Original Article

A study of association of ankle–brachial Index with cardiovascular risk factors in type 2 diabetes mellitus

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Abstract

Background: Ankle–Brachial Index (ABI) has a proven role in the baseline assessment of the individuals who are at a risk of cardiovascular diseases. Sparse data are available regarding the association of cardiovascular risk factors in type 2 diabetes mellitus (T2DM) and ABI from India.

Material and Methods: A cross-sectional study was conducted at a tertiary teaching hospital in South India among patients with T2DM during the period October 2014–June 2016. ABI was measured using vascular Doppler-sphygmomanometer. Independent cardiovascular risk factors were assessed and their association with ABI was studied.

Results: ABI was negatively correlated to cardiovascular risk factors such as age, body mass index, duration of T2DM, duration of hypertension and systolic blood pressure (SBP) and diastolic blood pressure (DBP) in the entire study population as well as in both genders separately. Among females, a statistically significant association of low ABI (<0.9) was observed with SBP and duration of hypertension only, whereas, in males, SBP, DBP and duration of T2DM were significantly associated with low ABI. Of note, among the individuals with proven coronary artery disease (CAD), statistically significant association with low ABI was also observed.

Conclusions: In our study, low ABI has been observed with increasing age, obesity, high systolic and DBPs, increasing the duration of diabetes and hypertension, however, with a distinctive statistically significant association in males and females. Among the individuals with documented CAD, a significant proportion had a low ABI.

Keywords: Ankle–Brachial Index, cardiovascular, risk factors, type 2 diabetes mellitus

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INTRODUCTION

As per the concept of common soil,[1] type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD) are described as consequences of immune inflammatory response to the oxidative insult. In addition, these also share a common genetic and experimental antecedent, and thus aptly described as ‘spring from the same soil’.

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The concept of cardiodiabetology, thus is, therefore, assuming global importance these days. The Multiple Risk Factor Intervention Trial[2,3] studies have established the fact that diabetic males are three times, and females six times more prone for developing CAD, suggesting diabetic state *per se*, a very special role. Cardiovascular disease is statistically found to be a more common cause

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of death in diabetes in comparison with microvascular complications.

Patients with T2DM have accelerated atherosclerosis. Peripheral artery disease (PAD), one of the peripheral vascular diseases, is a clinical manifestation of atherosclerosis. Ankle–Brachial Index (ABI) described first by Winsor[4] in 1950, is a simple as well as non-invasive procedure usually done for the diagnosis of PAD and its risk assessment. American Heart Association also recommended the measurement of ABI as a diagnostic criterion for the prevalence of PAD.[5] It is the ratio of resting systolic blood pressure (SBP) at ankle to that in arm. It has also been used as an indicator for the assessment of atherosclerosis and thus is extrapolated to the assessment of cardiovascular risk. A low ABI is an important risk factor for mortality among patients with history of stroke, angina (myocardial infarction) or DM.[6]

Many population-based studies have revealed the association of cardiovascular events in patients with T2DM and PAD. The present study is designed to study the association of ABI with independent cardiovascular risk factors in T2DM.

MATERIAL AND METHODS

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all the participants. We studied 257 T2DM patients (182 male) above 40 years of age who attended the Medicine Outpatient Department, Kasturba Medical College, Manipal, Karnataka, during the period October 2014–June 2016. T2DM was diagnosed according to the American Diabetes Association 2015 guidelines.[7] Patients over 40 years of age, patients with T1DM and other forms of diabetes, those using beta-blockers, calcium channel blockers, nitrates and hydralazine, patients in whom both lower limbs were amputated were excluded from the study.

Data regarding conventional risk factors such as age, duration of T2DM, hypertension, tobacco smoking, dyslipidaemia, alcohol consumption and diagnosis of CAD were recorded from all the patients. Height(m) and weight (kg) were measured and body mass index (BMI-kg/m^2) was calculated as weight (kg) divided by height (m)^2. As recommended by the American Society of Hypertension[8] using mercury sphygmomanometer, blood pressure was measured in the right forearm in sitting position. Two consecutive readings for each SBP and diastolic blood pressure (DBP) were recorded and the average was taken. Using the same mercury sphygmomanometer and vascular Doppler (VCOMIN 300 series) (VCOMIN®, Shenzen, China), the highest SBP reading in both the arms, on the brachial and radial artery, were recorded. The SBP in both legs was measured on the dorsalis pedis (DP) and posterior tibial (PT) arteries. The ABI of each leg was calculated by dividing the higher of the PT or DP SBP by the higher of the right or left arm SBP. Based on the ratio, patients were categorised into four categories: ABI of <0.9 (Category 1) which indicates a low ABI; ABI 0.9–1.1 (Category 2); ABI 1.1.–1.3 (Category 3) which are acceptable and normal ranges, respectively and ABI >1.3 (Category 4) denoted as high ABI. Among these, ABI of <0.9 indicates PAD and an assumption that they have significant cardiovascular risk.

Statistical analysis

All data were entered in a structured proforma and recorded in Microsoft Excel (Microsoft Corporation, Richmond, USA). Continuous variables are summarised as mean ± standard deviation, categorical variables are presented as percentages. Continuous variables were compared using one-way analysis of variance and Kruskal–Wallis test. *Post hoc* analysis for pair-wise comparison was done by Duncan's method. Categorical variables are compared by Chi-square test. Correlation between ABI and variables were analysed using Pearson's correlation coefficient. To determine the independent influences and association of individual risk factors on ABI, a multiple logistic regression analysis was done for both genders. The statistical software IBM SPSS Statistics Version 20 (IBM Corp Somers, NY, USA).

RESULTS

Two hundred and fifty-seven patients (182 men; 70.8%) with T2DM were included in the study. Their mean age was 56.9 ± 9.2. The comparison of baseline variables between men and women is shown in Table 1. Age, BMI, SBP, DBP, duration of T2DM and duration of hypertension, all were significantly higher in women than in men; ABI was similar in both the groups.

Table 1: Baseline characteristics of the study participants

Variables*	Males (*n*=182)	Females (*n*=75)
ABI	1.0±0.1	0.97±0.1
Age (years)	56.7±9.6	57.3±7.9
BMI (kg/m^2)	24.7±3.8	25.7±4.2
SBP (mmHg)	135.7±16.0	137.2±17.8
DBP (mmHg)	86.3±10.2	86.5±9.6
Duration of T2DM (years)	7.0±6.9	7.1±6.2
Duration of hypertension (years)	1.6±4.3	2.1±4.6

*All data are expressed as mean±SD.
SD=Standard deviation; ABI=Ankle-Brachial Index; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; T2DM=Type 2 diabetes mellitus

The distributions of cardiovascular risk factors across ABI according to sex are presented in Tables 2 and 3. In most of the patients, the ABI was between 0.9 and 1.1 (men 59.3%; women 54.7%) followed by <0.9 (men 30.8%: Women 29.3%) and 1.1–1.3 (7.7% in men; 14.7% in women). The prevalence of high ABI >1.3% was observed to be 2.2% in men and 1.3% in women.

The overall differences of means in different categories of ABI are shown in Table 2 (males) and Table 3 (females). Most of the hypertensives in T2DM (30.8% and 29.3%) were found in ABI values <0.9 in men and women. The highest mean values of SBP (144 ± 16.3) and DBP (90.5 ± 9.5) were observed in low ABI (<0.9) in men, whereas the highest mean values of BMI (26.8 ± 2.3), SBP (147.2 ± 17.7) and DBP (89.2 ± 9.1) in low ABI <0.9 were observed in women.

All the risk factors were negatively correlated with ABI in both men and women patients of T2DM [Table 4]. However, significant correlation was observed for SBP ($r = -0.355$, $P = 0.002$) and duration of hypertension ($r = -0.4$, $P = 0.0001$) in females, and for SBP ($r = -0.297$, $P = 0.0001$), DBP ($r = -0.27$, $P = 0.0001$) and duration of T2DM ($r = -0.155$, $P = 0.037$) in males. No significant correlation was found between age and BMI in both the sexes. In women, significant correlation was also not found between DBP and duration of T2DM. In men, duration of hypertension did not correlate significantly with ABI.

Table 4: Correlation analysis

Variables	Females		Males	
	r	*P*	*r*	*P*
Age	−0.216	0.063	−0.117	0.116
BMI	−0.023	0.847	−0.032	0.664
SBP	−0.355	0.002	−0.297	0.0001
DBP	−0.177	0.129	−0.27	0.0001
Duration of T2DM	−0.153	0.19	−0.155	0.037
Duration of hypertension	−0.4	0.0001	−0.109	0.144

ABI=Ankle-Brachial Index; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; T2DM=Type 2 diabetes mellitus

To determine the independent influences and association of individual risk factors on ABI, a multiple logistic regression analysis was done for both the genders [Table 5]. In women, a significant inverse association was observed between ABI and SBP (odds ratio [OR] 0.931, 95% confidence intervals [CIs] 0.871–0.995, $P = 0.035$), whereas in men, a significant inverse association was observed between ABI and BMI (OR 0.86, 95% CI 0.781–0.946, $P = 0.002$), SBP (OR 0.946, CI 0.908–0.985, $P = 0.007$) and duration of T2DM (OR 0.92, CI 0.866–0.977, $P = 0.007$). No association has been observed between age, DBP and duration of hypertension in both sexes. Association between ABI and duration of T2DM and BMI was not found in women.

Table 2: Distribution of cardiovascular risk factors across the ankle-brachial Index categories among males (*n*=182) with type 2 diabetes mellitus

Variable	ABI <0.9 (*n*=56)	ABI 0.9-1.1 (*n*=108)	ABI 1.1-1.3 (*n*=14)	ABI >1.3 (*n*=4)	Significance
Age (years)*	59.7±9.4	54.4±9.1	60.9±11.1	60.5±7.8	0.002
BMI (kg/m^2)*	26.0±3.5	23.8±3.5	25.1±4.6	28.0±7.9	0.02
SBP (mmHg)*	144±16.3	133.2±13.3	128.4±20.3	113.5±8.8	<0.001
DBP (mmHg)*	90.5±9.5	85.1±9.5	82.6±12.0	71.5±3.4	<0.001
Duration of T2DM (years)†	10.3±8.1	5.3±5.9	7.8±6.1	5.7±3.3	<0.001
Duration of hypertension (years)†	2.9±5.6	1.0±3.5	1.4±2.9	0.5±1.0	0.01

*One-way analysis of variance; †Kruskal-Wallis test. ABI=Ankle-brachial Index; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; T2DM=Type 2 diabetes mellitus

Table 3: Distribution of cardiovascular risk factors across the ankle-brachial Index categories among females (*n*=75) with type 2 diabetes mellitus

Variable	ABI <0.9 (*n*=22)	ABI 0.9-1.1 (*n*=41)	ABI 1.1-1.3 (*n*=11)	ABI >1.3 (*n*=1)	Significance
Age (years)*	60.1±8.4	55.8±6.6	56.3±9.5	72	0.047
BMI (kg/m^2)*	26.8±2.3	25.2±4.5	25.6±6.1	26.4	0.57
SBP (mmHg)*	147.2±17.7	132.4±15.9	134.5±18.4	144	0.014
DBP (mmHg)*	89.2±9.1	85.2±9.4	85.6±11.7	88	0.474
Duration of T2DM (years)†	9.6±6.9	5.6±5.3	6.9±7.0	15	0.06
Duration of hypertension (years)†	4.9±7.0	0.9±2.4	1.2±3.0	0	0.054

*One-way analysis of variance; †Kruskal-Wallis test. ABI=Ankle-brachial Index; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; T2DM=Type 2 diabetes mellitus

Table 5: Multiple logistic regression analysis

Clinical factors	Females			Males		
	OR	95% CI	*P*	OR	95% CI	*P*
Age (years)	0.973	0.896-1.056	0.507	0.977	0.939-1.018	0.267
BMI (kg/m^2)	0.901	0.781-1.040	0.155	0.86	0.781-0.946	0.002
SBP (mmHg)	0.931	0.871-0.995	0.035	0.946	0.908-0.985	0.007
DBP (mmHg)	1.108	0.985-1.247	0.088	1.028	0.965-1.094	0.39
Duration of T2DM (years)	0.955	0.862-1.059	0.383	0.92	0.866-0.977	0.007
Duration of hypertension (years)	0.862	0.721-1.029	0.101	1.031	0.940.9-1.13	0.512

ABI=Ankle-Brachial Index; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; T2DM=Type 2 diabetes mellitus; OR=Odds ratio; CI=Confidence interval

DISCUSSION

Our study demonstrated the prevalence of low ABI (<0.9) in the study population (30.4%) with 29.3% in females and 30.8% in males. These findings were in agreement with the results of earlier studies.[9-11] Low ABI was significantly associated with cardiovascular risk factors after adjusted for age in both sexes. In our study, among the entire study population, a significant negative correlation was observed between ABI and cardiovascular risk factors such as age, blood pressures (SBP and DBP), duration of T2DM and duration of hypertension; however, a significant association was not observed with respect to BMI.

Among males, a significant negative correlation was observed between ABI and SBP (144 ± 16.3 mmHg), DBP (90.5 ± 9.5 mmHg) and duration of diabetes (10.3 ± 8.1 years), and in females, significant negative correlation was observed with SBP (147.2 ± 17.7 mmHg) and duration of hypertension (4.9 ± 7.0 years). These negative correlations strengthen the hypothesis that a low ABI ≤0.9 is a useful diagnostic tool for detecting PAD and would also be considered as a strong predictor for cardiovascular morbidity and mortality in T2DM patients.

A significant association between low ABI with increasing age was observed in our study as in the other studies.[12-14] Age and BMI although were negatively correlated with ABI in both genders, a significant correlation was not observed. Statistically significant association had not been observed with other risk factors such as smoking, dyslipidaemia and alcohol consumption in the present study. The data in our study are in contrast to the known fact of the significant association of these risk factors demonstrated in multiple studies.[15,16] However, a lack of proper consensus of a complete data regarding these risk factors among the study population, probably might be the reason for contrasting results.

Of note, among the individuals with proven CAD, a high percentage of low ABI with statistically significant association was also observed. As the data on the presence of documented CAD in our study was limited, analysis of the presence of CAD with different ABI groups disclosed a remarkable percentage of individuals in the low ABI (<0.9) group and it underscores a significant association in comparison to the other groups. A systematic review[17] also reported similar observations and thus an emphasis on the necessity of incorporating ABI measurement as a potential tool in early recognition of the cardiovascular risk is recommended.

In the present study, among females with low ABI (<0.9), a significant association was not observed with duration of diabetes (9.6 ± 6.9 years), probably because of relatively low sample size of the female population in our study. Among males with low ABI (<0.9), the mean duration of diabetes (10.3 ± 8.1 years) in our study was found to be significant. This difference in means between the two studies stresses the importance of glycaemia levels and personal factors such as dietary habits and socioeconomic factors which exhibit indirect influence on the glycaemia levels, in addition to the duration of diabetes.

Among females, the mean duration of hypertension was 4.9 ± 7.0 years, and in males, it was observed to be 2.9 ± 5.7 years, and a significant association was observed in comparison to other groups among males. Majority of literature search focussed on the presence of hypertension in the study population rather than the duration of hypertension and our study was probably the first, in South India which spotlights on the duration of hypertension also as a significant risk factor.

Multiple logistic regression analysis done to assess the association of risk factors independently with ABI revealed a significant inverse association between ABI and SBP (OR: 0.931) in females, whereas in males, it showed a significant association between ABI and BMI (OR= 0.86), SBP (OR: 0.946) and duration of T2DM (OR: 0.92). Most of these results were in conjunction with the observations in studies.[13,18]

Our observations in comparison with other studies underscore the importance of ABI and its significant association with conventional cardiovascular risk factors. It highlights the significance of ABI in early assessment of cardiovascular risk and strengthens the debate in favour of utility of low ABI value as a powerful predictor of future cardiovascular disease. However, there is a need for a further prospective study with large sample size to strengthen our study is indubitable.

As a well-known fact, the incidence of cardiovascular risk is high in individuals with diabetes and requires a high and constant vigil, and assessment of ABI is a simple tool helpful in this process. The present study reveals negative and statistically significant association between ABI and cardiovascular risk factors such as age, high SBP and DBP, increasing duration of T2DM and hypertension which are distinct between males and females. The data emphasise on recommending the assessment of ABI in predicting cardiovascular outcomes in T2DM patients.

Since the study is cross-sectional, it does not show cause–effect relationship. Variables such as duration of T2DM, smoking and alcohol were self-reporting, and there were no records available for cross-verification. Dyslipidaemia status was taken into consideration whether or not the current cholesterol levels were measured for all patients. Concurrent glycaemic status and status of intake of drugs such as antihypertensives and hypolipidaemics were not taken into consideration to determine the exact concurrent status of respective blood pressure and lipid status. Further prospective study should be undertaken to determine the relationship between ABI distribution and cardiovascular diseases on follow-up.

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Conflicts of interest

There are no conflicts of interest.

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