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Increased Postoperative Glycemic Variability Is Associated with Increased Revision Surgery Rates in Diabetic Patients Undergoing Hip Fracture Fixation

Itay Ashkenazi †, Nissan Amzallag †, Shai Factor *, Nadav Graif, Or Shaked, Yaniv Warschawski, Tomer Ben-Tov and Amal Khoury

Tel Aviv Medical Center, Orhopaedic Division, Affiliated with the Faculty of Medicine, Tel Aviv University, Weizmann St. 6, Tel Aviv 6423906, Israel
* Correspondence: factor310@gmail.com; Tel.: +972-527360753; Fax: +972-74-7219810
† These authors contributed equally to this work.

Abstract: Background: An association between increased postoperative glycemic variability (GV) and inferior postoperative outcomes following hip arthroplasty procedures has been previously reported. However, the utilization of the GV to project surgical outcomes following the fixation of hip fractures has not been well established. The aim of this study is to assess the association between the postoperative GV of patients with diabetes mellitus (DM) and surgical outcomes following the fixation of a hip fracture. Methods: This is a retrospective analysis of 3117 consecutive cases of patients who underwent the fixation of hip fractures between 2011 and 2020. Patients with a DM diagnosis who had ≥3 postoperative glucose measurements during the first week after surgery and had a minimum of one-year follow-up were included. The coefficient of variation (the ratio of the standard deviation to the mean) was utilized to assess the GV. The final study population included 605 patients who were divided into three groups according to the extent of their GV. Short- and mid-term outcomes, including mortality, reoperations, readmissions, and postoperative infection rates were compared between the groups. Results: There was a non-significant trend towards increased rates of mortality ($p = 0.06$), readmissions ($p = 0.22$) and postoperative infections ($p = 0.09$) in the high GV group. The rate of revisions at the latest follow-up was significantly higher in the high GV group when compared to the two other groups ($p = 0.04$). Conclusion: For diabetic patients undergoing hip fracture fixation, a higher GV in the postoperative period was associated with increased rates of all-cause revision surgery and may be associated with increased mortality, readmission rates, and surgical site infections. Glucose levels of diabetic patients should be meticulously monitored and controlled in the postoperative period in an effort to contain the sequelae associated with elevated GV and to identify patients in need of closer observation and follow-up.

Keywords: fragility fractures; hip fractures fixation; diabetes mellitus; glucose variability

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1. Introduction

The increased morbidity and mortality associated with hip fractures are a major concern for health systems, especially within the growing elderly population [1,2]. While extracapsular fractures are usually treated by closed or open reduction and internal fixation, intracapsular fractures are treated based on both patient-related and fracture-related factors. Non-displaced intracapsular fractures usually involve in situ fixation to preserve the femoral head, while the management of displaced fractures mostly involves hip arthroplasty [3–5].

Diabetes mellitus (DM) is recognized as an independent risk factor for mortality and morbidity following surgical treatments for hip fractures [6,7]. Rapid fluctuations in glucose levels of patients with DM can lead to a variety of adverse effects, including compromised immune functions and increased oxidative stress [8,9], and it has been previously suggested that the glycemic variability (GV) is a strong predictor of adverse outcomes following surgery [10]. Specifically, increased GV has been previously associated with higher mortality rates in the general surgical population [9–11]. GV is assumed to contribute to postoperative complications through many possible mechanisms, including oxidative stress, immune dysfunction, microvascular damage, and impaired autonomic function [12].

In elective joint surgery settings, this increased risk is partially mitigated by preoperative optimization and GV control utilizing hemoglobin A1c (HbA1c) and Fructosamine as markers for glycemic control and as predictors of adverse outcomes following surgery [6,13]. However, the use of these markers in the trauma setting is limited, and data regarding their utility in this setting are scarce. In contrast, the coefficient of variation (calculated as the ratio between the standard deviation and the mean) of postoperative glucose levels has been previously utilized to assess the GV of patients undergoing hip arthroplasty in both the elective and the trauma setting, showing that increased GV is associated with inferior postoperative outcomes [14,15]. Limited studies have shown that increased postoperative glucose variability (GV) is associated with higher rates of mortality following hip fracture surgeries and may serve as a predictor for postoperative complications [16,17].

Nevertheless, the use of the coefficient of variation to assess the GV in diabetic patients specifically undergoing the fixation of a hip fracture is not well established, and the use of GV in this specific population to predict adverse events is lacking. This study aimed to assess the association between postoperative GV and the surgical outcomes following the urgent fixation of hip fractures in patients with DM. We hypothesize that an increase in GV will be associated with increased postoperative complications, specifically mortality and readmission rates.

2. Materials and Methods

2.1. Study Population

We conducted a retrospective review of data for all patients who were diagnosed with a femoral neck or trochanteric fracture (31A\31B according to the AO/OTA classification [18]) and underwent fracture fixation at a single academic tertiary care medical center between 1 January 2011 and 31 March 2020. Only patients with a DM diagnosis, who had $\geq$3 postoperative glucose measurements during the first week after surgery and had a minimum of one-year follow-up were included (Figure 1). This study was performed following institutional review board approval.

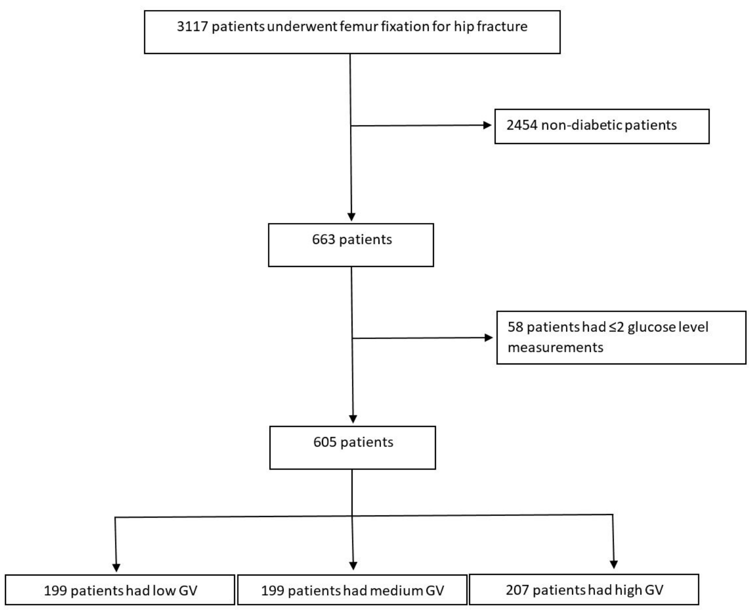

Figure 1. Study design. GV, glucose variability.

2.2. Data Collection

Patient baseline characteristics, laboratory results, and clinical outcomes at the latest follow-up were collected from our institution's electronic medical records database. The patient's baseline characteristics included age, sex, body mass index (BMI), the American Society of Anesthesiology (ASA) score, and the Charlson comorbidity index (CCI) [19]. Time to surgery was calculated as the time between emergency department admission and the time the surgery started. The findings were reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.3. Glucose Data Analyses

Glucose levels were evaluated using serum glucose testing. Routine laboratory values were taken on postoperative days 1 and 3 before breakfast, and further glucose level analyses were performed according to clinical needs. The mean glucose levels and standard deviation (SD) during hospitalization within a week after surgery were calculated using all available glucose readings. The coefficient of variation was calculated and used as a surrogate for GV [20]. The patients were divided into tertiles based on their GV levels: the highest third were in the "high GV" group, the lowest was in the "low GV" group, and the remaining were in the "medium GV" group. Glucose levels below 70 mg/dL (hypoglycemic) and above 200 mg/dL (hyperglycemic) were recorded.

2.4. Outcome Parameters

The principal outcomes of the study were readmissions, mortality, and the need for revisions of either infectious or non-infectious indications. The rates of readmissions at 30 and 90 days postoperatively were also assessed. Mortality was evaluated at 30 days, 90 days, and one year following the index surgery. The patient's electronic medical records and outpatient clinic reports were reviewed to evaluate the rates and indications of revision surgeries at the latest follow-up. Indications for revisions were categorized as infection and non-infection (i.e., cutout, conversion to hip arthroplasty, etc.). Postoperative infections during the follow-up period were identified and categorized as superficial or deep infections according to the definitions provided by the Centers for Disease Control and Prevention (CDC) [21].

2.5. Data Analyses

All analyses were performed using SPSS version 25 (IBM SPSS Statistics, Chicago, IL, USA). Demographic and clinical baseline characteristics were described as means with standard deviations for continuous variables and frequencies with percentages for categorical variables. Differences between the groups were analyzed using one-way ANOVA and *Chi*-squared (χ^2) tests as appropriate. *p*-values of less than 0.05 were considered statistically significant.

3. Results

The initial study population included 3117 cases of patients who underwent a hip fracture fixation. Following the exclusion of 2512 patients, the remaining study population consisted of 605 patients (Figure 1), who were subsequently stratified into three groups based on their postoperative GV: (1) low GV (lower tertile), (2) medium GV (middle tertile), and (3) high GV (highest tertile). Baseline demographics and comorbidities were comparable between groups (Table 1).

Although not statistically significant, the mortality rates at 30- and 90 days in the high GV group were higher than the corresponding rates in the medium GV and low GV groups ($p = 0.24$, $p = 0.29$, respectively). At one year following surgery, the trend towards higher mortality in the high GV cohort was more substantial ($p = 0.06$). Readmission rates at 30 days and 90 days were comparable between groups ($p = 0.81$, $p = 0.22$, respectively) (Table 2).

Table 1. Patient characteristics.

	Low GV	Medium GV	High GV	*p* Value
	n = 199	*n* = 199	*n* = 207	
Mean age, years (SD)	80.3 (10.2)	81.1 (10.4)	79.8 (9.3)	0.43
Female sex, *n* (%)	116 (58.3)	135 (67.8)	131 (63.3)	0.14
Mean BMI, kg/m^2 (SD)	25.6 (4.9)	25.6 (4.7)	24.8 (4.4)	0.14
ASA score, *n* (%)				0.8
1	2 (1)	1 (0.5)	0 (0)	
2	66 (33.2)	65 (32.7)	65 (31.7)	
3	119 (59.8)	122 (61.3)	124 (60.5)	
4	12 (6)	11 (5.5)	16 (7.8)	
Mean CCI score (SD)	5.9 (1.9)	5.9 (2.3)	5.8 (1.9)	0.92
Comorbidities, *n* (%)				
COPD	13 (6.5)	15 (7.5)	8 (3.9)	0.27
CHF	30 (15.1)	35 (17.6)	43 (20.8)	0.32
CKD	37 (18.6)	43 (21.6)	52 (25.1)	0.28
IHD	56 (28.1)	56 (28.1)	68 (32.9)	0.49
HTN	135 (67.8)	139 (69.8)	136 (65.7)	0.67
Time to surgery, days (SD)	1.49 (1.0)	1.42 (1.2)	1.55 (1.3)	0.54

SD, Standard deviation; BMI, body mass index; ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease; IHD, ischemic heart disease; and HTN, arterial hypertension.

Table 2. Outcome parameters.

	Low GV	Medium GV	High GV	*p* Value
	n = 199	*n* = 199	*n* = 207	
30-day mortality, *n* (%)	10 (5.0)	8 (4.0)	16 (7.7)	0.24
90-day mortality, *n* (%)	8 (4.0)	12 (6.0)	16 (7.7)	0.29
1-year mortality, *n* (%)	18 (9.0)	13 (6.5)	28 (13.5)	0.06
30 days readmission, *n* (%)	4 (2.0)	3 (1.5)	5 (2.4)	0.81
90 days readmission, *n* (%)	4 (2.0)	8 (4.0)	11 (5.3)	0.22
Revision of any cause, *n* (%)	5 (2.5)	3 (1.5)	12 (5.8)	0.04
Infectious	3 (1.5)	1 (0.5)	7 (3.4)	0.09
Non-infectious	2 (1.0)	2 (1.0)	5 (2.4)	0.37
Infection rates, *n* (%)				
SSI *	0 (0)	0 (0)	3 (1.4)	0.06
Deep †	3 (1.5)	1 (0.5)	4 (1.9)	0.43
Glucose levels ‡				
Mean glucose, mg/dL (SD)	159 (54.8)	173 (57.2)	182 (63.2)	<0.001
Patients with hypoglycemia events, *n* (%)	1 (0.5)	8 (4)	44 (21.3)	<0.001
Patients with hyperglycemia events, *n* (%)	70 (35.2)	112 (56.3)	159 (76.8)	<0.001
Patients with both hypo- and hyperglycemia events, *n* (%)	0 (0)	0 (0)	26 (12.6)	<0.001

GV, glucose variability; SSI, superficial site infection. * SSI diagnosis was made according to the CDC definition. † Deep infection was defined as infection not meeting the SSI definition. ‡ Glucose levels were collected at surgery and 1 week after surgery.

The rates of all-cause revisions were significantly higher for high GV patients when compared to the low and medium GV groups ($p = 0.04$). Similarly, high GV patients experienced higher rates of revisions due to infections, although not to a level of statistical significance ($p = 0.09$). Patients in the high GV group had significantly higher mean glucose levels ($p < 0.001$) and were significantly more likely to sustain an event of hypoglycemia ($p < 0.001$), hyperglycemia ($p < 0.001$), and both hypoglycemia and hyperglycemia events ($p < 0.001$) (Table 2).

4. Discussion

To the best of our knowledge, this is the largest study to assess the association between postoperative GV and surgical outcomes of patients with DM undergoing fixation of a hip fracture. The main findings of this study are as follows: (1) increased postoperative GV is associated with increased one-year mortality, although not clinically significant; and (2) patients with increased GV had increased rates of all-cause revision surgery and a non-significant trend towards increased rates of revisions due to infections.

Glycemic control has been increasingly recognized as an important factor in the management of patients with DM prior to undergoing elective surgery [6,13,22]. Moreover, there has been increasing evidence that postoperative glycemic control has an important role in the development of postoperative adverse events and requires further investigation [11,14]. Previous studies have shown that increased postoperative GV is associated with higher rates of mortality following hip fracture surgeries and that it may help in predicting postoperative complications. Long et al. [16] found that perioperative GV is an independent predictor of mortality in patients with diabetes undergoing surgical procedures for a hip fracture. Ashkenazi et al. [15] showed that higher GV in the postoperative period is associated with increased rates of mortality in diabetic patients following arthroplasty for hip fractures. Similarly, the findings of this current study suggest that increased GV is associated with increased all-cause revision rates. Additionally, increased GV was associated with increased one-year mortality, although there was a lack of statistical significance, most likely due to smaller sample sizes and limited statistical power. We assume that a larger sample size would provide statistical significance. Although our study findings did not demonstrate any other significant differences between the GV groups, they did reveal a trend towards worse outcomes in the high GV group for all of the measured outcomes, including mortality and readmission, emphasizing the importance of GV as a potential modifiable risk factor for mortality in this population. These findings contribute to the limited evidence on postoperative GV in patients undergoing hip fracture fixation, substantiating its potential use as a perioperative target to improve glycemic control and patient outcomes. Given the limited information currently available, it is important for healthcare providers to consider the potential impact of increased GV on their patients; the effective management of glucose variability involves a balanced diet, adequate sleep, and the proper monitoring and management of blood glucose levels, including the regular monitoring and adjustment of insulin doses, which can help minimize the effects of GV and reduce the risk of adverse outcomes [12]. Importantly, the clinical importance of postoperative GV is still debatable, as the association between the GV and adverse events is not necessarily causative, and other risk factors, such as age and BMI, can serve as confounding factors. Nevertheless, several risk factors, including age, BMI, and comorbidity index, were comparable between the study groups, partially addressing this issue. Moreover, even if not causative, this association has a clinical impact, as surgeons can use GV data to decide whether a patient needs closer follow-up and further postoperative monitoring. Regardless, additional high-quality research is needed to fully understand the relationship between glycemic variability and mortality and to develop effective strategies for managing glycemic control in patients with diabetes undergoing surgery.

The study has several limitations that need to be mentioned. Firstly, its retrospective design may introduce selection bias and bias due to a lack of follow-up. Additionally, laboratory values were only measured on postoperative days 1 and 3, and glucose levels were further measured based on clinical needs; as a result, some patients with uncontrolled glucose may have gone unnoticed or been considered to be under glycemic control, which could have affected the results. Furthermore, the findings of our study did not include preoperative HbA1c levels. Although the use of HbA1c for determining perioperative glycemic control has been questioned, there are several reports showing that patients with markedly elevated HbA1c levels are at increased risk of complications [17,23], which could have affected our results.

5. Conclusions

For diabetic patients undergoing hip fracture fixation, higher postoperative GV was associated with increased rates of all-cause revision surgery and may be associated with increased mortality, readmission rates, and surgical site infections. The glucose levels of diabetic patients must be meticulously monitored and controlled in the postoperative period in an effort to contain the sequelae associated with elevated GV and in order to identify patients in need of closer observation and follow-up.

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Data Availability Statement: Dataset available on request from the authors. The raw data supporting the conclusions of this article will be made available by the authors on request.

Conflicts of Interest: The authors declare that they have no conflicts of interest.

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