

Risk of hospitalization for diabetic macrovascular complications and in-hospital mortality with irregular physician visits using propensity score matching

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ABSTRACT

Aims/Introduction: The objective of the present study was to evaluate the risk of diabetic macrovascular complications and in-hospital mortality among diabetic patients with irregular physician visits.

Materials and Methods: We carried out a health insurance-based retrospective cohort study using claims data from diabetic patients who were newly hospitalized between April 2010 and September 2010 among beneficiaries of the Fukuoka National Health Insurance Organization. Regular visits were defined as physician visits for diabetes mellitus at least every 3 months between April 2009 and March 2010, whereas other visits or no visits were defined as irregular visits. We assigned 5,940 patients to the regular visit or the irregular visit groups using propensity score matching. We compared in-hospital mortality and hospitalization for diabetic macrovascular complications between the two groups by multiple logistic regression models.

Results: The irregular visit group had a significantly higher risk of hospitalization for acute myocardial infarction (AMI), ischemic heart diseases (IHDs) except AMI, all IHDs, all strokes and diabetic macrovascular complications than did the regular visit group. Adjusted odds ratios for AMI, IHDs except AMI, all IHDs, all strokes, and diabetic macrovascular complications were 3.52 (95% confidence interval [CI] 1.79–6.96), 1.25 (95% CI 1.02–1.54), 1.37 (95% CI 1.12–1.66), 1.29 (95% CI 1.04–1.60), and 1.28 (95% CI 1.10–1.48), respectively.

Conclusions: The present study shows that the irregular visit group had significantly higher risks of hospitalization for IHD and stroke among diabetic patients. Insurers need to motivate diabetic beneficiaries to make regular visits to physicians.

INTRODUCTION

Diabetes mellitus (DM) is a common chronic disease worldwide, and the global health expenditure on DM is expected to be at least 376 billion US dollars in 2010 and 490 billion US dollars in 2030¹. Especially among Asian countries, the prevalence of DM has rapidly increased in recent decades with economic development accompanied by changes in food supply and dietary patterns, technology transfer, and cultural admixtures².

In diabetic patients, the proportion of ischemic heart disease (IHD) is two- to fourfold higher³, the risk of stroke is approximately twofold greater⁴ and the risk of peripheral arterial disease (PAD) is approximately fourfold greater⁵ than in non-diabetic patients. In Japan, DM was reported as a risk factor for cardiovascular disease and coronary heart disease⁶, and DM is related to coronary heart disease among women and ischemic stroke among both sexes⁷. In addition, large nationwide cohort studies in Japan have suggested that DM and elevated glucose levels are associated with incident coronary heart

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disease⁸ and ischemic stroke⁹ in the general Japanese population.

In Japan, the National Diabetic Patients Survey reported that approximately 8.9 million people were strongly suspected of having DM¹⁰. Nevertheless, according to the National Health and Nutrition Survey carried out in 2009, just 2.37 million people received treatment for DM¹¹.

The Japanese government developed a set of indicators for health promotion for the period of 2001–2010, which is called “Healthy Japan 21” in financial year 2000. The midcourse review of these indicators reported that the proportion of adherence to treatment for DM and health guidance after health examinations slightly increased, but did not reach the targets¹². Subsequently, the number of patients with diabetic complications had increased beyond the target¹³.

However, there is no evidence of the effect of regular visits to physicians on in-hospital mortality of diabetic patients or the number of diabetic complications in Japan. Therefore, the objective of the present study was to evaluate the effect of irregular visits on diabetic macrovascular complications and in-hospital mortality among diabetic patients.

MATERIALS AND METHODS

Data Source

We obtained data of diabetic patients who were newly hospitalized to the general ward between April 2010 and September 2010 from fee-for-service claims data of the Fukuoka National Health Insurance Organization. We combined them with medical claims data of outpatient visits between April 2009 and March 2010. We assessed only the first hospitalizations among patients who had experienced several hospitalizations, after excluding patients who had received hemodialysis or peritoneal dialysis. From a previous study using Japanese medical claims data of fee-for-service¹⁴, we identified diabetic patients by the

diagnostic code of DM (International Classification of Diseases 10th revision [ICD-10] codes: E10–14) that they received when they were hospitalized.

Definition of Variables

Study variables included hospitalization for diabetic macrovascular complications, outcomes at discharge, age, sex, comorbidities and the use of insulin or oral hypoglycemic agents. Because Japanese medical claims data of the fee-for-service system often contain information on multiple diseases, diagnostic examinations and therapies, we converted primary diagnostic codes into six-digit codes of the Diagnosis Procedure Combination/Per-Diem Payment System (DPC/PDPS), which is a Japanese prospective payment system¹⁵. Then, we combined the six-digit diagnostic codes (base DPC), those of surgical procedures, adjuvant therapies and other diagnostic codes as comorbidities/complications, into 14-digit DPC codes. Finally, we estimated the most resource-intensive diseases by hospitalization costs, which were calculated based on the reimbursement rule of the DPC/PDPS, and defined these diseases as the primary disease. We also defined hospitalization for diabetic macrovascular complications, including IHD, stroke and PAD, as shown in Table 1.

Regular visits were defined as physician visits for DM at least every 3 months between April 2009 and March 2010, whereas other visits or no visits were defined as irregular visits. In other words, we counted months of physician visits by every quarter of the year, and defined physician visits throughout every quarter as regular visits. This timing was chosen because the expiry time of prescriptions is 3 months in the Japanese system of health insurance. Age was categorized into three groups: 64 years or younger, 65–74 years and 75 years or older. Medication for DM during hospitalization was categorized into four groups: no medication, oral hypoglycemic agents, insulin, and oral hypoglycemic agents and insulin.

Table 1 | Definition of diabetic macrovascular complications and International Classification of Diseases, 10th Revision codes for them

Diabetic macrovascular complications	Base DPC codes	Base DPC name	ICD-10 codes
All strokes			
Hemorrhagic stroke	010020	Subarachnoid hemorrhage, Unruptured cerebral aneurysm	I60.x
	010040	Non-traumatic intracranial hematoma(except for non-traumatic subdural hematoma)	I61.x, I62.9, I68.0, Q28.0–Q28.3
	010050	Non-traumatic subdural hematoma	I62.0, I62.1
Ischemic stroke	010060	Ischemic stroke	G45.x, G46.x, I63.x, I65.x, I66.x, I67.5, I67.9, I69.3, I97.8
All ischemic heart diseases			
AMI	050030	Acute myocardial infarction, recurrent myocardial infarction	I21.x, I22.x, I24.x
IHDs exopt AMI	050050	Angina pectoris, chronic myocardial infarction	I20.x, I25.x
PAD	050170	Arteriosclerosis obliterans	I74.0, I74.1, I74.2, I74.3, I74.4, I74.5, I74.8, I74.9, I70.0, I70.2, I70.8, I70.9, I72.0, I72.1, I72.4, I73.x

AMI, acute myocardial infarction; DPC, Diagnosis Procedure Combination; ICD-10, International Classification of Diseases, 10th Revision; IHDs, ischemic heart diseases; PAD, peripheral arterial disease.

Other lifestyle-related diseases (hypertension [I10] and hyperlipidemia [E78.0–78.5]) were assessed using ICD-10 codes from medical claims data during hospitalization. Furthermore, other comorbidities during hospitalization were assessed using ICD-10 codes and the Charlson Comorbidity Index (CCI) for all conditions, except for mild diabetes, diabetes with complications, cerebral vascular disease, acute myocardial infarction and unspecified peripheral vascular disease (I73.9)^{16,17}. The CCI was categorized into three categories: 0, 1 or 2, and 3 or higher¹⁸.

Statistical Analysis

Patient characteristics were constructed using frequencies and proportions for categorical variables, and using median and interquartile range for a continuous variable. Categorical variables were compared between the regular visit and irregular visit groups by Pearson's χ^2 -tests, and the continuous variable was compared between the two groups by the Mann–Whitney test.

Propensity score matching was carried out to formulate a balanced 1:1 matched study, and to compare risks of hospitalization for diabetic macrovascular complications and in-hospital mortality between the regular visit and irregular visit groups. According to previous studies on variable selection of propensity score matching^{19,20}, propensity scores were calculated by a logistic regression model to identify the relationships between irregular visits and sex, age, hypertension, hyperlipidemia, other comorbidities indicated in the CCI, and dummy variables for 62 residential municipalities in Fukuoka Prefecture (i.e., 61 variables). The Hosmer–Lemeshow test and the C statistic were used as an indicator of how well the logistic regression model fitted the data. Using the *SPSS* macro for propensity score matching²¹, each patient of the irregular visit group was matched with a unique control of the regular visit group within a caliper width of 0.02²². Finally, we assigned 5,940 patients to each group, and the C statistic was 0.620. The Hosmer–Lemeshow test did not reject the null hypothesis ($P = 0.227$).

Multiple logistic regression analyses were used to estimate adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) for irregular visits. For the first model, we set hospitalization for diabetic macrovascular complications as the dependent variable, and age, sex, hypertension, hyperlipidemia, medication for DM, and irregular visits as independent variables. For the second model, we set in-hospital mortality as the dependent variable, and independent variables included those in the first model, as well as the CCI. Statistical analyses were carried out using *PASW* version 18.0 (SPSS Inc., Chicago, IL, USA), and P -values <0.05 were regarded as statistically significant.

RESULTS

Descriptive Statistics

We identified 4,015 patients in the irregular visit group and 4,121 patients in the regular visit group. Patient characteristics are shown in Table 2. The proportion of those aged 75 years

or older in the regular visit group was significantly higher than that in the irregular visit group. The median number of months of physician visits in the regular visit group was 11 months (interquartile range [IQR] 3), whereas that in the irregular visit group was 2 months (IQR 5). The proportion of patients who received medications for DM in the regular visit group was significantly higher than that in the irregular visit group. The proportion of patients who had congestive heart failure in the regular visit group was significantly less than that in the irregular visit group, and the proportion of those who had pulmonary disease, cancer, or rheumatological disease was significantly higher than that in the irregular visit group. The proportion of patients who had hypertension or hyperlipidemia in the regular visit group was significantly higher than that in the irregular visit group. The proportion of patients hospitalized for AMI, IHDs except AMI, all IHDs, hemorrhagic stroke or all strokes in the regular visit group was significantly less than that in the irregular visit group. The mortality rate in the regular visit group was significantly less than that in the irregular visit group.

After propensity score matching, the proportion of patients who had congestive heart failure in the regular visit group was significantly less than that in the irregular visit group, and the proportion of those who had pulmonary disease or cancer was significantly higher than that in the irregular visit group (Table 3).

Multivariate Analyses

Table 4 shows comparisons of outcomes by physician visits after propensity score matching, and AORs and 95% CIs estimated by multiple logistic regression models. The irregular visit group had a significantly higher AMI (AOR 3.52; 95% CI 1.79–6.96), other IHDs except AMI (AOR 1.25; 95% CI 1.02–1.54), all IHDs (AOR 1.37; 95% CI 1.12–1.66), all strokes (AOR 1.29; 95% CI 1.04–1.60) and risk of hospitalization for diabetic macrovascular complications (AOR 1.28; 95% CI 1.10–1.48) than did the regular visit group.

DISCUSSION

We showed that there was a significant difference in the risk of hospitalization for IHD and stroke between the regular visit and irregular visit groups. The risk of hospitalization for AMI in the irregular visit group was higher than that in the regular visit group. The present study results suggest that regular visits might reduce hospitalization for diabetic macrovascular complications.

It is apparent that the regular visit group had higher adherence to treatments than did the irregular visit group. Several previous studies reported that lower adherence to medication for DM is associated with DM-related hospitalization^{23,24}. Patients who had not obtained at least 80% of their oral antihyperglycemic medication were reported to have a 2.53-fold higher risk of subsequent hospitalization among patients with type 2 diabetes²³. Similarly, patients who had a high level of

Table 2 | Patient characteristics according to physician visits

	Total (n = 8,136)	Regular visit group (n = 4,121)	Irregular visit group (n = 4,015)	P-value
Median age (years) [interquartile range]	77 [13]	78 [12]	77 [12]	0.133†
Age (years)				
<65	955 (11.7%)	437 (10.6%)	518 (12.9%)	
65–74	2,107 (25.9%)	1,114 (27.0%)	993 (24.7%)	0.001
75≤	5,074 (62.4%)	2,570 (62.4%)	2,504 (62.4%)	
Sex				
Male	4,191 (51.5%)	2,150 (52.2%)	2,041 (50.8%)	0.228
Female	3,945 (48.5%)	1,971 (47.8%)	1,974 (49.2%)	
Median no. months of physician visits [interquartile range]	7 [9]	11 [3]	2 [5]	<0.001†
Medication for diabetes				
No medication	4,382 (53.9%)	1,975 (47.9%)	2,407 (60.0%)	
OHA	1,925 (23.7%)	1,150 (27.9%)	775 (19.3%)	<0.001
Insulin	1,023 (12.6%)	523 (12.7%)	500 (12.5%)	
OHA + Insulin	806 (9.9%)	473 (11.5%)	333 (8.3%)	
Comorbidity				
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Congestive heart failure	2,379 (29.2%)	1,164 (28.2%)	1,215 (30.3%)	0.046
Chronic pulmonary disease	1,620 (19.9%)	870 (21.1%)	750 (18.7%)	0.006
Dementia	415 (5.1%)	208 (5.0%)	207 (5.2%)	0.824
Hemiplegia or paraplegia	192 (2.4%)	98 (2.4%)	94 (2.3%)	0.913
Mild liver disease	645 (7.9%)	349 (8.5%)	296 (7.4%)	0.067
Moderate or severe liver disease	202 (2.5%)	108 (2.6%)	94 (2.3%)	0.418
Cancer	1,620 (19.9%)	860 (20.9%)	760 (18.9%)	0.028
Metastatic solid tumor	353 (4.3%)	188 (4.6%)	165 (4.1%)	0.317
Peripheral vascular disease	274 (3.4%)	132 (3.2%)	142 (3.5%)	0.404
Peptic ulcer disease	1,816 (22.3%)	911 (22.1%)	905 (22.5%)	0.638
Rheumatological disease	332 (4.1%)	192 (4.7%)	140 (3.5%)	0.008
Renal disease	791 (9.7%)	420 (10.2%)	371 (9.2%)	0.148
Charlson Comorbidity Index				
0	2,491 (30.6%)	1,221 (29.6%)	1,270 (31.6%)	
1–2	3,423 (42.1%)	1,744 (42.3%)	1,679 (41.8%)	0.107
3≤	2,222 (27.3%)	1,156 (28.1%)	1,066 (26.6%)	
Other lifestyle-related disease				
Hypertension	5,327 (65.5%)	2,825 (68.6%)	2,502 (62.3%)	<0.001
Hyperglycemia	2,985 (36.7%)	1,654 (40.1%)	1,331 (33.2%)	<0.001
Hospitalizations for diabetic macrovascular complications				
AMI	62 (0.8%)	17 (0.4%)	45 (1.1%)	<0.001
IHDs except AMI	572 (7.0%)	266 (6.5%)	306 (7.6%)	0.040
All IHDs	634 (7.8%)	283 (6.9%)	351 (8.7%)	0.002
Hemorrhagic stroke	69 (0.8%)	24 (0.6%)	45 (1.1%)	0.008
Ischemic stroke	416 (5.1%)	196 (4.8%)	220 (5.5%)	0.139
All strokes	485 (6.0%)	220 (5.3%)	265 (6.6%)	0.016
PAD	95 (1.2%)	51 (1.2%)	44 (1.1%)	0.552
Diabetic macrovascular complications	1,214 (14.9%)	554 (13.4%)	660 (16.4%)	<0.001
In-hospital mortality	615 (7.6%)	268 (6.5%)	347 (8.6%)	<0.001

†Compared by Mann-Whitney test. Other comparisons made using χ^2 -test. AIDS/HIV, acquired immunodeficiency syndrome/human immunodeficiency virus; AMI, acute myocardial infarction; IHDs, ischemic heart diseases; OHA, oral hypoglycemic agents; PAD, peripheral arterial disease.

adherence were found to have the lowest hospitalization rates among patients with DM, hypertension, hypercholesterolemia or congestive heart failure²⁴.

To evaluate the risks of irregular visits more precisely, we separately estimated the rates and risks of hospitalization for stroke, IHD and PAD. We found that the risk of hospitaliza-

Table 3 | Patient characteristics according to physician visits after propensity score matching

	Total (n = 5,940)	Regular visit group (n = 2,970)	Irregular visit group (n = 2,970)	P-value
Median age (years) [interquartile range]	77 [12]	78 [12]	77 [12]	0.098†
Age (years)				
<65	567 (9.5%)	283 (9.5%)	284 (9.6%)	
65–74	1,627 (27.4%)	809 (27.2%)	818 (27.5%)	0.962
75≤	3,746 (63.1%)	1,878 (63.2%)	1,868 (62.9)	
Sex				
Male	3,137 (52.8%)	1,566 (52.7%)	1,571 (52.9%)	0.897
Female	2,803 (47.2)	1,404 (47.3%)	1,399 (47.1%)	
Median no. months of physician visits [interquartile range]	7 [9]	11 [2]	2 [5]	<0.001†
Medication for DM				
No medication	3,004 (50.6)	1,508 (50.8%)	1,496 (50.4%)	
OHA	1,490 (25.1%)	735 (24.7%)	755 (25.4%)	0.894
Insulin	803 (13.5%)	399 (13.4%)	404 (13.6%)	
OHA + Insulin	643 (10.8%)	328 (11.0%)	315 (10.6%)	
Comorbidity				
AIDS/HIV	0 (0.0%)	0 (0.0%)	0 (0.0%)	–
Congestive heart failure	1,803 (30.4%)	865 (29.1%)	938 (31.6%)	0.039
Chronic pulmonary disease	1,224 (20.6%)	646 (21.8%)	578 (19.5%)	0.029
Dementia	329 (5.5%)	159 (5.4%)	170 (5.7%)	0.533
Hemiplegia or paraplegia	147 (2.5%)	66 (2.2%)	81 (2.7%)	0.210
Mild liver disease	482 (8.1%)	259 (8.7%)	223 (7.5%)	0.087
Moderate or severe liver disease	158 (2.7%)	84 (2.8%)	74 (2.5%)	0.420
Cancer	1,260 (21.2%)	666 (22.4%)	594 (20.0%)	0.022
Metastatic solid tumor	277 (4.7%)	145 (4.9%)	132 (4.4%)	0.424
Peripheral vascular disease	218 (3.7%)	102 (3.4%)	116 (3.9%)	0.334
Peptic ulcer disease	1,392 (23.4%)	676 (22.8%)	716 (24.1%)	0.220
Rheumatological disease	234 (3.9%)	131 (4.4%)	103 (3.5%)	0.062
Renal disease	601 (10.1%)	297 (10.0%)	304 (10.2%)	0.763
Charlson Comorbidity Index				
0	1,703 (28.7%)	839 (29.1%)	864 (28.2%)	
1–2	2,505 (42.2%)	1,253 (42.2%)	1,252 (42.2%)	0.705
3≤	1,732 (29.2%)	878 (28.8%)	854 (29.6%)	
Other lifestyle-related disease				
Hypertension	4,183 (70.4%)	2,088 (70.3%)	2,095 (70.5%)	0.842
Hyperglycemia	2,354 (39.6%)	1,175 (39.6%)	1,179 (39.7%)	0.915

†Compared by Mann-Whitney test. Other comparisons made using χ^2 -test. AIDS/HIV, acquired immunodeficiency syndrome/human immunodeficiency virus; AMI, acute myocardial infarction; IHDs, ischemic heart diseases; OHA, oral hypoglycemic agents; PAD, peripheral arterial disease.

tion for IHD was higher than that of hospitalization for stroke. A prospective cohort study in Japan reported that the incidence rate of IHD (9.68 per 1,000 person-years) was higher than that of cerebrovascular attack (6.78 per 1,000 person-years) among elderly type 2 DM patients²⁵. The present results are consistent with the results of that previous study.

The present study results suggested that it would be effective for insurers to motivate beneficiaries with DM to have regular visits. Insurers, especially health insurance societies, promote lifestyle modifications aimed at enhancing health and the promotion of primary prevention²⁶. In addition to those health activities, the Japanese government has implemented “specific

health checkup and health guidance” in financial year 2008 to reduce the number of persons at high risk of lifestyle-related diseases, including DM. Because insurers can discover the insured at high risk of lifestyle-related diseases or those complications from specific health checkup data and incorporate that data to claims data, it is expected that insurers will develop a disease management program by using these data. To develop a disease management program, further experimental studies are necessary to evaluate the effect of interventions for making regular visits and economic effects.

There were some limitations of the present study. First, we only investigated beneficiaries of the Fukuoka National Health

Table 4 | Comparisons of outcomes and results of multiple logistic regression analyses by physician visit after propensity score matching

	Total	Regular visit group	Irregular visit group	P-value†	AOR 95% CI
Hospitalizations for AMI	47 (0.8%)	11 (0.4%)	36 (1.2%)	<0.001	3.52 [1.79–6.96]
Hospitalizations for IHDs except AMI	424 (7.1%)	192 (6.5%)	232 (7.8%)	0.044	1.25 [1.02–1.54]
Hospitalizations for all IHDs	471 (7.9%)	203 (6.8%)	268 (9.0%)	0.002	1.37 [1.12–1.66]
Hospitalizations for ischemic stroke	307 (5.2%)	141 (4.7%)	166 (5.6%)	0.143	1.17 [0.96–1.44]
Hospitalizations for hemorrhagic stroke	57 (1.0%)	21 (0.7%)	36 (1.2%)	0.046	1.22 [0.97–1.54]
Hospitalizations for all strokes	364 (6.1%)	162 (5.5%)	202 (6.8%)	0.030	1.29 [1.04–1.60]
Hospitalizations for PAD	68 (1.1%)	40 (1.3%)	28 (0.9%)	0.143	0.73 [0.45–1.19]
Hospitalizations for diabetic macrovascular complications	903 (15.2%)	405 (13.6%)	498 (16.8%)	0.001	1.28 [1.10–1.48]
In-hospital mortality‡	454 (7.6%)	209 (7.0%)	245 (8.2%)	0.079	1.17 [0.96–1.44]

†Comparison made using χ^2 -test. ‡Adjusted by sex, age, medications for diabetes, hypertension, hyperglycemia and Charlson Comorbidity Index. Other models adjusted by sex, age, medications for diabetes, hypertension, hyperglycemia. Hosmer-Lemeshow goodness for fit. $P = 0.940$, $P = 0.909$, $P = 0.706$, $P = 0.947$, $P = 0.684$, $P = 0.998$, $P = 0.129$, $P = 0.914$, $P = 0.070$, respectively. AMI, acute myocardial infarction; AOR, adjusted odds ratio; CI, confidence interval; IHDs, ischemic heart diseases; PAD, peripheral arterial disease.

Insurance Organization. Second, we could not investigate clinical information, such as family history, body mass index and other laboratory values (e.g., hemoglobin A1c). However, the present study included patients who did not have outpatient visits, although most previous studies did not include these patients.

In conclusion, the present study shows that the irregular visit group had significantly higher risks of hospitalization for IHD and stroke among diabetic patients. Strategies of insurers that motivate those beneficiaries with DM to make regular visits would be effective for reducing the risk of hospitalization for IHD and stroke.

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