airflow

The ultimate goal of OR design is to diminish the patient's exposure to the infecting organisms throughout the procedure. To pursue this aim, laminar airflow was introduced in 1964. However, there are controversies on the efficacy of laminar flow in reducing SSIs. Some studies stated that laminar flow could even increase the risk of SSIs (83). The CDC has no comment regarding

the use of laminar airflow in reducing SSI. Nevertheless, the CDC has released a guideline for the proper use of laminar airflow.

The ICM Comment

The ICM group believes that arthroplasty may be performed in ORs that are not equipped with laminar flows. The ICM has no comment in favor or against the use of laminar flows and recommends further studies (64).

Duration of the Operation

The risk of PJI has a direct link with the duration of the operation (84,85). Furthermore, the surgeon's surgical volume also has a potential effect on the rate of SSI; surgeons with lower number of surgeries tend to have higher rates of infection (86).

The ICM Comment

The ICM workgroup believes that the rate of SSI has a direct link with the duration of the surgery. They recommend that a coordinated effort must be made to minimize the surgical duration without compromising the procedure (64).

OR Traffic

The incidence of SSI is directly related to the OR traffic. OR traffic can increase the load of airborne microorganisms. Furthermore, more door openings due to higher traffic can interfere with laminar airflow, which can itself increase the rate of SSI (87–89).

The ICM Comment

The ICM recommended that OR traffic should be kept at a minimum (64).

Medical Equipment

Several studies have demonstrated that equipment contamination can occur during surgery (90–94). Givissis et al. investigated the contamination rate of suction tips and tried to correlate it with the development of subsequent deep wound infection (91). The authors reported a 54% rate of contamination in the suction tips. One of the cases developed deep SSI with the same organism that was isolated from the suction tip. The authors concluded that the contamination rate has a direct link with operation time. Therefore, they recommended that the suction tip should be changed every hour in long orthopaedic procedures. Davis et al. determined the contamination rates of glove tips (28.7%), syringe bags (20.0%), gown swabs (17.0%), base of light handles (14.5%), body of light handles (14.5%), sieve swabs (13.5), suction tips (11.4%), needles for deep closure (10.1%), skin blades (9.4%), and inside blades (3.2%) (90). Beldame et al. reported a significantly higher rates of contamination in gloves prior to prosthesis implantation and advised to change gloves before this step (95).

The ICM Comment

The ICM workgroup recommended changing suction tips every 60 minutes. Suction tips can be inserted into the femoral canal to evacuate fluid but should not be left there, where significant amounts of ambient air and particles are circulated that can potentially contaminate the case. Furthermore, the workgroup encourages surgeons to change their gloves at least every 90 minutes and after cementation. The ICM recommended further study on electrocautery devices and had no specific comment on their use (64).

Postoperative

Prevention of Late PJI

PJI may occur any time after the surgery. Episodic bacteremia can be a potential risk for PJI development. Certain medical procedures are more likely to cause bacteremia. In 2012, the AAOS released a new guideline on "The Prevention of Orthopaedic Implant Infections in Patients Undergoing Dental Procedures." The guideline is collaboration between the AAOS and the American Dental Association. It has three main recommendations(96).

1. "The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures.
2. We are unable to recommend for or against the use of topical oral antimicrobials in patients with prosthetic joint implants or other orthopaedic implants undergoing dental procedures.
3. In the absence of reliable evidence linking poor oral health to PJI, it is the opinion of the workgroup that patients with prosthetic joint implants or other orthopaedic implants maintain appropriate oral hygiene."

The ICM Comment

The ICM workgroup concluded that the use of prophylactic antibiotics prior to dental procedures in patients who have TJA in place should be based on the individual's risk factors and the complexity of the dental procedure.

Furthermore, in cases of viral infection, there is no role for oral antibiotics even for patients at higher risk.

The workgroup also concluded that for other minor surgical procedures such as endoscopy and colonoscopy, transient bacteremia could be minimized by administration of prophylactic antibiotics, especially in high-risk patients (97).

Conclusion

PJI is a serious complication with a significant morbidity and mortality. Several factors in the pre-, intra-, and postoperative periods are involved that can predispose a patient to develop PJI. Prevention is always better than treatment. One of the most important preoperative factors to reduce the risk of PJI is to optimize the patient's general health prior to elective arthroplasty. Evaluation of all patients in pre-assessment clinics prior to elective TJA is recommended. Preoperative prophylactic antibiotic administration should always be considered. Implementation of a surgical safety checklist can significantly reduce the

incidence of SSI and subsequent PJI. It is imperative to follow the recommendations of the CDC and the AAOS to minimize the risk of infection intraoperatively. Finally, patients who undergo TJA are always at risk of developing infection; therefore, it is essential to administer appropriate prophylactic antibiotics prior to certain medical procedures. Medical science is fluid in nature. Further research and developments may provide better insights for prevention of infection after orthopedic procedures.

Alisina Shahi MD
Javad Parvizi MD, FRCS
The Rothman Institute of Orthopaedics at Thomas Jefferson University, Philadelphia, PA

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