Association between Pulse Pressure and Coronary Heart Disease in Korean Elderly: The 7th Korean National Health and Nutrition Examination Survey (2016–2018)

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Background: Although the pulse pressure (PP) is an independent predictor of coronary heart disease (CHD), many physicians disregard its importance and there have been no recent studies on Korean elderly. We investigated the association between PP and CHD in Korean elderly through the nationwide, observational study.

Methods: This study included 4100 subjects aged ≥ 65 years from the 7th Korean National Health and Nutrition Examination Survey (2016–2018). Pulse pressure was calculated as the difference between the systolic blood pressure (SBP) and the diastolic blood pressure (DBP), and high PP was defined as ≥ 60 mmHg. Subjects diagnosed with angina pectoris or myocardial infarction were classified into the CHD group. Multivariate logistic regression analysis was performed to evaluate the association between PP and CHD.

Results: Among the subjects, the incidence of high PP was higher in women, while CHD was higher in men. Subjects with high PP were older, had higher SBP, lower DBP and higher FBG compared to subjects with normal PP. After adjustment for multiple covariates, participants with high PP had a higher risk for incidence of CHD with an OR of 1.361 (95% of CI: 1.077–1.719).

Conclusions: In this study, we found the significant association between PP and CHD in Korean elderly.

Key Words: Coronary heart disease, Elderly, Pulse pressure, Risk factor

INTRODUCTION

Coronary heart disease (CHD) is one of the leading causes of death worldwide [1,2]. Although CHD mortality has declined gradually [3], the incidence of CHD has increased as lifespan extends [4,5]. Since the incidence of CHD itself causes socioeconomic burden, the prevention of CHD is important.

CHD is a multifactorial disease [6,7]. As it is well known, various factors contribute to CHD such as aging, hypertension (HTN), dyslipidemia and smoking. Pulse pressure (PP) is the difference between the systolic blood pressure (SBP) and diastolic blood pressure (DBP). As already confirmed in several studies including the Framingham study, PP is an independent predictor of CHD [8,9]. Also, the measurement of PP is a non-invasive and cost-effective tool

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to predict the incidence of CHD simply measured in primary care settings [10]. Despite the usefulness of measuring PP, there was no recent study on Korean elderly. Thus, this study was aimed to find the correlation between PP and CHD in Korean elderly through the nationwide, large-scale observational study.

MATERIALS AND METHODS

1. Study subjects

This study was based on data from the 7th Korean National Health and Nutrition Examination Survey (KNHANES VII) conducted for 3 years (2016-2018). KNHANES VII is a population-based, cross-sectional study performed by the Korea Centers for Disease Control and Prevention (KCDC). The survey consisted of three parts: a health interview survey, a health examination survey, and a nutrition survey. The number of participants in the survey was 24,269. Among them, elderly aged over 65 years was 4,956. We excluded 856 participants with incomplete data such as height, weight, body mass index (BMI), waist circumference (WC), SBP, DBP readings, and blood chemistry test results. Finally, 4,100 subjects were analyzed in this study (Figure. 1). This study was conducted after obtaining approval for exemption from review by the Research Ethics Review Committee (Registration Number : K2021-0747-001).

2. Patient's demographic characteristics and clinical variables

Data regarding demographics and clinical variables including sex, age, smoking habits, and alcohol consumption were obtained using a health questionnaire. Sex was classified into male and female. In the smoking category, only current

smokers were classified as the smoking group. In the alcohol consumption category, according to the health questionnaire who consumed alcohol at least once a month over the last year were classified as alcohol consumption group. Comorbidities that can affect CHD such as diabetes mellitus (DM), dyslipidemia, and hypertension (HTN) were defined as those who were currently diagnosed by a physician.

Anthropometric data included measurement of weight, height, BMI, WC, SBP, and DBP. Weight, height and WC were measured following standardized protocols shown in KNHANES VII guidebook. Weight was measured using a GL-6000-20 (G-tech, Korea), height was measured with Seca 225 (Seca, Germany) or Seca 210 (Seca, Germany). BMI was calculated as weight in kilogram (kg) divided by height in m². WC was measured using a Seca 200 (Seca, Germany). Blood pressure was measured using a Baumanometer® Wall Unit 33 (0850) (Baum, USA), subjects with in a sitting position after taking 5-minute break. After three measurements, the average value of the 2nd and 3rd blood pressure was used as data.

Laboratory data included estimation of fasting blood glucose (FBG), total cholesterol (TC), high-density lipoproteincholesterol (HDL-C), low-density lipoproteincholesterol (LDL-C), and triglycerides (TG). Blood samples were obtained after fasting at least 8hrs with immediate pretreatment to minimize interference. The samples were analyzed by Labospect008AS (Hitachi/Japan) using enzymatic method and hexokinase UV.

3. Definition of high PP and CHD

PP was calculated as the difference between the SBP and DBP. High PP was defined as PP ≥ 60 mmHg [11]. In the evaluation of CHD, subjects with angina pectoris or my-

Figure 1. Flow diagram outlining the inclusion and exclusion criteria and the study design.

ocardial infarction diagnosed by a physician were classified into the CHD group.

4. Statistical analysis

General characteristics of the study subjects according to sex and the PP were analyzed using a chi-square test (continuous variables) and an independent t-test (categorical variables), and the results were presented in terms of mean, standard deviation, and percentage. The association with PP to variables was estimated using Pearson correlation analysis. TG values were analyzed after converting these into log values. To investigate the effect of variables on CHD, we performed multivariate logistic regression analysis was performed with PP, age, sex, smoking, alcohol consumption, DM, serum HDL-C, and LDL-C levels as independent variables with the diagnosis of CHD as the dependent variable (Model 1: non-adjusted, Model 2: adjusted for age, sex,

Model 3: further adjusted for smoking habits and alcohol consumption, Model 4 : further adjusted for DM, HDL-C, and LDL-C).

All statistical analyses were performed using the SPSS Statistics version. 27. Results were presented as of odds ratio and 95% confidence interval. The level of statistical significance in each analysis was defined as P-value <0.05.

RESULTS

1. General characteristics of subjects

General characteristics of the research subjects are shown in Table 1. The sample comprised 1,808 men (44.1%) and 2,292 women (55.9%). The mean age was 72.6 ± 5.0 and there was no significant difference between the two groups. Compared to male participants, the female participants had a higher BMI, higher SBP, higher PP (all $P < 0.001$). The

Table 1. General characteristics of research subjects (N=4,100)

	Total	Men (n=1808)	Women (n=2292)	P-value*
Age	72.6 ± 5.0	72.5 ± 4.9	72.8 ± 5.1	0.054
Weight (kg)	60.5 ± 9.8	65.3 ± 9.1	56.8 ± 8.6	<0.001
Height (cm)	158.0 ± 8.9	165.6 ± 5.7	151.9 ± 5.8	<0.001
BMI (kg/m^2)	24.2 ± 3.2	23.8 ± 2.9	24.6 ± 3.3	<0.001
WC (cm)	85.4 ± 9.0	86.9 ± 8.7	84.3 ± 9.1	<0.001
SBP (mmHg)	128.9 ± 17.5	126.7 ± 16.7	130.6 ± 17.9	<0.001
DBP (mmHg)	72.5 ± 9.9	72.2 ± 9.8	72.8 ± 9.9	0.066
PP (mmHg)	56.3 ± 15.2	54.5 ± 14.5	57.8 ± 15.6	<0.001
High PP (PP ≥ 60)	1561 (38.1)	601 (33.2)	960 (41.9)	<0.001
FBG (mg/dL)	108.0 ± 26.6	109.8 ± 28.4	106.6 ± 25.0	<0.001
TC (mg/dL)	184.5 ± 39.7	178.0 ± 37.9	189.6 ± 40.4	<0.001
HDL-C (mg/dL)	48.1 ± 11.9	46.1 ± 11.7	49.7 ± 11.7	<0.001
LDL-C (mg/dL)	109.5 ± 36.4	105.0 ± 34.5	113.1 ± 37.5	<0.001
TG (mg/dL)	134.2 ± 83.1	134.5 ± 80.5	134.0 ± 85.1	0.865
Current smoking [†]	377 (9.2)	327 (18.1)	50 (2.2)	<0.001
Alcohol (yes) [‡]	1,451 (35.4)	1,039 (57.5)	412 (18.0)	<0.001
HTN (yes) [§]	2,603 (63.5)	1,072 (59.3)	1,531 (66.8)	<0.001
DM (yes) [§]	1,078 (26.3)	503 (27.8)	575 (25.1)	0.048
Dyslipidemia (yes) [§]	1,390 (33.9)	446 (24.7)	944 (41.2)	<0.001
CHD (yes) [§]	331 (8.1)	183 (10.1)	148 (6.5)	<0.001

Data are expressed as mean $\pm$ standard deviation or n (%).

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; FBG, fasting blood glucose; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglycerides; HTN, hypertension; DM, diabetes mellitus; CHD, coronary heart disease.

*P-value were obtained by chi-square test (continuous variable) and independent t-test (categorical variable). [†]Current smokers were classified as smoking group. [‡]Participants who consumed at least one glass of alcohol every month over the last year were classified as alcohol consumption group. [§]Comorbidities were defined as those who were currently diagnosed by doctor.

incidence of high PP and CHD were 1561 (38.1%), and 331 (8.1%), respectively. The incidence of high PP was higher in women ($P<0.001$), while the CHD was higher in men. ($P<0.001$).

2. General characteristics of subjects according to high PP

General characteristics of the research subjects according to high PP are shown in Table 2. Individuals with high PP were older while they had higher SBP, lower DBP and higher FBG (all $P<0.001$). The high PP group was less likely to consume alcohol ($P=0.005$). More subjects were diagnosed with hypertension ($P<0.001$), diabetes mellitus ($P<0.001$) and dyslipidemia ($P=0.043$) in the high PP group.

3. Correlations between study variables and PP

Table 3 shows the correlation between the investigated variables and the PP. In the Pearson correlation analysis showed

that age, sex, FBG, and serum TG levels were associated with elevated in PP.

The serum LDL-C level was associated with reduced in PP.

4. Comparison of the CHD odd ratios according to high pulse pressure

Table 4 shows the OR and 95% CIs of multivariates adjusted logistic regression between high PP and the incidence of CHD. There was significant association between high PP and CHD without adjustment (Model 1). After adjustment for age and sex, individuals with high PP had a higher risk for incidence of CHD with an OR of 1.36 (95% of CI : 1.08-1.72). After additionally adjustment for serum HDL-C and LDL-C level and DM, the OR for CHD was 1.29 (95% CI: 1.03-1.82) (Model 4).

Table 2. General characteristics of research subjects according to PP (n=4,100)

	Total	Normal PP (n=1808)	High PP (n=2292)	P-value*
Age	72.6±5.0	71.7±4.9	74.1±4.8	<0.001
Weight (kg)	60.5±9.8	60.5±9.8	59.3±9.5	<0.001
Height (cm)	158.0±8.9	159.0±9.0	156.3±8.6	<0.001
BMI (kg/m ²)	24.2±3.2	24.2±3.2	24.2±3.1	0.791
WC (cm)	85.4±9.0	85.5±9.1	85.4±9.0	0.707
SBP (mmHg)	128.9±17.5	119.9±12.3	143.4±14.8	<0.001
DBP (mmHg)	72.5±9.9	73.0±9.3	71.8±10.7	<0.001
FBG (mg/dL)	108.0±26.6	106.8±26.2	109.9±27.1	<0.001
TC (mg/dL)	184.5±39.7	184.5±39.7	183.7±40.1	0.302
HDL-C (mg/dL)	48.1±11.9	47.9±11.8	48.4±11.9	0.218
LDL-C (mg/dL)	109.5±36.4	110.4±36.4	108.1±36.4	0.041
TG (mg/dL)	134.2±83.1	133.1±88.7	136.1±73.1	0.264
Current smoking [†]	377 (9.2)	243 (9.6)	134 (8.6)	0.289
Alcohol (yes) [‡]	1,451 (35.4)	940 (37.0)	511 (32.7)	0.005
HTN (yes) [§]	2,603 (63.5)	1,283 (50.5)	1,320 (84.6)	<0.001
DM (yes) [§]	1,078 (26.3)	595 (23.4)	483 (30.9)	<0.001
Dyslipidemia (yes) [§]	1,390 (33.9)	831 (32.7)	559 (35.8)	0.043
CHD (yes) [§]	331 (8.1)	183 (7.2)	148 (9.5)	0.009

Data are expressed as mean±standard deviation or n (%).

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure; FBG, fasting blood glucose; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TG, triglycerides; HTN, hypertension; DM, diabetes mellitus; CHD, coronary heart disease.

*P-value were obtained by chi-square test (continuous variable) and independent t-test (categorical variable). [†]Current smokers were classified as smoking group. [‡]Participants who consumed at least one glass of alcohol every month over the last year were classified as alcohol consumption group. [§]Comorbidities were defined as those who were currently diagnosed by doctor.

Table 3. Correlations among observed variable and PP

		PP	P-value
Pearson correlation coefficient*	Sex	0.107	<0.001
	Age	0.281	<0.001
	BMI (kg/m ²)	0.019	0.223
	WC (cm)	-0.001	0.971
	FBG (mg/dL)	0.062	<0.001
	TC (mg/dL)	-0.012	0.433
	HDL-C (mg/dL)	0.020	0.193
	LDL-C (mg/dL)	-0.033	0.034
	TG (mg/dL)	0.057	<0.001

BMI, body mass index; WC, waist circumference; FBG, fasting blood glucose; TC, total cholesterol; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; TGs, triglycerides; PP, pulse pressure.

*Pearson correlation coefficient was obtained by Pearson correlation.

Table 4. Comparisons of CHD odds ratio according to high PP (N=4,100)

Category		CHD odds ratio			
		Model 1	Model 2	Model 3	Model 4
PP	Normal PP	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
	High PP	1.35 (1.08-1.69)	1.35 (1.06-1.70)	1.35 (1.06-1.70)	1.29 (1.03-1.82)
	P-value	0.01	0.013	0.013	0.028

Model 1: non-adjusted. Model 2: adjusted for sex, age. Model 3: further adjusted for smoking, alcohol. Model 4: further adjusted for HDL-C, LDL-C, DM.

CHD, coronary heart disease; PP, pulse pressure.

DISCUSSION

In this cross-sectional study, we found the significant association between high PP and CHD in Korean elderly using data from KNHANES VII. As the previous studies, PP increased with age [8,12] and high PP was positively correlated with the incidence of CHD and related with higher SBP, lower DBP and higher FBG. Also, the association between PP and the incidence of CHD was consistent after adjustment for age, sex, smoking habits, alcohol consumption, serum HDL-C, LDL-C and DM. Previous studies have reported that high PP is an important component of the CHD risk. In the Framingham Heart Study, it was confirmed that high PP, as well as SBP and DBP, is a risk factors for CHD [13]. Assmann et al. [9] suggested that high PP is an independent determinant of CHD risk, even in those with normal pulse pressure. Glasser et al. [8] confirmed PP is related with incident CHD with no racial or regional differ-

ences in black and white. Selvaraj et al. [12] reported the prognostic value of PP and its association with multiple adverse cardiovascular outcomes.

However, in the study comparing central, and peripheral SBP and PP in Asian population, central SBP is more valuable than other blood pressure parameters for prediction of cardiovascular mortality [14]. In addition, though PP is identified as an independent risk factor for CHD, it is still controversial whether it should be the target of anti-hypertensive therapy [15].

PP is composed of various factors such as arterial stiffness, ventricular ejection, and timing of wave reflection. Among these, aging has a great influence on arterial stiffness which results in increased SBP and decreased DBP. The increased systolic afterload causes left ventricular hypertrophy (LVH) and left ventricular oxygen requirement [16]. Also, due to abnormalities in iso-volumetric relaxation, LVH increases the systolic period while decreasing the diastolic period [17]. In

this study, we confirmed positive correlation between age and PP and CHD, which is considered to be such a mechanism.

In this observational study, we found PP is positively related with high FBG. FBG is one of the diagnostic criteria for DM. It is well known that DM is a high risk factor for cardiovascular disease. In the study on arterial stiffness and glucose tolerance, poor glucose tolerance status was correlated with increased arterial stiffness and decreased arterial compliance even before the onset of DM [18]. The vessel wall is composed of collagen and elastin, which are influenced by hemodynamic forces and extrinsic factors including hormone, salt and glucose regulation [16-18]. As impaired glucose tolerance affects arterial stiffness, it is considered FBG and PP are in positive correlation.

The limitations of this study are as follows. First, we did not correct the possible impacts of hypertension on CHD. No investigation of the history of HTN drug treatment and subgroup analysis of the HTN and normotensive group was performed. Also, we did not consider other comorbidities (such as hyperthyroidism) which could affect blood pressure. Second, since this study is a cross-sectional study, we evaluated the association between variables, but it was difficult to explain an exact causal relationship or a predecessor relationship. Third, though we attempted to reduce the effects of confounders bias through by adjustment of covariates, some residual confounding may remain.

Despite these limitations, this study is meaningful in that it used large-scale, nationally-representative database to describe the association between pp and CHD in the Korean elderly population. Furthermore, we confirmed the importance of PP which can be easily used in daily clinical practice with recommendation to physicians to consider PP in addition to SBP and DBP.

In this study, we found the significant association between PP and CHD in Korean elderly. Our findings suggest the usefulness of clinical data of PP which are non-invasive and has easy clinical applicability in primary care settings. A prospective study on the association between PP and CHD in Korean elderly is needed.

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