

Review Article

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

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Abstract

Osteoarthritis 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 osteoarthritis 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 osteoarthritis 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 million people with knee osteoarthritis 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: Osteoarthritis, Total hip replacement, Total knee replacement, Periprosthetic infections, Risk factors

Introduction

Osteoarthritis 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 knee¹. Patients suffering either from hip or knee osteoarthritis are referring to orthopedic departments due to symptoms of pain and stiffness and disability to perform simple clinical activities¹. The hip and knee osteoarthritis 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 osteoarthritis is 40% in men and 47% in women population with normal body mass index (BMI) 3. For overweight people with BMI \geq 30%, the probability is elevated to 60%³. In the Johnston County Osteoarthritis Project, the prevalence of symptomatic osteoarthritis 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 osteoarthritis 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 1981⁷. Due to improvement of surgical techniques and targeted prophylactic antibiotic therapy, the prevalence of periprosthetic joint infection has minimized to 1-2% nowadays⁸. In 2003, 202,500 and 402,000 primary total hip and knee replacements, respectively, were carried out in USA⁸. During the same year, 36,000 revisions after total hip replacement and 32,700 revisions after total knee replacement were done⁸. 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 replacement⁸.

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 osteoarthritis. We choose to study bibliography for both periprosthetic hip and knee infections as being the two major weight-bearing joints operated for osteoarthritis 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 osteoarthritis 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 hospitalization⁹. 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 infection⁹.

Patients suffering from diabetes mellitus must be controlled preoperatively with hemoglobin A1c (HbA1c) or with a fasting blood glucose test¹⁰. Pre-existing diabetes mellitus is proven to be the most important risk factor for postoperative hyperglycemia that affects the immune defending system against infectious agents¹¹. 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 infections¹².

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 patients¹³. The rates of obese patients with joint osteoarthritis referring to orthopedic clinics for total hip or knee replacement have increased from 30% to 52% from 1990 to 2005 in USA¹⁴. 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 replacement¹⁵. They recorded 52 patients who experienced periprosthetic joint infection after a year from the primary surgery¹⁵. 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%¹⁵. In the same study, it seemed that the risk for periprosthetic joint infection is much more elevated when obesity coexists with diabetes mellitus¹⁵.

Additionally, malnourished patients who proceed with total hip or knee replacement have extremely high risk for infection after surgery, too¹⁶. 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 preoperatively¹⁶. According to Paul H et al, the presence of one or more markers that indicate malnutrition are independent risk factors for infection¹⁷. 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 study¹⁷.

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 site¹⁸. Patients with osteoarthritis must be advised to avoid smoking at least for 4 weeks prior surgery¹⁸.

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.

Greenky M et al., published their data from 15,222 patients who undergone 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 < 12 g/dl in women and Hgb < 13 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 staphylococci²². 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 period²⁹. 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 cumulatively²⁸.

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 USA²⁹. 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)²⁹. 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%), too²⁹.

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 women³⁰. Differences in skin characteristics, like skin pH, subcutaneous fat distribution, skin thickness, and circulating hormones are the more obvious reasons³⁰. 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 men³¹. Lübbecke 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 same³².

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 infection³³. They supported that comorbidities, like cardiac disease, and immunosuppressive illnesses, like rheumatoid arthritis that appear more usual in this age group is the main etiology for that³³.

According to Wilson MG et al., African-Americans are more prone for periprosthetic joint infection after total knee arthroplasty compared with white Caucasians³⁴. They supported that the reason for that is due to higher BMI of African Americans, intraoperatively compared with Caucasians³⁴. Collins TC et al., support that higher risk for postoperative infections among African Americans

is relevant to the prolonged duration of stay in hospital postoperatively³⁵.

The socioeconomic status of patients is another risk factor for periprosthetic joint infection after primary surgery³⁶. 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 countries³⁶.

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 Caucasians³⁷. 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 replacement³⁷.

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^{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^{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 anesthesia⁴⁰. General anesthesia causes peripheral vasodilatation diminishing blood and oxygen supply to the surgical site⁴⁰. Additionally, opioids and drugs used in general anesthesia suppress the defending mechanisms of immune system⁴⁰. 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 joint⁴⁰.

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 USA⁴¹. 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)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 minutes⁴¹. Obviously, the duration of operation is a more decisive factor for infections in total knee replacements compared with total hip replacements⁴¹.

Caution to traffic control in the operating room is another parameter that can affect the infectious risk⁴². 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 site⁴².

The type of air circulation and ventilation in orthopedic theaters for prevention of postoperative infections, was examined by Gastmeier P et al.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)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 infections⁴⁴. 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)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 prostheses⁴⁴. This is one of the reasons MOM bearing surfaces are rarely used nowadays⁴⁴. 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 COM⁴⁴.

Ever since, unicompartmental knee replacement versus tricompartmental total 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 Norway⁴⁵. 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] p=0.01)⁴⁵. The risk for infection may be one third in unicompartmental compared

with tricompartmental knee replacements⁴⁶. 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 fractures⁴⁵.

An article by Poultides 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 arthroplasty⁴⁷.

Engesaeter 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 rates⁴⁸. Among 56,275 patients with osteoarthritis who had total hip replacement, 252 revisions due to infection were recorded⁴⁸. Comparing risk of infection between uncemented and cemented arthroplasties with antibiotic-loaded cement, no differences were observed⁴⁸. On the other hand, cemented total hip arthroplasties without antibiotic had 1.8 times much more danger for infection⁵⁰. Every time that total hip arthroplasties are chosen to be cemented, orthopedic surgeons must ensure that they use antibiotic-loaded cement⁴⁸.

Perioperative antibiotic coverage

Perioperative antimicrobial prophylaxis consists of preoperative, intraoperative and postoperative prevention strategies against periprosthetic infections⁴⁹. 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 liters⁴⁹. Administration of cefazolin stops with the end of first postoperative day⁴⁹. In the case there is known allergic reaction (type 1) beta-lactams or Methicillin-resistant *Staphylococcus aureus* colonization the recommended alternatives are clindamycin and vancomycin⁴⁹.

According to Sewick A et al., vancomycin can't be the first line perioperative antimicrobial prophylaxis in colonized patients who are not MRSA resistant⁵⁰. Vancomycin is less effective compared with beta-lactams, needs more time to diffuse in tissues⁵⁰. Co-administration with cefazolin showed poor results in periprosthetic infections, but reduced infection rates by MRSA⁵⁰.

Skin preparation and draping

Current data support the use of chlorhexidine for skin preparation in the orthopedic theatre to sterilize the incision site⁵¹. Bosco JA et al, showed that chlorhexidine is a superior antimicrobial agent compared with iodine (Betadine) and alcohol-based solutions⁵¹.

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 not delay⁵⁸.

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%, respectively^{59,60}. 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 be 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 whole body, increasing the risk for periprosthetic infection when it functions insufficiently⁵⁷. 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 infection⁵⁷.

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 infection⁶⁵. In Florida (from 2009 to 2013), 4.7% of patients were readmitted with 33.39% of patients diagnosed with septic arthritis⁶⁵. 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 replacement⁷¹. Abblitt W et al., in a retrospective study, reviewed 167 patients treated with revision surgery due to periprosthetic joint infection, from 2003 to 2014⁷¹. 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 location⁷¹. Abblitt W et al., found a close association between positive blood cultures before joint replacement and the risk for future periprosthetic infection⁷¹. 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, Helmick CG, et al. Lifetime risk of symptomatic knee osteoarthritis. *Arthritis Rheum* 2008;59(9):1207-13.
4. Lawrence RC, Felson DT, Helmick 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 H, 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;(155):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):S4-5.
11. Jamsen E, Nevalainen PI, Eskelinen A, et al. Risk factors for perioperative hyper-glycemia 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

- Joint Arthroplasty? *Clin Orthop Relat Res* (2015) 473:175-182.
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;31(2):253-263.
 23. Hacek DM, Robb WJ, Paule SM, et al. Staphylococcus aureus nasal decolonization 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. Lübbecke 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(2):327-34.
 33. Soohoo NF, Farnig 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 C-C, 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. Gastmeier P, Breier AC, Brandt C. Influence of laminar airflow on prosthetic joint infections: a systematic review. *J Hosp Infect* 2012; 81:73-8.
 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 LI. 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. Aljaniipour.
 47. Poultsides LA, Triantafyllopoulos GK, Sakellariou VI, Memtsoudis 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. AlBuhairan 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(1):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.: CDO06353.
 53. Jaber FM, Parvizi 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.

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, Ghanem 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/advistmt/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.