Review Article

Risk factors for periprosthetic joint infection following total hip and knee arthroplasty

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Abstract
Osteoarthrosis is a common degenerative and progressive disease, involving the articular cartilage as well as the subchondral bone and the soft tissues in the hip and knee. The incidence of hip and knee osteoarthrosis has increased over the last twenty years and is expected to increase even further. Approximately, 40% of men and 47% of women over 65 years old suffer from symptomatic osteoarthrosis that eventually requires surgical treatment by an orthopedic surgeon. In 2010 around 2.5 million patients were operated for total hip replacement and around 4.7 people with knee osteoarthrosis had a total knee replacement in the United States of America. Acute periprosthetic joint infection, with Staphylococcus aureus being the most common and aggressive pathogen is a very threatening complication for the whole health status of the patient. The need for revision procedures due to periprosthetic hip infection is expected to be doubled in 2026 and is already doubled due to periprosthetic knee infection in 2015. The risk factors for hip and knee periprosthetic joint infections appear in the preoperative period, as well as intraoperatively and continue to be harmful both in the postoperative period and after the patient’s discharge from the hospital. The aim of this article is to present the variety of risk factors, associated with periprosthetic infections after total hip and knee replacements. Many risk factors can be controlled with the use of specific preventive and therapeutic interventions by orthopedic surgeons.

Keywords: Osteoarthrosis, Total hip replacement, Total knee replacement, Periprosthetic infections, Risk factors

Introduction

Osteoarthrosis is the most common form of degenerative joint disease affecting several joints like the first carpometacarpal joint of the hand, the spine and the two major weight-bearing joints of the hip and knee. Patients suffering either from hip or knee osteoarthrosis are referring to orthopedic departments due to symptoms of pain and stiffness and disability to perform simple clinical activities¹. The hip and knee osteoarthrosis prevalence vary from 1.9% to 4.7% for men and 2.5% to 6.6% for women, respectively². The lifetime risk probability for symptomatic knee osteoarthrosis is 40% in men and 47% in women population with normal body mass index (BMI) ³. For overweight people with BMI≥30%, the probability is elevated to 60%³. In the Johnston County Osteoarthritis Project, the prevalence of symptomatic osteoarthrosis was 16.7% for knees and 9% for hips among people over 45 years old⁴.

The total annual number for total hip and knee replacement, for patients suffering from osteoarthrosis is about 1.000.000 in the USA⁵. About 2.5 million (1.4 million of women and 1.1 million of men) patients submitted for total hip replacement and 4.7 million (3 million of women and 1.7 million of men) for total knee replacement in USA in 2010⁶. The prevalence for total joint replacement in USA is 5.26% for hips and 10.38% for knees⁶.

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Periprosthetic joint infection remains a timeless and aggravating complication for some patients, operated for total hip and knee replacement. According to Shurman D, 9.1% of total knee replacements were infected and a revision surgical procedure needed, in 1981. Due to improvement of surgical techniques and targeted prophylactic antibiotic therapy, the prevalence of periprosthetic joint infection has minimized to 1-2% nowadays. In 2003, 202,500 and 402,000 primary total hip and knee replacements, respectively, were carried out in USA. During the same year, 36,000 revisions after total hip replacement and 32,700 revisions after total knee replacement were done. The need for revision surgery after primary total hip replacement is expected to be doubled in 2026 and is already doubled in 2015 after total knee replacement.

The factors that increase the risk for periprosthetic joint infection after hip and knee replacement are broadly inspected and have been the point of interest and research. We will analyze the presence of these risk factors that can lead to periprosthetic joint infections, at pre-operative, intra-operative and post-operative periods.

**Method**

**Data sources**

This study was performed as a systematic review of a series of articles exploring potential risk factors for periprosthetic hip and knee infections following arthroplasty as a treatment for osteoarthrosis. We choose to study bibliography for both periprosthetic hip and knee infections as being the two major weight-bearing joints operated for osteoarthrosis with the highest infection rates among the rest. Additionally, we found only few review studies referring to both hip and knee periprosthetic infections, even though many patients have both hip and knee replacement during lifetime.

**Study selection and search strategy**

The authors searched for published articles as original and review studies on PubMed. We searched the electronic database of PubMed for articles written in English, between 2000 and 2018. Moreover, we mentioned two older articles. The first by Shurman D published in 1981 to emphasize deterioration of infection rates with the passing of time. The second by Wilson MG published in 1991 to present racial differences in the use of total knee arthroplasty for osteoarthrosis among older Americans. The quality of each study was also examined. Quality and risk of bias were assessed using Cochrane’s risk of bias tool (selection bias, performance bias, detection bias and reporting bias).

**Preoperative factors**

**Hyperglycemia and diabetes management**

Perioperative hyperglycemia is very common, up to 40%, for patients who undergo total hip or knee replacement during their hospitalization. A study by Mraovic B. et al. published in the Journal of Diabetes Science and Technology (JDST) in 2011, showed that patients with increased glucose in serum, above 200 mg/dl in the preoperative period, have a double risk for periprosthetic infection.

Patients suffering from diabetes mellitus must be controlled preoperatively with hemoglobin A1c (HbA1c) or with a fasting blood glucose test. Pre-existing diabetes mellitus is proven to be the most important risk factor for postoperative hyperglycemia that affects the immune defending system against infectious agents. The International Consensus Meeting Statement recommends glucose blood levels between 80 and 180 mg/dl and HbA1c<7% in the preoperative screening test to avoid periprosthetic infections.

**Obesity and nutritional disorders**

Obesity which is characterized by increase body mass index (BMI) is a skyrocketed phenomenon in western-industrial societies, and orthopedic surgeons deal with more obese patients. The rates of obese patients with joint osteoarthrosis referring to orthopedic clinics for total hip or knee replacement have increased from 30% to 52% from 1990 to 2005 in USA. Jamsen E et al. in a Finnish study investigated the risk for periprosthetic joint infection among 7,181 patients who underwent total hip or knee replacement. They recorded 52 patients who experienced periprosthetic joint infection after a year from the primary surgery. Patients with normal BMI (≤25 kg/m²) had a risk for periprosthetic joint infection approximately 0.37%, but adults with BMI greater or equal to 30 kg/m² had a risk around 4.66%. In the same study, it seemed that the risk for periprosthetic joint infection is much more elevated when obesity coexists with diabetes mellitus.

Additionally, malnourished patients who proceed with total hip or knee replacement have extremely high risk for infection after surgery. Serum markers that indicate establishment of malnutrition like leucocyte count less than 1500 cells/mm³, levels of transferrin less than 200 mg/dl and albumin levels below 3.5 g/dl must be checked preoperatively. According to Paul Het al, the presence of one or more markers that indicate malnutrition are independent risk factors for infection. Among 123 malnourished patients who had total hip or knee replacement, 9 patients (7%) had a periprosthetic joint infection which is statistically significant compared with 3 patients (1%) among 252 patients with normal BMI, in the same study.

**Smoking**

Patients who smoke have increased risk to develop an infection after total joint replacement due to vasoconstriction, insufficient blood and oxygen supply, and deterioration of circulating antimicrobial agents to the surgical site. Patients with osteoarthrosis must be advised to avoid smoking at least for 4 weeks prior surgery.
Anemia

Preexisting iron-deficiency anemia during preoperative period as well as excessive blood loss during intraoperative and postoperative periods, prolong hospital stay, increase the need for blood transfusion as well as the risk for periprosthetic joint infection19.

Greeney M et al., published their data from 15,222 patients who underwent total hip or knee replacement due to arthritis19. A significant ratio of patients approximately 19.6% referred to the hospital with preoperative anemia. Anemia determined as Hgb<1.2 g/dl in women and Hgb<1.3 g/dl in men19. About 4.3% of patients with anemia experience periprosthetic joint infection compared with 2% of people with normal hematocrit19. The need for blood transfusion was higher in the group of anemic patients (44%) compared to patients with normal hematocrit (13.4%)19. Additionally, the duration of hospital stay was extended in those with anemia (4.3 days) compared with normals (3.9 days), explaining the highest rates of postoperative infections19.

Intra-articular steroid injection increases the risk for periprosthetic infection?

Six clinical cohort studies were analyzed by Wang Q et al. describing the effect of preoperative intra-articular injection as a palliative therapy for osteoarthritis among 1,474 patients who were operated for total hip or knee replacement20. They found that 14 patients had deep and 72 patients superficial infections20. Another study by Jourdan M et al. found that the risk for periprosthetic joint infection was obviously elevated, only when the intra-articular injection was held in 3 months interval prior primary surgery21. Orthopedic surgeons must wait at least 6 months after the last intra-articular injection to proceed to joint replacement according to the same study21.

Colonization by Staphylococcus Aureus

Staphylococcus Aureus (SA) is the most usual isolated pathogen in periprosthetic joint infections along with coagulase-negative staphyloccoci22. SA colonizes anterior nares, axilla, inguinal and other body sites22. According to Hacek et al., the nasal cavity must be screened for SA and a 5-day mupirocin decolonization protocol has to be demonstrated preoperatively for positive tests, as the risk for periprosthetic joint infection can be decreased by 4-folds22.

Due to the highly aggressive behavior of SA a full body decolonization especially at axilla and inguinal it is recommended to use an at home protocol with chlorhexidine body wash the night before and the morning of the surgery day23.

Preoperative infections at distal sites

Preoperative infections affecting other body parts like the oral cavity, urinary tract and skin could be misdiagnosed if they are not inspected carefully and can lead to periprosthetic joint infections postoperatively24.

Preoperative bacteremia due to poor oral hygiene can threaten joint prostheses with oral pathogens leading to infection25. Total joint replacement following tooth extraction sometimes needs prophylactic antibiotic therapy although recent evidence doesn’t support it25. Certainly, major orthopedic surgeries like total hip and knee replacement must delay at least one week after dental procedure to give the appropriate period for oral mucus to be replaced as it is the most important barrier for pathogens to penetrate local vessels and cause bacteremia25.

According to Cordero-Ampuero J et al., the risk for periprosthetic joint infection in patients with asymptomatic bacteriuria is negligible so there is no need for prophylactic antibiotic therapy26. Among 228 patients who submitted total hip replacement, 8 persons had asymptomatic bacteriuria diagnosed from urine cultures26. Only one person developed periprosthetic joint infection, but cultures from the surgical site showed different pathogens between the joint and urinary tract26.

The skin of people that are going to be treated with joint replacement due to symptomatic osteoarthritis has to be inspected by orthopedic surgeons for the presence of atrophy, ulceration and lymphedema26. Absolute contraindications to proceed in total joint replacement are cellulitis, erysipelas and skin folliculitis26. Total hip or knee replacement with existing local eczema or atopic dermatitis is not prohibited if the skin is maintained clean and dry26.

Anticoagulant agents for prophylaxis from Deep vein thrombosis (DVT) prior surgery

Patients with past medical history of artificial biological heart valve replacement, deep vein thrombosis, cardiac arrhythmias e.g. atrial fibrillation, stroke, thrombophilia and other circulation illnesses receive anticoagulant therapy at home in the preoperative period28. Anticoagulant agents increase the risk for blood loosening, anemia, the formation of hematoma, insufficient closure and split of surgical wound, making ideal environment for excessive microbial contamination and spread of pathogens25.

According to McDougall C et al, the incidence of superficial and deep infections among patients who have total hip replacement is higher in those who received Warfarin postoperatively compared to those they didn’t28. The study group was composed by 89 patients who were under warfarin therapy and the control group included 179 patients who received aspirin 300 mg, 1 dose daily for 6 weeks28. The risk for superficial infection appeared to be significant higher in study group (13.5% in Warfarin group compared to 2.2% in aspirin group), as well as the risk of hematoma formation (28% in warfarin group compared with 4% in aspirin group)28. During the 5-year follow-up patients from the warfarin group had 9% danger to experience a deep infection compared to patients from the aspirin group who had only 2.2% risk28. When patients had to take Warfarin
alongside with Low Molecular Weight Heparin (LMWH) the risk for periprosthetic infection was elevated cumulatively\textsuperscript{28}. The effectiveness in thromboprophylaxis after total hip and knee replacement, as well as the ratio of postoperative complications between Warfarin and LMWH were studied in a retrospective study from the Global Orthopedic Registry (GLORY) among 3,755 patients in USA\textsuperscript{29}. The results of this study showed that patients who received LMWH were more susceptible in postoperative complications compared with Warfarin group (6.2% bleeding in LMWH group compared with 2.1% in Warfarin group), (29.4% need for blood transfusion in LMWH group compared with 22% in Warfarin group)\textsuperscript{39}. Postoperative periprosthetic infection found to be more common in LMWH group (1.6%), compared with Warfarin group (0.6%), and revision rates due to infection were higher in LMWH (2.4%) compared with Warfarin group (1.3%), too\textsuperscript{28}.

Individualized treatment in patients who are submitted in orthopedic departments for total joint replacement, taking into consideration the pros and cons among all medications for thromboprophylaxis will certainly minimize complication especially the risk for periprosthetic infections.

**Intraoperative factors**

**Factors that originate from patients’ profile**

Many studies support that the gender of the patients is a reasonable factor for the different ratio of postoperative complications between men and women\textsuperscript{30}. Differences in skin characteristics, like skin pH, subcutaneous fat distribution, skin thickness, and circulating hormones are the more obvious reasons\textsuperscript{30}. Skin normal flora differs between the two genders, as cultures from skin samples show that men are more prone in Staphylococcus Aureus colonization compared with women, and decolonization stills more difficult in men\textsuperscript{31}. Lübbeke A et al., supported that periprosthetic joint infection is most common in non-obese men compared with non-obese women, 16.1-folds more common in obese women, but comparing obese with non-obese men, the infectious ratio were the same\textsuperscript{32}.

Patient’s age seems to be another significant factor for infection following total hip or knee replacement. According to Soohoo et al., in a population study among 138,399 patients who submitted total hip arthroplasty in California from 1995 to 2005, patients between 55 to 74 years old are at greater risk to develop periprosthetic infection\textsuperscript{33}. They supported that the reason for that is due to higher BMI of African Americans, intraoperatively compared with Caucasians\textsuperscript{34}. Collins TC et al., support that higher risk for postoperative infections among African Americans is relevant to the prolonged duration of stay in hospital postoperatively\textsuperscript{35}.

The socioeconomic status of patients is another risk factor for periprosthetic joint infection after primary surgery\textsuperscript{36}. It is believed that patients with poor socioeconomic status, follow unhealthy lifestyle, and are hospitalized in poorer hygiene circumstances sometimes in hospitals with lack of antiseptic protocols in developing countries\textsuperscript{36}.

**Genetic susceptibility**

A very interesting and pioneer research study by Zhou X et al, supports that the presence of C allele and C/C genotype for the MBL-550 Single-Nucleotide-Polymorphism (SNP), A/A genotype for the MBL-54 SNP, as well as G allele for MBL-221 SNP, increase the risk for periprosthetic infections among Caucasians\textsuperscript{37}. On the other hand, the presence of G allele and G/G genotype for MBL-550 SNP decreases the risk for infections among Caucasians with total hip or knee replacement\textsuperscript{37}.

**The parameter of high qualified orthopedic surgeons in well experienced medical centers**

The incidence of periprosthetic infections is directly depended on the level of specialization of the health center and high experience of the medical staff in total hip and knee replacements. Early symptoms and signs of infections are diagnosed easier from well qualified doctors and nursing staff who are familiar with large number of patients operated for osteoarthritis\textsuperscript{38,39}. According to Kutz JN et al., the risk for periprosthetic infections is 50% lower between orthopedic surgeons who handle more than 50 total joint replacements annually, in hospitals with over 100 operated patients per year\textsuperscript{38,39}.

**Risk factors for infections associated with circumstances under the patient is operated**

In a retrospective study by Chang C et al., among 3,081 patients who had total hip or knee replacement in Taiwan between 2002 and 2006, showed that general anesthesia is associated with higher risk for periprosthetic infection compared with epidural or spinal anesthesia\textsuperscript{40}. General anesthesia causes peripheral vasodilatation diminishing blood and oxygen supply to the surgical site\textsuperscript{40}. Additionally, opioids and drugs used in general anesthesia suppress the defending mechanisms of immune system\textsuperscript{40}. On the other hand, epidural and spinal anesthesia maintain postoperative analgesia that bans peripheral vasodilatation and keep enough supply of antimicrobial agents in the operated joint\textsuperscript{40}.

The role of duration of the surgical procedure in total hip and knee replacement studied from Dicks K et al., in a retrospective study from 43 hospitals in USA\textsuperscript{41}. Among 42,187 total knee replacements, Dicks K et al, found that when the duration of operation was up to 1 hour the possibility for infection was 50% lower compared with operations ranged between 64 to 106 minutes (median
time 83 minutes)\textsuperscript{41}. In the same study, among 25,531 total hip replacements the risk for periprosthetic joint infection was 1.11% higher in patients who operated between 61 to 105 minutes (median time 80 minutes) compared to operations that exceeded more than 105 minutes\textsuperscript{41}. Obviously, the duration of operation is a more decisive factor for infections in total knee replacements compared with total hip replacements\textsuperscript{41}.

Caution to traffic control in the operating room is another parameter that can affect the infectious risk\textsuperscript{42}. Unnecessary overcrowded rooms by staff that moves inside and outside the room, with frequent opening and closing of the doors, may increase the inoculation of airborne microbes in the surgical site\textsuperscript{42}.

The type of air circulation and ventilation in orthopedic theaters for prevention of postoperative infections, was examined by Gastmeier P et al.\textsuperscript{43}. Among 75,000 total knee replacements and 120,000 total hip replacements in four countries (Germany, New Zealand, UK, USA) they found that Laminar flow system (air moves in a single direction along parallel flow lines) is not superior in prevention of postoperative infections compared with Plenum system (pressure greater inside than outside room) and Ex-flow system (air moves down and outwards the room)\textsuperscript{43}.

**The type of prostheses used and how they impact on infectious rates**

The bearing surface of the selected prosthesis in total hip replacements is crucial for complications like increased levels of serum metal ion, aseptic lymphocyte-dominated vasculitis-associated lesions and periprosthetic infections\textsuperscript{44}. A very recent study by Huang P et al. presented data from the Australian Orthopaedic Association National Joint Replacement Registry, comparing infection rates between Metal on Metal (MOM) and other bearing surfaces like Metal on Polyethylene (MOP), Ceramic on Metal (COM), Ceramic on Polyethylene (COP) and Ceramic on Ceramic (COM)\textsuperscript{44}. Among 200,076.879 patients, editors found that, revision for infection of MoM surfaces in primary hip replacement was 2.5%, compared to 0.8% for other type of prostheses\textsuperscript{44}. This is one of the reasons MOM bearing surfaces are rarely used nowadays\textsuperscript{44}. According to Huang P et al., the lowest risk for periprosthetic infections appears in Ceramicized Metal on Polyethylene and COP prostheses, with MOP and COC having an intermediate risk between MOM and COM\textsuperscript{44}.

Ever since, unicompartmental knee replacement versus tricompartmental knee replacement was another matter of issue between orthopedic surgeons. Furnes O et al., studied the 10 -year survival probability between the two techniques from 1994 to 2004 in Norway\textsuperscript{45}. They found that unicompartmental knee replacements have significant lower risk for infections compared with tricompartmental knee replacement (relative risk was 0.28 with 95% confidence interval, 0.10 to 0.74)\textsuperscript{45}. The risk for infection may be one third in unicompartmental compared with tricompartmental knee replacements\textsuperscript{46}. However, unicompartmental knee replacements are not preferred due to higher risk for other complications, like pain which needs revision, aseptic loosening of the tibial and femoral components and periprosthetic fractures\textsuperscript{45}.

An article by Poultssides LA et al., showed that when either unilateral or staged bilateral within one-year knee replacement was preferred, the infection risk for in-hospital infection was higher compared with one day bilateral total knee arthroplasty\textsuperscript{47}.

Engesæter L et al., collected data from the Norwegian Arthroplasty Register for the period between 1987 and 2003, investigating the role of cementation of total hip arthroplasties in infection rates\textsuperscript{48}. Among 56,275 patients with osteoarthritis who had total hip replacement, 252 revisions due to infection were recorded\textsuperscript{48}. Comparing risk of infection between uncemented and cemented arthroplasties with antibiotic-loaded cement, no differences were observed\textsuperscript{48}. On the other hand, cemented total hip arthroplasties without antibiotic had 1.8 times much more danger for infection\textsuperscript{50}. Every time that total hip arthroplasties are chosen to be cemented, orthopedic surgeons must ensure that they use antibiotic-loaded cement\textsuperscript{48}.

**Perioperative antibiotic coverage**

Perioperative antimicrobial prophylaxis consists of preoperative, intraoperative and postoperative prevention strategies against periprosthetic infections\textsuperscript{49}. Current data support the use of cefazolin (or cefuroxime) at a dose of 2 g/day (3 g for obese patients), between 30 to 60 minutes before the surgical incision. Intraoperative redosing is essential when the operation exceeds more than 4 hours and blood loss is over 2 liters\textsuperscript{49}. Administration of cefazolin stops with the end of first postoperative day\textsuperscript{49}. In the case there is known allergic reaction (type 1) beta-lactams or Methicillin-resistant Staphylococcus aureus colonization the recommended alternatives are clindamycin and vancomycin\textsuperscript{49}.

According to Sewick A et al., vancomycin can't be the first line perioperative antimicrobial prophylaxis in colonized patients who are not MRSA resistant\textsuperscript{50}. Vancomycin is less effective compared with beta- lactams, needs more time to diffuse in tissues\textsuperscript{50}. Co-administration with cefazolin showed poor results in periprosthetic infections, but reduced infection rates by MRSA\textsuperscript{50}.

**Skin preparation and draping**

Current data support the use of chlorhexidine for skin preparation in the orthopedic theatre to sterilize the incision site\textsuperscript{51}. Bosco JA et al. showed that chlorhexidine is a superior antimicrobial agent compared with iodine (Bedatine) and alcohol-based solutions\textsuperscript{51}.

Draping of surgical site with antiseptic agents can further deteriorate the risk for superficial and deep infections. A systematic review by Webster J et al., showed that adhesive
plastic skin drapes, do not reduce infection rates. On the contrary they seem to be less protective against pathogens according to new evidence, disputing previous studies52.

**Postoperative risk factors**

**Persistent drainage from surgical wound**

Persistent wound drainage, especially more than 48 hours postoperatively, must be monitored and make medical staff suspicious for complications like periprosthetic infection53. Surgical sites that continue to drain between 5 to 7 days after operation, are 12.5 times more susceptible to develop periprosthetic infection, compared to clean and dry sites54. Every next day the wound continues to drain, the risk for periprosthetic hip infection can reach 42% and 29% for periprosthetic knee infection55.

Medical conditions that delay wound healing and exceed wound drainage are diabetes mellitus, rheumatoid arthritis, smoking, old age, obesity, malnutrition and hypoalbuminemia56. The use of LMWH, for postoperative anticoagulation prophylaxis also increases the risk for delay drainage compared with aspirin and warfarin57.

**Postoperative distant infections**

According to Pulido L et al, among 9,245 persons who submitted total hip or knee arthroplasty, patients with postoperative urinary tract infection had 5-folds more risk to develop periprosthetic joint infection57, Iorio R et al., found increased risk for urinary tract infection and postoperative knee infection after primary arthroplasty in patients who were catheterized with indwelling catheters compared with straight catheters58. Urinary catheter removal is another significant factor for infections and must no delay59.

Postoperative nosocomial pneumonia is another complication that may lead to periprosthetic joint infection. According to Parvizi J and Pulido L, the incidence of nosocomial pneumonia after total hip and knee arthroplasty is 0.1% and 0.15%, respectively59. Streptococcus pneumonia being the most common pathogen isolated in pneumonia, can settle on hip or knee prostheses and cause infection61. Early signs and symptoms of postoperative pneumonia must early recognized by clinical and imaging examination and treated with appropriate medications61.

During immediate postoperative period, the anatomic skin barrier is disturbed. Postoperative subcutaneous hematoma formation creates ideal circumstances for pathogens to develop. Skin over surgical incision has to be clean and dry until sutures removal62.

Urinary tract infection, postoperative pneumonia, skin infections and non-well sterilized catheters for intravenous drug administration, can be the reason for postoperative bacteremia63. Murdoch Dr et al., defined periprosthetic joint infection due to postoperative bacteremia in those cases that happened 1 year after implantation64. Staphylococcus aureus is the most common pathogen found in postoperative bacteremia64. However, hospital-acquired is less aggressive compared with community-acquired staphylococcus aureus and difficult to distinguish whether joint site is the primary or secondary source of infection64.

**Postoperative cardiac complications**

Cardiovascular system consists of the pump and vascular network that transports blood, oxygen, nutrients, antimicrobial cells and molecules in the hole body, increasing the risk for periprosthetic infection when it functions insufficiently65. According to Pulido L et al., atrial fibrillation and infarction of the myocardium have 6.2 and 20.4 odds ratio, respectively, as independent predictors for periprosthetic infection67.

**Length of hospital stay and early readmissions due to infection**

The extended length of hospital stay increases patient’s exposure in nosocomial microbes and the risk for periprosthetic joint infection after total hip or knee replacement.

In California (from 2009 to 2011), 4.29% of patients were readmitted with 33.02% recorded readmissions due to infection66. In Florida (from 2009 to 2013), 4.7% of patients were readmitted with 33.39% of patients diagnosed with septic arthritis55. In Massachusetts (from 2010 to 2012), 3.92% of patients were readmitted with 35.2% for periprosthetic joint infection65. Staphylococcus Aureus was the most usual cultivated pathogen from septic samples65.

According to Barad SJ et al., the average hospital stays between 2009 and 2014 shortened from 2.0 to 1.3 days per year66. More patients are discharged directly at home with outpatient physical rehabilitation (from 9% to 53%) and less patients choose to move in a rehabilitation facility (from 41% to 1%)68. Postoperative readmission rates after 30 days still the same and savings were improved to $3,245 per patient66.

**Post-discharge factors**

**Postoperative dental procedures**

Daily dental manipulations like brushing and flossing as well as bad oral hygiene, cause transient bacteremia by oral microbes of the flora67. Dental procedures following total hip or knee replacement has been a long-standing issue between the American Academy of Orthopedic Surgeons (AAOS) and the American Dental Association (ADA) for being a risk factor for postoperative infections. The use of antibiotic prophylaxis prior hip and knee arthroplasties stills controversial in several case studies67. Berbari EF et al., found among 339 patients with total hip or knee replacement, that administration of antibiotic prophylaxis does not decrease the risk for postoperative infection prior a high-risk or low-risk dental procedure and must give only to specific patients68.
Orthopedic surgeons, dentists and infectious disease specialists recommended that “antibiotic prophylaxis is not indicated for most dental patients with total joint replacements”\(^{69}\), but AAOS redefined that “…clinicians have to consider antibiotic prophylaxis for all total joint replacement patients prior to any invasive procedure that may cause bacteremia.”\(^{70}\)

Orthopedic surgeons must encourage their patients to keep high quality oral hygiene. Meanwhile, more case studies have to be accomplished to define safe postoperative period for dental procedures as well as the necessity of antibiotic prophylaxis, due to the lack of evidence.

**Total hip or knee arthroplasty in patients with history of periprosthetic joint infection**

Hip and knee osteoarthritis being a degenerative and progressive disease is often detrimental for more than two joints at the same time in a single patient. People with multiple joint arthroplasties may have elevated risk for infection after a subsequent joint replacement. Patients with past medical history of periprosthetic joint infection have 19-20% more risk to develop a new infection in a future joint replacement\(^{71}\). Abblitt W et al., in a retrospective study, reviewed 167 patients treated with revision surgery due to periprosthetic joint infection, from 2003 to 2014\(^{71}\). Among these patients, 76 had multiple joint arthroplasties due to osteoarthritis. A significant number of this group (10/76), approximately 13%, operated for periprosthetic joint infection in a second location\(^{71}\). Abblitt W et al., found a close association between positive blood cultures before joint replacement and the risk for future periprosthetic infection\(^{71}\). In bacteremic patient the risk was 20% and in non-bacteremic patients 5.2%\(^{71}\). Patients with multiple arthroplasties planned for future joint replacement, must thoroughly be checked for septic loosening of their prostheses and positive blood cultures prior operation, especially if they have medical history of joint infection.

**Conclusion**

Every patient submitted for total hip or knee arthroplasty is exposed in various independent risk factors for postoperative joint infection. Some of them are patient-based factors being irreversible like the gender and race. Other ones are under the sphere of comorbidities that follow the patient like cardiovascular diseases and obesity which could be controlled. Improvement of the quality of antiseptic prophylaxis like adequate antibiotic prophylaxis and preferred type of prosthesis can also impact the risk for infection. A wide spectrum of factors, that have been analyzed above, affect the health of the patient from prior, during and after a total hip or knee joint replacement. We suggest that orthopedic surgeons in cooperation with infectious practitioners have to design population-based cohorts in order to develop evaluating infection scores. Tools like FRAX score for osteoporosis and Framingham Score for heart disease risk, are excellent paradigms for a new tool for periprosthetic joint infections estimating the significance of each risk factor in a total risk score. Patients may benefit from such a pioneer tool as they will be categorized in high and low risk groups for periprosthetic infections and improve their score under medical advice.

**References**

1. Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. Ann Rheum Dis 2014; 73:1323-1330.
2. Guillemin F, Rat A C, Mazieres B, Pouchot J, Fautrel B, Euler-Ziegler L, et al. Prevalence of symptomatic hip and knee osteoarthritis: A two-phase population-based survey. Osteoarthritis and Cartilage 2011; 19 (11): 1314-1322.
3. Murphy L, Schwartz TA, Helmiick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. Arthritis Rheum 2008;59(9):1207-13.
4. Lawrence RC, Felton DT, Helmiick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum 2008;58(1):26-35.
5. Steiner C, Andrews R, Barrett M, Weiss A. HCUP Projections: Mobility/Orthopedic Procedures 2003 to 2012. 2012. HCUP Projections Report # 2012-03. 2012 Sep 20. U.S. Agency for Healthcare Research and Quality.
6. Maradit K, Larson DR, Crowson CS, Kremers WK, Washington RE et al. Prevalence of Total Hip and Knee Replacement in the United States. J Bone Joint Surg Am 2015;97(17):1386-97.
7. Schurman DJ. Functional outcome of GUEPAR hinge knee arthroplasty evaluated with ARAMIS. Clin Orthop Relat Res 1981(115):118-132.
8. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007;89(4):780-5.
9. Mraovic B, Suh D, Jacovides C, et al. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. J Diabetes Sci Technol 2011;5: 412-8.
10. Standards of medical care in diabetes - 2016: summary of revisions. Diabetes Care 2016;39(Suppl 1):S4-S5.
11. Jamsen E, Nevalainen P, Eskelinen A, et al. Risk factors for perioperative hyperglycemia in primary hip and knee replacements. Acta Orthop 2015;86:175-82.
12. Parvizi J, Gehrke T. International consensus on periprosthetic joint infection: let cumulative wisdom be a guide. J Bone Joint Surg Am 2014;96:441.
13. Dixon JB. The effect of obesity on health outcomes. Mol Cell Endocrinol 2010; 316:104-8.
14. Fehring TK, Odum SM, Griffin WL, Mason JB, McCoy TH. The obesity epidemic: its effect on total joint arthroplasty. J Arthroplasty 2007; 22 (6 Suppl 2):71-6.
15. Jamsen E, Nevalainen P, Eskelinen A, et al. Obesity, diabetes, and preoperative hyperglycemia as predictors of periprosthetic joint infection: a single-center analysis of 7181 primary hip and knee replacements for osteoarthritis. J Bone Joint Surg Am 2012; 94:e101.
16. Cross MB, Yi PH, Thomas CF, Garcia J, Della Valle CJ. Evaluation of malnutrition in orthopaedic surgery. J Am Acad Orthop Surg 2014; 22:193-199.
17. Yi PH, Frank R, Vann E, Sonn K, et al. Is Potential Malnutrition Associated with Septic Failure and Acute Infection After Revision Total
18. Singh JA. Smoking and outcomes after knee and hip arthroplasty: a systematic review. J Rheumatol 2011; 38:1824-34.

19. Greenky M, Gandhi K, Pulido L, Restrepo C, Parvizi J. Preoperative Anemia in Total Joint Arthroplasty: Is It Associated with Periprosthetic Joint Infection? Clin Orthop Relat Res 2012; 470(10): 2695-2701.

20. Wang Q, Jiang X, Tian W. Does previous intra-articular steroid injection increase the risk of joint infection following total hip arthroplasty or total knee arthroplasty? A meta-analysis. Med Sci Monit 2014; 20: 1878-83.

21. Cancienne J, Werner B, Luetkemeyer L, Browne J. Does Timing of Previous Intra-Articular Steroid Injection Affect the Post-Operative Rate of Infection in Total Knee Arthroplasty? J Arthroplasty 2015; 30(11):1879-82.

22. Chirca I, Marculescu C. Prevention of Infection in Orthopedic Prosthetic Surgery. Infect Dis Clin North Am 2017;3(1):253-263.

23. Hacek DM, Robb WJ, Paule SM, et al. Staphylococcus aureus nasal colonisation in joint replacement surgery reduces infection. Clin Orthop Relat Res 2008; 466:1349-55.

24. Cordero-Ampuero J, de Dios M. What are the risk factors for infection in hemiarthroplasties and total hip arthroplasties? Clin Orthop Relat Res 2010;468(12):3268-3277.

25. Marmor S, Kerroumi Y. Patient-specific risk factors for infection in arthroplasty procedure. Orthop Traumatol Surg Res 2016; 102(1 Suppl): S113-9.

26. J Cordero-Ampuero, E González-Fernández, D Martínez-Vélez, J Esteban. Are antibiotics necessary in hip arthroplasty with asymptomatic bacteriuria? Seeding risk with/without treatment. Clin Orthop Relat Res 2013;471(12):3822-3829.

27. McDougall C, Gray H, Simpson P, Whitehouse S, Crawford R. Complications related to therapeutic anticoagulation in total hip arthroplasty. J Arthroplasty 2013;28(1):187-192.

28. McDougall C, Gray H, Simpson P, Whitehouse S, Crawford R. Complications related to therapeutic anticoagulation in total hip arthroplasty. J Arthroplasty 2013;28(1):187-192.

29. Wang Z, Anderson Jr. F, Ward M, Bhattacharyya T. Surgical Site Infections and Other Postoperative Complications following Prophylactic Anticoagulation in Total Joint Arthroplasty. PLoS ONE 9(4): e91755.

30. Kim M-K, Patel RA, Shinn AH, et al. Evaluation of gender difference in skin type and pH. J Dermatol Sci 2006;41(2):153-6.

31. Herwaldt LA, Cullen JJ, French P, et al. Preoperative risk factors for nasal carriage of Staphylococcus aureus. Infect Control Hosp Epidemiol 2004;25(6):481-4.

32. Liubeke A, Stern R, Garavaglia G, Zurcher L, Hoffmeyer P. Differences in outcomes of obese women and men undergoing primary total hip arthroplasty. Arthritis Rheum 2007;57(12):327-34.

33. Soohoo NF, Fargh E, Lieberman JR, Chambers L, Zingmond DS. Factors that predict short-term complication rates after total hip arthroplasty. Clin Orthop Relat Res 2010;468(9):2363-71.

34. Wilson MG, May DS, Kelly JJ. Racial differences in the use of total knee arthroplasty for osteoarthritis among older Americans. Ethn Dis 1994;4(1):57-67.

35. Collins TC, Daley J, Henderson WH, Khuri SF. Risk factors for prolonged length of stay after major elective surgery. Ann Surg 1999;230(2):251-9.

36. Webb BG, Lichtman DM, Wagner RA. Risk factors in total joint arthroplasty: comparison of infection rates in patients with different socioeconomic backgrounds. Orthopedics 2008;31(5):445.

37. Zhou X, Yishake M, Li J, et al. Genetic susceptibility to prosthetic joint infection following total joint arthroplasty: a systematic review. Gene 2015;563:76-82.

38. Katz JN, Barrett J, Mahomed NN, et al. Association between hospital and surgeon procedure volume and the outcomes of total knee replacement. J Bone Joint Surg Am 2004;86(9):1909-16.

39. Katz JN, Losina E, Barrett J, et al. Association between hospital and surgeon procedure volume and outcomes of total hip replacement in the united states medicare population. J Bone Joint Surg Am 2001; 83(11):1622-9.

40. Chang CC, Lin H-C, Lin H-W, Lin H-C. Anesthetic management and surgical site infections in total hip or knee replacement: a population-based study. Anesthesiology 2010;113(2):279-84.

41. Dicks K, Baker A, Durkin M, Anderson D, Moehring R et al. Short Operative Duration and Surgical Site Infection Risk in Hip and Knee Arthroplasty Procedures. Infect Control Hosp Epidemiol 2015;36(12):1431-1436.

42. Allo M, Tedesco M. Operating Room Management: Operative Suite Considerations, Infection Control. Surg Clin N Am 2005;85:1291-1297.

43. Gasteameier P, Breier AC, Brandt C. Influence of laminar airflow on prosthetic joint infections: a systematic review. J Hosp Infect 2012; 81:73-83.

44. Huang P, Lyons M, Sullivan M. The Infection Rate of Metal-on-Metal Total Hip Replacement is Higher When Compared to Other Bearing Surfaces as Documented by the Australian Orthopaedic Association National Joint Replacement Registry. HSSJ 2018; 14: 99-105.

45. Furnes O, Espehaug B, Lie SA, Vollset SE, Engesaeter LB, Havelin L. Failure mechanisms after unicompartmental and tricompartmental primary knee replacement with cement. J Bone Joint Surg Am 2007; 89(3):519-25.

46. B D Springer and J. Parvizi(eds.), Periprosthetic Joint Infection of the Hip and Knee, DOI 10.1007/978-1-4614-7928-4_2, © Springer Science + Business Media New York 2014. Chapter Risk Factors for Periprosthetic Joint Infection (p.15-40) B. Zmistowski and P. Alijannour.

47. Poultisides LA, Trantafyllopoulos GK, Sakellariou VI, Mermoutsoudis SG, Sculco TP. Infection risk assessment in patients undergoing primary total knee arthroplasty. Int Orthop 2018;42(1):87-94.

48. Engesaeter L, Espehaug B, Lie S, Furnes, Havelin L. Does cement increase the risk of infection in primary total hip arthroplasty? Revision rates in 56,275 cemented and uncemented primary THAs followed for 0-16 years in the Norwegian Arthroplasty Register. Acta Orthopaedica 2006; 77(3):351-358.

49. AlBuhran B, Hind D, Hutchinson A. Antibiotic prophylaxis for wound infections in total joint arthroplasty: a systematic review. J Bone Joint Surg Br 2008;90:915-9.

50. Sewick A, Makani A, Wu C, O’Donnell J, Baldwin KD, Lee GC. Does dual antibiotic prophylaxis better prevent surgical site infections in total joint arthroplasty? Clin Orthop Relat Res 2012;470:2702-7.

51. Bosco JA, Slover JD, Haas JP. Perioperative strategies for decreasing infection: a comprehensive evidence-based approach. J Bone Joint Surg Am 2010;92(11):232-9.

52. Webster J, Alghamdi A. Use of plastic adhesive drapes during surgery for preventing surgical site infection. Cochrane Database of Systematic Reviews 2015 Issue 4. Art. No.: CD006353.

53. Jaben FM, Parviz J, Haytmanek CT, Joshi A, Purtill J. Procrastination of wound drainage and malnutrition affect the outcome of joint arthroplasty. Clin Orthop Relat Res 2008;466(6):1368-71.

54. Saleh K, Olson M, Resig S, et al. Predictors of wound infection in hip and knee joint replacement: results from a 20-year surveillance program. J Orthop Res 2002;20(3):506-15.

55. Patel VP, Walsh M, Sehgal B, et al. Factors associated with prolonged wound drainage after primary total hip and knee arthroplasty. J Bone Joint Surg Am 2007;89(1):33-8.
Risk factors for periprosthetic joint infection following total hip and knee arthroplasty

56. Galat DD, McGovern SC, Larson DR, et al. Surgical treatment of early wound complications following primary total knee arthroplasty. J Bone Joint Surg Am 2009;91(1):48-54.
57. Pulido L, Qnemem E, Joshi A, Purtill JJ, Parvizi J. Periprosthetic joint infection: the incidence, timing, and predisposing factors. Clin Orthop Relat Res 2008;466(7):1710-5.
58. Iorio R, Healy WL, Patch DA, Appleby D. The role of bladder catheterization in total knee arthroplasty. Clin Orthop Relat Res 2000;380:80-4.
59. Parvizi J, Mui A, Purtill JJ, et al. Total joint arthroplasty: when do fatal or near-fatal complications occur? J Bone Joint Surg Am 2007;89(1):27-32.
60. Pulido L, Parvizi J, Macgibeny M, et al. In hospital complications after total joint arthroplasty. J Arthroplasty 2008;23(6 Suppl 1):139-45.
61. Berbari EF, Hanssen AD, Duffy MC, et al. Risk factors for prosthetic joint infection: case-control study. Clin Infect Dis 1998;27(5):1247-54.
62. Saleh K, Olson M, Resig S, et al. Predictors of wound infection in hip and knee joint replacement: results from a 20-year surveillance program. J Orthop Res 2002;20(3):506-15.
63. Ekkelenkamp MB, Van der Bruggen T, Van de Vijver DAMC, Wolfs TFW, Bonten MJM. Bacteremic complications of intravascular catheters colonized with Staphylococcus aureus. Clin Infect Dis 2008;46(1):114-8.
64. Murdoch DR, Roberts SA, Fowler Jr VG, et al. Infection of orthopedic prostheses after Staphylococcus aureus bacteremia. Clin Infect Dis 2001;32(4):647-9.
65. Zawadzki N, Wang Y, Shao H, Liu E, Chao Song C, et al. Readmission due to infection following total hip and total knee procedures: A retrospective study. Medicine (Baltimore) 2017;96(38): e7961.
66. Barad SJ, Howell S, Tom J. Is a shortened length of stay and increased rate of discharge to home associated with a low readmission rate and cost-effectiveness after primary total knee arthroplasty? Arthroplast Today 2015;4(1):107-112.
67. Zimmerli W, Sendi P. Antibiotics for prevention of periprosthetic joint infection following dentistry: time to focus on data. Clin Infect Dis. 2010;50(1):17-9.
68. Berbari EF, Osmon DR, Carr A, Hanssen AD, Baddour LM et al., Dental procedures as risk factors for prosthetic hip or knee infection: a hospital-based prospective case-control study. Clin Infect Dis 2010;50(1):8-16.
69. American Dental Association and American Academy of Orthopaedic Surgeons. Antibiotic prophylaxis for dental patients with total joint replacements, J Am Dent Assoc 2003, vol. 134 (pg. 895-8).
70. American Academy of Orthopaedic Surgeons, Antibiotic prophylaxis for bacteremia in patients with joint replacements Accessed 9 November 2009 Available at: http://www.aaos.org/about/papers/advstmt/1033.asp.
71. Jafari SM, Casper DS, Restrepo C, et al. Periprosthetic joint infection: are patients with multiple prosthetic joints at risk? J Arthroplasty 2012;27(6):877-80.