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Should Hemoglobin A1C be Used as an Predictor of Post-Operative Infection Risk With Total Knee Arthroplasty Surgery?

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PERMISSION

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Abstract

The incidence of diabetic patients requiring a total knee arthroplasty (TKA) is increasing exponentially overall due to the increased incidence of both orthopedic surgeries and diabetes diagnoses separately. Diabetes introduces an increased risk for several complications after surgery in general and more specifically for infection after a TKA. Poor glycemic control increases these risks greatly. A literature review was conducted in several databases to examine the efficacy of hemoglobin A1C in identifying those diabetic patients who are at increased risk of infection due to poor long-term glucose control. A total of 11 journal articles and studies were selected for analysis. The findings indicate while a hemoglobin A1C can be a useful tool to assessing overall glucose control, perioperative hyperglycemia more closely correlates with increased infection rates in TKA patients with diabetes.

A hemoglobin A1C greater than 8 is associated with increased risk of postoperative TKA infection. However, hemoglobin A1C was not found to be the superior glycemic marker to identify patients at a higher risk of infection. Perioperative glucose control should also be closely monitored and corrected accordingly to keep blood glucose below 200 mg/dL to achieve optimal outcomes, primarily in the immediate post-operative time frame. Both glycemic markers pose different implications when considering TKA outcomes and should be monitored in all diabetic patients throughout the perioperative period. If concern for infection is the primary purpose of monitoring or screening a patient, immediate preoperative or postoperative glucose levels are the most accurate indicators.

Background

Total knee arthroplasty (TKA) is one of the fastest growing surgical procedures in the United States. With any orthopedic procedure, a surgical site infection can be an unfortunate

complication that can result in poor outcomes or even a need for a revision surgery. While these are uncommon, a diagnosis of diabetes mellitus increases a patient's risk for an infection greatly (Kremers et al.,2014).

The incidence of diabetes mellitus type 2 is increasing rapidly in the United States. It is predicted that the prevalence of diabetes will be 9.9% worldwide by the year 2030 (Akiboye & Rayman, 2017). Incidentally approximately 50% of all diabetics have some degree of osteoarthritis. This is likely due to the aging population and the undisputed link between obesity and both diabetes and osteoarthritis. All of these contributing factors make it more likely than ever that a diabetic patient will need a TKA at some point in their lifetime (Yang et al., 2014).

Currently there is a fair amount of research on the overall complication risk diabetes poses in major procedures such as cardiothoracic surgery. While guidelines have been developed for preoperative patient risk assessments for those procedures, specific guidelines for orthopedic surgeries need to be developed. Approximately 8-22% of all orthopedic surgical patients have diabetes. This diagnosis alone increases a patient's risk of infection 3-5 times compared to the average healthy patient (Chrastil et al., 2015). If we are able to identify those patients at a high risk of infection due to poor glycemic control we have a better change at preventing infection rather than treating it after it occurs. Current evidence regarding use and accuracy of a hemoglobin A1C as a preoperative screening assessment for postoperative TKA infection risk remains unclear. (Kremers et al., 2014).

Case Report

A 45-year-old Caucasian female was seen in a primary care setting for a "diabetes recheck". She was advised to make an appointment with her primary care provider by a diabetes educator to discuss poorly controlled blood sugars. She had been non-compliant with routine

follow-ups prior to this visit and reports her fasting blood sugars range from 150 mg/dL to 200 mg/dL on average. She is currently taking metformin 500 mg twice daily for management of her type 2 diabetes mellitus. Other notable health history includes hypertension for which she takes Lisinopril 20 mg daily and hyperlipidemia which is well-managed with atorvastatin 20 mg daily. She acknowledged she takes her medications as prescribed and denied any further questions or concerns regarding her medication regimen. Besides her diabetes management she also reported concerns about increasing fatigue over the last "several months" and a 20-pound weight gain over the last year.

She has 2 small children at home and stated that "running around" with them limited her motivation to exercise or eat a healthy diet. Because of this she acknowledged that her weight gain was most likely due to lifestyle choices rather than a physiologic change. Her increasing fatigue had become more bothersome due to it interfering with her ability to play with her children. Her fatigue symptoms were vague and seemed to have developed with gradual onset over about 6 months. She denied any difficulty getting to sleep or staying asleep. She often felt "run down" and would take naps when able which was unusual for her.

A thorough physical exam was performed and was unremarkable aside from newly identified neuropathy on the bottom of both of the patient's feet. She denied noticing this prior to the visit and was completely unaware of when it had started. The skin on her feet was intact without evidence of erythema, calluses, or open wounds with adequate capillary refill. The neuropathy was not causing any pain or tingling sensation. Her vital signs were within acceptable ranges expect for a slightly elevated blood pressure of 148/98. After examination, laboratory tests completed included hemoglobin A1C, urine microalbumin, thyroid stimulating

hormone, and lipid panel. All results were within expected range aside from the hemoglobin A1C which was 8.5.

The elevated hemoglobin A1C indicated that the patient's diabetes was not in good control, so she was informed that her metformin would be increased to 1000 mg twice daily. Her blood pressure was elevated despite taking her Lisinopril as prescribed. The patient was motivated to make significant lifestyle modifications in terms of exercise and diet and did not want to increase her Lisinopril dose. She was educated on proper diabetic diet and recommended exercise of at least 30 minutes per day 5 days per week. It was determined both her fatigue and weight gain are likely due to lifestyle changes and will resolve with changing daily routine and healthier lifestyle choices. She was informed to keep follow ups with the diabetes educators as well as her primary care provider at a minimum of every 6 months. She will have her hemoglobin A1C rechecked in 3 months to determine efficacy of increased metformin dose. Lastly, diabetic foot care was discussed including increased risk of chronic wounds, routine feet checks by both the patient and medical professionals, and proper fitting footwear. The patient was scheduled to return to the clinic in 3 months for another diabetes recheck.

Literature Review

Several different databases were used for the purposes of this literature review. The first database used was the Cumulative Index of Nursing and Allied Health (CINAHL). This database specializes in nursing research. Initial search terms used were *diabetes* AND *knee replacement*. This resulted in 104 articles. Search parameters were then limited to articles published within the last 5 years to ensure the most current evidence was evaluated. The search term *infection* was then added to the previous search terms which resulted in 21 total articles, 5 of which were

directly related to diabetes and were evaluated in this review. All articles included were peer reviewed as well.

PubMed database was also used for this review. Initial search terms were *diabetes* AND *knee replacement* which yielded 341 total articles. When a 5-year time limitation was selected 195 articles remained. The term *infection* was again added to the search terms which resulted in 67 total articles. In this search the term *diabetes* was then exchanged for *hyperglycemia* which resulted in a total of 9 articles, 6 of which directly related to the topic of interest. It was determined that 4 articles from the previous CINAHL search were also included in the results of this search. The Cochrane Database of Systemic Reviews was then searched using the terms *diabetes* AND *knee replacement* AND *infection* which resulted in 11 total articles. Only one article directly related to hyperglycemia and surgery but was not specific to joint replacements, so it was not used for this review.

After examining the total articles, it was determined an insufficient number of articles were found to perform an adequate literature review. Google scholar was used as the final database search. Key search terms used were *diabetes* AND *knee replacement* AND *infection* AND *hyperglycemia.* Because this database is so large the terms were individually put in quotation marks to ensure the exact terms appeared in every result. An overwhelming total of 416 results were found. After the articles were limited to publication within the last 2 years, 260 remained. These were sorted by relevance to the intended topic and 4 articles were selected for this analysis to get a total of 11 journal articles and studies that were reviewed.

While all of the articles analyzed established that a diagnosis of diabetes increases the likelihood of adverse outcomes following TKA, several different implications regarding glycemic screening and control emerged when examining infection rates.

Many guidelines remain in place that indicate a hemoglobin A1C is an appropriate preoperative assessment test for diabetic patients. One of the key uses of this test prior to surgery is to assess a diabetic patient's overall glucose control across a longer time period. Several studies found that an elevated preoperative hemoglobin A1C increased rates of infection in TKA patients. Han and Kang (2013) identified a hemoglobin A1C greater than or equal to 8 was a positive predictor of TKA infection. This result was found to still be significant even when taking into consideration other factors such as other co-morbidities. Similar findings were presented by Akiboye and Rayman (2017) with the significant hemoglobin A1C threshold identified as greater than 7%. Whereas other studies found no correlation to hemoglobin A1C levels and infection rates at all (Iorio et al., 2012).

Perioperative hyperglycemia emerged as another contributing factor for increased infection risk in these patients, independent from elevated hemoglobin A1C. Fasting glucose monitoring is recommended in both the immediate preoperative and postoperative periods. Hyperglycemia in both timeframes was identified as significant in correlation to increased infection risk. A preoperative fasting blood glucose greater than 194 mg/dL was found to be more of a predictor of infection than a hemoglobin A1C alone (Chrastil et al., 2015). Schwartz & Lange (2017) identified perioperative glucose control as an important factor in TKA infection risk reduction but failed to identify any specific glucose control recommendations or guidelines.

Postoperative hyperglycemia is common in both diabetics and non-diabetics due to the physiological stress response surgery stimulates in the body. Lower thresholds for significant blood glucose readings of greater than 126 mg/dL were found to be significant when considered in the immediate postoperative period. Other postoperative blood glucose levels were examined at different lengths of time but the immediate time frame was identified as most highly correlated

with increased rates of infection (Reategui et al., 2015). It was also discussed that elevated fasting glucose of 200mg/dL in the post-operative period even up to 30 days after surgery increased risk of infection (Akiboye & Rayman, 2017).

One of the most notable studies examined for this review is a meta-analysis conducted by Liqing, Yuefeng, Ge, and Jiulong (2017) which examined six retrospective studies and included the largest patient sample size overall. This study found a positive correlation between both elevated hemoglobin A1C and perioperative hyperglycemia with infection rates after TKA. This is significant because it seems to summarize the general findings in the other studies examined above. Liqing et al. (2017) identified a more restrictive hemoglobin A1C level greater than 7% to be the threshold of increased infection risk. This is less conservative than the suggested 8% threshold identified by Han and Kang (2013). While a correlation between elevated perioperative glucose levels and infection rates was identified, optimal glucose levels were not clear which leaves room for further research (Liqing et al., 2013).

A single retrospective study presented findings that coincided with the large meta-analysis by Liqing et al. (2013). A hemoglobin A1C threshold of greater than 8% was also identified as a risk factor for infection along with a fasting glucose greater than 200mg/dL. These levels were determined to be risk factors both separately and when found simultaneously in the same patient (Hwang, Kim, Bamme, Na, & Kim, 2015). Important consideration should be given to the fact that each laboratory finding identifies different levels of glucose control (short term and long term) and each has different implications in the post-operative time period. This study also examined post-operative fasting glucose levels at different lengths of time and found that the preoperative glycemic labs (fasting blood sugar and hemoglobin A1C) were more indicative of true glycemic control than the post-operative lab values but did not identify if this is a more

accurate measure of infection risk. The implication that pre-operative glycemic markers are superior tools when simply assessing overall diabetic control is most likely due skewed hyperglycemia due to to increased stress in the postoperative period (Hwang et al., 2015).

While most articles acknowledged some relation to glucose control and infection rates, others determined that glucose control status did not alter infection risks at all. Kremers et al. (2014) did not find a correlation between elevated hemoglobin A1C and joint infections after TKA. It was determined that other co-morbidities were confounding contributors to joint infections rather than glycemic variability in the preoperative, perioperative, and postoperative time frames. This finding addresses the need to consider the implications a diabetes diagnosis has on the patient's overall health. The implications may be that these patients are generally unhealthier with other chronic conditions which leads to TKA infections rather than glucose control (Yang et al.,014).

These findings do seem to be somewhat of an outlier in the total rejection of glycemic variability increasing risk of infection in TKA. Based on these findings, simply considering the implications a diagnosis of diabetes carries with it in relation to surgical complication risks may be enough of a screening tool rather than serum lab work. Knowledge of this diagnosis alone may indicate to the surgeon that closer follow-up monitoring may be indicated for diabetic patients, no matter what level of control they currently have over their glucose levels (Kremers et al., 2014).

Another key factor to optimal outcomes after a TKA is routine follow-up. This is especially important for diabetics. This follow-up should be with the patient's primary care provider with the focus being on reduction of post-operative hyperglycemic episodes and early detection of symptoms indicating infection (Reategui et al., 2016). The primary care provider can

serve an integral role in post-operative glycemic monitoring and medication management to ensure glucose levels are kept within optimal range. This range may vary from one patient to the next which is where the primary care provider's knowledge about the individual patient's overall health is a useful tool for orthopedic surgeons to rely on for help with management (Wukich, 2015)

Conclusion

Overall, the benefit to checking a hemoglobin A1C prior to surgery lies in its indications for potential diabetes related complications that may further increase a likelihood of postoperative TKA infection. While a hemoglobin A1C alone may not directly predict infection rates, it can indicate a patient's risk of diabetic complications such as neuropathy or peripheral arterial disease which may increase complication rates after surgery, including infection (Wukich, 2015). A hemoglobin A1C threshold did emerge indicating a level greater than 8 may prompt a need for further assessments prior to surgery. However, hemoglobin A1C should not be used as a sole factor when assessing infection risk after TKA. Overall glucose control through the entire perioperative period needs to be closely monitored and corrected to truly reduce a diabetic patient's risk of infection following TKA. Per the Endocrine Society guidelines, all patients, diabetics and non-diabetics, should have a hemoglobin A1C and blood glucose level tested prior to surgery. However, this practice has yet to be implemented in many areas (Liqing et al., 2017). Research into exact optimal thresholds of both the hemoglobin AlC and fasting blood glucose immediately prior to after after surgery is still needed in the field of orthopedic surgery (Schwartz & Lange, 2017).

Learning Points

- Hemoglobin A1C serves as good indicator of overall diabetes control but may not have a superior predictive value over other glycemic markers when specifically determining infection risks for total knee arthroplasty. However, a hemoglobin A1C greater than 8 should prompt further evaluation and discussion with the patient as this indicates higher risk of poor outcomes in general due to increased risk of diabetes complications such as neuropathy or peripheral arterial disease.
- Preoperative AND postoperative fasting hyperglycemia greater than 200mg/dL may be a more accurate predictor of infection when compared to preoperative elevated hemoglobin A1C.
- Consider checking a fasting blood sugar at a preoperative assessment appointment in ADDITION to hemoglobin A1C to truly assess overall diabetes control. While a fasting blood sugar greater than 200 mg/dL may not indicate a need to postpone surgery, it indicates that the patient may need thorough glucose control during intraoperative and postoperative periods.
- Collaboration between the orthopedic team and the patient's primary care provider is imperative to promote optimal glycemic control before and after surgery.
- Patients education should include that insulin may be needed for a short time frame in the postoperative period to counteract stress-induced hyperglycemia that happens as a normal reaction to surgery.

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