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Hasan Hüseyin ÇELİK
Ruhuşen KUTLU
Selma ÇİVİ

RESEARCH

IS ANKLE BRACHIAL INDEX AND FRAMINGHAM RISK SCORE A PREDICTOR OF CARDIOVASCULAR DISEASES IN PEOPLE AGED ≥50 YEARS?

ABSTRACT

Introduction: Ankle-Brachial Index (ABI) has been shown to be a strong predictor of the extent and severity of cardiovascular diseases (CVD). We aimed to determine the early risk estimation of CVD by using ABI and Framingham risk score (FRS) in this study.

Materials and Method: In this study, 250 people aged ≥50 years were included. We calculated FRS of the participants using an automatic calculator. We calculated ABI by using the blood pressure data of the four extremities.

Results: The mean value of ABI was 1.13±0.12 (min=0.80, max=1.96). Of the participants, nine (3.6%) had low ABI (≤0.95). There were significant negative correlations between ABI and age, cigarette smoking, high blood pressure and FRS. In the people aged ≥60 years, ABI risk increase (≤0.95) was found to be 3.878 times greater compared with people aged <60 years. Among diabetics, the value for FRS1 was found to be 16.349 times greater compared to non-diabetics.

Conclusion: The prevalences of the main risk factors of CVD are quite high in the population. Screening the individuals aged 50 or more is necessary for the early diagnosis and management of main risk factors of CVD. Low ABI (≤0.95) and FRS can be used to estimate the risk of future cardiovascular events.

Key Words: Ankle Brachial Index; Cardiovascular Diseases/Epidemiology; Risk Factors.

ARAŞTIRMA

ANKE BRAKİAL İNDEKS VE FRAMİNGHAM RİSK SKORU 50 YAŞ VE ÜZERİNDE KARDİYOVASKÜLER HASTALIKLARIN BİR BELİRLEYİCİSİ MİDİR?

ÖZ

Giriş: Anke Brakial İndeks (ABİ) kardiyovasküler hastalıkların boyutunu ve şiddetini gösteren güçlü bir belirleyicidir. Bu çalışmada ABİ ve Framingham Risk Skoru (FRS) kullanarak kardiyovasküler hastalıkların erken risk tahminini tespit etmeyi amaçladık.

Gereç ve Yöntem: Bu çalışmaya 50 yaş ve üzerinde 250 kişi dahil edildi. Katılanların FRS değerleri otomatik olarak hesaplandı. Dört ekstremiteden alınan kan basınçlarını kullanarak ABİ değeri belirlendi.

Bulgular: ABİ ortalaması 1.13±0.12 (min=0.80, max=1.96) idi. Katılanların 9'unda (%3.6) ABİ değeri ≤0.95 idi. ABİ ile yaş, sigara içme, yüksek kan basıncı ve FRS arasında önemli derecede negatif korelasyon vardı. 60 yaş ve üzerindeki bireylerde 60 yaş altındakilere göre ABİ'deki risk artımı (≤0.95) 3.878 kez daha fazla idi. Diyabetiklerde FRS1 değeri diyabetik olmayanlara göre 16.349 kez daha fazla idi.

Sonuç: Kardiyovasküler hastalıkların temel risk faktörlerine toplumda oldukça sık rastlanır. Kardiyovasküler hastalıkların temel risk faktörlerinin erken tanı ve tedavisi için 50 yaş ve üzerindeki kişilerin taranması gereklidir. Düşük ABİ (≤0.95) ve FRS gelecekte oluşabilecek kardiyovasküler hastalıkların risk tahmininde kullanılabilir.

Anahtar Sözcükler: Ankle Brakial İndeks; Kardiyovasküler hastalık/epidemiyoloji; Risk Faktörleri.

İletişim *(Correspondance)*

Ruhuşen KUTLU
Konya Üniversitesi Meram Tıp Fakültesi, Aile Hekimliği Anabilim Dalı KONYA

Tlf: 0332 223 66 01
e-posta: ruhuse@yahoo.com

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Konya Üniversitesi Meram Tıp Fakültesi, Aile Hekimliği Anabilim Dalı KONYA

INTRODUCTION

Atherosclerotic vascular disease is a diffuse progressive condition that usually affects multiple vascular territories at the same time (1). Its manifestations are coronary heart disease (CHD), cerebrovascular disease (CVD), and peripheral arterial disease (PAD), which, taken together, have been the leading causes of death in adults for many decades (2). Cardiovascular disease is the first leading cause of death in all developed nations. As the population ages, the burden of cardiovascular disease is expected to increase (3).

Major cardiovascular and cerebrovascular events including myocardial infarction and stroke often occur in individuals without known pre-existing cardiovascular disease. The prevention of such events, including the accurate identification of those at risk, remains a serious public health challenge (4,5).

The ankle–brachial index (ABI) is the ratio of the ankle to brachial systolic blood pressure (3).

The ankle-brachial index (ABI) is a simple, inexpensive and non-invasive test used for the assessment of lower extremity arterial obstruction and for screening of patients with suspected PAD (6). ABI has been shown to be a strong predictor of subsequent cardiovascular events in patients with peripheral vascular disease in the middle-aged population and in older subjects (7,8). Major declines in resting and post-exercise ABI values are significantly associated with increased long-term mortality, and cardiac events (6).

Framingham Risk Score (FRS) is increasingly used in early risk identification of cardiovascular diseases. We calculated Framingham Risk Scores of the participants using an automatic calculator. The Framingham risk score includes the following items; age, sex, systolic blood pressure, total and high density lipoprotein cholesterol, LDL, diabetes mellitus, and smoking. We assigned participants to high risk, intermediate risk, and low risk groups based on tertiles of the calculated Framingham risk scores (4,9).

In this study, we aimed to study the relationship between Framingham Risk Score and Ankle-Brachial Index as a predictor of cardiovascular diseases in the middle-aged and older population.

MATERIALS AND METHOD

Study Design, Setting and Population

This cross-sectional study was conducted between 1st December 2009 and 31st August 2010. As the population ages, the burden of cardiovascular disease is expected to increase. Because of this reason, priority was given to a particular risk group (people aged ≥50 years). The research population of this study was comprised of 250 unselected people aged ≥50 years who presented with any problem to the Family Medicine Outpatient Clinic of the Meram Medical Faculty of Konya University. The study was approved by the ethical committee of Meram Medical Faculty of Konya University. An informed written consent was obtained from the participants. All participants responded to a questionnaire in a face-to-face manner. This questionnaire included the following items; sociodemografic characteristics, age, gender, marital status, education, chronic diseases, and the status of cigarette smoking. We excluded all participants with a history of cardiovascular disease, including myocardial infarction, stroke, peripheral arterial disease (intermittent claudication or surgery for noncardiac arterial disease), angina pectoris, or heart failure.

Systolic and Diastolic Blood Pressures

All patients were evaluated in the supine position after at least 5 minutes of resting. Systolic and diastolic blood pressures (DBP) of four extremities (right-left arms and legs) were measured with OMRON M2 sphygmomanometer. The mean value of the measured systolic blood pressures (SBP) was used for the analyses. The diagnosis of arterial hypertension was based on SBP ≥140 mmHg or DBP ≥90 mmHg or the use of antihypertensive medications (10).

Ankle-Brachial Index

We calculated the Ankle-Brachial Index (ABI) by using systolic blood pressure data. The resting ABI was determined by dividing the mean of systolic blood pressure at the ankle by the mean of the brachial systolic blood pressure. A low ankle brachial index is an indicator of atherosclerosis and has the potential to improve prediction. Some previous studies showed that patients with an ABI < 0.95 were at higher risk for cardiovascular events, compared with participants with an ABI >0.95 (11,12). In our study, the cut-off point of ABI was taken as 0.95 after Hooi and his colleagues (11).

Framingham Risk Score

Ten-year cardiovascular risk was calculated by using the Framingham risk scoring. The risk factors included in the Framingham calculation are age, gender, total cholesterol, HDL cholesterol, LDL cholesterol, systolic blood pressure, hypertension and the history of diabetes mellitus and smoking (4,9). We calculated Framingham Risk Scores (FRS) of the participants by using an automatic calculator (Figure 1) (4). FRS-1 was calculated by using total cholesterol and FRS-2 was calculated by using LDL-c. According to the NCEP/ATP III guidelines, subjects are considered to be at low risk if the estimated 10-year event rate is <10%, at high risk if the 10-year event rate is >20%, and at intermediate risk if the 10-year event rate is between 10% and 20% (13).

Smoking Status

Smoking is the most important preventable cause of morbidity and mortality worldwide (14). All participants were interviewed about present and past smoking habits. Current smokers were defined as those who had smoked 100 cigarettes and now smoking either everday (i.e., daily smokers) or irregularly (i.e., someday smokers). Ex-smokers had smoked at least 100 cigarettes in their lives but are not smoking currently. The minimum quitting period for the ex-smokers was accepted as 6 months. Never-smokers were defined as those who had never smoked (15).

Anthropometric Measurements

We measured the weight and height of the participants. Height was measured, to the nearest 0.5 cm, without shoes, back squared against the wall tape, eyes looking straight ahead. Weight was measured with a balance, to the nearest 100 grams, without shoes, in light undergarments. All measurements were taken twice. If the variation between the measurements was greater than 2 cm, a third measurement was taken. The mean of the two closest measurements was calculated. BMI was calculated as weight (in kilograms) divided by height (in meters) squared based on the World Health Organization classification (16). A body mass index (BMI) lower or equal to 18.5 kg/m^2 was defined as underweight, between 18.5 kg/m^2 and 24.9 kg/m^2 was considered as ideal weight (normal) for individuals. Overweight was defined as BMI between 25-29.9 kg/m^2, and obesity was defined as body mass index above 30 kg/m^2 (16).

Biochemical Studies

In all subjects, a fasting blood sample was collected in the morning after fasting for at least ten hours for analysis of the following biochemical parameters using standard techniques: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-c) low-density lipoprotein cholesterol (LDL-c), fasting blood glucose. We calculated Framingham Risk Scores of the participants using an automatic calculator by using the other risk factors together with LDL, HDL and total cholesterol. Diabetes was defined as fasting glycemia ≥126 mg/dL or treatment with insulin or hypoglycemic agents oral drugs (defined on the basis of the American Diabetes Association (ADA) guidelines 2007) (17,18). Dyslipidemia (DLP) was defined as TC ≥200 mg/dL or LDL-c ≥130 mg/dL, or HDL-c ≤40 mg/dL, or TG ≥150 mg/dL (17).

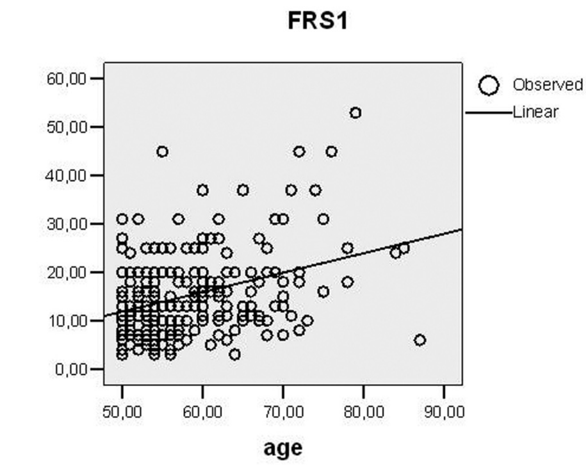

Figure 1— Linear regression analysis between age and FRS1. r^2 = Adjusted R square (r^2 = 0.119, **p = 0.000**)

Ethical Considerations

The study protocol was approved by the Ethics Committee of Meram Medical Faculty of Konya University and an informed written consent was obtained from the participants.

Statistical Analysis

The SPSS 13.0 statistical software package was used in data entry and analysis. The statistical analysis and evaluations were conducted by the authors. The minimum, maximum, mean, standard deviation, median and percentage values were used in the analysis of the data and chi-square test was used as the significance test. The significance level was taken as p<0.05. We used the Pearson's correlation coefficient and adjusted R square.

RESULTS

General Findings

Two hundred and fifty patients were included in the study. Of all the participants, 116 (46.4%) were male, 134 (53.6%) were female, the mean age was 58±7.35. The rate of cigarette smoking was 26.4% (46.9% among males, 9.0% among females).

Obesity

Obesity prevalence was found as 64.9% in females, 31.0% in males. Obesity rate was significantly higher in women than men (p<0.001).

Blood Pressure

According to JNC-7 criteria, 12.0% of the participants were found as normotensive, 39.6% pre-hypertensive, 38.0% stage-1 hypertensive, 10.4% stage-2 hypertensive.

Diabetes Mellitus

According to the basis of the American Diabetes Association Guidelines (ADA 2007), 55.6% were found as normoglycemic, 31.6% had impaired fasting blood glucose, and 12.8% had diabetes mellitus (11.2% in females, 14.6% in males). There was no significant difference in terms of manifest diabetes mellitus prevalence between males and females (χ^2=0.087, p=0.768).

Dyslipidemia

According to NCEP ATP III, 48.0% of the participants had high LDL-c (≥130 mg/dL), 46.0% high total cholesterol (≥200 mg/dL), 18.4% high triglycerides (≥150 mg/dL) and 54.0% low HDL-c (<40 mg/dL). Statistically, total cholesterol and LDL-c levels were significantly higher among females than males, [OR=2.032, %95CI; (1.223-3.375)], (p=0.016), [OR=1.541, %95CI; (0.934-2.543)], (p=0.034) respectively. HDL-c level was statistically lower in males than females [OR=3.192, %95CI; (1.893-5.383)], (p<0.001). No difference was found between females and males in triglyceride levels (p=0.560).

Ankle-Brachial Index

The mean value of ABI was 1.13±0.12 (min= 0.80, max=1.96). Of the participants, nine (3.6%) had low ABI (≤0.95). ABI levels were found to be significantly lower in smokers (p=0.006), ≥60-year-old participants (p=0.0045) and hypertensive patients (p<0.001). ABI was inversely and independently associated with age, cigarette smoking, and blood pressure. Gender, body mass index, total cholesterol, triglycerides, HDL-c and LDL-c were not significantly related to ABI (Table 1). In people aged ≥60 years, ABI risk increase (≤0.95) was found to be 3.878 times more compared with people aged <60 years [OR=3.878, %95 CI; (0.946-15.905)].

In males, ABI risk increase (≤0.95) was found to be 1.4 times higher compared with females [OR=1.464, %95 CI; (0.384-5.585)]. Furthermore, among male individuals, ≥10% FRS was found to be 1.971 times more compared with females [OR=1.971, %95 CI; (1.072-3.623)].

Framingham Risk Score

Mean values of FRS-1 and FRS-2 were found as 0.151±0.086 and 0.158±0.085 respectively. According to FRS-1, 36.8% of the participants had low, 34.8% had medium and 28.4% had high risk. On evaluation of the FRS-2 findings, we determined that 28.0% had low, 43.6% had medium, and 28.4% had high risk. Among the smokers, ≥10 FRS was found to be 2.780 times greater compared with non-smokers [OR=2.780, %95 CI; (1.241-6.228)]. The estimated 10-year event rate is was found to be 3.256 times more in the individuals having HDL-c ≤40 [OR=3.256, %95 CI; (1.754-6.044)].

There was a significant relation between diabetes mellitus, FRS1 and FRS2 (p<0.001). Among the diabetic people, FRS1 was found to be 16.349 times greater compared to non-diabetics. [OR=16.349, %95 CI; (2.199-121.558)], and FRS2 was found to be 6.103 times greater compared to non-diabetics [OR=6.103,%95 CI; (1.821-20.455)].

A mild but highly significant positive correlation existed between FRS1 and age (r=0.344, p<0.001). When linear regression analysis was done, FRS1 increase was attributed to age with 11.9% (r2=0.119) (Figure 1).

A mild but highly significant positive correlation existed between FRS2 and age (r=0.355, p<0.001). When linear regression analysis was done, FRS2 increase was attributed to age with 12.6% (r2=0.126, (p<0.001). (Figure 2).

Comparison of ABI and Framingham Risk Scoring

ABI was inversely and independently associated with FRS-1 and FRS-2 (p<0.001). Most of the patients having low ABI (88.9%) were also in the high risk group determined according to FRS (Table 2).

Table 1— Comparison of ABI and Cardiovascular Risk Factors

	ABI ≤0.95 (n=9)		ABI >0.95 (n=241)		Total (n=250)		Mean	p
Parameter	**n**	**%**	**n**	**%**	**n**	**%**		
Age								
<60	3	1.9	159	98.1	162	100.0	4.037	**0.045**
≥60	6	6.8	82	93.2	88	100.0		
Gender								
Male	5	4.3	111	95.7	116	100.0	0.313	0.576
Female	4	3.0	130	97.0	134	100.0		
Smoking status								
Current smoker	6	9.1	60	90.9	66	100.0	7.674	**0.006**
Never smoker	3	1.6	181	98.4	184	100.0		
Blood pressure (mmHg)								
<120/80 (normotensive)	–	–	30	100.0	30	100.0	12.720	0.001
120–139/80–89 (pre-hypertensive)	–	–	99	100.0	99	100.0		
140–159/90–99 (Stage–1 HT)	5	5.3	90	94.7	95	100.0		
≥160/≥100 (Stage–2 HT)	4	15.4	22	84.6	26	100.0		
Body mass index (BMI)								
<18.5 (underweight)	–	–	2	100.0	2	100.0	1.590	0.207
18.5–24.9 (normal)	3	7.5	37	92.5	40	100.0		
25–29.9 (overweight)	3	3.5	82	96.5	85	100.0		
≥30 (obesity)	3	2.4	120	97.6	123	100.0		
LDL-c (mg/dl)								
<130 (normal)	2	1.5	28	98.5	130	100	1.679	0.195
130–159 (borderline)	4	5.8	65	94.2	69	100		
160–189 (high)	3	7.7	36	92.3	39	100		
≥190 (very high)	–	–	12	100.0	12	100		
TG (mg/dl)								
<150 (normal)	6	3.8	153	96.2	159	100.0	0.162	0.687
150–199 (borderline)	2	4.4	43	95.6	45	100.0		
≥200 (high)	1	2.2	45	97.8	46	100.0		
Total cholesterol (mg/dl)								
<200	4	3.0	131	97.0	135	100.0	0.752	0.386
200–239 (borderline)	3	3.5	82	96.5	85	100.0		
≥240 (high)	2	6.7	28	93.3	30	100.0		
HDL-c (mg/dl)								
<40 (low)	7	59.3	128	40.7	135	100.0	2.116	0.146
≥40 (normal)	2	36.0	113	79.0	115	100.0		
Fasting blood glucose (mg/dl)								
<100 (normal)	3	2.2	136	97.8	139	100.0	1.864	0.172
100–125 (impaired fasting glucose)	4	5.1	75	94.9	79	100.0		
≥126 (manifest diabetes mellitus)	2	6.3	30	93.8	32	100.0		

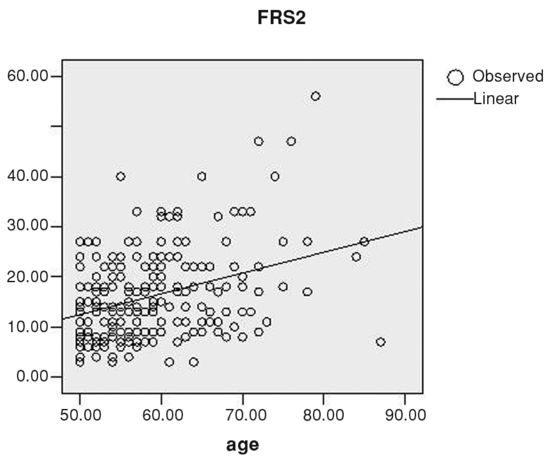

Figure 2— Linear regression analysis between age and FRS2. r^2 = Adjusted R square (r^2 = 0.126, **p = 0.000**)

DISCUSSION

Before concluding, the limitations of the study should be addressed. As the population ages, the burden of cardiovascular disease is expected to increase. The early risk estimation of CVD by using ABI and FRS is vital. Although the overall sample was relatively large, we could reach only a small group. In addition, although a quite close match, this study group is not entirely representative of the Turkish population. The study includes only the inhabitants of Konya.

Measuring the ABI is a valid procedure to confirm the diagnosis of PAD when this diagnosis is suspected on clinical grounds. Our current study shows that patients with a low ABI have a poorer prognosis with regard to cardiovascular morbidity and mortality. Thus, apart from being a diagnostic tool, the ABI can be used to detect those PAD patients who are at high risk for a future cardiovascular event. In those patients, preventive efforts should be focused on modification of risk factors such as hypertension, diabetes, smoking and hypercholesterolemia.

In this study, 250 unselected people aged ≥50 years were included. Ankle-Brachial Index (ABI) has been shown to be a strong predictor of extend and severity of cardiovascular diseases. Recent studies have presented the increase in total and cardiovascular risk associated with low ABI. In our study, the cut-off point of ABI was taken as 0.95 after Hooi et al. (11) and the mean value of ABI was 1.13±0.12 (min= 0.80, max=1.96). Of the participants, nine (%3.6) had low ABI (≤0.95). A significantnegative correlation existed between ABI and age, cigarette smoking and blood pressure. A significant correlation was observed between low ABI and Framingham Risk Scores. This result shows that low Ankle-Brachial Index (≤0.95) can be used to estimate the risk of future cardiovascular events.

In the previous studies, different ABI cut-off points were taken. These values were 1.1 (Diehm and his colleagues), 1.4 (Resnick), 1.01 (Hollander), 0.97 (van der meeer), 0.95 (Hooi), 0.9 (Papamichael, Feringa, Murabito, Lee, Leng Doobay) (2,3,6,7,11,19-24).

In their monitored prospective observational study, Diehm et al. found that the risk of mortality increased linearly in the lower ABI categories compared with an ABI≥1.1. Patients with a low ABI, who can be readily identified in a primary care setting, have a substantially

Table 2— Comparison of ABI and Framingham Risk Scoring

	ABI ≤0.95 (n=9)		ABI >0.95 (n=241)		Total (n=250)		Mean	p
	n	%	n	%	n	%		
Framingham risk score (FRS)-1 (According to total cholesterol)								
<10 (low risk)	–	–	92	100.0	92.0	100.0	13.647	0.001
10–19 (middle risk)	1	1.1	86	98.9	87	100.0		
≥20 (high risk)	8	11.3	63	88.7	71	100.0		
Framingham risk score (FRS)-2 (According to LDL-c)								
<10 (low risk)	–	–	70	100.0	70	100.0	12.910	0.001
10–19 (middle risk)	1	0.9	108	99.1	109	100.0		
≥20 (high risk)	8	11.3	63	88.7	71	100.0		

increased risk of mortality and severe vascular events. Patients with an ABI between 1.1 and 0.9 should be considered and followed up as borderline PAD cases. Particular attention should be paid to patients with PAD and previous vascular events as their risk is markedly increased (2).

Resnick et al. showed that the patients with low ABI were significantly older and more frequently had hypertension, higher triglycerides, total and LDL cholesterol, and lower HDL cholesterol compared to participants with normal ABI at baseline (19). Their results for age and blood pressure were similar to our study.

In Van der Meer's population-based cohort study, measurement of the ABI was suggested to be useful in people 50 years old or people are at high risk. The value of ABI <0.97 was found to be associated with increased risk of CHD (21).

Comparable to our results, Hooi et al. stated that the risk of cardiovasculer morbidity and mortality is increased in patients having a value of ABI <0.95 (11).

Papamichael et al. revealed that the value of ABI <0.90 was an independent predictor for cardiovascular events after adjustment for age, low-density lipoprotein cholesterol, carotid and femoral intima–media thickness, and Gensini score in their study on 165 consecutive patients who were referred to an institution for elective coronary angiography (7). In this study, smoking and diabetes mellitus were found to be independently related to ABI.

Doobay et al. detected that the sensitivity and specificity of a low ankle–brachial index to predict incident coronary heart diseases were 16.5% and 92.7% and cardiovascular mortality were 41.0% and 87.9%, respectively (3). FRS estimates the risk of having a heart attack or dying from heart disease within 10 years. We found significant correlation between low ABI and Framingham Risk Scores.

Fowkes et al. investigated 10-year total mortality, cardiovascular mortality and major coronary event rates in men and women using Framingham Risk Category and ABI at baseline for sixteen cohort studies combined in the ABI Collaboration. The results showed that a low ABI (0.90 or less) predicted vastly increased risks of 10-year cardiovascular mortality in both men and women. They found that the ABI provided independent risk information as compared with the FRS and, when combined with the FRS, a low ABI (≤ 0.9) approximately doubled the risk of total mortality, cardiovascular mortality and major coronary events across all Framingham risk categories (4).

CONCLUSION

The ABI is a relatively simple noninvasive procedure and is appropriate for use in a primary care setting. Framingham Risk Score shows the 10-year mortality, cardiovasculer mortality and major coronary event rate. In conclusion, ABI is a simple index related to the extent of atherosclerosis in coronary and noncoronary arterial beds, reflecting generalized atherosclerosis (25). Using ABI and FRS could be useful in assessing the risk for cardiovascular events in patients with coronary artery disease. FRS has shown to significantly underestimate the risk in population because of the exclusion of significant risk factors such as insulin resistance, obesity and family history. 10-year global risk of 20% or greater by FRS is considered to be a high risk and suitable for secondary prevention (25).

We could not find any study comparing Ankle Brachial Index with Framingham risk score in the literature. Our study directly shows the relationship between these methods. We emphasize in this study that using Framingham Risk Scoring and Ankle Brachial Index are important predictors of early risk estimation of cardiovascular diseases. We expect that our study which emphasizes the importance of early recognition in the primary care settings will contribute to the literature .

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