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Association Between Peripheral Arterial Disease Severity and Coronary Artery Disease Complexity.

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Abstract

Background: Peripheral arterial disease (PAD) and coronary artery disease (CAD) share a common pathophysiological basis rooted in systemic atherosclerosis and frequently coexist in the same patient. Despite this well-recognized overlap, the precise relationship between PAD severity and the anatomical complexity of CAD remains poorly defined, particularly in populations with a high burden of cardiometabolic risk factors. ***Methods:*** This prospective observational study enrolled 500 patients with angiographically confirmed CAD at a tertiary cardiac care center. PAD severity was graded using the Trans-Atlantic Inter-Society Consensus II (TASC II) classification, and CAD complexity was quantified using the SYNTAX score. Baseline demographic characteristics, clinical profiles, and cardiovascular risk factors were systematically recorded. Logistic regression analysis was used to identify independent predictors of disease severity. ***Results:*** The study cohort had a mean age of 62.8 ± 12.5 years, with a notable female predominance (356 [71.2%]). Diabetes mellitus (333 [66.6%]), hypertension (274 [54.8%]), and smoking (261 [52.2%]) were the most common risk factors. The majority of patients were asymptomatic at presentation (383 [76.6%]). A statistically significant association was observed between PAD severity and CAD complexity, with advanced TASC II lesions (types C and D) occurring more frequently among patients with high SYNTAX scores ($p < 0.001$). Patients with lower ankle-brachial index (ABI) values showed a greater proportion of severe disease across both classification systems. On multivariate analysis, diabetes mellitus (OR 1.33, 95% CI: 1.02-1.89), smoking (OR 1.69, 95% CI: 1.28-3.89), and SYNTAX score (OR 2.06, 95% CI: 1.56-3.55) emerged as independent predictors of disease severity. ***Conclusion:*** PAD is prevalent among patients with significant CAD and its severity closely mirrors the degree of coronary disease complexity, reflecting the diffuse and systemic nature of atherosclerosis. Routine peripheral vascular assessment in patients with CAD may improve risk stratification and facilitate more targeted management.

Keywords: Peripheral arterial disease (PAD), coronary artery disease (CAD), SYNTAX score, Trans-Atlantic Inter-Society Consensus II (TASC II) classification.

INTRODUCTION

Peripheral arterial disease is a widely prevalent but frequently underdiagnosed condition caused by atherosclerotic narrowing of arteries distal to the aortic bifurcation. It ranks as the third most common atherosclerotic manifestation after CAD and stroke, yet it often goes undetected in routine clinical practice owing to its silent presentation in a substantial proportion of affected individuals. (1,2) The shared pathophysiological substrate between PAD and CAD, driven by common risk factors including diabetes mellitus, hypertension, dyslipidemia, and physical inactivity, means that the two conditions frequently coexist. Their co-occurrence carries clinical significance, as affected patients face a considerably higher risk of adverse cardiovascular events and reduced long-term survival. (3)

Reported rates of PAD among patients with CAD vary considerably depending on the diagnostic method and the population studied. In Indian patients with CAD, an ABI-based screening study documented PAD in approximately 7.7% of cases, suggesting a relatively lower burden than that seen in Western cohorts. (4) Conversely, studies from the Middle East have described higher rates, with PAD detected in 12.8% of patients undergoing coronary angiography and 14.7% among those with confirmed CAD. (5) On the other side of this spectrum, the proportion of patients with PAD who harbor significant CAD ranges from 28% to 94%, underscoring a strong yet heterogeneous relationship between the two conditions. (6)

The biological link connecting PAD and CAD lies in the progressive nature of systemic atherosclerosis. Endothelial injury, lipid deposition, and sustained vascular inflammation drive plaque formation across multiple arterial territories

simultaneously. As atherosclerotic plaques advance, their destabilization and rupture can precipitate thrombotic occlusion, manifesting as acute ischemic events in both the coronary and peripheral circulations. (7) The concurrent involvement of these territories therefore signals advanced and diffuse disease rather than isolated vascular pathology.

Despite growing recognition of this overlap, the relationship between PAD severity and the anatomical complexity of coronary disease has not been adequately characterized, particularly in Indian populations where cardiometabolic risk profiles differ substantially from those of Western cohorts. The present study was therefore conducted to evaluate the association between PAD severity, as classified by the TASC II system, and CAD complexity, as quantified by the SYNTAX score, while also identifying independent risk predictors in this high-risk population.

MATERIALS AND METHODS

Study Design and Population

This prospective observational study was carried out at a tertiary cardiac care center (UNMICRC, Ahmedabad) between January 2021 and December 2022. Consecutive patients with clinically suspected and angiographically confirmed CAD were screened for enrollment. The study protocol received approval from the Institutional Ethics Committee , and written informed consent was obtained from every participant prior to any study procedure.

The study included patients admitted to the cardiology department with clinical features suggestive of coronary artery disease (CAD) and who had angiographically confirmed CAD. Patients who were unwilling to participate in the study were excluded. In addition, individuals with a prior history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), as well as those with incomplete clinical or investigational data, were also excluded from the study.

Data Collection

Detailed demographic characteristics, clinical history, and cardiovascular risk factor data including diabetes mellitus, hypertension, and smoking status were recorded using a structured case record form. A thorough clinical examination was performed in all patients, incorporating assessment of peripheral pulses and bilateral blood pressure measurements.

Assessment of Peripheral Arterial Disease

Ankle-Brachial Index (ABI): ABI was measured using a standard sphygmomanometer and a hand-held Doppler probe. The ratio of the higher ankle systolic pressure to the higher brachial systolic pressure was calculated for each limb. An ABI value below 0.90 was used as the diagnostic threshold for PAD. Patients were further stratified into mild (ABI 0.70-0.89), moderate (ABI 0.40-0.69), and severe (ABI < 0.40) disease categories based on established criteria.

TASC II Classification: The anatomical severity and morphological complexity of PAD lesions were graded according to the Trans-Atlantic Inter-Society Consensus II (TASC II) classification into four categories: Types A, B, C, and D, with Types C and D representing advanced and technically challenging lesions. Patients without hemodynamically significant peripheral lesions were classified as Type 0 (no PAD / normal peripheral vasculature) for the purposes of this analysis.

Coronary Angiography and SYNTAX Score

Coronary angiography was performed in all enrolled patients. All angiographic images were reviewed independently by two experienced interventional cardiologists. Disagreements were resolved through adjudication by a third observer, and a consensus score was recorded. Every coronary lesion causing at least 50% diameter stenosis in a vessel of 1.5 mm or more in diameter was scored according to the SYNTAX algorithm. Patients were subsequently grouped into three categories based on their total SYNTAX score: mild (< 22), moderate (22-32), and severe (> 32).

Operational Definitions

- Smoking: Encompassed both current and former smokers.
- Hypertension: Defined as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or current use of antihypertensive therapy.
- Diabetes Mellitus: Defined as fasting plasma glucose ≥ 126 mg/dL, random or two-hour postprandial glucose ≥ 200 mg/dL, or current use of antidiabetic medication.

Statistical Analysis

All analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were expressed as frequencies and proportions. Between-group comparisons were conducted using the independent samples t-test for continuous variables and the chi-square test for categorical data. Associations between continuous variables and SYNTAX score were evaluated using Pearson's correlation coefficient. Univariate logistic regression was performed to screen candidate predictors, followed by multivariate logistic regression incorporating variables that reached significance on univariate analysis. A two-tailed p-value below 0.05 was considered statistically significant.

RESULTS

Table 1 summarizes the baseline characteristics of the study population.

Table 1: Baseline Characteristics of the Study Population (N = 500)

Variables	N = 500, N (%)
Age (years)	62.8 ± 12.5
Gender	
Male	144 (28.8%)
Female	356 (71.2%)
Risk Factors	
Hypertension	274 (54.8%)
Diabetes Mellitus	333 (66.6%)
Smoking	261 (52.2%)
Symptom Status	
Asymptomatic	383 (76.6%)
Symptomatic	117 (23.4%)
LVEF (%)	45.20 ± 10.02
Extent of Coronary Disease	
Single Vessel Disease (SVD)	187 (37.4%)
Double Vessel Disease (DVD)	181 (36.2%)
Triple Vessel Disease (TVD)	132 (26.4%)

Legend: Demographic characteristics, cardiovascular risk factors, symptom status, left ventricular ejection fraction (LVEF), and extent of coronary artery disease among the study participants.

A total of 500 patients were enrolled, of whom 356 (71.2%) were female and 144 (28.8%) were male. The female predominance observed in this cohort is atypical for a CAD population and likely reflects referral patterns or specific characteristics of the study setting, which is discussed further in the limitations. Cardiovascular risk factors were common across the cohort, with diabetes mellitus recorded in 333 (66.6%), hypertension in 274 (54.8%), and smoking in 261 (52.2%) patients. Most participants were asymptomatic at the time of enrollment (383 [76.6%]). The mean LVEF was 45.20 ± 10.02%, reflecting considerable heterogeneity in baseline cardiac function. Regarding the extent of coronary involvement, single vessel disease (SVD) was present in 187 (37.4%) patients, double vessel disease (DVD) in 181 (36.2%), and triple vessel disease (TVD) in 132 (26.4%).

Table 2: Distribution of TASC II Categories in the Study Population

TASC II Category	N = 500, N (%)
0 (No PAD / Normal)	147 (29.4%)
A	129 (25.8%)
B	97 (19.4%)
C	81 (16.2%)
D	46 (9.2%)

Legend: Distribution of patients according to TASC II classification categories, including normal findings (Type 0) and lesion types A–D.

Among the study cohort, 147 (29.4%) patients had no detectable PAD lesions (TASC II Type 0) and were classified as normal. TASC II Type A lesions were found in 129 (25.8%) patients. Types B, C, and D were present in 97 (19.4%), 81 (16.2%), and 46 (9.2%) patients, respectively, indicating that a substantial proportion of the cohort harbored complex or advanced peripheral arterial lesions.

Table 3: Distribution of TASC II Types According to SYNTAX Score Category

TASC II Type	Mild SYNTAX (N=282)	Moderate SYNTAX (N=129)	Severe SYNTAX (N=89)	p-value
0 (No PAD)	107 (37.9%)	26 (20.2%)	17 (19.1%)	0.001
A	59 (20.9%)	43 (33.3%)	28 (31.5%)	0.01
B	49 (17.4%)	11 (8.5%)	3 (3.4%)	0.001
C	43 (15.3%)	26 (20.2%)	32 (36.0%)	0.0001
D	24 (8.5%)	23 (17.8%)	9 (10.1%)	0.02

Legend: Distribution of TASC II lesion types across mild, moderate, and severe SYNTAX score categories, with p-values comparing proportions across groups.

There was a statistically significant association between TASC II classification and SYNTAX score category ($p < 0.0001$). Normal peripheral vasculature (Type 0) was most prevalent in the mild SYNTAX group (107/282 [37.9%]) and progressively less common in the moderate (26/129 [20.2%]) and severe (17/89 [19.1%]) groups. TASC II Type C lesions followed the reverse trend, being least prevalent in the mild group (43/282 [15.3%]) and most common in the severe SYNTAX category (32/89 [36.0%]), indicating a clear parallel progression of PAD and CAD complexity.

Table 4: Distribution of TASC II Types According to ABI-Based Disease Severity

TASC II Type	Mild ABI (N=230)	Moderate ABI (N=200)	Severe ABI (N=70)	p-value
0 (No PAD)	80 (34.8%)	50 (25.0%)	10 (14.3%)	0.08
A	57 (24.8%)	57 (28.5%)	16 (22.9%)	0.5526
B	16 (7.0%)	47 (23.5%)	0 (0.0%)	< 0.001
C	54 (23.5%)	13 (6.5%)	34 (48.6%)	< 0.001
D	23 (10.0%)	33 (16.5%)	10 (14.3%)	0.8256

Legend: Distribution of TASC II lesion types according to ankle–brachial index (ABI)-based disease severity, with p-values comparing proportions across groups.

The distribution of TASC II lesion types varied significantly across ABI-defined severity groups for Types B and C (both $p < 0.001$). TASC II Type B lesions were clustered predominantly in the moderate ABI group (47/200 [23.5%]) and were entirely absent (0/70 [0%]) in patients with severe ABI impairment. In contrast, Type C lesions were disproportionately represented in the severe ABI group, accounting for 34/70 (48.6%) patients in that category. No significant difference was observed for TASC II Types 0, A, or D across ABI severity groups.

Table 5: Logistic Regression Analysis — Predictors of Disease Severity

Variable	OR	95% CI	p-value
Univariate Analysis			
Age	2.15	1.89 - 3.05	0.04
Sex	1.89	1.05 - 2.98	0.02
Diabetes Mellitus	1.52	1.05 - 2.78	0.03
Hypertension	1.12	1.09 - 2.59	0.04
Smoking	2.36	1.89 - 3.47	0.02
SYNTAX Score	2.55	1.56 - 3.02	0.001
Multivariate Analysis			
Age	0.98	0.77 - 1.68	0.09
Sex	0.76	0.55 - 1.89	0.10
Diabetes Mellitus	1.33	1.02 - 1.89	0.0001
Hypertension	0.99	0.65 - 1.59	0.125
Smoking	1.69	1.28 - 3.89	0.002
SYNTAX Score	2.06	1.56 - 3.55	0.004

Legend: Univariate and multivariate logistic regression analyses evaluating demographic, clinical, and angiographic predictors of peripheral arterial disease severity. Results are presented as odds ratios (OR) with 95% confidence intervals (CI).

On univariate logistic regression, advancing age (OR 2.15, 95% CI: 1.89-3.05, $p = 0.04$), male sex (OR 1.89, 95% CI: 1.05-2.98, $p = 0.02$), diabetes mellitus (OR 1.52, 95% CI: 1.05-2.78, $p = 0.03$), smoking (OR 2.36, 95% CI: 1.89-3.47, $p = 0.02$), and a higher SYNTAX score (OR 2.55, 95% CI: 1.56-3.02, $p = 0.001$) were all associated with greater disease severity. Following multivariate adjustment, three variables retained independent predictive significance: diabetes mellitus (OR 1.33, 95% CI: 1.02-1.89, $p = 0.0001$), smoking (OR 1.69, 95% CI: 1.28-3.89, $p = 0.002$), and SYNTAX score (OR 2.06, 95% CI: 1.56-3.55, $p = 0.004$). Age, sex, and hypertension did not independently predict disease severity after adjustment.

DISCUSSION

This study documents a substantial burden of peripheral arterial disease among patients with angiographically confirmed CAD and demonstrates a clear, graded association between PAD severity and the anatomical complexity of coronary lesions. The prevalence of advanced TASC II categories (types C and D) rose progressively with increasing SYNTAX score, and patients with the most severely reduced ABI values harbored the highest proportion of complex PAD lesions.

These observations support the view that atherosclerosis does not respect vascular boundaries and that disease severity in one territory reliably reflects the extent of involvement elsewhere. Diabetes mellitus, smoking, and SYNTAX score emerged as independent predictors on multivariate analysis, reinforcing the combined role of metabolic dysregulation, behavioral risk factors, and anatomical coronary burden in determining overall vascular severity.

The co-occurrence of PAD and CAD has been consistently described in prior literature, although reported prevalence figures differ markedly between studies. Data from United States-based cohorts have documented concomitant CAD in 55-80% of patients with established PAD, reflecting the systemic extent of the atherosclerotic process. (6) In contrast, an ABI-based screening study from India found PAD in only 7.7% of patients with CAD, a considerably lower figure that likely reflects differences in patient selection, diagnostic thresholds, and the population-specific distribution of risk factors. (4) Our results, derived from a tertiary cardiac center in western India, document a higher burden of complex PAD in patients with significant CAD and further demonstrate a graded relationship between PAD morphological complexity and SYNTAX-defined coronary severity, providing anatomical evidence for the parallel progression of atherosclerosis across vascular beds.

Another study reported a PAD prevalence of 17% in patients with CAD, with smoking and hypertension identified as the most prevalent risk factors. (8) Our cohort shows a comparably high burden of vascular severity, with the added dimension of angiographic risk stratification using both TASC II and SYNTAX scoring, lending greater precision to the characterization of disease complexity. Differences between our findings and those of prior studies are likely attributable to variations in diagnostic methodology and the degree of coronary disease confirmation required for enrollment.

Our finding that diabetes and smoking are independent predictors of combined PAD and CAD severity is consistent with large epidemiological studies from the United States, where smoking (OR 4.46), diabetes (OR 2.71), and hypertension (OR 1.75) were each significantly associated with PAD in a nationally representative sample. (9) Notably, hypertension did not retain independent significance in our multivariate model (adjusted OR 0.99), unlike in that cohort, a divergence that may relate to differences in disease severity, antihypertensive treatment prevalence, and the specific outcome definition used. The stronger contribution of diabetes and smoking in our population may reflect the particularly high cardiometabolic burden characteristic of Indian patients with premature and advanced atherosclerosis.

The ARIC study documented that a low ABI below 0.90 was associated with a two-to-three-fold increase in the odds of coronary heart disease events, positioning ABI as a marker of systemic atherosclerotic burden. (10) Our findings extend this observation by demonstrating that not only ABI magnitude but also TASC II morphological classification mirrors SYNTAX-defined coronary complexity. This adds a layer of granularity to the concept of integrated vascular risk, suggesting that anatomical PAD grading may carry information beyond what ABI alone provides.

The risk factor profile observed in this study was notably high, with diabetes (333 [66.6%]), hypertension (274 [54.8%]), and smoking (261 [52.2%]) predominating. This is broadly consistent with international and regional data, where these three factors have been repeatedly identified as the principal drivers of PAD development and progression. (11-14) Compared with a cohort from New York that reported hypertension in 89% and CAD in 74% of patients with vascular disease, (11) our population shows a relatively higher prevalence of diabetes and smoking, which may account for the greater degree of combined coronary and peripheral disease severity observed. Regional cardiometabolic risk patterns in India, characterized by early-onset insulin resistance and high tobacco use, likely contribute to this profile.

Limitations

Several limitations of this study merit consideration. As a single-center study conducted at a tertiary referral facility, the findings may not be fully generalizable to community-based or primary care populations, where disease severity is typically lower. The observational design precludes the establishment of causal directionality between PAD and CAD severity. Selection bias toward more advanced disease is an inherent feature of the tertiary care setting and should be acknowledged when interpreting the prevalence data. ABI measurements, while practical and widely used, may underestimate PAD severity in patients with heavily calcified arteries, a recognized limitation in diabetic patients who comprised a large proportion of this cohort. Finally, despite multivariate adjustment, residual confounding from unmeasured variables such as dietary patterns, physical activity, and medication adherence cannot be entirely excluded. The atypical female predominance in this cohort also warrants further investigation, as it may reflect a referral pattern specific to the study center rather than a true epidemiological feature.

CONCLUSION

This study establishes a clear association between PAD severity and CAD complexity, with advancing TASC II category paralleling increasing SYNTAX scores and greater ABI impairment. These findings affirm that atherosclerosis operates as a unified systemic process, with the degree of involvement in the peripheral circulation serving as a meaningful indicator

of coronary disease burden. Diabetes mellitus and smoking were identified as key modifiable drivers of combined vascular severity, highlighting their continued importance as targets for preventive intervention. Incorporating routine peripheral vascular assessment into the evaluation of patients with CAD has the potential to refine risk stratification, identify individuals at highest risk of adverse outcomes, and guide more comprehensive treatment strategies.

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