

The Influence of Diabetes Mellitus on Short-Term Outcomes of Patients with Bleeding Peptic Ulcers

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Purpose: Little information is available on the influence of diabetes mellitus on the short-term clinical outcomes of patients with bleeding peptic ulcers. The aim of this study is to investigate whether diabetes mellitus influences the short-term clinical outcomes of patients with bleeding peptic ulcers using a Japanese national administrative database. **Materials and Methods:** A total of 4863 patients treated by endoscopic hemostasis on admission for bleeding peptic ulcers were referred to 586 participating hospitals in Japan. We collected their data to compare the risk-adjusted length of stay (LOS) and in-hospital mortality of patients with and without diabetes mellitus within 30 days. Patients were divided into two groups: patients with diabetes mellitus (n=434) and patients without diabetes mellitus (n=4429). **Results:** Mean LOS in patients with diabetes mellitus was significantly longer than those without diabetes mellitus (15.8 days vs. 12.5 days, $p<0.001$). Also, higher in-hospital mortality within 30 days was observed in patients with diabetes mellitus compared with those without diabetes mellitus (2.7% vs. 1.1%, $p=0.004$). Multiple linear regression analysis revealed that diabetes mellitus was significantly associated with an increase in risk-adjusted LOS. The standardized coefficient was 0.036 days ($p=0.01$). Furthermore, the analysis revealed that diabetes mellitus significantly increased the risk of in-hospital mortality within 30 days (odds ratio=2.285, 95% CI=1.161-4.497, $p=0.017$). **Conclusion:** This study demonstrated that presence of diabetes mellitus significantly influences the short-term clinical outcomes of patients with bleeding peptic ulcers.

Key Words: Bleeding peptic ulcers, diabetes mellitus, health care quality, retrospective studies, databases

INTRODUCTION

Bleeding peptic ulcers are one of the most frequently encountered emergency conditions in daily practice for clinicians.^{1,2} The incidence of bleeding peptic ulcers patients with several chronic conditions has been increasing as a result of the aging of society in developed countries.³⁻⁵ In a recent report concerning bleeding peptic ulcers, Theocharis, et al.³ reported that the proportion of patients with chronic con-

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ditions had increased between 1995 and 2005 in Greece. Furthermore, some previous studies have suggested that the presence of chronic conditions is significantly associated with the clinical outcomes of patients with bleeding peptic ulcers.^{4,5}

Many researchers have investigated the influence of diabetes mellitus on clinical outcomes of patients with certain medical conditions or surgical procedures.⁶⁻⁹ In particular, many previous reports have shown strong associations between diabetes mellitus and cardiovascular diseases or interventional procedures, such as acute myocardial infarction or coronary stent implantation, and concluded that diabetes mellitus significantly influences the short-term clinical outcomes of patients with cardiac disease or procedure.^{8,9} It is plausible that diabetes mellitus is an independent predictor for the short-term clinical outcomes of these patients.

However, little information is available on the influence of diabetes mellitus on the short-term clinical outcomes of patients with bleeding peptic ulcers. Establishment of a relationship between diabetes mellitus and the clinical outcomes of patients with bleeding peptic ulcers could contribute to future studies about bleeding peptic ulcers and have significant implications for the quality of patient medical care.

In this study, we investigated the influence of diabetes mellitus on short-term clinical outcomes of patients with bleeding peptic ulcers. This study was achieved using a national administrative database associated with the Diagnosis Procedure Combination (DPC) system.

MATERIALS AND METHODS

Administrative database associated with the DPC system

Japanese case mix projects based on the DPC system were introduced to 82 academic hospitals (80 university hospitals, the National Cancer Centre and the National Cardiovascular Centre) in 2003.¹⁰⁻¹² Insurance reimbursement using the DPC system is quite prevalent in Japan, and the administrative database of the DPC system has increased the representation of acute care hospitals. As of 2007, data from approximately 450,000 inpatients have been compiled, representing approximately 90% of all acute care inpatient hospitalizations.¹⁰⁻¹²

The administrative database of the DPC system includes each patient's discharge summary and claim information, including principal diagnosis, comorbidities and complications during hospitalization. These data are coded in the In-

ternational Classification of Diseases and Injuries (ICD)-10th. In addition, this administrative database also contains detailed patients' information, such as all surgical procedures and medications that have been indexed in the original code. These codes are determined by the Ministry of Health, Labor and Welfare of Japan. The administrative database associated with the DPC system also includes the quantity and date of all care delivered on a daily basis.¹⁰⁻¹²

Study setting

We selected 4863 patients treated by endoscopic hemostasis on admission for bleeding peptic ulcers in 586 DPC participating hospitals (55 academic and 531 community hospitals) between April and December in 2008. These hospitals are dispersed throughout Japan and play a leading role in providing acute care medicine, advancing medical research, and educating students and medical residents.¹⁰⁻¹²

Using the data of comorbidities in the administrative database, patients were divided into two groups according to the presence of diabetes mellitus: patients with diabetes mellitus (n=434) and patients without diabetes mellitus (n=4429). In the present study, diabetes mellitus was defined as code E10-E14 (insulin dependent, non-insulin dependent, malnutrition-related diabetes mellitus, other specified diabetes, and other non-specified diabetes) in the ICD-10th.

The use of DPC data was permitted by all institution and hospitals that provided detailed data. The research protocol of the study was approved by the ethics committee of medical care and research of the University of Occupational and Environmental Health, Kitakyushu, Japan.

Study variables

We collected data in the administrative database with regard to the clinical characteristics of patients as follows: causes of bleeding peptic ulcers, gender, chronic comorbid conditions, sex, hospital type, use of ambulance transportation, use of a proton pump inhibitor, antiplatelet and anticoagulation drugs, frequencies of endoscopic hemostasis for recurrent bleeding and salvage surgery after endoscopic hemostasis, length of stay (LOS) and in-hospital mortality within 30 days after admission.

The causes of the bleeding peptic ulcers were defined in accordance with the ICD-10th: hemorrhagic gastric ulcer (K25.0, K25.2, K25.4 and K25.6) and hemorrhagic duodenal ulcer (K26.0, K26.2, K26.4 and K26.6). Elderly patients have a higher risk of recurrent bleeding or death than younger patients, and the patients were therefore stratified by age

into those aged <80 years and those aged ≥ 80 years, as described in a previous study.¹³ To assess the severities of chronic comorbid conditions except for diabetes mellitus, we used the Charlson Comorbidity Index (CCI) for every patient using the administrative database.¹⁰⁻¹² CCI was expressed as the score of comorbid conditions and was initially evaluated as a continuous variable. However, categorical variables defining three categories of severity of comorbidity were created to simplify the presentation of the results: 0, mild; 1, moderate; and 2 or more, severe.^{10,11} Hospital type was classified as academic or community.¹⁰⁻¹² In-hospital mortality within 30 days was evaluated, rather than overall in-hospital mortality, because this measure eliminates potential bias due to differences in LOS across hospitals and over time.¹⁴

Statistical analysis

The categorical data were compared using the chi-square test for categorical variables and the Mann-Whitney U test for continuous variables. In additional analyses, we used multiple linear regression models to identify the impact of the presence of diabetes mellitus on LOS, and addressed potential confounding variables in the case mix data by controlling for the severities of chronic comorbid conditions

and additional factors related to LOS, such as causes of bleeding peptic ulcers, age, gender, hospital type, use of ambulance transportation, use of a proton pump inhibitor, antiplatelet and anticoagulation drugs, and endoscopic hemostasis and salvage surgery during hospitalization. Because the distribution of LOS was skewed to the right, LOS was log-transformed in this model. Multiple logistic regression models were also used to identify the impact of the presence of diabetes mellitus on the in-hospital mortality within 30 days, considering the above factors.

All statistical analysis was performed using the STATA statistical software package version 9.0 (Stata Corporation, College Station, TX, USA). Values of $p < 0.05$ were considered to indicate statistical significance.

RESULTS

We identified a total of 4863 patients across 586 hospitals, comprising 3899 with hemorrhagic gastric ulcers, and 964 with hemorrhagic duodenal ulcers. The clinical characteristics and presentations of the patients are shown in Table 1. The mean age and proportions of elderly patients were sig-

Table 1. Clinical Characteristics and Presentations of Patients according to the Presence of Diabetes Mellitus

	Patients with DM	Patients without DM	<i>p</i> value
Number of patients	434	4429	
Causes of the bleeding peptic ulcers (%)			
Hemorrhagic gastric ulcer	79.9	82.5	0.206
Hemorrhagic duodenal ulcer	20.1	17.5	
Mean age [yrs (SD)]	66.5 (18.1)	64.3 (17.8)	0.016
Elderly patients [≥ 80 yrs, (%)]	26.7	19.7	0.001
Severities of chronic comorbid conditions (%)			
Mild	39.4	45.3	0.062
Moderate	44.9	40.7	
Severe	15.7	14.0	
Male patients (%)	67.7	67.0	0.772
Hospital type (%)			
Academic hospitals	5.9	6.7	0.556
Community hospitals	94.1	93.3	
Use of ambulance transportation (%)	39.4	40.5	0.671
Use of proton pump inhibitor (%)	85.9	86.8	0.602
Use of antiplatelet drugs (%)	4.2	4.1	0.959
Use of anticoagulation drugs (%)	2.8	3.0	0.836
Endoscopic hemostasis for recurrent bleeding (%)	13.0	14.2	0.476
Salvage surgery after endoscopic hemostasis (%)	0.9	0.6	0.594
Mean length of stay [days (SD)]	15.8 (18.7)	12.5 (10.3)	<0.001
In-hospital mortality within 30 days (%)	2.7	1.1	0.004

DM, diabetes mellitus; SD, standard deviation.

nificantly higher in patients with diabetes mellitus than those without diabetes mellitus. However, there were no significant differences between the two groups with regard to the proportion of the severities of chronic comorbid conditions, male patients, hospital type, use of ambulance transportation, use of proton pump inhibitor, antiplatelet and anticoagulation drugs, endoscopic hemostasis and salvage surgery during hospitalization. Significant variation in mean LOS was observed between groups (15.8±18.7 days in patients with diabetes mellitus vs. 12.5±10.3 days in patients without diabetes mellitus, $p<0.001$). Higher in-hospital mortality within 30 days was observed in patients with diabetes mellitus than in those without diabetes mellitus (2.7% vs. 1.1%, $p=0.004$).

Multiple linear regression analyses of factors associated with the LOS are represented in Table 2. After adjustment for potentially confounding demographic and clinical variables, diabetes mellitus was significantly associated with an increased LOS. The standardized coefficient was 0.036 days ($p=0.01$). Elderly patients, ambulance transportation, endoscopic hemostasis for recurrent bleeding and salvage surgery after endoscopic hemostasis were also significantly associated with an increased LOS (standardized coefficients: 0.152, 0.042, 0.056 and 0.1, respectively).

Multiple logistic regression analyses of factors associated

with the in-hospital mortality within 30 days are demonstrated in Table 3. In these analyses, diabetes mellitus significantly increased the risk of in-hospital mortality within 30 days [odds ratio (OR)=2.285, 95% CI=1.161-4.497, $p=0.017$]. Also, elderly patients, severe comorbid conditions, use of anticoagulation drugs, and salvage surgery after endoscopic hemostasis were associated with increased risks of in-hospital mortality within 30 days (OR: 2.138, 2.869, 2.835 and 10.546, respectively).

DISCUSSION

We conducted this study to investigate the influence of diabetes mellitus on short-term clinical outcomes of patients with bleeding peptic ulcers using the Japanese administrative database. The current study demonstrated that diabetes mellitus significantly increases in-hospital mortality and LOS in patients with bleeding peptic ulcers after adjustment for other chronic comorbid conditions and other factors.

Although there have been no studies with regard to LOS for the association between diabetes mellitus and bleeding peptic ulcers, our present findings about the influence of diabetes mellitus on in-hospital mortality to date are consis-

Table 2. Linear Regression Analysis of Factors Associated with Log-Transformed Length of Stay

Independent variables	Unstandardized coefficient	95% confidence interval	Standardized coefficient	<i>p</i> value
Intercept	2.173	(2.106, 2.241)		<0.001
Diabetes mellitus				
Patients with DM (reference: patients without DM)	0.089	(0.021, 0.157)	0.036	0.010
Causes of the bleeding peptic ulcers				
Hemorrhagic duodenal ulcer (reference: gastric ulcer)	-0.024	(-0.073, 0.023)	-0.014	0.316
Age				
Elderly patients (reference: younger patients)	0.265	(0.215, 0.316)	0.152	<0.001
Chronic comorbid conditions				
Moderate	-0.017	(-0.058, 0.024)	-0.011	0.426
Severe (reference: mild)	-0.004	(-0.063, 0.054)	-0.002	0.885
Sex				
Male (reference: female)	0.018	(-0.024, 0.061)	0.012	0.405
Hospital type				
Academic hospitals (reference: community hospitals)	-0.070	(-0.148, 0.007)	-0.025	0.075
Ambulance transportation	0.061	(0.021, 0.101)	0.042	0.002
Proton pump inhibitor	0.034	(-0.021, 0.090)	0.016	0.233
Antiplatelet drugs	-0.009	(-0.107, 0.088)	-0.002	0.848
Anticoagulation drugs	0.008	(-0.110, 0.128)	0.002	0.884
Endoscopic hemostasis for recurrent bleeding	0.117	(0.060, 0.175)	0.056	<0.001
Salvage surgery after endoscopic hemostasis	0.739	(0.537, 0.942)	0.100	<0.001

DM, diabetes mellitus.

tent with some previous studies.^{15,16} In a population-based cohort study in Denmark, Thomsen, et al.¹⁵ reported that the adjusted 30 days mortality rate ratio for bleeding peptic ulcer patients with diabetes mellitus to those without diabetes was 1.40 (95% CI=1.15-1.70). In a case-control study in the UK, Weil, et al.¹⁶ also reported that diabetes mellitus was a significant factor for poor outcomes of patients with peptic ulcer bleeding associated with non-steroidal anti-inflammatory drugs (OR=3.1, 95% CI=1.2-4.3).

The associations between diabetes mellitus and the in-

crease of in-hospital mortality and LOS may be explained by several factors. First, with regard to the association between diabetes mellitus and increased in-hospital mortality of patients with bleeding peptic ulcers, several studies suggested that diabetic angiopathy impairs mucosal integrity, leading to more severe ulcers,^{15,16} and that diabetes mellitus increases susceptibility to acute gastrointestinal injury and impairs mucosal healing.^{17,18} Therefore, the angiopathy related to diabetes mellitus may make the control of bleeding from the lesions more difficult and may influence in-hospital

Table 3. Logistic Regression Analyses of Factors Associated with In-Hospital Mortality Within 30 Days

Independent variables	Odds ratio	95% confidence interval	<i>p</i> value
Diabetes mellitus			
Patients with DM	2.285	(1.161, 4.497)	0.017
Patients without DM	1.000 (reference)		
Causes of the bleeding peptic ulcers			
Hemorrhagic duodenal ulcer	0.948	(0.486, 1.847)	0.876
Hemorrhagic gastric ulcer	1.000 (reference)		
Age			
Elderly patients	2.138	(1.195, 3.827)	0.010
Younger patients	1.000 (reference)		
Chronic comorbid conditions			
Moderate	1.769	(0.940, 3.328)	0.077
Severe	2.869	(1.407, 5.849)	0.004
Mild	1.000 (reference)		
Sex			
Male	0.840	(0.478, 1.475)	0.545
Female	1.000 (reference)		
Hospital type			
Academic hospitals	0.876	(0.270, 2.838)	0.826
Community hospitals	1.000 (reference)		
Ambulance transportation			
Used	0.970	(0.567, 1.660)	0.914
Not used	1.000 (reference)		
Proton pump inhibitor			
Used	0.646	(0.330, 1.264)	0.202
Not used	1.000 (reference)		
Antiplatelet drugs			
Used	0.693	(0.160, 2.999)	0.625
Not used	1.000 (reference)		
Anticoagulation drugs			
Used	2.835	(1.048, 7.668)	0.040
Not used	1.000 (reference)		
Endoscopic hemostasis for recurrent bleeding			
Performed	0.430	(0.153, 1.205)	0.109
Not performed	1.000 (reference)		
Salvage surgery after endoscopic hemostasis			
Performed	10.546	(3.446, 32.268)	<0.001
Not performed	1.000 (reference)		

DM, diabetes mellitus.

tal mortality of patients with bleeding peptic ulcers. Second, with regard to the association between diabetes mellitus and prolonged LOS, one possible explanation is that hospitalization was prolonged by high levels of blood sugar associated with hemorrhage from upper gastrointestinal lesions. Faigel, et al.¹⁹ reported that the glucose concentrations of patients with diabetic ketoacidosis were significantly elevated in cases of upper gastrointestinal hemorrhage. In addition, Bhatia, et al.²⁰ concluded that the admission and in-hospital blood glucose levels strongly positively correlated with the number of days of hospitalization. Several studies also showed a strong association between hyperglycemia and prolonged hospitalization.²¹⁻²³ Therefore, the hemorrhage from the lesions may contribute to the temporary high levels of blood sugar and lead to time-consuming glycemic control. As a consequence, LOS is prolonged in patients with bleeding peptic ulcers. These putative mechanisms may help explain the short-term clinical outcomes among patients with diabetes mellitus.

The strength of this study is its use of the clinical database. This administrative database can allow the assessment of a large number of patients, as well as the enrollment of a representative sample of patients with bleeding peptic ulcers for analysis in a community setting.¹⁰⁻¹² In addition, detailed medical data during hospitalizations such as all procedures and medications have been thoroughly coded.¹⁰⁻¹² This administrative database therefore enables a detailed evaluation of the quality of care and clinical outcomes, based on individual medical treatments for bleeding peptic ulcers with diabetes mellitus.

Several limitations of this study also warrant mention. First, we could not evaluate the history of diabetes mellitus or the circumstances of treatments for diabetes mellitus. Therefore, further clinical studies evaluating the relationship between diabetes mellitus and clinical outcomes in patients with bleeding peptic ulcers are required, taking account of the history or treatments of diabetes mellitus. Second, because this administrative database does not include endoscopic imaging data such as lesion size, stigmata of hemorrhage or laboratory test data such as hemoglobin, creatinine and blood urea nitrogen, we were unable to evaluate and control for some important clinical aspects of bleeding peptic ulcers. These clinical aspects of bleeding peptic ulcers may influence LOS and/or in-hospital mortality of patients. However, the subjects of this study comprised patients treated by endoscopic hemostasis on admission for bleeding peptic ulcers. Therefore, we think that our selection of pa-

tients minimizes any bias due to differences in the bleeding conditions of bleeding peptic ulcers, because almost all the patients were considered to be in a temporary hemostatic condition (in other words, almost all the patients were in the same condition at the baseline). For this reason, we believe that the administrative database used does not diminish the reliability of the present study.

Despite this limitation, the current study has implications for future research about the quality of patient care and health care policy decision making. The current study confirmed that diabetes mellitus significantly contributes to increased mortality and prolonged LOS of patients with bleeding peptic ulcers. Therefore, policy implementation of more appropriate medical treatments is necessary to achieve better clinical outcomes in patients with bleeding peptic ulcers and diabetes mellitus. One strategy for improving care for patients would be disease management programs, such as clinical practice guidelines (CPGs). As an example, CPGs for cardiovascular diseases in diabetes mellitus have been developed.²⁴ These CPGs contain detailed practical instructions for management of cardiovascular diseases in diabetic patients.²⁴ Some studies have reported that CPGs can improve the health outcomes of patients in terms of in-hospital mortality or LOS and concluded that CPGs were a significant independent predictor of clinical outcomes of patients.^{25,26} Therefore, we think that the preparation and institution of CPGs for bleeding peptic ulcers with comorbid diabetes mellitus would be a promising policy implementation for improving the short-term clinical outcomes of these patients. In addition, prospective monitoring of clinical outcomes of patients after introduction of CPGs should also be conducted in the future.

In conclusion, we have demonstrated that the presence of diabetes mellitus significantly influences the short-term clinical outcomes of patients with bleeding peptic ulcers using a national administrative database. The current findings could contribute to the policy implementation of disease management programs in patients with bleeding peptic ulcers and diabetes mellitus. To achieve better clinical outcomes for diabetic patients with bleeding peptic ulcers, CPGs for more appropriate medical treatments may be required in the future.

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