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Preexisting Diabetes and Risks of Morbidity and Mortality After Gastrectomy for Gastric Cancer

A Nationwide Database Study

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Abstract: The purpose of this study was to determine the risk of surgical mortality and morbidity in patients with diabetes mellitus (DM) undergoing a gastrectomy for gastric cancer (GC).

Using the Taiwan National Health Insurance Research Database, we identified 6284 patients who underwent gastrectomy for GC from 1999 to 2010. In addition, we created a non-DM control cohort consisting of 6268 patients who received gastrectomy during the same period.

Compared with the non-DM cohort, the DM cohort exhibited a higher prevalence of preoperative coexisting medical conditions, namely hypertension, hyperlipidemia, coronary artery disease, chronic kidney disease, chronic pulmonary disease, stroke, and cirrhosis. The

odds ratio (OR) of 30-day postoperative mortality after gastrectomy in the DM cohort was 1.04 (95% confidence interval 0.78–1.40) after we adjusted for covariates. The DM cohort did not exhibit a significantly higher risk of 30-day postoperative morbidities. Further analysis revealed that only patients with a history of a DM-related coma exhibited a higher risk of 30-day postoperative mortality (adjusted OR 2.46, 95% confidence interval 1.10–5.54). Moreover, the risk of 90-day postoperative mortality was significantly higher in patients with DM-related eye involvement, coma, peripheral circulatory disease, and renal manifestations, in comparison with the non-DM cohort.

The risk of 90-day mortality after gastrectomy for GC is higher in patients with DM-related manifestations than those without DM.

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Abbreviations: CI = confidence interval, DM = diabetes mellitus, GC = gastric cancer, NHIRD = National Health Insurance Research Database, OR = odds ratio, RCIPI = Registry of Catastrophic Illness Database.

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INTRODUCTION

Gastric cancer (GC) is among the most common cancers worldwide and causes considerable mortality, despite the declining trend in its incidence.^{1,2} GC can be attributed to several factors, including genetic factors,^{3,4} red meat diet,^{5,6} and *Helicobacter pylori* infection.⁷ Surgery, if feasible, is the only currently available treatment for GC.

Studies have reported that diabetes mellitus (DM) is associated with an increased risk of GC.^{8–11} In addition, a previous study demonstrated that patients with DM exhibited a significantly higher risk of GC mortality.¹² Furthermore, DM has been proposed to be an independent determinant of a greater risk of perioperative complications and mortality following various surgeries.^{13–15} Our previous study indicated that patients with DM exhibit higher risks of septicemia and acute renal insufficiency after undergoing hepatectomy for hepatocellular carcinoma.¹⁶ However, the effects of DM on the risk of perioperative morbidity and mortality after a gastrectomy for GC remain controversial.

Several previous studies investigating the surgical risk of patients with GC were limited by small sample sizes or were conducted at a single institution.^{17–20} Herein, we used data from the Taiwan National Health Insurance Research Database (NHIRD) to evaluate the postoperative risks of mortality and morbidity in patients with DM undergoing gastrectomy for GC on a nationwide scale. In addition, we investigated the effects of coexisting medical conditions and DM-related comorbidities on postoperative 30-day mortality in patients with DM.

MATERIALS AND METHODS

Data Resources

The Taiwan National Health Insurance program was established in 1995 and covers ~99% of the 23.7 million residents of Taiwan. We used electronic claims data from the NHIRD to establish a longitudinal cohort. All claims records contain data on all medical services used by beneficiaries of the NHI program, are released by the Bureau of National Health Insurance for public research, and are managed by the National Health Research Institutes. We analyzed data from the 2007–2011 Registry of Catastrophic Illness Database (RCIPD) of the NHIRD in this study. The RCIPD contains records on all confirmed cases of catastrophic illness, such as GC. Patients with catastrophic illness must submit pathology and related laboratory reports to receive a catastrophic illness certificate, which exempts these patients from copayments for all ambulatory visits and hospitalizations. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) was used to code diagnoses of diseases and gastrectomy procedures. The NHIRD files were connected with surrogate identification numbers to protect personal privacy. The research ethics committee of the institutional review board of China Medical University exempted this study from full review (CMU-REC-101–012).

Study Population

Our study was a population-based retrospective cohort study. We identified patients with GC (ICD-9-CM code: 151) who had undergone a partial gastrectomy (ICD-9-CM codes: 43.5, 43.6, 43.7, 43.81, 43.82, and 43.89) or total gastrectomy (ICD-9-CM codes: 43.91 and 43.99) according to the RCIPD records. All patients were aged over 20 years and underwent gastrectomy between 1999 and 2010. The date on which a patient first underwent gastrectomy served as the index date. We identified 6284 patients who were diagnosed with DM (ICD-9-CM code: 250) for the first time before the index date as the DM cohort. The comparison cohort ($n = 6269$) comprised patients without a history of DM who were randomly selected from the RCIPD and matched with the patients with DM in a 1:1 ratio according to age (each 5-year span), sex, and index year (supplementary Figure 1, <http://links.lww.com/MD/A411>).

We also used the propensity score matching method to select the DM and control cohorts. In this analysis, we matched the 2 cohorts in their baseline characteristics and risk factors (including age, sex, index year, monthly income, occupation, and the comorbidities history) in the 1:1 ratio. We were able to identify 3996 patients in DM and non-DM cohorts after propensity score matching (see supplementary Tables 1 and 2, <http://links.lww.com/MD/A411>).

Exposure Variables

We analyzed the sociodemographic information recorded before the index date, namely age, sex, monthly income, and occupation, as well as comorbidities, namely hypertension (ICD-9-CM codes: 401–405), coronary artery disease (CAD, ICD-9-CM codes: 410–414), chronic obstructive pulmonary disease (COPD, ICD-9-CM codes: 490–496), stroke (ICD-9-CM codes: 430–438), hyperlipidemia (ICD-9-CM code: 272), liver cirrhosis (ICD-9-CM codes: 571.2, 571.5, and 571.6), and chronic kidney disease (CKD, ICD-9-CM codes: 580–589).

The monthly income of individuals could be deduced according to their premium paid to the insurance bureau. For those with monthly income less than NT\$15,000, the premium

was NT\$900 per month. On the contrary, those who had monthly income higher than NT\$25,000 would pay more than NT\$1500 per month as the premium.

We calculated other potential risk factors of 30- and 90-day postoperative mortality present in the DM cohort between the date of DM diagnosis and the index date, namely the type of DM (type 1 ICD-9-CM codes: 250.x1 and 250.x3; type 2 ICD-9-CM codes: 250.x0 and 250.x2) by defining patients with ketoacidosis (ICD-9-CM code: 250.1), coma (ICD-9-CM codes: 250.2 and 250.3), renal manifestations (ICD-9-CM code: 250.4), eye involvement (ICD-9-CM code: 250.5), and peripheral circulatory disorder (ICD-9-CM code: 250.7).

Outcome Measure

The 30- and 90-day postgastrectomy mortality in the DM and non-DM cohorts was the primary outcome. The secondary outcomes included 10 major surgical postoperative complications that occurred within 30 and 90 days after operation, namely septicemia (ICD-9-CM code: 038), pneumonia (ICD-9-CM codes: 480–487), stroke (ICD-9-CM codes: 430–438), acute renal failure (ARF) (ICD-9-CM code: 584), wound infection (ICD-9-CM code: 998.59), wound dehiscence (ICD-9-CM codes: 998.83 and 998.3), acute myocardial infarction (ICD-9-CM code: 410), intraabdominal abscess (ICD-9-CM code: 682.2), intestinal obstruction (ICD-9-CM codes: 560.30, 560.39, and 560.8), and other intestinal complications (ICD-9-CM codes: 534, 564.2, 564.3, and 997.49).

Statistical Analysis

We described the distributions of age, sex, monthly income, and occupation, as well as hypertension and compared these distributions between the DM and non-DM cohorts by using the χ^2 test and Student *t* test. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using multivariate logistic regression to assess the association between DM and the risk of postoperative complications and mortality following a gastrectomy after we adjusted for age, sex, monthly income, occupation, and comorbidity history. The impact of differences in DM severity on 30- and 90-day postoperative mortality was determined using multivariate logistic regression, and DM severity was partitioned into 7 categories, namely ketoacidosis, coma, renal manifestations, eye involvement, peripheral circulatory disorders, type 1 DM, and type 2 DM. We also used multivariate logistic regression to examine the association between postoperative mortality (30- and 90-day) and coexisting hypertension, hyperlipidemia, ischemic heart disease, mental disorders, COPD, CKD, liver cirrhosis, hepatitis B, hepatitis C, stroke, and liver cancer in the DM cohort, and compared this association with that in the non-DM cohort.

We also analyzed the association between the adjusted OR of mortality (30- and 90-day) and the interaction between DM and total gastrectomy by using multivariate logistic regression. Logistic regression analysis was applied to calculate the propensity score and estimate the probability of the DM assignment base on baseline variables including index year, sex, age, residential area, parental occupation, and history of comorbidity. Finally, we used the logistic regression model stratification of the matched pairs to estimate the risk of postoperative complications and mortality between DM and non-DM cohorts.

All analyses were performed using the SAS 9.4 package (SAS Institute Inc, North Carolina). $P < 0.05$ in 2-tailed tests indicated significance.

RESULTS

The DM cohort and the non-DM cohort comprised 6284 and 6269 patients, respectively, who received a gastrectomy for GC during the study period (1999–2010). Table 1 shows the demographic characteristics and comorbidities of the 2 cohorts. Because we matched the 2 cohorts in age and sex, no significant difference in age and sex existed between the cohorts (Table 1). However, patients with DM tended to have a lower monthly income than did patients without DM (Table 1). As expected, the prevalence of comorbidities, namely hypertension, CAD, COPD, stroke, hyperlipidemia, liver cirrhosis, and CKD, was significantly higher in the DM cohort than in the non-DM cohort.

Next, we analyzed the postgastrectomy risks of morbidity and mortality in both cohorts. Multiple logistic regression model analysis revealed that, compared with the patients without DM, the patients with DM did not exhibit excessive risks of 30-day postgastrectomy mortality or morbidities (including 30- and 90-day postoperative mortality), as shown in supplementary Table 1, <http://links.lww.com/MD/A411>.

TABLE 1. Demographic characteristics of patients with and without diabetes after gastrectomy

	Diabetes				P
	No (N = 6269)		Yes (N = 6284)		
	n	%	n	%	
Age group, y*					0.99
20–55	610	9.73	610	9.71	
55–65	1160	18.5	1160	18.5	
65–75	2248	35.9	2252	35.8	
75+	2251	35.9	2262	36.0	
Mean (SD)†	70.0 (10.4)		70.1 (10.3)		0.54
Sex*					0.93
Women	2289	36.5	2299	36.6	
Men	3980	63.5	3985	63.4	
Monthly income (NTD)*					<0.0001
<15,000	3680	58.7	4054	64.5	
15,000–25,000	2089	33.3	1789	28.5	
≥25,000	500	7.98	441	7.02	
Occupation*					<0.0001
White collar	2520	40.2	2606	41.5	
Blue collar	2817	44.9	2593	41.3	
Others	932	14.9	1085	17.3	
Comorbidity history*					
Hypertension	3194	50.9	4827	76.8	<0.0001
Hyperlipidemia	1343	21.4	3402	54.1	<0.0001
CAD	2006	32.0	3079	49.0	<0.0001
CKD	822	13.1	1604	25.5	<0.0001
COPD	2256	36.0	2684	42.7	<0.0001
Stroke	1502	24.0	2322	37.0	<0.0001
Liver cirrhosis	180	2.87	301	4.79	<0.0001

CAD = coronary artery disease, COPD = chronic obstructive pulmonary disease.

* Chi-square test; white collar: civil services, institution workers, enterprise, business, and industrial administration personnel; blue collar: farmers, fishermen, vendors, and industrial laborers; others: retired, unemployed, and low-income populations; NTD: New Taiwan Dollars.

† Student *t* test.

To further verify our observation, we used the second method, propensity matching method, to select the DM and non-DM cohorts (n = 3996, respectively) from our database. As expected, there existed no differences in baseline characteristics and comorbidities between DM and non-DM cohorts after propensity matching (supplementary Table 2, <http://links.lww.com/MD/A411>). In the analysis after propensity score matching, we still did not find any statistically significant difference in postoperative complications and mortality (including 30 and 90 days) between the cohorts (supplementary Table 3, <http://links.lww.com/MD/A411>), which was consistent with the results obtained by the first analysis.

We further investigated whether DM-related complications are associated with the 30- and 90-day postgastrectomy risk of mortality (Tables 2 and 3). Patients who experienced a DM-related coma before undergoing a gastrectomy were associated with a significantly higher risk of 30-day postoperative mortality compared with the patients in the non-DM cohort (adjusted OR 2.46, 95% CI 1.10–5.54, Table 2). On the contrary, no difference was observed in the 30-day mortality rate between the patients without DM and patients with other DM-related morbidities, such as ophthalmological involvement, peripheral circulatory disorder, ketoacidosis, and nephropathy (Table 2). Compared with the non-DM cohort, the risk of 90-day postoperative mortality is higher in DM patients with eye involvement (adjusted OR 1.50, 95% CI 1.08–2.06), peripheral circulatory disorder (adjusted OR 1.69, 95% CI 1.23–2.33), coma (adjusted OR 2.02, 95% CI 1.24–3.30), and renal manifestations (adjusted OR 1.31, 95% CI 1.01–1.70) respectively. (Table 3)

We then investigated whether the risk of postoperative mortality is associated with coexisting morbidities in patients with DM (Tables 4 and 5). Most of the comorbidities, including hypertension, CAD, COPD, stroke, hyperlipidemia, and CKD, were not associated with an increased postoperative mortality risk in the diabetic patients, compared with the non-DM patients. However, patients with DM and concomitant cirrhosis exhibited a significantly higher 30-day postoperative mortality risk than did those without DM (adjusted OR 2.08, 95% CI 1.01–4.27, Table 4). But in risk of 90-day postoperative mortality, the DM cohort with particularly comorbidity (including hypertension, hyperlipidemia, CAD, CKD, COPD, stroke, and liver cirrhosis) had no statistically significant higher than non-DM cohort (*P* > 0.05; Table 5).

Next, we addressed whether diabetes is associated with different 30- and 90-day mortality risks in patients undergoing different extent of gastrectomy (ie, total gastrectomy or not). Based on the ICD coding, we were able to identify the subsets of patients undergoing total gastrectomy or not. Supplementary Tables 4 and 5, <http://links.lww.com/MD/A411> illustrate the joint effects of total gastrectomy and DM on the OR of 30- and 90-day mortality. Not surprisingly, we found that total gastrectomy was associated in marginal increase in the 30-day mortality rate (adjusted OR 1.39, 95% CI 0.93–2.09; supplementary Table 4, <http://links.lww.com/MD/A411>) and significantly elevated risk of 90-day mortality (adjusted OR 1.30, 95% CI 1.06–1.60; supplementary Table 5, <http://links.lww.com/MD/A411>) in nondiabetic cohorts. However, DM is not associated with increased 30- or 90- day mortality no matter whether the patients underwent total gastrectomy or not.

DISCUSSION

According to our research, this study was the first nationwide population-based study to investigate the effects of DM on the risk of surgical mortality and morbidity in patients

TABLE 2. Risk of 30-day postoperative mortality in patients with preoperative diabetes-related comorbidities, compared with nondiabetic patients

Outcomes	n	Deaths	Mortality, %	30-Day mortality adjusted OR (95% CI)
Without diabetes	6269	102	1.63	1.00
Type of diabetes				
Type 1	226	2	0.88	0.56 (0.14–2.32)
Type 2	6058	111	1.83	1.10 (0.82–1.48)
Preoperative diabetes-related eye involvement				
Without eye involvement	5793	104	1.80	1.09 (0.81–1.46)
With eye involvement	491	9	1.83	1.05 (0.52–2.13)
Preoperative diabetes-related PCD				
Without PCD	5834	104	1.78	1.08 (0.81–1.46)
With PCD	450	9	2.00	1.14 (0.56–2.30)
Preoperative diabetes-related ketoacidosis				
Without ketoacidosis	6173	110	1.78	1.08 (0.80–1.44)
With ketoacidosis	111	3	2.70	1.76 (0.54–5.72)
Preoperative diabetes-related coma				
Without coma	6144	106	1.73	1.05 (0.78–1.41)
With coma	140	7	5.00	2.46 (1.10–5.54)*
Preoperative diabetes-related renal manifestations				
Without renal manifestations	5344	93	1.74	1.07 (0.80–1.45)
With renal manifestations	940	20	2.13	1.16 (0.69–1.96)

OR = odds ratio, CI = confidence interval (adjusted for age, sex, monthly income [NTD], occupation, and comorbidity history), PCD = peripheral circulatory disorder.

* $P < 0.05$.

undergoing resection for GC. We observed that the patients with DM did not exhibit increased risks of major surgical complications or mortality compared with the patients without DM after we adjusted for covariates. However, patients with a

history of a DM-related coma exhibited an ~2-fold increased risk of postoperative mortality. However, other preoperative DM-related complications were not significantly associated with an increased risk of postoperative mortality after a

TABLE 3. Risk of 90-day postoperative mortality in patients with preoperative diabetes-related comorbidities, compared with nondiabetic patients

Outcomes	n	Deaths	Mortality, %	90-Day mortality adjusted OR (95% CI)
Without diabetes	6269	417	6.65	1.00
Type of diabetes				
Type 1	226	13	5.75	0.85(0.48–1.51)
Type 2	6058	416	6.87	1.01(0.87–1.18)
Preoperative diabetes-related eye involvement				
Without eye involvement	5793	378	6.53	0.97(0.83–1.13)
With eye involvement	491	51	10.4	1.50(1.08–2.06)*
Preoperative diabetes-related PCD				
Without PCD	5834	378	6.48	0.96(0.82–1.12)
With PCD	450	51	11.3	1.69(1.23–2.33)**
Preoperative diabetes-related ketoacidosis				
Without ketoacidosis	6173	419	6.79	1.00(0.86–1.16)
With ketoacidosis	111	10	9.01	1.41(0.72–2.76)
Preoperative diabetes-related coma				
Without coma	6144	408	6.64	0.98(0.84–1.15)
With coma	140	21	15.0	2.02(1.24–3.30)**
Preoperative diabetes-related renal manifestations				
Without renal manifestations	5344	338	6.32	0.96(0.82–1.12)
With renal manifestations	940	91	9.68	1.31(1.01–1.70)*

OR = odds ratio, CI = confidence interval (adjusted for age, sex, monthly income [NTD], occupation, and comorbidity history), PCD = peripheral circulatory disorder.

* $P < 0.05$.

** $P < 0.01$.

TABLE 4. Joint effects of coexisting medical conditions on 30-day postoperative mortality in patients with diabetes

Outcomes	n	Deaths	Mortality, %	30-Day mortality OR (95% CI)
No diabetes	6269	102	1.63	1.00
Diabetes with hypertension	4827	93	1.93	1.08 (0.79–1.48)
Diabetes with hyperlipidemia	3402	56	1.65	0.92 (0.65–1.31)
Diabetes with CAD	3079	68	2.21	1.11 (0.79–1.58)
Diabetes with CKD	1604	32	2.00	1.06 (0.68–1.64)
Diabetes with COPD	2684	60	2.24	1.20 (0.84–1.71)
Diabetes with stroke	2322	62	2.67	1.40 (0.98–2.00)
Diabetes with liver cirrhosis	301	9	2.99	2.08 (1.01–4.27)*

Preoperative diabetes was defined as the patient having at least 1 hospital admission or at least 2 visits for outpatient medical services related to diabetes. CAD = coronary artery disease, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, OR = odds ratio. Model manual adjusted for age, sex, monthly income (NTD), occupation, and comorbidity history.

* $P < 0.05$.

gastrectomy. The study results, which were obtained using a nationwide data set, indicated that GC surgery can be performed safely in patients with DM. However, attention should be devoted to perioperatively monitoring and managing patients with a history of DM-related neurologic symptoms.

Overall, our data indicated that the 30-day postoperative mortality rates were 1.63% for the non-DM cohort and 1.80% for the DM cohort; these rates are 2-fold to 3-fold higher than the mortality rates reported in randomized controlled studies.^{21,22} Several studies have demonstrated that the overall in-hospital mortality rate can be <1% when experienced surgeons perform the operation, irrespective of the extent of lymph node dissection.^{19,21,22} By contrast, a case series of 434 patients reported a mortality rate of 2.7% after a gastrectomy for GC.²³ The results of the present study were based on nationwide data and, therefore, may more accurately reflect the results of GC surgery in general practice.

Postoperative infection is among the major complications that can lead to severe sequelae and death following gastrectomy.²³ Severe postoperative infection can be due to pneumonia, bloodstream infection related to the central line, urinary tract infection, infected intraabdominal fluid accumulation, and anastomotic insufficiency.^{20,21} Patients with DM are generally susceptible to infection,²⁴ and previous studies have proposed that DM is a prognostic factor of postoperative infection

events.^{25,26} However, our data indicated that preoperative DM is not related to postoperative infection events; this finding is consistent with that of another study reporting that postoperative blood sugar, but not preexisting DM, predicts postoperative infection.²⁷ We recommend that future studies investigate whether our finding can be explained partly by greater postoperative glycemic control, which reduces the risk of postoperative septicemia.²⁸

Postoperative ARF is not an uncommon complication after major operations such as gastrectomy. Depending on the definition of ARF, the incidence of ARF varies among studies, ranging between 1% and 30% after cardiac bypass surgery²⁹ and between 5.8% and 6.7% after noncardiac surgery.^{30,31} In this study, the incidence of ARF after gastrectomy was 0.49% in the non-DM cohort and 0.68% in the DM cohort. Theoretically, DM might predispose patients to ARF development through various pathophysiological mechanisms, such as renal hemodynamic instability,³² endothelial cell injury,³³ and inflammatory processes.³⁴ Our previous study suggested that DM is related to an increased incidence of posthepatectomy ARF,¹⁶ which was not observed in the present study. Our results may be explained by improved perioperative management techniques, including the maintenance of hemodynamic stability during operation, amelioration of surgery-related inflammation, avoidance of vasoactive or nephrotoxic agents, and prevention of postoperative dehydration.

TABLE 5. Joint effects of coexisting medical conditions on 90-day postoperative mortality in patients with diabetes

Outcomes	n	Deaths	Mortality (%)	90-Day mortality OR (95% CI)
No diabetes	6269	417	6.65	1.00
Diabetes with hypertension	4827	350	7.25	0.99 (0.84–1.17)
Diabetes with hyperlipidemia	3402	211	6.20	0.86 (0.72–1.04)
Diabetes with CAD	3079	238	7.73	0.98 (0.82–1.19)
Diabetes with CKD	1604	136	8.48	1.14 (0.91–1.43)
Diabetes with COPD	2684	202	7.53	0.94 (0.78–1.15)
Diabetes with stroke	2322	216	9.30	1.20 (0.99–1.46)
Diabetes with liver cirrhosis	301	26	8.64	1.40 (0.91–2.15)

Preoperative diabetes was defined as the patient having at least 1 hospital admission or ≥2 visits for outpatient medical services related to diabetes. CAD = coronary artery disease, CI = confidence interval, CKD = chronic kidney disease, COPD = chronic obstructive pulmonary disease, OR = odds ratio. Model manual adjusted for age, sex, monthly income (NTD), occupation, and comorbidity history.

Postoperatively, cardiovascular events are often difficult to diagnose and may be overlooked because atypical symptoms may be masked by analgesics and physicians may not be alert. One study estimated that only 53% of patients with myocardial infarction exhibit a clinical sign or symptom that triggers a physician's awareness.³⁵ No significant difference in myocardial infarction between the DM and non-DM cohorts was observed in this study, possibly because myocardial infarction is underdiagnosed in patients with DM, and perioperative care has become sophisticated. Patients with DM have blunted pain perception, causing diagnosing myocardial infarction to be difficult. Balanced fluid therapy, blood pressure control, and pain management are essential for preventing postoperative cardiovascular events. Moreover, clinicians can currently use numerous medications that lower the risk of cardiovascular events.³⁵ Additional studies are required to clarify our observations.

In the present study, although total gastrectomy seemed to be associated with a decreased 30-day mortality in DM cohort, further analysis of 90-day mortality showed the trend disappeared. Moreover, total gastrectomy is associated with increased 90-day mortality in nondiabetic cohort (supplementary Table 5, <http://links.lww.com/MD/A411>). It is well-documented that total gastrectomy is associated with significant higher risks of postoperative morbidities and mortality, in comparison with subtotal gastrectomy.^{36,37} Total gastrectomy usually carries more unfavorable factors for postoperative recovery, such as technical difficulty, poorer oral intake due to lack of food reservoir, and more extensive lymphadenectomy, as well as possible splenectomy.^{37,38} Based on our database, we could not analyze the distribution and/or percentage of these unfavorable factors in the diabetic and nondiabetic cohorts. Further studies are therefore warranted.

We were unable to analyze some important preoperative parameters, which may affect the postoperative outcomes, such as cancer stages, performance status, activity of daily life, and American Society of Anesthesiologists score. Presumably, the DM group should have worse preoperative physical status than the non-DM group because the prevalence of comorbidities was higher in the DM group. Despite these unfavorable factors, we still could not demonstrate poorer surgical outcomes after gastrectomy in the DM group. Our finding suggested that DM per se may not affect the surgical results for those patients undergoing gastrectomy for GC.

We did not investigate the impact of cancer stage on 30- and 90-day surgical mortalities in the present study, due to lack of such data in NHIRD. The stage of cancer is a critical factor affecting not only long-term survival but also surgical outcomes. Although diabetes is associated with increased risk of GC,^{8–11} it remains unknown whether diabetic patients tend to have more advanced GC. Theoretically, surgery could be more difficult in patients with more advanced GC, which usually presented with larger tumor size, poorer nutritional conditions, and more extensive lymph node metastasis. The patients with more advanced GC therefore tend to experience more extensive surgical resection. As shown in supplementary Tables 4 and 5, <http://links.lww.com/MD/A411>, patients undergoing total gastrectomy exhibited higher surgical mortality risks than those who did not have total gastrectomy. Our findings supported that surgical risks may be higher in patients with later stages of GC. However, it has been shown that extended lymph node dissection did not increase the mortality or morbidity rate of resection for GC in experienced hands.³⁹ Further study will be necessary to address the effects of cancer stage on surgical mortality after resection of GC, especially in diabetic patients.

Some of the limitations should be mentioned which may be the unknown confounding factors or unmeasured biases relevant to this study: the NHIRD does not record a patient's individual data of the smoking amount, alcohol use, liver function, blood loss, and gastrectomy reconstruction method; this is a retrospective cohort study (unlike prospective studies); although the data from the inpatient database were strictly audited for the reimbursement purpose, we could not use the individual chart review for every subject to confirm the diagnoses' accuracy of DM, GC, and complications; a potentially selection bias should be considered because the study patients were identified by the inpatient admission with severe diseases or increased access to hospital care (such as these patients with mild DM and patients without hospital cares might have been excluded in this study). Although the above study limitations could cause the underestimation or overestimation of the risk of postoperative complications in DM patients, they should not produce the key bias based on the universal and population-based health insurance data.

In summary, we found that the risk of 90-day mortality after gastrectomy for GC is higher in patients with certain DM-related manifestations than those without DM. This nationwide study suggested that DM-related eye involvement, coma, peripheral circulatory disease, and renal manifestations are prognostic of poor surgical outcomes after gastrectomy for GC.

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