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Effect of Glycemic Control on Infection in Post Total Joint Replacements in the Diabetic  
Patient

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## PERMISSION

Title Effects of Glycemic Control on Infection in Post Total Joint Replacements in Diabetic Patients

Department Nursing

Degree Master of Science

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### **Abstract**

Total hip arthroplasty (THA) and total knee arthroplasty (TKA) are among the fastest growing and most expensive procedures in the United States. While these surgeries are considered comparatively safe, surgical site infections and especially prosthetic joint infections (PJI) are serious complications of THA and TKA. Post-operative joint infections are challenging to treat and manage along with being costly. These infections are becoming more prevalent due to an increase in prosthetic joints, an aging population and the prevalence of diabetes. Diabetes Mellitus has been considered a recognized hazard for surgical site infections after various surgical procedures. Diabetes can impede the body's capacity to recover from illness or injuries. In the case study presented a Type I diabetic patient is obtaining a preoperative history and physical for an upcoming total knee arthroplasty A literature review was conducted to evaluate the effects of glucose control in diabetic patients on post-operative total joint arthroplasty surgical site infections.

## Background

Almost 1 million total hip arthroplasty (THA) and total knee arthroplasty (TKA) procedures are performed each year in the United States with projections of more than four million of these procedures being done annually by the year 2030. The rate of prosthetic joint infection (PJI) in most institutions is 0.5 to 1.0 percent for THA and 0.5 to 2.0 percent for TKA (Beribari and Baddour, 2015). The risk of (PJI) is uncommon but when it transpires there is substantial morbidity and even with the appropriate treatment prognosis can be poor. Signs and symptoms of prosthetic joint infection may include pain, erythema, fever, swelling, and sinus tract formation. Synovial fluid aspiration is the best diagnosis modality. Treatment may include medical and/or surgical debridement or removal of the prosthesis. The highest number of THA and TKA is in those age 65 and older, but adults aged 40 to 60 are the fastest growing age group that these procedures are being performed on in the United States. Patient related risk factors for PJI include rheumatoid arthritis, diabetes type I and II, obesity, immunosuppressive therapy, smoking, and prior PJI. Risk factors that are modifiable include diabetes, obesity, and the use of immunosuppressive therapy. Prevention stratagems targeting these risk factors may decrease the incidence of PJI. These strategies include preoperative glucose monitoring and control in diabetic patients, decreasing the use of immunosuppressive drugs if able, and perioperative antibiotic therapy for obese patients (Shuman, 2013).

The Centers for Disease Control and Prevention, 2015 reports 29.1 million Americans have diabetes or 9.3% of the U.S. population. Of the 29.1 million, 21 million are diagnosed and 8.1 million are undiagnosed. Diabetes mellitus (DM) is a syndrome of

hyperglycemia, it includes Type I DM and Type II DM. Type I results from beta cell destruction leading to a total deficiency of insulin. The etiology can be related to hereditary factors or environmental factors such as viral infection such as the Coxsackie virus or mumps virus. Type II DM results from insulin resistance along with a defect in insulin secretion. The etiology can be hereditary or environmental. Environmental factors include obesity, a high carbohydrate diet, and/or sedentary lifestyle. DM can also be secondary to other disease factors such as pancreatic disease, hormone excess, medications such as glucocorticoids, and gestational diabetes. Infections are common in the individual with diabetes secondary to decreased tissue perfusion from vascular disease and impaired leukocyte function (Ferri, 2016). The burden of PJI in those patients with diabetes mellitus is expected to increase as the occurrence of DM continues to rise. It is projected that 27% of the U.S. population older than age 65 have been diagnosed with DM and 8-22% of arthroplasty patients have a diagnosis of DM. The rate of PJI is nearly three to five times higher in diabetics than in the overall total joint arthroplasty population (Chrastil et al., 2015). Numerous studies have been conducted to postulate if glycemic control plays a part in PJI. The following literature review summarizes study results using preoperative and/or perioperative glycemic indexes to project PJI risk and reduce the occurrence of PJI. Few studies have shown that preoperative HbA1c levels are good markers of the risk of postoperative PJI, while numerous studies have reported that hyperglycemia postoperatively is reliable predictor of postoperative PJI.

### **Case Report**

Mr. J. a 56-year-old Caucasian male was seen in the clinic for a preoperative history and physical needed for surgical clearance. He is scheduled for a total right knee

replacement in three weeks. His history of present illness is osteoarthritis of bilateral knees, he has continuous aching pain in the right knee that is concentrated in the right anterior and lateral knee area. He relates the pain does not radiate but intensifies when walking and is tolerable but he is ready for relief with surgery. He recently had a left total knee replacement done two months on Dec. 21, 2015 with no major complications by Dr. G. at Altru Medical Center. He did have nausea 24 hours post-operatively. He did not feel it was secondary to narcotic analgesics as he had the nausea prior to taking analgesics. Otherwise his recovery was without complications. Mr. J has a history of what he describes as brittle diabetes mellitus. He wears an insulin pump and relates his glucoses run between 100 and 160 consistently.

Mr. J works full time as a building contractor. He is married and continues to smoke one pack of cigarettes per day for the last 30 years. He drinks two beers per day and denies binge drinking. His family history includes his father who died at age 69 of a myocardial infarction and a brother who died at age 78 of a stroke. His mother is alive with no major health issues that he is aware of.

His past medical history is Type I diabetes, hypertension, hyperlipidemia, and osteoarthritis. His past surgical history includes bilateral wrist carpal tunnel repair, bilateral inguinal hernia repair, appendectomy, right knee arthroscopy for MCL tear, and as previous mentioned left total knee replacement in Dec. 2015.

His current medications are losartan 100mg daily, Novolog per insulin pump, simvastatin 80mg daily, and aspirin 81 mg daily. He has no known drug allergies.

His review of systems: Constitutional: denies fever or chills, denies weight loss. Denies head injury, retinopathy, hearing loss, dentures loose teeth, or any removable

appliance from his mouth. He denies any history of lung disease, dyspnea or cough, no history of heart disease and relates had a normal stress test two years ago. He denies abdominal pain, reflux, or heart burn. No history of urination difficulties, no dysuria or burning, although relates at times he urinates frequently. No history of anemia or gastrointestinal bleeding. Admits to osteoarthritis of right knee. Admits to continual aching pain of his right knee with activity although says is tolerable. Denies any history of a bleeding disorder.

The physical examination revealed a blood pressure of 158/94, temperature of 98.8° F, pulse of 76 and respiratory rate of 20. The head is normocephalic, good dentition, no loose teeth noted, nor oral lesions. The trachea is midline. Respirations are easy and non-labored with symmetrical thoracic expansion and clear lungs throughout all fields. The heart tones are moderate and regular with S1 and S2 present, no murmurs or S3 or S4. No jugular vein distention noted nor peripheral edema. Crepitus palpable in the right knee with 4/5 ROM. The patient is alert and oriented times four, his mood is appropriate and speech is fluent and forthright. Laboratory results revealed the RBCs to be low at 3.0 and hematocrit low at 34.5, the rest of the complete blood count was normal. The comprehensive medical panel was normal, of note the glucose was 96 and potassium level normal at 3.9. The EKG revealed normal sinus rhythm with no evidence of previous myocardial infarction. Centered on his history, physical, laboratory and EKG results the patient's diagnosis is Type I Diabetes mellitus managed per endocrinology, hypertension (currently elevated), osteoarthritis of the right knee, and tobacco abuse. A discussion was held with the patient regarding the elevated blood pressure reading, he relates he checks it twice a week at home and it typically runs around 130/80. The patient



is to check his BP daily at home for one week and then return to the clinic with his readings and the BP will be rechecked. In regards to the slightly low RBC and hematocrit the patient is to take ferrous sulfate 324mg twice daily on an empty stomach but if stomach upset occurs is to take with food. A lengthy discussion was held regarding tobacco effects on the body, including lung and bladder cancer, COPD, increased incidence of heart disease with combination of diabetes and smoking. He is agreeable to try a nicotine patch and will pick some up at the pharmacy. Encouragement was given for success. Addressed the need to abstain from smoking and alcohol use for a minimum of seven days prior to surgery or more if recommended by his surgeon.

In summary the patient is stable for right total knee arthroplasty scheduled for Feb. 29, 2016 if his blood pressure readings are less than 140/90, which I suspect they will. Mr. J did have post-operative nausea for 24 hours after his left total knee arthroplasty. I question if it was anesthesia related and patient is to discuss with anesthesia the day of surgery, he otherwise is low risk for complications based on above and his current reported stable glucose readings while on insulin pump.

### **Literature Review**

The patient in this case study is a Type I diabetic planning to have a total knee arthroplasty. Diabetes is known to play a role in surgical site infections. A literature review was conducted to determine if glycemic control preoperatively and/or perioperative plays a role in decreasing prosthetic joint infection. A literature search was conducted using the University of North Dakota's Harley French Library website to find knee replacement, hemoglobin A1C, and total joint replacement infections. Three search databases were utilized, PubMed, CINAHL, and SCOPUS.

The first search engine used was PubMed utilizing Medical subject headings, (MESH) using key words of *total joint replacement* further defined as *arthroplasty replacement/adverse events, diabetes, and infection*. After limiting the publishing date to eight years and the English language 20 articles were produced. After a review of the articles, five were considered pertinent to the subject. Another search in PubMed used the key words of *total joint replacement* further defined as *arthroplasty, replacement, diabetes, and infection* produced another 21 articles with one article deemed pertinent to the subject. The next MESH search used the key words of *total joint replacement* further defined as *arthroplasty replacement, infection, and diabetes mellitus*. This search produced 42 articles one of which was deemed pertinent to the subject. The next search engine used was CINAHL using the key words *total joint replacement, diabetes, and complications*. This search produced 26 articles, after careful review one new article was pertinent for the subject. The next search engine utilized was SCOPUS the search terms used were *hemoglobin A1C, total joint replacement, and infection*. After refining the search to the last eight years, medicine and articles a total of 31 articles were produced. After review of these articles four were deemed pertinent to the subject. A total of 11 articles were utilized for the literature search.

Nearly one million total hip and total knee arthroplasties are performed each year in the United States. It is projected that by the year 2030 four million will be performed annually in the U.S. The rate of prosthetic joint infection is nearly three to five times higher in diabetics than in the overall total joint arthroplasty population (Chrastil et al., 2015). Numerous studies have been conducted to determine the relationship of glycemic markers most strongly connected with the occurrence of surgical site infection in known

diabetic patients undergoing TKA and THA. Glycemic markers include hemoglobin A1C (HbA1c), fasting blood glucose, two-hour post prandial blood glucose readings, and random glucose readings. HbA1c is a glycosylate or glycated hemoglobin and provides a serologic marker for average systemic glucose concentration for the previous one to three months before measurement (Iorio et al., 2012).

Data from the majority of the studies conclude that the preoperative HbA1c is not an accurate predictive marker for postoperative total joint arthroplasty site infection. Most literature has shown that hyperglycemia with obesity are strong predictors of site infection post total joint arthroplasty.

### **Utilization of HbA1c as markers of diabetic control in predicting surgical site infection**

In the first retrospective study reviewed the authors defined diabetics with HbA1c levels less than 7% as controlled diabetes, and higher than 8% as uncontrolled diabetes. This study reviewed diabetic patients who had TKR and showed that a preoperative fasting blood glucose level >200 mg/dl and a HbA1c of 8% or higher were markers associated with superficial surgical site infections as compared to those patients with HbA1c less than 8% or fasting blood glucose less than 200mg/dl (Hwang, Kim, Bamne, Na, & Kim, 2015). Similarly, a second study by Han & Kang (2013) showed that preoperative HbA1c levels greater than 8% were associated with a significantly increased chance of postoperative wound complications after TKR. Both of these studies suggest tight control of glucose levels in the perioperative setting were correlated with decreased morbidity in the diabetic and nondiabetic patients. A third retrospective cohort study of 6088 diabetic patients from Veteran Association Hospital that underwent either a THR or

TKR showed a preoperative HbA1c of 7% or higher increased the odds by 22% of having at least one postoperative complication. Postoperative complications include superficial wound infection, deep wound infection, stroke, and urinary tract infection. The study showed no significance for superficial wound infection (0.9%) or deep wound infection (0.6%) in patients with an HbA1c of 7% or higher (Harris, Bowe, Gupta, Ellerbe, & Giori, 2013). In contrast to Han et al (2013), this study showed while there is an overall increased risk of complications post THR and TKR, the risk of infection with a preoperative HbA1c of 7% or higher was not significant. The authors suggested that surgeons should target the candidates who are at greater risk and that may benefit from preoperative attempts to reduce risk factors associated with HbA1c levels greater than 7%.

While diabetic patients are known to have an increased incidence of surgical interventions than nondiabetic patients, they also are at increased risk of surgical complications and increased length of hospital stay. Surgery can disturb the management of diabetes mellitus which can result in hyperglycemia in the post-operative period. In the fourth study reviewed, Iorio et al. (2012) concluded that there was no statistical significance discovered when comparing the well-controlled and poorly controlled HbA1c levels to predict infection after TKA. The study did show an increased likelihood of infection with TKA in diabetic patients than in the patients without diabetes but did not show that HbA1c levels are predictive of PJI. This is in conflict with the results that Han et al. (2013) and Hwang et al. (2015) produced reporting associated uncontrolled diabetes as evidenced by HbA1c levels greater than 8% are predictive of PJI. While Harris et al. (2013) noted an increased risk of infection according to HbA1c it was not of

significance. A fifth retrospective study by Stryker et al., (2013) noted a significant association between an HbA1c of 6.7% and higher with an increased risk of wound complications. The wound complications were not specific to infection and included hematomas, delayed healing or drainage, superficial infection, superficial necrosis and dehiscence. The sixth retrospective study using a cohort of 20,171 total hip and knee arthroplasty procedures again showed no association between HbA1c and PJI but did show a significantly higher risk of PJIs among diabetic patients using diabetic medications and patients with perioperative hyperglycemia. The results were attenuated after adjusting for body mass index and surgery type of THA or TKA, American Society of Anesthesiologist (ASA) score, and operative time, noting that obesity and hyperglycemia together increase the risk for PJI (Kremers et al., 2014). The majority of these studies reflect that preoperative HbA1c levels are not strong predictors of postoperative PJI.

### **Preoperative hyperglycemia and prediction of perioperative joint infection**

A large number of patients who have TKR are obese and obesity is associated with abnormal glucose metabolism which may progress in time to a diagnosis of diabetes. Diabetes and related hyperglycemia is associated with an increased rate of infection in knee arthroplasty. A retrospective study by Jansen, Nevalainen, Kalliovalkama, & Moilanen (2010) evaluated the effect of preoperative blood glucose levels on PJI. The results revealed higher postoperative infection rates with TKR in patients who had hyperglycemia in the preoperative screening. In those with a blood glucose of less than 110 mg/dl the infection rate during the one-year follow-up was 0.44%, glucoses of 110-125mg/dl the infection rate was 0.93%, and greater than or equal to 126mg/dl was 2.42%.

Like Kremers et al. (2014) it was also noted that obesity increased the rate of infected TKRs. The authors felt that hyperglycemia increases the risk of infection in both patients with diabetes and those without diabetes, but the risk is still somewhat unclear and they are suggesting that further studies are needed to confirm this hypothesis.

### **Relationship of postoperative hyperglycemia and TJA infections**

A large study using 13,272 diabetic patients from 153 Veteran Administration Hospitals showed there were no differences in the rate of PJI in the well-controlled diabetic patients (HbA1c less than 7%) compared to the poorly-controlled diabetic patients (HbA1c of 7% or greater). An increased mortality risk was noted within the first two years postoperatively in patients with an HbA1c of 7% or greater. Preoperative glucose levels correlated with significantly enhanced risk of developing PJI with an optimal cut-off glucose level of 194 mg/dl or greater. Also a modest increase in risk was noted when looking at the postoperative maximum blood glucose and averaging the patient's perioperative blood glucoses. Additionally, preoperative glucose levels of 194mg/dl or greater was associated with an increased risk of death (Chrastil et al., 2015). Similarly, a small study of 30 diabetic patients reported a significant risk for developing wound complications in patients with a mean postoperative blood glucose of greater than 200mg/dl and a maximum postoperative glucose of greater than 260mg/dl (Stryker et al., 2013). A retrospective study conducted in Spain of diabetic and nondiabetic patients showed similar results in that hyperglycemia in the immediate postoperative period showed a significant association between blood glucose levels drawn the day after surgery that were greater than 126mg/dl and infection. Infection included urinary tract infection, superficial wound infection, phlebitis, sepsis or prosthetic infection. Of note all

patients received infection prophylaxis with an intravenous antibiotic before and after surgery. This study showed no association between preoperative and intraoperative blood glucose results and infection (Reategui et al., 2015).

### **Controlled DM, uncontrolled DM, and no DM association to PJI**

A retrospective review study comparing patients with controlled DM, uncontrolled DM, and those with no diagnosis of DM showed that compared with patients with controlled DM, patients with uncontrolled DM had a significantly increased odds ratio of wound infection post THA and TKA. Patients with controlled diabetes showed no difference in wound infection as compared to those without diabetes. This was a large study with 920,555 nondiabetic patients, 105,485 patients with controlled DM, and 3973 patients with uncontrolled DM. Of note all patients with diabetes had significantly increased postoperative hospital charges adjusted for inflation, when compared to nondiabetic patients (Marchant, Viens, Cook, Vail, & Bolognesi, 2009). A comparable study but with a smaller sample size of 40,491 compared controlled DM, uncontrolled DM, and no DM wound infection rate and found no clear associations between poor glycemic control and wound infection. This study differed from Marchant et al. (2009) in that they had fewer patients classified as uncontrolled diabetics and the way that they defined poor glycemic control differed from Marchant et al. (2009). Marchant et al. (2009) defined poor control using an algorithm that was only based on ICD-9 codes. Adams et al. (2013) used both ICD-9 codes and laboratory based criteria to determine the diabetic status. All in all, they could not demonstrate that patients with uncontrolled DM had a higher risk of deep wound infection (Adams et al., 2013).

In summary of the 11 studies all but Hwang et al. (2015) had body mass index measurements greater than 30 which is considered obese. As previously described obesity and diabetes together are associated with increased risk of any infection. Six of the studies compared HbA1c levels to infection and only two of the studies had significant association with an elevated HbA1c and PJI, the other four studies did not show a significant association. Six of the 11 studies showed a significant risk of PJI in patients with hyperglycemia.

In summary, few studies have shown that preoperative HbA1c levels are good markers of the risk of postoperative PJI, while numerous studies have reported that hyperglycemia postoperatively is reliable predictor of postoperative PJI. Obesity and diabetes together are also associated with increased risk.

### **Learning Points**

- Fasting blood glucose greater than or equal to 200 could be used as a reference in recommending surgery or used to determine the timing of surgery for total joint arthroplasty to allow for optimization of glucose control prior to the procedure
- Hyperglycemia in the postoperative period is associated with a higher risk of PJI post total joint arthroplasty
- Obesity along with hyperglycemia is associated with a higher risk of PJI post total joint arthroplasty.
- The majority of retrospective studies have shown that preoperative HbA1c readings are not effective risk markers for predicting PJIs



- All the reviewed studies were retrospective cohort studies; no randomized control trials were found in the literature search. Randomized control trials would be beneficial and have a higher strength of recommendation taxonomy

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