

Advances in CT Perfusion Imaging Combined with High-Resolution Vessel Wall MRI for Ischemic Stroke

Wenjing Wang^{ID}, Daokai Gong*

Jingzhou Hospital Affiliated to Yangtze University, Jingzhou, China
Email: 15675661703@163.com, *dk_gong@163.com

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Abstract

CT perfusion imaging (CTP) and high-resolution magnetic resonance vessel wall imaging (HR-VWI) are two important modalities in the imaging assessment of ischemic stroke, providing complementary information from hemodynamic and vessel wall structural perspectives, respectively. CTP enables rapid quantification of the infarct core and ischemic penumbra in the acute phase, supporting decision-making reperfusion therapy, particularly in patients presenting beyond 6 hours from symptom onset. HR-VWI directly visualizes pathological changes of the vessel wall and offers unique advantages in differentiating etiologies such as atherosclerosis, arterial dissection, moyamoya disease and vasculitis. In recent years, the multimodal integration of these two techniques has gained increasing attention; however, related clinical studies remain in early stages, facing challenges including insufficient evidence, lack of technical standardization, and limited generalizability of artificial intelligence models. This review systematically summarizes the technical principles, clinical applications, and limitations of CTP and HR-VWI, with a focus on the current evidence and future directions for their combined use, aiming to inform precision imaging assessment in ischemic stroke.

Keywords

Ischemic Stroke, CT Perfusion Imaging, High-Resolution Magnetic Resonance Vessel Wall Imaging, Multimodal Imaging

1. Introduction

Ischemic stroke has become a major public health problem worldwide due to its high mortality and disability rates. With the acceleration of population aging, the

disease burden of ischemic stroke continues to rise, posing severe challenges to healthcare systems [1]. In the acute phase, the main task of neuroimaging is to rapidly identify patients suitable for reperfusion therapy [2]. CTP generates quantitative parametric maps of cerebral blood flow, cerebral blood volume, mean transit time, and time-to-maximum, which enable the assessment of tissue viability and differentiation between irreversibly damaged infarct core and potentially salvageable ischemic penumbra [3]. Studies have shown that patients with a small infarct core and a large penumbra derive significant clinical benefit from reperfusion therapy, regardless of whether they receive intravenous thrombolysis or endovascular treatment [3]. On the other hand, HR-VWI can directly visualize vessel wall structures, assess plaque components and vascular remodeling patterns, and help identify stroke etiologies, including atherosclerosis, arterial dissection, moyamoya disease, and vasculitis, while also evaluating plaque vulnerability and guiding individualized secondary prevention [4]. However, each modality has its limitations. CTP can assess cerebral hemodynamic status but cannot provide structural information of the vessel wall; HR-VWI can display the anatomical and pathological features of the vessel wall but cannot obtain real-time perfusion information of the brain parenchyma. Based on this complementarity, combining CTP with HR-VWI to construct a multimodal imaging evaluation strategy may provide a more comprehensive assessment for patients with ischemic stroke. This review aims to summarize the research progress of CTP and HR-VWI in ischemic stroke, with a focus on the principles and core parameters of the two techniques, their clinical applications and limitations, and the existing evidence and future directions for multimodal integration.

2. CTP: Principles and Clinical Applications

2.1. Technical Principles and Core Parameters of CTP

CTP is a dynamic acquisition technique that captures the transit of contrast agent through brain tissue [5]. In other words, as the contrast agent flows through the region of interest, the brain is repeatedly scanned to measure its relative increase, peak, and decrease, generating a time-attenuation curve [5]. Based on the time-attenuation curves obtained from the arterial input function (AIF) and venous output function (VOF), perfusion parameters are calculated for each voxel on the CTP maps that reflect different hemodynamic characteristics [5]. CTP generates multiple core hemodynamic parameters. Cerebral blood flow (CBF) reflects the volume of blood flowing through a given mass of brain tissue per unit time; cerebral blood volume (CBV) reflects the total volume of blood contained within a given mass of brain tissue; mean transit time (MTT) reflects the average time for blood to flow from arteries to veins; Tmax reflects the time to peak of the residue function [5] [6].

2.2. Clinical Applications in the Acute Phase

Upon arrival at the emergency department, in patients with suspected acute is-

chemic stroke, the decision to perform CTP examination depends on institutional protocols, clinical presentation, and the intended reperfusion-treatment strategy, rather than being a routine examination for all patients. Studies have shown that combining CTP with non-contrast CT improves diagnostic accuracy for detecting ischemia [7]. The primary value of CTP in the acute phase lies in patient selection for the late window (>6 hours from symptom onset). The DAWN and DEFUSE-3 trials extended the time window for endovascular therapy to 24 hours and 16 hours, respectively, both using CTP or DWI to screen for patients with salvageable penumbra [8] [9]. A secondary analysis of the MR CLEAN-LATE trial further demonstrated a significant interaction between penumbra volume and the effect of thrombectomy on functional outcomes (P for interaction < 0.001), with the greatest benefit observed in patients with penumbra ≥ 120 mL (adjusted common odds ratio = 6.89, 95% CI: 2.96 - 16.04), while a potential harmful trend was suggested in patients with penumbra ≤ 72 mL (adjusted common odds ratio = 0.49, 95% CI: 0.2 - 1.08) [10]. A meta-analysis of 14 studies comprising 5809 patients showed that compared with CTA alone, CTP/CTA was associated with reduced 90-day mortality (OR = 0.72, 95% CI: 0.60 - 0.87) and higher recanalization rates (OR = 1.42, 95% CI: 1.0 - 1.94), but the improvement in functional independence did not reach statistical significance [11]. Differences in core volume estimation across different post-processing software packages remain a major technical challenge limiting standardized application [12]. In addition, CTP provides valuable prognostic information in cerebral ischemia. A meta-analysis by Campbell *et al.* showed that the volume of hypoperfused tissue identified by $T_{max} > 6$ s was negatively associated with functional independence and functional improvement, whereas the definition of infarct core depends on the specific post-processing method and threshold applied (e.g., relative CBF < 30%) [13].

2.3. Limitations and Deficiencies Phase

The diagnostic accuracy of CTP in acute ischemic stroke remains a subject of debate. A systematic review of 11 studies reported a sensitivity of 69.9% and specificity of 87.7% for CTP [14]; another systematic review of 27 studies comprising 2,168 patients showed a pooled sensitivity of 82% (95% CI: 75% - 88%) and pooled specificity of 96% (95% CI: 89% - 99%) for CTP in diagnosing AIS, with sensitivity superior to non-contrast CT and comparable to CTA. No statistically significant differences in sensitivity or specificity were observed between patients undergoing CTP within 6 hours of symptom onset and those beyond 6 hours [15]. CTP does not always accurately predict the presence of ischemic stroke, and some ischemic lesions may be missed, leading to false-negative results. In addition, conditions such as extracranial carotid artery stenosis and proximal intracranial stenosis can mimic the perfusion patterns of acute cerebral ischemia, resulting in false-positive assessments. CTP techniques exhibit significant heterogeneity across institutions, with parameters influenced by scanner type, post-processing software differences, and optimization settings specific to large vessel occlusion stroke scenarios. Be-

yond image acquisition and post-processing techniques, the definition and calculation methods of perfusion parameters also represent important sources of variability [16].

3. High-Resolution Magnetic Resonance Vessel Wall Imaging: Principles and Clinical Applications

3.1. Abbreviations and Acronyms

The core principle of HR-VWI lies in suppressing the signal of flowing blood within the vessel lumen to achieve direct visualization of the vessel wall structure [17]. Traditional luminal imaging techniques rely mainly on intraluminal blood flow signals to indirectly assess vascular lesions; however, many cerebrovascular diseases have pathological changes that primarily occur in the vessel wall itself, and HR-VWI overcomes this limitation [18]. The main technical requirements for intracranial VW-MR imaging include: 1) high spatial resolution, 2) multi-planar 2D or 3D acquisition, 3) multiple tissue weightings, and 4) suppression of intraluminal blood and cerebrospinal fluid signals [19]. Intracranial artery wall thickness typically ranges from 0.3 to 0.6 mm; therefore, to accurately assess wall pathology, HR-VWI requires submillimeter spatial resolution, with isotropic resolution generally required to reach 0.4 - 0.7 mm [20]. In terms of core evaluation features, HR-VWI image interpretation is primarily based on wall morphology (concentric vs. eccentric thickening), plaque components (intraplaque hemorrhage, lipid core), vessel wall enhancement patterns, and remodeling index [21]. The patterns of wall thickening differ across etiologies: atherosclerosis frequently presents as eccentric wall thickening, whereas vasculitis often shows concentric wall thickening, and moyamoya disease usually demonstrates no wall enhancement [20]. These imaging features should be interpreted as supportive rather than definitive findings, because considerable overlap exists among intracranial atherosclerosis, vasculitis, dissection, and moyamoya vasculopathy, and no single pattern is pathognomonic for a specific etiology. Intraplaque hemorrhage appears as high signal intensity on T1-weighted sequences and is an important marker of vulnerable plaque [22]. The degree of plaque enhancement after contrast administration reflects inflammatory activity of the plaque and is significantly associated with the occurrence and recurrence of ischemic stroke [23].

3.2. Application of HR-VWI in Etiological Diagnosis

High-resolution magnetic resonance vessel wall imaging can directly visualize the structure of intracranial arterial walls and has unique value in the etiological differentiation of ischemic stroke [4]. Intracranial arterial diseases mainly include atherosclerosis, arterial dissection, moyamoya disease, and vasculitis. HR-VWI can effectively distinguish these different etiologies by displaying wall morphology, plaque components, and enhancement characteristics [4] [18]. In the assessment of atherosclerotic plaques, a study of 91 patients with symptomatic intracranial atherosclerotic stenosis showed that plaque burden was significantly corre-

lated with plaque enhancement $P = 0.037$, and ROC analysis determined that a contrast ratio ≥ 0.56 could effectively predict symptomatic Intracranial Atherosclerotic Stenosis (ICAS) [24]. In the differentiation of intracranial arterial dissection, HR-VWI can clearly demonstrate typical signs such as intramural hematoma, intimal flap, and double-lumen sign [4]. HR-VWI also has important value in differentiating moyamoya disease and vasculitis. Moyamoya disease may show vessel wall contrast enhancement on HR-VWI, and high-resolution vessel wall imaging contributes to the diagnosis and prognosis prediction of moyamoya disease [25]. Central nervous system vasculitis typically presents as concentric wall thickening and enhancement on HR-VWI [26]. HR-VWI can detect subtle mural inflammation in cases with normal luminal imaging, helping to differentiate Central Nervous System (CNS) vasculitis from other vascular diseases [27].

3.3. Limitations of HR-VWI

Although HR-VWI has unique value in the etiological diagnosis of ischemic stroke, its clinical adoption faces multiple constraints. Conventional 3T HR-VWI acquisition takes approximately 10 minutes per case, making it difficult to perform in emergency settings or in patients who cannot cooperate [28]. In addition, manual segmentation of the vessel wall and plaques requires continuous personnel training and is labor-intensive; the low contrast between the vessel wall and surrounding tissue, combined with reliance on expert experience, means that analysis of a single case often takes more than 30 minutes, severely affecting clinical efficiency [29]. Different centers lack unified standards for scanning parameters, sequence types, and interpretation criteria, making it difficult to directly compare and pool research findings [30]. A 2022 survey by the American Society of Neuroradiology showed that more than half of the participating centers had not incorporated HR-VWI into routine clinical practice, with the main reasons being lack of interpretive expertise (53.1%), insufficient technical support (46.4%), and limited knowledge of clinical applications (50.5%) [30]. Currently, there is no globally unified operational guideline for this technique, and diagnostic standards largely rely on expert consensus [30].

4. Multimodal Integration of CTP and HR-VWI

4.1. Complementarity Concept

CTP can effectively distinguish infarct core from ischemic penumbra by measuring parameters such as CBF, CBV, MTT, and Tmax [31], and has important screening value for endovascular treatment decisions in late-window patients presenting beyond 6 hours from symptom onset [10]; however, CTP cannot provide pathological information about the vessel wall itself. HR-VWI addresses this limitation by clearly displaying vessel wall morphology and plaque characteristics, including intraplaque hemorrhage, plaque enhancement, and remodeling patterns [32]. A prospective multicenter study showed that intraplaque hemorrhage was an independent risk factor for predicting ipsilateral stroke recurrence (HR = 6.64, 95%

CI: 1.23 - 35.8, $P = 0.028$) [33]. CTP and HR-VWI each have different informational emphases: the former quantitatively assesses ischemic penumbra volume in the acute phase to inform reperfusion therapy decisions, while the latter clarifies the nature of vessel wall pathology and recurrence risk in the subacute or chronic phase, guiding etiological classification and secondary prevention. The complementarity between the two modalities serves as the logical starting point for multimodal imaging integration.

4.2. Current Evidence for Combined Application Headings

Clinical studies directly evaluating the combined application of CTP and HR-VWI remain scarce. Direct combined-modality evidence. Li *et al.* retrospectively analyzed 78 patients with acute ischemic stroke due to middle cerebral artery stenosis, all of whom underwent both HR-VWI and CTP examinations. Multivariable analysis showed that poor collateral status assessed by CTP (HR = 2.87, 95% CI: 1.16 - 7.09, $P = 0.011$) and watershed infarction mechanism (HR = 3.28, 95% CI: 1.49 - 7.36, $P = 0.004$) were independent predictors of new ischemic lesions [34]. HR-VWI evidence in etiological diagnosis. In cryptogenic stroke, Roa *et al.* used 7T HR-VWI to prospectively screen 344 patients with negative conventional imaging and found that intracranial atherosclerotic disease was confirmed as the final stroke etiology in 65.8% of cases [35]. This study provides evidence for the diagnostic value of HR-VWI in a selected patient subgroup, but does not directly evaluate a combined CTP-HR-VWI strategy. CTP technical evidence. At the technical integration level, Pisani *et al.* compared the consistency of three automated CTP software packages in predicting final infarct volume and found good correlations in patients with near-complete or complete recanalization (Spearman correlation coefficients of 0.744, 0.711, and 0.600, respectively) [36]. This supports the feasibility of cross-platform CTP integration as a technical prerequisite for future combined analyses, but does not itself test a combined CTP-HR-VWI approach.

4.3. Clinical Application Value

The 2024 ACR Appropriateness Criteria indicate that advanced imaging modalities such as CT and MRI are useful for stroke diagnosis and subtype classification, providing an evidence-based framework for multimodal imaging strategies [37]. Regarding recurrence risk stratification, Wang *et al.*, based on a post-hoc analysis of the CMOSS study, found that CTP parameters $MTT > 6.5$ s (HR = 3.50, 95% CI: 1.19 - 10.30) and $rCBF \leq 0.5$ (HR = 7.36, 95% CI: 2.27 - 23.85) independently predicted ischemic stroke recurrence [38]. Shao *et al.* Reported that a total plaque count > 4.5 and the coexistence of intracranial and extracranial enhancing plaques were independent risk factors for recurrence (AUCs of 0.787 and 0.710, respectively) [39]. These findings suggest that CTP perfusion parameters and HR-VWI plaque features each contribute to recurrence prediction, and their combined use may facilitate a more comprehensive assessment of stroke recurrence risk. In terms of individualized treatment, vulnerable plaque features identified by HR-

VWI may provide additional information for risk stratification and can assist clinicians in refining secondary prevention strategies. However, treatment decisions should primarily follow the established stroke mechanism and current clinical guideline recommendations; plaque imaging alone does not independently dictate the choice of dual antiplatelet therapy or anticoagulation. In the AI domain, Gao *et al.* developed a habitat radiomics and vision transformer fusion model based on HR-VWI to identify high-risk plaques and predict stroke recurrence, achieving a test set AUC of 0.960 [40]. Fan *et al.* constructed an attention-based deep learning ensemble model, Trans-CNN, which achieved a test set AUC of 0.912 for recurrence prediction [41]. These technologies provide a foundation for future deep integration of CTP and HR-VWI information. However, high-level studies directly evaluating the combined use of both modalities on clinical outcomes remain scarce, and further prospective multicenter research is needed for validation.

Proposed staged clinical workflow. Based on the available evidence, a practical clinical pathway can be considered. In the hyperacute setting, patients with suspected large vessel occlusion should first undergo non-contrast CT and CT angiography, with CTP added when the clinical presentation suggests a late window (>6 hours) or when the stroke mechanism remains unclear. If CTP demonstrates a perfusion deficit without a corresponding large vessel occlusion on CTA, or if the infarct pattern is atypical (e.g., watershed infarction, multiple scattered small infarcts), HR-VWI may be added in the subacute phase for etiological assessment, plaque characterization, and secondary prevention planning. This stepwise integration aims to balance the time sensitivity of acute reperfusion decisions with the diagnostic precision offered by vessel wall imaging.

5. Challenges and Future Directions

The clinical translation of the combined CTP and HR-VWI application still faces multiple difficulties. The most prominent issue is the lack of evidence-prospective studies directly evaluating the impact of combined use on clinical outcomes remain scarce, and existing evidence is predominantly based on retrospective analyses. One study, including 78 patients with middle cerebral artery stenosis that employed both HR-VWI and CTP, is one of the few pieces of evidence for combined application; however, its main focus was on short-term recurrence risk stratification rather than clinical outcome validation [34]. Although deep learning has made considerable progress in acute ischemic stroke imaging, current evidence mainly centers on automated detection, segmentation, and outcome prediction using single modalities, while research specifically targeting multimodal information fusion remains in its early stages [42]. Technical heterogeneity and lack of standardization are also important limiting factors: different post-processing software packages show marked discrepancies in core volume estimation [12], and centers have yet to reach a consensus on HR-VWI scanning parameters and interpretation criteria [30]. The sensitivity of artificial intelligence in detecting distal vessel occlusion remains suboptimal; a meta-analysis reported a pooled sensitivity of 64%

(95% CI: 53% - 74%) for AI in detecting M2 segment occlusion [43]. The time efficiency of clinical workflows is also a concern—HR-VWI acquisition typically taking 10 to 15 minutes per case, making it difficult to perform routinely in the hyperacute setting. Future research should prioritize the development of standardized databases, interpretable AI-driven multimodal fusion algorithms, and the validation of combined strategies in stratified clinical pathways to determine their actual impact on patient functional outcomes and recurrence rates.

Author Contributions

Conceptualization, W.W. and D.G.; investigation, W.W.; writing—original draft preparation, W.W.; writing—review and editing, D.G.; supervision, D.G. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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