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Assessment of carotid artery hemodynamic profile in young patients presenting with acute coronary syndrome – a cross-sectional study from a tertiary care center in South India

Kannan Murugesan[1], Ramachandran Paramasivam[2], Hariharakrishnan Ramamoorthy[3], Kannan Kumaresan[4]

[1]Senior Resident, [2,3]Assistant Professor, [4]Professor and Head, Department of Cardiology, Government Stanley Medical College, Chennai, Tamil Nadu, India

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ABSTRACT

Background: Coronary artery disease (CAD) prevalence in young individuals is rising, particularly in South Asian populations. Carotid artery hemodynamic parameters and their relation with CAD have not been studied much in young patients. **Aims and Objectives:** The aim of the study was to study the relationship between Carotid artery hemodynamic parameters, and CAD severity in young patients. **Materials and Methods:** A cross-sectional and single-center study was conducted involving consecutive patients undergoing coronary angiography due to acute coronary syndrome and aged under 40. Carotid ultrasonography and Doppler were performed to assess Carotid artery hemodynamic parameters. Gensini and SYNTAX scores were used to evaluate the severity and complexity of CAD. A total of 136 patients were included in the study. **Results:** The mean age was 36.24±4.030 years, with 92 males. CAD patients demonstrated significantly increased carotid intima-media thickness (CIMT) (0.730±0.157 vs. 0.488±0.09; P<0.001) and resistive index (RI) in the right internal carotid artery (RICA) (P=0.004). Carotid blood flow velocities were significantly reduced in CAD patients, including peak systolic velocity (PSV) in both the RICA and left ICA (LICA) (P<0.05) and end-diastolic velocity of the RICA (P=0.049). Mean SYNTAX 9.526±6.762 and mean Gensini 23.403±18.58. CIMT correlated significantly with CAD complexity in terms of vessels involved (P=0.036) and of SYNTAX score (P=0.046). CIMT, PSV RICA, PSV LICA, and RI RICA are the significant CAD predictors. **Conclusion:** CIMT and Carotid artery hemodynamic parameters are valuable predictors of CAD occurrence, severity, and complexity even in young individuals, highlighting their clinical utility in risk assessment for this population.

Key words: Coronary artery disease; Carotid intima-media thickness; Carotid artery hemodynamics; Coronary artery disease in young

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INTRODUCTION

Coronary artery disease (CAD) continues to be a major global health issue, affecting people of all ages and from all geographical locations. Although long thought to be an illness mostly affecting the elderly, CAD is now affecting younger people. Current epidemiological statistics support the increase in the prevalence of CAD in young people, especially in South Asian groups.[1,2] According to recent studies, the frequency and incidence of CAD are on the rise among individuals under 40 years old in India.[3,4] South Asians are prone to CAD at a young age; in this community, patients under 40 years old account for 25% of all myocardial infarctions (MIs), while patients under 50 years old account for more than 50% of CAD deaths.[5] Early occurrence of CAD in patients from South Asia was

Address for Correspondence:
Dr. Kannan Kumaresan, Professor and Head, Department of Cardiology, Government Stanley Medical College, Chennai, Tamil Nadu, India. **Mobile:** +91-9094011522. **E-mail:** manju_kannan2000@yahoo.co.in

reported in the INTERHEART study, with a prevalence of 11.7% in India in patients aged below 40 years.[6]

The association between the severity of CAD and Carotid artery hemodynamics is exciting. Widely accepted as a measure of subclinical atherosclerosis, Carotid intima-media thickness (CIMT) has been thoroughly studied in older CAD populations and has proven predictive value for cardiovascular events.[7,8] Similar to this, Carotid artery hemodynamic parameters – such as blood flow velocity and arterial stiffness – have been linked to the etiology of CAD and may provide important information about the complexity and severity of the illness.[9,10]

Atherosclerotic plaque rupture or erosion is the underlying pathogenesis, as seen in older patients; the younger patients are also likely to have the same pathophysiological process for developing atherosclerosis. Young patients are at risk for premature atherosclerosis through both traditional and non-traditional risk factors.[11] The use of subclinical atherosclerosis markers such as CIMT and Carotid artery hemodynamic parameters such as peak systolic velocity (PSV), end-diastolic velocity (EDV), and resistive index (RI), as predictive markers, are poorly documented in the literature for young patients with CAD, particularly those under the age of 40.

The prevalence of CAD in the young population is alarmingly rising, so it is worth a study to assess whether these non-invasive markers can be used as predictive factors for CAD in the young population or not. Thus, our work aims to fill this gap in the literature by assessing the relationship between Carotid artery hemodynamic parameters and the complexity and severity of CAD, particularly acute coronary syndrome, in a group of young patients.

Aims and objectives

To study the relationship between Carotid artery hemodynamic parameters, and Coronary artery disease (CAD) severity in young patients.

MATERIALS AND METHODS

Study design

This is a cross-sectional and single-center study.

Study population and setting

Patients presenting with the acute coronary syndrome, receiving coronary angiography at a tertiary care center in Chennai, Tamil Nadu, India were included in the study.

Inclusion and exclusion criteria

Patients presenting with acute coronary syndrome (Unstable angina, non-ST-segment elevation MI, or ST-segment elevation MI [STEMI]) with age <40 were included in the research. The participants with other systemic illnesses such as chronic kidney disease, patient's post-coronary revascularization, and sub-optimal images for measurement were excluded from the study. The CAD group consisted of participants with more than 50% luminal stenosis in any major coronary artery on coronary angiography, whereas the non-CAD group consisted of individuals with normal coronaries and minimal CAD.

Data collection

A thorough history with clinical examination and standard laboratory tests, such as complete blood count, renal function test, lipid profiles, fasting blood glucose tests, and cardiac biomarkers, were performed on all recruited patients. To evaluate CIMT and Carotid artery hemodynamic parameters, Doppler investigations, and Carotid ultrasonography were also carried out. CIMT was assessed with linear vascular ultrasound and Carotid artery hemodynamic parameters using high-resolution ultrasound Doppler at the internal carotid artery, carotid bulb, and common carotid artery (CCA) following recognized methods.

Study tools

To collect data, we used a semi-structured questionnaire. Using a linear array transducer and high-resolution ultrasonography, CIMT measurements were acquired. The CCA, carotid bulb, and internal carotid artery were among the predetermined sites where CIMT was assessed. The average value of the CIMT was determined by measuring the distance between the media-adventitia and lumen-intima interfaces on either side of the carotid artery. CIMT was measured at a distance of at least 5 mm below the distal end of CCA, along a 10 mm long straight segment of the artery free of atherosclerotic plaque. Doppler ultrasonography techniques were used to evaluate Carotid artery hemodynamic parameters. Measurements were made of variables such as RI, PSV, and EDV.[10]

The SYNTAX score and GENSINI score, two well-known scoring systems, were used to determine the severity of CAD. We assessed the severity of CAD using the Gensini score, a summation of the individual coronary segment scores based on the degree of narrowing and its topographical importance. The complexity of CAD was evaluated by Syntax score, where each coronary lesion showing stenosis ≥50% of the diameter in vessels ≥1.5 mm is scored separately. The total SYNTAX score was calculated by summing up the scores from individual lesions using an online SYNTAX calculator (http://www.syntaxscore.com).[12,13]

Ethical consideration

The institutional review board reviewed the study protocol and granted ethical approval. Written informed consent was obtained from the study subjects. Privacy of participant's data and confidentiality was strictly maintained throughout the study process.

Statistical analysis

The study population's clinical and demographic features were compiled using descriptive statistics. Categorical variables were shown as frequencies and percentages, whereas continuous variables were given as mean±standard deviation or median (interquartile range). To find the factors associated with CAD severity as determined by SYNTAX and GENSINI scores, a Chi-squared test or independent t-test was carried out. Pearson's correlation coefficients were calculated to assess the relationships between CIMT, carotid hemodynamic parameters, and CAD severity scores. A P<0.05 was considered statistically significant. All statistical analyses were conducted using SPSS version 21.

RESULTS

Baseline characteristics and carotid artery hemodynamic parameters of CAD and non-CAD patients (n = 136)

A total of 136 patients were included in the study. Out of which 77 had significant CAD. Baseline characteristics and Carotid artery hemodynamic parameters are compared in Table 1. The mean age was 36.24±4.030 with the youngest patient at the age of 20. There were 92 males and 44 females. Smoking (54.5% vs. 10.2%; P<0.001), alcohol consuming (50.6% vs. 13.6%; P<0.001), high-density lipoprotein cholesterol (P–0.049), low-density lipoprotein cholesterol (P–0.002), triglycerides (P<0.001) and total cholesterol (P<0.001) were significantly associated with CAD than Non-CAD. No significant difference between the groups was seen regarding body mass index, diabetes, and hypertension. Carotid plaque was present in 38.4% of CAD patients (<0.001). Mean CIMT (0.730±0.157 vs. 0.488±0.093; P<0.001) was significantly increased in CAD patients (Figure 1). Carotid blood flow velocities were significantly reduced in the CAD group when compared with the non-CAD group, such as PSV in Right ICA (RICA) (P=0.002), in Left ICA (LICA) (P=0.027) and EDV of RICA (P=0.049). The RI in RICA was significantly increased in CAD patients (P=0.004). These parameters in other locations also had the same nature but were not statistically significant.

Demographic and clinical characteristics among patients with CAD (n = 77)

Mean CIMT was found to be increased in patients with left main disease than in those with single vessel disease (SVD) (0.95±0.07 vs. 0.72±0.12, P=0.036). Among 77

Table 1: Correlation of baseline characteristics and carotid artery hemodynamic parameters between coronary artery disease and non-coronary artery disease patients (n=136)

Parameters	CAD (n=77)	Non-CAD (n=59)	P-value
Age (years)	35.66±4.459	37±3.274	0.014
Sex			
Male	65 (84.4)	27 (45.8)	<0.001
Female	12 (15.6)	32 (54.2)	
BMI	26.31±4.44	27.214.66	0.257
Smoker	42 (54.5)	6 (10.2)	**<0.001**
Alcohol consumer	39 (50.6)	8 (13.6)	**<0.001**
Diabetes	18 (23.45)	9 (15.3)	0.239
Hypertension	20 (26)	12 (20.3)	0.443
HDL-C	43.39±6.62	45.787.34	**0.049**
LDL-C	86.01±23.858	73.6921.20	**0.002**
TGL	153.75±48.79	114.7618.41	**<0.001**
Total cholesterol	158.97±24.02	141.8821.91	**<0.001**
Mean CIMT (mm)	0.730±0.15	0.480.09	**<0.001**
PSV			
CCA			
Right	46.45±9.05	47.5410.61	0.528
Left	44.10±8.90	51.3710.86	**<0.001**
ICA			
Right	49.49±9.58	55.2811.59	**0.002**
Left	53.83±11.71	58.009.34	**0.027**
EDV			
CCA			
Right	14.53±3.76	17.093.74	**<0.001**
Left	16.89±4.45	18.274.95	0.095
ICA			
Right	22.69±9.72	25.525.64	**0.049**
Left	20.61±9.62	22.465.56	0.190
RI			
CCA			
Right	0.68±0.07	0.630.05	**<0.001**
Left	0.65±0.06	0.620.06	**0.046**
ICA			
Right	0.62±0.09	0.580.05	**0.004**
Left	0.62±0.08	0.600.04	0.206

CAD: Coronary artery disease, BMI: Body mass index, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, TGL: Triglyceride, CIMT: Carotid intima-media thickness, CCA: Common carotid artery, ICA: Internal carotid artery, PSV: Peak systolic velocity, EDV: End diastolic velocity, RI: Resistive index, P<0.05 is considered statistically significant

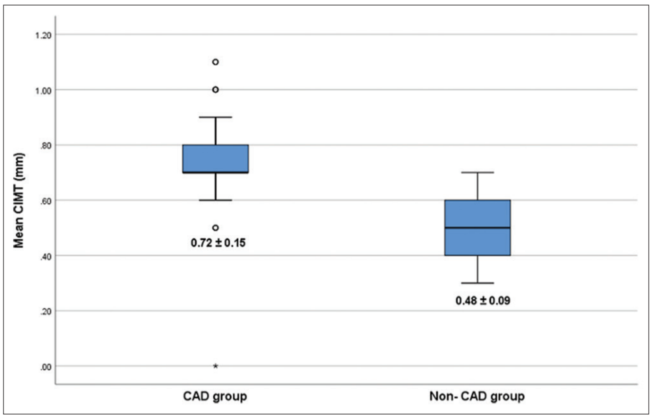

Figure 1: Correlation of carotid intima-media thickness with coronary artery disease versus non-coronary artery disease

CAD patients, 61 patients were presented with STEMI. Out of which, 43 presented with anterior wall myocardial infarction (70.5%), and 18 with inferior wall myocardial infarction (29.5%). CAG revealed 66 out of 77 had SVD (85.7%), out of which the majority (n=50) had SVD of LAD (75.7%). Mean SYNTAX 9.526±6.762 and mean Gensini 23.403±18.58. The association of demographic and clinical characteristics among patients with CAD done by univariate logistic regression analysis is shown in Table 2. Notable findings include smoking (OR=10.60, P<0.001), alcohol consumption (OR=6.54, P<0.001), elevated triglyceride levels (OR=10.66, P<0.001), and total cholesterol (OR=1.84, P=0.017). Higher mean CIMT was also significantly associated with CAD (P<0.001). In addition, lower PSV in the ICA and higher RI in the right ICA showed significant associations with CAD (P<0.05 for both). Other parameters were not significant. These findings emphasize the importance of these variables in assessing CAD risk.

Correlation of CIMT and other parameters with severity and complexity of CAD (n = 77)

Pearson correlation analysis was done between CIMT and other parameters with the severity and complexity of CAD as measured by SYNTAX and GENSINI scores (Table 3). Among these parameters, total cholesterol showed significant positive correlations with both SYNTAX (correlation factor=0.271, P=0.017) and GENSINI (correlation factor=0.338, P=0.003) scores. Mean CIMT demonstrated a positive correlation with SYNTAX scores (correlation factor=0.228, P=0.046), and with Gensini scores (correlation factor=0.201, P=0.08) indicating an association between increased CIMT and CAD severity (Figures 2 and 3). Among the Carotid artery measurements, RI exhibits a positive correlation, and other parameters like PSV and EDV were negatively correlated with SYNTAX and Gensini but not statistically significant. There was a positive correlation between CIMT and Syntax and Gensini scores.

Correlation of traditional risk factors with severity and complexity of CAD (n = 77)

Student's t-test analysis was done to assess the correlation of traditional risk factors with the severity and complexity of CAD, as measured by SYNTAX and GENSINI scores

Table 2: Association of demographic and clinical characteristics with coronary artery disease (n=77)

Variables	OR	95% CI	P-value
BMI			
Overweight	0.68	0.217–2.18	0.526
Obese	0.62	0.250–1.55	0.312
Smoker	10.60	4.075–27.57	**<0.001**
Alcohol consumer	6.54	2.744–15.60	**<0.001**
Diabetes	1.69	0.700–4.10	0.239
Hypertension	1.37	0.609–3.09	0.443
Dyslipidemia	3.57	1.42–8.9	**0.005**
HDL-C	1.66	0.75–3.71	0.209
LDL-C	4.03	0.45–35.44	0.209
TGL	10.66	3.05–37.26	**<0.001**
Total Cholesterol	1.84	1.57–2.15	**0.017**
Mean CIMT (mm)	46519451	150521–14377089237	**<0.001**
PSV			
ICA			
Right	0.948	0.916–0.982	**0.003**
Left	0.964	0.932–0.996	**0.029**
EDV			
ICA			
Right	0.959	0.920–1.00	0.051
Left	0.972	0.932–1.014	0.193
RI			
ICA			
Right	1062.5	7.17–157444	**0.006**
Left	21.648	0.180–2597.1	0.208

CAD: Coronary artery disease, BMI: Body mass index, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, TGL: Triglycerides, CIMT: Carotid intima-media thickness, CCA: Common carotid artery, ICA: Internal carotid artery, PSV: Peak systolic velocity, EDV: End diastolic velocity, RI: Resistive index, OR: Odds ratio, CI: Confidence interval, P<0.05 is considered statistically significant

Table 3: Correlation of carotid intima-media thickness and other parameters with severity and complexity of coronary artery disease (n=77)

Parameters	Syntax		Gensini	
	Correlation factor	P-value	Correlation factor	P-value
Age (years)	0.252	0.027	0.283	**0.013**
HDL-C	0.045	0.696	−0.026	0.825
LDL-C	0.144	0.212	0.295	**0.009**
TGL	0.179	0.119	0.106	0.358
Total cholesterol	0.271	0.017	0.338	**0.003**
Mean CIMT (mm)	0.228	0.046	0.201	0.08
PSV				
CCA				
Right	−0.178	0.121	−0.146	0.206
Left	−0.097	0.402	−0.132	0.253
ICA				
Right	−0.042	0.716	−0.041	0.722
Left	−0.061	0.599	−0.139	0.226
EDV				
CCA				
Right	−0.124	0.284	−0.110	0.342
Left	−0.027	0.816	−0.108	0.349
ICA				
Right	−0.096	0.406	− 0.090	0.434
Left	−0.037	0.750	−0.048	0.675
RI				
CCA				
Right	0.279	0.114	0.035	0.764
Left	0.027	0.816	0.108	0.349
ICA				
Right	0.041	0.726	0.063	0.586
Left	0.140	0.224	0.092	0.426

CAD: Coronary artery disease, BMI: Body mass index, HDL-C: High-density lipoprotein cholesterol, LDL-C: Low-density lipoprotein cholesterol, TGL: Triglyceride, CIMT: Carotid intima-media thickness, CCA: Common carotid artery, ICA: Internal carotid artery, PSV: Peak systolic velocity, EDV: End diastolic velocity, RI: Resistive index, P<0.05 is considered statistically significant

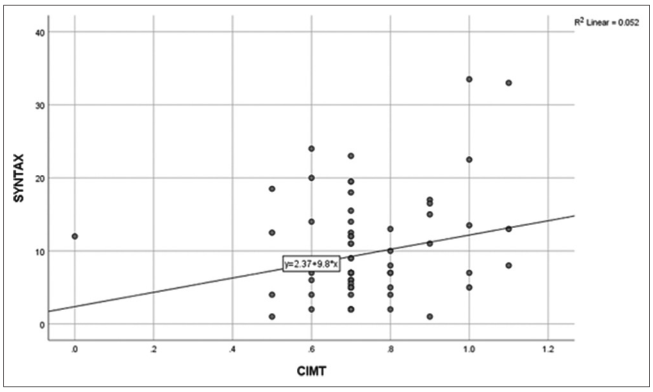

Figure 2: Correlation of carotid intima-media thickness with syntax score

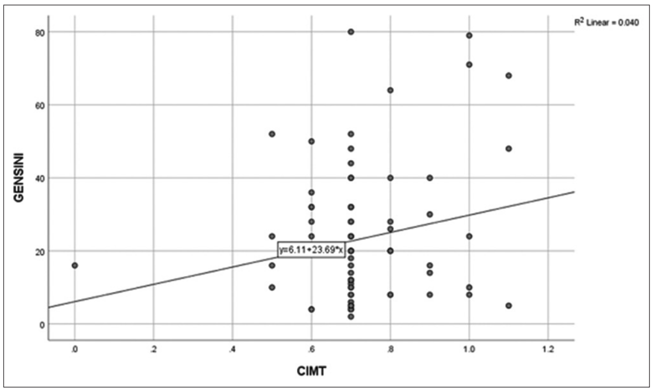

Figure 3: Correlation of carotid intima-media thickness with Gensini score

(Table 4). Significant associations were observed between smoking and CAD severity, with smokers exhibiting higher SYNTAX score (11.45±7.84, P=0.005) and Gensini score (27.57±20.05, P=0.030) compared to non-smokers (SYNTAX: 7.21±4.23, Gensini: 18.40±15.47). Similarly, alcohol consumption showed a significant association with CAD severity, as individuals consuming alcohol have higher SYNTAX score (11.19±8.22, P=0.028) and Gensini score (27.33±20.16, P=0.060) compared to non-consumers. However, no significant associations were observed between diabetes, hypertension, dyslipidemia, and CAD severity based on SYNTAX and GENSINI scores.

DISCUSSION

There is no universal definition of premature CAD. Forty-five or 55 years is the age cutoff used in most studies, whereas 65 years in older studies. Recently, a threshold of 49 years for men has been suggested to define premature CAD.[14] However, studies assessing young CAD patients (under 40) are extremely sparse. The current literature notes that premature atherosclerosis with plaque rupture or plaque erosion is the most common etiology, accounting for almost 90% of acute MI in young adults under 45. The remaining 10% of cases are secondary to non-plaque etiologies that include spontaneous coronary artery dissection, coronary vasospasm, hypercoagulability, coronary embolic phenomena, autoimmune-mediated inflammation, and drug-induced occlusions.[11] Young people, especially in South Asian regions are becoming more and more affected by CAD, and about a decade earlier than the Western population. Many studies have proven the association of traditional risk factors and genetic factors for the causation of CAD in this young population.

Table 4: Correlation of traditional risk factors with severity and complexity of coronary artery disease (n=77)

Variables	Syntax		Gensini	
	Mean±SD	P-value	Mean±SD	P-value
Smoker				
Yes (n=42)	11.45±7.84	0.005	27.57±20.05	0.030
No (n=35)	7.21±4.23		18.40±15.47	
Alcohol consumer				
Yes (n=39)	11.19±8.22	0.028	27.33±20.16	0.060
No (n=38)	7.81±4.30		19.38±16.09	
Diabetes				
Yes (n=18)	11.13±7.48	0.250	26.56±19.46	0.414
No (n=59)	9.03±6.51		22.44±18.36	
Hypertension				
Yes (n=20)	9.79±4.59	0.567	24.56±12.24	0.359
No (n=57)	8.77±7.39		22.10±20.31	
Dyslipidemia				
Yes (n=25)	9.57±6.49	0.939	24.32±19.68	0.766
No (n=52)	9.44±6.95		22.96±18.21	

CAD: Coronary artery disease, CIMT: Carotid intima-media thickness, P<0.05 is considered statistically significant

As premature atherosclerosis is the most common cause of CAD, non-invasive predictors of subclinical atherosclerosis can be helpful in the prevention and management of this condition.[15] The CIMT is at present the best-studied sonographic marker for early atherosclerotic vascular wall lesions. Several studies and meta-analyses demonstrated the utility of CIMT and other Carotid artery hemodynamic parameters and their association with CAD.[7,8] Our goal was to investigate the link that exists between Carotid artery hemodynamic parameters, and the severity of CAD in this young population (under 40 years of age).

As with earlier studies, our study also demonstrated the association of traditional risk factors like smoking, alcohol consumption, and dyslipidemia with CAD and those are also strongly correlated with the severity and complexity of CAD as assessed by SYNTAX and Gensini scores.[5] Our study demonstrated that diabetes and hypertension were not significantly associated with CAD in this young population complying with the results of earlier studies.[16]

Our study revealed that the majority of the young patients had SVD (85.7%), out of which the majority had SVD of LAD (75.7%) as by previous studies.[17] Significant variations in Carotid artery measurements were found in our investigation between the CAD and non-CAD groups. Consistently linked to CAD was elevated CIMT, a measure of subclinical atherosclerosis, supporting earlier observations.[18-20] First, the Kuopio Ischemic Heart Disease study demonstrated an association of CIMT with future coronary events, as every 0.1-mm rise of thickness was associated with an 11% increased risk of MI during follow-up.[21] Subsequently, many other large clinical studies, including the atherosclerosis risk in communities study, the cardiovascular health study the carotid atherosclerosis progression study, the malmo diet and cancer study, and the Rotterdam Study, showed that CIMT can be used to assess incident CVD risk, but these studies evaluated mainly older patients.[22] In this study, we found a similar association in the young population too. Furthermore, our study showed a correlation between CIMT and both the severity and increasing complexity of CAD. With this, our study provides evidence that CIMT can be used as a non-invasive marker for predicting CAD and its severity, even in the young population.

Carotid artery blood flow velocities have been studied in CAD patients. It was found that the peak blood flow velocities are reduced in CAD patients. An important reason for the reduction in blood flow velocity was attributed to reduced cardiac output.[23] Researchers studied a physiological attempt to restore blood flow velocity by intimal thickening and subsequent lumen reduction as a compensating mechanism in vascular aging. The reduction of peak blood flow velocity was attributed to a failure in this compensating mechanism or endothelial dysfunction in CAD patients.[24] In some cross-sectional studies it has been reported that an increased arterial stiffness was observed in patients with MI or congestive heart failure, and also, the degree of peripheral vascular resistance has more effect on the occurrence of CAD than does atherosclerosis itself. Very few studies in the past have analyzed the RI as the predictor of CAD.[25] In our study also we found the decreased PSV and elevated RI in the carotid arteries, which were suggestive of compromised hemodynamics in individuals with CAD, highlighting the possible use of carotid hemodynamic measures in CAD risk assessment. However, these hemodynamic parameters were not significantly correlated with the severity and complexity of CAD.

The current investigation highlighted the significance of these variables in CAD risk assessment among young persons by identifying them as significant predictors of CAD, like smoking, alcohol use, hypertriglyceridemia, increased total cholesterol, with increased CIMT, diminished PSV, and increased RI of the internal carotid artery. CIMT and Carotid artery hemodynamic parameters continued to be strong predictors of CAD and its complexity in this young cohort, despite the majority of cases being mild-to-moderate CAD presentations.

Limitations of the study

Although our study offers insightful information about the relationship between young patients' Carotid artery hemodynamics and their risk of developing CAD, there are a few limitations to take into account. The small sample size and single-center design might restrict how broadly applicable our results can be. Furthermore, the study's cross-sectional design makes it impossible to determine the causes of the variables. It is essential to do bigger cohort prospective studies with long-term follow-ups in the future to confirm our results and clarify the underlying mechanisms causing these relationships.

CONCLUSION

This study underscores the importance of evaluating Carotid artery hemodynamic parameters in CAD risk assessment among young populations. From this study, we suggest that, along with CIMT, these parameters can be implemented as early markers of subclinical atherosclerosis in the young population for targeted preventive strategies and to mitigate the burden of CAD in this vulnerable demographic group.

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AVAILABILITY OF DATA AND MATERIAL

The datasets analyzed during this study are available from the corresponding author on reasonable request.

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Authors' Contributions:
KM- Definition of intellectual content, literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation and submission of the article; **RP**- Concept, design, clinical protocol, manuscript editing, literature survey and preparation of figures; **HR**- Design of study, statistical analysis, and interpretation; **KK**- Review manuscript, coordination, and manuscript revision.

Work attributed to:
Department of Cardiology, Government Stanley Medical College, Chennai, Tamil Nadu, India.

Orcid ID:
Kannan Murugesan - https://orcid.org/0000-0002-3049-7033
Ramachandran Paramasivam - https://orcid.org/0009-0003-4314-1719
Hariharakrishnan Ramamoorthy - https://orcid.org/0009-0006-2569-782X
Kannan Kumaresan - https://orcid.org/0009-0001-9235-0571

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