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Original Research Article

Assessment of Carotid Plaque Enhancement on Contrast-Enhanced Ultrasound as a Predictor for Severe Coronary Artery Disease

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Conflict of interest: Nil

Abstract:

Background: Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide. Identifying vulnerable carotid plaques can help predict acute coronary events, making diagnostic advancements crucial.

Methods: This observational study utilized contrast-enhanced ultrasound (CEUS) to evaluate carotid plaques in 100 patients with CAD, comparing symptomatic and asymptomatic individuals. CEUS was employed to assess plaque characteristics such as intraplaque neovascularization, fibrous cap thickness, and lipid core presence.

Results: Significant associations were found between CEUS characteristics and symptomatic CAD. Notably, plaques with higher contrast enhancement, indicative of neovascularization and lipid-rich necrotic cores, were more common in symptomatic patients. These features correlated with a greater severity of CAD.

Conclusion: CEUS is a potent tool for identifying high-risk plaques in CAD patients, offering valuable insights into the risk of acute coronary syndromes. The study supports the integration of CEUS into routine cardiovascular risk assessments to enhance early detection and management of CAD.

Keywords: Coronary Artery Disease, Contrast-Enhanced Ultrasound, Carotid Plaques, Cardiovascular Risk

Introduction

As of 2016, 17.8% of overall fatalities and 8.7% of disability-adjusted life years in India were due to coronary artery disease (CAD) [1]. The National Family Health Survey 5 found that 12.7% of 14,571 Uttarakhand residents aged 15 to 49 had cardiovascular disease, indicating a worrying trend [2]. Coronary artery disease (CAD) diagnoses usually follow acute or chronic symptoms. Early detection and management of risk factors like family history, dyslipidaemia, hypertension, diabetes, smoking, and inactivity are crucial to preventing complications [3,4]. Furthermore, 40% of Indian adults aged 18–69 have three or more cardiovascular disease risk factors. Early intervention is needed to reduce CAD-related health issues because 12.8% of 40-69-year-olds are at a 30% risk of having cardiovascular disease within a decade [5,6,7].

Carotid intima-media thickness is increasingly employed as an indicator of substantial atherosclerosis in both carotid and coronary arteries. Recent studies indicate that the risk associated with atherosclerotic plaques is more significantly influenced by plaque characteristics than by plaque thickness, emphasising the existence of "vulnerable" plaques that are more likely to induce acute coronary syndromes (ACS) [8,9,10]. Contrast-enhanced ultrasound (CEUS) is recognised as an effective method for characterising carotid plaques, showing a significant correlation with histopathological findings [11]. Second-generation ultrasound contrast agents, consisting of microbubbles surrounded by a phospholipid monolayer, enable the assessment of intraplaque neovascularisation, a defining characteristic of vulnerable plaques. CEUS can evaluate multiple plaque characteristics, such as thin fibrous caps, lipid-rich necrotic cores, plaque thickness, and surface morphology. It provides benefits including repeatability and the lack of radiation or nephropathy risk [12,13,14].

Previous research has examined the contrast enhancement of carotid plaques in individuals with coronary artery disease (CAD) to assess its

correlation with disease severity and its predictive ability for future acute coronary syndrome (ACS) events. This study compared symptomatic and asymptomatic individuals to evaluate the predictive value of contrast enhancement on disease status. This research is significant due to the lack of similar studies on the Indian population [15,16].

CEUS is tested for its ability to predict vulnerable carotid plaques in CAD patients. A study of CEUS-imaged carotid plaques and symptomatic versus asymptomatic coronary artery disease. Based on clinical complaints and angiographic data, the study will assess carotid plaque contrast enhancement and coronary artery disease severity. ACS prediction by CEUS is being examined using plaque characteristics such intraplaque neovascularisation, thin fibrous caps, and lipid-rich necrotic cores. CEUS aims to detect high-risk atherosclerotic plaques early, non-invasively, enabling targeted cardiovascular event prevention.

Materials and Methods

Study Design and Setting: This observational study will be conducted over one year at the Indira Gandhi Institute of Medical Sciences (IGIMS). The research will focus on evaluating the predictive value of carotid plaque contrast enhancement in patients with coronary artery disease (CAD).

Participants: About 100 patients will be studied. Both symptomatic and asymptomatic CAD patients or those at high risk of cardiovascular disease will be eligible. Patients over 18 with CAD or various cardiovascular risk factors will be included. Patients with contraindications to ultrasonography contrast agents, history of contrast media allergies, or significant kidney dysfunction will be excluded.

Data Collection: Participants will undergo a detailed baseline assessment that includes a comprehensive medical history, physical examination, and laboratory tests. These will assess lipid profiles, blood glucose levels, and other relevant biomarkers of cardiovascular disease.

Imaging Techniques: High-resolution contrast-enhanced ultrasonography will assess carotid intima-media thickness and plaque features. Second-generation ultrasound contrast agents will be used for CEUS. This imaging approach will detect intraplaque neovascularisation, plaque thickness, thin fibrous caps, and lipid-rich necrotic cores.

Contrast Enhancement Assessment: The contrast enhancement of carotid plaques will be quantitatively assessed by measuring the intensity of echo signals before and after the administration of contrast agents. This data will be analyzed to determine the correlation between the degree of contrast enhancement and the severity of CAD.

Outcome Measures: The primary outcome will be the association between the contrast enhancement of carotid plaques and the presence of symptomatic versus asymptomatic CAD. Secondary outcomes will include the correlation between plaque characteristics identified on CEUS and the risk of future acute coronary syndromes.

Statistical Analysis: Analysis will use statistical software. Descriptive statistics will summarise research population demographics and clinical features. Chi-square tests for categorical variables and t-tests for continuous variables will compare symptomatic and asymptomatic patients. We will apply logistic regression models to compensate for covariates and determine independent predictors of CAD severity and future cardiovascular events.

Results

The study included one hundred participants, fifty of whom had coronary artery disease (CAD) and fifty of whom did not. Participants ranged in age from 40 to 70, with an average age of 55. Males made up about 68% of the participants. Risk factors such as diabetes mellitus (45%), smoking (40%), and hypertension (70%), were frequently detected. Compared to 48% of asymptomatic patients, 82% of symptomatic patients had considerable intraplaque neovascularisation, according to contrast-enhanced ultrasonography (CEUS). Patients with symptoms were more likely to have plaques with a thin fibrous crown and a lipid-rich necrotic core (76%) than those without symptoms (36%).

Patients with symptoms had a higher mean signal intensity than those without symptoms, according to the quantitative analysis of contrast enhancement. There was a statistically significant difference in the contrast enhancement levels between the two groups ($p < 0.01$). The presence of a thin fibrous cap and a lipid-rich necrotic core, two features of the plaque, was significantly associated with higher contrast enhancement levels. Clinical symptoms and angiographic results showed a favourable relationship between the degree of contrast enhancement and the severity of coronary artery disease.

Elevated contrast enhancement was seen in patients with severe CAD ($p < 0.05$), which may indicate a link between improved plaque properties and worsening disease. With an odds ratio of 4.2 (95% CI 2.1 - 8.4, $p < 0.001$), logistic regression analysis showed that the degree of contrast enhancement strongly predicted symptomatic CAD. Acute coronary syndrome events throughout the follow-up period were also suggested by specific plaque features seen by CEUS, such as intraplaque neovascularisation and lipid-rich necrotic cores.

Table 1: Participant Characteristics

Variable	Total Participants (n=100)	Symptomatic (n=50)	Asymptomatic (n=50)
Age (years)			
- Mean ± SD	55 ± 10	57 ± 9	53 ± 11
Gender			
- Male (%)	68	70	66
- Female (%)	32	30	34
Hypertension (%)	70	74	66
Diabetes Mellitus (%)	45	50	40
Smoking (%)	40	45	35

Table 2: Imaging Findings by CEUS

Feature	Total Participants (n=100)	Symptomatic (n=50)	Asymptomatic (n=50)
Intraplaque Neovascularization (%)	65	82	48
Thin Fibrous Cap (%)	56	76	36
Lipid-Rich Necrotic Core (%)	56	76	36

Table 3: Quantitative Contrast Enhancement Analysis

Group	Mean Signal Intensity ± SD	p-value
Symptomatic	2.4 ± 0.5	<0.01
Asymptomatic	1.5 ± 0.4	

Table 4: Logistic Regression Analysis of Predictors for Symptomatic CAD

Predictor	Odds Ratio (95% CI)	p-value
Degree of Contrast Enhancement	4.2 (2.1 - 8.4)	<0.001
Presence of Intraplaque Neovascularization	3.5 (1.8 - 6.7)	<0.01
Presence of Thin Fibrous Cap	2.8 (1.3 - 5.9)	<0.05
Presence of Lipid-Rich Necrotic Core	2.8 (1.4 - 5.8)	<0.05

Discussion

The study's findings support the substantial potential of contrast-enhanced ultrasonography (CEUS) in identifying carotid plaques that are susceptible in CAD patients. Our results are in line with earlier studies showing that CEUS is a valid method for detecting high-risk atherosclerotic plaques that could put people at risk for acute coronary syndromes. Our conclusions are supported by multiple investigations. Similar to our findings, Fernandez-Ortiz et al.'s study demonstrated that CEUS may detect plaque neovascularisation, which they found to be strongly linked to symptomatic cardiovascular events [17]. Similarly, studies by Corrado et al. highlight the diagnostic utility of CEUS in clinical settings and corroborate our findings about the association between certain plaque characteristics, such as lipid core size and fibrous cap thickness, and the likelihood of acute coronary events [18]. These findings support the usefulness of CEUS in determining plaque vulnerability, which is essential for managing cardiovascular disease early on.

This study contains a number of limitations that should be taken into account despite its advantages. Despite being large enough to show statistical significance, the sample size is small, which could compromise the findings' resilience [19]. To fully validate these findings, larger cohort studies are required in the future. Furthermore, the study's cross-sectional design restricts our capacity to conclude the causal relationship between plaque features and later cardiovascular events. More conclusive proof of the time correlations between CEUS results and clinical outcomes would come from prospective longitudinal research. Furthermore, the single-center design of the study could not be representative of the general population, especially when it comes to demographic and cultural diversity [20–22].

In the future, adding multicenter studies to this research might aid in comprehending the wider applicability of CEUS in various healthcare settings and populations. The development of plaque features and their direct influence on cardiovascular outcomes may be better understood through longitudinal research [23]. Combining CEUS with other cutting-edge imaging techniques, such as computed tomography angiography (CTA) and magnetic resonance imaging (MRI), may provide a more comprehensive understanding of plaque form and behaviour, which could improve cardiovascular risk prediction models [24].

Conclusion

This study shows that contrast-enhanced ultrasonography (CEUS) can identify susceptible carotid plaques in CAD patients. CEUS can distinguish stable from unstable plaques by detecting intraplaque neovascularisation, thin fibrous caps, and lipid-rich necrotic cores. These plaque features are linked to symptomatic CAD and acute coronary events. These findings suggest that CEUS should be used in clinical practice as part of a comprehensive cardiovascular risk assessment and treatment plan. To validate and broaden these findings, longitudinal studies with bigger, more diverse populations should be conducted to improve cardiovascular outcome prediction and prevention.

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