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Analysis of Ankle-Brachial Index, Waist-Hip Ratio, Ejection-Fraction, Obesity, Smoking, Alcohol Habits, Diabetes and Hypertension as Independent Predictors of Complexity and Severity of Coronary Artery Disease

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Abstract

Background: The present study was conducted to examine the association between various coronary risk factors and clinical parameters, with special emphasis on ankle-brachial index, in predicting the severity and complexity of coronary artery disease. Methods: Patients diagnosed with coronary artery disease at our hospital between September-2012 and December-2014 were examined in this study. Selected patients were screened for cardiovascular risk factors including diabetes, hypertension, smoking, and alcohol habits as well as for clinical parameters including body-mass index, waist-hip ratio, ankle-brachial index, and ejection fraction. All patients underwent coronary angiography and were evaluated for severity of coronary artery disease (based on number of vessels involved) and complexity of coronary angiographic lesions (measured by computer-assisted Syntax score calculator). The collected data were analyzed to determine the role of cardiovascular risk factors and clinical parameters as predictors of complexity and severity of coronary artery disease. Results: A total of 211 patients (mean age: 54.64 ± 9.9 years; 81% males) with coronary artery disease were analyzed. Findings revealed that diabetes mellitus ($p < 0.001$), hypertension ($p < 0.001$), smoking habits ($p = 0.036$), and low ankle-brachial index ($p < 0.001$) were independent predictors of complex coronary artery disease as measured by Syntax score. Significant associations were also evident between severity of coronary artery disease and diabetes mellitus ($p < 0.001$), hypertension ($p < 0.001$), and ankle-brachial index ($p < 0.001$). Conversely, other cardiovascular risk factors including body-mass index, alcohol habits, wait-hip ratio, and ejection fraction did not exhibit significant associations with severity and complexity of coronary artery. Conclusions: The early diagnosis of coronary artery can be predicated by evaluating diabetes, hypertension, and smoking habits in patients presenting with acute coronary syndrome. In addition, ankle-brachial index can be used as an effective non-invasive bed-side tool, as an al-

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ternative to Syntax score, in predicting the severity and complexity of coronary artery disease.

Keywords

Ankle-Brachial Index, Cardiovascular Risk Factors, Coronary Artery Disease, Peripheral Arterial Disease, Predictor, Syntax Score, Waist-Hip Ratio

1. Introduction

Coronary artery disease is a leading cause of morbidity and mortality worldwide. In recent years, there has been an increasing trend in the prevalence of associated cardiovascular risk factors such as diabetes mellitus, hypertension, smoking, alcohol, dyslipidemia, and obesity among patients with coronary artery disease [1]. Several studies have also identified a significant association between these cardiovascular risk factors and severity and complexity of coronary artery disease [2]-[5]. In recent years, a high prevalence of peripheral arterial disease has been noted among patients with coronary artery disease [6]. Ankle-brachial index (measured <0.9) is an effective non-invasive tool to detect peripheral arterial disease. Since coronary artery disease and peripheral arterial disease are manifestation of atherosclerotic process, it is considered that ankle-brachial index may also reflect coronary atherosclerotic burden [7]. Few studies have also shown a link between ankle-brachial index and Syntax score, a lesion based angiographic scoring system introduced as a tool to grade the complexity of coronary lesions [7] [8]. However, there are no such studies from India till date. With this background, the present study was conducted to study the relation between various coronary risk factors and clinical parameters, with special emphasis on ankle-brachial index, in predicting the severity and complexity of coronary artery disease.

2. Methods

2.1. Study Population

Patients with coronary artery disease presenting to the Osmania General Hospital, Hyderabad between September-2012 and December-2014 were analyzed in this study. Inclusion criteria included 1) age ≥18 years, 2) presentation of ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), or unstable angina 3) diagnosis of coronary artery disease by coronary angiography, and 4) willingness to sign informed consent. Patients with chronic stable angina, dilated cardiomyopathy, ischemic cardiomyopathy and chronic kidney disease were excluded from the study.

2.2. Data Collection

Selected patients were screened for diabetes and hypertension. Data on smoking and alcohol habits for each patient were also recorded. Body-mass index (BMI) was calculated by dividing body weight (kilograms) by height (meters) squared. Based on BMI data, patients were divided in normal (18.5 - 25 kg/m^2), overweight (25 - 30 kg/m^2), and obese (>30 kg/m^2) categories. Similarly, waist-hip ratio was evaluated as the ratio of circumference of the waist to that of the hips. Subsequently, patients were divided in to two groups based on the cut-off value for waist-hip ratio set at 1.0 for men and 0.85 for women. All patients were also evaluated for ankle-brachial index by measuring the systolic blood pressure from both brachial arteries and from both the dorsalis pedis and posterior tibial arteries using the Doppler device after the patient has been at rest in the supine position for 10 minutes. The cut-off level for ankle brachial index was <0.9. Left-ventricular ejection fraction was measured by echocardiography, and the cut-off level was <55%. Moreover, the severity of coronary artery disease and number of vessels with significant stenosis or occlusion were noted based on angiographic assessment. Syntax score of coronary angiographic lesions was calculated using computer-assisted Syntax score calculator. Based on the Syntax score data, patients were distributed in to three groups, namely mild (<22), intermediate (22 - 32) and high (>32) Syntax score.

2.3. Statistical Analysis

Continuous data are presented as means and standard deviations, while categorical data are presented as fre-

quencies and percentages. Chi-square test was used to analyze the association of cardiovascular risk factors and clinical parameters in predicting the complexity and severity of coronary artery disease. A two-sided alpha level of 0.05 was used to identify statistically significant association. All data were analyzed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15.

3. Results

3.1. Baseline Demographics

A total of 211 patients with coronary artery disease were analyzed in this study. Mean age of the study population was 54.64 ± 9.99 years (range: 26 - 80 years). Majority of patients belonged to 51 - 60 years age group. Of recruited patients, 171 (81%) were male and 40 (19%) were female. Diabetes mellitus was present in 75 (35.5%) patients, while hypertension was present in 131 (62.1%) patients. Smoking and binge alcohol habits were reported in 51.2% and 37.4% of patients respectively. In addition, about one-third of patients with coronary artery disease were identified to have clinical or subclinical peripheral arterial disease, as measured by abnormal ankle-brachial index. Other baseline characteristics are described in **Table 1**.

3.2. Predictors of Complexity of Coronary Artery Disease

Findings of the analysis of association between cardiovascular risk factors and complexity of coronary artery disease, as measured by Syntax scores, are described in **Table 2**. We found that diabetes mellitus ($p < 0.001$), hypertension ($p < 0.001$), smoking habits ($p = 0.036$), and low ankle-brachial index ($p < 0.001$) were independent predictors of complex coronary artery disease. On the other hand, the associations between Syntax scores and body-mass index, alcohol habits, wait-hip ratio, and left-ventricular ejection fraction were found to be statistically insignificant.

3.3. Predictors of Severity of Coronary Artery Disease

Findings of the analysis of association between cardiovascular risk factors and severity of coronary artery disease, as measured by number of vessels involved, are described in **Table 3**. Significant associations were evident between severity of coronary artery disease and diabetes mellitus ($p < 0.001$), hypertension ($p < 0.001$) and ankle-brachial index ($p < 0.001$). Other cardiovascular risk factors or clinical parameters did not exhibit significant associations.

4. Discussion

Ankle-brachial index is the ratio of the systolic blood pressure measured at the ankle to that measured at the

Table 1. Baseline and clinical characteristics of enrolled patients.

Variable	211 patients
Age (years)	54.64 ± 9.99
Males	171 (81.0%)
Diabetes mellitus	75 (35.5%)
Hypertension	131 (62.1%)
Smoking	108 (51.2%)
Alcohol	79 (37.4%)
Body-mass index (kg/m^2)	24.22 ± 3.60
Waist-hip ratio	1.02 ± 0.09
Ankle-brachial index	0.98 ± 0.10
Ejection fraction (%)	53.65 ± 9.62

Data are expresses as mean ± SD for continuous variables and as frequency (percentage) for categorical variables.

Table 2. Analysis of association between cardiovascular risk factors and Syntax score.

Variable	Category	Syntax score*			p value†
		Mild (n = 126; 59.7%)	Moderate (n = 37; 17.5%)	Severe (n = 48; 22.7%)	
Cardiovascular risk factors					
Diabetes mellitus	Yes (n = 75; 35.5%)	28 (13.3%)	16 (7.6%)	31 (14.7%)	**<0.001**
	No (n = 136; 64.5%)	98 (46.4%)	21 (10.0%)	17 (8.1%)	
Hypertension	Yes (n = 131; 62.1%)	62 (29.9%)	29 (13.7%)	40 (19.0%)	**<0.001**
	No (n = 80; 37.9%)	63 (29.9%)	9 (4.3%)	8 (3.8%)	
Smoking	Yes (n = 108; 51.2%)	73 (34.6%)	13 (6.2%)	22 (10.4%)	0.036
	No (n = 103; 48.8%)	53 (25.1%)	24 (11.4%)	26 (12.3%)	
Alcohol	Yes (n = 79; 37.4%)	53 (25.1%)	11 (5.2%)	15 (7.1%)	0.237
	No (n = 132; 62.6%)	73 (34.6%)	26 (12.3%)	33 (15.6%)	
Clinical parameters					
Body-mass index	Normal (n = 127; 60.2%)	82 (38.9%)	21 (10.0%)	24 (11.4%)	0.378
	Overweight (n = 72; 24.1%)	39 (18.5%)	13 (6.2%)	20 (9.5%)	
	Obese (n = 12; 5.7%)	5 (2.4%)	3 (1.4%)	4 (1.9%)	
Waist-hip ratio	>1 for men; >0.85 for women (n = 58; 27.5%)	40 (19.0%)	7 (3.3%)	11 (5.2%)	0.222
	<1 for men; <0.85 for women (n = 153; 72.5%)	86 (40.8%)	30 (14.2%)	37 (17.5%)	
Ankle-brachial index	<0.9 (n = 70; 33.2%)	18 (8.5%)	17 (8.1%)	35 (16.6%)	**<0.001**
	≥0.9 (n = 141; 66.8%)	108 (51.2%)	20 (9.5%)	13 (6.2%)	
Ejection fraction	<55% (n = 111; 52.6%)	63 (29.9%)	22 (10.4%)	26 (12.3%)	0.581
	≥55% (n = 100; 47.4%)	63 (29.9%)	15 (7.1%)	22 (10.4%)	

*Data are expresses as frequency (percentage); †Chi-square test; ABI: Ankle-brachial index; BMI: Body-mass index.

brachial artery. Initially, this index was proposed as an easy, reliable, and noninvasive tool to determine the presence and severity of lower-extremity peripheral arterial disease [9]. In current practice, the ankle-brachial index can also be used as an indicator of coronary atherosclerosis even in the absence of symptoms of peripheral arterial disease [10]. In addition, the inverse relationship between ankle-brachial index and cardiovascular risk factors as well as its association with cardiovascular events (myocardial infarction, stroke and death) has been well established [11] [12]. However, Indian studies determining the role of ankle-brachial index as a predictor of severity of coronary artery disease are limited. In this regard, we examined the association between ankle-brachial index and coronary artery disease severity. We found that ankle-brachial index could be a useful method in assessing both the atherosclerotic risk factors and the degree of coronary involvement in suspected patients.

In the present study, most of the patients belonged to age group of 51 - 60 years. It is known that ageing leads to decreased ankle-brachial index as a result of arterial stiffening [13]. Further, a significant male predominance is commonly observed in majority of studies on coronary artery disease and peripheral arterial disease. In similar lines, about 80% of patients with coronary artery disease were male in the present study. Such gender-related differences in peripheral artery disease may be attributable to smaller baseline calf muscle area in women [14].

Metabolic syndrome is also a significant risk factor for coronary artery disease as well as peripheral arterial disease. In a study of 3041 adults aged ≥40 years, the age-adjusted prevalence of peripheral arterial disease among participants with and without high glucose was 5.9% and 3.6% respectively (p = 0.075), and with and without abdominal obesity was 4.2% and 3.7% respectively (p = 0.337) [15]. In addition, another trial suggested that diabetes is associated with increased atherogenicity and complexity of the disease, measured by Syntax

Table 3. Analysis of association between cardiovascular risk factors and severity of coronary artery disease.

Variable	Category	Coronary vessels involved*					p value†
		Recanalized (n = 12; 5.7%)	SVD (n = 79; 37.4%)	DVD (n = 59; 28.0%)	TVD (n = 58; 27.5%)	TVD + LMCA (n = 3; 1.4%)	
Cardiovascular risk factors							
Diabetes mellitus	Yes (n = 75; 35.5%)	2 (0.9%)	15 (7.1%)	27 (12.8%)	30 (14.2%)	1 (0.5%)	**<0.001**
	No (n = 136; 64.5%)	10 (4.7%)	64 (30.3%)	32 (15.2%)	28 (13.3%)	2 (0.9%)	
Hypertension	Yes (n = 131; 62.1%)	7 (3.3%)	35 (16.6%)	43 (20.4%)	43 (20.4%)	3 (1.4%)	**<0.001**
	No (n = 80; 37.9%)	5 (2.4%)	44 (20.9%)	16 (7.6%)	15 (7.1%)	0 (0.0%)	
Smoking	Yes (n = 108; 51.2%)	7 (3.3%)	48 (22.7%)	25 (11.8%)	27 (12.8%)	1 (0.5%)	0.210
	No (n = 103; 48.8%)	5 (2.4%)	31 (14.7%)	34 (16.1%)	31 (14.7%)	2 (0.9%)	
Alcohol	Yes (n = 79; 37.4%)	3 (1.4%)	36 (17.1%)	21 (10.0%)	19 (9.0%)	0 (0.0%)	0.244
	No (n = 132; 62.6%)	9 (4.3%)	43 (20.4%)	38 (18.0%)	39 (18.5%)	3 (1.4%)	
Clinical parameters							
Body-mass index	Normal (n = 127; 60.2%)	7 (3.3%)	50 (23.7%)	35 (16.6%)	32 (15.2%)	3 (1.4%)	0.725
	Overweight (n = 72; 24.1%)	5 (2.4%)	24 (11.4%)	22 (10.4%)	21 (10.0%)	0 (0.0%)	
	Obese (n = 12; 5.7%)	0 (0.0%)	5 (2.4%)	2 (0.9%)	5 (2.4%)	0 (0.0%)	
Ankle-brachial index	<0.9 (n = 70; 33.2%)	1 (0.5%)	8 (3.8%)	24 (11.4%)	36 (17.1%)	1 (0.5%)	**<0.001**
	≥0.9 (n = 141; 66.8%)	11 (5.2%)	71 (33.6%)	35 (16.6%)	22 (10.4%)	2 (0.9%)	
Waist-hip ratio	>1 for men; >0.85 for women (n = 58; 27.5%)	4 (1.9%)	27 (12.8%)	13 (6.2%)	13 (6.2%)	1 (0.5%)	0.454
	<1 for men; <0.85 for women (n = 153; 72.5%)	8 (3.8%)	52 (24.6%)	46 (21.8%)	45 (21.3%)	2 (0.9%)	
Ejection fraction	<55% (n = 111; 52.6%)	7 (3.3%)	43 (20.4%)	28 (13.3%)	31 (14.7%)	2 (0.9%)	0.887
	≥55% (n = 100; 47.4%)	5 (2.4%)	36 (17.1%)	31 (14.7%)	27 (12.8%)	1 (0.5%)	

*Data are expresses as frequency (percentage); †Chi-square test; SVD: Single vessel disease; DVD: Double vessel disease; TVD: Triple vessel disease; LMCA: left main coronary artery.

score [3]. However, the correlation of Syntax score with disease severity or number of vessels involved has been reported rarely. In the present study, we found a significant association between diabetes status and severity and complexity of coronary artery disease. We also observed that increase in BMI was associated increase in severity of coronary artery disease, but the association was statistically insignificant. This may be due to the influence of other cardiovascular risk factors. Waist-hip ratio is another major component of the metabolic syndrome, and indicates atherosclerotic burden of the patients. About 27.5% of patients displayed abnormal waist-hip ratio in present study. However, no association was observed between waist-hip ratio and severity/complexity of coronary artery disease. Similarly, left-ventricular dysfunction showed no association with severity and complexity of coronary artery disease. It is known that hypertension is one of the most established risk factor of coronary artery disease. In the present study, we identified that the complexity of coronary artery lesions was higher among hypertensive patients. It was also observed that incidence of multi-vessel coronary artery disease were higher among hypertensive patients than among non-hypertensive patients.

In the present study, a strong association was also observed between severity of coronary artery disease and presence of coexisting peripheral arterial disease, as measured by ankle-brachial index. Further, an abnormal ankle-brachial index was associated with increased risk of multi-vessel coronary artery disease. A recent study by Ikeda et al has also shown an association between ankle-brachial index and the complexity of the coronary lesion with Syntax score [16]. Papamichael *et al*. have reported similar findings regarding the use of ankle-brachial index as the main variables for predicting the extent and severity of coronary disease, especially in male

patients and those with diabetes [17]. These findings highlight the potential role of ankle-brachial index as a non-invasive tool to predict coronary artery disease severity and complexity of coronary artery disease in patients with suspected coronary artery disease. The potential mechanisms that might underlie this association include the progressive occlusion of arteries and vascular disease that leads to occlusion of the cerebral arteries, cerebral tissue loss and hence vascular dementia. There is also an evidence of a strong positive association between peripheral arterial disease and inflammation, which has been inferred in the pathogenesis of atherosclerosis. However, making more accurate decisions for using this method in the prevention, diagnosis, prediction of severity and complexity, and prognostication of coronary artery disease needs further studies with large sample sizes.

Study Limitations

The present study has several limitations. It is a single-center study; hence, scope of the finding might be limited. Further, the findings of the study were substantiated from comparatively smaller sample-size data. Duration of risk factors was not taken into consideration for analyzing the data, which can also be considered as another limitation of the present study. Data on coronary risk factors treatment condition are also lacking. Therefore, we recommend fellow researchers to conduct a multi-center study involving large-sample size for further investigation and confirmation of present findings.

5. Conclusion

We examined the role of ankle-brachial index, waist-hip ratio, ejection-fraction, obesity, smoking/alcohol habits, diabetes and hypertension as independent predictors of complexity and severity of coronary artery disease. About one-third of study participants with coronary artery disease were reported to have clinical or subclinical peripheral arterial disease. We found that early diagnosis of coronary artery can be predicated by evaluating diabetics, hypertension, and smoking habits in patients presenting with acute coronary syndrome. In addition, ankle-brachial index can be used as an effective non-invasive bed-side tool, as an alternative to Syntax score, in predicting the severity and complexity of coronary artery disease.

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