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

A Nationwide Database Study

Ming-Shian Tsai, MD, Yu-Chiao Wang, MSc, Yin-Hsien Kao, PhD, Long-Bin Jeng, MD, and Chia-Hung Kao, MD

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 6286 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.

INTRODUCTION

Gastric cancer (GC) is among the most common cancers worldwide and causes considerable mortality, despite the declining trend in its incidence.¹² GC can be attributed to several factors, including genetic factors,³,⁴ red meat diet,⁵,⁶ 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 NHIC 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 998.83), 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 χ2 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 morbidity (including 30- and 90-day postoperative mortality), as shown in supplementary Table 1, http://links.lww.com/MD/A411.

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 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 0.39–2.09; 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.
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 a ~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 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.

### 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.
Joint effects of coexisting medical conditions on 90-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.

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| 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 exhibited a clinical sign or symptom that triggers a physician’s awareness.\(^25\) 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.\(^10\) 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.

REFERENCES

1. Tanaka K, Kiyohara Y, Kubo M, et al. Secular trends in the incidence, mortality, and survival rate of gastric cancer in a general Japanese population: the Hisayama study. Cancer Causes Control. 2005;16:573–578.
2. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. J Clin Oncol. 2006;24:2137–2150.
3. Deng N, Goh LK, Wang H, et al. A comprehensive survey of genomic alterations in gastric cancer reveals systematic patterns of molecular exclusivity and co-occurrence among distinct therapeutic targets. Gut. 2012;61:673–684.
4. Hu Z, Ajani JA, Wei Q. Molecular epidemiology of gastric cancer: current status and future prospects. Gastrointest Cancer Res. 2007;1:12–19.
5. Pourfarzi F, Whelan A, Kaldor J, et al. The role of diet and other environmental factors in the causation of gastric cancer in Iran—a population based study. Int J Cancer. 2009;125:1953–1960.
6. Tsugane S, Sasazuki S. Diet and the risk of gastric cancer: review of epidemiological evidence. Gastric Cancer. 2007;10:75–83.
7. Yanoaka K, Oka M, Ohata H, et al. Eradication of Helicobacter pylori prevents cancer development in subjects with mild gastric atrophy identified by serum pepsinogen levels. Int J Cancer. 2009;125:2697–2703.
8. Inoue M, Iwasaki M, Otani T, et al. Diabetes mellitus and the risk of cancer: results from a large-scale population-based cohort study in Japan. Arch Intern Med. 2006;166:1871–1877.
9. Yamagata H, Kiyohara Y, Nakamura S, et al. Impact of fasting plasma glucose levels on gastric cancer incidence in a general Japanese population the Hisayama study. Diabetes Care. 2005;28:789–794.
10. Zendehdel K, Nygren O, Östenson C-G, et al. Cancer incidence in patients with type 1 diabetes mellitus: a population-based cohort study in Sweden. J Natl Cancer Inst. 2003;95:1797–1800.
11. Sekikawa A, Fukui H, Maruo T, et al. Diabetes mellitus increases the risk of early gastric cancer development. *Eur J Cancer*. 2014;50:2065–2071.

12. Tseng C-H. Diabetes conveys a higher risk of gastric cancer mortality despite an age-standardised decreasing trend in the general population in Taiwan. *Gut*. 2010;60:774–779.

13. Herlitz J, Wognsen GB, Emanuelsson H, et al. Mortality and morbidity in diabetic and nondiabetic patients during a 2-year period after coronary artery bypass grafting. *Diabetes Care*. 1996;19:698–703.

14. McAlister FA, Man J, Bistritz L, et al. Diabetes and coronary artery bypass surgery: an examination of perioperative glycemic control and outcomes. *Diabetes Care*. 2003;26:1518–1524.

15. Yeh CC, Liao CC, Chang YC, et al. Adverse outcomes after noncardiac surgery in patients with diabetes: a nationwide population-based retrospective cohort study. *Diabetes Care*. 2013;36:3216–3221.

16. Tsai MS, Lin CL, Chang SN, et al. Diabetes mellitus and increased postoperative risk of acute renal failure after hepatectomy for hepatocellular carcinoma: a nationwide population-based study. *Ann Surg Oncol*. 2014;21:3810–3816.

17. Wu C-W, Lo S-S, Shen K-H, et al. Surgical mortality, survival, and quality of life after resection for gastric cancer in the elderly. *World J Surg*. 2000;24:465–472.

18. Tuujinaka T, Sasaki M, Yamamoto S, et al. Influence of overweight on surgical complications for gastric cancer: results from a randomized control trial comparing D2 and extended para-aortic D3 lymphadenectomy (JCOG9501). *Ann Surg Oncol*. 2007;14:355–361.

19. Park D, Lee HJ, Kim HH, et al. Predictors of operative morbidity and mortality in gastric cancer surgery. *Brit J Surg*. 2005;92:1099–1102.

20. Viste A, Hau`gstvedt T, Eide GE, et al. Postoperative complications and mortality after surgery for gastric cancer. *Ann Surg*. 1988;207:7–13.

21. Sano T, Sasaki M, Yamamoto S, et al. Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy—Japan Clinical Oncology Group study 9501. *J Clin Oncol*. 2004;22:2767–2773.

22. Deguchi M, Sasaki M, Calgaro M, et al. Morbidity and mortality after D1 and D2 gastrectomy for cancer: interim analysis of the Italian Gastric Cancer Study Group (IGCSCG) randomised surgical trial. *Eur J Surg Oncol (EJSO)*. 2004;30:303–308.

23. Gil-Rendo A, Martinez-Regueira F, Martinez AS, et al. Risk factors related to operative morbidity in patients undergoing gastrectomy for gastric cancer. *Clin Transl Oncol*. 2006;8:354–361.

24. Pozzilli P, Leslie RD. Infections and diabetes: mechanisms and prospects for prevention. *Diabet Med*. 1994;11:935–941.

25. Yanaga K, Matsumata T, Hayashi H, et al. Effect of diabetes mellitus on hepatic resection. *Arch Surg*. 1993;128:445–448.

26. Pessaux P, van den Broek MA, Wu T, et al. Identification and validation of risk factors for postoperative infectious complications following hepatectomy. *J Gastrointest Surg*. 2013;17:1907–1916.

27. Ramos M, Khalpey Z, Lipsitz S, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. *Ann Surg*. 2008;248:585–591.

28. Dronge AS, Perkal MF, Kancir S, et al. Long-term glycemic control and postoperative infectious complications. *Arch Surg*. 2006;141:375–380.

29. Rosner MH, Okusa MD. Acute kidney injury associated with cardiac surgery. *Clin J Am Soc Nephrol*. 2006;1:19–32.

30. Biteker M, Dayan A, Tekkesin AI, et al. Incidence, risk factors, and outcomes of perioperative acute kidney injury in noncardiac and nonvascular surgery. *Ann Surg*. 2014;207:53–59.

31. Weingarten TN, Gurrieri C, McCaffrey JM, et al. Acute kidney injury following bariatric surgery. *Obes Surg*. 2013;23:64–70.

32. Ramseayer DV, Garvin JL. Tumor necrosis factor-alpha: regulation of renal function and blood pressure. *Am J Physiol Renal Physiol*. 2013;304:F1231–1242.

33. Hempel A, Maasch C, Heinze U, et al. High glucose concentrations increase endothelial cell permeability via activation of protein kinase C alpha. *Circ Res*. 1997;81:363–371.

34. Gao G, Zhang B, Ramesh G, et al. TNF-alpha mediates increased susceptibility to ischemic AKI in diabetes. *Am J Physiol Renal Physiol*. 2013;304:F515–521.

35. Devereaux P, Goldman L, Yusuf S, et al. Surveillance and prevention of major perioperative ischemic cardiac events in patients undergoing noncardiac surgery: a review. *Can Med Assoc J*. 2005;173:779–788.

36. Robertson C, Chung S, Woods S, et al. A prospective randomized trial comparing R1 subtotal gastrectomy with R3 total gastrectomy for antral cancer. *Ann Surg*. 1994;220:176–182.

37. Bozzetti F, Marubini E, Bonfanti G, et al. Subtotal versus total gastrectomy for gastric cancer: five-year survival rates in a multi-center randomized Italian trial. *Ann Surg*. 1999;230:170–178.

38. Csendes A, Burdiles P, Rojas J, et al. A prospective randomized study comparing D2 total gastrectomy versus D2 total gastrectomy plus splenectomy in 187 patients with gastric carcinoma. *Surgery*. 2002;131:401–407.

39. Siewert JR, Böttcher K, Stein HJ, et al. Relevant prognostic factors in gastric cancer: ten-year results of the German Gastric Cancer Study. *Ann Surg*. 1998;228:449–461.