

Recent Advances in the Use of Bioinformatics and Artificial Intelligence for Detecting Carotid Plaques

Songrui Zhu^{1*}

¹ Department of Radiology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China

*Correspondence: Songrui Zhu

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Abstract:

Vulnerable carotid plaques are a major cause of ischemic stroke. Traditional imaging assessment methods primarily rely on the degree of luminal stenosis and qualitative plaque characteristics, but they lack sufficient sensitivity in predicting stroke risk. In recent years, artificial intelligence (AI)-based radiomics and machine learning (ML) technologies have enabled high-throughput quantitative analysis of medical images, significantly improving the ability to identify high-risk plaques. This study provides a systematic review of the latest advances in the application of radiomics and machine learning to the assessment of carotid artery plaques, with a focus on imaging modalities such as ultrasound (US), computed tomography angiography (CTA), and magnetic resonance imaging (MRI).

Keywords:

Carotid Plaque, Ischemic Stroke, Artificial Intelligence

1. Introduction

Rupture of atherosclerotic plaques in the carotid artery and subsequent thrombus formation are among the primary mechanisms leading to ischemic stroke. Traditional risk assessment relies on the degree of stenosis and plaque morphological features (such as ulceration and calcification), but these indicators have limited accuracy and sensitivity in predicting stroke risk [1]. In recent years, the emergence of radiomics has provided new methods for the quantitative analysis of large-scale medical imaging datasets, and the application of AI and ML has further improved the accuracy of plaque risk assessment [2].

2. Fundamentals of Bioinformatics and Artificial Intelligence

2.1. Radiomics

Bioinformatics is a technique for high-throughput extraction of quantitative features (such as texture, morphology, and wavelet transforms) from medical images, combined with machine learning algorithms to build predictive models. The main workflow includes: image acquisition and preprocessing (denoising, normalization), lesion segmentation (manual or automatic ROI delineation), feature extraction (first-,

second-, and higher-order texture features), feature selection and modeling (LASSO regression, random forests, etc.), and model validation (ROC curves, cross-validation) [3]. Bioinformatics extracts and analyzes quantitative features from medical images, converting this data into clinically applicable indicators to provide deeper insights into the pathological mechanisms, prognosis, and treatment response of diseases. Although the field lacks uniformity in definitions, nomenclature, and evaluation methods—which makes cross-study comparisons difficult—imaging omics features are typically categorized into morphological features (e.g., shape, size), statistical features (e.g., intensity distribution), model-based features (e.g., fractal analysis), and transform-domain features (e.g., wavelet features). The Imaging Biomarker Standardization Initiative (IBSI) has proposed guidelines to standardize feature extraction and promote reproducibility of results. However, differences in imaging protocols and feature extraction methods remain major obstacles to clinical translation. Future efforts must focus on strengthening methodological standardization and validation to fully realize the potential of radiomics in precision medicine [4].

2.2. Machine Learning and Deep Learning

Artificial intelligence (AI) refers to computer systems that simulate human cognitive functions to solve complex tasks. In the field of medical imaging, this is primarily manifested through machine learning (ML) and deep learning (DL), which form a hierarchical relationship: ML is one of the implementation methods of AI, while DL is an advanced branch of ML [5]. Traditional machine learning (ML) methods (such as SVM and random forests) are primarily used for the analysis of radiomic features. Deep learning (DL) methods (such as CNNs, ResNets, and DenseNets) can automatically extract high-level features directly from images without the need for manual curation. The core difference lies in their learning paradigms: supervised learning relies on labeled data to predict diseases by establishing a mapping relationship between input features and target outputs; Unsupervised learning, on the other hand, mines intrinsic patterns from unlabeled data and offers unique advantages in identifying novel imaging biomarkers or patient subgroups. Specifically in radiological applications, supervised learning methods excel in diagnostic tasks such as lesion classification, while unsupervised techniques can reveal underlying disease phenotypes, providing new perspectives for precision medicine. The synergistic application of both approaches will more fully unlock the clinical value of medical imaging data.

As a key branch of machine learning, deep learning employs a multi-layered neural network architecture and demonstrates unique advantages when handling complex tasks. Unlike traditional machine learning, which relies on manually extracted features, deep learning directly processes raw data through its ability to learn representations, automatically constructing multi-level feature representations. This has enabled it to achieve breakthrough progress in medical imaging problems that traditional algorithms struggle to solve [6]. Of particular note is the development of hybrid learning paradigms: semi-supervised learning enhances model generalization by combining a small number of labeled samples with a large volume of unlabeled data; self-supervised learning, on the other hand, leverages the intrinsic structure of the data to generate supervisory signals, significantly reducing reliance on costly manual labeling. This adaptive feature extraction not only overcomes the shortcomings of traditional methods—such as heavy reliance on experts and time-

consuming processes—but also provides a new research dimension for uncovering latent correlations between pathological features in medical images.

3. Imaging characteristics of plaque vulnerability

In the past, the degree of carotid artery stenosis was considered a key indicator for assessing stroke risk. This view was primarily based on studies conducted in the 1980s and 1990s, which emphasized the efficacy of carotid endarterectomy (CEA) in patients with severe stenosis (70%–99%) [7]. However, recent studies have found that relying solely on the degree of stenosis may have significant limitations: most patients with severe stenosis are actually asymptomatic (annual symptom conversion rate <1%), and approximately one-third of patients with anterior circulation strokes have stenosis of less than 50%. This contradiction highlights the critical role of plaque stability in risk assessment—features of vulnerable plaques (such as a lipid necrotic core, ruptured fibrous cap, or intramural hemorrhage) may have greater predictive value than stenosis severity alone [8].

The Carotid Plaque RADS system proposed by the Saba team offers a solution to this problem [9]. This system integrates three categories of indicators through multimodal imaging: (1) core features (maximum wall thickness, lipid necrotic core, fibrous cap integrity, etc.); (2) auxiliary features (positive remodeling, plaque burden, calcification patterns); and (3) modifying factors (post-stenting status, history of CEA), thereby establishing a standardized framework for stroke risk stratification. Ultrasound, as the preferred screening tool, can provide an initial assessment of plaque burden and fibrous cap thickness (Class 3a). If hyperechoic areas adjacent to the lumen are detected (suggesting a lipid core covered by a thin fibrous cap, plaque rupture, or intraluminal thrombus), further confirmation with high-resolution imaging is required (Classes 3b–4c). This advancement marks a paradigm shift in carotid risk assessment from “lumen stenosis” to “plaque vulnerability,” providing a new basis for personalized treatment decisions.

3.1. Lipid-rich necrotic core

As the earliest pathological feature of atherosclerotic plaque formation, the development of LRNCs begins at the lipid streak stage. As macrophages phagocytose lipids and transform into foam cells, secondary cell necrosis leads to the accumulation of extracellular lipid pools, ultimately resulting in the formation of LRNCs [10]. On magnetic resonance imaging, LRNC appears as isointense or slightly hyperintense on fat-suppressed T1-weighted images but exhibits slightly hypointense signal on MPRAGE sequences, which aids in distinguishing it from intraplaque hemorrhage. Contrast-enhanced imaging can further distinguish between non-enhancing LRNC and markedly enhanced fibrous cap structures. Although the risk associated with LRNC is relatively lower than that of other high-risk plaque features, it may still lead to clinical symptoms. More importantly, LRNC is progressive: it may increase in volume and may evolve into higher-risk plaque features such as fibrous cap rupture, intraplaque hemorrhage, or ulceration [11]. Clinical studies have shown that intensive statin therapy can significantly reduce the volume of LRNCs. Notably, this therapeutic effect is time-dependent: while short-term (3-month) treatment yields limited results, significant volume reduction can be observed with continuous treatment for over 1 year, and long-term treatment (3 years) can even reduce LRNC volume by up to 50%. This finding holds significant clinical value: continuous imaging follow-up not only allows for the assessment of dynamic changes in LRNCs

but also enables objective monitoring of the therapeutic effects of statins, providing a crucial basis for the precision treatment of atherosclerosis.

3.2. Intra-plaque hemorrhage

Intra-plaque hemorrhage (IPH) is considered a key marker of vulnerable plaques, and its pathogenesis is primarily associated with the rupture of immature neovascularization on the plaque surface. As the high-risk plaque feature with the strongest evidence to date, IPH not only promotes rapid plaque growth but is also closely associated with ipsilateral neurological symptoms and significantly increases the risk of future stroke. Technologies for imaging IPH have undergone significant evolution: traditional T1-weighted MRI identifies hemorrhagic foci based on the high signal intensity of blood metabolites (such as methemoglobin); subsequently developed MPRAGE sequences further enhance T1 contrast in IPH regions [12]. In recent years, some institutions have begun adopting synchronized non-contrast angiography and intramural hemorrhage (SNAP) technology. By optimizing the signal contrast between blood flow and hemorrhagic tissue, this sequence has significantly improved the sensitivity and specificity of IPH detection. These technological advancements have transformed IPH from a mere pathological feature into a precisely identifiable clinical warning sign, providing critical imaging evidence for stroke risk stratification [13].

Multiple studies have confirmed that IPH in carotid plaques is significantly associated with ipsilateral ischemic events, such as stroke or transient ischemic attack. In both asymptomatic and symptomatic patients, the presence of IPH substantially increases the risk of future ischemic events. It is worth noting that while some studies suggest that high signal intensity on imaging may further indicate an increased risk of ischemia, this view remains controversial [14]. Recent clinical observations have shown that IPH is more common in specific high-risk groups, including elderly men, smokers, and patients with hyperlipidemia or hypertension. In addition, the incidence of IPH is significantly higher in the left carotid artery than in the right, although the exact mechanism remains unclear [15]. Recent studies have also shown that, in patients with mild to moderate carotid artery stenosis, the presence of IPH and total plaque volume may both be significant predictors of ipsilateral stroke recurrence. These findings suggest that, in clinical practice, special attention should be paid to patients with IPH-particularly those with multiple risk factors-in order to optimize stroke prevention strategies [14].

3.3. Plaque Ulcers

Plaque ulceration refers to defects in the surface of the fibrous cap of an atherosclerotic plaque, manifesting as depressions, erosions, or fissure-like changes. This structural defect is primarily caused by thinning of the fibrous cap due to local inflammatory reactions or hemodynamic stress. Its pathophysiological basis warrants significant clinical attention: ulceration leads to the direct exposure of the plaque's internal components to the bloodstream, which not only accelerates the process of plaque instability but may also trigger thrombus detachment, resulting in distal embolic events. Although some recent studies have found no significant association between the presence of ulcers and the side of symptoms, the majority of evidence supports the notion that ulcers increase the risk of ipsilateral ischemic events [16]. Research data indicate that ulcerated plaques are not only significantly associated with ischemic events but may also influence stroke severity. It is worth noting that the

clinical significance of ulceration may involve a “threshold effect”: while its role is relatively clear in plaques with severe stenosis (e.g., >70%), further research is needed to confirm its harmful effects in plaques with mild to moderate stenosis. In clinical practice, it should be recognized that plaque ulceration, as one of the key characteristics of vulnerable plaques, poses a risk not only due to structural damage but also because it reflects a highly unstable pathological state of the plaque. Therefore, even “quiescent” ulcers identified on imaging require active medical intervention and close follow-up.

3.4. Fiber cap rupture

Fibrous caps, as a key component of atherosclerotic plaques, begin to form during the early stages of plaque development. Composed primarily of smooth muscle cells that have migrated into the vascular lumen, they play an indispensable protective role in maintaining plaque stability by effectively isolating vulnerable plaque contents—such as necrotic lipid cores and intraplaque hemorrhages—from the blood flow environment [11]. From a pathological perspective, an intact and thick fibrous cap can withstand hemodynamic stress and indicates that the plaque is relatively stable; conversely, a thinned or ruptured fibrous cap is a high-risk feature, signaling a potential risk of ischemic events. It is important to note that the precise assessment of the fibrous cap poses significant technical challenges. Even with high-resolution carotid plaque surface coils, accurately determining the integrity of the fibrous cap remains difficult. Therefore, the comprehensive term “thinned or ruptured fibrous cap” (TRFC) is commonly used in clinical practice to describe the severity of the lesion. Recent research evidence indicates a clear association between TRFC and cerebrovascular ischemic events. Furthermore, it is worth noting that plaque surface irregularities (even if they do not meet TRFC criteria) may also have significant clinical implications; studies suggest that these often accompany a lipid necrotic core or intraplaque hemorrhage and may increase the risk of subsequent vascular events. From a clinical practice perspective, assessing the state of the fibrous cap is not only valuable for predicting stroke risk but may also serve as a key factor in guiding treatment decisions. For patients in whom TRFC has been identified, intensified antiplatelet therapy and closer follow-up monitoring should be considered. In the future, with advances in imaging technology, quantitative analysis of the fibrous cap may provide a more precise basis for personalized treatment.

4. Guidelines for the Treatment of Carotid Plaques

Currently, surgical decisions for CEA are primarily based on the degree of arterial stenosis and perioperative risks, with criteria drawn from the findings of the North American Symptomatic Carotid Endarterectomy Trial (NASCET) and the European Carotid Surgery Trial (ECST) [17]. According to these criteria, surgical intervention or stent placement is recommended only for symptomatic patients with stenosis $\geq 50\%$. However, recent studies have shown that the degree of stenosis is closely associated with features of vulnerable plaques (such as intraplaque hemorrhage, ulceration, and rupture of the fibrous cap), and the success of NASCET and ECST may be partly attributed to interventions targeting high-risk plaques. It is worth noting that many symptomatic plaques are classified as non-severe stenosis ($<50\%$) under NASCET criteria, yet their biological behavior may still pose a high risk. Consequently, an increasing number of scholars are calling for a revision of current treatment guidelines to incorporate imaging features of plaque vulnerability into the evaluation system for

surgical indications. Furthermore, the volume of lipid necrotic core (LRNC), the integrity of the fibrous cap, and specific types of intraplaque calcification also hold potential clinical value. In the future, a multimodal, individualized decision-making model combining hemodynamic assessment with plaque biological characteristics is expected to provide more precise treatment options for patients with carotid artery disease. Currently, there remains a lack of sufficient evidence-based data regarding the medical management of vulnerable carotid plaques, and no clear clinical guidelines have been established. Existing management strategies are largely based on expert consensus: all patients with unexplained ischemic stroke (ESUS) should receive standard medical therapy (including high-intensity statin therapy and dual antiplatelet therapy for 3 weeks, followed by long-term monotherapy with aspirin), while further evaluation via magnetic resonance angiography (MRA) to determine the need for surgical intervention is recommended. This perspective specifically notes that carotid endarterectomy (CEA) should be considered for patients with intra-plaque hemorrhage (IPH) and/or ulceration who experience recurrent strokes [18].

5. Conclusions

In recent years, magnetic resonance imaging has made significant advances in the assessment of carotid atherosclerotic plaques. There is now a deep understanding of the identification and clinical significance of both high-risk features (such as Intra-plaque hemorrhage and capsular rupture) and stable features (such as calcifications). This development is driving a shift in clinical decision-making from a reliance solely on the assessment of stenosis severity toward a multidimensional evaluation that incorporates plaque characteristics. In the future, with advances in imaging technology and the accumulation of clinical evidence, the plaque characteristics provided by MRI will increasingly become a key basis for predicting stroke risk and formulating individualized treatment plans. This requires clinicians to continuously update their knowledge base and promptly grasp the potential impact of emerging imaging biomarkers on diagnostic and treatment guidelines, particularly maintaining up-to-date judgment on core issues such as the early identification of high-risk plaques and the selection of optimal intervention timing.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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