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ORIGINAL RESEARCH

Intertrochanteric Fracture Surgery Patients with Diabetes Mellitus are Prone to Suffer Perioperative Neurological and Endocrine/Metabolic Complications: A Propensity-Score Matched Analysis

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Background: In older adults, the recovery after hip fracture surgery is not always to be well expected due to high risks of adverse outcomes including perioperative complications and mortality. We aimed to evaluate the intertrochanteric fracture (IF) patients with diabetes mellitus (DM) and receiving surgical fixation with intramedullary nail on the perioperative complications, total hospital costs (THC), length of hospital stay (LOS), and mortality.

Methods: In this retrospective cohort study, among 487 consecutive intertrochanteric fracture patients with age over 65 years and treated surgically by using intramedullary nail between Jan. 2015 and Mar. 2020, 353 patients were included, including 81 with DM and 272 without DM. After using propensity-score matched (PSM) analysis, 80 patients remained in each group. The perioperative complications, 30-day, 90-day, 1-year, and 2-year survival rates, THC, and LOS were observed and compared between two groups. Overall survival was compared by Kaplan–Meier method.

Results: No significant between-group differences were found in 30-day, 90-day, 1-year, and 2-year mortality rates, THC, LOS, and other perioperative complications after PSM and McNemar's tests (all $p>0.05$), except for neurological complications ($p<0.004$) and endocrine/metabolic complications ($p<0.001$). At a mean follow-up time of 36.2 months, there were no statistically significant differences between the groups based on the Kaplan–Meier survival curve ($p=0.171$, log-rank).

Conclusion: IF surgery patients with DM are more prone to suffer perioperative neurological and endocrine/metabolic complications and they should be managed individually while being aware of these risks henceforth. Further high evidence clinical trials are needed to expand in DM patients with IF.

Keywords: hip fracture, older adults, perioperative complications, mortality, propensity-score matched

Introduction

Given the rise in population age and the growing number of older people with osteoporosis, the prevalence of hip fractures is currently increasing at an accelerated pace. Such situation is more pronounced in developing countries such as China. In China, the number of older people over 60 years old is as high as 17.9% of the total population by 2018–related number reaching 249 million and the number is up to 450 million by 2050, comprising over thirty percent of the total population.[1] Wang et al[2] also reported in their study that the older population in China comprised nearly two-fifth of all older population worldwide. Intertrochanteric fractures (IF), as one of the major orthopedic clinical problems in the

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hip area, is a common cause of illness, disability, and mortality in older people which leads to heavy socioeconomic pressure on society.

Previous literature indicates that the prognosis for these patients is generally poor because of preexisting severe comorbidities, delay of surgery, anemia, and adverse reactions following blood transfusion, which is related to perioperative morbidity and mortality.[3–9] As one of the major comorbidities, diabetes mellitus (DM) is a worldwide epidemic with a devastating impact on multiple organ systems. Previous studies have reported that DM not only has impacts on fracture risk and bone healing procedure but also affects cardiovascular and renal systems.[10,11] It also has been reported that DM has a significant role in decreasing disability and survival rates in elderly hip fractures.[12]

To the best of our knowledge, multiple factors including surgical delay, American Society of Anesthesiologists grade (ASA), anemia, anesthesia type, and blood transfusion are associated with adverse outcomes, making it difficult to analyze the direct relationship between DM and adverse outcomes following IF fracture surgery when considering these potential confounders. In addition, a substantial proportion of previous studies[12–14] have shown that DM patients are prone to functional impairment while others[15,16] have suggested these patients are not particularly associated with adverse outcomes. However, studies on the effects of DM on perioperative complications and mortality in older patients with IF are still lacking. The aim of this study was to evaluate the IF surgically treated patients combined with DM on the perioperative complications and mortality.

Patients and Methods

Study Design, Participants and Groups

The population for this analysis comprised all enrolled patients over 65 years presenting with IF at a single Level I trauma center in China between Jan. 2015 and March. 2020 who complied with the study inclusion and exclusion criteria. We included hip fracture patients who were 65 years or older, had an admission delay <48 hours, underwent hip surgery by using proximal femoral nail anti-rotation (PFNA), and received a minimum of one-year follow-up. Patients who had multiple fractures or injuries or pathological or open hip fractures, received conservative treatment due to severe comorbidities or refused surgery were excluded. Patients were retrospectively assigned to two groups according to DM comorbidity: group A with DM and group B without DM. According to WHO 2019 criteria, DM is diagnosed when HbA1c is 6.5% or greater or antidiabetic medicines or insulin are currently being taken. That is, patients who use insulin or noninsulin pharmacologic methods to control their diabetes were categorized as patients with DM, while patients without DM were defined as patients who either have no history of diabetes or currently are using only diet modifications to control their diabetes. The protocol for the research project has been approved by the institutional review board (IRB) of Binzhou People's Hospital. The present study conforms to the Declaration of Helsinki. All patients involved gave informed consent and all data were anonymized before the analysis to safeguard patient privacy.

Patient characteristics were extracted as follows: gender, age, age group (65–69, 70–79, and 80–89), body mass index (BMI, normal with BMI<24 kg/m2, overweight with 24≤BMI<28 kg/m2 and obesity with BMI≥28 kg/m2), injury mechanism, fracture type (stable or unstable according to the AO/OTA classification), ASA, surgical delay, anesthesia type (general anesthesia or regional anesthesia), surgery duration, intraoperative blood loss, and rate and volume of transfusion.

Outcome Assessments

Data regarding total numbers of antidiabetic and therapy medications including insulin, diet, and oral antidiabetic drugs were collected. Totally, we found that two-third of patients were oral antidiabetic users, whereas one-third received insulin. The follow-up started at the date of enrollment in the cohort and the endpoint was the date of death or the end of the study, whichever came first. Time and the leading cause of death were recorded. Then, 30-day, 90-day, 1-year, and 2-year survival states and perioperative complications were identified. The perioperative complications were recorded as severe complications (consisting of pulmonary embolisms, sudden cardiac death, stroke, acute myocardial infarction, acute cerebral infarction, heart failure, and respiratory failure, etc.), pulmonary complications (consisting of pulmonary infection, respiratory insufficiency, pleural effusion, and atelectasis, etc.), cardiac complications (consisting of new-onset cardiac arrhythmia, ischemic heart disease, hemodynamic instability, and cardiac dysfunction, etc.), neurological complications (consisting of transient ischemic attack and delirium, etc.), hematological complications (consisting of deep vein thrombosis and anemia, etc.) and endocrine/metabolic complications (consisting of stress hyperglycemia, electrolyte disorder, hypoproteinemia, and metabolic or endocrine disturbances, etc.). We also recorded total hospital costs (THC) and length of hospital stay (LOS) for analysis.

Statistical Analysis

The continuous variables were evaluated for normality by using the Shapiro–Wilk test. The data were reported as frequency and percentage for categorical variables and as mean and standard deviation (SD) for continuous variables. To compare these data, we used *t*-test and chi-square for continuous and categorical variables, respectively. Otherwise, nonnormally distributed groups were presented as the median (interquartile range) and compared by Mann–Whitney *U*-test. To minimize selection bias and potential confounding effects, we carried out adjustments for differences in baseline characteristics between the two groups utilizing propensity score matching (PSM) by using a 1:1 ratio. Logistic regression analysis using covariates including gender, age, age group, BMI, injury mechanism, fracture type, ASA, surgical delay, anesthesia type, surgery duration, intraoperative blood loss, and rate and volume of transfusion was used to obtain the propensity-score and performed via the caliper matching method with the value of calipers limited to 0.04. After PSM, McNemar's tests were used to examine the association of DM with perioperative complications and mortality. All data analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM, Armonk, NY, USA). The *p*-value of <0.05 was considered to be statistically significant.

Results

From Jan. 2015 and Mar. 2020, a total of 487 consecutive IF patients were screened and assessed for eligibility to enroll. A total of 134 patients were eliminated by the exclusion criteria. Among these, 21 patients were under the age of 65 years; 39 patients received conservative treatment; 46 patients had an admission delay >48 hours; 5 patients had multiple fractures or injuries, pathological or open hip fractures; then 23 patients were lost to follow-up. Finally, 353 patients, including 81 in group A with DM and 272 in group B without DM met our inclusion and exclusion criteria (Figure 1).

The baseline characteristics of patients in the two groups are summarized in Table 1. Almost one-quarter of fractures (22.9%, n = 81) with DM compared to three quarters (77.1%, n = 272) without DM included. The majority of patients (71.6% in group A and 63.2% in group B) were female and aged over 70. Most of the patients were classified as ASA class II–IV. Other patient characteristics were statistically equivalent between both groups including BMI, injury mechanism, anesthesia type, surgery duration, intraoperative blood loss, and rate and volume of transfusion. Besides, characteristics including the ASA grade ($p<0.001$) and surgical delay ($p=0.009$) were significantly different between the two groups. After PSM, there were 80 matched patients in each group, and all the baseline characteristics were balanced between the two cohorts (Table 1).

Pre-matching and post-matching results, including perioperative complications, and 30-day, 90-day, 1-year, and 20-year mortality, are shown in Table 2. The statistical distribution showed that cardiac complications were not significantly different between the two groups after PSM ($p=0.730$), although the differences were significant before PSM ($p=0.046$). However, neurological complications were significantly different between the two groups after PSM ($p=0.004$) while statistically equivalent before PSM ($p=0.958$). In terms of endocrine/metabolic complications, patients with DM had a significantly larger proportion compared with patients without DM both before and after PSM ($p<0.001$). No significant difference was observed in other complications, THC, LOS, and mortality rates before and after PSM although marginally significant in 1-year and 2-year mortalities after PSM ($p=0.050$ and $p=0.053$, respectively), which need to be interpreted with caution. Crude mortality rate was 0.89% at 30 days, with no significant difference between the two groups before and after PSM.

The mean follow-up was 36.2 months. At the end of the study, the overall mortality rate of all patients was 17.6%. Before PSM, the mortality rates in patients with and without DM were 24.7% and 15.4%, respectively. After PSM, the

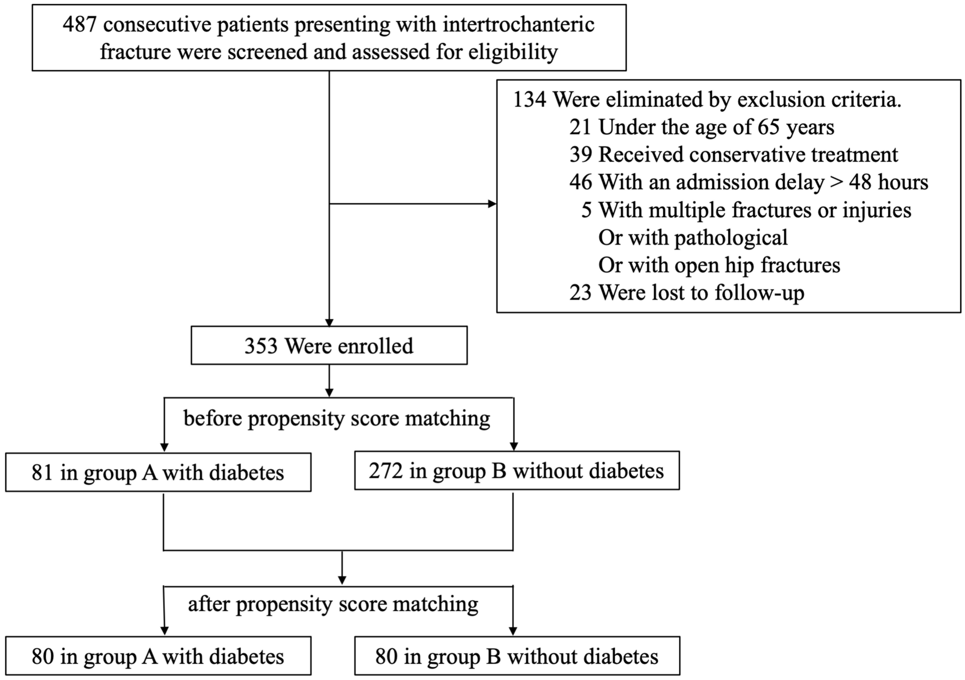

Figure 1 Flow diagram of included patients.

rates were 25.0% vs 36.3%. However, the Kaplan–Meier survival curve showed no significant difference between the two groups regarding cumulative survival rate (Figure 2, p=0.171, log-rank).

Discussion

In the current study, we found higher ASA grade and longer surgical delay in patients with DM than in patients without DM. IF surgery patients with or without DM seem to be comparable except for perioperative neurological complications and endocrine/metabolic complications.

To the best of our knowledge, functional outcomes after hip fracture surgeries are likely to be multifactorial. Numerous studies[17–20] have shown that gender, advanced age, comorbidities, transfusion requirement and volume, and higher ASA-grade were predictors of morbidity and mortality after hip fracture surgery. Additionally, the impact of other factors, such as type of anesthesia, duration of operation, and intraoperative blood loss, and surgical delay has not been consistently demonstrated.[18,21–23] However, in our study, none of these baseline characteristics and pre-existing morbidities showed statistically significant differences between the two groups, which ruled out the possible confounder effect of these factors by using the method of PSM.

Our results implied that patients with DM were more prone to suffer neurological complications and endocrine/metabolic complications, which is consistent with Golinvaux et al.[16] According to Novak et al,[24] DM seemed to be associated with progressive metabolic disturbance in the cerebrovascular bed which may affect blood flow and accelerate the white matter degeneration, suggesting possible explanations for our results to an extent. Regarding the baseline characteristics of patients, a greater percentage of patients had an ASA grade 3 or 4 as well as longer surgical delay in patients with DM than patients without DM, indicating that DM patients had an increased risk of developing additional comorbidities which required optimizing. Given this, early identification and optimizing pre-operative management of DM individuals is important to secure less perioperative neurological and endocrine/metabolic complications, leading to early mobilization and quick recovery.

It is well known that perioperative pulmonary complication is related to reduced chest ventilation capacity in bedridden patients, pre-existing morbidities, and exposure to nosocomial pathogens or pneumonia following hip fracture is common.[25] The incidence of postoperative pneumonia for the general population undergoing orthopaedic surgery is

Table 1 Patient Characteristics at Baseline[§]

Variables	Pre-Matching			Post-Matching		
	Group A with DM (n=81)	Group B without DM (n=272)	*p* value	Group A with DM (n=80)	Group B without DM (n=80)	*p* value
Gender			0.165			0.607
Male	23 (28.4%)	100 (36.8%)		23 (28.7%)	26 (32.5%)	
Female	58 (71.6%)	172 (63.2%)		57 (71.3%)	54 (67.5%)	
Age	77.9±6.6	78.1±6.8	0.842	78.0±6.5	79.5±6.4	0.139
Age group			0.172			0.164
65–69	11 (13.6%)	46 (16.9%)		10 (12.5%)	7 (8.8%)	
70–79	36 (44.4%)	90 (33.1%)		36 (45.0%)	27 (33.8%)	
80–89	34 (42.0%)	136 (50.0%)		34 (42.5%)	46 (57.5%)	
BMI			0.315			0.456
Normal	43 (53.1%)	170 (62.5%)		43 (53.8%)	50 (62.5%)	
Overweight	28 (34.6%)	75 (27.6%)		27 (33.8%)	20 (25.0%)	
Obesity	10 (12.3%)	27 (9.9%)		10 (12.4%)	10 (12.5%)	
Injury mechanism			0.348			0.497
Fall	79 (97.5%)	256 (94.1%)		78 (97.5%)	80 (100.0%)	
Violent	2 (2.5%)	16 (5.9%)		2 (2.5%)	0 (0.0%)	
Fracture type			0.497			0.874
Stable	41 (50.6%)	126 (46.3%)		40 (50.0%)	41 (51.2%)	
Unstable	40 (49.4%)	146 (53.7%)		40 (50.0%)	39 (48.8%)	
ASA grade			<0.001*			0.095
I	0 (0.0%)	38 (14.0%)		0 (0.0%)	3 (3.8%)	
II	16 (19.8%)	81 (29.8%)		16 (20.0%)	11 (13.8%)	
III	38 (46.95)	91 (33.5%)		38 (47.5%)	28 (35.0%)	
IV	24 (29.6%)	51 (18.8%)		23 (28.7%)	32 (40.0%)	
V	3 (3.7%)	11 (4.0%)		3 (3.8%)	6 (7.5%)	
Surgical delay	6.5±2.5	5.5±2.9	0.009*	6.5±2.5	6.0±3.2	0.269
Anesthesia type			0.446			0.342
General	36 (44.4%)	108 (39.7%)		35 (43.8%)	41 (51.2%)	
Regional	45 (55.6%)	164 (60.3%)		45 (56.2%)	39 (48.8%)	
Surgery duration	97.5±30.2	98.3±32.7	0.840	97.9±30.1	93.3±28.3	0.318
Intraoperative blood loss	200 (100, 300)	200 (100, 300)	0.292	200 (100, 300)	200 (100, 300)	0.593
Transfusion rate			0.767			0.593
Yes	57 (70.4%)	196 (72.1%)		57 (71.3%)	60 (75.0%)	
No	24 (29.6%)	76 (27.9%)		23 (28.7%)	20 (25.0%)	
Transfusion volume	2 (0, 6)	2 (0, 6)	0.790	2 (0, 6)	2 (0, 6)	0.761

Notes: [§]Values are presented as the number (%). Age, surgical delay, and surgery duration are presented as the mean ± standard deviation. Intraoperative blood loss is presented as the median (interquartile range). *p < 0.05, statistical significance.
Abbreviations: DM, diabetes mellitus; BMI, body mass index; ASA, American Society of Anesthesiologists.

0.7%[26] and with a range of 0.45% to 14.4%.[27] Bohl et al[28] indicated that advanced age, functional dependency, increased operative time, previous COPD, and diabetes are risk factors for developing postoperative pneumonia. After ruling out the possible confounder effect of multiple factors, our study showed individuals with comorbid DM might not increase the incidence of pulmonary complications. Previous studies have also shown that good postoperative recovery for older hip fracture patients was not expected due to poor surgical tolerance and have a tendency for anemia, which has been demonstrated with significant adverse outcomes.[3,4] However, there was no significant difference in transfusion volume and rates between the two groups no matter before or after PSM based on our results.

Although a number of published researches[6,7,29,30] have previously performed survival analyses for older hip fracture patients, the PSM method which has advantages in controlling for a variety of potential confounding was not involved. In our 36.2 months follow-up in average, 17.6% of patients died at the end of this study, suggesting a lower mortality rate

Table 2 Patient Complications and Outcomes[§]

Variables	Pre-Matching			Post-Matching		
	Group A with DM (n=81)	Group B without DM (n=272)	*p* value	Group A with DM (n=80)	Group A without DM (n=80)	*p* value
Severe complications			0.670			0.593
Yes	20 (24.7%)	61 (22.4%)		20 (25.0%)	23 (28.7%)	
No	61 (75.3%)	211 (77.6%)		60 (75.0%)	57 (71.3%)	
Cardiac complications			0.046*			0.730
Yes	26 (32.1%)	58 (21.3%)		25 (31.3%)	23 (28.7%)	
No	55 (67.9%)	214 (78.7%)		55 (68.8%)	57 (71.2%)	
Pulmonary complications			0.909			0.184
Yes	9 (11.1%)	29 (10.7%)		9 (11.3%)	15 (18.8%)	
No	72 (88.9%)	243 (89.3%)		71 (88.7%)	65 (81.2%)	
Neurological complications			0.958			0.004*
Yes	7 (8.6%)	23 (8.5%)		7 (8.8%)	21 (26.3%)	
No	74 (91.4%)	249 (91.5%)		73 (91.2%)	59 (73.7%)	
Hematological complications			0.341			0.752
Yes	43 (53.1%)	128 (47.1%)		43 (53.8%)	41 (51.2%)	
No	38 (46.9%)	144 (52.9%)		37 (46.2%)	39 (48.8%)	
Endocrine/metabolic complications			<0.001*			<0.001*
Yes	81 (100.0%)	170 (62.5%)		80 (100.0%)	51 (63.7%)	
No	0 (0.0%)	102 (37.5%)		0 (0.0%)	29 (36.3%)	
Death			0.055*			0.123
Yes	20 (24.7%)	42 (15.4%)		20 (25.0%)	29 (36.3%)	
No	61 (75.3%)	230 (84.6%)		60 (75.0%)	51 (63.7%)	
30-day mortality			0.362			1.000
Yes	1 (1.2%)	1 (0.4%)		1 (1.3%)	1 (1.3%)	
No	80 (98.8%)	271 (99.6%)		79 (98.8%)	79 (98.8%)	
90-day mortality			0.453			0.493
Yes	3 (3.7%)	6 (2.2%)		3 (3.8%)	6 (7.5%)	
No	78 (96.3%)	266 (97.8%)		77 (96.3%)	74 (92.5%)	
1-year mortality			0.692			0.050
Yes	8 (9.9%)	23 (8.5%)		8 (10.0%)	17 (21.3%)	
No	73 (90.1%)	249 (91.5%)		72 (90.0%)	63 (78.8%)	
2-year mortality			0.105			0.053
Yes	17 (21.0%)	37 (13.6%)		17 (21.3%)	28 (35.0%)	
No	64 (79.0%)	235 (86.4%)		63 (78.2%)	52 (65.0%)	
THC	50397±17,461	49,350±17,992	0.644	50,529±17,531	53,460±22,992	0.366
LOS	13.7±4.6	13.7±5.9	0.995	13.7±4.6	14.2±6.2	0.583

Notes: [§]Values are presented as the number (%). THC and LOS are presented as the mean ± standard deviation. *$p < 0.05$, statistical significance.
Abbreviations: DM, diabetes mellitus; THC, total hospital costs; LOS, length of hospital stay.

than previous findings,[6,7,29] which may be attributed to the conservative treatment cases being excluded. The survival analysis showed that there was no significant difference between the two groups. Such quantitative analyses have both empirical and theoretical strengths for orthopedists to better manage DM patients and to optimize interventions for these frail population in the future.

We do acknowledge that our study has certain limitations, including its retrospective design and the data being collected in a single center. We did not control all risk factors, such as smoking and other unknown confounders, which

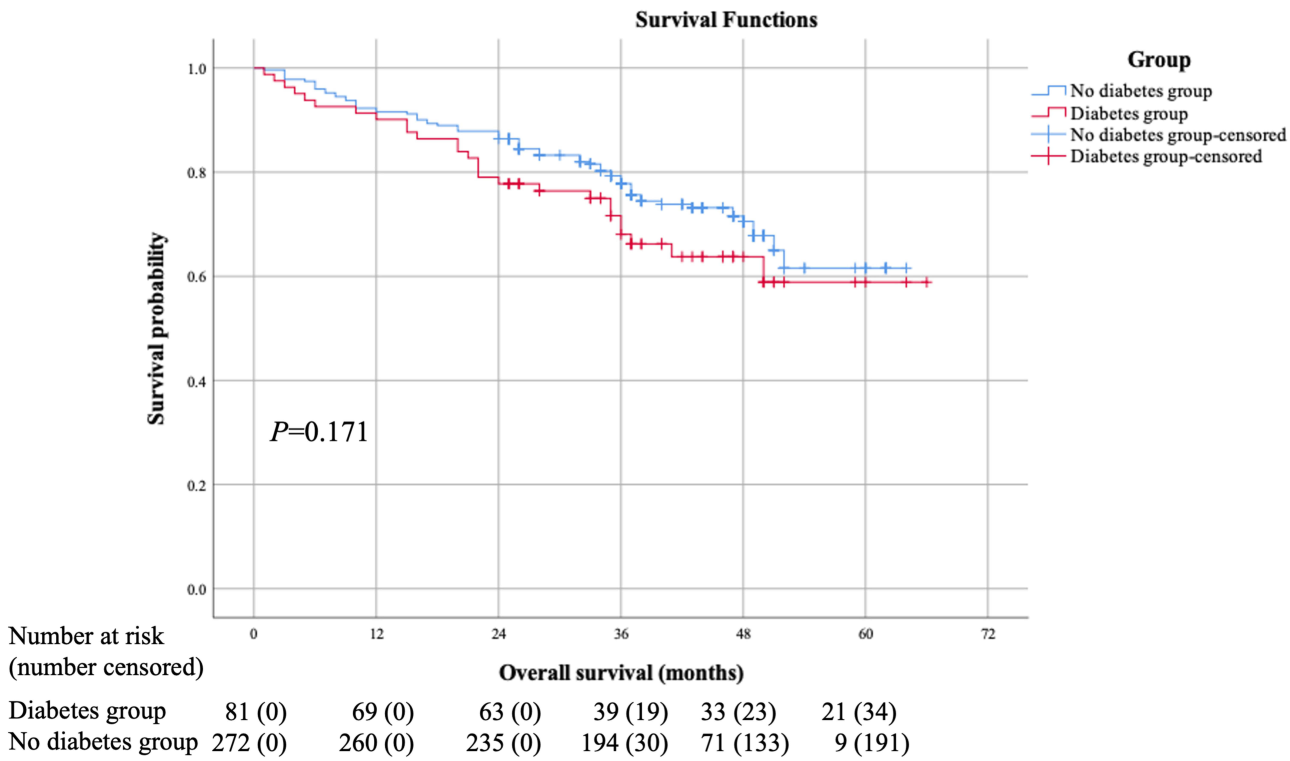

Figure 2 Kaplan-Meier survival curves for older patients with or without diabetes mellitus after intertrochanteric fracture surgery. The Kaplan-Meier survival curve showed no significant difference between the two groups of patients on cumulative survival rate. (Figure 1, *P* = 0171, log-rank).

may potentially influence the findings. Although HbA1c is a reliable indicator of long-term glycemic control, providing a picture of patients' average blood glucose levels during the previous two to three months,[31] conflicting results have been reported regarding mortality and postoperative complications after orthopedic procedures including hip fracture surgery.[32,33] Through this study, we aimed to compare the adverse outcomes following hip fracture surgery in DM and non-DM patients. The study did not have specific indicators of DM and interventions to further explore the specific treatment and its associated influence. Certainly, further studies, multicenter and with larger cohorts are needed to explore the specific indicators and glycemic control for outcome change interventions, achieving the goal of clarifying the association between various severities of diabetes and adverse outcomes after hip fracture surgery in elderly patients. However, we provide a comparative study containing multiple relative contributions of patient, fracture, anesthetic, surgical, and transfusion factors, which is still lacking in the literature, and those on DM patient cohort with PSM method is non-existent. The strength of this study includes the PSM method we used and the specific cohort of patients who received surgery by single internal fixation, which eliminated the effects of possible confounding variables. Finally, the cohort comprises a relatively large sample size and has a long-term follow-up.

Conclusions

In conclusion, IF surgery patients with DM are more prone to suffer perioperative neurological and endocrine/metabolic complications and they should be managed individually while being aware of these risks henceforth. Further high evidence clinical trials are needed to expand on these findings in DM patients with IF.

Abbreviation

IF, intertrochanteric fractures; DM, diabetes mellitus; ASA, American Society of Anesthesiologists; PFNA, proximal femoral nail anti-rotation; BMI, body mass index; THC, total hospital costs; LOS, length of hospital stay; PSM, propensity score matching.

Data Sharing Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Statement of Ethics

The protocol for the research project has been approved by the institutional review board (IRB) of Binzhou People's Hospital. The present study conforms to the Declaration of Helsinki. All patients involved gave informed consent and all data were anonymized before the analysis to safeguard patient privacy.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declared no potential conflicts of interest.

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