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Kristina Gresh

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Hyperglycemia and Total Knee Arthroplasty Healing

Kristina Gresh, BSN, RN

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Title Hyperglycemia and Total Knee Arthroplasty Healing

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Abstract

Diabetes is a common medical issue affecting 30.3 million Americans with about 10.7 million people being between the ages of 45 and 64 (CDC, 2017). Uncontrolled diabetes can lead to major health complications including heart disease, stroke, neuropathy, nephropathy, retinopathy, increased infection risk and hearing problems (Mayo Clinic, 2018). Patients with a diagnosis of diabetes who are undergoing complex orthopedic surgery, such as a total knee replacement, require more pre- and postop planning to optimize their healing and recovery from surgery. Patient S is a 63 year old female who presented to the clinic for a routine preoperative appointment for a total left knee replacement. She has a history of smoking, nightly alcohol use, type 2 diabetes (T2DM), hypertension and hyperlipidemia. After a thorough review of the literature using both CINAHL and PubMed databases, 425 articles were initially identified. English language, five to eight years old or less, and peer reviewed were used as limitations. This reduced the related articles to 102. Upon further review, 10 were identified as relevant for this review. Based on the findings in the articles reviewed, recommendations regarding the care of a diabetic patient before and after total knee arthroscopy were identified to reduce postoperative complications and optimize healing time. These recommendations provide a road map for the provider to help the patient to achieve the best possible healing and recovery from their surgery possible.

Keywords: Diabetes, total knee replacement, hyperglycemia, glycemic control, total knee arthroscopy, diabetes and wound healing

Hyperglycemia and Total Knee Arthroscopy Healing

Background

Diabetic patients face higher surgical risks than those without diabetes who plan for elective surgeries. Patient S presented to the clinic for a routine preoperative examination for a left total knee arthroplasty. She is 63 years old and has a medical history including hypertension, T2DM, arthritis and hyperlipidemia. She plans to have an elective left total knee replacement sometime in the next two weeks.

According to Yang et al. (2014) hyperglycemia affects wound healing by delaying the synthesis of collagen as well as impairing the bones ability to produce osteoclasts for healing. Delayed healing coupled with the higher risk of surgical site infection, pneumonia, blood transfusions and blood clots makes total knee arthroplasty in diabetic patients more complicated (Akiboye & Rayman, 2017). Delayed healing time can affect all aspects of a patients' life including, but not limited to, their mental, physical and emotional health. It can lead to loss of income due to not being able to work as well as have a long and lasting effect on their overall health and wellness.

Glycemic control after total knee arthroplasty has demonstrated a reduced risk of surgical site infections (Akiboye & Rayman, 2017). Research has shown in general surgery, controlling hyperglycemia with a basal bolus regimen was linked to a lower incidence of pneumonia, wound infection, bacteremia, respiratory failure and acute renal failure (Akiboye & Rayman, 2017). In the postoperative period, it is recommended for medical professionals to test diabetic patients' blood glucose levels four times per day and treat any blood glucose reading higher than 216 mg/dl (Akiboye & Rayman, 2017). Blood supply is a critical component for proper functionality and healing of bone tissue, providing oxygen, nutrients and minerals

essential in bone regeneration (Marin, Luyten, Van der Schueren, Kerckhofs & Vandamme, 2018). Hyperglycemia can inhibit these critical steps in bone and surgical healing due to damage of the vessel wall, reduced blood flow and inhibition of the immune response.

Case Report

Patient S presented to the clinic for a preoperative clearance for a left total knee replacement surgery. She does not currently have a surgery date but is hopeful to have it done sometime in the next two weeks. She has no history of injury to her left knee but reported she has significant arthritis. She has never tried a joint injection or done any physical therapy for her knee pain. She occasionally will take acetaminophen or ibuprofen for her knee pain but states it does not help very much. She has tried ice and heat in the past with short term relief of her pain. She does not take any prescription pain medications. After evaluation by an orthopedic surgeon, she has decided it is time for a left knee arthroplasty. She works at a bank and does mostly sit throughout the day. She is married and smokes a half pack per day (ppd) as well as drinks two glasses of wine each night. She is interested in quitting smoking and a discussion about options she has for that were reviewed. She plans to start by calling the North Dakota Quit Line for assistance with patches. She has tried a few times to quit in the past but is more motivated at this time due to her upcoming surgery.

Past medical history for Patient S included hypertension, hyperlipidemia, arthritis and T2DM. For medication, she takes 10mg of lisinopril daily, 1000mg of metformin twice daily, 20 mg of simvastatin and 81mg of aspirin daily. She reported taking her medications every day as prescribed. She did not regularly check her blood sugars as she felt they were controlled by her medications. She denied any recent episodes or history of hypoglycemia. Family medical history is unremarkable.

Upon physical examination of Patient S, she was alert, oriented and answered questions appropriately. Her vital signs were as follows: blood pressure 142/92, heart rate 78, respiratory rate 24 and oral temperature 98.6. She denied any recent illnesses, fever, chills, night sweats, nausea or vomiting. Her ears, nose and throat examination were unremarkable. Lung sounds were clear, heart rate regular and she denied any shortness of breath, chest pain, dizziness or lower extremity edema. Bowel sounds were audible and she denied any abdominal pain, constipation or diarrhea. Upon inspection of her left knee, she had no obvious deformity, redness, bruising, crepitus or swelling. Her left knee was tender to palpation, with passive range of motion and with normal activity that is worse at the end of the day and keeps her up sometimes at night. She is able to ambulate without assistance of a cane or walker but reports the pain has limited her physical activity.

After her examination, a CBC was ordered for a baseline hemoglobin and hematocrit due to the potential for blood loss during the surgery. A CMP was also ordered to check her electrolytes, kidney and liver function. Due to her age, her history of hypertension, hyperlipidemia, type 2 diabetes, smoking and daily alcohol use, an EKG was also ordered to rule out any rhythm abnormality. All studies came back within normal limits. A recommendation was made for her to go ahead with her surgery as planned with acknowledgement of the risks of surgery due to her age, health history, history of daily smoking and alcohol use.

Literature Review

To better understand the physical obstacles a diabetic patient's body faces in healing after a total knee arthroscopy, one must look at the physiologic differences in bone and vascular health of diabetic patients. When providers understand the physiologic differences, they can help optimize healing for diabetic patients postoperatively. T2DM is very common and is predicted

to be the seventh leading cause of death by 2030 (Marin et al., 2018). In T2DM, hyperglycemia occurs due to insulin resistance caused by islet b-cell dysfunction in the pancreas (Marin et al., 2018). Increased blood sugars cause damage to the vasculature walls and can lead to the inhibition of delivery of oxygen, nutrients, and osteoprogenitor cells to the repair sites needed for healing (Marin et al., 2018). The exact effect of T2DM on the physiology of bone cell regeneration, osteoclast and osteoblast activity, is not fully known. However, their functionality and healing properties are observed to be slowed (Marin et al., 2018). At the microscopic level, it has been identified that osteoblasts are differentiated to a more adipogenic lineage in T2DM patients following a bone fracture or surgical repair and causes more fat tissue in the bone regrowth that slows healing (Marin et al., 2018). Studies have also shown that hyperglycemia can delay the synthesis of collagen, therefore delaying wound healing (Yang, et al., 2014). High glucose levels interfere with protein function, impair endothelial cell function, inhibit nitric oxide production and suppress normal immune function (Engoren, Schwann & Habib, 2014). If Patient S does not have good control of her blood sugar levels before and after her total knee arthroscopy, she is at a higher risk of delayed healing due to dysfunction at the cellular level in her healing properties and immune response.

Ackinzi et al. (2014) performed a study looking at the wound fluid in patients with and without hyperglycemia. They wanted to see what elements were missing for proper wound healing in patients with hyperglycemia to better identify why wounds of those patients had delayed healing. Ackinzi et al. (2014) reported that wound healing occurs in several stages with neutrophils and macrophages as the key elements in the inflammatory stage. They in turn produce pro-inflammatory cytokines TNF-a and IL-1B which attract fibroblasts and epithelial cells to the wound or incision site for healing (Ackinzi et al., 2014). In patients with diabetes,

they found that these pro-inflammatory cytokines are higher in non-healing wounds or incisions (Ackinzi et al., 2014). This study followed 54 postsurgical cases with 13 patients having a preoperative diagnosis of T2DM, 41 were nondiabetic but, after follow up, four additional patients were diagnosed with T2DM (Ackinzi et al., 2014). Ackinzi et al. (2014) were specifically looking at the activation of the Plg system, which when metabolized by the liver helps to produce plasmin which in turn helps with wound healing. The activation of this system also activates protein uPA and receptor site uPAR that assists with wound healing (Ackinzi et al., 2014). In patients with hyperglycemia, whether from T2DM or stress induced, these important proteins and processes are inhibited and therefore delay the healing time as the body does not have the proper proteins, blood and oxygen supply to assist with healing.

Sathya, Davis, Taveira, Whitlatch & Wu (2013) performed a study in the perioperative phase of blood sugar control and the effect on surgical outcomes. Risks associated with perioperative hyperglycemia have been identified as increased ventilator dependence, atrial fibrillation, wound infection and increased risk of mortality (Sathya et al., 2013). Sathya et al. conducted a search of current research articles and found 754 that were related to blood sugar control, diabetes and surgical outcomes. They narrowed their article review to six and completed a meta-analysis of the data. Sathya et al. concluded that in the perioperative environment, moderate control of blood glucose levels between 150–200 mg/dl, during or immediately after surgery, was associated with a significantly lower risk of mortality and stroke in patients with diabetes (Sathya et al., 2013). Currently there are no standard protocols or recommendations from the American Diabetic Association for blood sugar control in the pre- and postoperative diabetic patient. There are critical care protocols for the control of glucose levels, but these were found to be no more beneficial for use in postoperative patients than using a moderate control

scale (Sathya et al., 2013). They recommended more research be done to develop a more finite protocol to manage blood sugar control in the pre- and postoperative diabetic patient.

For patient S, it is unknown what her blood sugar levels run as she did not regularly test them. To get a better idea of how well she would do in the postoperative period with recovery and healing, a better assessment of her blood sugar levels should occur. She should be recommended to check her blood sugar levels three to four times per day in preparation for her surgery to see if any medications need to be added to her regimen to get blood sugar levels under control. Glycemic control between 150-200mg/dl, according to Saytha et al., (2013), can help optimize her healing and minimize the risk of other adverse events following surgery.

According to Amusat et al. (2014), observational studies have concluded that the greatest amount of pain relief and functional recovery occur in the first six months following a total knee arthroplasty. Up to this point, little research had been done in differentiating the recovery pattern for diabetic patients separate from non-diabetic patients. Amusat et al. (2014) sought to perform a study looking at the recovery patterns of nondiabetic and diabetic patients postoperatively of a total knee arthroscopy. A total of 405 patients participated with 60 reportedly having diabetes. Median age of the participants was 68 with 62% of the total patient population female. Of those 60 diabetic patients, 19 reported that diabetes impacted their activities of daily living severely. Amusat et al. (2014) identified three groups to report on during the study: nondiabetic, diabetic and diabetic with impact on daily living. At the first, third and six month recheck appointments, the 19 diabetic patients with impact on daily living reported higher pain levels and continued lower functioning levels (Amusat et al., 2014). Overall, at the one month check, there was no statistically significant difference in pain or function among all three groups (Amusat et al., 2014). However, at the third and six month recheck, the diabetic group with impact on daily

living had higher rates of pain and continued poor physical functioning level in accomplishing their daily activities (Amusat et al., 2014). Overall, different patterns of recovery were noted in the three groups in the postoperative recovery period. Patients' with diabetes that impacted their daily living reported difficulty with ambulation, completing activities of daily living and overall higher levels of pain were reported during follow up (Amusat et al., 2014).

For patient S, diabetes does not adversely affect her life or impact her activities of daily living. It is not known how well controlled her blood sugars are as she did not regularly check them. Based on Amusat et al. study's findings, her recovery and healing in the first six months after surgery could be comparable to those who are nondiabetic. However, she does have other confounding factors that could potentially play into delayed healing time such as regular alcohol use and smoking a half ppd. This coupled with her history of hypertension and sedentary life style could also offer a higher risk of postoperative complications, reduced functionality and delayed healing. She should be advised to stay active, encouraged to quit smoking and to monitor her blood sugars closely to help aid in the healing process postoperatively.

Glycemic control strategies are important during the postoperative period to reduce blood glucose to normal levels. Surgery and anesthesia can elicit a stress response in both diabetic and nondiabetic patients (Akiboye & Rayman, 2017). The stress response can increase hormones and cytokines that raise glucose levels and increase insulin resistance (Akiboye & Rayman, 2017). In a study conducted by Gallagher, Erich, Gattermeyer & Beam (2017), 301 patients were treated with an insulin protocol after surgery based on three different glucose testing points; a point of care test in the PACU greater than 140 mg/dl, a point of care test at nine pm on their surgical night greater than 180 mg/dl or point of care test before breakfast in the morning after surgery greater than 140 mg/dl. If any one of those was elevated, the patient qualified for the insulin

protocol therapy to help with blood sugar control. Total patient participation was 489 with 187 of those patients undergoing a total knee arthroscopy (Gallagher, Erich, Gattermeyer & Beam, 2017). For 220 of these participants a Hgb A1C was available with 37 being diabetic, 105 falling in the prediabetes category and 78 were in the normal range (Gallagher, Erich, Gattermeyer & Beam, 2017).

The use of the standardized protocol for subcutaneous insulin treatment of postoperative stress induced hyperglycemia was effective in both diabetic and nondiabetic patients (Gallagher, Erich, Gattermeyer & Beam, 2017). For nondiabetic patients, the stress induced hyperglycemia typically resolved with insulin use within 48 hours. For diabetic patients, they were on the protocol longer due to their more erratic response to insulin and increased glycemic variability, especially if poorly controlled prior to surgery. Gallagher, Erich, Gattermeyer & Beam (2017) recommend diabetic patients who are poorly controlled see an endocrinologist prior to elective orthopedic surgery. For Patient S if her blood sugar levels prior to surgery are elevated or if her A1C is above nine, it may be wise to send her to endocrinology prior to surgery to get her blood sugars more controlled. A postoperative infection would most definitely delay her healing time with the possibility of increased risk of a host of other postoperative complications such as pulmonary embolism, DVT, limb amputation, sepsis or death.

An additional study performed by Robertson, Geddes, Ridley, McLeod & Cheng (2012) researched whether or not a preoperative diagnosis of diabetes had an effect on the healing and functionality level after a total knee arthroplasty versus patients with no diagnosis of diabetes. They looked at a test group of 291 people post total knee arthroplasty who had a preoperative diagnosis of diabetes versus the control group of nondiabetic patients which consisted of 3228 people (Robertson et al, 2012). In the first year post surgery, the diabetic group demonstrated

stiffer knee joints, decreased functionality scores, decreased range of motion and decreased flexion that those in the nondiabetic group (Robertson et al, 2012). They concluded that this is not enough of a functional set back to not offer total knee arthroplasty to diabetic patients. It is something to consider when counseling patients prior to surgery that they understand the healing time and recovery to functionality for daily living activities can be delayed due to diabetes and other comorbidities (Robertson et al, 2012). Patient S should be counseled regarding the possible delay in healing time and return to functionality for her knee due to her diabetes and other comorbidities. It is important for her to have all the information so she can be prepared for a possible longer recovery time and what adjustments that will mean for her life.

One article during the literature review found no basis of difference in risk factors for increased healing time or other surgical complications between nondiabetic and diabetic patients. Clement, MacDonald, Burnett and Breusch (2013) found in their research that comorbidities played a higher role in postoperative adverse events than the diagnosis of diabetes alone. They studied total knee arthroplasty in diabetic patients and how that affected their mobility, functionality via the Oxford Knee Score and overall satisfaction with their surgery. The Oxford Knee Score is a questionnaire of 13 questions asking the patient to rate their pain, mobility and confidence level with performing activities of daily living. Totals are then added together with a highest potential score of 48 points which gives the provider a scale of confidence of where the patient is at in their healing; rated by poor, moderate, good or excellent. During their study period, they had 2,392 total knee arthroplasty patients with 275 having a diabetes diagnosis before surgery (Clement, MacDonald, Burnett and Breusch, 2013). They found that overall diabetes does not independently predict patient outcomes even though it presents high risk of complications for the patient, especially when comorbidities are present; such as liver or heart

disease, depression, vascular disease, anemia or back pain (Clement, MacDonald, Burnett and Breusch, 2013). In Patient S's case, this is a true statement. It is not diabetes alone that puts her at increased risk of postoperative complications and delayed healing time, it is the combination of her social and medical history that complicates the surgery for her along with a sedentary lifestyle.

Learning Points

When caring for patients who are diabetic and planning for elective total knee arthroscopy, education for the patient is one of the highest priorities in preparing them and optimizing their health for the safest surgical outcomes possible. These are just a few of the important points to consider when planning their pre and postoperative care:

- Hyperglycemia impairs leucocytes function causing immunocompromise with increased risk of infection, impaired skin and bone healing and increased risk of mortality (Akiboye & Rayman, 2017).
- Hyperglycemia adversely effects wound healing in diabetics because of the delay in synthesis of collagen as well as the impaired bone metabolism with dysfunctional osteoblasts (Yang, et al., 2014).
- People with diabetes require more planning and care before, during and after orthopedic procedures to ensure the safest delivery of their procedure and minimizing the potential harm to this group of patients (Akiboye & Rayman, 2017).
- Moderate control of blood glucose levels between 150–200 mg/dl, during or immediately after surgery, was associated with a significantly lower risk of mortality and stroke in patients with diabetes (Sathya et al., 2013). Checking blood sugar levels 4 times a day

was recommend and it was noted keeping blood sugar levels between 150-200 mg/dl helps to minimize adverse events for diabetic patients (Sathya et al., 2013).

- Recovery over the first six months postoperatively after total knee arthroscopy is slower in patients whose diabetes affects their activities of daily living (Amusat, et al., 2014).

Overall, controlling blood sugar levels pre- and postoperatively will assist with healing time and decreasing a diabetic patient's overall risk of adverse events. A collaborative approach is necessary to optimize the patient's chance of an uncomplicated recovery. Even with controlling blood sugars, other risks still exist for diabetic patients. More research needs to be done to develop optimal blood sugar control protocols for diabetic patient undergoing total knee arthroplasty. Our goal is to assist with decreasing that risk and make the surgical and postoperative environment safer for the patient at hand.

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