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Arthroplasty

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Reducing the risk of infection after total joint arthroplasty: preoperative optimization

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Abstract

Total joint arthroplasty (TJA) is one of the most commonly performed procedures in orthopedic surgery, and as the demand for TJA increases over time, the number of concurrent complications such as surgical infection will also increase. There are multiple risk factors that independently increase the risk of surgical site infection (SSI) and periprosthetic joint infection (PJI) after surgery. These modifiable risk factors can be identified in preoperative clinic screening visits that gives physicians the opportunity to provide specific intervention that can decrease patient infection risk. The risk factors that are known to significantly increase the risk of PJI and/or SSI include MSSA/MRSA colonization, rheumatoid arthritis, cardiovascular and renal disease, obesity, diabetes mellitus, hyperglycemia, anemia, malnutrition, tobacco use, alcohol consumption, depression, and anxiety. Patients who present with one or more of these risk factors require intervention with a multidisciplinary approach including patient education, counseling, and follow-up. Preoperative patient optimization for high risk TJA patients can significantly decrease PJI and SSI risk while improving surgical outcomes and patient care.

Introduction

The number of total joint arthroplasties (TJAs) performed has increased over time, and the projected growth for total knee arthroplasty (TKA) and total hip arthroplasty (THA) from 2005 to 2030 is approximately 673 and 174%, respectively [1]. However, this growth in surgical procedures is associated with an increase in the number of surgical complications, such as periprosthetic joint infection (PJI). In order to reduce postoperative complications, infections should be prevented by engaging in patient optimization and targeted intervention of potential risk factors.

Patients' risk for infection can be evaluated preoperatively with screening methods and transparent patient-provider communication, as patients undergoing TJA often have medical comorbidities or follow lifestyle activities that increase the risk for developing PJI and/or surgical site infection (SSI). The most common modifiable risk factors in 80% of eligible arthroplasty patients are obesity, anemia, malnutrition, and diabetes mellitus [2]. Other factors which warrant preoperative screening include methicillin sensitive *Staphylococcus aureus* (MSSA) and methicillin resistant *Staphylococcus aureus* (MRSA) colonization, rheumatoid arthritis, tobacco and alcohol use, renal failure, cardiovascular issues, depression, and medication use [3]. Some risk factors are more common in patients greater than 64 years of age, who often have longer hospital length of stay (LOS), which is an independent risk factor for PJI, and may have 5-times greater mortality compared to younger patients [4, 5].

Preoperative screening should occur at the initial visit, evaluating for factors such as obesity and diabetes, which may require longer intervention times. These preoperative clearance visits usually occur 2–6 weeks prior to surgery to allow adequate time for intervention and treatment, such as *Staphylococcus aureus* screening to permit sufficient time for the antibiotic treatment to be medically effective [6]. Each risk factor has an individual component that contributes to a heightened risk for SSI/PJI, and patients with more than one major risk factor or comorbidity are at an even greater risk for PJI development. These patients require intervention using a dynamic approach of risk factor recognition, medical

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treatment, education, and long-term engaged outlook to prevent risks from recurring. The purpose of this review is to identify specific modifiable risk factors that can be addressed preoperatively to optimize patients and reduce the risk of infection after TJA.

MSSA/MRSA

Patients with pre-existing MSSA and/or MRSA colonization have an increased risk for developing postoperative orthopaedic SSI/PJI [7]. MRSA was the cause of 23% of primary THA SSIs and 21% revision THA SSIs [6]. These infected cases are difficult to treat and often result in unfavorable postoperative outcomes for patients, such as increased mortality and longer LOS [8]. Therefore, preoperative screening for MSSA/MRSA may be beneficial since *S. aureus* genotype screening shows that 80% of infections result from patients' clonal nasal flora [9].

Medical providers often perform MSSA/MRSA nares swabbing preoperatively in order to identify the presence of these organisms, although other sites can be swabbed including the axilla and perineum. Nasal swabbing successfully detected 66% of carriers, and overall detection rates reached 82% when both nosal and perineal swabbing were conducted [10–12]. If MSSA and/or MRSA is detected, the most common treatment involves the intranasal application of topical mupirocin ointment twice daily and 5 days of daily chlorhexidine body wash immediately prior to surgery [10, 13]. If a patient is MRSA positive, antibiotic prophylaxis with vancomycin is added to the usual regimen of cefazolin prior to surgery (Fig. 1).

MSSA/MRSA surveillance in patient populations has demonstrated that this intervention reduces infections and is cost-effective. Decolonization following nasal mupirocin application and antiseptic body washes decreased MRSA-related SSIs from 2.3 to 0.3% [14]. The cost of the nasal swab test and treatment ranges from $100 to $300 based on how many swabs are collected, insurance reimbursement, and decolonization regimen used. With decolonization rates exceeding 50%, the cost analysis of this regimen was deemed cost-effective and finically dominant from the hospital and third-party payer perspectives [15]. Success of this preoperative decolonization protocol was predicted in another study to save one hospital $230,000 [16]. The overall cost savings from avoided medical costs of treating infections

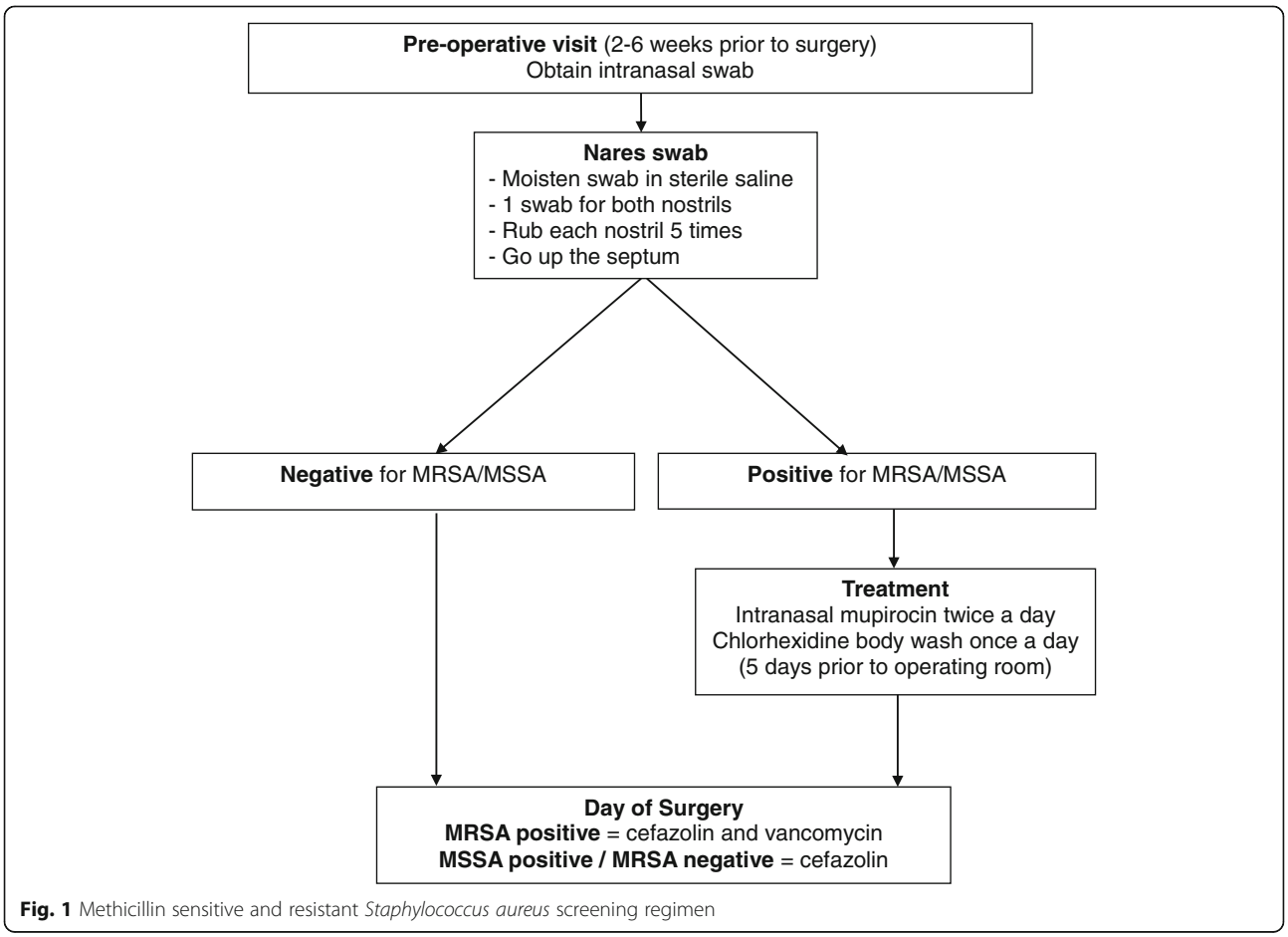

Fig. 1 Methicillin sensitive and resistant *Staphylococcus aureus* screening regimen

and health benefits significantly outweighed the cost of MSSA/MRSA screening swabs and decolonization [15].

Rheumatoid arthritis

The presence of rheumatoid disease is associated with a 3.7% increase in PJI which escalates with greater chronicity of rheumatoid disease [17]. This inflammatory disease impacts immune system function and adversely affects wound healing. The immunosuppression prescription medications often given to rheumatoid arthritis patients also contributes to increased infection risk [17]. Therefore, it is strongly recommended that preoperative clinic visits for patients with rheumatoid disease include education and guidance for modified medication regimens leading up to orthopaedic surgical procedures. These non-biologic disease modifying antirheumatic drugs (DMARDs) should be discontinued before surgery due to their long half-lives and resulting elimination of underlying disease suppression [13]. Associated drug treatments often increase patients' risk for developing mycobacterial and opportunistic infections [13]. Therefore, altered medication regimens include stopping biologics (i.e. rituximab and belimumab) before surgery and scheduling an arthroplasty date at the end of the dosing cycle for these specific medications. Patients should also be advised to stop the following medications at least 4 weeks before surgery: infliximab (REMICADE®), adalimumab (HUMIRA®), certolizumab (CIMZIA®) golimumab (SIMPONI®), and etanercept (ENBREL®), which should be stopped 15 days before the procedure [18]. At least 1 week before surgery, it should be noted that tofacitinib should also be stopped. These medications should only be started again after the healing process is complete with no signs of infection [3]. The medications that can be continued are methotrexate, leflunomide, hydroxychloroquine, sulfasalazine, mycophenolic acid (myfortic), azathioprine, mizoribine, cyclosporine, and/or prograf [19].

The use of corticosteroids to treat rheumatoid arthritis is another risk factor for infection where the degree of infection risk is directly proportional to steroid dosage [20]. These steroids increase the risk of infection due to depressed immune function with reduced phagocytosis, adhesion, leukocyte function, and vascular permeability [13]. Therefore, patients undergoing arthroplasty should ideally decrease the dosage of steroids prior to surgery to under 5 mg/day [21]. However, if this is not possible, the current daily dose of glucocorticoids should be given on the day of surgery if taking < 15 mg instead of giving perioperative supraphysiologic doses referred to as "stress doses" [19].

Cardiovascular diseases

Cardiovascular disorders are linked to higher postoperative complications and PJI rates. Conditions such as myocardial infarction, atrial fibrillation [5], congestive heart failure [22], hypertension [23], pulmonary circulation disorders, peripheral valvular disease, and valvular disease are significant risk factors for PJI development [22]. TJA patients with atrial fibrillation also have an increased need for blood transfusion and prolonged LOS by approximately 3 days with higher complications and readmissions [24]. TKA patients with preexisting cardiac comorbidities have 16 times greater 30-day mortality compared to those without any cardiovascular conditions [25]. During the preoperative consultation, a complete cardiovascular history should be obtained to identify preexisting conditions that can increase the risk for postoperative complications. Some patients with prior cardiovascular issues scheduled for elective orthopaedic surgery should also be cleared by a cardiologist, as these screenings and interventions can reduce postoperative complications. These patients may benefit from undergoing echocardiography and subsequent optimization before undergoing surgery [26].

Anticoagulation medications for treating cardiovascular conditions, such as heparin, warfarin, or clopidogrel, have also been associated with increased PJI risk [24, 27]. These therapies can interfere with wound healing by causing complications such as hematoma, excessive wound drainage, and bleeding that can further predispose patients to PJI [27]. These anticoagulation regimens are often monitored using laboratory tests, such as international normalized ratio (INR), prothrombin (PT) and partial thromboplastin time (PTT). Higher preoperative INR levels have been associated with PJI in TJA patients [28]. INR levels above 1.5 among TJA aseptic revision patients were 2-times more likely to develop PJI [27]. Therefore, it is recommended that preoperative screening should include INR levels that should be <= 2 prior to surgery [29]. Patients on anticoagulation therapy may need to be seen at thrombosis clinics for proper therapy management and standardization of INR levels. These patients should also stop anticoagulation medications before surgery to decrease their risk of increased bleeding, wound complications, and infection. Some patients with myocardial infarction or atrial fibrillation may be able to change anticoagulation regimens and use protocols that may lead to less hematoma formation [5].

Renal failure and dialysis

Renal system disease and renal failure patients are known to have greater surgical complications, such as infection, morbidity, and mortality after orthopaedic procedures [30, 31]. Multiple preoperative factors that predict the severity of renal disease progression can also highlight underlying, related comorbidities. Preoperative serum creatine level is an indicator of kidney problems and should be under 1.0 mg/dl [32]. The creatinine

clearance formula predicts renal clearance in patients that takes body mass index (BMI) and age into consideration while measuring 24-h creatinine excretion [33]. Hemoglobin and potassium levels should also be checked since these patients often have anemia or hyperkalemia. If this is the case, preoperative hemoglobin should be corrected to > 10 g/dL and potassium < 5 mEq/L. [26] consultation with providers multiple providers is especially important to preoperatively correct and monitor fluid management, antibiotics, urea, glucose, and electrolyte levels in patients who often display imbalances [34]. Coexisting risk factors should also be taken into consideration and treatment plans are devised since factors such as nutrition/diet and lifestyle activities can individually predispose patients to increased infection risk with amplifying effects.

Dialysis patients have an even greater risk of postoperative infection, as these patients have weakened immune systems that slow the healing process [35]. TKA patients on dialysis have increased mortality (5.8%), early complications (58%), and deep infections (13%) [36] while THA patients on hemodialysis have 1-year mortality rates of 6.3% and patients with prior renal transplant also have high rates of mortality at 4.4% [37]. Overall, dialysis can increase the risk of infection up to 4-times compared to patients not on dialysis [31]. If medically feasible, dialysis patients may benefit from renal transplant prior to TJA to reduce their risk of infection [38]. However, if a patient is unable to receive a kidney transplant, dialysis techniques can be changed to potentially improve surgical outcomes by using bicarbonate-based dialysate and other biocompatible dialyzers [39]. Furthermore, infection rates are lower with preoperative hemodialysis compared to peritoneal dialysis, which is linked to higher amounts of skin and enteric flora [40]. Thus, preoperative consultation with nephrologists is recommended to reduce the risk of postoperative infection after altered dialysis regimens [31].

Obesity

Obesity is another common modifiable risk factor for surgical infections, as almost 40% of the population is classified as obese with a body mass index (BMI) greater than or equal to 30 kg/m^2 [41]. Obese orthopaedic surgery patients have doubled risk of developing a SSI [42]. Particularly for PJI, a prospective multi-site study reported that obese TKA patients were 6.7 times more likely to sustain a PJI while obese THA patients had a 4.2 times higher risk for developing a PJI [43].

Furthermore, surgeons experience challenging technical approaches, longer operating time, and more tissue dissection when performing surgery in obese patients. These patients are faced with a larger incision, more blood loss, slower healing, and longer recovery time that can make them more vulnerable to developing an SSI [10], prosthetic loosening, and the need for future revision surgery [44]. The operative time increases by 1 min for every extra 1 kg/m^2 in body mass [45], which quickly accumulates for severely obese patients and put them in a very high infection risk. Postoperative outcomes are also jeopardized with increased pain and continued risk of osteoarthritis, as one pound of body weight equates to an extra four to six pounds of mechanical pressure on the knee joint [44].

The increased infection rates associated with obesity are also linked to the amount of adipose tissue which has higher bacterial counts [46]. Such characteristics of adpisoe tissue in obese patients are associated with altered surgical wound healing due to venous insufficiency [47, 48] and decreased vascularity [49], which lead to decreased oxygen supply to healing tissue and related oxidative stress [50], increased macrophage levels leading to acute inflammation [51], and other adverse healing effects. This is related to adipose tissue anatomy which can increase the amount of dead space in the wound and further delay healing [52]. Specifically, morbidly obese TKA patients (BMI < 40 kg/m^2) had increased wound healing complications (22%) compared to normal BMI patients (2%) due to this increased dead space [53].

Other studies assessing adipose tissue properties have shown a relationship with higher counts of CD8 (+) effector T cells in epididymal adipose tissue, yet less regulatory T cells and CD4 (+) helper cells in obese mice [54]. This pathophysiological relationship with these immune cells in adipose tissue shows their influence on inflammation and decreased immunity associated with obesity [46]. Additionally, in obese THA patients, there were increased levels of cytokine mediators including interleukin (IL)-1 beta, IL-6, and tumor necrosis factor (TNF)-α levels. This is correlated to an increased postoperative proinflammatory state for obese patients that can lead to increased pain and slower recovery [55]. The expression of these inflammatory factors in peripheral blood lymphocytes have been notably imbalanced with obesity.

Therefore, the procedural BMI cut-off for elective TJA for most surgeons is 40 kg/m^2 [56], while some surgeons may follow or are mandated to follow a cut-off of 35 kg/m^2. Preoperative obesity screening should be implemented at least 6 weeks prior to surgery in order to give obese patients enough time to lose weight and improve their lifestyle before surgery in a safe and healthy manner. These patients should also have their glucose levels and blood counts tested, nutritional levels checked, along with cardiac and renal function assessed [56]. Patient education should also be included in the visit to inform patients of complications associated with obesity and the importance of losing weight before surgery.

Providers may also refer patients to nutritionists and recommend exercise programs.

Diabetes mellitus and hyperglycemia

TJA patients with blood sugar abnormalities are also at an increased risk for postoperative infections and other complications. Since the surgical process alters eating patterns and increases stress, this affects the body's blood sugar response by increasing insulin resistance making diabetic and hyperglycemic patients especially vulnerable to adverse surgical outcomes [57].

Diabetes mellitus

Pooled data for arthroplasty patients with diabetes in the U.S. displayed a significantly higher risk for SSI development with an odds ratio of 1.26 after the data *plural* were adjusted for hyperglycemia and BMI [58]. The odds ratio for development of an SSI was 2.8 [59]–3.4 for orthopaedic surgery patients with a preoperative serum glucose level of > 125 mg/dL or a postoperative level of > 200 mg/dL [60]. It has also been reported that diabetic TJA patients with unmanaged diabetes have a 2.8 higher PJI risk than non-diabetic patients [61].

Higher infection rates can be related to the decreased production of cytokines and formation of new blood vessels found at the wound site that make diabetic individuals more vulnerable to infection [62]. Furthermore, diabetic patients often have concomitant comorbidities associated with their condition, such as atherosclerosis that decreases proper wound healing, neuropathy that can lead to further musculoskeletal trauma, and vitamin D deficiency that can weaken bone [63]. Arthroplasty patients with diabetes treated with insulin have also been shown to have higher rates of 30-day readmission [64], longer LOS, and other renal, respiratory, and cardiac complications [65]. Multiple approaches have been implemented for optimizing diabetic patient health, such as preoperative screening for HbA1c levels (less than 7, 7.7 and 8%) and implementing glucose management programs to maintain healthy glycemic values and control.

Hyperglycemia

In addition to diabetes, hyperglycemia increases infection rates due to its impact on the immune system and the healing process. This glycemic condition alters the role of leucocytes that can lead to an immunocompromised state and consequential deep tissue infection from surgery due to decreased innate immune function [66]. Since operating antagonizes insulin, surgery may predispose people to hyperglycemia which reduces the functional ability of leukocytes to fight infection [67, 68]. Arthroplasty patients who had hyperglycemic levels (> 137 mg/dL) the morning after surgery had an increased risk of developing PJI [69]. One study assessing primary TKA patients with perioperative glucose levels over 6.9 mmol/L displayed a 4-fold increase of PJI development compared to patients with normal glucose levels of < 6.1 mmol/L. [70] Accordingly, patients should have fasting blood sugar levels with or without the presence of ketones in their urine checked on the day of surgery [71]. Therefore, it is crucial for hyperglycemia to be managed before orthopedic surgery even though research is still exploring effective interventions in the perioperative and postoperative settings [57].

Diabetes and hyperglycemia intervention

Preoperative identification of diabetic and hyperglycemic patients allows for proper intervention to optimize health before proceeding to surgery, which can significantly decrease SSI/PJI risk. Standard glucose monitoring and patient management should be implemented to keep glucose levels < 200 mg/dL and HgbA1C < 7% [72], which includes integrative care from primary care providers, endocrinology, rheumatology, internal medicine, and nutritional counseling with other educational outreach. Depending on a patient's preoperative levels, surgeons will most likely suggest strict glycemic monitoring and control programs to help patients drop levels within the normal range; however, this can take some patients up to 6 months [73, 74]. Other alternative effective preoperative screening tools include glucose challenge tests (plasma or capillary glucose, GCTpl and GCTcap, respectively) and random plasma or capillary glucose (RPG or RCG respectively) [75]. Research has shown that GCTpl is the least expensive screening tool with subsequent effective screening results in high-risk patient populations [76]. The Medicare cost of using this screening tool over 3 years is $180,635 compared to the costs associated with no screening of $205,966 [75].

There have been successful outcomes with tight intraoperative glycemic control and the use of a basal bolus insulin regime that reduces rates of wound infection, bacterial counts, and acute respiratory and renal failure [77]. One study implementing an evidence-based approach to manage blood sugar in hyperglycemic patients effectively reduced SSI rates after THA and TKA [78]. Hyperglycemia and diabetes can also be treated with insulin after surgery, however, using a "sliding scale" with insulin correction is not routinely recommended as it can cause further complications and actually worsen hyperglycemia [57].

Anemia

Anemia is classified by the World Health Organization (WHO) as hemoglobin levels less than 13 g/dL in men and less than 12 g/dL in women [79]. Anemia is detected in as many as 35% of elective orthopaedic surgery patients [80] and leads to increased LOS, infection, and mortality [81]. Research has identified preoperative anemia as an

independent risk factor for PJI [82], as patients with low preoperative hemoglobin and hematocrit are more likely to receive transfusions and use anticoagulation medications that can also increase infection risk [3, 5, 83].

Patients with anemia should be referred to hematologists and other specialists to identify the cause of anemia in order to properly devise a treatment plan. Preoperative and intraoperative treatment has successfully reduced infection rates in anemic patients with the collaboration of surgeons, anesthesiologists, immunohaematologists, and other specialists [84]. Screening for anemia should be conducted around 30 days prior to surgery with blood work assessing complete blood count, iron (ferritin), vitamin B_{12} [85] and folic acid [86]. Causes may be malnutrition, chronic renal insufficiency, or chronic inflammatory disease [85]. For instance, if a patient is anemic due to low iron, physicians should not include administration of human erythropoietin (rHuEPO) because it will most likely lead to an adverse response to erythropoiesis and inhibit treatment [87].

For those with low iron contributing to their anemia, oral iron supplements (325 mg TID), vitamin B_{12} (1 mg), or folic acid (5 mg) taken 4 weeks before surgery can help improve patient's laboratory levels before surgery to decrease their risk of infection [86]. This inexpensive and simple approach is recommended for patients who do not urgently need surgery. If oral iron cannot be tolerated, such as in elderly patients, intravenous iron can be administered since it is faster-acting, safe, and has minimal side effects [84]. This treatment should work within 2–3 weeks to replenish iron levels and can raise hemoglobin levels by 1-3 g/dL after 1 month [88, 89]. Intravenous iron sucrose treatment has been proven especially beneficial in hip fracture patients which displayed less need for postoperative transfusions compared to patients without treatment [90]. Other intravenous iron formulations have also been effective in high doses with cost-effective benefits including ferric carboxymaltose, low molecular weight iron dextran, sodium ferric gluconate, or iron isomaltoside-1000 [84, 88]. If intravenous treatment does not result in normal hemoglobin levels within the expected time period, a dose of subcutaneous rHUEPO is advised [84].

Alternatively, preoperative erythropoietin helps to stimulate epoetin alpha (Epogen) which is a natural glycoprotein created by renal pericapillary cells in reaction to reduced oxygen tension, often found in conjunction with anemia or chronic obstructive pulmonary disease [91]. Epogen acts on bone marrow to stimulate red blood cell (RBC) differentiation and maturation, thereby increasing total RBC mass in anemic patients [91]. Its use has been approved by the Food and Drug Administration (FDA) in anemic patients with hemoglobin levels between 10 and 12 g/dL [92]. The use of erythropoietin is associated with decreased transfusion rates and consequently less PJI in TJA patients [93]. However, there are serious side effects with the administration of epoetin alpha, such as cardiovascular events, thromboembolic events, stroke, mortality, and tumor growth [94]. It is also expensive and can cost $3500 for a daily dose for 15 days and up to $2000 when administered weekly for 4 weeks [91]. Therefore, it is recommended that preoperative screening to identify the cause of anemia and eliciting respective alternative treatments should be considered before using Epogen.

The economic benefits of preoperative treatment for anemic patients undergoing elective orthopaedic surgery have revealed significant financial savings. Research assessing the economic costs associated with anemic orthopaedic surgery patients who followed preoperative treatment compared to those who did not reported a shortened LOS by 0.7 days and lower readmission rates by 5% that resulted in approximately $185,000 of savings [95]. Another large study was conducted by the Government of Ontario to assess the cost of implementing preoperative treatment programs for anemic patients undergoing cardiac and prostate surgeries, THA, and TKA. The programs costed $3 million to apply in practice, but healthcare savings reached $39 million with avoided surgical and postoperative complication costs [96]. Therefore, preoperative anemic screening with appropriate targeted treatment can significantly reduce SSI/PJI while also saving money.

Malnutrition

Malnutrition often coexists with anemia and is another independent predisposing risk factor for orthopaedic surgical infections [97]. As many as 50% of orthopaedic surgery patients are malnourished and it is often not identified or treated preoperatively, which can lead to further complications [98]. Malnourishment can lead to suppressed immune responses, apathy, cardiac and renal complications [99], sarcopenia, hematoma formation [100], and impaired wound healing [101]. This is due to depleted protein reserves and inhibited proteoglycan and collagen synthesis which reduces wound healing capacity [10]. These various complications are especially prevalent in patients over 55 years of age undergoing TJA that often have other comorbidities that contribute to increased infection rates [100].

Nutrition markers can be checked easily with routine preoperative blood tests at least 2 weeks before surgery to identify at-risk patients and determine which metabolic markers are abnormal. Laboratory blood tests that indicate malnourishment include the following: albumin < 3.5 g/dL, prealbumin < 18 mg/dL, total protein < 6.0 g/dL, total lymphocyte count < 1500 cells/mm^3, iron < 45 μg/dL, serum transferrin < 200 mg/dL, and 25-hydroxyvitamin D

(25OHD) < 30 ng/mL [102]. Low albumin levels in THA patients were directly correlated to a 6-fold increase in 30-day mortality and major morbidity [103]. Low transferrin levels are also known to be an independent correlated risk factor for surgical infections [104] and predictive of delayed wound healing in THA patients [105]. Lymphocyte counts are often used as a nutrition marker even though studies relating them to wound healing and infection rates in orthopaedic surgery are not conclusive. Some studies have shown that low preoperative total lymphocyte counts were not predictive of malnutrition in some patients [106] and may not contribute to orthopaedic surgery infection [107] while others have shown that they did correlate with SSI [108], deep infection, excessive wound drainage [109], protein deletion associated with bone mineral density [110], and immunosuppressive effects [10] making patients vulnerable to infection.

Other significant markers are low iron, vitamin D, and total protein levels. Decreased iron levels are predictive of anemia and reduced protein counts that inhibit wound repair and overall healing [10]. Vitamin D is important for bone and muscle health, calcium regulation, and control of immune responses [111]. Low preoperative serum 25-hydroxyvitamin D (25OHD) in primary arthroplasty patients correlate with PJI and aseptic joint loosening [112]. Other preoperative screening tests for malnutrition incorporate alternative factors, such as preoperative total lymphocyte counts, albumin, transferrin, skin antigen testing, arm circumference, and triceps skin fold metrics. The results of these tests have been positively correlated to malnutrition status in orthopaedic patients [107]. TJA patients who were screened for malnutrition used similar integrated anthropoetric metrics such as the triceps skinfold, arm and calf muscle circumference, while also using standardized nutritional measurement tools, such as the Rainey-MacDonald nutritional index and the Mini Nutritional Assessment [102].

Malnourished patients should be given nutritional supplements daily for at least 14 days prior to their surgery date [113]. Specifically, diabetic and geriatric patients will need supplements that are low in sugar with strict glucose control, but also high in protein, vitamins and minerals.

Smoking and alcohol use

Lifestyle factors including substance use, misuse and abuse further predispose TJA patients to increased SSI, morbidity, and mortality [114]. This is primarily due to their effects on wound healing and the introduction of foreign chemical materials into the body [115, 116]. These factors have detrimental physical and emotional or behavioral effects on patients who may be noncompliant to medical instructions and experience withdrawal effects resulting in other adverse outcomes [115]. Therefore, preoperative screening for lifestyle risk factors can help prevent infection development and may improve surgical outcomes.

Tobacco use

Approximately 15.5% of American adults still report daily cigarette smoking even though the prevalence has decreased from 2005 to 2015 [117]. However, there has been no significant decrease in this rate from 2015 to 2016 [117]. The prevalence of smokers among TJA patients is also alarmingly high [118]. Cigarette smoking and the use of other tobacco products are known to have serious adverse health effects linked to the presence of 4000 hazardous chemicals, such as carbon monoxide, cyanide, nicotine, and other carcinogenic polycyclic aromatic hydrocarbons (PAHs) [119]. The health complications associated with these chemicals have also been shown to interfere with bone healing leading to reduced bone cell metabolic activity mostly attributable to nicotine [120], along with inhibited collagen synthesis and vasoconstriction which prolongs healing time [121], leads to wound necrosis, and weakens immune responses directly leading to infection [122]. This has been related to a decreased inflammatory response due to reduced immune cell chemotactic responses, oxidative bactericidal processes, and migratory ability [123]. Consequently, patients who smoke before surgery have significantly more postoperative complications and infection-related loosening with greater rates of revision surgery [114, 118]. This has led to increased national medical costs by $170 billion [124] and prolonged LOS by 4 days [125].

The direct association between smoking and PJI and consequential aseptic prosthetic loosing is a major concern for arthroplasty surgeons. For THA patients who smoked preoperatively, 1.5% of patients developed PJI with an overall 2.71-fold increased risk of postoperative infection [126]. This increased infection risk was also noted in TKA patients who smoke preoperatively [127] in whom smoking attributed to a 10.4% increase in SSI when calculated with a population-attributable fraction [128]. The frequency and length of time of smoking are influential when assessing patients' infection and complication risk [129].

Another important factor which should be assessed when patients are seeking TJA is dental hygiene that is often negatively affected by tobacco use, alcohol consumption, and malnutrition. Tobacco use often results in poor dental hygiene that can influence infection risk after surgery [130]. Surgeons should make sure that patients do not have any ongoing dental infections or incomplete dental procedures before surgery and also do not present with decayed teeth, abscess, gingivitis, or periodontitis [72].

Since smoking is a modifiable risk factor, most researches suggest that smoking cessation programs should begin 6–8 weeks before surgery to effect changes [131], with a minimum time of 4 weeks [123, 132]. With a longer cessation period, postoperative complications are expected to decrease proportionally [133]. Orthopaedic surgery trauma patients following a 4 week smoking cessation program displayed reduced postoperative complication rates [129]. These patients displayed improved tissue oxygenation, inflammatory responses, and bone metabolism after smoking cessation for 4 weeks [123]. Some patients who may not follow such recommendations for an extended period of time can also abstain from smoking the day of surgery, which has shown less drastic but still significant reductions in SSI [134]. The most effective smoking cessation therapy programs have included a combination of weekly counseling sessions with a trained smoking cessation therapy nurse and nicotine replacement therapy at least 4 weeks preoperatively [135]. Other nicotine replacement therapies can include prescription medications such as buproprion SR (Zyban) or varenicline tartrate (Chantix), or over-the-counter products such as nasal sprays, nicotine patches, gum, and inhalers [136]. Smoking cessation can be verified with a simple serum cotinine test with a value ≤ 10 ng/dL [137], but it is important to note that even the use of nicotine patches will cause this test to be positive for nicotine.

This integrative approach has been proven to be cost-effective while also consequentially resulting in life-long health benefits if smoking is not continued postoperatively. More involved intensive therapy programs are cost-effective due to more significant net benefit with quality adjusted life year economic savings ranging from $1108-$4542 [138]. Patients who follow these programs and are persuaded to quit smoking preoperatively are at reduced risk for perioperative and postoperative complications that shortens their LOS and minimizes the need for additional surgery and treatment. Preoperative screening should include patient smoking history and the use of the Physician Quality Reporting System, which has been successful using physician-reported quality measures for Medicare [139] to reduce patient risk. Therefore, surgical patient optimization with preoperative screening, healthcare advising, and nicotine replacement treatment can significantly improve postoperative outcomes and reduce infection rates [140, 141].

Alcohol consumption

Another modifiable lifestyle factor that is harmful to patients undergoing TJA is alcohol consumption. Patients with diagnosed alcohol abuse undergoing TJA have increased immediate postoperative complications such as stroke, surgical infections, blood clots, delirium, pneumonia, arrhythmia, gastrointestinal bleeding, and shock [142] along with longer LOS, and behavioral issues in TJA patients [116]. Excessive alcohol consumption is associated with organ dysfunction, cardiac insufficiency, varied hemostatic function, and immunosuppression that can be exacerbated in patients under increased surgical stress [143].

Chronic alcohol use increases an individual's risk for additional medical problems due to its effect on the body. Long-term alcohol use predisposes patients to infection as it alters the immune system and T cell-mediated responses. Increased infection rates are further attributed to subdued cytotoxic lymphocyte ratio, inhibited interferon gamma:IL-10 ratio, and heightened levels of plasma IL-10 in alcoholics, suggesting overall suppression of whole blood cell responses [144]. Furthermore, among primary TJA patients, high alcohol consumption (> 168–252 g/week) was linked to a higher incidence of PJI at 1 year postoperatively compared to non-drinkers, low to moderate drinkers (> 0–168 g/week), or excessive drinkers (> 252 g/week) [145]. Excessive consumers displayed increased postoperative complications with deep venous thrombosis and increased 1 year mortality rates [145]. Researchers concluded that preoperative guidance and intervention for patients with low-to-moderate alcohol consumption can potentially be more lenient when suggesting abstinence, but preoperative abstinence should still be enforced for high and excessive drinkers [145].

Therefore, it is important to preoperatively screen every patient for a detailed alcohol history and quantify their usage and frequency. Screening measures used to identify at-risk patients include the Alcohol Use Disorders Identification Test (AUDIT-C), which is a self-reported questionnaire where each point on the 12-point scale attributed to alcohol consumption correlates to a 29% average increase in the number of surgical complications [142]. Healthcare professionals can also administer the Complications Evaluation Questionnaire (CEQ) to patients to assess the overall effects of alcohol and other lifestyle risk factors, such as tobacco [115]. Providers should also keep in mind that self-reported consumption levels can be underestimated and that alcohol abuse is defined as consuming at least 5 or more standard drinks per day [143].

Patients who follow professional alcohol cessation programs or cease alcohol intake have displayed improved reversal effects after abstinence. With alcohol cessation, organ dysfunction can be reversed over time and hemostasis can be improved within 4–8 weeks of alcohol abstinence [143]. After 3–4 weeks of abstinence, wound-healing capability is restored with significantly reduced postoperative morbidity and LOS [116]. Furthermore, within 1–2 months, cardiac and immune function can normalize, and external stress responses can be reduced

after 3 months of alcohol cessation. This intervention should be multi-disciplinary and include counseling sessions, motivational health dialogue [143], pharmacological mediation, relapse prophylaxis with frequent follow-up, and medications if needed for withdrawal or alcohol substitution [146]. Such products that can be used include benzodiazepines for withdrawal [147], acamprosate [148], and opioid antagonists [149] for dependence, or disulfiram for short-term cessation [150].

Such an integrative preoperative approach for patients at risk can reduce postoperative complications and medical costs. Programs incorporating preoperative screening and counseling for patients have been proven cost-effective with medical savings around $1755 per quality adjusted life year [151]. These screening programs are important to identify preoperative alcohol misuse in TJA patients so that providers can intervene to implement effective multi-modal cessation programs to reduce infections and complications.

Depression and anxiety

Lifestyle factors such as malnutrition, overeating, tobacco use, and alcohol consumption can be associated with altered emotional states and psychological conditions. Depression is a strong predictor of postoperative pain tolerance as it has been linked to decreased pain tolerance and increased postoperative infection and mortality [22, 152]. TKA patients with preoperative anxiety and/or depression were 6 times more likely to report dissatisfaction with long-term postoperative outcomes and had a longer LOS by 1 day compared to patients without either form of psychological distress [153]. Anxiety and depression often coexist and are both risk factors for TJA complications [154, 155], such as PJI [22, 156], due to the impact on the body's immune response [157].

These adverse effects and increased infection rates can be explained by immunosuppression caused by depression leading to unregulated immune activation from inhibited T-cell activity [158] and affected serotonin pathways [152]. Genes in this pathway have been found with single nucleotide polymorphisms (SNPs) associated with depressive symptoms and unbalanced immune function linked to suppressed immunity and postoperative infections [152]. This condition leads to altered neurotrophic factor circulation and leukocyte responses [159]. Furthermore, a relationship between depression and inflammatory responses has also been identified. Also, higher levels of allelic variants have been expressed in depressed patients [160]. The etiology of depression has been linked to the expression of genes involving inflammatory molecules and enzymes. For instance, cytokines and enzymes involved in mediating the inflammatory response (cyclo-oxygenase2 [COX-2] and phospholipase2 [PLA2]) have been detected in depressed patients [152]. Other genetic variants are also associated with the biological mechanisms where depression develops from an altered innate immune system. This is linked to gene expression of IL-1β, TNF-α, C-reactive protein (CRP) and SNPs in the IL-1β, IL-6 and IL-11 genes that contribute to reduced efficacy of anti-depressant therapy [160]. Such altercations may prompt physicians and researchers to preoperatively detect these genetic variants in patients to assess their risk level. Due to these serious effects of depression presenting with altered immunomodulary responses that may lead to increased surgical complications and infection, depression and anxiety screening should be a routine part of preoperative assessments.

Screening for these emotional conditions is simple and can be conducted in clinics in a short amount of time. Common screening tools for depression and anxiety are the Patient Health Questionnaire-2 and -9 [152], the Hospital Anxiety and Depression Scale, and Beck's Depression Inventory [161]. Preoperative screening and identification for the stage of depression is important because patients can also develop depression after surgery. Those with a history of preoperative depression are at a higher risk to relapse after surgery. The development of postoperative depression may be higher in orthopaedic surgery patients compared to other surgical specialties and can occur as soon as 2 days after surgery [162]. Preoperative evaluation and screening protocols should integrate and advise treatment from a psychologist or psychiatrist while specifically reviewing realistic patient expectations to avoid postoperative depression during recovery. Screening should also pay attention to the common comorbidities and lifestyle activities mentioned previously that often exist with depression and anxiety. Providers and counselors need to be patient with treatment and intervention outcomes, since most approaches for depression often fail or take a long time to produce positive results [152]. Preoperative screening and discussion with patients undergoing arthroplasty may reduce postoperative complications and PJI rates after appropriate intervention and therapy programs.

Conclusion

In conclusion, all patients undergoing TJA are at risk for infection and complications, however, various predisposing modifiable risk factors have been identified that significantly increase SSI/PJI risk development. Medical comorbidities and lifestyle factors that independently increase one's risk for SSI and/or PJI are MSSA/MRSA colonization, rheumatoid arthritis, cardiovascular and renal diseases, obesity, diabetes mellitus, hyperglycemia, anemia, malnutrition, tobacco use, alcohol consumption, depression, and anxiety. Comprehensive education and intervention are crucial to the optimization of TJA patients prior to surgery, as one study revealed that 80% of TJA cases had at least one modifiable risk factor present,

with 46% of patients being obese, 29% anemic, 26% malnourished, and 20% diabetic [2]. Patients who were candidates for revision arthroplasty also require critical surveillance since researchers also reported that 93% of these patients had at least one modifiable risk factor present with anemia, urinary tract infection, and human immunodeficiency virus (HIV) being the most prevalent in this group, respectively [2]. Therefore, these reports support the need for preoperative patient screening to identify these risk factors before TJA along with the establishment of multi-disciplinary relationships with orthopaedic surgeons and respective care teams to improve patient outcomes. The resulting impact of implementing these preoperative protocols with widespread diligence and awareness may improve TJA infection prevention while providing satisfying patient care and surgical outcomes.

Abbreviations

25OHD: 25-hydroxyvitamin D; AUDIT-C: Alcohol use disorders identification test; BMI: Body Mass Index; CEQ: Complications Evaluation Questionnaire; COX-2: Cyclo-oxygenase-2; CRP: C-reactive protein; DMARDs: Disease modifying antirheumatic drugs; Epogen: Epoetin alpha; FDA: Food and Drug Administration; GCTcap: Capillary glucose; GCTpl: Plasma glucose; HIV: Human immunodeficiency virus; IL: Interleukin; INR: International normalized ratio; LOS: Length of stay; MRSA: Methicillin resistant *Staphylococcus aureus*; MSSA: Methicillin sensitive *Staphylococcus aureus*; PAHs: Polycyclic aromatic hydrocarbons; PJI: Periprosthetic joint infection; PLA2: Phospholipase 2; PT: Prothrombin; PTT: Partial thromboplastin time; RBC: Red blood cell; RCG: Random capillary glucose; rHuEPO: Human erythropoietin; RPG: Random plasma glucose; SNPs: Single nucleotide polymorphisms; SSI: Surgical site infection; THA: Total hip arthroplasty; TJA: Total joint arthroplasty; TKA: Total knee arthroplasty; TNF: Tumor necrosis factor; WHO: World Health Organization

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