

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

## ค่าอ้างอิงสำหรับดัชนีการสูงขึ้นของคลื่นความดันเลือดแดงและความเร็วของคลื่นความดันเลือดแดง ในอาสาสมัครไทยสุขภาพดี

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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) increased with age. AI and AI@HR75 were significantly higher in women than men, whereas baPWV was significantly higher in men than women ( $P < 0.05$ ). 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 ภาวะหลอดเลือดแดงแข็งเป็นตัวชี้วัดที่สำคัญที่บ่งชี้ถึงการเริ่มต้น และ/หรือการดำเนินของโรคหัวใจและหลอดเลือด ปัจจุบันวิธีการแบบไม่รุกรานที่ใช้ในการประเมินสภาวะหลอดเลือดคือ การวัดดัชนีการสูงขึ้นของคลื่นความดันเลือดแดง (AI) และความเร็วของคลื่นความดันเลือดแดง (PWV) การศึกษานี้ทำการศึกษาในอาสาสมัครสุขภาพดีจำนวน 80 คน อายุระหว่าง 30–60 ปี

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(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 ในขณะที่ผู้ชายมีค่า baPWV สูงกว่าผู้หญิงอย่างมีนัยสำคัญ ( $P<0.05$ ) โดยสรุปข้อมูลค่าอ้างอิงเพื่อประเมินสภาวะหลอดเลือดแดงแข็งในประชากรไทยที่มีสุขภาพดีจะเป็นประโยชน์ต่อการบริหารจัดการด้านสาธารณสุข โดยเป็นดัชนีสำคัญต่อการพยากรณ์โรคหลอดเลือดและหัวใจ

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

**คำสำคัญ :** สภาวะหลอดเลือดแดงแข็ง, ความเร็วของคลื่นความดันเลือดแดง, ดัชนีการสูงขึ้นของคลื่นความดันเลือดแดง

## 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) [1]. 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 [2]. 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 [3].

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 [4]. The two major non-invasive methods used for assessing arterial stiffness are PWV and augmentation index (AI) [5].

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 [6]. 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

The aim of this study is 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 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 [7]. 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 [8]. 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 [8]. 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) [9].

### 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 III, 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.

### 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 measure-

ments 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).

## 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 [10]. 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 ( $23.5 \pm 8.1$  vs.  $17.6 \pm 9.0\%$ ,  $P < 0.05$ ), 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,  $P < 0.05$ ) [9]. 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. [11].

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 [12].

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 [13].

In conclusions, this study reported that aging is the most important influencing factor of arterial stiffness and is reported for the first time that AI and baPWV in

middle-aged Thais. 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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**Table 1** Characteristics, anthropometric and the blood biochemistry profiles of all subjects.

| Parameters                         | Men<br>(n= 40) | Women<br>(n= 40) | P value |
|------------------------------------|----------------|------------------|---------|
| <b>Anthropometric measurements</b> |                |                  |         |
| 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 <sup>2</sup> )           | 22.8 ± 3.1     | 22.8 ± 2.9       | 0.954   |
| <b>Biochemical measurements</b>    |                |                  |         |
| 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<br>(n= 40) | Women<br>(n= 40) | P value |
|---|----------------|------------------|---------|
| <b>Central arterial measurements</b>    |                |                  |         |
| 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   |
| <b>Peripheral arterial measurements</b> |                |                  |         |
| 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.



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

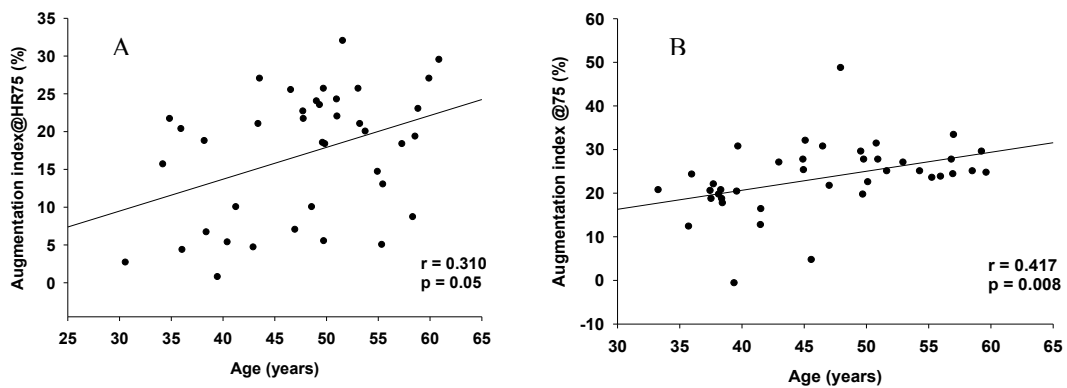
| Parameter                          | Group I<br>(n= 21) | Group II<br>(n= 31)       | Group III<br>(n= 28)     | P value |
|------------------------------------|--------------------|---------------------------|--------------------------|---------|
| <b>Anthropometric measurements</b> |                    |                           |                          |         |
| Age (years)                        | 37.0 ± 2.3         | 46.2 ± 3.2 <sup>#</sup>   | 55.5 ± 3.1 <sup>*†</sup> | <0.001  |
| Height (cm)                        | 161.9 ± 7.1        | 161.3 ± 7.8               | 160.6 ± 8.1              | 0.841   |
| BMI (kg/m <sup>2</sup> )           | 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 <sup>†</sup>  | 0.018   |
| <b>Biochemical measurements</b>    |                    |                           |                          |         |
| FBG (mg/dL)                        | 79.6 ± 8.1         | 85.6 ± 6.8 <sup>#</sup>   | 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 <sup>#</sup> | 111.3 ± 42.0             | 0.016   |

All data are presented as mean ± S.D. <sup>#</sup> significant between group I and II, \* significant between group I and III, <sup>†</sup> 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.

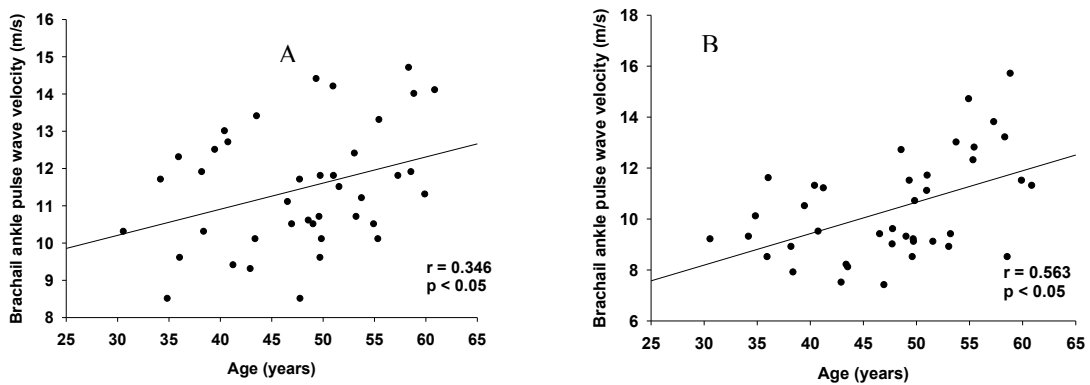
**Table 4** Central and peripheral arterial pressures and augmentation index of the participants according to the decade of age.

| Parameter                               | Group I<br>(n= 21) | Group II<br>(n= 31)       | Group III<br>(n= 28)      | P value |
|---|--------------------|---------------------------|---------------------------|---------|
| <b>Central arterial measurements</b>    |                    |                           |                           |         |
| Systolic pressure (mmHg)                | 92.1± 9.7          | 103.9 ± 11.5 <sup>#</sup> | 105.4 ± 11.2 <sup>*</sup> | 0.029   |
| Diastolic pressure (mmHg)               | 63.7 ± 7.9         | 70.3 ± 9.7 <sup>#</sup>   | 66.7 ± 9.3                | 0.045   |
| Mean arterial pressure (mmHg)           | 74.9 ± 8.2         | 81.5 ± 9.8 <sup>#</sup>   | 79.6 ± 9.3                | 0.045   |
| Pulse pressure (mmHg)                   | 33.4 ± 4.9         | 33.6 ± 7.1                | 38.7 ± 7.6 <sup>*†</sup>  | 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 <sup>*†</sup>  | <0.001  |
| Augmentation index (%)                  | 20.5 ± 8.4         | 24.2 ± 8.9                | 28.1 ± 7.6 <sup>*†</sup>  | <0.001  |
| Augmentation index@HR75 (%)             | 16.0 ± 8.4         | 21.1 ± 10.4               | 23.3 ± 6.6 <sup>*</sup>   | 0.004   |
| baPWV (m/s)                             | 10.0 ± 1.5         | 10.4 ± 1.7                | 12.1 ± 1.9 <sup>*†</sup>  | <0.001  |
| <b>Peripheral arterial measurements</b> |                    |                           |                           |         |
| 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 <sup>#</sup>   | 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 <sup>#</sup>  | 82.9 ± 10.0 <sup>†</sup>  | 0.012   |

All data are presented as mean ± S.D. <sup>#</sup>significant between group I and II, <sup>\*</sup> significant between group I and III, <sup>†</sup>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.



**Figure1** Relationship between augmentation index@HR75 and age in male (A) and female (B) subjects.



**Figure 2** Relationship between brachial ankle pulse wave velocity and age in male (A) and female (B) subjects