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Associations Between the Continuity of Ambulatory Care of Adult Diabetes Patients in Korea and the Incidence of Macrovascular Complications

Young-Hoon Gong, Seok-Jun Yoon, Hyeyoung Seo, Dongwoo Kim

Department of Preventive Medicine, Korea University College of Medicine, Seoul, Korea

Objectives: The goal of this study was to identify association between the continuity of ambulatory care of diabetes patients in South Korea (hereafter Korea) and the incidence of macrovascular complications of diabetes, using claims data compiled by the National Health Insurance Services of Korea.

Methods: This study was conducted retrospectively. The subjects of the study were 43 002 patients diagnosed with diabetes in 2007, who were over 30 years of age, and had insurance claim data from 2008. The macrovascular complications of diabetes mellitus were limited to ischemic heart disease and ischemic stroke. We compared the characteristics of the patients in whom macrovascular complications occurred from 2009 to 2012 to the characteristics of the patients who had no such complications. Multiple logistic regression was used to assess the effects of continuity of ambulatory care on diabetic macrovascular complications. The continuity of ambulatory diabetes care was estimated by metrics such as the medication possession ratio, the quarterly continuity of care and the number of clinics that were visited.

Results: Patients with macrovascular complications showed statistically significant differences regarding sex, age, comorbidities, hypertension, dyslipidemia and continuity of ambulatory diabetes care. Visiting a lower number of clinics reduced the odds ratio for macrovascular complications of diabetes. A medication possession ratio below 80% was associated with an increased odds ratio for macrovascular complications, but this result was of borderline statistical significance.

Conclusions: Diabetes care by regular health care providers was found to be associated with a lower occurrence of diabetic macrovascular complications. This result has policy implications for the Korean health care system, in which the delivery system does not work properly.

Key words: Diabetes mellitus, Diabetes complications, Continuity of care, Primary health care

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Corresponding author: Seok-Jun Yoon, MD, PhD
73 Inchon-ro, Seongbuk-gu, Seoul 136-705, Korea
Tel: +82-2-2286-1412 Fax: +82-2-927-7220
E-mail: yoonsj02@korea.ac.kr

INTRODUCTION

The epidemiological traits of diseases are changing. The proportion of chronic disease is increasing in South Korea (hereafter Korea), as well as worldwide [1]. Diabetes is one of the most common chronic diseases. According to a study of the global burden of disease that quantified the health status of populations, diabetes accounts for 1.89% of the total disease burden worldwide [2], and accounts for 4.45% of the total disease bur-

den in Korea [2,3] The International Diabetes Federation has estimated that the number of diabetes patients worldwide was 382 million in 2013, and that the number of people with the disease will rise beyond 592 million in less than 25 years [4].

In addition to the problems caused by uncontrolled blood sugar itself, such as hypoglycemia or diabetic ketoacidosis, diabetes leads to microvascular and macrovascular complications. Ischemic heart disease, a macrovascular complication, accounts for a large proportion of mortality in patients with diabetes [5,6]. Ischemic stroke, another macrovascular complication, also makes a considerable contribution to premature mortality and is associated with a large socioeconomic burden, because stroke leads to a loss of function and patients often require a long period of rehabilitation [7]. As the number of patients with diabetes increases, the incidence of the complications of diabetes will also increase.

It is known that hypertension, smoking, dyslipidemia, and uncontrolled blood sugar level are major risk factors for the development of macrovascular complications [8]. Many of these risk factors, such as blood sugar levels, hypertension and dyslipidemia are managed on ambulatory diabetes care settings. Thus, the adherence of diabetes patients to treatment and the continuity of ambulatory care are important factors affecting the development of macrovascular complications in diabetes patients. Several studies dealing with the medication adherence of diabetes patients have shown that medication non-adherence was associated with higher rates of hospitalization and mortality caused by diabetes and cardiovascular diseases [9,10]. Kim et al. [11], in a study using National Health Insurance claim data, suggested that continuity of ambulatory diabetes care can lead to improvements in health outcomes such as hospitalization, mortality, and national costs. However, these studies did not show that the continuity of ambulatory diabetes care directly affects the development of macrovascular complications.

In this study, by using National Health Insurance Service (NHIS) claim data, we examined the associations among demographic and socioeconomic characteristics, utilization patterns of ambulatory care and the incidence of macrovascular complications by dividing newly diagnosed patients with diabetes into two groups: one comprised of patients who developed macrovascular complications, and one comprised of patients who did not. Kim et al. [11] showed that the care of newly diagnosed diabetic patients tends to involve poor follow-up, and that continuity of care in the first year was the most powerful explanatory variable for predicting outcomes in the following year. Based on these findings, we examined patients newly diagnosed with diabetes in 2007, and identified the following factors reflecting the continuity of ambulatory care in 2008 medication adherence, number of visited clinics and quarterly continuity. We then evaluated the development of macrovascular complications in these patients from 2009 to 2012. We then attempted to ascertain how the factors reflecting continuity of ambulatory diabetes care affected the occurrence of macrovascular complications.

METHODS

In study, we used the raw data of NHIS claims from all people aged 30 years or older in six metropolitan cities in Korea (Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) from 2007 to 2012 (n=6 844 158). The macrovascular complications associated with diabetes were limited to ischemic heart disease and ischemic stroke. To diabetes care managed mostly in outpatient settings, continuity of ambulatory care was estimated by the following three metrics that can be assessed using NHIS claim data. Medication adherence was identified by the medication possession ratio, which was calculated based the number of days covered by prescriptions for diabetes as the main sick and first sub sick claim code. On the assumption that patients who utilized one clinic had a regular medical provider, the number of visited clinics during 2008 was identified for each patient. Quarterly continuity was also measured by the numbers of the quarters that visits were made more than once through the year.

We classified patients' conditions according to the International Classification of Disease, 10th revision. Patients with diabetes were defined as those who had claims with one of the following codes more than once: E10 (insulin-dependent diabetes mellitus), E11 (non-insulin-dependent diabetes mellitus), E12 (malnutrition-related diabetes mellitus), E13 (other specified diabetes mellitus), or E14 (unspecified diabetes mellitus) [12]. Main sick and first sub sick claim codes were used in this process. New cases of diabetes were defined as those who had no claims with codes associated with diabetes from 2001 to 2006, and then had claims with these codes in 2007.

In order to identify the patients in whom macrovascular complications occurred, we used main sick claim code and all other sub sick claim codes. Cases of ischemic heart disease were defined as cases coded as I20 (angina pectoris), I21 (acute myo-

cardial infarction), I22 (subsequent myocardial infarction), I23 (certain current complications following acute myocardial infarction), I24 (other acute ischemic heart diseases), or I25 (chronic ischemic heart disease). Ischemic stroke was defined as cases coded as I63 (cerebral infarction), I64 (stroke, not specified as hemorrhage of infarction), I65 (occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction), I66 (occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction), I67 (other cerebrovascular diseases), I69 (sequelae of cerebrovascular disease), or G45 (transient cerebral ischemic attacks and related syndromes).

This study was designed to assess the characteristics of the ambulatory diabetes care of newly diagnosed patients before the occurrence of macrovascular complications (Figure 1). Of the patients newly diagnosed with diabetes in 2007 (n=121 892) who had claim data for codes corresponding to the relevant macrovacular complications, and we excluded patients who experienced macrovascular complications from 2001 to 2008 (n=78 037), and ultimately established a study population including patients newly diagnosed with diabetes in 2007 who had used medical services in 2008 (n=43 002). The demographic and socioeconomic characteristics of the study subjects in 2007 were then analyzed (Table 1).

The study subjects were divided into two groups. One included patients with claim data using codes associated with macrovascular complications from 2009 to 2012. The other included patients who did not use codes associated with macrovascular

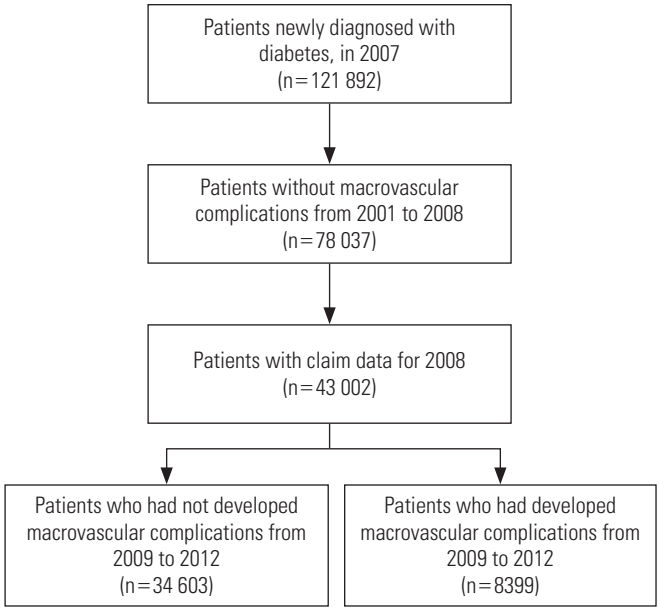

Figure 1. Flow chart of study subjects selection.

complications from 2009 to 2012. The chi-square test was used to identify the variables that were related to each patient's general characteristics at the time of the diabete diagnosis and to medical utilization traits one year after diagnosis.

The demographic and socioeconomic characteristics were sex, age, Charlson comorbidity index (CCI) [13], accompanying hypertension and/or dyslipidemia, and health insurance premium level. The CCI was obtained to adjust each patient's health status through an analysis of the claim data including the following diseases: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, mild liver disease, diabetes without chronic complications, diabetes with chronic complications (except ischemic heart disease, ischemic stroke), hemiplegia or paraplegia, renal disease, any malignancy including leukemia and lymphoma, moderate or severe liver disease, metastatic solid

Table 1. Baseline characteristics of patients newly diagnosed with diabetes in 2007

	n (%)
Sex	
Male	22 451 (52.21)
Female	20 551 (47.79)
Age (y)	
30-39	3306 (7.69)
40-49	10 247 (23.83)
50-59	13 326 (30.99)
60-69	9996 (23.25)
70-79	4942 (11.49)
≥80	1185 (2.76)
Charlson cormobidity index	
0	26 238 (61.02)
1	2994 (6.96)
2	10 933 (25.42)
≥3	2837 (6.6)
Hypertension and dyslipidemia	
None	11 805 (27.45)
Only hypertension	15 096 (35.11)
Only dyslipidemia	4809 (11.18)
Both	11 292 (26.26)
Health insurance premium level	
1	7629 (17.75)
2	6605 (15.37)
3	7928 (18.44)
4	9554 (22.23)
5	11 271 (26.22)

tumor, and AIDS/HIV. Hypertension and dyslipidemia, which are well-known risk factors for the occurrence of macrovascular complications [8], were also used to adjust for risk by dividing patients into four groups: those with no hypertension or dyslipidemia, those with hypertension only, those with dyslipidemia only, and those with both hypertension and dyslipidemia. Health insurance premiums, which initially had 20 levels, were rescaled to five levels and used to reflect each patient's income level [12]. Medicaid patients were included in health insurance premium level 1.

Variables affecting the development of macrovascular complications of diabetes that were found to be significant using the chi-square test were then used for multivariate logistic regression analysis. All statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, USA) and SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). A p-value <0.05 was considered to indicate statistical significance.

RESULTS

Of the patients newly diagnosed with diabetes in 2007, 78 037 had no macrovascular complications by the end of 2008. Newly diagnosed patients who made no claims in 2008 were excluded, and 43 002 patients remained, whose general characteristics are shown in Table 1. Diabetes was more common in males than in females, and 78% of patients were 40 to 69 years of age. The most common CCI score was zero, followed by 2. Regarding the risk factors for macrovascular complications, 35.11% had hypertension only, 11.18% had dyslipidemia only, 26.26% had both hypertension and dyslipidemia, and 27.45% had neither hypertension nor dyslipidemia. Regarding to health insurance premium, more patients had higher health insurance premium levels.

The demographic and socioeconomic characteristics as well as the parameters reflective of ambulatory diabetes care for

Table 2. Comparison of the demographic and socioeconomic characteristics and factors reflecting continuity of ambulatory care between the patients with and without macrovascular complications during 2009-2012

	Complications (–) n (%)	Complications (+) n (%)	p-value
Sex			<0.001
Male	18 286 (52.7)	4165 (49.5)	
Female	16 317 (47.3)	4234 (50.4)	
Age			<0.001
30-39	2969 (8.6)	337 (4.0)	
40-49	8848 (25.6)	1399 (16.7)	
50-59	10 889 (31.5)	2437 (29.0)	
60-69	7544 (21.8)	2452 (29.2)	
70-79	3512 (10.1)	1430 (17.0)	
≥80	841 (2.4)	344 (4.1)	
Charlson comorbidity index in 2007			<0.001
0	21 302 (61.6)	4936 (58.8)	
1	2262 (6.5)	732 (8.7)	
2	8854 (25.6)	2079 (24.8)	
≥3	2185 (6.3)	652 (7.8)	
Hypertension and dyslipidemia in 2007			<0.001
None	9981 (28.8)	1824 (21.7)	
Hypertension	11 827 (34.2)	3269 (38.9)	
Dyslipidemia	4067 (11.8)	742 (8.8)	
Both	8728 (25.2)	2564 (30.5)	
Health insurance premium level in 2007[1,2]			0.18
1	6141 (17.8)	1488 (17.7)	
2	5377 (15.5)	1228 (14.6)	
3	6380 (18.4)	1548 (18.5)	
4	7689 (22.2)	1865 (22.2)	
5	9002 (26.0)	2269 (27.0)	
Medication possession ratio for 2008 (%)[1]			0.001
<80	14 934 (48.8)	3548 (46.5)	
≥80	15 686 (51.2)	4082 (53.5)	
No. of visited clinics for 2008[1]			<0.001
1	24 653 (72.5)	5422 (65.1)	
2	7033 (20.7)	2042 (24.5)	
3	1726 (5.1)	605 (7.3)	
≥4	597 (1.8)	257 (3.1)	
Quarterly continuity for 2008[1]			<0.001
1	5653 (16.3)	1039 (12.4)	
2	3180 (9.2)	656 (7.8)	
3	3285 (9.5)	805 (9.6)	
4	22 485 (65.0)	5899 (70.2)	

The complications evaluated in this study were ischemic heart disease and ischemic stroke.
[1]There are missing data related to these indices.
[2]Health insurance premium level 1 includes Medicaid patients.

the groups with and without macrovascular complications from 2009 to 2012 are shown in Table 2. The relationships between these two groups and those variables, age, sex, CCI, hypertension/dyslipidemia, health insurance premium level, medication possession ratio, the number of visited clinics and quarterly continuity were examined by the chi-square test. Most variables showed statistically significant differences between two groups, with the exception of health insurance premium levels.

Based on the above analysis, multiple logistic regression was conducted using variables found to be significant covariates such as sex, age, CCI, hypertension/dyslipidemia and metrics reflecting the continuity of ambulatory diabetes care. The method of selecting the variables was backward elimination. Age, CCI, hypertension/dyslipidemia, and the number of visited clinics showed statistically significant. C statistics of this logistic regression model was 0.62.

Table 3 shows multiple logistic regression analyses of risk factors of continuity of ambulatory care among the group of patients with macrovascular complications. The number of visited clinics was only metric reflecting the continuity of ambulatory diabetes care that was related to the development of macrovascular complications. As the number of clinics a patient visited increased, the odds ratio for macrovascular complications increased linearly. The odds ratio also higher among patients with medication possession ratio below 80%, but this result was of borderline statistical significance. Quarterly continuity, the metric assessing continual clinic visits during the year, did not show a statistically significant relationship with the development of macrovascular complications.

Table 3. Multiple logistic regression analyses of risk factors among the group of patients with macrovascular complications

Variables	Coefficient	SE	OR (95% CI)	*p*-value
MPR (%)				
<80	0.06	0.03	1.06 (0.99, 1.14)	0.06
≥80			1.00 (reference)	-
No. of visited clinics				
1			1.00 (reference)	-
2	0.21	0.03	1.23 (1.16, 1.31)	<0.001
3	0.37	0.05	1.45 (1.31, 1.60)	<0.001
≥4	0.56	0.08	1.75 (1.50, 2.04)	<0.001
Quarterly continuity				
1	-0.01	0.05	0.99 (0.89, 1.10)	0.88
2	-0.04	0.05	0.96 (0.86, 1.07)	0.46
3	0.02	0.05	1.02 (0.93, 1.12)	0.66
4			1.00 (reference)	-

Adjusted for sex, age, Charlson comorbidity index, and hypertension/dyslipidemia.
SE, standard error; OR, odds ratio; CI, confidence interval; MPR, medication possession ratio.

DISCUSSION

Several studies have shown that chronic disease patients, including diabetes patients, with a higher continuity of care have better health outcomes [14,15] and lower hospitalization rates [16,17], than patients with a lower continuity of care. In this study, three parameters reflecting the continuity of ambulatory diabetes care were analyzed, and it was found that visiting fewer clinics was associated with a lower occurrence of macrovascular complications [11]. As explained above, it was assumed that visiting fewer clinics indicated that patients had a regular medical provider, and conversely, that visiting many clinics indicated that patients did not have a regular provider. The health care delivery system in Korea does not work properly, and patients can freely select their medical provider [18]. These dynamics could lead to discontinuous care, which could increase the risk of overusing health care services, potentially compromising patients' health outcomes. Therefore, patients with chronic disease should have a regular medical provider. This is especially important for diabetes patients, as the above mentioned risk factors of macrovascular complications, including hypertension, dyslipidemia, obesity and smoking, as well as blood sugar levels, can be managed in the outpatient setting.

According to the UK Prospective Diabetes Study, the occurrence of macrovascular complications is not necessarily proportional to the duration of diabetes, in contrast to microvascular complications [19]. Lee et al. [20] compared macrovascular complications in an early onset group (≤ five years) and a late onset group (> five years). Kim et al. [11] found that patterns of ambulatory diabetes care in the early phase of the disease are potential indicators predicting outcomes in the next year. Therefore, we analyzed patterns of ambulatory care in the year after diagnosis and their effects on the development of macrovascular complications. In order to prevent a confusion of cause and effect, study population was comprised of patients who did not have claims involving diabetes and macrovascular complications from 2001 to 2006 and 2001 to 2007, respectively.

This study has several limitations. The first problem is the validity of the claim data. The claim data were drawn from insur-

ance records instead of medical records, and may reflect inaccurate diagnoses. In order to increase the accuracy of the estimations, the age of the study population was restricted to over 30 years, and a wash-out period of six years was implemented. The incident cases of ischemic heart disease and ischemic stroke were defined using a seven year wash-out period and were restricted to patients with diabetes. Due to the limitations of data, a precise algorithm to increase the validity of our estimates, such as an analysis of the utilization of prescribed drugs or procedures, was not applied.

The second problem is metrics that were used in this study. The medication possession ratio is frequently used as a surrogate indicator of medication adherence [21,22]. However, it does not reflect whether the patients take the drugs in question. But to use the medication possession ratio showing statistically borderline significance on development of macrovascular complications, the use of more precise indicator that better reflect medication adherence would lead a more significant result. Using the health insurance premium level to estimate patients' income level likewise does not accurately reflect the economic status of patients.

Third, smoking, HbA1c levels, and obesity which are known risk factors for macrovascular complications of diabetes, were not considered. We attempted to adjust for other risk factors by using the codes indicating hypertension and dyslipidemia. Lee et al. [20] showed that the early macrovascular complication group, with a duration of diabetes of less than five years, was older than the group with late complications and had a higher proportion of smoker. This is a considerable limitation, since the pathologic mechanisms underlying the development of diabetic macrovascular complications, include cell injury through hyperglycemia and atherosclerosis [23,24].

In order to determine the number of patients who received medical treatment during the first year after they were diagnosed with diabetes, we excluded patients with no claims of medical treatment in 2008 from the group of patients who were newly diagnosed in 2007. A total of 35 035 patients (44.8%) were excluded from the 78 037 newly diagnosed patients without previous macrovascular complications. Since several reasons could account for not using health care, including death, immigration and poor adherence, those patients were excluded. However, since this group could include patients with poor adherence, the results of this study may be biased. Therefore, any interpretation of this study should clearly note that it was restricted to the study of diabetic patients who had claim data in 2008.

Despite these limitations, this study has the strength of being a large-scale longitudinal study investigating the occurrence of macrovascular complications of diabetes that included entire population of 6 cities, corresponding to 14% of the national population in 2007, over a six-year follow-up period. Although previous studies used indirect dependent variables such as hospitalization or death, this study attempted to identify the development of diabetic macrovascular complications that may have been associated with poor adherence to ambulatory diabetes care. In conclusion, the results of this study have the policy implication that primary care physicians, in the role of regular medical providers play a crucial role in the management of diabetes.

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CONFLICT OF INTEREST

The authors have no conflicts of interest with the material presented in this paper.

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