Effect of Obesity on P-Wave Parameters in a Chinese Population

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Objective: To study the association between obesity and P-wave duration and dispersion (P_d) in order to evaluate the potential risk for atrial fibrillation development in Chinese subjects using the definitions applied for Asian populations.

Methods: The study population consisted of 40 obese (body mass index (BMI) $\geq$ 25 Kg/m^2, according to the World Health Organization classification for the Asian population) subjects and 20 age- and sex-matched normal weight controls. Maximum P-wave duration (P_{max}), minimum P-wave duration (P_{min}), and P_d were carefully measured using a 12-lead electrocardiogram, while the presence of interatrial block (IAB; P $\geq$ 110 ms) was assessed.

Results: There were no significant differences between the two groups regarding age, sex, history of hypertension or diabetes, and hyperlipidemia. Compared to controls, BMI, left atrial diameter (LAD), and interventricular septal thickness were increased, while P_{max} (111.9 $\pm$ 9.3 vs 101.1 $\pm$ 6.0 ms, $P < 0.01$) and P_d (47.9 $\pm$ 9.3 vs 31.8 $\pm$ 6.9 ms, $P < 0.01$) were significantly prolonged in the obese group. P_{min} was similar between the two groups. The prevalence of IAB was significantly greater in the obese subjects. Pearson's correlation analysis showed that there were positive correlations between P_d and BMI ($r = 0.6$, $P < 0.001$), as well as between P_d and LAD ($r = 0.366$, $P < 0.05$).

Conclusion: Our data suggest that obesity is associated with increased P_{max} and P_d, and increased prevalence of IAB, parameters that have been associated with atrial fibrillation. The correlation of these electrocardiogram parameters with LAD indicates an association between increased BMI and atrial remodeling in Asian subjects.

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obesity; P-wave duration; P-wave dispersion; interatrial block; atrial fibrillation

Obesity represents a global problem with significant health consequences. The prevalence of obesity in China is continuously increasing following the global trends.[1,2] It is well known that obesity is associated with increased prevalence of hypertension, coronary artery disease, diabetes mellitus, and metabolic syndrome.[3] On the other hand, atrial fibrillation (AF) is a rapidly evolving epidemic associated with increased cardiovascular morbidity and mortality.[4,5] Recent data indicate that obesity is independently related to the development of AF,[6–9] while left atrial dilation may be involved in this association.[10]

P-wave dispersion (P_d) is a novel electrocardiographic marker. It has been proposed that it reflects the prolongation of intraatrial and interatrial conduction time and the discontinuous inhomogeneous propagation of sinus impulses.[11,12] However, the difference of P-wave duration in different leads may be a simple vector projection phenomenon.[12] Pd is defined as the difference between the maximum and the minimum P-wave duration calculated on a 12-lead surface electrocardiogram (ECG). Prolonged P_d and maximum P-wave duration (P_{max}) have been proposed as independent predictors for the development or

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recurrence of AF in patients with various cardiovascular diseases.[13–18] Previous studies have demonstrated that P_d and P_{max} are more prolonged in obese patients,[19–21] whereas weight loss in these subjects has been associated with decreased P_d.[20,22] However, in these studies the participants were of European origin having greater body mass index (BMI) compared with Asian people.[23] In the present study we investigated the effect of obesity on P-wave duration and P-wave dispersion (P_d) in order to evaluate the potential risk for AF development in Chinese subjects using the World Health Organization (WHO) definitions applied for Asian populations.[23,24] Moreover, we evaluated the prevalence of interatrial block (IAB) a novel index of atrial conduction abnormality which has been associated with AF.[25,26]

MATERIALS AND METHODS

Study Population

Between January 1, 2007 to June 30, 2008, 162 consecutive subjects had angiographically proven normal epicardial coronary arteries and sinus rhythm when underwent coronary angiography in the context of investigation for coronary artery disease. Among these subjects, 42 were excluded because they were taking antiarrhythmic drugs including beta-blockers, while 36 patients who had electrolyte disturbances, thyroid disease, chronic obstructive pulmonary disease, obstructive sleep apnea (OSA), valvular heart disease, congenital heart disease, cardiomyopathy, left ventricular dysfunction, prior pacemaker implantation, history of AF, left or right bundle branch block, and atrioventricular conduction abnormalities on the 12-lead ECG were also not included in the study. After excluding another three subjects due to low P-wave amplitude in three or more ECG leads, there were 40 obese subjects (BMI $\geq$ 25 Kg/m^2, according to the WHO classification for the Asian population[23,24]), who were included in the study. From the remaining 41 subjects, 20 age and sex-matched normal weight controls (BMI < 23 Kg/m^2) were selected. Our study was approved by the ethics committee of Second Hospital of Tianjin Medical University and written informed consent was obtained from all patients.

Weight and height were measured using a standardized protocol at admission to our hospital. BMI was calculated by dividing weight in kilograms by the square of the height in meters. Blood samples were collected after a 12-hour overnight fast for determination of plasma glucose, total cholesterol, low-density lipoprotein, high-density lipoprotein-cholesterol, and triglyceride levels.

Twelve-Lead Surface ECG

Twelve-lead surface ECG was recorded from all patients in the supine position at a paper speed of 50 mm/s and a sensitivity of 10 mm/mV (CardiMax FX-7402, FUKUDA DENSHI Corp. Tokyo, Japan). In order to avoid diurnal variations, we obtained the ECG recordings during the same time interval (from 9 AM to 11 AM). All patients were breathing freely and were not speaking during the ECG acquisition.

P-Wave Duration Measurements

The P-wave duration was measured manually in all of the simultaneously recorded 12 leads of the surface ECG. Two experienced investigators unaware of the clinical characteristics of the study participants measured the P-wave durations. For greater accuracy, all measurements were performed with calipers and magnifying lenses. P-wave duration was measured from the onset to the end of the P wave. The onset and offset of the P wave were defined as the junction between the P-wave pattern and isoelectric line. Maximum and minimum P-wave duration (P_{max} and P_{min}, respectively) were carefully recorded. P_{max} was defined as the longest P-wave duration, and P_{min} was as the shortest P-wave duration. Pd was calculated as the difference between P_{max} and P_{min} ($P_d = P_{max} - P_{min}$). IAB was defined as a prolonged P-wave duration ($\geq$110 ms).[25,26] All of the measurements were repeated 3 times and average values were recorded. The intraobserver and interobserver variations for all measurements were less than 5% and therefore nonsignificant.

Echocardiography

A transthoracic echocardiography was performed in all patients using the Vivid-7 system equipped with a 2–4 MHz transducer (GE Medical Systems, Milwaukee, WI, USA). Parasternal long- and short-axis, apical four chamber, and two chamber views were obtained, and left ventricular systolic and diastolic function was evaluated. Left atrial diameter (LAD), interventricular septal thickness and left ventricular end-diastolic diameter were assessed for each patient. Left ventricular ejection fraction was determined from apical four-chamber views using the Simpson's biplane formula. All echocardiographic data were analyzed by the same investigator who was blind to clinical status of the participants.

Statistical Analysis

Continuous variables are presented as mean ± SD and categorical variables as percentages. Kolmogorov Smirnov test was used to assess the normality of distribution of the continuous variables and all variables were normally distributed. Statistical analysis was performed using the Student's *t*-test for continuous variables and Chi-square test to compare categorical variables. The relationship between variables was analyzed with Pearson correlation. A P value < 0.05 was considered statistically significant. All data analyzed using SPSS 11.5 Statistical Package Program for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

The clinical and echocardiographic characteristics of the study population are presented in Table 1. There were no significant differences between the two groups regarding age (54 ± 10 vs 50 ± 9 years), sex (males 80% vs 75%), history of hypertension or diabetes, blood pressure, total cholesterol and low-density lipoprotein cholesterol levels. There was a trend toward higher triglyceride and lower high-density lipoprotein cholesterol levels in obesity subjects, but the difference was not statistically significant. Compared with controls, BMI (29.4 ± 3.0 vs 21.5 ± 2.0 Kg/m^2, P < 0.01), Left atrial diameter (37.6 ± 7.3 vs 29.6 ± 4.8 mm, P < 0.01), and interventricular septal thickness (9.8 ± 2.7 vs 8.0 ± 1.9 mm, P < 0.05) were significantly increased in the obese subjects. However, there were no statistically significant differences between the left ventricular end-diastolic diameter and left ventricular end-diastolic diameter.

P-wave measurement results are listed in Table 2. P_{max} (111.9 ± 9.3 vs 101.1 ± 6.0 ms, P < 0.001) and P_d (47.9 ± 9.3 vs 31.8 ± 6.9 ms, P < 0.01) were significantly prolonged in the obese group while P_{min} was similar between the 2 groups (64.5 ± 12.8 vs 69.3 ± 5.6 ms, P > 0.05). In our study, the longest P-wave duration was observed in the inferior leads (II, III, AVF) 108.2 ± 5.8 ms and the shortest duration in V1-V2 67.8 ± 7.6 ms. With regard to IAB, a statistically significant difference was evident between the 2 groups (Table 2). Pearson's correlation analysis showed that there were positive correlations between P_d and BMI (r = 0.6, P < 0.001), P_d and LAD (r = 0.366, P < 0.05).

Table 1. Baseline Clinical and Echocardiographic Characteristics of Study Population

	Obese Subjects (n = 40)	Controls (n = 20)	P Value
Sex (male %)	32 (80)	15 (75)	NS
Age (years)	54 ± 10	50 ± 9	NS
BMI (Kg/m^2)	29.4 ± 3.0	21.5 ± 2.0	**<0.01**
Hypertension (%)	13 (32.5)	5 (25)	NS
Diabetes mellitus (%)	5 (12.5)	2 (10)	NS
SBP (mmHg)	133 ± 18	127 ± 16	NS
DBP (mmHg)	80 ± 10	83 ± 11	NS
Fasting glucose (mmol/L)	5.87 ± 1.84	5.31 ± 1.90	NS
Total cholesterol (mmol/L)	4.9 ± 0.9	5.0 ± 0.5	NS
LDL cholesterol (mmol/L)	2.9 ± 0.8	3.0 ± 0.6	NS
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.5 ± 0.4	NS
Triglycerides (mmol/L)	1.8 ± 0.8	1.4 ± 0.7	NS
LAD (mm)	37.6 ± 7.3	29.6 ± 4.8	**<0.01**
LVEDD (mm)	45.5 ± 3.6	44.1 ± 3.2	NS
IVST (mm)	9.8 ± 2.7	8.0 ± 1.9	**<0.05**
LVEF (%)	58.8 ± 6.9	65.2 ± 6.5	NS
Medications			
Statin (%)	11 (27.5)	6 (30)	NS
ACEIs or ARBs (%)	7 (17.5)	3 (15)	NS
CCBs (%)	8 (20)	3 (15)	NS
Diuretics (%)	3 (7.5)	1 (5)	NS

Bold indicates a significant difference between the two groups. BMI = body mass index; NS = not significant; SBP = Systolic blood pressure; DBP = diastolic blood pressure; LDL-c, low-density lipoprotein; HDL-c, high-density lipoprotein; LAD = left atrial diameter; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; IVST = interventricular septum thickness ACEIs = angiotensin-converting enzyme inhibitors; ARBs = angiotensin receptor blockers; CCBs = calcium channel blockers.

DISCUSSION

In the current study, we demonstrated that P_{max} and P_d were significantly higher while the prevalence of IAB was greater in Chinese obese subjects

Table 2. P-wave Duration Measurements of Study Population

	Obese Subjects (n = 40)	Controls (n = 20)	P Value
Heart rate (bpm)	72 ± 13	69 ± 7	NS
IAB n (%)	31 (77.5)	6 (30)	<0.01
P_{max} (ms)	111.9 ± 9.3	101.1 ± 6.0	<0.01
P_{min} (ms)	64.5 ± 12.8	69.3 ± 5.6	NS
P_d (ms)	47.9 ± 9.3	31.8 ± 6.9	<0.01

IAB = interatrial block; NS = not significant; bpm = beat per minute.
P-wave duration ≥ 110 ms in any electrocardiographic lead was regarded as IAB.

compared to age and sex-matched normal weight controls. In addition, there was a positive correlation between P_d and LAD. To the best of our knowledge, no study to date has examined the effect of obesity on P-wave indices in Asian populations who have much lower BMI than westerns.

Recently, it was suggested that obesity may be an important risk factor for the development of AF.[6–9] Dublin et al.[7] showed that AF risk was higher in subjects with increased BMI than those with normal BMI. Moreover, a recent meta-analysis of 16 studies including 123,249 patients showed that obesity increased the risk of AF by 49% in the general population, but failed to demonstrate an association between obesity and AF in postcardiac surgery patients.[8] The potential mechanisms between obesity and AF are still not fully understood. Left atrial enlargement and left ventricular hypertrophy, which are very common findings in obese subjects, may have a particular role. Interestingly, some clinical conditions related to obesity such as metabolic syndrome, diabetes, hypertension, and OSA may also contribute to the development of AF.[3] Last, autonomic dysfunction, inflammation, and oxidative stress may be implicated in this setting.[9,27]

P_d represents a noninvasive electrocardiographic marker that may reflect the prolongation of intraatrial and interatrial conduction time as well as the discontinuous inhomogeneous propagation of sinus impulses,[11] or simply it may be a vector projector phenomenon.[12] Regardless of the underlying mechanisms, prolonged P_d and P_{max} have been suggested as independent predictors for the development or recurrence of AF in patients with acute myocardial infarction,[13] hypertrophic cardiomyopathy,[14] atrial septal defect,[15] rheumatic mitral stenosis,[16] and after elective cardioversion[17] or coronary artery bypass surgery.[18] Also, P_d seems to be a useful predictor of AF in patients with hyperthyroidism,[28] chronic obstructive pulmonary disease,[29] and OSA.[30] Previous studies have shown that P_d and P_{max} are prolonged in obese subjects compared with normal weight controls in European countries,[19–21] while weight loss by a predefined program or bariatric surgery in obese subjects is associated with decreased P_d.[20,22] In our study, we enrolled a group of obese patients defined according to the WHO classification for the Asian population (BMI ≥ 25 Kg/m^2).[23,24] The mean BMI in our obese subjects was 29.4 Kg/m^2, a much lower value compared to the BMI (38.1–52.6 Kg/m^2) of obese subjects who enrolled in previous European studies.[19–21] Our analysis showed that obesity is associated with increased P_d and P_{max} as well as with increased prevalence of IAB. The prevalence of IAB is more than 40% in hospitalized patients although it is commonly ignored.[25,26] IAB may represent a useful predictor of AF in several settings.[25,26]

Left atrial dilation, atrial conduction prolongation, and autonomic imbalance in obese subjects could be the underlying mechanisms for the prolonged P_d and P_{max}. Our study also demonstrated that there was a positive correlation between P_d and LAD, indicating the association between increased BMI and atrial remodeling in Asian subjects. It could also be speculated that the increased P-wave dispersion which is associated with abnormal geometry (increased LAD) is due to the projection phenomenon.

In the present study, we excluded the patients taking any antiarrhythmic drugs which may have potential influence on P-wave indices. In addition, patients with coronary artery disease, OSA, electrolyte disturbance, associated cardiac and pulmonary disease were also excluded. The prevalence of hypertension, diabetes, and hyperlipemia were similar between obese groups and sex-age-matched controls. Medications such as statins, angiotensin-converting enzyme inhibitors and angiotensin receptors, calcium channel blockers were also matched in both groups.

Study Limitations

This study has some limitations. First, the small sample size in a selected population is an important limitation of our study. Second, multivariate regression analysis was unfeasible because of the small study population. Third, P waves were measured manually and not by digital methods. However, both methods have been reported to produce similar results.[31] It should also be acknowledged that data related to metabolic syndrome prevalence were unavailable. However, the prevalence of hypertension, diabetes, and hyperlipemia were similar between obesity and control groups.

CONCLUSIONS

Our data suggest that obesity in Asian subjects is associated with increased P_{max} and P_d, as well as with increased prevalence of IAB, parameters that have been associated with AF. The correlation of these indexes with the LAD indicates the association between increased BMI and atrial remodeling in Asian subjects. In addition larger studies are needed to elucidate the exact prognostic value of these ECG indexes in this setting.

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