

# Impact of type 2 diabetes on postoperative outcome after hip fracture: nationwide population-based study in Taiwan

Tien-Ching Lee <sup>1,2,3</sup>, Yu-Li Lee,<sup>4</sup> Jian-Chih Chen,<sup>5,6</sup> Chung-Hwan Chen,<sup>1,3,6</sup> Pei-Shan Ho<sup>7</sup>

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For numbered affiliations see end of article.

**Correspondence to**  
Professor Pei-Shan Ho;  
[peishan1103@gmail.com](mailto:peishan1103@gmail.com)

## ABSTRACT

**Summary** The impact of diabetes mellitus (DM) on hip fracture (HFx) is still controversial. We used nationwide population-based data in Taiwan to observe postoperative outcomes of HFx in patients with type 2 diabetes mellitus (T2DM) and found that the impact of T2DM may be related to medication of blood glucose control.

**Objective** Published studies evaluating diabetic patients with HFx have shown controversial outcomes. We assessed the impact of T2DM on postoperative outcomes after HFx in elderly patients using the nationwide population database in Taiwan.

**Research design and methods** We used data from the National Health Research Institute in Taiwan to recruit patients who had undergone operations for HFx between 2000 and 2009. The recruited patients with T2DM were divided into the oral antidiabetic drug (OAD) cohort and the insulin cohort according to the use or non-use of insulin. Patients without DM were propensity score matched in a 1:1 ratio by four variables. We used the  $\chi^2$  test, linear regression and Cox proportional hazards model to assess variables, including length of hospital stay, medical cost, complications, early readmission, and 1-year mortality.

**Results** We identified 5490 subjects in total. The insulin cohort exhibited prolonged hospital stay (11.8 days), higher medical costs, more complications within 30 and 90 after hip surgery, earlier readmission, and higher 1 year mortality rate (25.8%) than the OAD and non-DM cohorts. The OAD cohort had longer hospital stay (10.1 days) and higher readmission rate but fewer complications and mortality rates (14.9%) than the non-DM cohort.

**Conclusions** After matching confounding factors, the T2DM with OAD control groups were not associated with higher complication or mortality rates but were associated with higher readmission rates. However, diabetic patients with insulin control have poor outcome. The impact of T2DM on the postoperative outcomes of patients with HFx may be related to blood glucose control medication.

## INTRODUCTION

Diabetes mellitus (DM) is a common, worldwide chronic metabolic disease with increasing incidence in the last decade.<sup>1,2</sup> In 2017, 425 million adults had DM globally, and this number is projected to grow to 629 million

## Significance of this study

### What is already known about this subject?

► Published studies evaluating diabetic patients with hip fracture (HFx) show controversial outcome.

### What are the new findings?

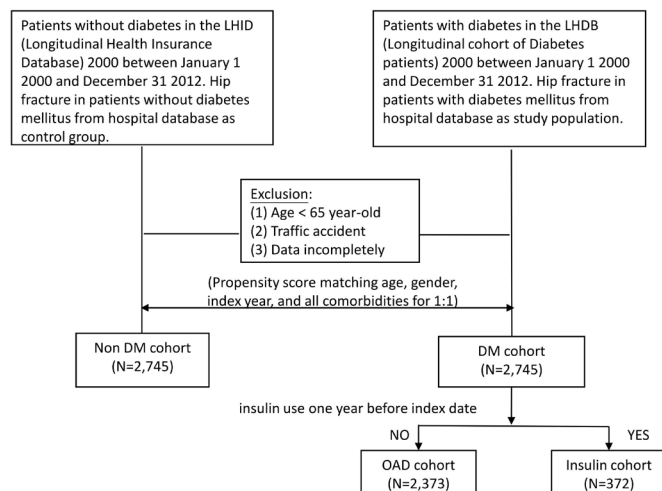
► After matching confounding factors, the patients with type 2 diabetes with oral antidiabetic agent control were not associated with higher complication or mortality rates but were associated with higher readmission rates.  
► We found that the impact of type 2 diabetes mellitus (T2DM) on the postoperative outcomes of patients with HFx may be related to blood glucose control medication.

### How might these results change the focus of research or clinical practice?

► These findings will contribute to improve the pre-operative workup and counseling of patients with T2DM with HFx who need surgery.

adults by 2045.<sup>3</sup> It is estimated that more than 20% of Taiwanese adults aged >65 years are affected by DM.<sup>4</sup> The prevalence of osteoporosis increases with population aging as well.<sup>5</sup> Therefore, DM and osteoporosis often coexist in older adults.<sup>6–8</sup>

Osteoporotic hip fractures (HFx's) in the elderly population cause high mortality and adverse outcomes.<sup>9–12</sup> The 1-year mortality rate following HFx is 15%–20%.<sup>9–13</sup> Previous studies demonstrated that patients had decreased mobility; lower quality of life; increased dependence on family, care givers, and social services; and increased physical, mental, and financial burden following HFx.<sup>14–20</sup> Janghorbani *et al* demonstrated that both type 1 and 2DM are associated with higher risk for HFx in men and women.<sup>21</sup> In addition, patients with type 2 diabetes mellitus (T2DM) are reported to have a higher HFx



**Figure 1** Flow diagram of the selected study subjects. DM, diabetes mellitus; OAD, oral antidiabetic.

risk compared with patients without DM for a given age and bone mineral density or for a given Fracture Risk Assessment Tool score.<sup>22</sup> Several studies have evaluated DM and surgical management of Hfx<sup>23–28</sup>; however, the impact of DM on the postoperative outcome in patients with Hfx remains controversial.

In this regard, we analyzed national population data from the National Health Insurance Research Database (NHIRD) at the National Health Research Institute in Taiwan to clarify the effect of T2DM on postoperative complication rate, length of hospital stay, early readmission rate, and mortality within 1 year after Hfx.

## METHODS

### Data sources

This study was performed using data from the Longitudinal Cohort of Diabetes Patients (LHDB 2000), which contains random samples from 120 000 patients with newly diagnosed DM enrolled from the 2000 Registry of National Health Insurance (NHI) beneficiaries, in addition to the Longitudinal Health Insurance Database (LHID 2000), which comprises registration files for the insured population and medical claims for 1 000 000 randomly sampled NHI patients enrolled from the 2000 Registry of NHI beneficiaries in the NHI program of Taiwan. Implemented in 1995, the NHI program provides comprehensive healthcare for more than 23 million residents in Taiwan, covering more than 99% of the entire population. The details regarding the database generation area are available online ([http://nhird.nhri.org.tw/date\\_cohort.html](http://nhird.nhri.org.tw/date_cohort.html)).

### Study population

Discharge codes (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes 820–820.9) and medical codes for internal fixation or hemiarthroplasty (ICD-9-CM codes 79.15, 79.35, and 81.52) in the LHDB 2000 were used to identify patients with Hfx with T2DM who had undergone operations

between 1 January 2000 and 31 December 2012. Subjects with T2DM were selected based on ICD-9-CM code 250 of outpatient claims with prescription of antidiabetic medications (including oral agents and insulin) for 3 months at least within 1 year. The first hospital admission date for Hfx was considered the index date. The exclusion criteria were inpatients aged <65 years, those with malignancy-associated fractures (ICD-9-CM codes 733.14 and 733.15), those involved in major traffic accidents, or those who died during the index admission (figure 1). In addition, to avoid possible confounding effects on complication and mortality rates, patients who underwent operations on the pelvis, femur, and hip regions before the index date were also excluded. The final cohort of patients with Hfx with T2DM consisted of 2745 subjects and was divided into two groups according to the antidiabetic medications used 1 year before the index date. Patients with records of the insulin prescription from an outpatient department for at least 3 months were classified as the insulin cohort group. We recorded the following information: (1) length of hospital stay, (2) operation type (internal fixation or arthroplasty), (3) comorbidities experienced before or at the time of the index date based on the Charlson Comorbidity Index (CCI),<sup>18</sup> and (4) the main diagnosis code for readmission.

### Control cohort

The control group was selected from LHID 2000 using the same criteria as for the study group, but subjects with T2DM were excluded. Each patient with Hfx was propensity score matched for 1:1 by four variables, including age, sex, index date, and CCI within the same follow-up period using SAS software V.9.3. The CCI did not include the diagnosis of DM because subjects were DM-free before the index date. A total of 2745 subjects served as the matched control cohort.

### Outcome measures

This study analyzed three outcomes: (1) medical cost and length of hospital stay of index admission based on inpatient expenditures by admissions from NHIRD; (2) complications (including acute myocardial infarction, acute stroke, acute renal failure, deep wound infection, pneumonia, postoperative hemorrhagic anemia, septicemia, acute gastrointestinal ulcer, and pulmonary embolism) and readmissions within 30 and 90 days after index admission based on the records of inpatient expenditures by admissions from NHIRD; and (3) mortality within 1 year after index admission.

### Statistical analysis

We used the  $\chi^2$  test to compare the demographic data of patients with Hfx with and without T2DM. Linear regression was used to compare the medical cost during index admission with adjustment for age, sex, payroll bracket table, anesthesia type, and CCI. We used Cox proportional hazards model to assess variables, including complications, early readmission, and 1-year mortality.

**Table 1** Demographic data among patients with hip fractures in the non-DM and DM cohorts

	Non-DM cohort (n=2745)	OAD cohort (n=2373)	P value	Insulin cohort (n=372)	P value
	n (%)	n (%)		n (%)	
<b>Age (years)</b>					
65–69	214 (7.8)	175 (7.4)		31 (8.3)	
70–74	387 (14.1)	341 (14.4)	0.518	63 (16.9)	0.614
75–79	610 (22.2)	485 (20.4)		83 (22.3)	
80–84	732 (26.7)	645 (27.2)		94 (25.3)	
≥85	802 (29.2)	727 (30.6)		101 (27.2)	
Mean±SD	80.52 (7.37)	80.25 (6.86)		79.39 (6.88)	
<b>Sex</b>					
Female	1611 (58.7)	1420 (59.8)	0.403	193 (51.9)	0.013
Male	1134 (41.3)	953 (40.2)		179 (48.1)	
<b>Payroll bracket table</b>					
<NT 15 000	1853 (67.5)	1621 (68.3)	0.205	245 (65.9)	0.709
≥NT 15 000	892 (33.5)	752 (31.7)		127 (34.1)	
<b>Anesthesia type</b>					
Regional	1866 (68.0)	1636 (68.9)	0.459	261 (70.2)	0.396
General	879 (32.0)	737 (31.1)		111 (29.8)	
<b>Operation method</b>					
Internal fixation	1526 (55.6)	1369 (57.7)	0.131	225 (60.5)	0.074
Hemiarthroplasty	1219 (44.4)	1004 (42.3)		147 (39.5)	
<b>Charlson Comorbidity Index score</b>					
≤1	945 (34.4)	814 (34.3)	0.354	109 (29.3)	0.004
=2	654 (23.8)	604 (25.5)		74 (19.9)	
>2	1146 (41.7)	955 (40.2)		189 (50.8)	

DM, diabetes mellitus; NT, New Taiwan Dollar; OAD, oral antidiabetic drug.

All analyses were performed using SAS software V.9.3 and IBM SPSS Statistics software V.19.

## RESULTS

A total of 5490 subjects who underwent Hfx surgery met the study criteria and were divided into the non-DM cohort (n=2745), oral antidiabetic drug (OAD) cohort (n=2373), and insulin cohort (n=372) according to the

use or non-use of medications for DM (table 1). The median length of the index hospital stay was 9 days. Among these patients, 3224 (58.7%) were female and 2266 (41.3%) were male, with a mean age of 78.75 years. Of these, 43.2% of the patients underwent joint replacement, and the remaining 3120 (56.8%) underwent internal fixation. The average length of index hospital stay in the OAD (10.1 days) and insulin (11.8

**Table 2** Medical cost (NT\$) during index admission among patients with hip fractures in the non-DM, OAD and insulin cohorts

	Mean (SD)	Model I		Model II	
		β (95% CI)	P value	β (95% CI)	P value
Non-DM cohort	74 865.2 (47 220.2)	Ref			
OAD cohort	75 825.1 (53 618.9)	1038.6 (–1684.8 to 3762.1)	0.455	Ref	
Insulin cohort	91 721.8 (89 961.0)	7927.5 (5021.4 to 10 833.7)	<0.001	14 996.34 (8508.0 to 11 775.5)	<0.001

Adjusted for age, sex, payroll bracket table, anesthesia type, and Charlson Comorbidity Index score.

Model I: comparison among the non-DM (ref), OAD, and insulin cohorts.

Model II: comparison between the OAD (ref) and insulin cohorts.

DM, diabetes mellitus; NT, New Taiwan; OAD, oral antidiabetic drug; ref, reference.

**Table 3** Complication rate among patients with hip fractures in the non-DM, OAD, and insulin cohorts

	Complication				Model I		Model II	
	No		Yes		Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
	n	(%)	n	(%)				
Within 30 days								
Non-DM cohort	2602	(94.8)	143	(5.2)	Ref			
OAD cohort	2284	(96.2)	89	(3.8)	0.73 (0.56 to 0.95)	0.020	Ref	
Insulin cohort	341	(91.7)	31	(8.3)	1.59 (1.07 to 2.34)	0.021	2.21 (1.46 to 3.34)	<0.001
Within 90 days								
Non-DM cohort	2485	(90.5)	260	(9.5)	Ref			
OAD cohort	2191	(92.3)	182	(7.7)	0.81 (0.67 to 0.98)	0.028	Ref	
Insulin cohort	320	(86.0)	52	(14.0)	1.49 (1.10 to 2.01)	0.009	1.81 (1.33 to 2.47)	<0.001

Adjusted for age, sex, payroll bracket table, anesthesia type, and Charlson Comorbidity Index score.

Model I: comparison among the non-DM (ref), OAD, and insulin cohorts.

Model II: comparison between the OAD (ref) and insulin cohorts.

DM, diabetes mellitus; OAD, oral antidiabetic drug; ref, reference.

days) cohorts was longer than that in the non-DM cohort (9.7 days), with significance after adjusting for age, sex, payroll bracket table, anesthesia type, and CCI score. The medical costs in the insulin cohort during the index admission were significantly higher than those in the other two groups ( $p < 0.001$ , table 2).

In the insulin cohort, the complication rate within 30 and 90 days was significantly higher than that in the other two groups, with adjusted HRs of 1.59 (95% CI 1.07 to 2.34) and 1.49 (95% CI 1.10 to 2.01), respectively (table 3).

Although the non-DM cohort had the lowest readmission rate within 30 and 90 days among these groups (table 4), the OAD cohort had a lower 1-year mortality rate (14.9%) compared with the non-DM (17.6%) and insulin (25.8%) cohorts (table 5).

## DISCUSSION

Some studies have demonstrated that patients with T2DM with HFr have an increased risk of postoperative cardiac complications,<sup>23 24</sup> renal dysfunction,<sup>23 25</sup> urinary retention,<sup>26</sup> extended length of hospital stay,<sup>24</sup> and early readmission.<sup>27</sup> However, Golinvaux *et al* reported conflict results showing little difference in perioperative risk among geriatric patients with HFr with non-insulin-dependent or insulin-dependent DM compared with those without DM.<sup>28</sup>

Our results demonstrate that T2DM negatively impacts postoperative outcome, including hospital stay, complication rate, and early readmission rate after adjusting for age, sex, payroll bracket table of insurance, anesthesia type, and CCI. Furthermore, the insulin-dependent cohort had higher hospital expenses,

**Table 4** Readmission rate among patients with hip fractures in the non-DM, OAD, and insulin cohorts

	Readmission				Model I		Model II	
	No		Yes		Adjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
	n	(%)	n	(%)				
Within 30 days								
Non-DM cohort	2438	(88.8)	307	(11.2)	Ref			
OAD cohort	2082	(87.7)	291	(12.3)	1.16 (1.06 to 1.25)	0.001	Ref	
Insulin cohort	308	(82.8)	64	(17.2)	1.60 (1.38 to 1.85)	<0.001	1.39 (1.20 to 1.61)	<0.001
Within 90 days								
Non-DM cohort	1602	(58.4)	1143	(41.6)	Ref			
OAD cohort	1270	(53.5)	1103	(46.5)	1.12 (0.95 to 1.31)	0.182	Ref	
Insulin cohort	157	(42.2)	215	(57.8)	1.51 (1.15 to 1.98)	0.003	1.38 (1.05 to 1.81)	0.020

Adjusted for age, sex, payroll bracket table, anesthesia type, and Charlson Comorbidity Index score.

Model I: comparison among the non-DM (ref), OAD, and insulin cohorts.

Model II: comparison between the OAD (ref) and insulin cohorts.

DM, diabetes mellitus; OAD, oral antidiabetic drug; ref, reference.

**Table 5** Mortality among patients with hip fractures in the non-DM, OAD, and insulin cohorts

	Mortality				Model I Adjusted HR (95% CI)	P value	Model II Adjusted HR (95% CI)	P value
	No		Yes					
	n	(%)	n	(%)				
Non-DM cohort	2263	-82.4	482	-17.6	Ref			
OAD cohort	2020	(85.1)	353	(14.9)	0.86 (0.75 to 0.98)	0.026	Ref	
Insulin cohort	276	(74.2)	96	(25.8)	1.48 (1.19 to 1.85)	<0.001	1.69 (1.35 to 2.13)	<0.001

Adjusted for age, sex, payroll bracket table, anesthesia type, and Charlson Comorbidity Index score.

Model I: comparison among the non-DM (ref), OAD, and insulin cohorts.

Model II: comparison between the OAD (ref) and insulin cohorts.

DM, diabetes mellitus; OAD, oral antidiabetic drug; ref, reference.

longer length of stay, more complications, and higher mortality compared with the OAD cohort. These findings are consistent with most published studies<sup>24 27 29 30</sup> but in conflict with Golinvaux *et al's* result.<sup>28</sup> To the best of our knowledge, this work is the first population-based study to evaluate the effect of T2DM on postoperative outcome after Hfx with at least 1 year of follow-up. We found that patients with Hfx with T2DM bear the risk of longer hospital stay and short-term readmission rate.

Interestingly, the OAD cohort exhibited a higher early readmission rate but lower complication and 1-year mortality rate compared with the non-DM cohort. Furthermore, the insulin cohort had the highest readmission, complication, and 1-year mortality rates. The most common causes of early readmission in the OAD and insulin cohort were endocrine, nutritional, and metabolic diseases and immunity disorders (International Classification of Diseases, Ninth Revision: 240–279) (online supplementary file 1). It is well known that diabetic patients typically have more coexisting comorbidities. Diabetes is associated with multiple organ systems and adverse effects on fracture healing, bone remodeling rate, and infection.<sup>31</sup> Insulin exerts pleiotropic effects by regulating local growth factors.<sup>32</sup> Our results indicate that the preoperative use of insulin may play an important role in postoperative outcome in patients with Hfx.

A possible explanation for the higher complication and 1-year mortality rates in the non-DM cohort is that the matching variables in this study include CCI, which contains chronic diseases, including DM. Results show that matched non-DM cohort may have more comorbidities compared with the non-DM general population. We observed that patients with T2DM with regular OAD control did not carry higher complication or mortality rates compared with patients without DM after matching age, sex, payroll bracket table, anesthesia type, and CCI.

In the present study, patients with T2DM under control with OAD only did not show a higher risk of short-term complications and 1-year mortality. Based on the current analysis of this study, our results imply that subjects with long-term insulin use have poorer postoperative outcome after Hfx. Nevertheless, a

prospective study involving a large cohort of patients with non-insulin-dependent DM, insulin-dependent DM, and no DM carefully monitoring preoperative functional status, personal habits, hemoglobin A1c (HbA<sub>1c</sub>), blood glucose, and postoperative complications to more accurately evaluate the impact of perioperative glucose control on surgical outcome following Hfx is still needed.

This study has several limitations. First, we divided the patients with Hfx with T2DM into the OAD and insulin cohort in order to roughly represent the control status of T2DM. However, it cannot be a definitive representation of the severity of T2DM. Second, the NHI database was not designed for academic research; hence, miscoding of diagnosis might have occurred. The coding error could be compensated using medication codes for DM control and procedure codes for Hfx (internal fixation or hemiarthroplasty). Third, the NHI database does not include patient's functional status, personal habits (eg, smoking and alcohol use), severity of comorbidities (eg, heart function and renal function), patient compliance, nutritional status, biochemical data (eg, HbA<sub>1c</sub>), time to surgery, quality of postoperative care, and falls. Thus, unknown confounding factors may exist. Moreover, the effect of antiosteoporotic medication in preventing secondary fracture may have been overlooked due to the short (up to 1 year) follow-up duration in this study.

In conclusion, our results indicate that T2DM negatively impacts postoperative outcome, including hospital stay and early readmission rate after Hfx. Patients with T2DM with preoperative insulin use carry higher medical cost and complication rate as well as 1-year mortality rate. These findings may provide a valuable foundation for future prospective studies to explore the relationship between preoperative diabetes control and postoperative outcome after Hfx.

#### Author affiliations

<sup>1</sup>Orthopaedic Research Center, College of Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>2</sup>Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>3</sup>Department of Orthopedics, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>4</sup>Division of Endocrinology and Metabolism, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

<sup>5</sup>Department of Orthopedics, Kaohsiung Municipal Siaogang Hospital, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>6</sup>Department of Orthopedics, College of Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>7</sup>Faculty of Dental Hygiene, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

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**Data availability statement** All data relevant to the study are included in the article or uploaded as supplementary information. Data are available upon reasonable request.

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#### ORCID iD

Tien-Ching Lee <http://orcid.org/0000-0002-1510-8079>

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