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ORIGINAL ARTICLE

Correlation of vascular risk age with pulse wave velocity in young patients with low absolute cardiovascular risk

Düşük mutlak kardiyovasküler riske sahip genç hastalarda vasküler risk yaşının nabız dalga hızı ile korelasyonu

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ABSTRACT

Objective: The systematic coronary risk evaluation (SCORE) estimates the 10-year risk of fatal cardiovascular disease (CVD), and its application is recommended. The absolute risk of CVD, independent of risk factors, is relatively low in young individuals. Expressing the risk as their "risk age" may aid in understanding the risk. This study aimed to demonstrate a possible correlation between vascular risk age, SCORE risk value, and the level of subclinical atherosclerosis evaluated using a pulse wave velocity (PWV) device.

Methods: This work was designed to be a cross-sectional study. The SCORE 10-year fatal CVD risk and vascular risk age were calculated for patients below the age of 50 years and without any previous diagnosis of atherosclerotic disease or equivalents. The PWV of each patient was measured non-invasively using a PWV device.

Results: The study population included a total of 300 patients with a mean age of 35.1±9.5 years. The mean PWV and mean vascular age of the entire study population were 6.3±1.3 m/s and 44.3±5.5 years, respectively, and the median 10-year risk of fatal CVD score was 0.4 (0.04-2.74). There was a positive correlation between PWV and the 10-year risk of fatal CVD (r=0.613; *P*<0.001) and vascular risk age (r=0.684; *P*<0.001).

Conclusion: Despite their young age and low to moderate 10-year risk of fatal CVD (<1%-5%) according to the SCORE chart, patients with a high vascular risk age were found to have high PWV values. These results show that calculations of vascular risk age might be used to assess the risk of fatal CVD in young patients and correlate with subclinical atherosclerosis.

ÖZET

Amaç: Sistematik Koroner Risk Değerlendirmesi (SCORE), 10 yıllık ölümcül kardiyovasküler hastalık (KVH) riskini tahmin etmekte ve uygulanması Avrupa Kardiyoloji Derneği tarafından tavsiye edilmektedir. Risk faktörlerinden bağımsız olarak ölümcül KVH mutlak riski, genç insanlarda nispeten düşüktür. Riskin "risk yaşı" olarak ifade edilmesi, riskin anlaşılmasına yardımcı olabilir ve gerekli yaşam tarzı değişikliklerinin uygulanmasını kolaylaştırabilir. Temel amaç, vasküler risk yaşı ve SCORE risk değeri ile nabız dalga hızı (PWV) ölçümü ile gösterilen subklinik ateroskleroz seviyesi arasındaki ilişkiyi ortaya koymaktır.

Yöntemler: Bu çalışma kesitsel bir çalışma olarak tasarlandı. Elli yaş altında, daha önce herhangi bir aterosklerotik hastalık tanısı veya diabetes mellitus ve kronik böbrek hastalığı gibi eşdeğerleri olmayan hastalarda SCORE risk skalasına göre 10 yıllık ölümcül KVH riski hesaplandı. Her bir hastanın nabız dalga hızı, PWV cihazı kullanılarak non-invaziv olarak ölçüldü.

Bulgular: Çalışmaya toplam 300 hasta (156 kadın, 144 erkek) alındı ve yaş ortalaması 35.1±9.5 yıldı. Tüm çalışma popülasyonunun ortalama PWV değeri 6.3±1.3 m/sn ortalama vasküler risk yaşı 44.3±5.5 yıl ve medyan 10 yıllık ölümcül KVH risk skoru 0.4 (0.04-2.74) idi. PWV ile 10 yıllık ölümcül KVH riski (r=0.613; *p*<0.001) ve vasküler risk yaşı (r=0.684; *p*<0.001) arasında pozitif korelasyon saptandı.

Sonuç: SCORE tablosuna göre genç yaşlarına ve 10 yıllık düşük ölümcül kardiyovasküler hastalık riskine (<%1) rağmen, yüksek vasküler risk yaşı olan hastaların yüksek PWV değerlerine sahip oldukları bulundu. Bu sonuçlar, vasküler risk yaşının hesaplanmasının, genç hastalarda KVH riskinin değerlendirilmesinde kullanılabileceğini ve subklinik ateroskleroz ile ilişkili olabileceğini göstermektedir.

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Guidelines on cardiovascular disease (CVD) prevention recommend that advice about risk factor modification should be based on an individual's total CVD risk.[1, 2] Several systems are available to assess absolute risk according to conventional risk factors. Of these, the most commonly used are based on the Framingham project in the United States of America and the systematic coronary risk evaluation (SCORE) in Europe.[2-4] SCORE is the system recommended by the European guidelines on CVD prevention.[2, 5]

Risk factor modifications, particularly pharmacotherapy, are based on absolute risk because individuals at high absolute risk will derive the greatest benefit from them.[2] However, the absolute risk is associated primarily with age. A young person with a very high relative risk owing to multiple risk factors may still have a low absolute risk.[2]

In 2008, a new concept of cardiovascular risk was published as a result of the Framingham study: the age of the heart or the vascular age, that is, the age of the vascular system of a patient with different cardiovascular risk factors.[3] This age is calculated as the age a person would be with the same calculated cardiovascular risk but whose risk factors were all within normal ranges. The concept of vascular age can be useful in identifying young people in whom low to moderate absolute risk may conceal higher relative risk.[2, 6-8]

Arterial stiffness is defined as irreversible damage to vessels from age and cardiovascular risk factors and is associated with CVD-related morbidity and mortality.[9, 10] Arterial stiffness can be measured by an augmentation index (the ratio of augmentation pressure to aortic pulse pressure [Alx]) and PWV that represents a measure of wave reflection and arterial stiffness.[11] PWV and AIx increase with age and are closely associated with CVD risk factors such as hypertension and coronary artery disease.[12, 13]

There are many studies showing the relationship between PWV, Alx, and arterial stiffness in elderly patients; however, the number of studies exploring the PWV and Alx in the young is very limited. There are deficiencies in treatment algorithms for young patients with a high relative risk of CVD. This study aimed to demonstrate a possible correlation between vascular age, SCORE value, and the level of subclinical atherosclerosis assessed by a PWV device.

Abbreviations:

BP	*Blood pressure*
CVD	*Cardiovascular disease*
LDL	*Low-density lipoprotein*
PWV	*Pulse wave velocity*
SCORE	*Systematic coronary risk evaluation*

METHODS

This cross-sectional study was conducted in patients below the age of 50 years and without any previous diagnosis of atherosclerotic disease or equivalents who were admitted for routine screening to the cardiology department at Hacettepe University Hospital between 2014 and 2016. Patients with known atherosclerotic vascular disease and equivalent diseases such as diabetes mellitus and chronic kidney disease were excluded. The impact of age on risk was minimized by enrolling only men and women between the ages of 18 and 50 and calculating vascular age and 10-year risk of CVD according to risk factors.

The inclusion criteria were: (i) age >18 years; (ii) having atherosclerotic risk factors such as hypertension, hypercholesteremia, and cigarette smoking with no known atherosclerotic disease; and (iii) informed written consent. The exclusion criteria were: (i) chronic atrial fibrillation or any other type of arrhythmia; (ii) history of myocardial infarction, unstable angina, ischemic stroke, and/or peripheral artery disease; (iii) diabetes mellitus and renal failure; (iv) heart failure, according to New York Heart Association classification; and (v) malignancy or any clinical condition associated with poor prognosis. All protocol procedures were conducted in accordance with the Declaration of Helsinki, and the study was approved by Ethics Committee of Hacettepe University (Approval Date: July 9, 2014; Approval Number: GO 14/388-07). Informed consent was obtained from all participants.

A detailed medical history, findings from physical examinations, and blood samples for routine laboratory tests after at least 8 hours of fasting were obtained from all participants. Their body weight and height were measured, and standard office blood pressure (BP) readings were recorded after 10 minutes of rest.

Arterial stiffness is affected by atherosclerosis risk factors, particularly hypertension and age, and

is used as an indicator of subclinical organ damage.[7] Many studies have shown that it is an independent risk factor for fatal and non-fatal CVD.[10] Carotid-femoral PWV is the gold standard for measuring aortic stiffness.[14] However, these devices are not commonly used in daily clinical practice. One reason could be that current measurement devices have serious limitations in terms of time consumption and operator requirements. Measuring PWV using the oscillometric method was found to be safe and accurate, similar to the results of studies comparing the oscillometric method with invasive and tonometric measurements.[14-16] Tonometry is fairly simple technique to learn and has good inter- and intra-operator reproducibility.[17]

The PWV measurement is based on the principle that the pressure pulse generated by the left ventricular ejection travels at a speed determined by the size, shape, and properties of the artery.[18] PWV is determined by measuring the pulse wave in 2 places on an artery and dividing the distance between measurement sites by the difference in time between the 2 pulses. It is preferable to measure the pulse wave between 2 points on the same artery; however, if this is not possible, the pulse wave of a branching artery can be used as a substitute for the proximal wave.[15] A Mobil-O-Graph (Mobil-O-Graph, Germany) records oscillometric brachial BP and pulse waves and calculates aortic BP and Alx as a measure of wave reflections and PWV as a measure of arterial stiffness. A higher PWV indicates higher peripheral vascular stiffness.[15] In our study, participants were assessed for arterial wall stiffness in the brachial region at the upper extremity after at least 8 hours of fasting and no smoking. A Mobil-O-Graph was used to obtain PWV, aortic BP, and Alx.

High-risk countries' SCORE risk scale and the website *www.heartScore.org* were used to calculate the age of vascular risk. Turkey is classified as a high-risk country.[2] The risk factors considered were age, sex, smoking, total cholesterol level, and systolic BP levels. We accepted the normal BP limit to be <130/85 mm Hg based on current information.[2, 7, 8] A total cholesterol level of 5 mmol/L (190 mg/dL) was considered normal.[2, 19] For example, a 40-year-old male participant with a total cholesterol level of 225 mg/dL and systolic BP of 160 mm Hg was found to have a SCORE risk of 1% and vascular age of 55 years. On the SCORE risk chart, a vascular age could not be calculated for patients younger than 40. In our study, the vascular risk age of patients under 40 was calculated assuming that they were 40.

Statistical analysis

Normally distributed data were evaluated using the Kolmogorov-Smirnov test. Continuous variables with normal distribution were expressed as mean± standard deviation. Abnormal distribution was expressed as median (min-max), and categorical variables were expressed as percentages when appropriate. Comparisons of numerical variables between the 2 groups were analyzed using the paired sample t-test and Mann-Whitney U test. Comparisons of categorical variables between the 2 groups were analyzed using chi-square and Fisher exact tests. The relationship between numerical variables was studied using Pearson correlation analysis. Statistical analyses were performed using the Statistical Package for Social Sciences software version 20.0 (IBM Corp.; Armonk, NY, USA). A p value of 0.05 was considered statistically significant.

The primary endpoint of the study was to demonstrate the possible correlation between vascular age and PWV. In the literature, a highly significant correlation (r=0.91, p<0.0001) was found between Mobil-O-Graph and standard PWV measuring devices.[15] According to these findings, when alpha is accepted as 0.05, power is taken as 80%, and at least 41 participants must be included for a 0.50 correlation.

RESULTS

Baseline demographics and clinical characteristics of the participants are presented in Table 1. The study population included 156 women and 144 men with a mean age of 35.1±9.5 years. Women were significantly older than men (37.0±9.9 vs 33.0±9.0; p<0.001). The incidence of hypertension was 13%, and women were more hypertensive (5.2% men vs 20.2% women) (p=0.003). The smoking rate in the study population was 41.5%, which included 59.4% of men and 25% of women (p<0.001).

The calculated mean risk age was 46.1±5.2 for men, 42.7±5.3 for women and 44.3±5.5 for the entire study population, and this difference between sexes was found to be statistically significant. As with risk age, male patients were found to have a higher

Table 1. Baseline demographics and clinical characteristics of the participants

Variables	Entire study population (n=300)	Women (n=156)	Men (n=144)	*p*
Age (years)	35.1±9.5	37.0±9.9	33.0±9.0	<0.001*
Height (cm)	166.8±8.2	162.7±5.5	171.3±8.3	<0.001*
Body weight (kg)	72.7±13.6	67.2±12.4	78.7±12.4	<0.001*
BMI (kg/m²)	26.1±4.5	25.5±5.0	26.9±4.1	0.013*
Waist circumference	88.5±9.1	85.2±10.2	90.2±8.0	<0.001*
Current smokers	41.5%	25%	59.4%	<0.001*
Hypertension	13%	20.2%	5.2%	0.003*
Hyperlipidemia	19%	20.2%	17.7%	0.721
Family history of CVD	41%	50%	31.3%	0.007*
Physical inactivity	47.5%	61.5%	32.3%	0.001*
Vascular risk age (years)	44.3±5.5	42.7±5.3	46.1±5.2	<0.001*
10-year risk of fatal CVD (SCORE) (%)	0.4 (0.04-2.74)	0.06 (0.04-1.85)	0.99 (0.40-2.74)	<0.001*

**p* value <0.05 is statistically significant.
Continuous variables with normal distribution are expressed as mean±standard deviation.
Abnormal distribution is expressed as a median (min-max), numerical variables are presented as the median and interquartile range, and categorical variables are expressed as percentages when appropriate.
BMI: body mass index; CVD: cardiovascular disease.

Table 2. Laboratory, ambulatory blood pressure monitoring, and pulse wave velocity data

Variables	Entire study population (n=300)	Women (n=156)	Men (n=144)	*p*
Total cholesterol (mg/dL)	205.0±46.9	190.1±43.3	221.2±46.5	<0.001*
Triglyceride (mg/dL)	126 (42-412)	107 (42-375)	165 (47-412)	0.001*
LDL cholesterol (mg/dL)	119.5 (39-255)	116 (39-255)	144 (39-255)	0.001*
HDL cholesterol (mg/dL)	51.0±14.2	52.4±14.6	49.4±13.8	0.069
Heart rate (bpm)	81.2±12.6	78.4±12.3	84.2±12.4	<0.001*
Mean SBP (mmHg)	122.2±16.8	121.7±19.3	122.7±13.5	0.606
Mean DBP (mmHg)	76.8±11.7	76.7±12.6	76.8±10.7	0.940
Mean MBP (mmHg)	97.3±12.4	97.2±14.3	97.4±10.1	0.890
AIx@75 (%)	22 ([-5]-111)	21 ([-5]-39)	24 (4-49)	0.044*
Cardiac Output (mL/kg)	4.3±0.6	4.2±0.6	4.5±0.5	<0.001*
Pulse wave velocity (m/s)	6.3±1.3	5.9±1.1	6.6±1.3	<0.001*

**p* value <0.05 is statistically significant.
Continuous variables with normal distribution are expressed as mean ± standard deviation.
Abnormal distribution is expressed as a median (min-max), numerical variables are presented as the median and interquartile range, and categorical variables are expressed as percentages when appropriate.
LDL: low-density lipoprotein; HDL: high-density lipoprotein; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; AIx@75: heart rate-adjusted augmentation index.

10-year risk of fatal CVD than women (0.99% vs, 0.06%, p<0.001).

Along with these data, height, body weight, body mass index (BMI), and waist circumference were found to be statistically higher in men; and hypertension, physical inactivity, and family history of CVD were significantly higher in women.

Total cholesterol levels were 221.2±46.5 mg/dL in men, 190.1±43.3 mg/dL in women, and 205.0±46.9 mg/dL in the whole study population (p<0.001). The

Table 3. Variables related to pulse wave velocity and 10-year risk of fatal CVD levels

	10-year risk of fatal CVD (SCORE)		Pulse wave velocity (m/s)	
Variables	r	*p*	r	*p*
10-year risk of fatal CVD (SCORE)	-	-	0.613	<0.001*
Pulse wave velocity	0.613	<0.001*	-	-
Age	0.272	0.015*	0.463	<0.001*
Vascular risk age	0.843	<0.001*	0.684	<0.001*
Height	0.071	0.319	-0.107	0.132
Body weight	0.299	0.005*	0.280	0.011*
BMI	0.292	0.006*	0.374	<0.001*
Waist circumference	0.162	0.160	0.099	0.393
Total cholesterol	0.520	<0.001*	0.435	<0.001*
Triglyceride	0.481	<0.001*	0.353	<0.001*
LDL cholesterol	0.523	<0.001*	0.443	<0.001*
HDL cholesterol	-0.105	0.140	-0.059	0.406
Mean SBP	0.298	0.005*	0.528	<0.001*
Mean MDP	0.255	0.029*	0.477	<0.001*
Mean DBP	0.083	0.242	0.308	<0.001*
Heart rate	0.260	0.023*	0.071	0.316
AIx@75	0.016	0.817	0.207	0.003*
Cardiac Output	0.064	0.369	0.204	0.004*

**p* value <0.05 is statistically significant.
Logarithmic transformation applied to 10-year risk of fatal cardiovascular disease risk, triglyceride LDL cholesterol, AIx@75 variables.
BMI: body mass index; CVD: cardiovascular disease risk; LDL: low-density lipoprotein; HDL: high-density lipoprotein; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; AIx@75: heart rate-adjusted augmentation index.

median triglyceride level (107 mg/dL vs 165 mg/dL, p=0.001) and median low-density lipoprotein (LDL) cholesterol levels (116 mg/dL vs 144 mg/dL, p=0.001) were higher in men than in women. The mean PWV was 6.3±1.3 m/s in the whole study population, and the mean PWV in male patients was higher than in female patients (5.9±1.1 m/s vs 6.6±1.3 m/s, P<0.001). Heart rate, cardiac output, and AIx values were significantly higher in men. Table 2 summarizes laboratory, ambulatory BP monitoring, and PWV data.

Table 3 summarizes the variables related to the 10-year risk of fatal CVD (SCORE risk chart) and PWV. A moderate correlation was found between the 10-year fatal CVD risk (SCORE risk scheme) and PWV (r=0.613; p<0.001). Meanwhile, there was a strong correlation between vascular risk age and 10-year risk of fatal CVD (SCORE risk chart) and PWV (r=0.843, p<0.001; r=0.684, p<0.001; respectively). Age, body weight, BMI, total cholesterol, triglyceride, LDL cholesterol, systolic BP, mean arterial BP, and heart rate were also positively correlated with the 10-year risk of fatal CVD. In addition, a positive correlation was found between BMI; total cholesterol; triglycerides; LDL cholesterol; systolic, diastolic, and mean arterial BP and PWV and other variables that constitute the risk factors.

DISCUSSION

Atherosclerotic vascular disease is the leading cause of death globally, and the primary prevention of cardiovascular events is a healthcare priority. A key challenge to primary prevention efforts is identifying individuals who could be candidates for more intensive medical interventions. European guidelines on CVD prevention in clinical practice recommend using the SCORE chart system to assess absolute 10-year risk of fatal CVD (%) events; however, this model is very dependent on chronological age as a surrogate for atherosclerotic burden.[2] There is a particular problem related to young people with low to

moderate absolute risk and multiple risk factors. The relative risk chart helps illustrate how a young person with a low to moderate absolute risk may be at a substantially high and reducible relative risk.[2]

There is a need to identify younger subjects at risk for CVD so that preventive measures may be instituted before occlusive vascular disease occurs. Noninvasive methods are used frequently in daily practice for this. The best known of these are coronary calcium scoring, an ankle-brachial index, a carotid duplex scan, and PWV. PWV is currently the method preferred over the others because it can be used rapidly in daily practice, is cheap, and does not have any side effects. However, most information concerning the prognostic value of noninvasive measures of arterial function and structure have been derived from the study of older populations. Therefore, it is important to establish the relationship between the concept of vascular age and the arterial stiffness measured by PWV.

The measurement of oscillometric PWV is generally considered to be the simplest, most robust noninvasive and reproducible method for determining arterial stiffness. Carotid-femoral PWV is a direct measurement and corresponds to the widely accepted propagation model of the arterial system.[14, 20] Although there are different methods by which to evaluate arterial stiffness, carotid-femoral PWV has emerged as the gold standard.[14, 20] Studies comparing PWV measurement with the oscillometric method and invasive and tonometric measurements found it to have similar safety and accuracy.[15, 21, 22] A Mobil-O-Graph records oscillometric brachial BP and pulse waves and calculates PWV, aortic BP, and Alx as a measure of wave reflections and arterial stiffness. A higher PWV indicates higher peripheral vascular stiffness.[15, 20, 23]

Boutouyrie et al.[24] have revealed that 1,045 hypertensive patients followed for 5.6 years with PWV were significantly associated with the occurrence of a coronary event. Laurent et al.[25] followed 1,715 patients with essential hypertension for an average of 7.9 years and reported that PWV significantly predicted the occurrence of stroke. As a result of many similar studies, PWV was considered as end-organ damage in the cardiovascular system in adult patients, with increased arterial stiffness identified as an independent risk factor for future CVD.[7, 8]

The literature shows a strong association of PWV with age and BP;[23] however, findings regarding its association with other risk factors have been inconsistent, particularly in young individuals.[26] However, in some studies using PWV in young patients, a correlation was found between age and risk factors and arterial stiffness. Kotsis et al.[27] have shown that increased 24-hour systolic BP variability is associated with arterial stiffness in healthy young volunteers. The study of professional athletes and swimmers demonstrated that arterial stiffness is lower in aerobic-trained athletes than in sedentary individuals.[28] Sehestedt et al.[29] found a correlation between PWV and SCORE in participants with a SCORE value <5%. This suggests that PWV measurement may be particularly useful in low-risk individuals, such as younger individuals with a genetic disposition for CVD or obese smokers with SCORE values <5%, and could provide essential information that would influence lifestyle counseling.

In a study by Kılıç,[30] the relationship between PWV was examined according to the age distribution of healthy adults and results showed a positive correlation between age and PWV from the very young to the elderly. In this study, the average PWV value was found to be 5.57 in healthy adults in aged 30-39 without any risk factors.[30] In our study, the patients had risk factors, their mean age was 35.1±9.5 years, and the mean PWV value was 6.3±1.3. These results suggest that PWV in a group of young patients may correlate with CVD risk even if there are no risk factors.

There are no studies in patients with low to moderate 10-year risk of fatal CVD <1-5% with a high vascular age and multiple risk factors. In addition, there is limited evidence showing that subclinical atherosclerosis was higher in these patients.[31] In this cross-sectional study, we demonstrated that increased PWV in young patients with a low to moderate absolute risk but high relative risk and high vascular age. These data imply that a young individual with low absolute risk but high relative risk could have stiffer arteries than a patient with real low risk suggesting established vascular damage.

In our study, although the mean age, frequency of physical inactivity, hypertension, and history of CVD in the family were higher in female participants than in male participants, the 10-year fatal risk of CVD

(%) and risk age were higher in men. We believe that sex, BMI, waist circumference, and the high rate of smoking in men is a major determinant of these results. Similarly, PWV and AIx were found to be higher in men than in women, and this difference was statistically significant.

Although the rate of hypertension was higher in women, all patients with hypertension were receiving medical treatment and there was no difference in BP values between men and women. Laurent et al.[10] reported that aortic stiffness measured by the PWV device is significantly associated with the risk of all-cause and cardiovascular mortality in patients with essential hypertension. However, only 483 of the 1,980 patients in this study were receiving antihypertensive treatment, and the mean BP measured was 148/89 mm Hg.[10] In other studies showing a relationship between hypertension and PWV, BP averages were similarly high; however, a multivariate Cox model including previous antihypertensive treatment (yes/no) among other classic risk factors revealed that the predictive value of PWV remained significantly and independently associated with an increased risk of CVD.[24] The fact that participants with hypertension in our study population were younger and normotensive under treatment may have masked the effect of hypertension on arterial stiffness.

When young smokers and non-smokers without known CVD were compared, the former showed an increased arterial stiffness as measured by PWV. In our study, the PWV, vascular age, and absolute 10-year risk of fatal CVD were high in men. This result suggests that a male sex and smoking are the most important risk factors in younger patients.[32, 33]

Not surprisingly, correlation analysis showed that age, body weight, BMI, total cholesterol, triglyceride, LDL cholesterol, systolic BP, mean arterial BP, heart rate, and risk age levels were also positively correlated with the 10-year risk of fatal CVD. PWV levels correlated positively with age, body weight, BMI, total cholesterol, triglyceride, LDL cholesterol, systolic BP, mean BP, diastolic BP, AIx, and cardiac output.

Routine screening with imaging modalities is generally not recommended in clinical practice as a way to predict future CVD events, but imaging modalities in the CVD risk assessment are particularly applicable to patients with low to moderate risk as risk modifiers.[2] Therefore, coronary artery calcium scoring, atherosclerotic plaque detection by carotid artery scanning, and ankle-brachial index are recommended for CV risk assessment.[2] The use of PWV is not routinely recommended but can be used in combination with vascular age in patients with low absolute risk and a high relative risk because it is noninvasive, inexpensive, and easily accessible.

Limitations

Our study had many limitations. First, the cross-sectional design of this study prevented the evaluation of the temporal sequence of events. The gold standard method of PWV measurement is an invasive measurement with a catheter. However, the validity of the Mobil-O-Graph device–a noninvasive method–has been proven in many studies. The sample size was small, and studies with larger patient numbers are required. In patients under 40, the SCORE 10-year risk of fatal CVD was calculated assuming their age to be 40 years. This may have affected the results of the study. PWV measurements were managed solely by the same trained observer.

Conclusion

We found that participants with very low risk (<1%) according to the SCORE chart but multiple other risk factors and a high vascular age, had higher PWV. Our results showed that measuring aortic stiffness with PWV can help to identify those at high risk of CVD who may benefit from more aggressive management. However, to be able to evaluate the prognostic value of PWV, prospective studies in patients with very low risk are needed.

Ethics Committee Approval: Ethics committee approval was received for this study from the Ethics Committee of Hacettepe University (Approval Date: July 9, 2014; Approval Number: GO 14/388-07).

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REFERENCES

1. Detection NCEPEPo, Adults ToHBCi. Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III): International Medical Pub; 2002. [Crossref]
2. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts)Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016;37:2315-81.
3. D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care. Circulation 2008;117:743-53. [Crossref]
4. Conroy R, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987-1003. [Crossref]
5. Perk J, De Backer G, Gohlke H, Graham I, Reiner Z, Verschuren M, et al. 'European Guidelines on cardiovascular disease prevention in clinical practice (version 2012)' The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Eur Heart J 2012;33:1635-701. [Crossref]
6. Cuende JI, Cuende N, Calaveras-Lagartos J. How to calculate vascular age with the SCORE project scales: a new method of cardiovascular risk evaluation. Eur Heart J 2010;31:2351-8. [Crossref]
7. Task Force for the management of arterial hypertension of the European Society of Hypertension; Task Force for the management of arterial hypertension of the European Society of Cardiology. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Blood Press 2013;22:193-278. [Crossref]
8. Williams B, Mancia G, Spiering W, Rosei EA, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021-104. [Crossref]
9. Hung C-S, Lin J-W, Hsu C-N, Chen H-M, Tsai R-Y, Chien Y-F, et al. Using brachial-ankle pulse wave velocity to associate arterial stiffness with cardiovascular risks. Nutr Metab Cardiovasc Dis 2009;19:241-6. [Crossref]
10. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, et al. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. Hypertension 2001;37:1236-41. [Crossref]
11. Safar ME, Levy BI, Struijker-Boudier H. Current perspectives on arterial stiffness and pulse pressure in hypertension and cardiovascular diseases. Circulation 2003;107:2864-9. [Crossref]
12. Fantin F, Mattocks A, Bulpitt CJ, Banya W, Rajkumar C. Is augmentation index a good measure of vascular stiffness in the elderly? Age Ageing 2007;36:43-8. [Crossref]
13. Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, et al. Arterial stiffness, wave reflections, and the risk of coronary artery disease. Circulation 2004;109:184-9. [Crossref]
14. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J 2006;27:2588-605. [Crossref]
15. Weiss W, Gohlisch C, Harsch-Gladisch C, Tölle M, Zidek W, van der Giet M. Oscillometric estimation of central blood pressure: validation of the Mobil-O-Graph in comparison with the SphygmoCor device. Blood Press Monit 2012;17:128-31. [Crossref]
16. Wassertheurer S, Kropf J, Weber T, van der Giet M, Baulmann J, Ammer M, et al. A new oscillometric method for pulse wave analysis: comparison with a common tonometric method. J Hum Hypertens 2010;24:498-504. [Crossref]
17. Wilkinson IB, Fuchs SA, Jansen IM, Spratt JC, Murray GD, Cockcroft JR, et al. Reproducibility of pulse wave velocity and augmentation index measured by pulse wave analysis. J Hypertens 1998;16:2079-84. [Crossref]
18. London GM, Guerin AP. Influence of arterial pulse and reflected waves on blood pressure and cardiac function. Am Heart J 1999;138:S220-S4. [Crossref]
19. Mach F, Baigent C, Catapano AL, Koskinas KC, Casula M, Badimon L, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk: The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). Eur Heart J 2020;41:11-188.
20. Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. J Hypertens 2012;30:445-8. [Crossref]
21. Wassertheurer S, Kropf J, Weber T, van der Giet M, Baulmann J, Ammer M, et al. A new oscillometric method for pulse wave analysis: comparison with a common tonometric method. J Hum Hypertens 2010;24:498-504. [Crossref]
22. Hametner B, Wassertheurer S, Kropf J, Mayer C, Eber B, Weber T. Oscillometric estimation of aortic pulse wave velocity: comparison with intra-aortic catheter measurements. Blood Press Monit 2013;18:173-6. [Crossref]
23. Zhong Q, Hu M-J, Cui Y-J, Liang L, Zhou M-M, Yang Y-W, et al. Carotid-femoral pulse wave velocity in the prediction of cardiovascular events and mortality: an updated systematic review and meta-analysis. Angiology 2018;69:617-29. [Crossref]
24. Boutouyrie P, Tropeano AI, Asmar R, Gautier I, Benetos A, Lacolley P, et al. Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longi-

tudinal study. Hypertension 2002;39:10-5. [Crossref]
25. Laurent S, Katsahian S, Fassot C, Tropeano AI, Gautier I, Laloux B, et al. Aortic stiffness is an independent predictor of fatal stroke in essential hypertension. Stroke 2003;34:1203-6. [Crossref]
26. Cecelja M, Chowienczyk P. Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. Hypertension 2009;54:1328-36. [Crossref]
27. Kotsis V, Stabouli S, Karafillis I, Papakatsika S, Rizos Z, Miyakis S, et al. Arterial stiffness and 24 h ambulatory blood pressure monitoring in young healthy volunteers: the early vascular ageing Aristotle University Thessaloniki Study (EVA-ARIS Study). Atherosclerosis 2011;219:194-9. [Crossref]
28. Nishiwaki M, Takahara K, Matsumoto N. Arterial stiffness in young adult swimmers. Eur J Appl Physiol 2017;117:131-8. [Crossref]
29. Sehestedt T, Jeppesen J, Hansen TW, Wachtell K, Ibsen H, Torp-Pedersen C, et al. Risk prediction is improved by adding markers of subclinical organ damage to SCORE. Eur Heart J 2010;31:883-91. [Crossref]
30. Kılıç A. Reference pulse wave velocity values in a healthy, normotensive Turkish population. Turk Kardiyol Dern Ars 2019;47:373-8. [Crossref]
31. Wibetoe G, Ikdahl E, Rollefstad S, Olsen IC, Bergsmark K, Kvien TK, et al. Discrepancies in risk age and relative risk estimations of cardiovascular disease in patients with inflammatory joint diseases. Int J Cardiol 2018;252:201-6. [Crossref]
32. Seet RC, Loke WM, Khoo CM, Chew SE, Chong WL, Quek AML, et al. Acute effects of cigarette smoking on insulin resistance and arterial stiffness in young adults. Atherosclerosis 2012;224:195-200. [Crossref]
33. Lerant B, Christina S, Olah L, Kardos L, Csiba L. The comparative analysis of arterial wall thickness and arterial wall stiffness in smoking and non-smoking university students. Ideggyogy Sz 2012;65:121-6.

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