Reference Values for Augmentation Index and Brachial-Ankle Pulse Wave Velocity in Healthy Thai Subjects

ค่าอ้างอิงสำหรับดัชนีการสูงขึ้นของคลื่นความดันเลือดแดงและความเร็วของคลื่นความดันเลือดแดงในอาสาสมัครไทยสุขภาพดี

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ABSTRACT

Arterial walls are stiffening with age. Arterial stiffness is a novel marker for initiation and/or progression of cardiovascular disease (CVD). Currently, the non-invasive methods used for assessment of arterial stiffness are augmentation index (AI) and pulse wave velocity (PWV). A total of 80 identified healthy Thai subjects; aged 30-60 years (40 men, 40 women) were recruited in this study. Using applanation tonometry, AI and brachial-ankle PWV (baPWV) were assessed. Results of this study showed that baPWV and AI adjusted at heart rate 75 beats/min (AI@HR75) values increased with advancing age in all subjects(P < 0.005). AI and AI@HR75 were significantly higher in women than men (23.5 ± 8.1 vs. 17.6 ± 9.0%, P < 0.05), whereas baPWV was significantly higher in men than women (11.5 vs. 10.4 m/s, P< 0.05). In conclusion, data of the reference values of arterial stiffness in Thai healthy population will be beneficial to public health surveillance as it is a powerful predictor of CVD.

บทคัดย่อ

หลอดเลือดแดงจะแข็งยิ่งขึ้นเมื่ออายุมากขึ้น ภาวะหลอดเลือดแดงแข็งเป็นตัวชี้วัดที่สำคัญที่บ่งชี้ถึงการเริ่มต้นและ/หรือการดำเนินของโรคหัวใจและหลอดเลือด ปัจจุบันการประเมินสภาวะหลอดเลือดแบบไม่รุกรานคือ การวัดดัชนีการสูงขึ้นของคลื่นความดันเลือดแดง (AI) และความเร็วของคลื่นความดันเลือดแดง (PWV) การศึกษานี้ทำการศึกษาในอาสาสมัครสุขภาพดีจำนวน 80 คน อายุระหว่าง 30-60 ปี (ชาย 40 คน, หญิง 40 คน) ทำการวัด AI และ baPWV โดยใช้เทคนิค applanation tonometry ผลการศึกษาพบว่าค่า baPWV, AI และ AI ที่ปรับค่าที่อัตราเต้นหัวใจ 75 ครั้ง/นาที (AI@HR75) มีค่าเพิ่มขึ้นตามอายุ ผู้หญิงมีค่า AI และ AI@HR75 สูงกว่าผู้ชายอย่างมีนัยสำคัญ(23.5 ± 8.1 vs. 17.6 ± 9.0% ตามลำดับ, P < 0.05) ในขณะที่ผู้ชายมีค่า baPWV สูงกว่าผู้หญิงอย่างมีนัยสำคัญ (11.5 vs. 10.4 m/s, P< 0.05). โดยสรุปข้อมูลค่าอ้างอิงเพื่อประเมินสภาวะหลอดเลือดแดงแข็งในประชากรไทยที่มีสุขภาพดีจะเป็นประโยชน์ต่อการให้บริการทางด้านสาธารณสุข ต่อการพยากรณ์โรคหลอดเลือดและหัวใจ

Key Words: Arterial stiffness, Pulse wave velocity, Augmentation index

คำสำคัญ: สภาวะหลอดเลือดแดงแข็ง ความเร็วของคลื่นความดันเลือดแดง ดัชนีการสูงขึ้นของคลื่นความดันเลือดแดง

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Introduction

Arterial stiffness is increased when elastic properties of the arterial wall are reduced. Arterial stiffness is the gold standard marker for initiation and/ or progression of cardiovascular disease (CVD) (Sugawara et al., 2005). Increasing arterial stiffness is closely associated with cardiovascular risk factors that induce dysregulation of the balance between collagen and elastin, resulting in overproduction of abnormal collagens and decreased production of normal elastin (Tomiyama and Yamashina, 2010). These alterations lead to increased pulse wave velocity (PWV), especially central elastic arteries, and increase in systolic blood pressure (SBP) and pulse pressure (PP) resulting to promote cardiac hypertrophy and myocardial ischemia (Meaume et al., 2001).

Numerous non-invasive methods are currently used to diagnose and evaluate distensibility of artery and to assess arterial stiffness. Measurement of arterial stiffness have been recommended in the risk stratification for CVD (Ai et al., 2011). The two major non-invasive methods used for assessing arterial stiffness are PWV and augmentation index (AI) (Shim, 2011).

Currently, the reference values of arterial stiffness in various nationalities have been reported, such as groups of European origins and Asia (e.g. Japan, China and Korea). To our knowledge, there is very limited information about arterial stiffness in Thai population. A recent study by our group has evaluated the arterial stiffness in elderly Thais (Khontong et al., 2012). Further investigation of arterial stiffness in Thai population with widen age ranges is required, which is the objective of this study.

Objectives of the study

To assess the arterial stiffness in middle-aged healthy Thais and to determine the relationship between arterial stiffness and age in healthy Thais.

Methodology

Study population

A total of 80 consecutive subjects ranging in middle aged healthy Thai (age range 30 to 60 years). All subjects are northeastern Thais who reside in the northeast of Thailand. Subjects are apparently healthy without present illness as indicated from the reports of their Health Stations. A "healthy subject" was defined followed the NCEP ATP III criteria: blood pressure (BP) <130/85 mmHg, fasting glucose <110 md/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 (Ma et al., 2009). Personal and family history, lifestyle habits, previous and present illness and use of medications were assessed using standardized questionnaire.

This study was approved by the Khon Kaen University Ethics Committee for Human Research (No. HE531391 and HE531392). All participants gave written consent before enrollment into the study.

Measurements of arterial stiffness

The arterial stiffness was evaluated by using SphygmoCor device (AtCor Medical, West Ryde, Australia). After resting in the supine position for 15 minutes, radial pulse wave was measured by using a hand held probe placed on the radial artery and 10–15 subsequent images were recorded (Virdis et al., 2012). Radial pressure waveform is transformed into aortic pressure waveform by pulse wave analysis using a validated transfer function. Three successive measurements were recorded. The AI was the difference between the second and the first systolic peak given as a percentage of the aortic pulse pressure. Peripheral and central pulse pressures were defined as the difference between systolic and diastolic BP derived from the brachial BP (Virdis et al., 2012). AI values have been normalized at a heart rate of 75 beats/min and expressed as AI@HR75. The PWV has assessed with the same device by recording waveforms at the brachial and ankle sites sequentially. The system uses a tonometer and ECG leads connected to an electronics module. The subject's peripheral artery pressure wave and ECG waveform were recorded. From these measurements, the SphygmoCor software is able to estimate PWV between the brachial and ankle sites (baPWV). Simultaneously recorded ECG is used to calculate wave transit time. The distance traveled by the pulse wave is measured over the body surface and the baPWV is then calculated as distance/time (m/s) (Khontong et al., 2012).

Laboratory measurements

On the next day, fasting blood samples about 8 mL were collected for routine hematological and biochemical assays at Srinagarind Hospital, including CBC, fasting blood sugar, uric acid, lipid profiles, liver and kidney function tests.

Statistical analysis

Results are present as the mean ± S.D. Comparison between the two groups are used Student unpaired t-test or chi square test. Pearson correlation analysis was used to assess the relationship between variables. P value less than 0.05 was considered significant.

Results

Clinical characteristics

This study was comprised of 80 participants (40 males and 40 females). Subjects with age between 30-39, 40-49, and 50-59 years are defined as group I, II and II, respectively. The clinical characteristics of all subjects are shown in Table 1. There was no difference in age, BMI, blood glucose, total cholesterol and LDL-cholesterol levels between men and women. In contrast, male subjects had a higher body weight and triglyceride levels (P <0.05). The HDL-C was significantly higher in female subjects compared with male subjects (P<0.001). The clinical characteristics of all subjects according to the decade of age are shown in Table 3, the level of FBG and TG were significantly higher in age range 40-49 years (P < 0.05). However, all significant values are within normal ranges.

Table 1 Characteristics, anthropometric and the blood biochemistry profiles of all subjects.

Parameters	Men (n= 40)	Women (n= 40)	P value
Anthropometric measurements			
Age (years)	47.7 ± 7.9	46.4 ± 7.7	0.466
Body weight (kg)	63.3 ± 10.4	55.4 ± 7.5	<0.001
BMI (kg/m^2)	22.8 ± 3.1	22.8 ± 2.9	0.954
Biochemical measurements			
FBG (mg/dL)	85.7 ± 9.5	82.4 ± 7.0	0.079
TC (mg/dL)	203.4 ± 48.9	196.8 ± 31.4	0.842
LDL-C (mg/dL)	132.9 ± 42.4	122.6 ± 31.5	0.222
HDL-C mg/dL)	48.0 ± 13.9	58.8 ± 13.5	<0.001
TG (mg/dL)	128.1 ± 55.5	102.1 ± 39.8	0.033

All data are presented as mean ± SD. BMI, Body mass index; FBG, Fasting blood glucose; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TG, Triglyceride.

Table 2 Central and peripheral arterial pressures and augmentation index of the participants.

Parameter	Men (n= 40)	Women (n= 40)	P value
Central arterial measurements			
SBP (mmHg)	105.6 ± 11.3	99.6 ± 10.6	0.016
DBP (mmHg)	70.9 ± 9.1	63.7 ± 8.2	<0.001
MAP (mmHg)	82.4 ± 9.3	75.7 ± 8.4	0.001
PP (mmHg)	34.8 ± 6.7	35.9 ± 7.5	0.479
HR (beats/min)	66.6 ± 12.8	66.3 ± 8.4	0.519
AP (mmHg)	7.8 ± 4.2	10.3 ± 4.6	0.014
AI(%)	21.6 ± 8.2	27.6 ± 8.2	0.002
AI@HR75 (%)	17.6 ± 9.0	23.5 ± 8.1	0.003
baPWV (m/s)	11.5 ± 1.6	10.4 ± 2.0	0.005
Peripheral arterial measurements			
SBP (mmHg)	116.4 ± 10.6	108.1 ± 11.0	<0.001
DBP (mmHg)	69.8 ± 9.1	62.8 ± 8.2	<0.001
MAP (mmHg)	85.4 ± 8.9	77.9 ± 8.4	<0.001
PP (mmHg)	46.6 ± 7.6	45.3 ± 8.1	0.453
AI (%)	77.6 ± 13.4	81.6 ± 11.7	0.163

All data are presented as mean ± S.D. SBP, Systolic pressure; DBP, Diastolic pressure; MAP, Mean arterial pressure; PP, Pulse pressure; HR, Heart rate; AP, Augmentation pressure; AI, Augmentation index; AI@75, Augmentation index at a heart rate of 75 beats/min; baPWV, Brachial ankle pulse wave velocity.

Distribution of the arterial measurements

In both sex participants, there was no significant difference in pulse pressure and heart rate obtained from central arterial measurements, and pulse pressure and AI obtained from peripheral arterial measurements. Central and peripheral systolic, diastolic, mean arterial pressure and baPWV were significantly higher in male than female subjects (P < 0.05). Data distribution of the arterial measurements according to the decade of age show that DBP and MAP obtained from central arterial measurements were no significant difference among age groups. However, those values are within normal ranges. The female subjects had greater mean values of central augmentation pressure (AP), AI and AI@75 than male subjects (P < 0.05) in Table 2. In addition PP, AP, AI, AI@75 and baPWV were significantly higher in older subjects when divided according to the decade of age (P < 0.005, Table 4)

AI@75 was correlated with age in both male (R = 0.310, p = 0.05, in Fig. 1) and female subjects (R = 0.417, p < 0.05, in Fig. 2). In addition, baPWV was significantly correlated with age in both male (R = 0.346, p < 0.05, in Fig. 3) and female subjects (R = 0.563, p < 0.05, in Fig. 4).

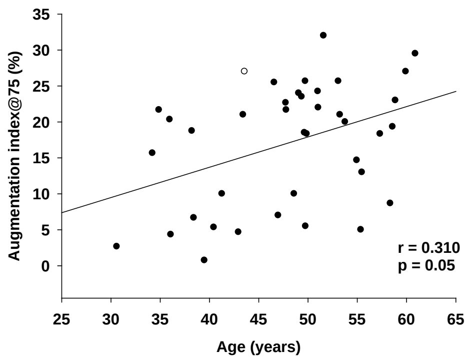

Figure 1 Relationship between augmentation pressure and age in male subjects.

Table 3 Characteristics, anthropometric and the blood biochemistry profiles of the participants according to the decade of age

Parameter	Group I (n= 21)	Group II (n= 31)	Group III (n= 28)	P value
Anthropometric measurements				
Age (years)	37.0 ± 2.3	46.2 ± 3.2#	55.5 ± 3.1*†	<0.001
Height (cm)	161.9 ± 7.1	161.3 ± 7.8	160.6± 8.1	0.841
BMI (kg/m^2)	21.8 ± 3.3	23.2 ± 3.1	23.0 ± 2.5	0.226
Waist (cm)	75.5 ± 10.0	79.6 ± 7.9	82.5 ± 7.4†	0.018
Biochemical measurements				
FBG (mg/dL)	79.6 ± 8.1	85.6 ± 6.8#	85.4 ± 9.5	0.025
TC (mg/dL)	180.8 ± 39.8	205.3 ± 40.6	207.3 ± 39.5	0.054
LDL-C (mg/dL)	56.3± 16.3	50.2 ± 11.9	55.1 ± 16.2	0.134
HDL-C mg/dL)	108.1 ± 34.8	132.3 ± 38.1	135.8 ± 35.1	0.025
TG (mg/dL)	101.4 ± 39.8	127.7 ± 40.2#	111.3 ± 42.0	0.016

All data are presented as mean ± S.D. #significant between group I and II, * significant between group I and III, †significant between group II and III, BMI, Body mass index; FBG, Fasting blood glucose; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; TG, Triglyceride.

Table 4 Central and peripheral arterial pressures and augmentation index of the participants according to the decade of age

Parameter	**Group I** (**n= 21)**	**Group II** (**n= 31)**	**Group III** (**n= 28)**	**P value**
Central arterial measurements				
Systolic pressure (mmHg)	92.1± 9.7	103.9 ± 11.5#	105.4 ± 11.2*	0.029
Diastolic pressure (mmHg)	63.7 ± 7.9	70.3 ± 9.7#	66.7 ± 9.3	0.045
Mean arterial pressure (mmHg)	74.9 ± 8.2	81.5 ± 9.8#	79.6 ± 9.3	0.045
Pulse pressure (mmHg)	33.4 ± 4.9	33.6 ± 7.1	38.7 ± 7.6*†	0.008
Heart rate (beats/min)	65.5 ± 11.3	68.5 ± 11.1	64.7 ± 10.1	0.347
Augmentation pressure (mmHg)	7.0 ± 3.3	8.5 ± 4.7	11.2 ± 4.6*†	<0.001
Augmentation index (%)	20.5 ± 8.4	24.2 ± 8.9	28.1 ± 7.6*†	<0.001
Augmentation index@HR75 (%)	16.0 ± 8.4	21.1 ± 10.4	23.3 ± 6.6*	0.004
baPWV (m/s)	10.0 ± 1.5	10.4 ± 1.7	12.1 ± 1.9*†	<0.001
Peripheral arterial measurements				
SBP (mmHg)	108.5 ± 10.0	113.4 ± 12.7	113.8 ± 11.3	0.232
DBP (mmHg)	62.7 ± 5.4	69.2 ± 9.7#	65.8 ± 9.3	0.029
MAP (mmHg)	75.7 ± 7.7	84.0 ± 10.0	81.8 ± 9.3	0.087
PP (mmHg)	45.8 ± 6.3	44.2 ± 8.5	48.0 ± 8.1	0.181
AI (%)	72.8 ± 10.9	81.5 ± 14.7#	82.9 ± 10.0†	0.012

All data are presented as mean ± S.D. #significant between group I and II, * significant between group I and III, †significant between group II and III, Systolic pressure; DBP, Diastolic pressure; MAP, Mean arterial pressure; PP, Pulse pressure; HR, Heart rate; AP, Augmentation pressure; AI, Augmentation index; AI@75, Augmentation index at heart rate of 75 beats/min; baPWV, Brachial ankle pulse wave velocity.

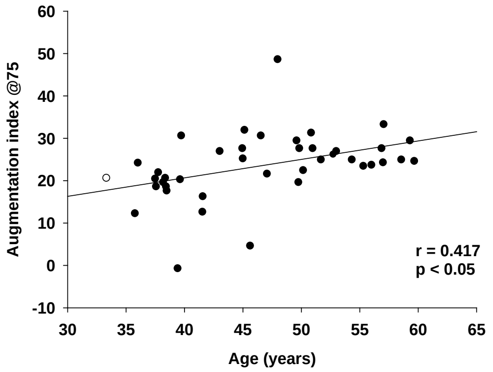

Figure 2 Relationship between augmentation pressure and age in female subjects.

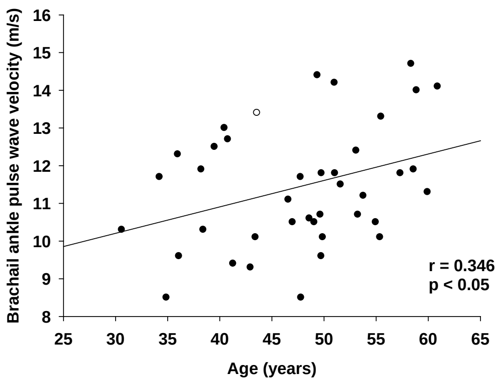

Figure 3 Relationship between brachial ankle pulse wave velocity and age in male subjects.

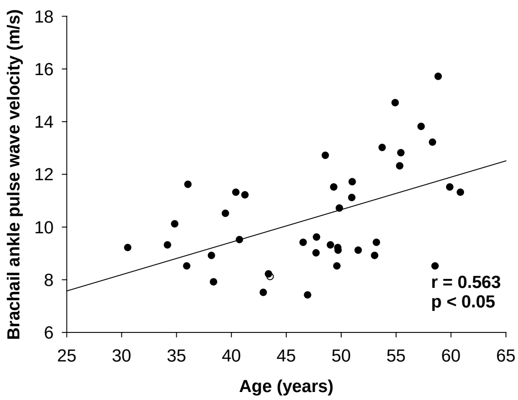

Figure 4 Relationship between brachial ankle pulse wave velocity and age in female subjects

Discussion and Conclusions

Changes in arterial structure and function are major determinants for clinical cardiovascular event. Arterial stiffness assessment has been recommended for CVD risk stratification. The reference values of baPWV can be used as marker for arterial elasticity. Numerous studies concluded that vascular stiffness increases with advancing age, young women have lower PWV values than men (Wang et al., 2009). In this study, baPWV, PP, AP, and AI adjusted at heart rate 75 beats/min (AI@HR75) values increased with advancing age ($P < 0.005$). Central AI and AI@HR75 were significantly higher in women than men (23.5 ± 8.1 vs. 17.6 ± 9.0%, $P < 0.05$), whereas baPWV was significantly higher in men than women (11.5 vs. 10.4 m/s, $P < 0.05$). In agreement with previous studies, our group has evaluated the arterial stiffness in elderly Thais (age range 70-79), the results showed that arterial stiffness increases with age, male had higher baPWV values than female subjects (~12 vs. 11 m/s), whereas AI@HR75 was significantly higher in women than men (26.4 vs. 20.1, $P < 0.05$) (Khontong et al., 2012). Some studies demonstrated that estrogen has beneficial effect on arterial stiffness. It is possible that the influence of age on the artery may be different in males and females during different periods with the varied levels of estrogen and androgen. (Tomiyama et al., 2003).

AP, AI and AI@75 were higher in female than male subjects. Previous study suggested that the shorter height in females might cause the arterial wave reflections occurred earlier where the distance from the heart to reflection point is shorter (McGrath et al., 2001).

Ageing is one of the major influential factors for arterial stiffness. We observed that the AI@75 and baPWV of both males and females were positively correlated with age. With aging, structural of arterial wall changes as a consequence of fractures of the elastic lamina, increase in collagen fiber, focal media smooth muscle cell necrosis and calcification. These changes may decrease timing of forward and backward pulse wave and the consequent increase central SBP leading to target organ damage (Laurent, 2012).

In conclusions, this study is reported for the first time that baPWV was higher in males, whereas AP, AI and AI@75 were higher in female healthy Thais. The baPWV and AI@75 of both males and females were positively correlated with age. However, further investigation of arterial stiffness is needed in large population. Information about arterial stiffness in healthy Thais will be beneficial for prevention of atherosclerosis and in facilitating primary screening of potential CVD patients.

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