The Journal of Arthroplasty xxx (2016) 1–4

Contents lists available at ScienceDirect

The Journal of Arthroplasty

journal homepage: www.arthroplastyjournal.org

Original Article

Effect of Hypoglycemia on the Incidence of Revision in Total Knee Arthroplasty

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ARTICLE INFO

Article history:
Received 25 March 2016
Received in revised form
9 June 2016
Accepted 11 July 2016
Available online xxx

Keywords:
total knee arthroplasty
revision
hypoglycemia
knee replacement
revision arthroplasty

ABSTRACT

Background: It is well established that diabetic patients undergoing total knee arthroplasty (TKA) are more susceptible to infection, problematic wound healing, and overall higher complication rates. However, a paucity in current literature exists. The purpose of this study was to determine the effect of hypoglycemia on TKA revision (rTKA) incidence by analyzing a national private payer database for procedures performed between 2007 and 2015 Q1 Q2.

Methods: A retrospective review of a national private payer database within the PearlDiver Supercomputer application for patients undergoing TKA with blood glucose levels from 20 to 219 mg/mL, in 10-mg/mL increments, was conducted. Patients who underwent TKA were identified by Current Procedural Terminology (CPT) and International Classification of Disease (ICD) codes. Glucose ranges were identified by filtering for Logical Observation Identifiers Names and Codes within the PearlDiver database. Patients with diagnosed diabetes mellitus type I or II were excluded by using ICD-9 codes 250.00-250.03, 250.10-250.13, and 250.20-250.21. rTKA causes including mechanical loosening, failure/break, periprosthetic fracture, osteolysis, infection, pain, arthrofibrosis, instability, and trauma were identified with CPT and ICD-9 codes. Statistical analysis was primarily descriptive.

Results: Our query returned 264,824 TKAs, of which 12,852 (4.9%) were revised. Most TKAs were performed with a glucose of 70-99 mg/mL (26.1%), followed by 100-109 mg/mL (18.5%). Patients with TKAs performed with glucose 20-29 mg/mL had the highest rate of revision (17.2%; $P < .001$). Infection was the most common cause of revision among all glucose ranges ($P < .001$).

Conclusion: Infection remains one of the most common causes of rTKA irrespective of glucose level. Our results suggest that hypoglycemia may increase revision rates among TKA patients. Tight glycemic control before and during surgery may be warranted.

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Diabetic patients undergoing total knee arthroplasty (TKA) are more susceptible to adverse outcomes [1,2]. Hyperglycemia contributes to the pathogenesis of surgical site infection, delays in wound healing, and higher postoperative complications [3-8]. However, few studies have reported on the effect of hypoglycemia during the perioperative period [9,10]. To our knowledge, no study has reported on the effects of hypoglycemia in TKA patients. Some literature suggests that low perioperative glucose levels may contribute to variations in outcomes [11,12].

The measured serum glucose level before surgery is primarily dependent on the length of preoperative fasting and effects of antiDiabet Medications. Traditionally, strict overnight fasting was employed to prevent pulmonary aspiration. However, recent anesthesia guidelines now recommend a 2-hour and 6-hour fast for clear fluids and solids, respectively, in elective surgery patients [13,14]. This fasting period influences the metabolic state of the patient and may subsequently impact the stress response following surgery, which elicits metabolic, hormonal, and hemodynamic responses that may be amplified in an over-fasted state. Extended fasting before surgery leads to a shift of the carbohydrate metabolism, disturbed glycogen formation, and enhanced endogenous

No author associated with this paper has disclosed any potential or pertinent conflicts which may be perceived to have impending conflict with this work. For full disclosure statements refer to http://dx.doi.org/10.1016/j.arth.2016.07.014.

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http://dx.doi.org/10.1016/j.arth.2016.07.014
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glucose production, which prolongs the decline in insulin sensitivity [11,13,15-17]. Thus, insulin resistance might impair recovery following TKA [13]. The transient state of insulin resistance may lead to a period of hyperglycemia lasting for 2-3 weeks following surgery, predisposing the patient to hyperglycemic postoperative risk factors, increased protein catabolism, and reduced muscle strength [13,18,19].

Preoperative hypoglycemia has been associated with in-hospital mortality in patients undergoing operative procedures [20]. However, there is paucity in current literature investigating the effects of hypoglycemia on TKA. The purpose of this study was to determine the effect of hypoglycemia on TKA revision (rTKA) incidence by analyzing a national private payer database for procedures performed between 2007 and 2015 Q1 Q2.

Methods

A retrospective review of a national private payer database within the PearlDiver Supercomputer application (Warsaw, IN) for patients undergoing TKA between 2007 and 2015 with glucose levels ranging from 20 to 219 mg/mL, in increments of 10 mg/mL, was conducted. The PearlDiver database is a publicly available Health Insurance Portability and Accountability Act–compliant national database compiled from a collection of private payer records. This database contains Current Procedural Terminology (CPT) and International Classification of Diseases, Ninth Revision (ICD-9) codes.

Patients who underwent TKA were identified by CPT-27447 and ICD code 81.54. Preoperative glucose ranges on the day of surgery were identified by filtering for Logical Observation Identifiers Names and Codes within the PearlDiver database. Patients with diagnosed diabetes mellitus (DM) type I or II were excluded by using ICD-9 codes 250.00-250.03, 250.10-250.13, and 250.20-250.21. The revision variables were identified with CPT codes 27486, 27487, ICD-9 codes 00.80-00.84 and 81.55, which code for revision TKAs. Causes for revision were identified with ICD-9 codes 996.40-47, 996.49, 996.66-67, 996.77-78, 718.46, 718.56, and 718.86. These code for mechanical loosening, failure/break, periprosthetic fracture, osteolysis, infection, pain, arthrofibrosis, instability, and trauma.

Statistical analysis of this study was performed with Minitab version 17 (State College, PA) and was primarily descriptive with analysis of variance to determine significance where appropriate.

Results

Our query returned a total of 264,824 TKAs during the study period. Of these, 12,852 (4.9%) were revised. The majority of TKAs were performed with a glucose level ranging 70-99 mg/mL (26.1%), followed by 100-109 mg/mL (18.5%). Patients with glucose of 20-29 mg/mL had the highest rate of revision (17.2%; $P < .001$) following the index procedure. A complete breakdown of TKAs and subsequent rTKAs performed with respective glucose ranges studied is shown in Table 1 and Figure 1. Infection was the most common cause of revision among all studied glucose ranges ($P < .001$). Other causes of revision in the respective glucose ranges are listed in Table 2.

Table 1
TKA and rTKA Glucose Ranges and Revision.

Glucose (mg/mL)	TKA	rTKA	Revision Incidence (%)
210-219	3179	189	5.9
200-209	3777	234	6.2
190-199	4661	275	5.9
180-189	5589	314	5.6
170-179	6972	365	5.2
160-169	8791	467	5.3
150-159	11,337	594	5.2
140-149	14,584	746	5.1
130-139	18,688	965	5.2
120-129	25,031	1224	4.9
110-119	34,850	1661	4.8
100-109	48,881	2180	4.5
70-99	69,098	2922	4.2
60-69	5843	404	6.9
50-59	2164	166	7.7
40-49	950	93	9.8
30-39	330	36	10.9
20-29	99	17	17.2
Total	264,824	12,852	4.9

Discussion

Although previous studies have primarily reported on the postoperative complications among diabetic patients following surgery, few have investigated the significance of hypoglycemia [1]. Our paper is among the first to evaluate the influence of hypoglycemia in the setting of TKA. Several reports have demonstrated high complication risks among diabetic patients undergoing major joint arthroplasty; such reported postoperative complications include infection, deep vein thrombosis, stroke, acute coronary syndromes, and poor wound healing [3-7]. However, perioperative management of glycemic control remains challenging and may predispose the patient to hypoglycemia. Here, we demonstrate that hypoglycemia may be a risk factor for postoperative revision following primary TKA.

The primary results of our study found that rTKA incidence increases as glucose levels decline from the normal range. Additionally, we demonstrate that the most common cause of rTKA in the setting of hypoglycemia remains as infection.

Preoperative fasting and antidiabetic medications may predispose patients to perioperative hypoglycemia. Thus, diabetic medications are often adjusted or omitted to help minimize perioperative hypoglycemia [21-23]. Because of this, several authors have advocated that scheduled surgeries be performed during morning hours for diabetic patients [22,24,25]. Prevention of perioperative hypoglycemia is important, as it has been associated with increased hospital costs and length of stay, likelihood of discharge to a skilled nursing facility, greater mortality, and poor outcomes [21,26-29]. Both low-normal blood glucose and hyperglycemic patients being treated preoperatively are especially at risk of developing perioperative hypoglycemia [21]. In a retrospective review, Drews et al [21] demonstrated that patients with low-normal blood glucose, defined as 70-89 mg/mL, were at greater risk of developing perioperative hypoglycemia than were hyperglycemic patients being treated with insulin; however, hyperglycemic insulin-treated patients were more likely to experience severe hypoglycemia (blood glucose <50 mg/mL). This is particularly important in renal disease and elderly patients, where insulin clearance is prolonged [21,30,31].

Our study demonstrated that the rate of revision increased as glucose ranges deviated from normal. We found that patients with blood glucose between 20 and 29 mg/mL had nearly triple the risk of revision. Additionally, it was shown that infection was the leading cause of revision for hypoglycemic patients undergoing TKA. This is suggestive of an association between hypoglycemia and postoperative infection, although the role, if any, is unknown. Despite numerous studies demonstrating a correlation between hyperglycemia and postoperative infection, no literature evaluating the association between hypoglycemia and postoperative infection is available [7,8,32,33]. Kremer et al. postulated that the role of preoperative glucose testing in all joint arthroplasty patients

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