■ Original Article

The Relationship between Heart Rate Variability and Aortic Knob Width

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Background: The aortic knob width (AKW) and the heart rate variability (HRV) were suggested to be related to development of cardiovascular diseases. However, the relationship between them has not been investigated; thus, this study aimed to determine this relationship.

Methods: This study included 587 Koreans aged 18–79 years. Their physical measurements, medical and social histories, blood test findings, and chest radiographs were obtained. The HRV parameters included the standard deviation of the N-N interval (SDNN), root mean square of successive differences (RMSSD), approximate entropy (ApEn), total power (TP), very low frequency (VLF), low frequency (LF), high frequency (HF), and LF/HF ratio, which were measured for 5 minutes. The AKW was measured on chest radiographs by a single reviewer.

Results: The AKW was significantly correlated with the HRV parameters, except for the LF/HF ratio. However, RMSSD and ApEn were not significantly related to the AKW in women. After dividing the participants into quartile groups, the AKW was significantly related to the SDNN, RMSSD, TP, VLF, LF, and HF. The HRV parameter values decreased in the higher AKW quartile groups, the HRV parameter values decreased. After adjusting for sex, drinking status, exercise habits, smoking status, waist circumference, and triglyceride, low-density lipoprotein cholesterol, fasting blood sugar, and glycated hemoglobin levels, the AKW showed significant negative associations with the HRV parameters, except for the LF/HF ratio.

Conclusion: The AKW is significantly associated with the HRV parameters of SDNN, RMSSD, ApEn, TP, VLF, LF, and HF.

Keywords: Heart Rate Variability; Aortic Knob Width; Cardiovascular Diseases; Thoracic Aorta

INTRODUCTION

Heart rate variability (HRV) evaluates the activity of the autonomic nervous system (ANS) noninvasively. The normal activity of the ANS is determined by a balance between the sympathetic and parasympathetic activities. In the cardiovascular system, an imbalance in the ANS results in the fluctuation of the heart rate. Low HRV parameters were found to be associated with atherosclerotic plaque progression, congestive heart failure, myocardial infarction, arrhythmia, sudden cardiac death, diabetic neuropathy, hypertension, dyslipidemia, and older age.[1-3] Several studies showed that HRV may indicate a current illnesses or serve as a warning sign for various cardiac diseases, such as arrhythmia, myocardial infarction, coronary heart disease, and heart failure.[1,2,4,5]

The aortic knob width (AKW) is an important parameter in chest radiography and may be an early indicator of cardiovascular diseases. It can be increased by changes in elasticity or by increased pressure flow in the aorta (e.g., in systemic hypertension and aortic dissection), and in the presence of the aortic arch calcification, atherosclerosis, and cardiovascular diseases.[6-10]

No studies have investigated the correlation between the HRV and AKW, which is an important index of cardiovascular risk. This study aimed to investigate the relationship between these factors.

METHODS

1. Subjects

A total of 696 Korean adults aged 18–79 years who visited a health screening center for regular check-ups between January 2015 and July 2016 were considered for inclusion in this study. Subjects with a history of arrhythmia, atrial fibrillation, angina pectoris, myocardial infarction, cerebrovascular disease, major depression, thyroid disease, malignancy, and infectious diseases were excluded. Pregnant women and those who presented with incomplete questionnaires were also excluded. Out of the 696 subjects, 109 subjects were excluded, and the remaining 587 subjects were examined. All participants provided written informed consent prior to inclusion.

2. Clinical Examination and Blood Assays

Medical, social, and lifestyle histories, including drinking status, exercise habits, and smoking status, were collected using self-administered questionnaires. Based on the current drinking status, patients were divided into alcoholic drinkers and non-drinkers, while based on the current smoking status they were divided into smokers and non-smokers. Only those who exercised regularly 3 or more times in a week were assigned to the exercise group.

The height and weight of participants were measured using an automatic digital stadiometer (GM-1000; NEO GM TEC, Incheon, Korea). Body mass index was calculated as body weight divided by height squared (kg/m²). Waist circumference was measured at the midpoint between the rib cage's lower border and the iliac crest. Blood pressure

Table 1. Characteristics of the study participants

Characteristic	Total (N=587)	Men (N=351)	Women (N=236)	P-value
Age (y)	46.85±12.89	48.81±12.57	43.93±12.83	<0.001
Aortic knob width (mm)	32.08±5.54	33.94±5.28	29.30±4.71	<0.001
Body mass index (kg/m²)	24.02±3.51	25.01±3.25	22.55±3.37	<0.001
Waist circumference (cm)	81.02±10.34	85.47±8.66	74.39±9.02	<0.001
Systolic BP (mm Hg)	118.18±14.02	122.26±12.28	112.10±14.286	<0.001
Diastolic BP (mm Hg)	70.99±10.09	73.32±9.54	67.52±9.93	<0.001
Total cholesterol (mg/dL)	199.68±38.06	202.19±38.04	195.94±37.87	0.051
Triglyceride (mg/dL)	119.69±88.46	142.43±100.664	85.86±49.98	<0.001
High-density lipoprotein cholesterol (mg/dL)	55.73±14.50	51.11±1 1.97	62.60±15.23	<0.001
Low-density lipoprotein cholesterol (mg/dL)	120.63±33.90	124.40±33.86	115.01±33.23	0.001
Fasting blood sugar (mg/dL)	92.95±20.38	95.69±23.67	88.88±13.17	<0.001
Glycated hemoglobin levels (%)	5.56±0.70	5.63±0.75	5.45±0.60	0.002
Mean heart rate (ms)	70.38±9.85	69.34±9.41	71.93±10.30	0.002
SD of all normal-to-normal intervals (ms)	32.53±13.81	32.75±14.38	32.22±12.94	0.649
Root mean square of successive differences (ms)	23.44±12.46	22.92±12.96	24.21±11.67	0.221
Approximate entropy	0.97±0.11	0.97±0.11	0.96±0.11	0.870
TP* (ms²)	6.40±0.93	6.41±0.96	6.40±0.89	0.896
Very LF (ms²)	5.54±1.09	5.54±1.11	5.55±1.07	0.947
LF (ms²)	5.03±1.09	5.08±1.13	4.95±1.03	0.167
HF (ms²)	4.62±1.16	4.55±1.21	4.73±1.07	0.056
LF/HF ratio	2.67±4.13	2.90±3.97	2.33±4.34	0.102

Values are presented as mean±SD. All data were analyzed by independent t-test. P-values refer to comparisons between men and women.
BP, blood pressure; SD, standard deviation; TP, total power; LF, low-frequency; HF, high-frequency.
*Short-term estimate of the TP of power spectral density.

(BP) was measured using an automated sphygmomanometer (FT-500R; Jawon Medical, Kyungsan, Korea) after 5 minutes of stabilization.

Blood samples were collected the following morning after fasting for at least 8 hours. The laboratory tests included assessment of the total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood sugar (FBS), and glycated hemoglobin (HbA1c) levels.

3. Measurement of the Aortic Knob Width

The aortic knob is best visualized on frontal chest radiographs. The AKW was measured along the horizontal line from the point of the trachea's lateral edge to the aortic knob's left lateral wall.[7,11] To minimize possible errors, all measurements were performed by one reviewer.

4. Heart Rate Variability Measurement

For accurate measurement, the following conditions were maintained: (1) a room temperature of 23°C–25°C and noise was avoided; (2) participants were asked to avoid consuming caffeine and smoking 2 hours before the examination; and (3) participants were asked to relax and not move or speak during the examination.

The HRV parameters were measured using a HRV analyzer (SA-3000P; Medicore Co. Ltd., Seoul, Korea) for 5 minutes. The HRV provides significant information on the regulatory function and balance status of the ANS.

All HRV parameters were calculated on 'normal-to-normal' (N-N) inter-beat intervals (N-N intervals) caused by normal heart contrac-

tions paced by the sinus node depolarization. Assessed parameters were measured by the time domain and frequency domain.[2] The time domain parameters used in this study included the standard deviation of the N-N interval (SDNN), root mean square of successive differences (RMSSD), and approximate entropy (ApEn). The SDNN is the square root of the variance and is a marker of total power (TP) in HRV.[1] Furthermore, it reflects both parasympathetic and sympathetic activities. The RMSSD is the square root of the mean squared differences of successive N-N intervals. This parameter estimates high-frequency variations in the heart rate in short-term N-N recordings and reflects an estimate of parasympathetic activities. The ApEn is the quantification of the regularity and complexity of the HRV; the higher the ApEn, the higher the tachogram's complexity.

The frequency domain parameters used in this study included the TP (0–0.4 Hz), very low frequency (VLF, 0–0.4 Hz), low frequency (LF, 0.04–0.15 Hz), high frequency (HF, 0.15–0.4 Hz), and LF/HF ratio. The TP mainly shows the level of both parasympathetic and sympathetic activities; a decreased TP indicates that the individual is under chronic stress or has some underlying disease. TP is strongly associated with the risks of sudden cardiac death and all-cause death after myocardial infarction. VLF is an additional indicator of sympathetic function. LF reflects sympathetic and parasympathetic activities in short-term measurements and sympathetic activities in long-term measurements. HF reflects the parasympathetic or vagal activity of the ANS; a reduced HF is related to aging, electrical instability of the heart, and chronic stress. The LF/HF ratio is an index that quantifies the overall balance between the sympathetic and parasympathetic nervous sys-

Table 2. Relationships between aortic knob width and investigated variables

Variable	Total		Men		Women	
	R	P-value	R	P-value	R	P-value
Age (y)	0.583	<0.001	0.5110	<0.001	0.661	<0.001
Body mass index (kg/m²)	0.406	<0.001	0.193	<0.001	0.498	<0.001
Waist circumference (cm)	0.464	<0.001	0.227	<0.001	0.474	<0.001
Systolic BP (mm Hg)	0.424	<0.001	0.206	<0.001	0.506	<0.001
Diastolic BP (mm Hg)	0.349	<0.001	0.192	<0.001	0.388	<0.001
Total cholesterol (mg/dL)	0.083	<0.001	-0.061	0.255	0.249	<0.001
Triglyceride (mg/dL)	0.248	<0.001	0.093	0.082	0.308	<0.001
High-density lipoprotein cholesterol (mg/dL)	-0.265	<0.001	-0.064	0.229	-0.212	0.001
Low-density lipoprotein cholesterol (mg/dL)	0.116	<0.001	-0.096	0.072	0.346	<0.001
Fasting blood sugar (mg/dL)	0.275	<0.001	0.206	<0.001	0.322	<0.001
Glycated hemoglobin levels (%)	0.296	<0.001	0.253	<0.001	0.302	<0.001
Mean heart rate (ms)	-0.145	<0.001	-0.040	0.459	-0.197	0.002
Standard deviation of all normal-to-normal intervals (ms)	-0.207	<0.001	-0.223	<0.001	-0.257	<0.001
Root mean square of successive differences (ms)	-0.143	<0.001	-0.144	0.007	-0.116	0.075
Approximate entropy	-0.113	<0.001	-0.148	0.006	-0.091	0.162
TP* (ms²)	-0.244	<0.001	-0.290	<0.001	-0.234	<0.001
Very LF (ms²)	-0.159	<0.001	-0.186	<0.001	-0.152	<0.001
LF (ms²)	-0.269	<0.001	-0.362	<0.001	-0.246	<0.001
HF (ms²)	-0.255	<0.001	-0.269	<0.001	-0.199	<0.001
LF/HF ratio	0.020	0.629	-0.009	0.865	-0.008	0.905

All correlation coefficients were obtained by Pearson's correlation analysis.
BP, blood pressure; TP, total power; LF, low-frequency; HF, high-frequency.
*Short-term estimate of the TP of power spectral density.

tems. A high LF/HF ratio indicates an increased sympathetic activity or reduced parasympathetic activity. All frequency domain parameters were transformed into natural logarithm.

5. Statistical Analysis

All continuous variables were analyzed using the independent t-test. Pearson's correlation analysis was conducted to determine the association between the HRV parameters and the AKW. To evaluate the trends of each HRV parameter according to the AKW quartiles, the P-value for trend was obtained using the analysis of covariance, after adjusting for age, drinking status, smoking status, and exercise habits. Multiple regression analysis was used to investigate the relationship between each of the HRV parameters and the AKW. All analyses were two-tailed, and P-values <0.05 were considered statistically significant. All statistical analyses were performed using PASW SPSS for Windows ver. 18.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

The study included a total of 587 participants: 351 men and 236 women. The mean patient age was 46.85±12.89 years. The mean AKW was 32.08±5.54 mm in the general study population, 33.94±5.28 mm in men, and 29.30±4.71 mm in women. No significant differences were found between men and women in any HRV parameter, except for the mean heart rate (Table 1).

The AKW was significantly negatively associated with all HRV parameters in all participants, except for the LF/HF ratio. In men, the AKW was significantly negatively associated with SDNN (ms), RMSSD (ms), ApEn, TP, VLF, LF, and HF. In women, the AKW was significantly negative associated with SDNN (ms), TP, VLF, LF, and HF (Table 2).

After adjusting for drinking status, exercise habits, smoking status, waist circumference, and triglyceride, LDL-C, FBS, and HbA1c levels, all HRV parameters decreased as the AKW quartile increased (Table 3).

The AKW was significantly associated with the SDNN (R^2=0.310, P<0.001), RMSSD (R^2=0.306, P=0.048), ApEn (R^2=0.306, P=0.001), TP (R^2=0.320, P<0.001), VLF (R^2=0.303, P=0.004), LF (R^2=0.337, P<0.001), and HF (R^2=0.315, P<0.001) after adjusting for sex, drinking status, exercise habits, smoking status, waist circumference, and triglyceride, LDL-C, FBS, and HbA1c levels (Table 4).

DISCUSSION

The HRV parameters were not significantly different between men and women, except for the mean heart rate. As the quartile of the AKW increased, the HRV parameters decreased. This negative correlation was enhanced in the multiple regression analysis after adjusting for significant variables.

In contrast, a previous study has shown that the RMSSD and HF, which reflect parasympathetic activities, were higher in women than in men.[12] Moreover, the quartile of each AKW was higher in men than

Table 3. Trends of each heart rate variability parameter according to quartiles of AKW

	Variable	Quartiles of AKW				P-value for trend
		Q1	Q2	Q3	Q4	
Total	Range of AKW (mm)	20.74–27.88	27.89–31.72	31.73–35.15	35.16–75.00	
	SDNN (ms)	37.64±13.99	32.95±12.31	31.60±13.97	27.89±13.14	<0.001
	RMSSD (ms)	26.15±14.18	23.52±11.16	22.77±10.10	21.27±23.80	0.001
	TP (ms^2)	6.77±0.75	6.49±0.88	6.30±0.99	6.05±0.94	<0.001
	VLF (ms^2)	5.86±0.99	5.57±1.08	5.48±1.16	5.26±1.05	<0.001
	LF (ms^2)	5.46±0.93	5.21±1.00	4.85±1.11	4.59±1.11	<0.001
	HF (ms^2)	4.99±1.03	4.74±1.05	4.51±1.14	4.23±1.27	<0.001
Men	Range of AKW (mm)	22.02–30.45	30.46–33.50	33.51–36.69	36.70–75.00	
	SDNN (ms)	37.74±14.11	32.31±12.86	32.32±14.52	28.61±14.72	<0.001
	RMSSD (ms)	25.56±14.76	22.50±11.33	22.78±11.11	20.86±14.00	0.025
	TP (ms^2)	6.84±0.74	6.43±0.95	6.33±0.99	6.02±0.97	<0.001
	VLF (ms^2)	5.90±0.99	5.54±1.12	5.49±1.21	5.24±1.00	<0.001
	LF (ms^2)	5.64±0.92	5.18±1.06	4.92±1.07	4.56±1.21	<0.001
	HF (ms^2)	5.00±1.02	4.57±1.13	4.50±1.13	4.12±1.38	<0.001
Women	Range of AKW (mm)	20.74–25.93	25.94–28.50	28.51–32.00	32.10–47.33	
	SDNN (ms)	37.42±13.93	33.95±11.71	30.55±13.19	26.83±10.37	<0.001
	RMSSD (ms)	26.99±13.38	25.13±10.81	22.75±10.92	21.89±10.84	0.009
	TP (ms^2)	6.66±0.76	6.58±0.76	6.27±0.99	6.08±0.91	<0.001
	VLF (ms^2)	5.81±0.99	5.6±1.03	5.46±1.07	5.29±1.13	0.006
	LF (ms^2)	5.20±0.89	5.25±0.92	4.73±1.18	4.62±0.96	<0.001
	HF (ms^2)	4.99±1.03	5.00±0.87	4.53±1.16	4.40±1.09	<0.001

Values are presented as mean±standard deviation. Analyzed by analysis of variance after adjusting for age, drinking status, exercise habits, and smoking status. P-value for trend was obtained by using analysis of covariance after adjusting for age, drinking status, exercise habits, and smoking status.
AKW, aortic knob width; SDNN, standard deviation of all normal-to-normal intervals, RMSSD, root mean square of successive differences; TP, short-term estimate of the total power of power spectral density; VLF, very low-frequency; LF, low-frequency; HF, high-frequency.

Table 4. Multiple linear regression analysis of the association between the aortic knob width with the heart rate variability parameters

Variable	β±standard error	R^2	Adjusted R^2	P-value
Standard deviation of all normal-to-normal intervals (ms)	-0.054±0.014	0.310	0.299	<0.001
Root mean square of successive differences (ms)	-0.031±0.16	0.306	0.301	0.048
Approximate entropy	-5.815±1.805	0.306	0.295	0.001
TP* (ms^2)	-1.011±0.213	0.320	0.309	<0.001
Very LF (ms^2)	-0.520±0.181	0.303	0.292	0.004
LF (ms^2)	-1.109±0.180	0.337	0.327	<0.001
HF (ms^2)	-0.736±0.172	0.315	0.304	<0.001

Multiple regression analysis was performed after adjusting for sex, drinking status, exercise habits, smoking status, waist circumference, and triglyceride, low-density lipoprotein cholesterol, fasting blood sugar, and glycated hemoglobin levels.
TP, total power; LF, low-frequency; HF, high-frequency.
*Short-term estimate of the total power of power spectral density.

in women in this study; this result is consistent with that of a previous study.[13]

Previous studies have indicated that HRV and the AKW are associated with the increased risk for cardiovascular diseases.[1,4,7,8,14,15] However, the relationship between the AKW and HRV has not been yet elucidated. Except for the RMSSD and ApEn in the women, the AKW was highly correlated with the SDNN, RMSSD, ApEn, TP, VLF, LF, and HF. This relationship between AKW and HRV may be explained by several factors. First, both the HRV and AKW were found to be associated with coronary instability.[1,12] Second, increased BP in the aorta induces widening of the aortic knob. A low SDNN at a young age indicates an increased risk of hypertension.[1,16] Third, common factors, including age, hypertension, metabolic syndrome, atherosclerosis, and diabetes mellitus, were found to be associated with the AKW widening and decreased HRV.[1,16-20] Finally, unstable hemodynamics causing aortic arch calcification is presumed to be related to an imbalance in the ANS activity.[9,10,21,22]

The HRV parameters were divided into two categories: time domain and frequency domain. The parameters of the time domain were the SDNN, RMSSD, and ApEn, while the parameters of the frequency domain were the TP, VLF, LF, HF, and LF/HF ratio.[1,4,14] The data obtained from short-term (5 minutes) recordings should be processed with frequency domain methods, whereas time domain analyses should be performed to analyze 24-hour, long-term recordings.[1] This study used the 5-minute measurement method, and the frequency domain parameters were matched well regardless of sex. Therefore, we can assume that the frequency domain parameters matched better in the correlation analysis between the AKW and HRV.

This study has several limitations. The long-term analysis (24-hour measurement) is more accurate than the short-term analysis (5-minute analysis). However, the short-term analysis is less expensive, saves time, and is convenient for the participants. A large number of subjects should be investigated in future studies to clarify the relationship between the AKW and HRV parameters.

Despite these limitations, HRV can be a useful factor in evaluating the change in AKW associated with cardiovascular disease. If an individual has a significantly higher AKW than the average age group, we can assume that such an individual has low SDNN and TP (represent-

ing HRV). The result was obtained using chest radiography; thus, HRV may be used clinically as an indicator of possible cardiovascular diseases. Further research is needed to determine how HRV can be used as a clinical factor to evaluate cardiac risks, and how to apply the relationship between the AKW and HRV. In addition, it is necessary to investigate the relationship between the AKW and HRV in metabolic syndrome and the change in this relationship according to age and sex.

In conclusion, the HRV parameters were significantly associated with the AKW in the Korean population of this study.

CONFLICT OF INTEREST

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

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