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Research Progress on the Relationship Between Carotid Artery Plaques and Ischemic Stroke Based on CTA Imaging

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Abstract

Ischemic stroke accounts for more than 80% of all stroke cases and is closely related to carotid artery plaques. Early and accurate diagnosis and risk assessment are crucial for improving prognosis. Computed tomography angiography (CTA), as an efficient and non-invasive imaging technique, plays a significant role in the diagnosis and treatment of ischemic stroke. This article reviews the research progress of carotid CTA in this field, including plaque feature analysis, ischemic stroke risk prediction, and the application of the Plaque-RADS scoring system. It also points out technical limitations and prospects for future development, providing references for clinical practice and scientific research.

Keywords: computed tomography angiography, ischemic stroke, carotid artery plaques, plaque vulnerability

1. Introduction

Ischemic stroke is one of the leading causes of disability and mortality worldwide, accounting for more than 80% of all stroke cases (Wu J, Zou Y, Meng X, Fan Z, van der Geest R, Cui F, et al., 2024). Its pathogenesis is often related to atherosclerosis, particularly the formation, rupture, and thromboembolism of carotid artery plaques. According to statistics, there are approximately 13 million new stroke cases globally each year, with about 25%–30% closely associated with carotid artery stenosis or plaque vulnerability. Due to the high incidence, high recurrence rate, and significant societal burden of ischemic stroke, early and accurate diagnosis and risk assessment are crucial for improving patient prognosis.

Computed tomography angiography (CTA) is an efficient and non-invasive imaging technique. By intravenous injection of contrast agent combined with rapid CT scanning, it can clearly display the anatomical structure of the carotid arteries, plaque morphology, and hemodynamic characteristics. Since its clinical application in the 1990s, CTA technology has been continuously optimized, evolving from single-slice spiral CT to current spectral CT and ultra-high-resolution CTA, significantly improving image quality and diagnostic accuracy. Compared to traditional ultrasound and magnetic resonance angiography (MRA), CTA offers unique advantages such as fast scanning speed, high spatial resolution, and the ability to assess calcified plaques. It has become an important tool for etiological screening and preoperative evaluation of ischemic stroke.

This review aims to systematically summarize the research progress of carotid CTA imaging in the field of ischemic stroke, focusing on its application in plaque feature analysis, ischemic stroke risk prediction, and the Plaque-RADS scoring system. It will also analyze current technical limitations and prospect future development directions, providing references for clinical practice and scientific research.

2. Application of CTA in Carotid Plaque Feature Analysis

The nature and characteristics of carotid atherosclerotic plaques are key to predicting stroke risk. With the integration of CTA, radiomics, and artificial intelligence, precise identification and quantitative analysis of plaques have become possible, providing a basis for early intervention in ischemic stroke.

2.1 Identification of Plaque Characteristics

CTA is highly reliable for judging the degree of stenosis in intracranial and extracranial arteries and is commonly used for detecting carotid plaques (Liu, Y., & Hui, P., 2024). In recent years, classification models combining artificial intelligence and radiomics have significantly improved the accuracy of identifying plaque characteristics. For example, Buckler et al. (2023) prospectively collected CTA images and paired atherosclerotic plaque specimens from patients who underwent carotid endarterectomy at two centers. Based on pathological results, plaques were classified into normal, stable, and unstable categories. Using machine learning to classify vascular cross-sectional samples from 496 development cohorts and 408 validation cohorts, the results showed that the model achieved 93% accuracy in identifying unstable plaques. Shan et al. (2023) retrospectively analyzed CTA and contrast-enhanced ultrasound (CEUS) data from 74 patients (total 110 plaques). Using CEUS-defined plaque contrast enhancement as an indicator of intraplaque neovascularization (judging plaque vulnerability), plaques were divided into vulnerable and stable groups. Then, through radiomics feature selection, 10 key features related to neovascularization were identified, and prediction models were constructed using 7 algorithms including logistic regression and random forest. The random forest model achieved an AUC of 0.93, confirming the potential of CTA in distinguishing plaque characteristics.

Intraplaque hemorrhage (IPH) is a core feature of vulnerable plaques and is closely associated with increased stroke risk (Larson AS, Nasr DM, Rizvi A, Alzuabi M, Seyedsaadat SM, Lanzino G, et al., 2021). Studies suggest that a CT value <25 HU can serve as an indicator for IPH (Saba L, Francone M, Bassareo PP, Lai L, Sanfilippo R, Montisci R, et al., 2018). However, high-resolution magnetic resonance imaging (MRI), due to its higher specificity and sensitivity, is considered the best imaging technique for identifying IPH, with the defined standard being an MRI signal intensity of IPH reaching 1.5 times that of adjacent muscle tissue (Zhou T, Jia S, Wang X, Wang B, Wang Z, Wu T, et al., 2019). Zhang et al. (2022) conducted a multicenter retrospective study incorporating multimodal data, including 64 patients who underwent both carotid CTA and high-resolution vessel wall MRI. Using MRI results as the gold standard, patients were divided into IPH and non-IPH groups. LASSO regression was used to select CTA radiomics features, which were combined with clinical factors to build a prediction model. The results showed that this model achieved a diagnostic accuracy of 84.2% (AUC=0.811) in the external validation set, significantly better than the pure clinical model (accuracy 78.9%, AUC=0.761), confirming the supplementary value of CTA radiomics features in IPH identification. Eisenmonger et al. (2016) developed a CT prediction model integrating plaque features such as the positive rim sign, maximum soft plaque thickness, degree of stenosis, and ulceration, achieving an AUC as high as 0.94 for predicting IPH, further validating the reliability of multi-parameter CT assessment in determining plaque characteristics.

2.2 Quantitative Analysis of Plaque Features

Intelligent analysis technologies based on CTA have promoted the shift of plaque assessment from subjective judgment to objective quantification, with deep learning and semi-automatic quantification methods being important advancements. Zhu et al. (2022) used the nnU-Net deep learning framework to achieve automated assessment of carotid stenosis and plaque features. Validated with 93 patients, the model showed high accuracy for calcified plaque segmentation (Dice coefficient = 0.795), and excellent agreement with radiologists' diagnoses for stenosis degree judgment (Kappa=0.930). More importantly, this system reduced the assessment time from 296.8 seconds for traditional manual analysis to 27.3 seconds, significantly improving clinical efficiency. Meanwhile, Chrencik et al. (2019) developed a semi-automatic quantitative analysis method focusing on precise measurement of plaque morphology and composition. Through the analysis of 93 carotid arteries from 50 patients, this method demonstrated excellent reproducibility in measuring plaque volume (ICC=0.96) and calcified components (ICC=0.99), capable of detecting volume changes as small as 4%, providing a precise tool for monitoring plaque progression.

3. Application of CTA in Ischemic Stroke Risk Prediction

Traditional carotid assessment focuses on the degree of stenosis, but recent studies have shown that plaque vulnerability features (such as ulceration, lipid core, intraplaque hemorrhage, etc.) have higher predictive value for stroke risk. CTA, through multi-parameter analysis, provides substantial evidence for ischemic stroke risk prediction.

3.1 Combined Prediction Based on Radiomics and Clinical Features

Radiomics can high-throughput mine imaging features from medical images, extracting quantitative data information difficult for the human eye to recognize for analysis. Li et al. (2025) used radiomics and traditional risk factors to build a combined model, achieving an AUC of 0.878, which was about 15% higher than the traditional clinical model; the 9 optimal radiomics features screened mainly reflected plaque heterogeneity and surface irregularity, providing new indicators for risk stratification. Shi et al. (2023) further found that plaque ulceration (OR=6.106) and the rim sign (OR=3.285) were the most predictive morphological features. In summary, radiomics, by mining the potential quantitative features of plaques and combining them with traditional clinical risk factors and key morphological features (such as plaque ulceration, rim sign), can significantly improve the performance of ischemic stroke risk prediction models, providing a more accurate basis for clinical risk stratification and decision-making.

3.2 Predictive Value of Calcification Features

The relationship between calcified plaques and stroke risk is controversial, with some considering them protective and others suggesting they indicate vulnerability. However, recent research has clarified the predictive value of calcification configuration and found that the napkin-ring sign (NRS) is an important marker. Pisu et al. (2024) classified calcified plaques into 6 morphological subtypes through a multicenter study and established 5 prediction models using clinical variables and calcification grading. The ML-All-G model (including plaque grading and all other variables) confirmed that calcification configuration (rather than mere presence) is a key determinant of stroke risk, especially the napkin-ring sign on the right artery in elderly and hyperlipidemia patients, which is significant for identifying symptomatic patients. Meanwhile, Wu et al. (2024) found that the number of NRS plaques was an independent risk factor for stroke. The AUC for identifying acute ischemic stroke (AIS) using ipsilateral NRS plaques reached 0.86, confirming that NRS is closely related to ischemic stroke and can serve as an important indicator for identifying high-risk AIS patients in emergency settings, providing a basis for early anti-atherosclerotic treatment.

3.3 Optimization of Prediction Models with Novel Biomarkers

Furthermore, the addition of novel biomarkers has further optimized prediction models. Luo et al. (2025) compared the perivascular fat density (PFD) at the most stenotic plaque level between symptomatic and asymptomatic patients, finding that PFD was significantly correlated with plaque burden and soft plaque thickness ($P<0.05$). PFD, along with the degree of stenosis, plaque burden, and soft plaque thickness, served as predictors for symptomatic carotid plaques. After incorporating PFD, the prediction model's AUC increased from 0.631 to 0.846. Moreover, research (2025) confirmed that PFD also has important predictive value for stroke recurrence. Multivariate Cox analysis showed that PFD was associated with recurrent stroke or transient ischemic attack (TIA), and the event-free survival rate was significantly lower in the high PFD group. Research (2024) also found that non-alcoholic fatty liver disease

(NAFLD), as an indicator of systemic metabolic abnormality, could independently predict stroke/TIA recurrence. The combined model built with clinical data and plaque features showed the best predictive performance, with an AUC of 0.79, providing a new target for secondary stroke prevention.

4. CTA-Related Standardized Assessment System: Application of the Plaque-RADS Scoring System

Traditional carotid assessment relies on the degree of stenosis but may underestimate the risk of some vulnerable plaques. The proposal of the Carotid Plaque Reporting and Data System (Plaque-RADS) has standardized plaque assessment, compensating for this deficiency. Saba et al. (2023) proposed Plaque-RADS, aiming to establish a standardized imaging assessment system for carotid plaques. Addressing the lack of consensus in reporting carotid plaque characteristics, the study constructed a standardized classification system through expert consensus and multimodal imaging analysis. It not only includes traditional quantitative assessment of stenosis but also supplements qualitative analysis of plaque morphological features (such as thickness, ulceration, hemorrhage, etc.), providing a unified assessment standard for clinical practice.

On this basis, multiple studies have confirmed the value of Plaque-RADS in stroke risk assessment, showing significant advantages especially in patients with mild to moderate stenosis. Song et al. (2025) proposed a CTA-modified Plaque-RADS for patients with embolic stroke of undetermined source (ESUS), finding that the proportion of high-risk plaques (≥ Grade 3: thickness ≥3 mm, ulceration, or hemorrhage volume >50 mm^3) on the stroke-ipsilateral side was significantly higher than on the contralateral side. This confirmed that the system can assist in identifying vulnerable plaque phenotypes, especially suitable for etiological screening in ESUS patients with stenosis degree <50%. Further, Huang et al. (2025) confirmed through a large-sample retrospective study (n=1,378) that the Plaque-RADS grade was significantly correlated with stroke risk (P<0.001). Moreover, in patients with mild to moderate stenosis, those with Plaque-RADS ≥ Grade 3 had a significantly increased stroke risk. Combining Plaque-RADS with stenosis grading improved the net reclassification index, suggesting it can compensate for the blind spots of traditional stenosis assessment. Additionally, Qian et al. (2025) innovatively combined Plaque-RADS with pericarotid fat density (PFD) to construct a comprehensive risk index (CRI). They found that the combined model (stenosis degree + Plaque-RADS + PFD) had significantly better predictive efficacy for stroke recurrence than any single indicator (AUC=0.892), providing new ideas for personalized prevention in patients with mild to moderate stenosis.

5. Limitations of CTA

Although CTA has significant advantages in carotid plaque assessment, it still has technical limitations: First, the ionizing radiation generated during the examination (He Y, Li Y, Chen Y, Feng L, Nie Z, 2014) may pose potential harm to patients. Second, the use of iodine contrast agent may cause adverse reactions such as allergies or renal impairment (Yamada K, Kawasaki M, Yoshimura S, Shirakawa M, Uchida K, Shindo S, et al., 2016). Furthermore, when the CT value of calcified plaque areas is close to that of the enhanced vessel lumen, it can reduce the diagnostic sensitivity for plaque ulceration, affecting assessment accuracy. Therefore, the optimal diagnostic technique should be selected based on the specific circumstances of the patient.

6. Summary and Outlook

Carotid CTA has become a key technical means for evaluating carotid atherosclerotic lesions. Its clinical value is mainly reflected in two aspects: measurement of luminal stenosis degree and characterization of vulnerable plaques. Existing studies have confirmed that imaging features of vulnerable plaques (such as IPH, LRNC, thin fibrous cap, or specific calcification patterns) are significantly correlated with the occurrence of ischemic stroke events (Baradaran H, Eisenmenger LB, Hinckley PJ, de Havenon AH, Stoddard GJ, Treiman LS, et al., 2021). With the innovation of CT technology, carotid assessment has progressed from traditional stenosis measurement to the stage of analyzing plaque microstructure. The application of artificial intelligence and radiomics has further achieved breakthroughs from plaque feature assessment to micro-information detection. Current research focuses on the clinical translational value of vulnerable plaque feature biomarkers, including their role in treatment decision-making mechanisms and optimal intervention strategies for different plaque characteristics (Saba L, Saam T, Jäger HR, Yuan C, Hatsukami TS, Saloner D, et al., 2019). Future work requires more clinical studies to clarify the association between plaque features and risk prediction models for cerebral ischemic events to guide individualized treatment. Simultaneously, integrating machine learning, deep learning, and radiomics to explore the intrinsic relationship between imaging phenotypes and histopathological features will open new directions for the precise diagnosis and treatment of carotid atherosclerosis.

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