

The Association of Self-Reported Coronary Heart Disease with Diabetes Duration in Korea

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Background: This study aimed to investigate the association of diabetes duration with self-reported coronary heart disease (CHD) in Korea.

Methods: Among data from 34,145 persons compiled in the third Korean National Health and Nutrition Examination Survey in 2005, laboratory test and nutritional survey data from 5,531 persons were examined. The participants were asked to recall a physician's diagnosis of CHD (angina or myocardial infarction).

Results: Age- and sex-adjusted relative risk for CHD was 1.51 (95% confidence interval [CI], 0.64 to 3.59; not significant) for diabetes with duration of <1 year, 2.27 (95% CI, 1.14 to 4.54; $P=0.020$) for diabetes with a duration of 1 to 5 years, and 3.29 (95% CI, 1.78 to 6.08; $P<0.001$) for diabetes with a duration >5 years, compared with non-diabetes as a control. Even after adjusting for age, sex, current smoking status, waist circumference, hypertension, triglycerides, high density lipoprotein cholesterol, and fasting plasma glucose, relative risk for CHD was 2.87 (95% CI, 1.01 to 8.11; $P=0.047$) in diabetes with a duration of 6 to 10 years and 4.07 (95% CI, 1.73 to 9.63; $P=0.001$) in diabetes with duration of >10 years with non-diabetes as a control.

Conclusion: CHD prevalence increased with an increase in diabetes duration in Korean men and women. Recently detected diabetes (duration <1 year) was not significantly associated with CHD prevalence compared to non-diabetes. However, diabetes of a duration of >5 years was associated with an increase in CHD compared to non-diabetics after adjusting for several CHD risk factors.

Keywords: Coronary disease; Diabetes mellitus; Duration

INTRODUCTION

Cardiovascular disease (CVD) is well-known as a leading cause of death in patients with type 2 diabetes mellitus (T2DM) [1]. T2DM is associated with a 2-fold increase in the risk for CVD [2-4]. Similar to patterns seen in Western countries, coronary artery disease (CAD) is very prevalent in Koreans with T2DM. The Committee of the Korean Diabetes Association on the Epidemiology of Diabetes Mellitus performed a nationwide survey regarding the status of glycemic control and diabetic complications in 2006. The prevalence of CAD, including angina, myocardial infarction (MI), coronary artery bypass graft,

and primary intervention was 8.7% in diabetic patients [5].

In several studies, diabetes without previous coronary heart disease (CHD) showed equivalent risk for future development of CHD when compared to non-diabetes with established CHD, supporting the view that diabetes is a coronary risk equivalent to previous history of CHD [6-9]. However, a recent meta-analysis established that patients with diabetes are at lower risk of developing total CHD events compared with non-diabetics with established CHD, indicating that diabetes is not a coronary risk equivalent [10]. Diabetes duration could be an important determinant for CHD in T2DM, as a longer duration of diabetes is associated with an increased risk of

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CVD [11-15].

Despite the rapidly growing prevalence of diabetes in Korea and the importance of CHD in the management of diabetes, there have been no reports regarding the association of the duration of diabetes with CHD in the general Korean population. Therefore, we investigated this issue using data obtained in a nationwide representative sample from the third Korea National Health and Nutrition Examination Survey (KNHANES III).

METHODS

Study population

This study was based on data obtained from the KNHANES III among non-institutionalized civilians in the Republic of Korea. The survey, which was conducted by the Korean Ministry of Health and Welfare in 2005, was a nationwide representative study using a stratified and multistage probability sampling design for the selection of household units. The survey consisted of health interview, health behavior, health examination, and nutrition components. A total of 34,145 individuals from these sampling frames were included in the health interview survey. Among them, 5,531 persons aged 18 to 99 years were identified as participants, and participated in laboratory tests and a nutritional survey.

Health examination survey and laboratory test

Trained interviewers visited each participant's dwelling and administered a standardized questionnaire on smoking and regular exercise. A dietary recall method was used to collect data on food items consumed by participants during the past 24 hours. The participants were also asked to recall a physician's diagnosis of CHD (angina or MI). Height and weight were obtained using standardized techniques and equipment. Height was measured to the nearest 0.1 cm using a portable stadiometer (Seriter, Bismarck, ND, USA). Weight was measured to the nearest 0.1 kg using a Giant-150N calibrated balance-beam scale (Hana, Seoul, Korea). Body mass index (BMI) was calculated by dividing weight by height squared (kg/m^2). Waist circumference (WC) was measured on standing participants with a soft tape midway between the lowest rib and the iliac crest. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured by standard methods using a sphygmomanometer with the patient in a sitting position. Three blood pressure measurements were made at 5-minute intervals and

the average of the second and third measurements was used in the analysis. Blood samples were collected in the morning after fasting for at least 8 hours. Fasting plasma glucose (FPG), total cholesterol (TC), triglyceride (TG), and high density lipoprotein cholesterol (HDL-C) levels were measured in a central and certified laboratory, using an Advia 1650 (Siemens, Tarrytown, NY, USA). Low density lipoprotein cholesterol (LDL-C) was estimated indirectly using the Friedwald formula: $\text{LDL-C} = \text{TC} - [\text{HDL-C} + (\text{TG}/5)]$, for subjects with TG levels $< 400 \text{ mg/dL}$.

Statistical analyses

Data are presented as mean \pm standard deviation or percent. Statistical analysis was performed using SPSS for Windows (SPSS, Chicago, IL, USA). ANCOVA was used to estimate clinical and biochemical characteristics and the prevalence of CHD according to the presence of diabetes after adjusting for age, current smoking, WC, hypertension, TG, and HDL-C in each sex (Tables 1 and 2). ANCOVA was done for comparison of CHD according to diabetes duration in each sex (Table 3). Logistic regression analyses were done for CHD with age, sex, current smoking, WC, hypertension, HDL-C, TG, FPG, and duration of diabetes as covariates (Table 4). Statistical significance was defined as $P < 0.05$.

Ethics statement

This study was approved by the Institutional Review Board of the Ilsan Paik Hospital (IB-2-1112-047).

RESULTS

The study population ranged in age from 18 to 99 years and included 2,368 men and 3,163 women. Mean age was 45 years (46 years in men, 45 years in women). Mean BMI was $23.7 \pm 3.3 \text{ kg}/\text{m}^2$ ($24.0 \pm 3.1 \text{ kg}/\text{m}^2$ in men, $23.5 \pm 3.4 \text{ kg}/\text{m}^2$ in women). Prevalence of diabetes was 8.7% (10.8% in men, 7.2% in women). Prevalence of CHD was 1.9% (1.7% in men, 2.1% in women).

Table 1 presents the age and age-adjusted clinical characteristics of the study population of adult Korean men. The participants were divided into three groups: non-diabetes, newly-detected diabetes, and previously-diagnosed diabetes (diabetes duration, median 5 years [range, 0 to 53 years]). With increased diabetes duration, BMI, WC, BP, FPG, TG, and age all increased. Serum HDL-C decreased according to the extent of

Table 1. Age and age-adjusted clinical characteristics of the study population of adult Korean men (n=2,368)

Characteristic	Non-diabetes (n=2,113)	Newly detected diabetes (n=84)	Previously diagnosed diabetes (n=171)	P for trend
Age, yr	45.2±0.3	54.1±1.4	58.0±0.8	<0.001
Household income, KRW/mo	234±3	272±17	216±12	NS
Current smoking, %	44.4±1.1	52.5±5.4	47.0±3.9	NS
Exercise x3/wk, %	32.5±1.0	35.1±5.1	39.4±3.6	NS
Daily calories intake, kcal	2,343±21	2,315±106	2,320±74	NS
Daily fat intake, g/day	49.1±0.8	41.8±4.1	50.2±2.9	NS
Daily alcohol intake, g/day	16.6±1.0	34.4±5.3	20.2±3.7	NS
BMI, kg/m ²	23.9±0.1	25.1±0.3	24.5±0.2	0.001
Waist circumference, cm	83.8±0.2	87.9±1.0	86.3±0.7	<0.001
SBP, mm Hg	122.3±0.3	128.9±1.6	124.0±1.2	0.012
DBP, mm Hg	80.6±0.2	83.9±1.1	79.7±0.8	NS
BP medication, %	9.8±0.6	12.3±3.2	26.2±2.3	<0.001
HTN, %	26.6±0.9	38.6±4.7	42.1±3.3	<0.001
Fasting plasma glucose, mg/dL	92.3±0.4	157.6±2.2	136.7±1.5	<0.001
LDL-C, mg/dL	113.0±0.7	112.0±3.8	112.3±2.5	NS
Triglyceride, mg/dL	151.4±3.3	297.6±16.7	212.2±11.9	<0.001
HDL-C, mg/dL	42.7±0.2	40.6±1.1	39.3±0.8	<0.001
Coronary heart disease, %	1.5±0.3	1.5±0.3 (P=0.966) ^a	4.6±1.0 (P=0.003) ^a	0.005
Coronary heart disease, % ^b	1.5±0.3	1.9±1.4 (P=0.755) ^a	4.6±1.0 (P=0.003) ^a	0.004

Values are presented as mean or %±SEM. NS, not significant; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP, blood pressure; HTN, hypertension (current antihypertensive medication or SBP ≥140 mm Hg or DBP ≥90 mm Hg); LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol. ^avs. non-diabetes, ^bPrevalence of coronary heart disease after adjusting for age, current smoking, waist circumference, HTN, triglyceride, and HDL-C.

the increase in diabetes duration. CHD prevalence was increased according to the extent of increase in diabetes duration. This results was unchanged even after adjusting for age, current smoking, WC, hypertension (HTN), TG, and HDL-C.

Table 2 summarizes the findings concerning age and age-

Table 2. Age and age-adjusted clinical characteristics of the study population of adult Korean women (n=3,163)

Characteristic	Non-diabetes (n=2,940)	Newly detected diabetes (n=59)	Previously diagnosed diabetes (n=164)	P for trend
Age, yr	45.4±0.3	55.7±1.9	63.2±0.9	<0.001
Household income, KRW/mo	230±3	224±21	221±13	NS
Current smoking, %	4.2±0.4	4.6±2.7	7.6±1.6	0.049
Exercise x3/wk, %	33.3±0.9	31.1±6.2	40.1±3.8	NS
Daily calories intake, kcal	1,794±13	1,800±94	1,805±57	NS
Daily fat intake, g/day	36.4±0.5	34.7±3.7	37.3±2.3	NS
Daily alcohol intake, g/day	2.6±0.2	5.3±1.6	2.2±1.0	NS
BMI, kg/m ²	23.4±0.1	25.4±0.4	24.0±0.3	0.002
Waist circumference, cm	78.0±0.2	84.3±1.2	81.6±0.7	<0.001
SBP, mm Hg	116.0±0.3	123.9±1.9	120.0±1.2	<0.001
DBP, mm Hg	74.6±0.2	78.1±1.3	73.5±0.8	NS
BP medication, %	11.3±0.6	18.3±3.9	40.1±2.4	<0.001
HTN, %	20.7±0.7	32.5±4.6	37.6±2.8	<0.001
Fasting plasma glucose, mg/dL	89.6±0.3	159.6±1.9	130.3±1.1	<0.001
LDL-C, mg/dL	114.9±0.5	128.6±3.9	110.0±2.4	NS
Triglyceride, mg/dL	110.7±1.4	168.7±9.9	162.1±6.1	<0.001
HDL-C, mg/dL	47.4±0.2	43.2±1.4	43.9±0.9	<0.001
Coronary heart disease, %	1.8±0.2	4.1±1.9 (P=0.221) ^a	7.3±1.1 (P<0.001) ^a	<0.001
Coronary heart disease, % ^b	1.8±0.3	3.7±1.9 (P=0.338) ^a	6.7±1.2 (P<0.001) ^a	<0.001

Values are presented as mean or %±SEM. NS, not significant; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; BP, blood pressure; HTN, hypertension (current antihypertensive medication or SBP ≥140 mm Hg or DBP ≥90 mm Hg); LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol. ^avs. non-diabetes, ^bPrevalence of coronary heart disease after adjusting for age, current smoking, waist circumference, HTN, triglyceride, and HDL-C.

adjusted clinical characteristics of adult Korean women in the study population. The participants were divided into the aforementioned three groups (diabetes duration, 5 years [range, 0 to 35 years]). With increased diabetes duration, BMI, WC, BP, FPG, TG, age, and proportion of current smoking were in-

Table 3. Coronary heart disease according to diabetes duration in each sex

	Non-diabetes	Diabetes			P for trend
		Diabetes with duration of <1 yr	Diabetes with duration of 1-5 yr	Diabetes with duration of >5 yr	
Men					
No.	2,113	95	86	74	
Diabetes duration, yr			2 (1-5)	12 (6-53)	
Age-adjusted, %	1.5±0.3	1.2±1.3 (P=0.846) ^a	3.4±1.4 (P=0.173) ^a	6.8±1.5 (P<0.001) ^a	0.001
Multiple factors-adjusted, % ^b	1.4±0.3	2.5±1.5 (P=0.478) ^a	4.1±1.5 (P=0.078) ^a	7.7±1.6 (P<0.001) ^a	0.001
Women					
No.	2,940	71	79	73	
Diabetes duration, yr			2 (1-5)	11 (6-35)	
Age-adjusted, %	1.8±0.3	4.5±1.7 (P=0.109) ^a	6.0±1.6 (P=0.011) ^a	8.9±1.7 (P<0.001) ^a	<0.001
Multiple factors-adjusted, % ^b	1.7±0.3	6.1±2.0 (P=0.034) ^a	6.1±1.7 (P=0.012) ^a	9.7±1.9 (P<0.001) ^a	<0.001

Values are presented as mean or % ± SEM.

^avs. non-diabetes, ^bPrevalence of coronary heart disease after adjusting for age, current smoking, waist circumference, hypertension, triglyceride, high density lipoprotein cholesterol, and fasting plasma glucose.

Table 4. Logistic regression analyses for coronary heart disease with age, sex, current smoking, waist circumference, HTN, HDL-C, triglyceride, fasting plasma glucose, and duration of diabetes as covariates

Variable	OR (95% CI)	P value
Age	1.05 (1.04-1.07)	<0.001
Male	0.86 (0.55-1.34)	0.494
Current smoking	0.74 (0.41-1.33)	0.310
Waist circumference	1.00 (0.98-1.03)	0.816
HTN	2.01 (1.29-3.14)	0.002
HDL-C	0.97 (0.95-1.00)	0.017
Triglyceride	1.00 (1.00-1.00)	0.772
Fasting plasma glucose	1.00 (0.99-1.01)	0.330
Diabetes vs. non-diabetes		0.012
Diabetes with duration of <1 yr	1.89 (0.70-5.14)	0.213
Diabetes with duration of 1-5 yr (2 [1-5])	2.12 (1.00-4.50)	0.050
Diabetes with duration of 6-10 yr (9 [6-10])	2.87 (1.01-8.11)	0.047
Diabetes with duration of >10 yr (15.5 [11-53])	4.07 (1.73-9.63)	0.001

HTN, hypertension (current antihypertensive medication or SBP ≥140 mm Hg or DBP ≥90 mm Hg); HDL-C, high density lipoprotein cholesterol; OR, odds ratio; CI, confidence interval.

creased. CHD prevalence showed an increasing trend according to increased diabetes duration. After adjusting for several

CHD risk factors, this increasing CHD trend was unchanged. There was no difference in self-reported CHD prevalence between non-diabetes and newly-detected diabetes by gender. However, the prevalence of self-reported CHD in previously-diagnosed diabetes was significantly higher compared to that in non-diabetes after adjusting for several risk factors (Tables 1 and 2).

Table 3 summarizes the CHD data according to diabetes duration in each sex. The participants were arbitrarily divided according to diabetes duration (non-diabetes and duration of <1 year, 1 to 5 years, and >5 years) to allow similar numbers in each diabetes group. After adjusting for age and several CHD risk factors, CHD showed an increasing trend according to diabetes duration in men. Diabetes of a duration of <1 year or 1 to 5 years did not differ in CHD prevalence compared to non-diabetes. However, CHD prevalence with diabetes of duration of >5 years was significantly higher than with non-diabetes after adjusting for several risk factors (7.7±1.6% vs. 1.4±0.3%, P<0.001). Women also presented an increasing trend in CHD according to diabetes duration. There was no difference in CHD prevalence between non-diabetes and diabetes of a duration of <1 year. However, CHD prevalence with diabetes of a duration of >5 years was significantly higher than that of non-diabetes after adjusting for several risk factors (9.7±1.9% vs. 1.7±0.3%, P<0.001). Contrary to the findings regarding men, women with diabetes of <1 year or 1 to 5 years in duration showed a significantly higher prevalence of CHD compared to

those of non-diabetes after adjusting for several risk factors.

After adjusting for age and sex, logistic regression analysis showed that the relative risk for CHD was 1.51 (95% confidence interval [CI], 0.64 to 3.59; not significant) in diabetes with a duration of <1 year, 2.27 (95% CI, 1.14 to 4.54; $P=0.020$) in diabetes with a duration 1 to 5 years, and 3.29 (95% CI, 1.78 to 6.08; $P<0.001$) in diabetes with a duration >5 years, compared with non-diabetes as a control.

Table 4 summarizes the findings of logistic regression analyses for CHD with age, sex, current smoking, WC, HTN, HDL-C, TG, FPG, and duration of diabetes as covariates. After adjusting for all these factors, relative risk for CHD was 2.87 (95% CI, 1.01 to 8.11; $P=0.047$) in diabetes with a duration of 6 to 10 years and 4.07 (95% CI, 1.73 to 9.63; $P=0.001$) in diabetes with duration of >10 years with non-diabetes as a control. After adjusting for several parameters in addition to age and sex, participants with a diabetes duration of 1 to 5 years did not show a significant difference in CHD compared to non-diabetes.

DISCUSSION

The principal finding of the present study is that the prevalence of CHD increased with an increase in diabetes duration in Korean men and women. In particular, diabetes of a duration of 6 to 10 years showed about a 2.9-fold increase of CHD and diabetes with >10 years of duration showed about a 4.1-fold increase compared to non-diabetes, even after adjusting for several CHD risk factors. As far as we know, this is the first study reporting the association between diabetes duration and a risk of CHD in the general Korean population.

T2DM is associated with an increased risk of CVD [2-4]. It has been suggested that people with diabetes without a prior MI have a similar risk of CHD to those without diabetes who have had a MI [4]. Various studies from different population cohorts have provided varying conclusions regarding the validity of the concept of coronary risk equivalent in patients with diabetes [6-9,16-19], with the results of some studies supporting coronary risk equivalent [6-9], while others did not [16-19]. In a recent meta-analysis [10], patients with diabetes were at a lower risk of developing total CHD events compared with patients without diabetes with established CHD, indicating that diabetes is not a coronary risk equivalent. Due to the limitation of a cross-sectional study design, we could not examine this issue. However, the lack of a difference in self-re-

ported CHD between non-diabetes and recently-detected diabetes supports the suggestion that the presence of diabetes itself, irrespective of severity or duration of diabetes, may not be an equivalent CHD risk factor when compared to a history of previous CHD in the Korean population.

In most studies to have examined the issue, diabetes duration was found to be associated with an increased risk of CVD [11-15,20,21]. Diabetes is associated with increases in traditional risk factors for CVD, including hypertension and dyslipidemia, increased oxidative stress, increased tissue glycosylation, and platelet and fibrinolytic disorders that can lead to a procoagulant state [22,23]. After adjusting for age, sex, and CHD risk factors, the risk of CHD found by the Framingham heart study was 1.38 times higher for each 10-year increase in the duration of diabetes (95% CI, 0.99 to 1.92) [20]. After adjusting for age, smoking, social class, BMI, physical activity, and alcohol intake, the relative risk of major CHD events in a British regional heart study was 1.67 (95% CI, 1.01 to 2.75) in participants with <7 years diabetes duration, 2.65 (95% CI, 1.31 to 5.35) in participants with 7 to 12 years diabetes duration, and 2.67 (95% CI, 1.46 to 4.88) in participants with >12 years diabetes duration as compared to non-diabetes (P for trend <0.0001) [21]. According to a United States-based study regarding the impact of diabetes mellitus and prior MI [11], when compared with non-diabetic men, patients with diabetes diagnosed ≤ 5 years previously had a relative risk of 1.48 (95% CI, 1.27 to 1.72) and those with a diagnosis exceeding 26 years had a relative risk of 1.91 (95% CI, 1.43 to 2.55). In this study, we observed an increase in self-reported CHD with a longer duration of diabetes. This was especially true in participants with the longest duration of diabetes (>10 years; median, 15.5 years) with an approximately 4.1-fold increase of CHD compared to non-diabetes, even after adjusting for several CHD risk factors. Despite the limitations of this study, the data strongly suggests that a longer duration of diabetes markedly increases the risk of CHD in the general Korean population, irrespective of other CHD risk factors.

The association of diabetes duration with severity of CAD has been reported previously. A positive significant correlation between CAD severity (Gensini score) and duration of diabetes mellitus ($r=0.362$, $P=0.004$) has been reported [24]. These factors had a positive linear relationship with the Gensini score, suggesting that as the duration of diabetes increases, the severity of CAD will increase with multiple and tighter lesions, especially if the diabetes is poorly controlled. A Korean study

[25] reported the relationship between coronary arterial lesion on coronary angiogram and clinical CHD risk factors. The relative risk of CHD in participants with >10 years diabetes duration was 2.6 (95% CI, 1.4 to 5.1; $P=0.003$), as compared to participants with ≤ 10 years diabetes duration.

Presently, the prevalence of CHD according to increased diabetes duration was markedly increased in women compared to men. Traditional CHD risk factors were more prevalent in men. A study regarding gender difference and the effect of diabetes duration on CHD mortality was previously done using NHANES data [8]. After adjusting for age, race, smoking, HTN, serum cholesterol level, and BMI, the hazard ratio of fatal CHD was 1.5 (95% CI, 0.9 to 2.5) for a diabetes duration <10 years and 4.8 (95% CI, 3.0 to 7.8) for a diabetes duration ≥ 10 years in women. In men, the hazard ratio of fatal CHD was 2.0 (95% CI, 0.9 to 2.5) for a diabetes duration of <10 years, and 2.6 (95% CI, 3.0 to 7.8) for a diabetes duration of ≥ 10 years. The reason for the markedly increased CHD with increased diabetes duration in women is not clear. Several reports have suggested some possible explanations [26-30]. The first possibility is that CHD risk factors such as HTN and dyslipidemia could be more prominent in women than in men [26-29]. Another possibility is that diabetes may alter estrogen-related protective mechanisms [30].

A limitation of this study was that the history of CHD was not obtained from the hospital records, but was based on the questionnaire that required recall by participants of a physician's diagnosis of CHD (angina or MI). Due to the possibility of recall bias and the limitation of the cross-sectional study design, we could not confirm the results of this study. Therefore, another longitudinal study is warranted. Secondly, the reported duration of diabetes might be underestimated because the actual onset of diabetes frequently precedes clinical diagnosis by several years. Although the strength of our study was its nationally representative data, there could be some limitations in terms of generalization of these results to general the Korean population, because we did not account for the primary sampling units, stratification, and sampling weights of the KNHANES.

In conclusion, as diabetes duration increases, the prevalence of self-reported CHD increased in Korean men and women. Recently-detected diabetes was not associated with a difference in self-reported CHD prevalence compared to non-diabetes. However, diabetes with duration of 6 to 10 years showed an approximately 2.9-fold increase in self-reported CHD, and

diabetes >10 years in duration showed an approximately 4.1-fold increase compared to non-diabetes, even after adjusting for several CHD risk factors. The data suggests that more active surveillance of CHD should be done as the duration of diabetes increases.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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