นิพนธ์ต้นฉบับ ■ Original Article

การประเมินสภาวะความแข็งของหลอดเลือดแดงส่วนกลางในคนไทยสุขภาพดีโดยเทคนิคแบบไม่รุกราน

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Assessment of Central Arterial Stiffness in Healthy Thais by Non-invasive Technique

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หลักการและวัตถุประสงค์: สภาวะความแข็งของหลอดเลือดแดงส่วนกลางเป็นตัวแปรอิสระของการเกิดโรคและการเสียชีวิตจากโรคหัวใจและหลอดเลือด ค่าความเร็วของคลื่นชีพจรจากหลอดเลือดแคโรติดถึงหลอดเลือดฟีโมรัล (cfPWV) เป็นดัชนีชี้วัดมาตรฐานของการประเมินสภาวะความแข็งของหลอดเลือดแดงส่วนกลาง อย่างไรก็ตามข้อมูลเกี่ยวกับค่า cfPWV ในประชากรไทยนั้นมีน้อยมาก ดังนั้นการศึกษานี้จึงมีวัตถุประสงค์เพื่อวัดค่าปกติของ cfPWV ในคนไทยที่มีสุขภาพดี

วิธีการศึกษา: อาสาสมัครสุขภาพดีที่เข้าร่วมในการศึกษานี้มีอายุระหว่าง 20 ถึง 60 ปี จำนวนทั้งหมด 163 ราย (เพศหญิง 82 ราย และชาย 81 ราย) อาสาสมัครแบ่งเป็น 4 กลุ่มตามช่วงอายุ ช่วงละ 10 ปี ทำการวัดความดันเลือดส่วนปลายและความดันเลือดส่วนกลาง รวมทั้ง cfPWV ด้วยวิธีไม่รุกรานโดยใช้เทคนิค applanation tonometry

ผลการศึกษา: ความดันเลือดซิสโทลิกและความดันชีพจรของหลอดเลือดแดงส่วนกลางมีค่าสูงขึ้นตามอายุ ค่าเฉลี่ย cfPWV ในกลุ่มชายและหญิงมีค่าเพิ่มขึ้นตามอายุ นอกจากนี้ยังพบว่า cfPWV มีความสัมพันธ์กับอายุและความดันเลือดของหลอดเลือดแดงส่วนกลาง

สรุป: การศึกษานี้ให้ข้อมูลเกี่ยวกับค่าปกติของ cfPWV ในอาสาสมัครสุขภาพดี ความดันเลือดปกติและไม่มีความผิดปกติทาง

Background and Objective: Central arterial stiffness is an independent predictor of cardiovascular morbidity and mortality. Carotid-femoral pulse wave velocity (cfPWV) is regarded as the gold standard marker of central arterial stiffening. However, there is limited information available on the values of cfPWV in Thai population. Therefore, the current study aimed to measure the normal values of cfPWV in healthy Thais.

Methods: A total of 163 identified healthy subjects (82 female, 81 male), aged 20-60 years were recruited in this study. The subjects were divided into 4 age groups with 10-year intervals. Blood pressures of peripheral and central arteries and cfPWV were measured non-invasively by using the applanation tonometry.

Results: The systolic blood pressure and pulse pressure of central artery increased progressively with age. The mean values of cfPWV in men and women were increased with age. Moreover, cfPWV was correlated with age and central blood pressure.

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เมแทบอลิก cfPWV มีค่าสูงขึ้นชัดเจนในคนไทยสุขภาพดีที่มีอายุมากกว่า 50 ปี

คำสำคัญ: ความแข็งของหลอดเลือดแดงส่วนกลาง, ความเร็วของคลื่นชีพจรจากหลอดเลือดแคโรติดถึงหลอดเลือดฟีโมรัล, คนไทย

Conclusion: The present study provides normal values of cfPWV in healthy, normotensive and non-metabolic disorder subjects. A pronounced increase in cfPWV was demonstrated in healthy Thais aged over 50 years.

Keywords: central arterial stiffness, carotid-femoral pulse wave velocity, Thai population.

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Introduction

Cardiovascular diseases (CVD) are a group of disorders of the heart and blood vessels, including coronary heart disease (CHD), stroke, congenital heart defects and peripheral artery disease. CVD continue to be the main cause of morbidity and mortality of the population worldwide, including Thais. CVD remain responsible for about one-third or more of all deaths in individuals over age 35[1]. According to the World Health Organization (WHO) data published in 2017, CHD deaths in Thailand reached 63,151 or 12.61% of total deaths[2], and CHD is the second cause of deaths among Thai population.

Aging of the cardiovascular system is the platform from which CVD are launched[3]. Based on the accumulated evidence, it is widely known that arterial wall thickening and dilation are the major structural changes that occur in the large elastic arteries during aging. With advanced age, the structure and function of the arterial wall are altered as a consequence of fracture of elastin and increased deposition of collagen fiber[4]. Stiffening of the conduit vessels is a result from loss of elasticity of the artery wall, reducing arterial storage capacity as well as increasing the speed of the propagating pulse along the arterial wall. That is, for a given ventricular stroke volume, arterial stiffness is a major determinant of pulse pressure due to the combined influence on the capacitive effects of the artery wall to absorb the pulsatile energy and the wave propagation effects that influence peripheral wave reflection. These factors form the underlying mechanisms of the gradual increase in systolic pressure with age, especially after the 5th decade[5], leading to the development of isolated systolic hypertension in the elderly and to an increased cardiovascular risk[6]. Therefore, increased systolic pressure, pulse pressure and arterial pulse wave velocity (PWV) are powerful independent predictors of cardiovascular morbidity and mortality[7]. Since arterial stiffness is a strong predictor of cardiovascular events and all-cause mortality in various populations, especially elderly[8], thus, early detection of arterial stiffness is recommended for decreasing the mortality rate of CVD.

The carotid-femoral PWV (cfPWV) is a gold standard for assessing large artery stiffening since it reflects vessel status predominantly in the central aorta and proximal elastic arteries[9]. Currently, cfPWV has received much attention as a marker for cardiovascular aging and a prognostic biomarker for CHD. Many studies reported the reference values of cfPWV in various ethnic groups from European origins and Asia (e.g. China, Japan and Korea). To our knowledge, there is limited information available on the values of central arterial stiffness in healthy Thais. Therefore, the purpose of this study is to assessing of central arterial stiffness by measuring of cfPWV in an apparently healthy Thai population.

Methods

Study population

This cross-sectional study was conducted on 163 subjects (82 female, 81 male) with age ranging from 20 to 60 years and divided into 4 groups with age including 21-30 years (19 female, 23 male), 31-40 years (20 female, 20 male), 41-50 years (22 female, 18 male), and 51-60 years (21 female, 20 male). All subjects are apparently healthy without present illness by physical examination and medical record from the Chest Unit of Srinagarind Hospital, Amphoe Mueang, Khon Kaen province, Thailand. A healthy subject was defined following the criteria provided by the modified NCEP ATP III criteria[10]: blood pressure (BP) < 130/85 mm/Hg, fasting glucose < 110 mg/dL, high-density lipoprotein cholesterol (HDL-C) > 40 mg/dL in men and >50 mg/dL in women, triglycerides < 150 mg/dL, and waist circumference < 90 cm in men and < 80 cm in

women, and no history of myocardial infarction, unstable angina, severe arrhythmias, pulmonary embolism, dissecting aneurism, severe aortic stenosis, stroke, renal insufficiency and pulmonary disease. The study protocol has been approved by the Khon Kaen University Ethics Committee for Human Research (HE591358). All subjects gave written informed consent before enrollment into the study.

Measurements

Age, gender, and smoking were self-reported. Height and weight was measured while participant was in a standing position wearing indoor clothes and no shoes. Body mass index (BMI) was calculated as weight (kg) divided by square of height (m^2). Waist circumference (cm) was taken with a tape measure as the point midway between the costal margin and iliac crest in the midaxillary line, with subject standing and breathing normally, and hip circumference (cm) was measured at the widest point around the greater trochanter. The venous blood sample was collected for clinical chemistry assay.

After physical examination by physician, the participant was asked to lie in supine position for at least 15 minutes in a quiet room with controlled temperature. The peripheral blood pressure is measured on the left upper arm for three times consecutively using Dinamap Carescape v100. The averaged values of the three blood pressure recordings are used.

The central arterial blood pressure and cfPWV were assessed non-invasively in all subjects by using SphygmoCor device (AtCor Medical, West Ryde, Australia). In brief, the radial waveform was recorded for 30 s by placing the probe on the left radial artery. The aortic (central) pressure wave was derived from the radial tonometric signal by a generalized transfer function available on the SphygmoCor system. The values of central blood pressure were obtained from the aortic pulse wave. The cfPWV was assessed by sequential recordings of the arterial pressure waveforms at the left carotid artery and left femoral artery. The distance between the two arterial sites was measured. Pulse transit time was the average of 10 consecutive beats. The cfPWV was calculated as the ratio of the distance in meters to the transit time in seconds.

Statistical Analysis

Results are presented as the mean + SD. All statistical analyses were performed using a standard software package (Stata version 13, Stata Corp., College Station, TX, USA). A two-way analysis of variance (ANOVA) was used to assess differences between men and women in different age intervals, and in case of a significant F test, Bonferroni' posthoc was used to find individual differences. Pearson correlation analysis was used to assess the relationship between variables. A value of $p < 0.05$ was considered statistically significant.

Results

The characteristic, anthropometric and blood chemistry of all subjects are shown in Table 1. The mean (SD) age was 40.6 (11.2) years. The weight, height, BMI, waist, hip circumference, blood glucose, and triglyceride in men were significantly higher than women, whereas HDL-cholesterol in women was significantly higher than men. The peripheral systolic and diastolic blood pressures were slightly higher in men than women. Although the anthropometrics, blood pressures and some of the blood chemistry levels were different between genders, the values were found to lie within normal range, suggesting that all of study subjects are apparently healthy.

Central and peripheral blood pressures of men and women are shown in Table 1. The peripheral systolic blood pressure (SBP), diastolic blood pressure (DBP), and central DBP were slightly higher in men than women (Table 1 & Figure 1). The pulse pressure (PP) of central and peripheral blood pressures was not different. Moreover, central SBP and PP increased progressively with age in all subjects, especially in women (Figure 2). The increase in central blood pressures was more prominent in subjects over 40 years (Figure 2)

Figure 3 displays the cfPWV values in all subjects. There was a progressive increase in cfPWV with age (5.5 m/s in 21-30 y, 5.8 m/s in 31-40 y, 6.2 m/s in 41-50 y, and 7.2 m/s in 51-60 y, Figure 3A), and this tendency is more pronounced after 50 years old in both men and women (Figure 3B & C). The univariate correlations revealed that age was highly correlated with cfPWV ($r = 0.553$, $p < 0.001$, Table 2). Moreover, central SBP, DBP and PP were also correlated with cfPWV ($p < 0.05$, Table 2).

Table 1 Characteristic, anthropometric, blood chemistry and peripheral blood pressure of all subjects.

Parameter	All (n = 163)	Men (n = 81)	Women (n = 82)	P-value
Anthropometric				
Age (years)	40.6±11.2	39.6±11.5	41.7±10.9	0.235
Weight (kg)	59.9±8.8	65.3±7.1	54.6±6.8	<0.001
Height (cm)	164.2±7.8	169.8±5.8	158.7±5.2	<0.001
BMI (kg/m^2)	21.9±1.8	22.5±1.7	21.3±1.7	<0.001
Waist (cm)	77.4±6.5	81.4±5.4	73.5±5.0	<0.001
Hip (cm)	82.6±6.9	87.0±5.7	78.4±5.2	<0.001
Blood chemistry				
Blood glucose (mg/dL)	88.8±7.0	90.5±7.1	87.0±6.5	0.001
Total cholesterol (mg/dL)	175.1±23.2	176.8±21.5	173.4±24.8	0.360
Triglyceride (mg/dL)	93.5±32.8	100.0±31.3	87.2±33.3	0.012
HDL-cholesterol (mg/dL)	62.5±15.1	58.9±14.1	66.1±15.2	0.002
LDL-cholesterol (mg/dL)	123.8±22.5	125.4±22.2	122.2±22.8	0.375
Central blood pressure				
SBP (mmHg)	108.2±8.8	108.5±8.5	107.9±9.1	0.662
DBP (mmHg)	73.9±8.3	75.8±8.8	72.2±7.4	0.005
PP (mmHg)	34.1±8.6	32.8±7.6	35.4±9.4	0.051
Peripheral blood pressure				
SBP (mmHg)	118.4±9.2	120.7±8.7	116.2±9.1	0.001
DBP (mmHg)	72.9±8.2	74.7±8.6	71.1±7.5	0.004
PP (mmHg)	45.5±9.5	46.0±8.8	45.0±10.2	0.530

Data are presented as mean ± SD. P values indicate significant differences between men and women. BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

Discussion

The measurement of cfPWV is a well-known method for the quantification non-invasive arterial stiffness and currently considered as the gold standard marker of arterial stiffness due to its simplicity, accuracy, reproducibility, and predictive value[11]. Therefore, cfPWV is a highly reliable prognostic parameter for cardiovascular morbidity and mortality. The expert consensus advises the use of 10 m/s as a new cut-off value for cfPWV[12]. This value of cfPWV is an indicative of large artery stiffening and a predictive of atherosclerosis or future cardiovascular events.

In this study, we demonstrated the normal values of cfPWV in healthy Thais, aged between 20-60 years. The mean values of cfPWV rise progressively with increasing age. These findings are consistent with previous studies in different ethnic groups, such as argentinean[11], south african[13] and korean[14].

Large arteries become stiffer with age due to alterations in their morphology and the composition of their major structural proteins, elastin and collagen[15]. cfPWV was correlated with age and central

Table 2 The univariate correlations among age, cfPWV, central SBP, central DBP, and central PP in all subjects.

	Age	cfPWV	Central SBP	Central DBP	Central PP
Age	1.000				
cfPWV	0.553*	1.000			
Central SBP	0.423	0.436*	1.000		
Central DBP	0.040*	0.256*	0.472*	1.000	
Central PP	0.378*	0.191*	0.539*	-0.467*	1.000

Data are presented as correlation (r). *p < 0.05; cfPWV, carotid-femoral pulse wave velocity; SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

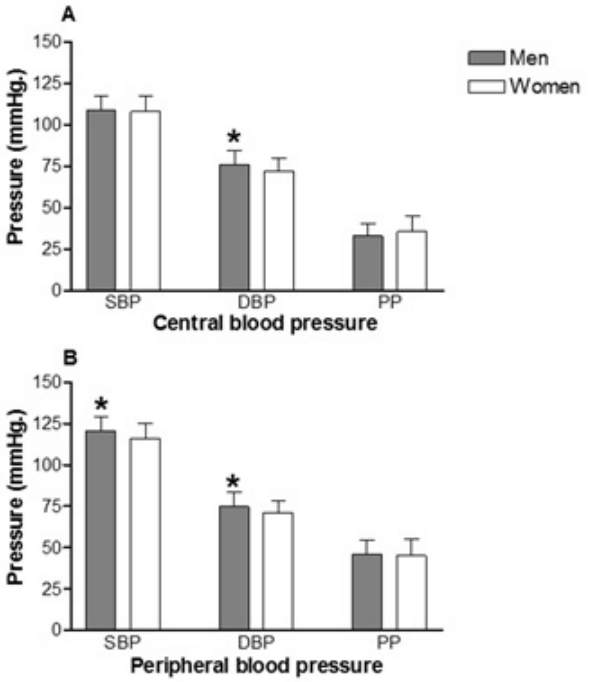

Figure 1 Central (A) and peripheral (B) blood pressures in all subjects. Each bar represents the mean ± SD. *p < 0.05 compared between men and women. SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

blood pressure. The central blood pressure was also increased with age. It has been suggested that blood pressure elevation directly affects remodeling of blood vessels by increasing medial stress and hypertrophy, which leads to arterial stiffening. On the other hand, arterial stiffness may be a preexisting condition that contributes to the development of high blood pressure[16].

Conclusion

The normal values of cfPWV in healthy Thais are correlated with age and central blood pressure. The reference values of cfPWV may be beneficial for primary health care interventions and facilitating the screening of patients with risk of CVD. Further investigation of arterial stiffness is required in the larger population.

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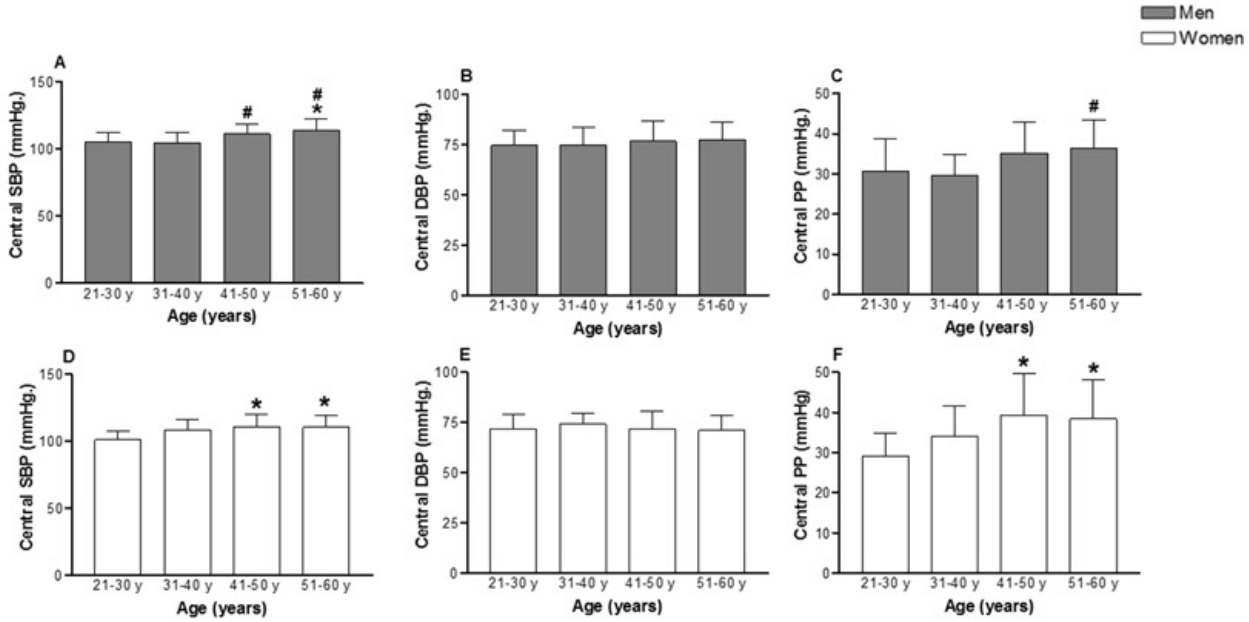

Figure 2 Central blood pressures in men (A, B, C) and women (D, E, F) subjects according to the decade of age. Each bar represents the mean ± SD. *p < 0.05 compared with 21-30 years. #p < 0.05 compared with 31-40 years. SBP, systolic blood pressure; DBP, diastolic blood pressure; PP, pulse pressure.

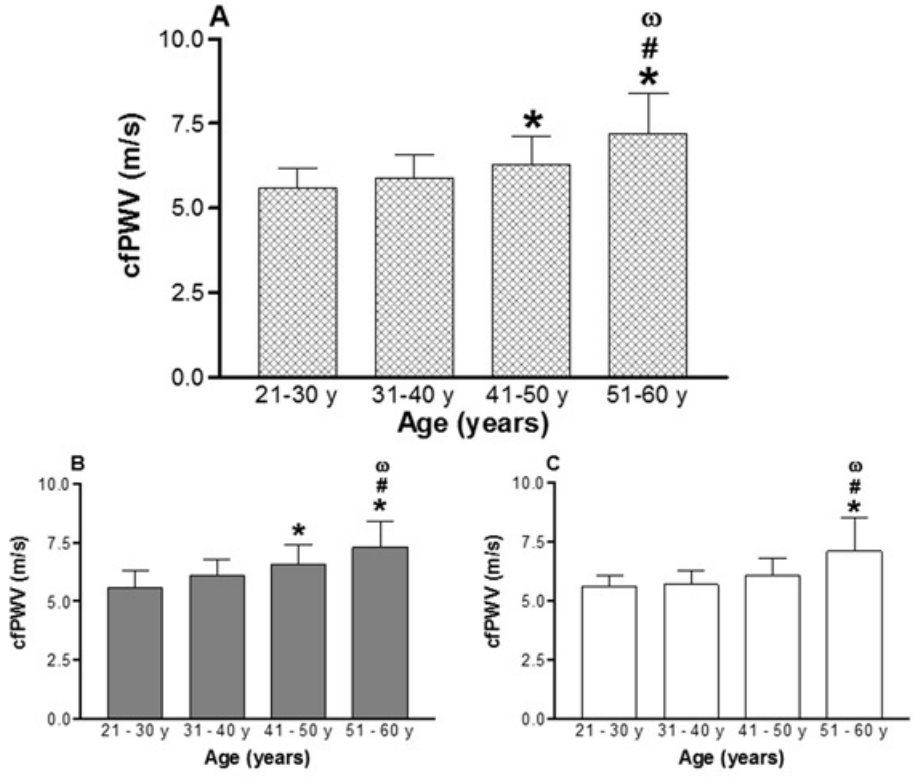

Figure 3 Distribution of cfPWV in all subjects (A), men (B), and women (C) according to the decade of age. Each bar represents the mean ± SD. *p < 0.05 compared with 21-30 years, #p < 0.05 compared with 31-40 years, and $^{\omega}$p < 0.05 compared with 41-50 years. cfPWV, carotid-femoral pulse wave velocity.

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