ORIGINAL ARTICLE

Reference pulse wave velocity values in a healthy, normotensive Turkish population

Sağlıklı Türk popülasyonunda nabız dalga hızının normal aralıkları

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ABSTRACT

Objective: Pulse wave velocity (PWV) is the primary determiner of arterial stiffness. In daily practice, the normal range of arterial stiffness is based on large multi-center studies conducted in the USA, Europe, Asia, and Australia. The goal of this study was to identify the reference values of brachial PWV in a healthy, normotensive Turkish population with no cardiovascular risk factors.

Methods: This retrospective study involved healthy, adult Turkish participants from Ankara. A total of 353 consecutive, normotensive individuals were enrolled in the study between September 2017 and January 2018 according to strict inclusion criteria, Normal PWV and 95% confidence interval values were acquired for 353 patients (mean age: 55.03±15.38 years; range: 20–95 years) who were divided into 6 age groups.

Results: The mean PWV was 7.75±1.89 m/s (range: 4.25–15.90 m/s). The PWV had a positive linear correlation with age (r^2=0.94; p=0.00). The PWV increased gradually by an average of 5% to 9% with each decade of life until the age of 50 years, after which the average PWV increased by 16%.

Conclusion: To the best of our knowledge, this study is the first to define PWV reference values via brachial measurement in a healthy, normotensive Turkish population. These data provide important information for daily clinical practice in Turkey.

ÖZET

Amaç: Nabız dalga hızı (PWV) atardamar sertliğinin iyi bilinen öngördürücülerindendir. Günlük pratiğimizde kullandığımız PWV'nin normal aralıkları Amerika, Avrupa, Asya ve Avustralya'da yapılan çok merkezli çalışmalardan elde edilmiştir. Bu çalışmanın amacı kardiyovasküler risk faktörü taşımayan sağlıklı Türk popülasyonunda PWV'nin normal aralıklarını saptamaktır.

Yöntemler: Çalışma sağlıklı Türk katılımcılarda geriye dönük olarak dizayn edildi. Çalışmaya Eylül 2017 ve Ocak 2018 yılları arasında 353 normotansif sağlıklı katılımcı dahil edildi. Hastalar yaşlarına göre altı gruba ayrılarak PWV'nin normal aralıkları tespit edildi.

Bulgular: Ortalama PWV 7.75 m/s ±1.89 (dağılım: 4.25–15.90) olarak bulundu. PWV artış hızı yaş ve yaş grupları ile pozitif korelasyon göstermektedir (r^2=0.94; p=0.00). Türk toplumunda PWV her on yıllık artış hızı %5–9 arasında değişirken bu oran elli yaş ve üzerinde %16 olarak tespit edilmiştir.

Sonuç: Bildiğimiz kadarı ile literatürdeki sağlıklı Türk popülasyonunda brakiyal yolla PWV'nin normal aralıklarının tespit edildiği ilk çalışmadır. Çalışmamızda yaşa göre PWV'nin normal aralıkları tanımlanmıştır. Bu çalışma günlük klinik pratikte kullanmamız için önemli veriler sağlamaktadır.

Arterial stiffness, which is an index of vascular aging, has been shown to be an independent predictor for the development of cardiovascular (CV) diseases.[1–4] Pulse wave velocity (PWV) is considered the main determiner of arterial stiffness. Pulse wave analysis, central aortic pressure, and the augmentation index (AIx) may also provide extra information for risk stratification and evaluation of the effectiveness of treatment.[5] A large number of epidemiological studies have verified that measurement of the carotid to femoral PWV is the gold standard for arterial stiffness assessment.[3,6] PWV can also be calculated in other

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arterial pathways, such as the heart–brachial, heart–carotid, and femoral–ankle segments. In recent years, the brachial–ankle PWV has been widely used in Asian countries.[7] Many devices have been developed to measure arterial stiffness using the brachial pathway and 24-hour aortic and brachial systolic blood pressure (BP). Devices that measure brachial PWV may be more useful than those that determine aortic PWV (carotid-femoral arteries) due to easy use and the high reproducibility of the brachial PWV in routine daily clinical practice. However, more studies and data are needed. PWV reference values have, thus far, most often been obtained from multi-center registries in the USA,[8] Europe,[9] Asia,[10] and Australia.[11]

Despite the great significance of PWV in clinical practice, there are currently no brachial PWV reference values for a healthy, normotensive Turkish population. The goals of this study were not only to define the reference values of brachial PWV in a healthy, normotensive Turkish population with no CV risk factors, but also to determine the relationship and proportional change of brachial PWV with aging.

METHODS

Study population

This retrospective survey included 353 consecutive, healthy, normotensive, adult Turkish participants enrolled between September 2017 and January 2018 according to the following inclusion criteria: 1) office BP <140/90 mm Hg or 24-hour ambulatory BP <130/80 mm Hg (based on the European Society of Cardiology guidelines), and 2) no use of antihypertensive drugs or a history of hypertension. The exclusion criteria were defined as the presence of diabetes (fasting blood glucose ≥126 mg/dL, glycated hemoglobin N 6.5%, 2-hour post-load plasma glucose N 200 mg/dL, or use of antidiabetic drugs), chronic kidney disease, hepatic failure, previous CV disease (myocardial infarction, stroke, congestive heart failure, coronary revascularization, including use of vascular stents), valvular heart disease, arrhythmia, stroke, any previous diagnosed sleeping disorder, and current smoking. A "normal" population was defined as subjects having optimal or normal BP values (according to office blood pressure measurement) and no additional CV risk factors. The study protocol was approved by the local ethics committee, and informed consent was obtained from each of the participants. The clinical and demographic information of the volunteers participating in the study that was used included age, gender, and body surface area (BSA) data. Patient laboratory information regarding fasting glucose levels, creatinine levels, fasting serum lipid status, and urinary albumin excretion were also noted. Hyperlipidemia was described as a total cholesterol level >240 mg/dL or the use of lipid-lowering drugs. The BSA was calculated using the following formula: BSA (m^2) = ([Height (cm) × Weight (kg)]/3600)½.

Abbreviations:

AIx	*Augmentation index*
BP	*Blood pressure*
BSA	*Body surface area*
CI	*Confidence interval*
CV	*Cardiovascular*
PWV	*Pulse wave velocity*

Twenty-four-hour ambulatory blood pressure monitoring

Office BP, ambulatory BP, and arterial stiffness were measured using a Mobil-O-Graph arteriograph system consisting of a Mobil-O-Graph PWA measurement device and HMS CS analysis software (IEM GmbH, Stolberg, Germany). This monitoring system allows for the recording and display of a complete BP profile throughout the day and night with parameters that include nocturnal values and blood pressure variations. Three cuffs of different sizes (small, medium, large) are provided by the manufacturer. Each participant's arm circumference was measured in a quiet room with an ambient temperature of between 20°C and 22°C to ensure the correct cuff was used. Patient office BP data were acquired after the subjects had rested for at least 5 minutes in a seated position. Since the value could affect the AIx results, the subjects were required to refrain from eating and from drinking alcohol, coffee, or tea for at least 12 hours prior to the measurement. The average value of duplicate measurements was computed before and after an ambulatory Holter recording. Simultaneous brachial BP, PWV, and AIx measurements provided by the oscillometric Mobil-O-Graph arteriograph were taken at 20-minute intervals during the day (8:00 am-10 pm) and 30-minute intervals at night (10 pm-8 am).

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 23.0 software (IBM Corp., Armonk, NY, USA). Measured and calculated values were expressed as mean value±SD. A $p<0.05$ was considered statistically significant. Differences between groups were evaluated using analysis of variance and Bonferroni's post hoc test.

RESULTS

The original cohort comprised 805 individuals. In all, 452 subjects were excluded due to previous diabetes, CV diseases, or a current smoking habit, a BP over the limit for optimal or normal, or the use of BP-lowering drugs. Thus, the analysis was conducted on 353 apparently healthy adults. The baseline demographic and clinical features of all of the study groups are shown in Table 1. The mean age of the participants was 55.03±15.38 years (range: 20–95 years). The mean PWV was 7.75±1.89 m/s (range: 4.25–15.90 m/s). The laboratory characteristics of the study groups are provided in Table 2. Table 3 presents the mean PWV, range, and 95% confidence interval (CI) for each of the 6 age groups. The SD of the 3 oldest age groups (range: 50–95 years) was higher than that of the 3 youngest groups (range: 10–49 years) and indicated a rise in the scatter of the PWV with the aging process. Similarly, in subjects younger than 70 years of age, the minimum and maximum values of the 95% CI demonstrated a lower dispersion in the PWV data than that observed in older participants. Figures 1 and 2 illustrate a linear rise in PWV with increased age at the individual (r^2=0.94; p=0.00) and group level. The PWV gradually increased by an average of 5% to 9% with each decade of life until the age of >50

Table 1. Demographic characteristics and hemodynamic data of the study group

	All subjects (n=353)
Age (years)	55±15 (range: 20–95)
Female, n (%)	76 (21.5)
Body surface area (m^2)	1.88±0.19
Office SBP (mm Hg)	121±13
Office DBP (mm Hg)	74±10
24-h SBP (mm Hg)	116±8
24-h DBP (mm Hg)	71±6
24-h MAP (mm Hg)	92±6
24-h heart rate (beats/min)	74±9
24-h PP (mm Hg)	45±7
Daytime SBP (mm Hg)	118±8
Daytime DBP (mm Hg)	73±7
Daytime MAP (mm Hg)	93±6
Daytime heart rate (beats/min)	76±10
Daytime PP (mm Hg)	45±8
Nighttime SBP (mm Hg)	111±10
Nighttime DBP (mm Hg)	66±7
Nighttime MAP (mm Hg)	87±8
Nighttime heart rate (beats/min)	67±9
Nighttime PP (mm Hg)	45±7
Central SBP (mm Hg)	111±13
Central DBP (mm Hg)	76±11
Central pulse pressure (mm Hg)	35±10
Cardiac output (l/min)	4.84±0.78
PWV (m/s)	7.75±1.89
AIx (%)	26.62±10.81

AIx: Augmentation index; DBP: Diastolic blood pressure; MAP: Mean arterial pressure; PP: Pulse pressure; PWV: Pulse wave velocity; SBP: Systolic blood pressure.

Table 2. Laboratory characteristics of the study group

	All subjects (n=467)
	Mean±SD
Glucose (mg/dL)	106±28
BUN (mg/dL)	31±11
Creatinine (mg/dL)	0.86±0.22
Creatinine clearance (mL/min)	84±21
Uric acid (mg/dL)	5.06±1.48
T. Chol. (mg/dL)	201±43
Triglyceride (mg/dL)	155±84
HDL-C (mg/dL)	50±12
LDL-C (mg/dL)	121±36
NonHDL-C (mg/dL)	154±8
Total bilirubin	0.62±0.33
HBG (mg/dL)	13.5±1.4
HTC (%)	41±4
WBC (K/uL)	8±2.14
Neutrophils (mm^3)	4.98±1.91
Lymphocytes (mm^3)	2.23±0.73
Platelet ($\times 10^9$/L)	267±69
MPV (fL)	9.15±1.28

BUN: Blood urea nitrogen; T. Chol.: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; HBG: High blood glucose; HTC: Hematocrit; WBC: White blood cell count; MPV: Mean platelet volume.

Table 3. Brachial PWV for each age group in the study population

Age group (years)	n	Mean PWV (m/s)	SD	95% CI lower–upper limit	Range
10–29	28	4.87	0.40	4.71–5.02	4.25–5.85
30–39	35	5.57	0.41	5.43–5.72	4.7–6.45
40–49	53	6.28	0.44	6.15–6.40	5.45–7.8
50–59	93	7.47	0.52	7.36–7.58	6.55–9.65
60–69	74	8.72	0.64	8.57–8.87	6.65–10.15
>70	70	10.42	1.15	10.15–10.70	7.65–15.90
Total	353	7.75	1.89	7.55–7.94	4.25–15.90

PWV: Pulse wave velosite; SD: Standard deviation; CI: Confidence interval.

years, after which the average PWV increased by 16%. With the exception of the fifth group (age: 60–69 years), which had PWV values of 8.64±0.61 m/s (men) versus 9.01±0.66 m/s (women) (p=0.04), there were no significant differences in PWV between genders. Higher PWV values were seen in both women (8.52±1.28 m/s versus 5.74±0.71 m/s; p=0.00) and men (9.42±1.72 m/s versus 5.66±0.69 m/s; p=0.00) in subjects over 50 years of age when compared with those aged <50 years (Fig. 3). The differences in the PWV data were chiefly determined by age, particularly between the young and elderly subjects, regardless of gender (p=0.01).

DISCUSSION

Our study defined age- and gender-specific reference values for PWV in 353 healthy Turkish individuals. The PWV was observed to increase linearly with the age of the study participants. Aging is a continuous deterioration of basic physiological functions, and

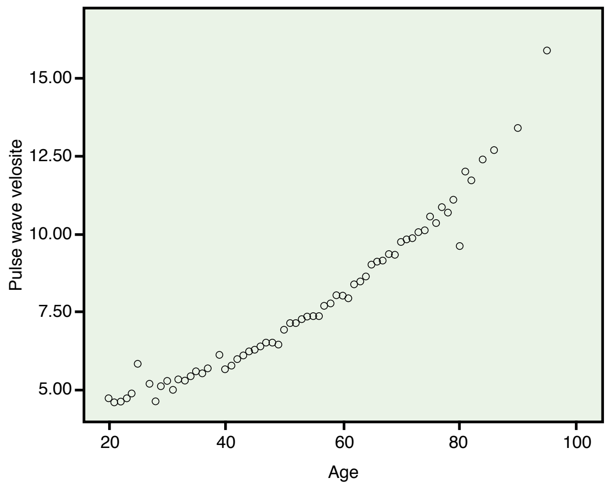

Figure 1. Scatter graph showing the relationship between mean pulse wave velocity (PWV) and age (years) in the study population (n=353; mean and 95% confidence interval).

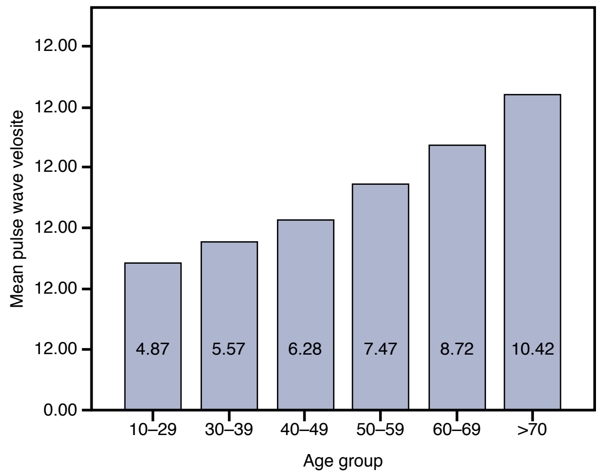

Figure 2. Evolution of the mean value of the pulse wave velocity (mean±SD) according to age group.

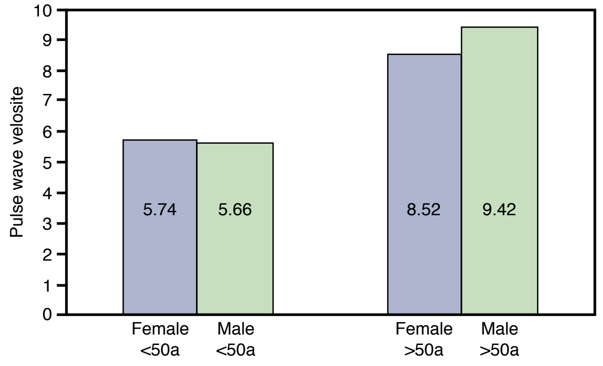

Figure 3. Mean value of pulse wave velocity (PWV; meters per second) showing significant differences between subjects ≤50 years and those >50 years of age. A gender difference in PWV was only seen in the fifth age group.

it influences all systems in the organism. One of the most affected by this progressive process is the vascular system, with initial molecular alterations in the medial layer of the elastic arteries. Degeneration of elastic fibers is caused by increased collagenous tissue, resulting in progressive stiffening of the arterial wall.[12] As a result of cardiac contraction, peripheral pulse waves are created. In stiffened arteries, the pulse wave moves more rapidly, causing overlap of the progressive wave and reflected wave in the arterial lumen, possibly explaining the increased risk for CV and cerebrovascular diseases.[4] PWV analysis is currently considered the gold standard method of determining arterial stiffness, due to its accuracy, simplicity, predictive value, and reproducibility.[13]

At present, a gender difference in arterial stiffness is a controversial issue. Except for the fifth group (age: 60–69 years), no significant differences in the PWV were observed between men and women in our study.[14] This result is similar to several large population-based studies in which the gender difference in PWV was absent or without clinical significance (<0.1 m/s).[11,15,16] In an investigation aimed at deciphering the PWV reference values for normotensive individuals in Argentina, there was no statistically significant difference found in the PWV between men and women (6.81 m/s versus 6.89 m/s, respectively).[14] In contrast, in Brazil, a significant and clinically relevant difference in PWV between genders was observed, and, furthermore, the inclination of the age-related increase in PWV was similar between men and women for both the healthy sample and the entire study population.[17] Differences in socioeconomic conditions and race may contribute to explaining the inconsistent relationship between gender and PWV reported in the published literature.

Arterial stiffness, which is the predictive measurement of the vascular age, has been linked to CV disorders and mortality.[3,4] Nakano et al.[18] demonstrated that patients who have a PWV above 10 m/s, have a 30% greater risk of cerebrovascular disease than those with a lower PWS in Japanese patients, and another study found that an increased PWV level was a strong predictor of CV mortality in patients with a PWV over 13 m/s.[19] The difference between these 2 studies regarding the detection reference values may be related to socioeconomic aspects, individual factors, measurement instrument, or sample size. In the present study, we included 353 healthy, normotensive Turkish individuals and used the baseline data from another study of normotensive, non-dipper status in the healthy population. The current study design was based on strict exclusion criteria. These criteria included the presence of diabetes (fasting blood glucose ≥126 mg/dL, glycated hemoglobin N6.5%, 2-hour post-load plasma glucose N200 mg/dL, or use of antidiabetic drugs), chronic kidney disease, hepatic failure, previous CV disease (myocardial infarction, stroke, congestive heart failure, coronary revascularization, including use of vascular stents), valvular heart disease, arrhythmia, stroke, any sleeping disorder, and smoking. These strict exclusion criteria were required for the reliability of our PWV reference values.

Since PWV is an age-dependent parameter, to orient both risk stratification and evaluation of the effectiveness of treatment, physicians need to know the normal PWV range in general populations, and an estimated dispersion for each decade of human life. Our research demonstrated that the normal range of PWV with a corresponding 95% CI for each age group, which is relevant and important clinical data in terms of aortic stiffness. Ankara is the capital of Turkey and, according to the Turkish Statistical Institute, represents the general population in many aspects, such as gender, age distribution, literacy rate, socioeconomic level, and the maternal–infant mortality rate. To the best of our knowledge, this study is the first to define PWV reference values via brachial measures, based on a healthy, normotensive Turkish population in Ankara. Another notable finding was the disproportionate rise in PWV across different age groups. It suggested an adverse change in vascular elasticity that is positively correlated with advances in age and all age groups in the Turkish population. The effect was most apparent after the age of 50 years (Fig. 3), which is consistent with previous research.[14]

Conclusion

To our knowledge, this article is the first to define reference PWV values via brachial measures in a healthy, normotensive Turkish population in Ankara. Analysis of this cohort demonstrated that PWV values were positively correlated with the aging process. No association was observed between gender and PWV. The data provide important information for daily clinical practice.

Limitations

The current study has several limitations. First, as in other literature research, the study subjects consisted of both normotensive dipper and normotensive non-dipper subjects. Normotensive non-dipping status might be associated with autonomic nervous system dysfunction, sleep-apnea, or orthostatic hypotension, and therefore might have affected the PWV values. Second, it was single-center study of a relatively small number of participants. Despite these limitations, we believe that the study provides important information for daily clinical practice.

Ethics Committee Approval: The study protocol was approved by the Ankara Training and Reseach Hospital Local Ethics Committee (date: 18.10.2017, no: 21/229).

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Keywords: Aging process; arterial stiffness; pulse wave velocity.

Anahtar sözcükler: Yaşlanma süreci; atardamar sertliği; nabız dalga hızı.