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Original Article

Relationship between plaque morphology and symptomatology in carotid endarterectomy patients: Which plaques are more dangerous?

Ayse Gul Bayazit[1], Burak Toprak[1], Abdulkadir Bilgic[2]

[2]Mersin City Education and Research Hospital, Department of Cardiovascular Surgery, Mersin, Türkiye
[1]Mersin University Faculty of Medicine Hospital, Department of Cardiovascular Surgery, Mersin, Türkiye

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Abstract

Aim: Stroke ranks as the third leading cause of death worldwide after myocardial infarction and cancer. Carotid artery stenosis, primarily due to atherosclerotic plaque buildup, can result in transient ischemic attacks (TIAs) and stroke. Carotid endarterectomy (CEA) is a key treatment for symptomatic and asymptomatic patients with severe stenosis, with plaque characteristics—whether stable or unstable—affecting symptom risk and outcomes. Examining the link between plaque morphology and symptoms is essential for surgical decision-making. This study assesses the relationship between plaque characteristics and symptoms in CEA patients at Mersin University, focusing on stability differences between symptomatic and asymptomatic cases.

Material and Methods: In this retrospective cohort study, 152 symptomatic and asymptomatic CEA patients were analyzed. Plaques were classified as stable or unstable based on surface smoothness, ulceration, thrombus presence, and intraplaque hemorrhage. Key demographics, comorbidities, and imaging data from ultrasonography, computed tomography (CT), angiography, and magnetic resonance (MR) Angiography were reviewed.

Results: Stable plaques were more common in asymptomatic patients, while unstable plaques with features such as ulceration and thrombus were predominantly observed in symptomatic cases. A significant correlation was found between unstable plaques and neurological symptoms, suggesting that preoperative plaque assessment could be vital for surgical planning.

Conclusion: This study suggests that integrating plaque morphology with stenosis severity in CEA planning may enhance treatment success and reduce neurological risks. Assessing unstable plaque characteristics offers improved risk prediction, potentially supporting better long-term outcomes.

Keywords: Carotid artery, endarterectomy, atherosclerosis, plaque characterization

INTRODUCTION

Cerebrovascular diseases, notably ischemic stroke, represent a leading cause of global morbidity and mortality, ranking as the third most common cause of death worldwide [1]. Given the high burden of stroke, understanding and mitigating factors contributing to carotid plaque instability has become a crucial aspect of preventive cardiovascular care. While the degree of carotid artery stenosis is well-established as a predictor of neurological outcomes, recent studies emphasize the critical role of plaque morphology in symptom manifestation, highlighting the need for a more comprehensive evaluation of these features in surgical decision-making. Carotid artery stenosis, primarily due to atherosclerotic plaque accumulation, significantly impacts morbidity and mortality rates, particularly in developed countries [2]. Atherosclerotic plaques accumulating within the carotid arteries narrow the vessel lumen, reducing cerebral perfusion and leading to clinical presentations such as transient ischemic attacks (TIAs) and ischemic strokes [3].

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Corresponding Author: Burak Toprak, Mersin City Education and Research Hospital, Department of Cardiovascular Surgery, Mersin, Türkiye
Email: brk.tprk@gmail.com

Surgical intervention is often pursued in the treatment of high-grade carotid artery stenosis. Carotid endarterectomy (CEA) is a widely adopted surgical method for patients with symptomatic or asymptomatic severe stenosis, with its efficacy demonstrated across various clinical studies [4,5]. All surgical procedures were performed exclusively using patch closure to optimize long-term patency and reduce the risk of restenosis, as this technique was deemed the most appropriate for all cases based on anatomical and clinical considerations. Recent studies, such as Rothwell et al.'s analysis on the impact of medical management and surgical outcomes, continue to support the role of CEA in reducing neurological risks in patients with significant stenosis [2,6,7]. For asymptomatic patients, CEA has shown benefits for stenoses exceeding 70% [8,9]. However, relying solely on the degree of stenosis in making surgical decisions is not always considered optimal; factors such as plaque characteristics warrant consideration as well [10].

The stability or instability of atherosclerotic plaques holds significant implications for disease progression and surgical decision-making. Stable plaques typically have smooth surfaces, dense fibrous structures, and high levels of calcification, making them less likely to embolize. Conversely, unstable plaques have irregular surfaces, often containing thrombus and ulcerations, which heighten the risk of embolization. Such plaque structures are major contributors to serious neurological symptoms, including stroke and TIA [11,12].

Multiple studies have shown that unstable plaques are more frequently observed in symptomatic patients, increasing the need for surgical intervention [13,14]. For example, studies by Warlow et al. indicate that unstable plaques have a higher probability of embolizing, thus elevating the risk of neurological complications [15]. The relationship between plaque morphology and symptomatology underscores the importance of considering not only stenosis severity but also plaque structure in surgical decision-making [16]. Furthermore, assessing plaque morphology is critical for postoperative outcomes, as patients with unstable plaques may face higher risks of surgical complications [17].

Today, advanced imaging techniques play a crucial role in characterizing plaque morphology in patients with carotid artery stenosis. Techniques such as ultrasonography (USG), color Doppler USG (CDUS), computed tomography (CT), CT angiography (CTA), magnetic resonance angiography (MRA), and digital subtraction angiography (DSA) are widely used for classifying plaques as stable or unstable [18,19]. These methods evaluate not only the degree of stenosis but also features such as plaque surface structure, ulceration, thrombus, and calcification presence. While stable plaques generally show higher calcification, unstable plaques are more likely to contain thrombus and ulceration, enabling risk analysis based on plaque morphology [20,21]. Our findings revealed a significant association between unstable plaque morphology and symptomatic presentations, underscoring the need to identify plaque stability during clinical evaluations and its potential impact on improving patient outcomes. Recent advancements in imaging modalities, such as high-resolution magnetic resonance imaging and molecular imaging, have further enhanced our understanding of plaque instability and its role in predicting neurological events [22].

MATERIAL AND METHODS

Data Collection

This retrospective study included 152 patients who underwent CEA at Mersin University Faculty of Medicine from August 1, 2015, to November 9, 2018. This retrospective cohort study analyzed data from patients who underwent carotid endarterectomy between 2015 and 2018 at Mersin University Faculty of Medicine. Patients were categorized into two groups—stable and unstable plaques—to assess the effect of plaque stability on symptom presence. The equal number of patients with stable and unstable plaques in this study reflects a systematic selection process based on predefined inclusion criteria rather than a randomized distribution. This balance ensures a clear comparison between the two groups but may not represent the natural distribution in the broader patient population. Inclusion criteria were patients undergoing carotid endarterectomy for symptomatic or asymptomatic stenosis of >50% as assessed by CTA or MRA. Exclusion criteria included previous carotid interventions, incomplete medical records, and coexisting conditions that could independently impact neurological outcomes. Medical records provided demographic data and cardiovascular risk factors (hypertension, diabetes, and hyperlipidemia). The mean age of the study population was 65 ± 10 years, with a significant proportion presenting with hypertension (75.0%) and diabetes mellitus (34.9%). Concomitant coronary artery disease was observed in 48% of patients, and peripheral artery disease was present in 15%. Sequential or staged procedures were performed for patients requiring additional vascular interventions. Due to the retrospective nature of the study, randomization methods were not applicable. All patients included in the study received preoperative medical treatment consisting of atorvastatin, acetylsalicylic acid, and clopidogrel. These medications were administered as part of the standard preoperative protocol to optimize vascular health and minimize thromboembolic risks prior to carotid endarterectomy. The uniform use of these treatments ensures a consistent baseline of medical management across the study population, which may influence plaque stability and symptomatology. Imaging techniques, including USG, CDUS, CTA, and MRA, were used to classify plaques, with intervention thresholds set at 70% stenosis for asymptomatic and 50% for symptomatic

patients. Plaques excised during surgery were categorized into two main groups based on characteristics such as surface smoothness, ulceration, thrombus, and intraplaque hemorrhage: stable and unstable plaques. Plaque thickness was not measured intraoperatively in this study. Atherosclerosis risk factors were managed preoperatively with atorvastatin, acetylsalicylic acid, and clopidogrel, which were continued postoperatively unless contraindicated. Risk stratification was guided by clinical assessments, including lipid profiles and other relevant cardiovascular risk markers. As this was a retrospective study, blinding methods were not employed. Stable plaques exhibited a smooth surface and high calcification, whereas unstable plaques displayed irregular surfaces, ulceration, and thrombus features. The primary endpoint was the association between plaque morphology (stable vs. unstable) and the presence of neurological symptoms such as TIA or stroke. These characteristics were documented and classified accordingly.

Statistical Analysis

Statistical analyses were performed using both parametric and non-parametric tests, as per the recommendations of our Faculty's Biostatistics Department, which conducted the statistical evaluations. Sample size was determined via a power analysis by the same department. The Central Limit Theorem enabled the use of parametric tests without a normality test. The sample size was determined based on a power analysis conducted by the Biostatistics Department, ensuring a statistical power of 80% to detect differences in plaque morphology between symptomatic and asymptomatic patients. A non-probability convenience sampling method was used to include all eligible patients within the study period. Risk factor statistics, including mean, standard deviation, minimum, and maximum values, were calculated for continuous variables, while frequency and percentages were determined for categorical variables. Relationships between categorical variables were evaluated using the Chi-square test, and independent group comparisons were conducted using Student's t-test. For stable and unstable plaques where a relationship with symptomatology was predicted, the odds ratio was calculated. Statistical significance was set at $p<0.05$. Data were analyzed using licensed statistical software e-Picos (NY, New York) and MedCalc. Results were organized and presented in tables for clarity and ease of interpretation.

Ethical Approval

Ethical approval for the study was obtained from the Ethics Committee of Mersin University Faculty of Medicine on June 24, 2020 (approval number 448). Informed consent was obtained from all participants in accordance with ethical guidelines. The study protocol was prepared in accordance with ethical guidelines and confidentiality principles. This study adhered to the principles of the Declaration of Helsinki and followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. This study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants.

RESULTS

Plaque stability was not significantly associated with gender, smoking, hypertension, diabetes, or hyperlipidemia. However, unstable plaques were more common in symptomatic patients (58.3%), while asymptomatic patients mainly had stable plaques (70.5%), indicating a meaningful link between plaque stability and symptom presence. Specific symptoms like TIA and amaurosis fugax showed no significant association with plaque stability (Table 1).

The analysis of specific preoperative symptoms, including TIA, Amaurosis Fugax, motor aphasia, hemiparesis, and hemiplegia, showed no statistically significant association with plaque stability (all p-values>0.05). Although patients with TIA and motor aphasia had a slight tendency toward unstable plaques, these findings were not conclusive. This suggests that while unstable plaques generally increase the likelihood of symptoms, specific neurological presentations may depend on additional factors beyond plaque morphology alone (Table 1).

The study's findings highlight that while general cardiovascular risk factors such as hypertension, diabetes, and hyperlipidemia are prevalent in both stable and unstable plaque groups, they do not significantly influence plaque stability in isolation. However, unstable plaques are significantly more associated with symptomatic cases, suggesting that plaque morphology should be a critical consideration in clinical evaluations to anticipate potential symptom development. Further research might focus on additional biological or imaging markers that could clarify the influence of plaque characteristics on specific symptom types.

This table shows a significant association between symptom status and plaque stability in carotid endarterectomy patients (p=0.001). Symptomatic patients were more likely to have unstable plaques (58.3%) than stable ones (41.7%), while asymptomatic patients predominantly had stable plaques (70.5%). These findings suggest that unstable plaques may increase the likelihood of symptomatic presentation, emphasizing the importance of plaque stability assessment in evaluating symptom risk in carotid artery disease (Table 2).

This combined analysis suggests that there is a statistically significant relationship between overall symptomatic status and plaque stability, with symptomatic patients more likely to have unstable plaques (odds ratio=3.34, $p<0.05$). This finding underscores that plaque instability is a critical factor in the presence of symptoms, likely due to the increased risk of rupture or thromboembolic events associated with unstable plaques (Table 3).

However, when examining specific symptoms such as TIA, Amaurosis Fugax, Motor Aphasia, Hemiparesis, and Hemiplegia individually, no significant associations with plaque stability were observed. This suggests that while unstable plaques contribute to a higher likelihood of symptomatic presentation overall, they do not necessarily correlate with specific neurological symptoms. The data indicate that the symptomatic effects of unstable plaques might involve multifactorial interactions rather than direct associations with particular symptom types.

Table 1. Plaque characteristics, demographic and clinical features (n=152)

Characteristic	Stable plaque, n (%)	Unstable plaque, n (%)	p-value
Total patients (n)	76 (50.0)	76 (50.0)	-
Gender			0.37
Female	24 (31.6)	19 (25.0)	
Male	52 (68.4)	57 (75.0)	
Smoking status			0.62
Non-smoker	43 (56.6)	40 (52.6)	
Smoker	33 (43.4)	36 (47.4)	
HT			0.71
No	18 (23.7)	20 (26.3)	
Yes	58 (76.3)	56 (73.7)	
DM			0.61
No	48 (63.2)	51 (67.1)	
Yes	28 (36.8)	25 (32.9)	
HPL			0.51
No	42 (55.3)	46 (60.5)	
Yes	34 (44.7)	30 (39.5)	
Symptom status			0.001
Asymptomatic	31 (70.5)	13 (29.5)	
Symptomatic	45 (41.7)	63 (58.3)	
Preoperative symptoms			Various
TIA no	67 (52.8)	60 (47.2)	0.13
TIA yes	9 (36.0)	16 (64.0)	
Amaurosis fugax no	73 (49.7)	74 (50.3)	0.65
Amaurosis fugax yes	3 (60.0)	2 (40.0)	

HT: hypertension, DM: diabetes mellitus, HPL: hyperlipidemia, TIA: transient ischemic attack; Statistical tests: Chi-square test was used for the independence of categorical data, and Student's t-test for age differences between groups (significance set at $p<0.05$)

Table 2. Relationship statistics between symptomatic/asymptomatic status and plaque stability (n=152)

Symptom status	Stable, n (%)	Unstable, n (%)	p-value
Symptomatic (n=108)	45 (41.7)	63 (58.3)	0.001
Asymptomatic (n=44)	31 (70.5)	13 (29.5)	

$p<0.05$ considered significant; Chi-square test was applied to assess the relationship between symptom status and plaque stability

Table 3. Relationship between specific symptoms and plaque characteristics (n=152)

Symptom	Stable, n (%)	Unstable, n (%)	Odds ratio	95% CI (lower-upper)	p-value
Transient ischemic attack (TIA)					
No (n=127)	67 (52.8)	60 (47.2)	Reference		0.13
Yes (n=25)	9 (36.0)	16 (64.0)	0.5	0.21-1.22	Not significant
Amaurosis fugax					
No (n=147)	73 (49.7)	74 (50.3)	Reference		0.65
Yes (n=5)	3 (60.0)	2 (40.0)	1.52	0.25-9.37	Not significant
Motor aphasia					
No (n=127)	67 (52.8)	60 (47.2)	Reference		0.13
Yes (n=25)	9 (36.0)	16 (64.0)	0.5	0.21-1.22	Not significant
Hemiparesis					
No (n=94)	50 (53.2)	44 (46.8)	Reference		0.32
Yes (n=58)	26 (44.8)	32 (55.2)	0.71	0.37-1.38	Not significant
Hemiplegia					
No (n=143)	73 (51.0)	70 (49.0)	Reference		0.5
Yes (n=9)	3 (33.3)	6 (66.7)	0.48	0.11-1.99	Not significant
Overall symptomatic	45 (41.7)	63 (58.3)	3.34	1.57-7.08	Significant (p<0.05)

Chi-square test was applied to assess the relationship between each symptom and plaque stability; Odds ratios were calculated with stable plaques as the reference group; p<0.05 was considered statistically significant

DISCUSSION

Our study provides compelling evidence that unstable plaque characteristics, such as surface irregularities and thrombus formation, play a pivotal role in symptom manifestation in patients with carotid artery stenosis. These morphological features, indicative of higher embolic potential, reinforce the need for integrating plaque stability assessments into routine preoperative evaluations to enhance patient outcomes. Literature indicates that unstable plaques carry a high risk for thromboembolic events and are frequently observed in symptomatic patients [22,23]. Our findings resonate with this, showing that unstable plaques not only correlate with symptoms but significantly heighten the likelihood of critical neurological events, thus making plaque stability assessment an indispensable tool in preoperative evaluation. For instance, previous studies have reported that plaques with irregular surfaces, ulcerations, and thrombus are associated with embolic risk [24,25]. Our study similarly found that plaques with these characteristics were more prevalent among symptomatic patients, emphasizing the importance of detecting such features in preoperative evaluations to improve outcome prediction. Postoperative complications included transient ischemic attacks (2.6%), minor strokes (1.3%), and restenosis within the follow-up period (3.9%). Patients with unstable plaques exhibited a higher incidence of minor strokes, suggesting a possible link between plaque morphology and perioperative outcomes. In contrast, stable plaques are generally observed in asymptomatic patients and are associated with a lower risk of neurological complications [26,27]. Accordingly, many studies emphasize the need for plaque morphology assessment in the surgical decision-making process [28,29].

CEA is commonly performed in patients with carotid artery stenosis to reduce neurological complications. The NASCET and ECST trials have shown that CEA reduces neurological events in symptomatic patients with high-grade stenosis [30,31]. In asymptomatic patients, CEA has been found to be more beneficial than medical therapy for stenosis of 70% or greater [32,33]. However, to enhance treatment success, it is recommended to consider not only the degree of stenosis but also the stability or instability of the plaque [34,35]. Our study also observed that plaque morphology is a critical factor guiding surgical decision-making. This finding contributes to the growing body of evidence supporting the integration of detailed plaque assessment into routine care, suggesting that this could refine patient outcomes beyond traditional stenosis-focused approaches.

Imaging methods play a significant role in evaluating the relationship between plaque morphology and symptomatology. Emerging imaging modalities, including high-resolution

ultrasound and molecular imaging, have demonstrated superior capabilities in identifying plaque stability and vulnerability [36,37]. The literature reports that plaque assessments, particularly those using CDUS and CTA, are successful in identifying unstable plaque characteristics such as thrombus and ulceration [38,39]. Considering the high diagnostic accuracy of CDUS and CTA for high-risk plaque features, these tools should be prioritized in clinical protocols for stratifying risk in patients with varying degrees of stenosis. Our study confirms these findings, showing that CDUS and CTA effectively detected unstable plaques among symptomatic patients, supporting the role of these imaging modalities in identifying high-risk patients and refining treatment approaches. Identifying unstable plaques, which are more commonly observed in symptomatic patients, aids in making more accurate treatment decisions [40]. Therefore, by enhancing the decision-making process with morphology-based criteria, healthcare providers can offer a more proactive approach in preventing potentially fatal complications.

Limitations of the Study

This study has several limitations that should be acknowledged. Firstly, the retrospective nature of data collection introduces potential biases, such as incomplete or inconsistent data recording, which may influence the study outcomes. Secondly, the relatively small sample size of 152 patients limits the generalizability of the findings. This specific cohort may not fully represent the broader demographic or clinical characteristics of all patients undergoing carotid endarterectomy, especially in diverse populations with varying risk factors and healthcare practices. Plaque thickness was not measured intraoperatively in this study. Atherosclerosis risk factors were managed preoperatively with atorvastatin, acetylsalicylic acid, and clopidogrel, which were continued postoperatively unless contraindicated. Risk stratification was guided by clinical assessments, including lipid profiles and other relevant cardiovascular risk markers. Future research involving larger, prospective cohorts is necessary to validate and expand upon these findings.

CONCLUSION

This study highlights that plaque morphology, particularly the presence of unstable plaques, is crucial in predicting symptom risk in carotid artery stenosis, as unstable plaques are more prevalent in symptomatic patients and linked to increased neurological complications. CEA remains an effective treatment, especially for symptomatic high-grade stenosis, but incorporating plaque stability into decision-making enhances risk assessment. Non-invasive imaging techniques, such as USG, CDUS, and CTA, are recommended for their accuracy in identifying unstable plaques, helping prevent complications. A morphology-focused approach in treatment algorithms may reduce stroke risk and improve patient outcomes, emphasizing the need for further research to refine treatment strategies based on plaque characteristics.

Ethics Committee Approval: Ethical approval for the study was obtained from the Ethics Committee of Mersin University Faculty of Medicine on June 24, 2020 (approval number 448). The study protocol was prepared in accordance with ethical guidelines and confidentiality principles.

Patient Consent for Publication: This study was conducted in accordance with the Declaration of Helsinki, and informed consent was obtained from all participants.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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