The Optimal Time for Blood Glucose Measurements in Patients Who Underwent Primary or Revision Total Joint Arthroplasty: A Retrospective Review

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Abstract

Background Perioperative hyperglycemia is a risk factor for postoperative complications after total joint arthroplasty (TJA). However, the most optimal timing to detect blood glucose and the extent of elevation of postoperative glucose remain unknown. Our study investigated differences in perioperative blood glucose fluctuations between primary and revision groups to determine optimal timing for glycemic control. Methods We retrospectively evaluated medical records of 1,788 TJA patients from October 2013 to November 2018. We examined blood glucose values collected within 6 days perioperatively. Each time point's findings were evaluated with descriptive statistics. Glucose variability was assessed by coefficient of variation (CV). Differences in glucose levels were compared between primary and revision groups. Results The final cohort included medical records of 1,480 patients (1,417 primary, 63 revision). Mean glucose values were highest on postoperative day 1 (117±35 and 132±50 mg/dL) in primary and revision groups, respectively (P <0.001). Postoperative day 1 included the highest number of hyperglycemic patients (glucose >100 mg/dL) with 66.4% and 75.5% in primary and revision groups, respectively. The CV of primary and revision group nondiabetic and diabetic patients was 6.85% and 9.02% and 12.83% and 15.31%, respectively. Conclusions Postoperative day 1 was the most sensitive time for glucose control. Hyperglycemia occurred on postoperative day 1 in most patients who underwent TJA in both groups. Primary group diabetics and revision group had higher postoperative glycemic fluctuations than primary group nondiabetics. Our results reveal the need for specialized protocols for clinicians to detect and monitor hyperglycemia in patients under different situations.

Background

Total joint arthroplasty (TJA) is a surgical procedure to treat late the stage of osteoarthritis, and to improve the quality of life for patients. However, more complications have been diagnosed than before, as the number of TJA surgeries has increased. Common complications include prosthetic joint infection (PJI), aseptic implant loosening, surgical site infection (SSI), and venous thromboembolism, which increase the cost of care, prolong hospital stays, and compromise patient outcomes. Recently, more surgical and patient-related risk factors for postoperative complications, including age, obesity, malnutrition, diabetes mellitus (DM), blood transfusion, prior infection, and hyperglycemia, were confirmed by several studies[1–3]. Hyperglycemia is a significant risk factor for postoperative complications in TJA, even independent of diabetes status[1, 3, 4]. Many experts attempted to determine a threshold for glycemic control. Kheir et al.[1] investigated the impact of postoperative blood glucose levels on PJI after elective TJA and determined a threshold for glycemic control. They found a linear relationship between postoperative blood glucose levels and PJI with an optimal cutoff of 137 mg/dL. Specifically, researchers attempted to determine the best time point to monitor glucose levels to obtain timely control of glucose. Nathan et al.[5] suggested that glucose should be measured within the first 24 hours after TJA. In their study, they found that 9 PM on the night of surgery was the most sensitive time for detecting hyperglycemia in both diabetic and nondiabetic patients. Efforts should be made to control glucose levels to a steady state, and to reduce the fluctuations of blood glucose levels. Understanding the fluctuations of glucose levels is crucial for clinicians to manage the blood glucose level properly, to decrease the variability and fluctuations of blood glucose in a timely manner, and eventually, to reduce the rate of complications postoperatively. Though some researchers demonstrated the variability of glucose levels in TJA patients during the perioperative period, and the acute fluctuations of blood glucose level within 24 h after surgery, an exact conclusion regarding the most optimal timing to detect blood glucose, and to what extent glucose values would become elevated postoperatively in TJA patients remains unknown. Therefore, we investigated the variability and fluctuations of blood glucose levels within 6 days postoperatively, and compared primary TJA with revision patients by examining the blood glucose levels on multiple days postoperatively, to determine the differences and variabilities of the blood glucose values. Additionally, we aimed to determine the optimal time for detecting the blood glucose, which can aid clinicians to control blood glucose levels in a timely manner in clinical practice.

Methods

This retrospective study involved the review of 1,788 medical records of patients who were admitted to the orthopedic department of our hospital from October 2013 to November 2018. Inclusion criteria were as follows: patients who underwent total knee arthroplasty (TKA) or total hip arthroplasty (THA) as either primary surgical procedure or revision. Following our institutional review board's approval, we collected data from all patients whose blood glucose levels were recorded at different times preoperatively and postoperatively. The requirement for informed consent was waived due to the retrospective design of our study. The exclusion criteria were as follows: (1) preoperative diagnosis of rheumatoid arthritis, ankylosing spondylitis, and malignancy; (2) no surgical record; (3) lack of blood glucose values within 6 days either preoperatively or postoperatively. Finally, the medical records of 1,417 primary and 63 revision TJA patients were included in the study (**Fig. 1**). Demographic information (age, sex, type of procedure, date of administration, date of discharge), comorbidities (malignancy, rheumatoid arthritis, ankylosing spondylitis, DM, and hypertension), operative details (type of anesthesia, date of surgery performed, start time, end time, and duration of surgery), and complications (PJI, periprosthetic osteolysis, aseptic loosening,

periprosthetic fracture, dislocation, and SSI) were extracted from the medical records. The SSI and PJI were based on the Centers for Disease Control (CDC) definition and the Musculoskeletal Infection Society (MSIS) criteria [6, 7]. The medial parapatellar approach was used for TKA, and the posterior lateral approach was used for THA.

Blood glucose values were based on serum glucose levels in venous samples which were recorded within six preoperative and postoperative days. All glucose samples were drawn in the morning (around 7 AM) after the patient underwent nighttime fasting for a minimum of 6 hours. The diagnosis of DM was based on the past medical history or the ADA criteria regarding the blood glucose levels after admission. DM patients were supplied diabetic diets while others were supplied routine diets by hospital canteen. All the patients were restricted solids for at least 8 hours and liquids for 2 hours before surgery. Either general or spinal anesthesia was performed. Postoperatively, some patients received analgesic pump. Within 6 hours, all patients were given lactated ringers or glucose saline intravenously. In case of liquid-induced hyperglycemia, supplementary insulins were added to glucose liquid in diabetic patients. DM patients were initiated insulin sliding scale or antidiabetic drugs. The fixed amount of carbohydrate diet was supplied for DM patients at each meal by hospital canteen. Generally, DM patients were under regular fingertip glucose level monitoring and the adjustment of oral medications or insulin according to the glucose level. Nonsteroidal anti-inflammatory drugs, for example, loxoprofen or celecoxib, were used to relieve pain postoperatively. Routine serum blood tests were ordered for all patients determined by chief doctors and the situation of patients. After discharge, patients underwent regular follow-up according to the schedule made by our department.

Many studies have demonstrated the association of blood glucose levels (with certain thresholds) and PJI. Therefore, we classified the glucose values into several intervals to identify the hyperglycemic state of each patient at each time point based on previous experiments[1, 4, 5, 8-12]. According to the definition from the American Diabetes Association (ADA)[8] and the data published by Nathan et al.[5], the normal status was defined as fasting blood glucose values < 100 mg/dL. Glucose values between 100 mg/dL and 126 mg/dL were defined as elevated hyperglycemia. The other three separate thresholds of serum glucose values were used to define hyperglycemia: > 126 mg/dL as strict, >137 mg/dL as intermediate, and >180 mg/dL as lenient[1, 4, 9-12]. Glycemic variability was evaluated by calculating the coefficient of variation (CV), which is the ratio of the standard deviation to the mean of blood glucose levels[13, 14].

Statistical Analysis

The patients were divided into primary and revision groups. For the demographic features, age differences were analyzed with the use of an independent t test, and categorical variables were calculated with use of a chi-square test. The Mann-Whitney U test was applied for the divergence in glycemic status. The distribution of glucose levels (mean, standard deviation, median, range, and hyperglycemic intervals) was performed in each time point for the primary and revision groups. The variability and fluctuations of blood glucose values were revealed by boxplots that included the line of mean and CV (defined as the ratio of the standard deviation to the mean of blood glucose levels). To evaluate the differences between each pair of time points, we used a Kruskal-Wallis H test for comparisons, and the *P* value was adjusted by Bonferroni analysis. The Mann-Whitney U test was then used to compare the blood glucose values between the primary and revision groups, between patients with and without DM. Variables with a *P* value of <0.05 were considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corporation, Armonk, New York).

Results

Demographic features and general glycemic status

After applying the inclusion and exclusion criteria, medical records of 1,480 patients (1,417 primary and 63 revision) were included in our study. The demographic features and glycemic status of the patients are shown in **Table 1**. The average age (and SD) of primary and revision patients was 63.3 ± 12.3 years and 65.5 ± 11.1 years, respectively. There were no significant differences in age and sex ratio between the groups (*P* = 0.17 and *P* = 0.10, respectively). In the revision group, 84.1% of patients were diagnosed with a hip problem. In contrast, half of the patients in the primary group were diagnosed with a hip problem (*P* < 0.001). There were 184 (13.0%) and 12 (19.0%) primary and revision patients, respectively, with a previous diagnosis of DM. The distribution of DM was similar between the groups (*P* = 0.17). For hypertension and anesthesia, no significant differences were revealed in the primary and revision groups. In the primary patients, the mean (± SD) blood glucose values were 93 ± 26 mg/dL preoperatively, 109 ± 32 mg/dL postoperatively, and 103 ± 31 mg/dL in total. For the revision group, the mean blood glucose values were 94±28 mg/dL preoperatively, 121±45 mg/dL postoperatively, and 111±42 mg/dL in total. Significant differences were noted between the primary and revision patients for glucose levels after surgery (*P* = 0.01).

Table 2 and Fig. 2 show the indications for revision surgery. Most patients required revision surgery due to osteolysis or aseptic loosening (43/63). The remaining patients required revision surgery for dislocation (9/63), PJI (7/63), SSI (2/63), and periprosthetic fracture (2/63).

Fluctuations of perioperative blood glucose values

Primary total joint arthroplasty patients

Among the primary total joint arthroplasty patients, the mean glucose values measured in the preoperative days (PRD) were 93±26 mg/dL. The mean glucose values of postoperative days (POD) were 109±32 mg/dL (POD1~6: 117±35, 104±26, 105±29, 100±24, 96±21, 99±38 mg/dL, respectively) (**Table 3.1**). The mean glucose levels at POD1 were significantly higher than those at all other time points ($P < 0.001$). There were no significant differences for the mean glucose values postoperatively between PODs 2 and 3, 3 and 4, 4 and 5, or 5 and 6 (**Table 4**). From PODs 1 to 6, the mean glucose levels gradually declined and became stable (CV%: 7.14) (**Table 3.1**, **Fig. 3A**). The mean glucose levels at POD1 in nondiabetic patients were significantly higher than those at all other time points ($P < 0.001$). There was no significant difference for the mean glucose levels postoperatively between PODs 2 and 3, 3 and 4, 4 and 5, or 5 and 6 (**Table 4**). From PODs 1 to 6, the mean glucose levels gradually declined and stabilized (CV%: 6.85) (**Table 3.2**, **Fig. 3B**). Further examination of the primary TJA group revealed that diabetics, compared to nondiabetics (NDM), had mean glucose values at POD1 that were only significantly higher than those measured preoperatively ($P < 0.001$) (**Table 4**), and variability of the glucose values was higher in the diabetic patients within the primary group (CV%: 9.02) (**Table 3.2**, **Fig. 3C**).

We further classified patients with hyperglycemia into four groups (> 100 mg/dL as elevated, > 126 mg/dL as strict, >137 mg/dL as intermediate, and >180 mg/dL as lenient). POD1 had the highest number of hyperglycemic patients, with glucose values of > 126 mg/dL, accounting for 29.4% of the patients. POD1 also had the highest number of patients (37.0%) in slightly elevated hyperglycemic status. For POD1, a total of 66.4% of patients in the primary group had hyperglycemic status (> 100 mg/dL), far more than other days (**Table 3.1**). When the primary patients were further grouped by DM status, 63.7% of NDM and 85.0% of DM patients were hyperglycemic (> 100 mg/dL) on POD1 (**Table 3.2**).

Revision surgery patients

In the revision TJA group, the mean glucose values on POD1 (132±50 mg/dL) were significantly higher than on the PRDs ($P < 0.001$). There were no significant differences for the mean glucose levels between PODs 2 and 3, 3 and 4, 4 and 5, or 5 and 6 (**Table 4, Table 5.1**). The CV was 8.82% postoperatively and the glucose values displayed large fluctuations (**Table 5.1, Fig. 4A**). The mean glucose values at POD1 (121±36 mg/dL) in revision surgery NDM patients were significantly higher than that in PRDs ($P < 0.001$). There was no significant difference for the mean glucose levels postoperatively between PODs 2 and 3, 3 and 4, 4 and 5, or 5 and 6 (**Table 4, Table 5.2**). For the NDM group, PODs 1 to 6, the CV was 12.83% and the glucose values displayed large fluctuations (**Table 5.2, Fig. 4B**). However, compared to the NDM group, there were no significant differences for glucose values between each time point, and the variability of glucose values was higher in the DM group (CV%: 15.31) (**Table 4, Table 5.2, Fig. 4C**).

The highest number of hyperglycemic revision group patients (75.5%), with glucose values of > 100 mg/dL, was on POD1, which was far higher than that on the other days (**Table 5.1**). When stratified by diabetes status, 69.1% of NDM and 100% of DM patients were hyperglycemic (> 100 mg/dL) on POD1 (**Table 5.2**).

Comparison between the groups

Primary vs. Revision Groups

The glucose values of the primary and revision groups were separately collected and compared (primary vs. revision, mg/dL): PRD: 93±26 vs. 94±28; POD1: 117±35 vs. 132±50; POD2: 104±26 vs. 110±39; POD3: 105±29 vs. 107±26; POD4: 100±24 vs. 108±33; POD5: 96±21 vs. 116±56; and POD6: 99±38 vs. 126±46. For the PRDs, the glucose levels of both primary and revision groups were within normal limits. Glucose levels exhibited greater elevations in the revision compared to the primary group after surgery, but the difference was statistically significant only for POD1 ($P = 0.018$) (**Table 6.1, Fig. 5**). Additionally, the revision group had a larger population of hyperglycemic patients, with glucose levels (> 126 mg/dL) on POD1 (strict, intermediate, lenient hyperglycemia: 29.4%, 19.7%, 5.0% in primary group vs. 49.1%, 30.2%, 11.3% in revision group), and greater glucose variability postoperatively (CV%: 7.14 in primary group vs. 8.82 in revision group) (**Table 3.1, Table 5.1**).

Diabetic vs. Nondiabetic Groups

The mean glucose values were higher in patients with DM than for NDM patients for each time point in the primary and revision groups (**Table 6.2**). Among all patients, significant differences in glucose values were demonstrated for all perioperative time points ($P < 0.05$). Except for POD6, the glucose values were statistically significant for each time point in primary group patients ($P < 0.05$). For the patients

who underwent revision TJA, significant differences in glucose values were exhibited in PRD, and PODs 1, 4, 5, and 6 ($P < 0.05$) (**Table 6.2, Fig. 6A-C**).

Discussion

In our study, we extended the glucose monitoring through 6 days after TJA. We found that POD1 had the highest blood glucose levels perioperatively. The majority of hyperglycemic patients were identified on the 1st day after TJA surgery; therefore, investigating the blood glucose levels at this time point may be warranted. Also, compared to that in the NDM patients in the primary TJA group, the glucose variability was greater in patients with DM within the primary group and DM or NDM patients in the revision group, indicating that perioperative glucose assessment throughout whole week was useful for those patients.

The clear association between postoperative glucose levels and postoperative complications has been supported by many studies, in which some of the former studies considered diagnosis of DM as a critical risk factor for postoperative complications including PJI, SSI, and aseptic implant loosening[1, 3, 15-17]. Hyperglycemia, which is independent from DM, was considered to be a risk factor for perioperative complications of surgical procedures including PJI by previous studies[2], is receiving more attention in the clinic [1, 5, 9, 10, 18]. Notably, the literature shows that examining the blood glucose level and assessing glucose variability are more effective and precise for predicting postoperative infections[3]. Some articles reported that early postoperative glucose control was a predictor of nosocomial infections[19, 20]. Specifically, Varady et al.[5] examined the blood glucose values within POD1 in patients who underwent TJA, and they found that 9 PM on the night of surgery had the highest number of hyperglycemic patients, suggesting that this time point may be the most sensitive for detecting hyperglycemia in both DM and NDM patients. However, the above studies lacked multiple consecutive monitoring of postoperative glucose for over 1 week after the surgical procedure and there is no consensus regarding how glucose levels vary perioperatively. Different from their data, which are limited to within 24 h, our study included not only the observation of the glucose fluctuations in PRDs, but also for 6 days postoperatively. In our study, the peak of blood glucose levels appeared in the first 24 h after surgery in the primary and revision groups. Our findings suggest that the blood glucose values for TJA patients remain within normal limits before surgery and increase substantially within the first days of TJA, and then postoperative glucose values decrease mildly and tend toward normal in the NDM patients within the primary group. CDC published a guideline in 2017, which recommended that for all patients regardless of DM status, it is better to control blood glucose levels to less than 200 mg/dL during surgery[6]. Moreover, previous studies reported the cutoff of glucose levels to minimize the risk of postoperative complications, suggesting that clinicians have better control over glucose levels below the cut off value. For example, Kwon et al.[11] studied the relationship of perioperative hyperglycemia and insulin administration on outcomes in general surgery. They revealed that glucose levels controlled under 130 mg/dL had promising outcomes. Kheir et al.[1] found that hyperglycemia was associated with periprosthetic joint infection, with an optimal cutoff of 137 mg/dL. Mraovic et al.[9] investigated the association between hyperglycemia and infection that requires surgical intervention after TKA and THA. They found that postoperative blood glucose values of more than 140 mg/dL increased more than two-fold the risk of infection in TJA patients. Kremers et al.[4] demonstrated a significantly higher risk of PJI among patients with perioperative hyperglycemia (blood glucose value > 180 mg/dL). In our study, we classified hyperglycemia into different levels and found that the total number of hyperglycemic patients was the highest on POD1 among all measured days. Therefore, for both the primary and revision groups, the blood glucose values increased significantly on POD1, and POD1 also had the largest population of hyperglycemic patients, indicating that POD1 was the most critical and sensitive day for clinicians to monitor blood glucose. On POD1, the glucose values were higher than the cut off values for many patients, which suggested an increased risk of postoperative complications. Doctors should be aware that monitoring and gaining control of glucose values on POD1 can minimize the time the patient spends in a hyperglycemic status, which can eventually decrease postoperative complications and improve clinical outcomes.

Effective management of hyperglycemia can help to improve surgical outcomes in patients with TJA[21]. Several studies suggested that feasible glycemic control is beneficial to reduce postoperative mortality, length of stay, and complications[22-24]. Additionally, glycemic control is considered to be a critical procedure to decrease the risk of adverse outcomes after surgery. Understanding blood glucose variability could help doctors to monitor and control blood glucose at a stable level[3]. The principal step is to determine which perioperative day is best to monitor and strictly control glucose levels. However, the best time point to control the blood glucose remains controversial. Continuous glucose monitoring (CGM) is used to obtain continuous measurements of perioperative glucose values for the patient through a specific device which more readily facilitates the identification of blood glucose fluctuations[25, 26]. CGM of blood glucose was reported by some studies in several fields of medicine, including orthopedic[27, 28]. Maeda et al.[29] performed CGM analysis in 20 patients who underwent THA or TKA, and found that higher blood glucose levels, and larger fluctuations were detected postoperatively, especially until POD2. Shohat et al.[3, 15] focused on the associations between hyperglycemia and adverse outcomes in patients who underwent orthopedic surgery and TJA. They demonstrated that higher glucose variability in the postoperative period was associated with increased rates of in-hospital complications, including infection. In our study, from PODs 1 to 6, the mean glucose levels

gradually declined and became stable in nondiabetic patients in the primary group. For diabetics in the primary and DM or NDM in revision groups, the glucose values varied dramatically postoperatively. Significantly greater fluctuations were seen in patients with DM or in the revision group. Unlike the patients without DM in the primary group, patients with DM or in the revision group should undergo careful monitoring of the blood glucose level and receive more attention to identify the fluctuations of blood glucose, suggesting that clinicians should strictly monitor the glucose level throughout whole postoperative week.

In patients with variable situations or characteristics, the glucose level could exhibit different types of variations. For the primary TJA, Varady et al.[5] found that 9 PM on the night of surgery had the highest percentage of hyperglycemic patients. Also, researchers focused much on the glucose state and control of glucose levels for DM patients, and neglected to monitor the hyperglycemic status in patients without DM. Thus, patients without DM may have experienced more infections related to their elevated blood glucose levels, whereas DM patients only showed a trend toward significance[1]. However, no solid conclusion regarding the glucose variability in diabetic and revision patients can be drawn. In our study, we extended our research on diabetic and revision patients, and compared with multivariable statistics that included: a) primary versus revision; b) DM versus NDM. We found that diabetic patients in the primary and revision groups had higher postoperative glucose values. The percentage of hyperglycemic patients in the revision group on POD1 was higher than the primary group. In terms of CV and fluctuations as shown in boxplots, the DM and revision patients had larger fluctuations postoperatively. In NDM patients in the primary TJA group, the majority of patients who were hyperglycemic were identified on POD1 after TJA and the blood glucose tended to stabilize within 1 week postoperatively, indicating that for these patients, we could monitor the blood glucose on POD1 only. However, we suggested that in primary diabetics and revision patients, we should monitor the blood glucose values not only in POD1 but also throughout the whole week after surgery, to get the hyperglycemia in control as early as possible to prevent postoperative complications. The significant differences revealed in these groups have a number of important implications for clinicians to consider, to help gain control over blood glucose levels, and for future research to study the effects on the postoperative blood glucose values. Further, we found a large population of patients with hyperglycemia after surgery that were not diagnosed DM. These patients may be ignored in clinical practice. Therefore, monitoring of blood glucose levels is critical for the patients with high risk, even if they were not diagnosed with DM. For patients with hyperglycemia, who do not have DM preoperatively, this should be taken into consideration to timely control the glucose level under the critical cut off value.

This study prolonged the length of perioperative glycemic measurement time to identify the time point with highest glucose values and determine the most optimal time point for measurement of the blood glucose levels in primary and revision patients with and without DM. Our investigation and findings not only specifically and thoroughly identified glucose status and fluctuations, but also a formula of instruction for clinicians to use to manage blood glucose levels, so the patients can benefit from early glycemic control, and minimize the time that they spend in a hyperglycemic state, decreasing the risk of postoperative complications. To our knowledge, our study is the first to find the optimal day for postoperative measuring by extending nearly a week consecutive monitoring after TJA in a large sample size. Further, a critical feature of this study was the comparison of glucose levels and glucose fluctuations between the multiple factors including primary vs. revision, and DM vs. NDM. However, there were some limitations to this study. First, the information about what each patient ate was not precise. Though dinner is available at a specific time, it is possible that a patient might refused feeding even after dinner was provided, or might have already taken other food before or after dinner. Second, this is a retrospective study conducted at one medical center, reducing the ability of generalizing the findings to other institutions, and limiting us to monitoring blood glucose in standardized frequency. Not all the patients have blood glucose measured at each time point we investigated and HbA1c was unable to record due to the lack of relevant medical information. Prospective studies with measurement of glucose values in a fixed interval for all patients and correlation to HbA1c would be valuable to better document and identify the most proper timing of evaluations. Third, compared to the primary group, the number of patients in the revision group was relatively small. Recruiting more revision patients in a future study would allow for this group to be better represented.

Conclusions

Our study highlights that POD1 had the highest blood glucose levels, and the highest proportion of patients with hyperglycemia perioperatively, which suggested that POD1 may be the most sensitive time to detect hyperglycemia. Greater attention should be paid to the measurement of blood glucose levels of TJA patients frequently after surgery, especially for patients who either had DM or underwent revision surgery, because glucose fluctuations were higher for these patients within 6 days after surgery. Clinicians must be aware of the incidence of perioperative hyperglycemia, especially within the first 24 h after surgery, and strategies may need to be carried out to control glucose levels in order to avoid postoperative complications triggered by hyperglycemia.

Abbreviations

ADA, American Diabetes Association; CDC, Centers for Disease Control; MSIS, Musculoskeletal Infection Society; DM, Diabetes mellitus; NDM, Nondiabetes mellitus; PJI, Prosthetic joint infection; SSI, Surgical site infection; THA, Total hip arthroplasty; TKA, Total knee arthroplasty; TJA, Total joint arthroplasty; POD, Postoperative day; PRD, Preoperative day; CGM, Continuous glucose monitoring; CV, Coefficient of variation; IQR, Interquartile range; SPSS, Statistical Package for the Social Sciences

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of First Affiliated Hospital of Sun Yat-sen University. The requirement for informed consent was waived due to the retrospective design of our study.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

There are no conflicts of interest to declare.

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Authors' contributions

YY, ZZ, PS contributed to the idea and design of the study. YY, BP, GX, WC contributed to data collection, data analysis and drafted the manuscript. All authors contributed to the interpretation of results and manuscript revision. All authors read and approved the final manuscript.

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References

1. Kheir MM, Tan TL, Kheir M, Maltenfort MG, and Chen AF. Postoperative blood glucose levels predict infection after total joint arthroplasty. J Bone Joint Surg Am. 2018;100:1423-31.
2. Eka A and Chen AF. Patient-related medical risk factors for periprosthetic joint infection of the hip and knee. Ann Transl Med. 2015;3:233.
3. Shohat N, Restrepo C, Allierezaie A, Tarabichi M, Goel R, and Parvizi J. Increased postoperative glucose variability is associated with adverse outcomes following total joint arthroplasty. J Bone Joint Surg Am. 2018;100:1110-7.
4. Kremers HM, Lewallen LW, Mabry TM, Berry DJ, Berbari EF, and Osmon DR. Diabetes mellitus, hyperglycemia, hemoglobin A1c and the risk of prosthetic joint infections in total hip and knee arthroplasty. J Arthroplasty. 2015;30:439-43.
5. Varady NH, Schwab PE, Jones T, Collins JE, Fitz W, and Chen AF. Optimal timing of glucose measurements after total joint arthroplasty. J Arthroplasty. 2019;34:S152-S8.
6. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA surgery. 2017;152:784-91.
7. Parvizi J, Zmistowski B, Berbari EF, Bauer TW, Springer BD, Della Valle CJ, et al. New definition for periprosthetic joint infection: From the workgroup of the musculoskeletal infection society. Clin Orthop Relat Res. 2011;469:2992.

8. Chamberlain JJ, Johnson EL, Leal S, Rhinehart AS, Shubrook JH, and Peterson L. Cardiovascular disease and risk management: Review of the american diabetes association standards of medical care in diabetes 2018. Ann Intern Med. 2018;168:640-50.
9. Mraovic B, Suh D, Jacovides C, and Parvizi J. Perioperative hyperglycemia and postoperative infection after lower limb arthroplasty. J Diabetes Sci Technol. 2011;5:412-8.
10. Chrastil J, Anderson MB, Stevens V, Anand R, Peters CL, and Pelt CE. Is hemoglobin A1c or perioperative hyperglycemia predictive of periprosthetic joint infection or death following primary total joint arthroplasty? J Arthroplasty. 2015;30:1197-202.
11. Kwon S, Thompson R, Dellinger P, Yanez D, Farrohki E, and Flum D. Importance of perioperative glycemic control in general surgery: A report from the surgical care and outcomes assessment program. Ann Surg. 2013;257:8-14.
12. King JT, Goulet JL, Perkal MF, and Rosenthal RA. Glycemic control and infections in patients with diabetes undergoing noncardiac surgery. Ann Surg. 2011;253:158-65.
13. Siegelaar SE, Holleman F, Hoekstra JB, and DeVries JH. Glucose variability; does it matter? Endocr Rev. 2010;31:171-82.
14. Rodbard D. Clinical interpretation of indices of quality of glycemic control and glycemic variability. Postgrad Med. 2011;123:107-18.
15. Shohat N, Foltz C, Restrepo C, Goswami K, Tan T, and Parvizi J. Increased postoperative glucose variability is associated with adverse outcomes following orthopaedic surgery. Bone Joint J. 2018;100-B:1125-32.
16. Shohat N, Muhsen K, Gilat R, Rondon AJ, Chen AF, and Parvizi J. Inadequate glycemic control is associated with increased surgical site infection in total joint arthroplasty: A systematic review and meta-analysis. J Arthroplasty. 2018;33:2312-21.e3.
17. Kremers HM, Schleck CD, Lewallen EA, Larson DR, Van Wijnen AJ, and Lewallen DG. Diabetes mellitus and hyperglycemia and the risk of aseptic loosening in total joint arthroplasty. J Arthroplasty. 2017;32:S251-s3.
18. Reategui D, Sanchez-Etayo G, Nunez E, Tio M, Popescu D, Nunez M, et al. Perioperative hyperglycaemia and incidence of post-operative complications in patients undergoing total knee arthroplasty. Knee Surg Sports Traumatol Arthrosc. 2015;23:2026-31.
19. Pomposelli JJ, Baxter JK, Babineau TJ, Pomfret EA, Driscoll DF, Forse RA, et al. Early postoperative glucose control predicts nosocomial infection rate in diabetic patients. JPEN J Parenter Enteral Nutr. 1998;22:77-81.
20. Furnary AP, Zerr KJ, Grunkemeier GL, and Starr A. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. Ann Thorac Surg. 1999;67:352-60; discussion 60-2.
21. Buchleitner AM, Martinez-Alonso M, Hernandez M, Sola I, and Mauricio D. Perioperative glycaemic control for diabetic patients undergoing surgery. Cochrane Database Syst Rev. 2012:CD007315.
22. Simha V and Shah P. Perioperative glucose control in patients with diabetes undergoing elective surgery. JAMA. 2019;321:399-400.
23. Kang ZQ, Huo JL, and Zhai XJ. Effects of perioperative tight glycemic control on postoperative outcomes: A meta-analysis. Endocr Connect. 2018;7:R316-R27.
24. Shohat N, Muhsen K, Gilat R, Rondon AJ, Chen AF, and Parvizi J. Inadequate glycemic control is associated with increased surgical site infection in total joint arthroplasty: A systematic review and meta-analysis. J Arthroplasty. 2018;33:2312-21 e3.
25. Boom DT, Sechterberger MK, Rijkenberg S, Kreder S, Bosman RJ, Wester JP, et al. Insulin treatment guided by subcutaneous continuous glucose monitoring compared to frequent point-of-care measurement in critically ill patients: A randomized controlled trial. Crit Care. 2014;18:453.
26. Keenan DB, Mastrototaro JJ, Voskanyan G, and Steil GM. Delays in minimally invasive continuous glucose monitoring devices: A review of current technology. J Diabetes Sci Technol. 2009;3:1207-14.
27. Madhu SV, Muduli SK, and Avasthi R. Abnormal glycemic profiles by cgms in obese first-degree relatives of type 2 diabetes mellitus patients. Diabetes Technol Ther. 2013;15:461-5.
28. Rasbach LE, Atkins AE, Milaszewski KM, Keady J, Schmidt LM, Volkening LK, et al. Treatment recommendations following 3-day masked continuous glucose monitoring (CGM) in youth with type 1 diabetes. J Diabetes Sci Technol. 2014;8:494-7.
29. Maeda Y, Nakamura N, Tsujimoto T, and Sugano N. Higher blood glucose and larger fluctuations detected postoperatively using continuous glucose monitoring: A preliminary study following total knee or hip arthroplasty. J Exp Orthop. 2019;6:15.

Tables

Table 1
Demographic Features and Glycemic status of Patients Underwent Total Joint Arthroplasty

Group and Variable	Primary	Revision	*P* Value
No. of patients	1417	63	
Age*	63.3±12.3	65.5±11.1	0.17[a]
Sex†			0.10[b]
Female	1012 (71.4%)	39 (61.9%)	
Male	405 (28.6%)	24 (38.1%)	
Joint†			<0.001 [b]
Hip	604 (42.6%)	53 (84.1%)	
Knee	813 (57.4%)	10 (15.9%)	
Diabetes Mellitus†			0.17 [b]
Diabetic	184 (13.0%)	12 (19.0%)	
Nondiabetic	1233 (87.0%)	51 (81.0%)	
Blood pressure†			0.23 [b]
Hypertension	580 (40.9%)	42 (66.7%)	
Nonhyperension	837 (59.1%)	21 (33.3%)	
Anesthesia†			0.28 [b]
Spinal	1032 (72.8%)	43 (68.3%)	
General	385 (27.2%)	20 (31.7%)	
Glycemic status (mg/dL)*			
Preoperation (within 6 days)	93±26	94±28	0.81[c]
Postoperation (within 6 days)	109±32	121±45	0.01 [c]
Total	103±31	111±42	0.55 [c]

TJA, total joint arthroplasty. *Data are presented as the mean ± standard deviation. †Data are presented as the number (percentage) of patients.
[a] *P* value was calculated by independent T test. [b] *P* value was calculated by chi-square test. [c] *P* value was calculated by Mann-Whitney U test.
$P < 0.05$ indicates a significant difference between groups.

Table 2
Indications for Revision Surgery

Diagnosis	Number
Periprosthetic joint infection	7
Osteolysis/Aseptic loosening	43
Periprosthetic fracture	2
Dislocation	9
Surgical site infection	2
Total	63

Table 3.1
Perioperative Glucose Levels of the Primary Total Joint Arthroplasty Population

Day	Cases (n)	Glucose Level (mg/dL)								CV (%)†
		Mean±SD	Median	Range	Normal* (<100mg/dL)	Elevated* (100-126mg/dL)	Strict* (>126mg/dL)	Intermediate* (>137mg/dL)	Lenient* (>180mg/dL)	
PRD	1463	93±26	88	47-367	1133 (77.4%)	229 (15.7%)	101 (6.9%)	69 (4.7%)	20 (1.4%)	
POD1	1158	117±35	110	40-383	388 (33.5%)	429 (37.0%)	341 (29.4%)	228 (19.7%)	58 (5.0%)	7.14
POD2	470	104±26	97	45-227	255 (54.3%)	154 (32.8%)	61 (13.0%)	45 (9.6%)	10 (2.1%)	
POD3	217	105±29	97	67-239	119 (54.8%)	66 (30.4%)	32 (14.7%)	22 (10.1%)	9 (4.1%)	
POD4	205	100±24	94	54-202	132 (64.4%)	46 (22.4%)	27 (13.2%)	18 (8.8%)	4 (2.0%)	
POD5	177	96±21	94	61-238	126 (71.2%)	40 (22.6%)	11 (6.2%)	7 (4.0%)	2 (1.1%)	
POD6	143	99±38	92	52-391	99 (69.2%)	26 (18.2%)	18 (12.6%)	13 (9.1%)	4 (2.8%)	

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
*Data are presented as the number (percentage) of measurement.
†Postoperative glucose variability was assessed using a coefficient of variation (the ratio of the standard deviation to the mean glucose level).

Table 3.2
Perioperative Glucose Levels of Diabetic and Nondiabetic Patients Underwent Primary Total Joint Arthroplasty

Day	Cases (n)	Glucose Level (mg/dL)								CV (%)†
		Mean±SD	Median	Range	Normal* (<100mg/dL)	Elevated* (100-126mg/dL)	Strict* (>126mg/dL)	Intermediate* (>137mg/dL)	Lenient* (>180mg/dL)	
Diabetic										
PRD	194	118±45	109	47-317	81 (41.8%)	53 (27.3%)	60 (30.9%)	45 (23.2%)	14 (7.2%)	
POD1	153	144±47	139	40-364	23 (15.0%)	35 (22.9%)	95 (62.1%)	77 (50.3%)	26 (17.0%)	9.02
POD2	59	132±40	131	58-227	15 (25.4%)	14 (23.7%)	30 (50.8%)	26 (44.1%)	7 (11.9%)	
POD3	29	127±41	115	79-230	10 (34.5%)	6 (20.7%)	13 (44.8%)	8 (27.6%)	5 (17.2%)	
POD4	36	116±35	114	54-202	13 (36.1%)	8 (22.2%)	15 (41.7%)	9 (25.0%)	3 (8.3%)	
POD5	19	113±26	103	83-182	6 (31.6%)	9 (47.4%)	4 (21.1%)	3 (15.8%)	1 (5.3%)	
POD6	17	125±77	101	52-391	8 (47.1%)	4 (23.5%)	5 (29.4%)	5 (29.4%)	2 (11.8%)	
Nondiabetic										
PRD	1269	90±18	86	52-367	1052 (82.9%)	176 (13.9%)	41 (3.2%)	24 (1.9%)	6 (0.5%)	
POD1	1005	113±30	108	58-383	365 (36.3%)	394 (39.2%)	246 (24.5%)	151 (15.0%)	32 (3.2%)	6.85
POD2	411	100±21	97	45-205	240 (58.4%)	140 (34.1%)	31 (7.5%)	19 (4.6%)	3 (0.7%)	
POD3	188	101±24	95	67-239	109 (58.0%)	60 (31.9%)	19 (10.1%)	14 (7.4%)	4 (2.1%)	
POD4	169	97±20	94	65-191	119 (70.4%)	38 (22.5%)	12 (7.1%)	9 (5.3%)	1 (0.6%)	
POD5	158	94±20	90	61-238	120 (75.9%)	31 (19.6%)	7 (4.4%)	4 (2.5%)	1 (0.6%)	
POD6	126	96±28	90	63-306	91 (72.2%)	22 (17.5%)	13 (10.3%)	8 (6.3%)	2 (1.6%)	

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
*Data are presented as the number (percentage) of measurement.
† Postoperative glucose variability was assessed using a coefficient of variation (the ratio of the standard deviation to the mean glucose level).

Table 4
Comparison of Glucose Values Between Adjacent Time Point in Primary and Revision TJA Patients

Group	*P* value*					
	PRD vs. POD1	POD1 vs. POD2	POD2 vs. POD3	POD3 vs. POD4	POD4 vs. POD5	POD5 vs. POD6
Primary						
Nondiabetics	< 0.001	< 0.001	1.000	1.000	1.000	1.000
Diabetics	< 0.001	1.000	1.000	1.000	1.000	1.000
Total	< 0.001	< 0.001	1.000	1.000	1.000	1.000
Revision						
Nondiabetics	< 0.001	0.453	1.000	1.000	1.000	1.000
Diabetics	0.102	1.000	1.000	1.000	1.000	1.000
Total	< 0.001	0.459	1.000	1.000	1.000	1.000

PRD, preoperative day; POD, postoperative day.
**P* value was calculated by Kruskal-Wallis H test and adjusted by Bonferroni analysis.
$P < 0.05$ indicates a significant difference between groups.

Table 5.1
Perioperative Glucose Levels of the Total Revision Joint Arthroplasty Population

Day	Cases (n)	Glucose Level (mg/dL)								CV (%)†
		Mean±SD	Median	Range	Normal* (<100mg/dL)	Elevated* (100-126mg/dL)	Strict* (>126mg/dL)	Intermediate* (>137mg/dL)	Lenient* (>180mg/dL)	
PRD	66	94±28	86	65-265	50 (75.8%)	11 (16.7%)	5 (7.6%)	3 (4.5%)	1 (1.5%)	
POD1	53	132±50	121	76-337	13 (24.5%)	14 (26.4%)	26 (49.1%)	16 (30.2%)	6 (11.3%)	8.82
POD2	17	110±39	101	68-194	7 (41.2%)	6 (35.3%)	4 (23.5%)	4 (23.5%)	1 (5.9%)	
POD3	16	107±26	102	77-184	8 (50.0%)	6 (37.5%)	2 (12.5%)	1 (6.2%)	1 (6.2%)	
POD4	15	108±33	92	74-180	9 (60.0%)	3 (20.0%)	3 (20.0%)	3 (20.0%)	1 (6.7%)	
POD5	11	116±56	97	65-230	6 (54.5%)	3 (27.3%)	2 (18.2%)	2 (18.2%)	2 (18.2%)	
POD6	8	126±46	109	77-189	4 (50.0%)	1 (12.5%)	3 (37.5%)	3 (37.5%)	2 (25.0%)	

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
*Data are presented as the number (percentage) of measurement.
†Postoperative glucose variability was assessed using a coefficient of variation (the ratio of the standard deviation to the mean glucose level).

Table 5.2
Perioperative Glucose Levels of Diabetic and Nondiabetic Patients Underwent Revision Total Joint Arthroplasty

Day	Cases (n)	Glucose Level (mg/dL)								CV (%)†
		Mean±SD	Median	Range	Normal* (<100mg/dL)	Elevated* (100-126mg/dL)	Strict* (>126mg/dL)	Intermediate* (>137mg/dL)	Lenient* (>180mg/dL)	
Diabetics										
PRD	14	117±51	104	70-265	6 (42.9%)	3 (21.4%)	5 (35.7%)	3 (21.4%)	1 (7.1%)	
POD1	11	176±72	158	108-337	0 (0.0%)	2 (18.2%)	9 (81.8%)	7 (63.6%)	3 (27.3%)	15.31
POD2	4	148±54	163	70-194	1 (25.0%)	0 (0.0%)	3 (75.0%)	3 (75.0%)	1 (25.0%)	
POD3	6	111±12	113	90-122	1 (16.7%)	5 (83.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
POD4	4	148±39	160	92-180	1 (25.0%)	0 (0.0%)	3 (75.0%)	3 (75.0%)	1 (25.0%)	
POD5	4	168±65	171	101-230	0 (0.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	2 (50.0%)	
POD6	4	163±32	171	122-189	0 (0.0%)	1 (25.0%)	3 (75.0%)	3 (75.0%)	2 (50.0%)	
Nondiabetics										
PRD	52	88±12	86	65-121	44 (84.6%)	8 (15.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
POD1	42	121±36	111	76-281	13 (31.0%)	12 (28.6%)	17 (40.5%)	9 (21.4%)	3 (7.1%)	12.83
POD2	13	99±27	101	68-176	6 (46.2%)	6 (46.2%)	1 (7.7%)	1 (7.7%)	0 (0.0%)	
POD3	10	104±32	88	77-184	7 (70.0%)	1 (10.0%)	2 (20.0%)	1 (10.0%)	1 (10.0%)	
POD4	11	93±15	90	74-119	8 (72.7%)	3 (27.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
POD5	7	87±15	85	65-112	6 (85.7%)	1 (14.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
POD6	4	88±8	89	77-95	4 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
*Data are presented as the number (percentage) of measurement.
†Postoperative glucose variability was assessed using a coefficient of variation (the ratio of the standard deviation to the mean glucose level).

Table 6.1
Comparison of Glucose Levels Between Primary and Revision Groups

Day	Mean Glucose Level (mg/dL)		*P**
	Primary†	Revision†	
PRD	93±26	94±28	0.811
POD1	117±35	132±50	0.018
POD2	104±26	110±39	0.872
POD3	105±29	107±26	0.542
POD4	100±24	108±33	0.557
POD5	96±21	116±56	0.493
POD6	99±38	126±46	0.089

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
†Data are presented as the mean ± standard deviation.
**P* value was calculated by Mann-Whitney U test. $P < 0.05$ indicates a significant difference between groups.

Table 6.2
Comparison of Glucose Levels Between Diabetic and Nondiabetic Groups in Primary and Revision TJA Patients

Day	Both			Primary			Revision		
	Mean Glucose Level (mg/dL)		*P**	Mean Glucose Level (mg/dL)		*P**	Mean Glucose Level (mg/dL)		*P**
	Diabetic†	Nondiabetic†		Diabetic†	Nondiabetic†		Diabetic†	Nondiabetic†	
PRD	118±46	90±18	<0.001	118±45	90±18	<0.001	117±51	88±12	0.032
POD1	146±49	113±31	<0.001	144±47	113±30	<0.001	176±72	121±36	0.002
POD2	133±41	100±21	<0.001	132±40	100±21	<0.001	148±54	99±27	0.163
POD3	125±38	102±25	<0.001	127±41	101±24	<0.001	111±12	104±32	0.181
POD4	119±36	96±20	<0.001	116±35	97±20	0.002	148±39	93±15	0.018
POD5	122±40	93±19	<0.001	113±26	94±20	<0.001	168±65	87±15	0.012
POD6	132±72	96±27	0.003	125±77	96±28	0.070	163±32	88±8	0.029

PRD, preoperative day; POD, postoperative day; SD, standard deviation.
†Data are presented as the mean ± standard deviation.
**P* value was calculated by Mann-Whitney U test. $P < 0.05$ indicates a significant difference between groups.

Figures

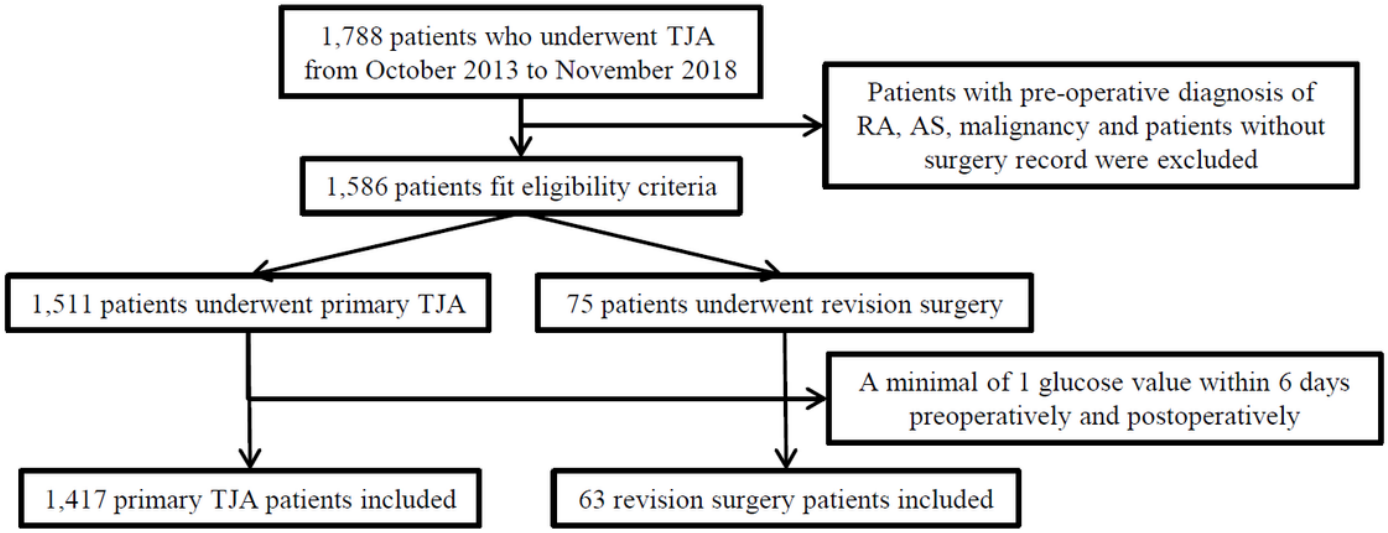

Figure 1

Flow diagram of study selection. TJA, total joint arthroplasty; RA, rheumatoid arthritis; AS, ankylosing spondylarthritis

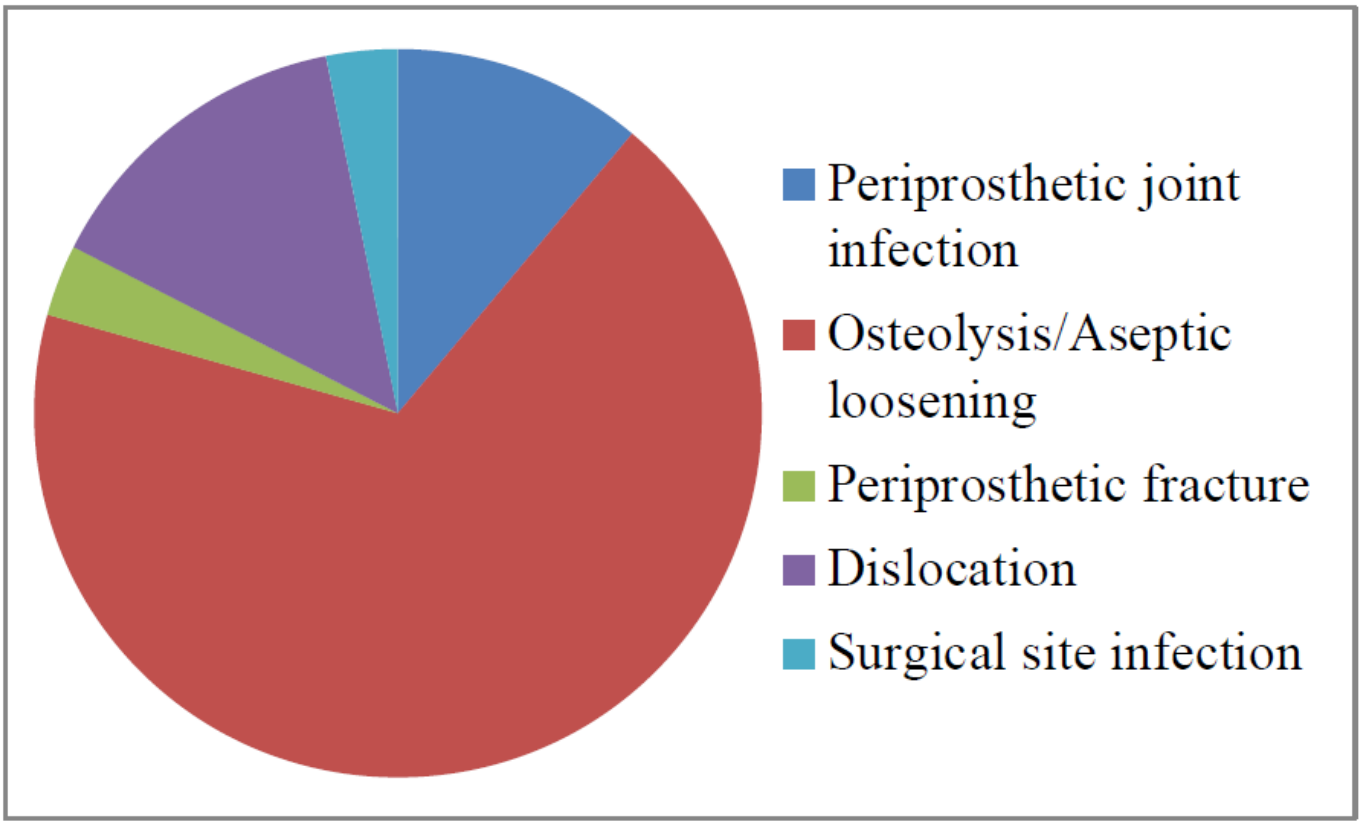

Figure 2

Distribution of indications for revision surgery.

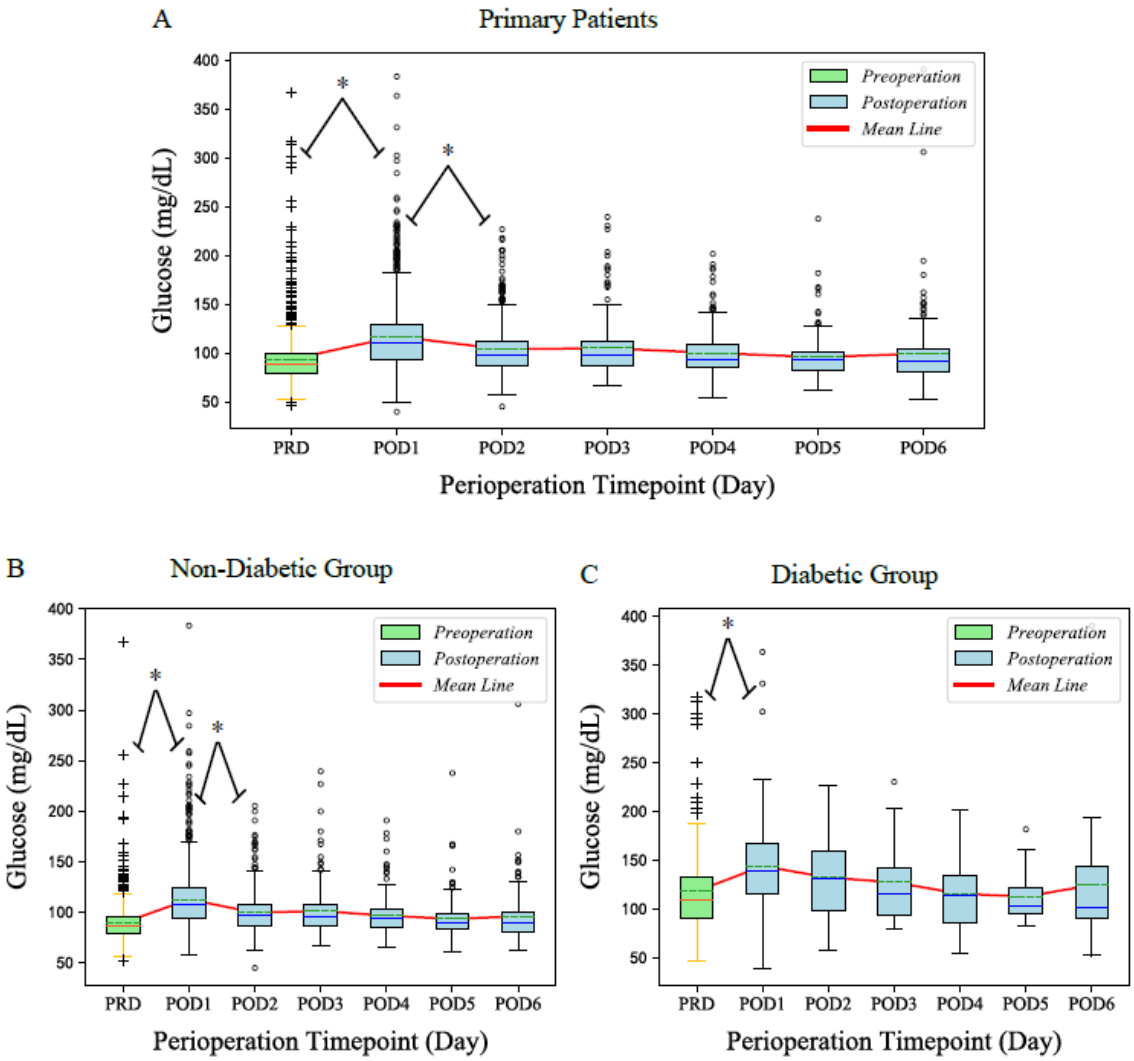

Figure 3

A-C. Boxplots of glucose values for each time point in primary total joint arthroplasty patients. The asterisks indicate a significant difference between groups. The P values was calculated by Kruskal-Wallis H test and corrected by Bonferroni analysis. $P < 0.05$ indicates a significant difference between groups. Solid lines within the box indicate median, top and bottom lines of box equal interquartile range (IQR), whiskers indicate values within 1.5 IQR of the top or bottom of the box, and circle or plus symbols represent outliers. Dashed lines within the box indicate mean and red line represents the fluctuations of mean. PRD indicates preoperative day. POD indicates postoperative day and the number represent day after surgery. Fig. 3A. The fluctuations of glucose values for each time point in primary total joint arthroplasty patients. With the increase of days postoperatively, the blood glucose levels tend to stabilize within 6 days. Fig. 3B. and Fig. 3C. The fluctuations of glucose values for each time point in primary total joint arthroplasty patients grouped by diabetes mellitus. Compared to the nondiabetic group, the fluctuations of blood glucose levels within 6 days postoperatively was larger in the diabetic patients.

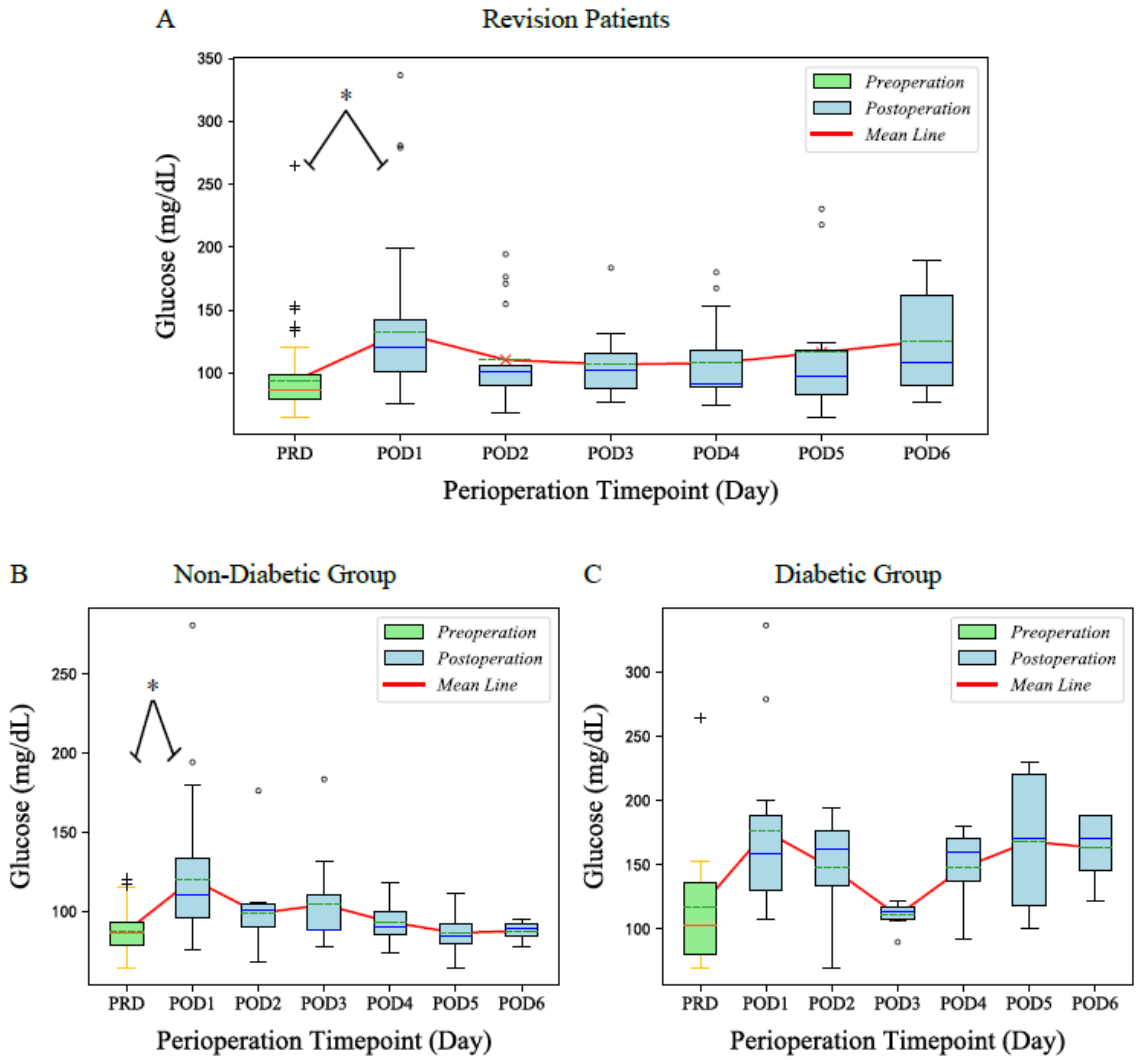

Figure 4

A-C. Boxplots of glucose values for each time point in revision total joint arthroplasty patients. The asterisks indicate a significant difference between groups. The P values was calculated by Kruskal-Wallis H test and corrected by Bonferroni analysis. $P < 0.05$ indicates a significant difference between groups. Solid lines within the box indicate median, top and bottom lines of box equal interquartile range (IQR), whiskers indicate values within 1.5 IQR of the top or bottom of the box, and circle or plus symbols represent outliers. Dashed lines within the box indicate mean and red line represents the fluctuations of mean. PRD indicates preoperative day. POD indicates postoperative day and the number represent day after surgery. Fig. 4A. The fluctuations of glucose values for each time point in revision total joint arthroplasty patients. Fig. 4B. and Fig. 4C. The fluctuations of glucose values for each time point in revision total joint arthroplasty patients grouped by diabetes mellitus. In above groups, the blood glucose values significantly fluctuate within 6 days postoperatively.

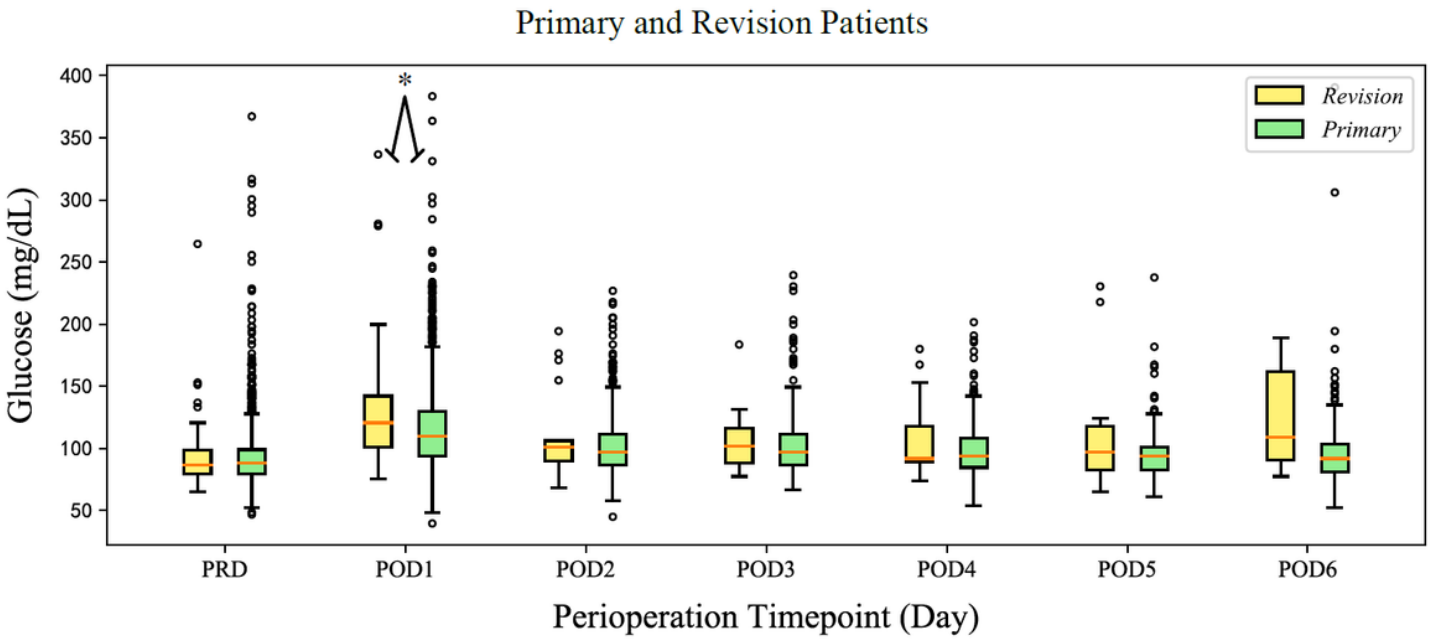

Figure 5

Comparisons of glucose values between primary and revision total joint arthroplasty groups. The asterisks indicate a significant difference between groups. The glucose levels was significantly different in postoperative day 1 between primary and revision groups. The P values was calculated by Mann-Whitney U test. $P < 0.05$ indicates a significant difference between groups. Solid lines within the box indicate median, top and bottom lines of box equal interquartile range (IQR), whiskers indicate values within 1.5 IQR of the top or bottom of the box, and circle symbols represent outliers. PRD indicates preoperative day. POD indicates postoperative day and the number represent day after surgery.

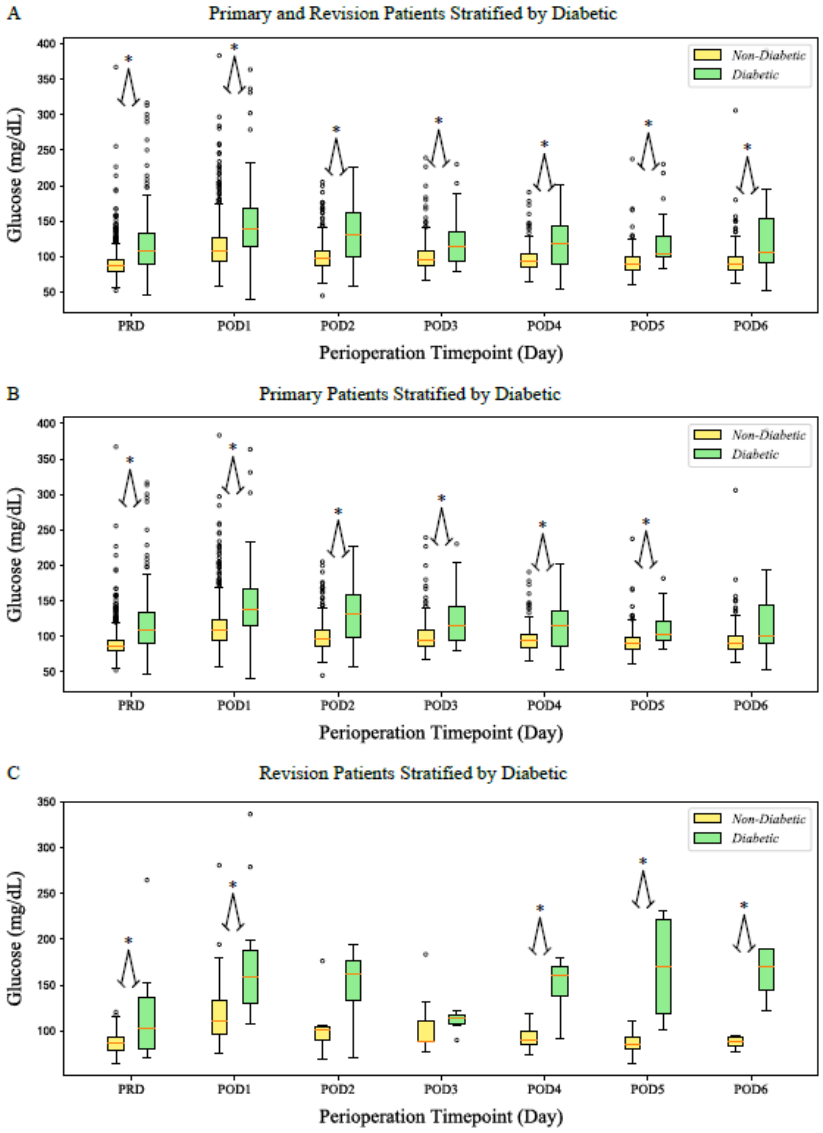

Figure 6

A-C. Comparisons of glucose values between nondiabetic and diabetic groups. The asterisks indicate a significant difference between groups. The P values was calculated by Mann-Whitney U test. $P < 0.05$ indicates a significant difference between groups. Solid lines within the box indicate median, top and bottom lines of box equal interquartile range (IQR), whiskers indicate values within 1.5 IQR of the top or bottom of the box, and circle symbols represent outliers. PRD indicates preoperative day. POD indicates postoperative day and the number represent day after surgery. Fig. 6A. The primary and revision patients. Fig. 6B. The primary patients only. Fig. 6C. The revision patients only. In above groups, most of the diabetic patients had higher glucose levels than nondiabetic patients.