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REVIEW ARTICLE

Clinical value of computed tomography angiography and perfusion imaging for assessing functional prognosis and cognitive impairment after ischemic stroke

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Abstract

Ischemic stroke is a leading cause of disability and cognitive impairment in China. Accurate prediction of functional outcomes is crucial for formulating treatment strategies and improving patient prognosis. Computed tomography angiography (CTA) and computed tomography perfusion (CTP), established techniques for assessing cerebral hemodynamics, hold significant potential but require a more systematic synthesis of evidence in predicting neurological recovery and cognitive dysfunction. This review aims to comprehensively evaluate the existing evidence and clinical utility of CTA and CTP in assessing functional prognosis and cognitive impairment in patients with ischemic stroke. We conducted a narrative synthesis based on a systematic search of relevant literature up to August 2025 in databases including PubMed and the China National Knowledge Infrastructure. The focus is on research advances in areas where CTA and CTP are applied, such as defining the infarct core and ischemic penumbra, assessing collateral circulation, diagnosing vascular cognitive impairment (VCI), and integrating these techniques with 3D printing technology. We found that CTP quantifies infarct core and salvageable penumbra through parametric maps/software (e.g., RAPID), guiding reperfusion therapy in extended windows; CTA/CTP collateral assessment (e.g., HIR) predicts functional outcomes; and CTA/CTP identifies large-vessel pathologies and hypoperfusion as early VCI biomarkers, with CTA 3D printing expanding personalized surgical planning. However, the field currently lacks standardized assessment protocols suitable for routine clinical application, and the reliability and generalizability of predictive models in real-world practice remain to be firmly established. The potential of artificial intelligence in assisting CTA and CTP image analysis and model construction has yet to be fully exploited.

Keywords: Ischemic stroke; Computed tomography angiography; Computed tomography perfusion; Ischemic penumbra; Collateral circulation

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1. Introduction

The accelerating aging of the population and the persistently high prevalence of risk factors such as hypertension, diabetes, and hyperlipidemia have contributed to stroke-related deaths in developing countries, accounting for two-thirds of global stroke mortality and placing a substantial burden on affected families and societies. China has the highest prevalence of stroke globally, and the stroke prevention and management strategies face substantial challenges.[1] In terms of stroke subtypes, compared with other ischemic stroke subtypes, patients with atherosclerotic stroke and cardioembolic stroke tend to have worse short-term outcomes and higher risks of disability and mortality.[2,3] In addition, cardioembolic stroke is more prone to recurrence. Both atherosclerotic stroke and cardioembolic stroke are characterized by sudden onset and rapid progression of focal or global neurological deficits.[4] Therefore, it is essential to develop and apply rapid, accurate, and safe imaging methods to assess functional prognosis and guide treatment strategies.

Non-contrast computed tomography (NCCT) is widely used as the first-line imaging method for stroke screening due to its speed and availability. However, NCCT has limitations in early infarct detection, ischemic penumbra assessment, identification of posterior circulation lesions, and long-term prognosis prediction.[5] In this context, multimodal computed tomography (CT) imaging, especially CT angiography (CTA) and CT perfusion (CTP), has been used as a powerful tool to identify acute ischemic stroke (AIS) and predict neurological functional outcomes. Contrast-enhanced 3D reconstruction provides detailed vascular anatomical information for CTA. CTP can acquire tissue-level perfusion information and obtain intuitive quantitative indices through automated software processing, which can segment the ischemic core and penumbra intuitively, quantitatively assess collateral circulation,[5] and further predict functional outcomes and post-stroke cognitive impairment.

In recent years, many reviews have reported the application of CTA and CTP in the management of AIS. Most previous reviews have focused on diagnostic performance, technical principles, extension of reperfusion time windows, or treatment decision-making in the acute phase.[6,7] A comprehensive review of the predictive value of CTA or CTP for neurological functional prognosis is still lacking. The application of CTA and CTP in the growing field of post-stroke cognitive impairment has not been summarized. Therefore, we summarized the current evidence to explain the applications and mechanisms of CTA and CTP in the evaluation of functional prognosis and post-ischemic stroke cognitive impairment. This includes their roles in defining the ischemic penumbra, assessing collateral circulation, diagnosing vascular cognitive impairment (VCI), and integrating with 3D printing technology. Figure 1 provides an overview of these imaging modalities and their applications. Table 1 presents the core viewpoints of the most significant literature reviewed in this article and summarizes their key limitations, while the subsequent text discusses current challenges and potential future directions.

2. Imaging characteristics and hemodynamic parameter applications of CTA and CTP

The CTA and CTP have become two mature imaging techniques for the clinical evaluation of cerebral hemodynamics and cerebral perfusion in patients with AIS, enabling rapid guidance of reperfusion therapy selection.[19,20] In terms of imaging principles, CTA is a bolus contrast-tracking technique designed to visualize the macrovasculature. Following the intravenous injection of an iodinated contrast agent, a series of rapid, thin-slice CT scans is performed from the aortic arch to the cranial vertex within 15–20 s, capturing the first pass of the contrast agent through the cerebral arteries. The acquired imaging data undergoes sophisticated post-processing utilizing techniques such as 2D maximum-intensity projection and 3D multiplanar reconstruction. These computational methods are essential for generating high-resolution, 3D angiographic representations of the cerebral vascular architecture. This reconstructed vascular mapping yields comprehensive anatomical details regarding vessel patency, the degree of stenotic lesions, the presence of complete occlusions, and the status of collateral circulatory pathways.[6] The principal advantage of this methodology is its demonstrated high accuracy and sensitivity for detecting large-vessel occlusion (LVO) stroke. Furthermore, the technique has demonstrated clinical utility in assessing leptomeningeal collateral circulation patterns and has shown significant value in predicting functional outcomes for patients receiving endovascular thrombectomy.[21,22] Notwithstanding its diagnostic strengths in identifying large-vessel pathologies, the efficacy of CTA diminishes considerably when applied to non-LVO stroke etiologies. In such clinical scenarios, where occlusive pathology involves smaller, distal cerebral arteries or manifests as purely hemodynamic insufficiency, information provided by CTA alone may be insufficient for comprehensive diagnosis and therapeutic planning. This inherent limitation has consequently elevated the importance of CTP in the diagnostic algorithm.

Meanwhile, CTP is a kinetic tracer technique that characterizes cerebral perfusion status. Compared to

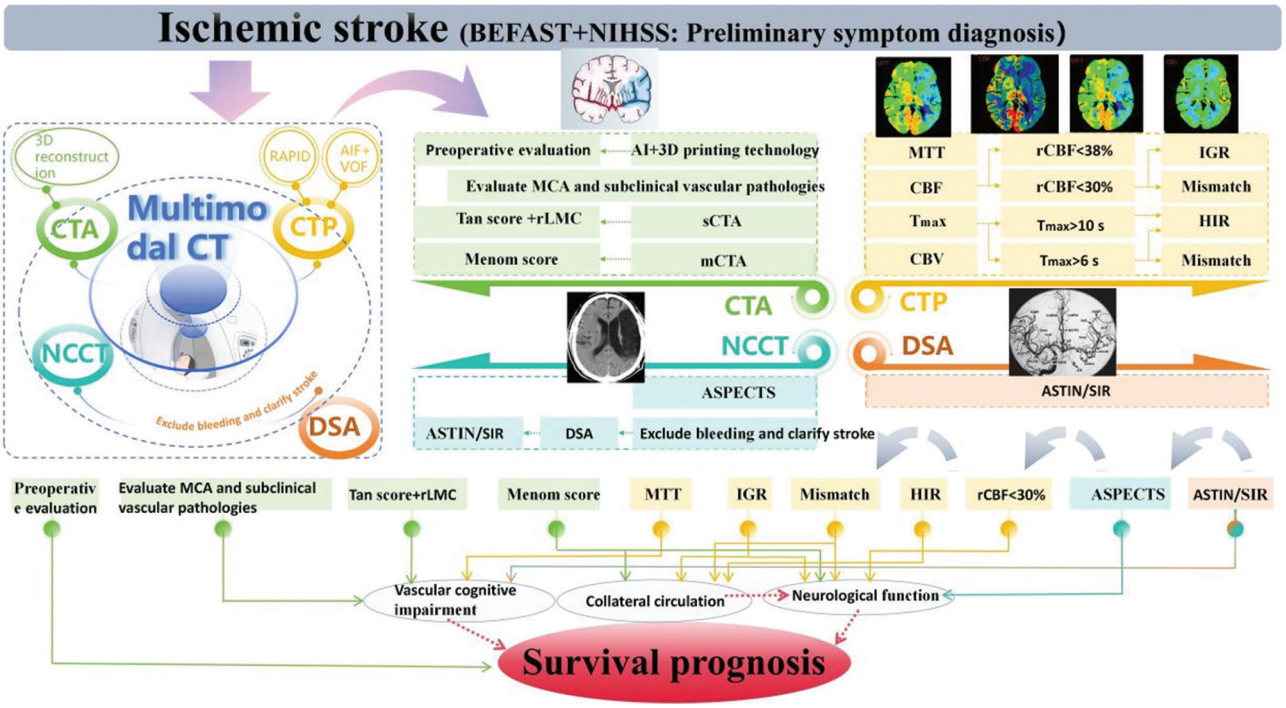

Figure 1. Overview diagram of this review. The yellow areas represent regions associated with CTP, the orange areas with DSA, the turquoise areas with CTA, and the aqua areas with NCCT. Created with BioRender. Zhou, C. (2025). https://BioRender.com/s3armw9.

Abbreviations: AI: Artificial intelligence; ASPECTS: Alberta Stroke Program Early Computed Tomography Score; ASTIN: American Society of Interventional and Therapeutic Neuroradiology; BEFAST: Balance, Eyes, Face, Arm, Speech, Time; CBF: Cerebral blood flow; CBV: Cerebral blood volume; CT: Computed tomography; CTA: Computed tomography angiography; CTP: Computed tomography perfusion; DSA: Digital subtraction angiography; HIR: Hypoperfusion intensity ratio; IGR: Infarct growth rate; MCA: Middle cerebral artery; mCTA: Multi-phase computed tomography angiography; MTT: Mean transit time; NCCT: Non-contrast computed tomography; NIHSS: National Institutes of Health Stroke Scale; rCBF: Reduced cerebral blood flow; rLMC: Regional leptomeningeal collateral; mCTA: Single-phase computed tomography angiography; SIR: Society of Interventional Radiology.

CTA, it can provide information on both macrocirculation and microcirculation and offers greater clinical utility for evaluating cerebral infarction in non-LVO subtypes.[7,23] After administering a venous bolus of contrast, repeated CT acquisitions are performed over a specific region of brain tissue (typically lasting 40–60 s), dynamically tracking the transit of contrast into the arteries, then into the capillaries and parenchyma, and finally into the veins. The change in signal intensity resulting from contrast arrival in the tissue, measured in Hounsfield units, is proportional to the concentration of contrast at each time point, allowing time–density curves to be generated for each voxel in the region of interest.[6] Based on the central volume principle, key perfusion parameters are calculated from these curves: (i) cerebral blood flow (CBF), representing the volume of blood flow per unit time per unit mass of tissue (mL/100 g/min), is proportional to the maximum slope of the tissue time–density curve; (ii) cerebral blood volume (CBV), reflecting the total volume of flowing blood within the vasculature in a given region (mL/100 g), is proportional to the area under the tissue time–density curve; (iii) mean transit time (MTT), the average time for blood to traverse the cerebral capillary network (in seconds), can be derived from the ratio of CBV to CBF based on the central volume theorem; and (iv) time to maximum (T_{max}), the time taken for the residue function to reach its maximum, indicating hemodynamic delay.[7,24] These parameters and their combinations can be widely applied to the delineation of the infarction core and ischemic penumbra in ischemic stroke, evaluation of collateral circulation status, and further assessment of functional prognosis.

3. CTP in defining the infarct core and ischemic penumbra

3.1. Definitions and clinical implications of infarct core and penumbra

During cerebral ischemia, regions of poor cerebral arterial perfusion, insufficient oxygen supply, and glucose deficiency in brain tissue can occur, triggering a cascade of disruptions in cellular energy metabolism and ultimately resulting in cerebral infarction characterized by neurological dysfunction.[24] The infarcted territory is classified into

Table 1. Summary of key findings and limitations from the current review

References	Methodology	Statistical model	Main findings	Limitations
Czap *et al.*[5]	Review	-	CTA has high sensitivity for identifying large-vessel occlusion. CTP can evaluate brain tissue perfusion and identify ischemic core and penumbra.	CTA may miss arterial lesions smaller than 2 mm, as well as lesions in the skull base and in other locations. CTP may underestimate or overestimate the ischemic core, leading to bias in predicting prognosis.
Sarraj *et al.*[8]	A prospective, randomized controlled trial	Use generalized odds ratio (OR) and Wilcoxon–Mann–Whitney probability of superiority to quantify the magnitude of therapeutic efficacy.	Patients with larger T_{max} (>10 s) and lesion volumes were less likely to achieve better functional prognosis while bearing a higher risk of neurological deterioration. Provide strong high-level evidence for expanding the indications for thrombectomy to patients with large infarctions.	Early termination of the trial resulted in an insufficient sample size, limited efficacy of subgroup analysis, an open-label design, non-compliance with imaging standards for some patients, limited use of intravenous thrombolysis, and limited population representativeness.
Sui *et al.*[9]	A retrospective cohort study design	Evaluating the predictive ability of the large infarct core for poor prognosis using univariate and multivariate logistic regression analysis.	CTP ≥70 mL is more accurate than ASPECTS ≤5 in predicting the adverse functional prognosis of EVT patients, especially in the early stages within 6 h of onset.	The sample size is limited, there is selection bias, ASPECTS is subjective, and CTP may overestimate the core.
Liebeskind *et al.*[10]	*Post hoc* subgroup analysis of a prospective, randomized, multicenter, controlled clinical trial (DAWN trial)	Using a generalized linear mixed model, set a binomial distribution and logit linking function to evaluate the interaction effect between treatment mode and collateral status.	During the 6–24 h late time window, collateral circulation status is an important biomarker for predicting treatment response and long-term prognosis.	The use of single-phase CTA instead of multi-phase CTA or perfusion imaging (such as HIR), which better reflects hemodynamics, may lead to misjudgment of collateral status.
Chatterjee *et al.*[11]	A prospective cohort study	Spearman's correlation analysis is used to explore correlations among variables, including those between the rLMC score and the ASPECTS score, and the rLMC score and three-month mRS.	The rLMC scoring system based on multi-phase CTA is a simple, reliable, and prognostic imaging biomarker.	This study has a small sample size, does not conduct multivariate analysis and blinded evaluation, and is limited to the anterior cycle.
Lee *et al.*[12]	A retrospective cohort study	Use receiver operating characteristic (ROC) curve analysis to evaluate the ability of various imaging parameters (e.g., ASPECTS, single-phase CTA collateral, multi-phase CTA collateral, and their combinations) to predict different infarct volume thresholds.	The combination of ASPECTS and CTA collateral score can significantly improve predictive ability for a small infarct core (< 31 mL).	In clinical practice, patients with ASPECTS <4 are usually not scheduled for MRI, resulting in a low proportion of such patients in the study and limiting the complete validation of the core prediction model for large infarction.
Seners *et al.*[13]	A retrospective, multicenter, observational cohort study	Multivariate logistic regression analysis of the relationship between core IGR and 90-day functional outcomes.	HIR ≥0.40 is the strongest predictor of fast infarct core growth during inter-hospital transfer. Patients with rapidly increasing core infarct volume have significantly lower rates of positive outcomes (28% vs. 49%) and higher rates of death/severe disability (39% vs. 24%) compared to patients with slow infarct core growth.	HIR is mostly obtained after transportation, and the experiment is based on MRI, which may introduce selection bias and fail to cover all patient populations.

(Cont'd)

Table 1. ***(Continued)***

References	Methodology	Statistical model	Main findings	Limitations
Wouters *et al.*[14]	A prospective, multicenter observational cohort study	Use stepwise logistic regression to analyze the relationship between IGR and 90-day mRS score. Poor collateral circulation was associated with a 2.45-fold increase in the risk of rapid infarct growth (IGR >10 mL/h) during interhospital transfer (OR=2.45, 95% CI=1.62–3.71).	HIR ≥0.5 and core volume ≥7.5 mL indicate rapid infarct expansion during transfer. Independent predictive factors for infinite growth. Rapid infarct expansion is associated with poorer 90-day functional prognosis.	CTP evaluates the initial core volume, and diffusion-weighted MRI evaluates the final core volume. There is a systematic deviation in core volume measurements between the two techniques, potentially leading to the overestimation of IGR.
Wang *et al.*[15]	A retrospective, observational cohort study	Construct a multivariate logistic regression model to assess whether the multi-phase Menon score is an independent predictor of favorable outcomes.	Multi-phase CTA collateral scores not only outperform single-phase scores but also demonstrate comparable efficacy to CTP parameters in predicting clinical outcomes.	Multi-phase CTA images were computationally simulated from raw whole-brain CTP data rather than acquired through actual independent multi-phase CTA scans, potentially limiting the generalizability and clinical applicability of the results.
Jakimovski *et al.*[16]	A prospective cohort study	Spearman's correlation analysis and multiple linear regression analysis are used to construct the model.	Cerebrovascular reactivity dysfunction may lead to an inadequate response to high perfusion demands, exacerbating mitochondrial stress, neuronal damage, and cognitive decline.	The limitations include the absence of healthy controls, a small sample size, the use of invasive perfusion techniques, and a cross-sectional design that hinders the establishment of causality.
Makin *et al.*[17]	A systematic review and meta-analysis	-	Although lacunar strokes have small lesions, the incidence of cognitive impairment is as high as 30%, which is comparable to that of non-lacunar strokes.	All included studies were observational, which carries the risks of selection bias, information bias, and confounding bias. The imaging criteria for stroke subtyping were not standardized.
Seidlová *et al.*[18]	A prospective cohort study	Spearman's rank correlation coefficient and Kendall's Tau-b correlation coefficient were used to assess the correlations among various measurement indicators.	The integration of CTA and 3D printing technology is feasible and effective, enabling the generation of high-fidelity, patient-specific carotid artery stenosis models.	This technique is constrained by factors such as single-material usage, absence of distal resistance, and standardized wall thickness, all of which currently prevent it from fully replicating the complex biomechanical environment *in vivo*.

Abbreviations: ASPECTS: Alberta Stroke Program Early Computed Tomography Score; CT: Computed tomography; CTA: Computed tomography angiography; CTP: Computed tomography perfusion; EVT: Endovascular therapy; HIR: Hypoperfusion intensity ratio; IGR: Infarct growth rate; MRI: Magnetic resonance imaging; mRS: Modified Rankin Scale; rLMC: Regional leptomeningeal collateral.

the infarct core and ischemic penumbra. While both regions exhibit functional disorders, the penumbra retains salvageable potential, as timely restoration of blood flow can reverse ischemic injury and restore cerebral function in this area.[25] Without reperfusion, the ischemic penumbra will eventually grow into an irreversible core infarct area, and the volume of the infarct core is significantly correlated with the patient's clinical prognosis. The smaller the infarct core, the more likely the patient is to achieve a favorable prognosis.[26] In a prospective study utilizing CTP parameters to quantify infarct core volume, Sarraj *et al.*[8] found that patients with larger T_{max} (>10 s) and larger lesion volumes were less likely to achieve a better functional prognosis (modified Rankin Scale [mRS] score: 0–2) while bearing a higher risk of neurological deterioration (median infarct core volume: 107 mL in patients with neurological deterioration). Therefore, establishing the core–penumbra mismatch ratio and achieving rapid reperfusion of the ischemic penumbra are key to improving functional prognosis. Concurrently, CTP-based quantification of infarct core volume enhances the accuracy of predicting post-treatment neurological recovery.

3.2. Advantages and clinical utility of CTP in core–penumbra delineation

At present, diffusion-weighted magnetic resonance imaging (MRI) and computed tomography (e.g., CTP) have high specificity, sensitivity, and accuracy in determining the final core infarct volume in stroke patients and have been applied in many large-scale clinical trials.[8,27,28] However, compared with CTP, MRI has limited availability in emergency situations. In contrast, CTP can become the preferred imaging examination for cerebral perfusion assessment in acute stroke management.

CTP plays an important role in identifying the ischemic core and penumbra and can accurately distinguish ischemic cores with reduced CBF (rCBF) from normal brain tissue. The concept of defining rCBF <30% as the ischemic core and T_{max} >6 s as the ischemic penumbra has been widely validated. CTP provides critical imaging evidence for reperfusion therapy in patients beyond the standard therapeutic time window by calculating the core–penumbra mismatch ratio. Although current CTP technology still has limitations in defining the infarct core and ischemic penumbra (such as the "ghost infarct core" phenomenon and the imaging–neuropathological gap), its future development should move beyond the static dichotomous framework and evolve toward a dynamic, multidimensional assessment paradigm. Some scholars suggest that integrating multiparametric imaging, cerebral tissue vulnerability, dynamic metabolic imaging, and molecular biomarkers can enable more precise delineation of "salvageable tissue."[29] This dynamic model, which synthesizes imaging and biomolecular metabolic information, can correct the current overestimation bias in infarct core assessment, reflect the processes of neural injury and repair, and thereby establish a new paradigm for personalized neuroprotective strategies.[29]

Multiple randomized clinical trials have demonstrated that, as first-line treatment strategies, the two main endovascular therapy (EVT) techniques—contact aspiration and stent retriever thrombectomy—show no significant differences in successful recanalization rates, 90-day functional outcomes (measured by mRS scores), or the incidence of adverse events.[30,31] For example, in the ASTER trial, successful reperfusion rates (defined as modified thrombolysis in cerebral infarction score corectionis, in the ASTER trial, successful reperfusion rates (defined as reatment stra.[31] Furthermore, no significant differences were observed between the two approaches in improvement in the 24-h National Institutes of Health Stroke Scale score or 90-day mortality.[32]

Some studies have also explored the efficacy of combined techniques (contact aspiration and stent retriever). The ASTER2 trial indicated that the combined approach did not significantly improve the final successful reperfusion rate nor lead to substantial improvements in clinical outcomes.[33-35] It is noteworthy, however, that the addition of contact aspiration following failed stent retriever thrombectomy may achieve earlier reperfusion.[35] In 2018, the DAWN and DEFUSE 3 trials used automated CTP analysis software (RAPID) to evaluate the volume of ischemic cores defined as rCBF <30%. The results showed that patients receiving EVT in extended windows had better functional outcomes compared to those receiving standard medical care alone. These studies have demonstrated that CTP extends the time window for EVT based on safe and effective assessment of core infarction and has been shown to have therapeutic effects.[36,37] Subsequently, the ANGEL-ASPECT and SELECT2 trials confirmed the efficacy of EVT in patients with anterior circulation LVO by utilizing CTP-defined large core infarction (core infarction volume of 70lume mL in ANGEL0ASPECT trial and ≥50 mL in SELECT2 trial).[8,38] In a subsequent study investigating the superiority of CTP in predicting the prognosis of stroke patients with large core infarction, Sui *et al.*[9] defined large core infarction using two criteria: (i) NCCT Alberta Stroke Program Early CT Score (ASPECTS) ≤5, and (ii) relative CBF <30% with lesion volume ≥70 mL. The results showed that both methods of defining large core infarction patients had elevated rates of poor functional outcomes (3-month mRS: 4–6), mortality, symptomatic intracranial hemorrhage, and hemorrhagic transformation. Notably, large core infarction defined by CTP could become an independent predictor of outcomes in patients undergoing EVT within 6 h and showed superior predictive performance across all treatment time windows compared to NCCT-based criteria. Numerous studies have shown great superiority and clinical significance of CTP in delineating the ischemic core and penumbra, demonstrating its pivotal role in guiding treatment decisions.

4. Assessment of collateral circulation by CTA and CTP

4.1. Clinical significance and imaging assessment of collateral circulation

Cerebral collateral circulation constitutes a compensatory vascular network that maintains perfusion in ischemic territories following cerebral arterial occlusion. Developed collateral circulation is associated with higher recanalization rates, improved tissue reperfusion, smaller final core infarct volume, a lower risk of hemorrhagic transformation, and favorable clinical outcomes.[25,39] Rapid and accurate imaging evaluation of the responsible blood vessels and their collateral circulation can guide treatment decisions and predict the functional prognosis of patients.[10] Digital subtraction angiography is currently the gold standard for evaluating collateral circulation, primarily using the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASTIN/SIR) scale.[40] Given its invasive nature and time constraints, it is not suitable for assessing collateral circulation in hyperacute settings. Therefore, evaluation methods for CTA and CTP of collateral circulation have attracted much attention.

4.2. CTA-based collateral assessment and its predictive value for prognosis

CTA is currently a commonly used non-invasive imaging method for assessing collateral circulation. It demonstrates high anatomical consistency with digital subtraction angiography for intracranial arterial imaging. CTA primarily provides anatomical information on collateral circulation. Single-phase CTA (sCTA) evaluates the leptomeningeal collaterals by describing the vascular conditions during the arterial phase. The validated scales mainly include the Tan score[10] and the regional leptomeningeal collateral (rLMC) score.[11] Several studies have examined the predictive value of sCTA for functional prognosis in patients with ischemic stroke. Liebeskind *et al.*[10] used the Tan score to evaluate collateral circulation in the DAWN trial and identified developed collateral circulation as a significant predictor of achieving a 90-day mRS score of 0–2 post-EVT. Among patients achieving an mRS score of 0–2, 43.7% (31/71) had developed collateral circulation, 30.8% (16/52) had moderate collateral circulation, and 17.7% (6/34) had poor collateral circulation (p=0.026). Meanwhile, the rLMC score provides a quantitative assessment of collateral circulation, demonstrating a significant correlation with the ASPECT score. The rLMC score can also predict the functional prognosis of acute stroke patients after thrombolytic therapy.[11,41]

At present, compared with sCTA, collateral circulation assessment based on multi-phase CTA (mCTA) has attracted increasing attention for assessing functional prognosis in stroke patients.[42] mCTA is a time-resolved vascular imaging technology that can capture three distinct phases (arterial, early venous, and late venous), reflecting vascular filling efficiency, blood flow clearance, and delayed perfusion dynamics, and providing a more accurate and comprehensive evaluation of secondary collateral circulation. Using mCTA, collateral circulation is evaluated with the grading system introduced by Menon, a qualitative 6-point scale. This scale categorizes collateral supply based on the extent and prominence of vascular enhancement after comparing the occluded territory with the contralateral normal side. The collateral supply is classified as poor (grades 0–1), intermediate (grades 2–3), or good (grades 4–5).[43]

The prognostic value of mCTA-based collateral assessment was confirmed in two recent studies. Scholars analyzed data from the Prove IT dataset[44] and found that favorable collateral circulation grading was associated with better functional prognosis in patients receiving both endovascular and standard drug treatments. In addition, Lee *et al.*[12] enhanced the predictive ability for stroke prognosis with smaller core infarct volumes by combining mCTA with the ASPECTS collateral score. These collateral assessment methods have opened up new avenues for CTA to predict the prognosis of stroke patients.

4.3. Methods for assessing collateral circulation in CTP and their predictive value for prognosis

CTP provides critical functional information on collateral circulation status by integrating quantitative cerebral perfusion parameters (e.g., CBF, T_{max}) with qualitative CTA findings, enabling a more comprehensive hemodynamic evaluation. The hypoperfusion intensity ratio (HIR) was first proposed by Olivot *et al.*[45] in 2014. It is defined as the volumetric ratio of T_{max} >10 s to T_{max} >6 s regions. HIR is considered to have a strong correlation with collateral circulation (r = 0.82, p<0.001), and a high HIR (>0.4) can serve as a reliable indicator for identifying patients with rapid progression of core infarction volume during interhospital transport, which is related to infarct growth rate (IGR) and clinical prognosis.[13,45] In addition, another study compared the average CBV value of the infarcted area with that of the contralateral normal area (CBV ratio) and found a correlation between a higher CBV ratio and better collateral circulation.[46] Notably, the volumetric threshold of rCBF <38% emerged as a superior predictor of favorable collateral status compared with HIR- and CBV-ratio-based criteria. Furthermore, studies have also proposed a combination of CTP parameters and time, namely IGR—the ratio of core infarct growth volume to time. The commonly used clinical definition method is based on the clear onset time of the patient and the ratio of the core infarct volume obtained by CTP imaging at admission to the time from onset to imaging examination.[47,48] The categories of fast progressors (IGR >10 mL/h) and slow progressors (IGR <10 mL/h) are closely related to collateral circulation status. Slow progressors often exhibit superior collateral networks (odds ratio [OR]: 2.45, 95% CI: 1.62–3.71) and better functional prognosis (mRS 0–2: 54.3% vs. 22.1%).[14] Although numerous studies currently focus on CTP-based collateral circulation assessment methods, with some providing reference for predicting stroke prognosis, there is no approved perfusion parameter application method in medical guidelines to evaluate collateral circulation.

4.4. Comparison and exploration of the combined application of multimodal computed tomography in evaluating collateral circulation

Emerging studies have increasingly focused on comparing the efficacy of sCTA, mCTA, and CTP parameters in predicting the prognosis of AIS. Wang *et al.*[15] simulated the collateral circulation assessment methods of sCTA and mCTA to evaluate their prognostic performance in

patients with AIS. Their study found that the multi-phase Menon score is an independent predictor of reliable prognosis in patients with anterior circulation LVO-related AIS. Its predictive performance was superior to that of the single-phase Menon score and did not differ significantly from that of CTP parameters (T_{max} >6 s and rCBF <30%).

There is growing recognition that the functional prognosis of ischemic brain tissue is not determined unidirectionally by arterial supply, but is bidirectionally influenced by the efficiency of the entire cerebral circulatory system. This integrated circulatory system comprises two essential components: Arterial inflow, chiefly facilitated by collateral circulation, and venous outflow, which constitutes the microcirculatory drainage pathway. On the arterial side, robust collateral circulation sustains perfusion to ischemic territories, thereby retarding the transition of penumbral tissue to irreversible infarction.

Similar to the cerebral arterial system, the cerebral venous system also plays a critical role in maintaining homeostasis of the central nervous system. The cerebral venous system accommodates approximately 70% of total CBV; impairment of its autoregulatory function may manifest as cerebral venous congestion, which can trigger cerebral metabolic abnormalities and ultimately lead to severe neurological deficits. The drainage capacity of the venous system may influence prognosis by regulating perfusion efficiency at the tissue level. The efficacy of venous outflow is particularly important for the clearance of metabolic byproducts and the preservation of tissue homeostasis.[49]

A crucial pathophysiological aspect lies in the functional interdependence between the arterial and venous systems. Compromised arterial collateral circulation can potentiate the development of ischemic cerebral edema, whereas impaired venous reflux may further exacerbate such edema, establishing a self-perpetuating cycle that elevates intracranial pressure and ultimately undermines cerebral perfusion.[50] Thus, the maintenance of optimal functional outcomes depends critically on the homeostatic equilibrium within this "inflow–outflow" circuit. This intricate relationship underscores the necessity for comprehensive hemodynamic assessment in AIS. Consequently, the concept of the cerebral collateral cascade has been proposed.[51,52] This concept involves assessing the extent of collateral circulation and venous outflow volume via CTA and evaluating tissue-level collateral circulation through HIR. Its application in clinical practice, using multimodal CT, may enhance our ability to identify stroke patients who genuinely benefit from reperfusion therapy.

5. CTP and CTA in VCI

5.1. VCI

Previous clinical studies on ischemic stroke have mostly focused on the resulting somatic functional impairments, while often overlooking the associated cognitive deficits. In recent years, early identification and intervention for cognitive dysfunction have garnered increasing attention, with an increasing number of studies focusing on the diagnostic and evaluative roles of CTA and CTP in various types of cognitive impairments.[53] Among these, VCI and Alzheimer's disease have emerged as primary research directions. VCI is a prevalent form of cognitive dysfunction. It is classified into two major subtypes based on vascular etiology: (i) Cognitive deficits secondary to large-vessel stenosis/occlusion and (ii) cerebral small-vessel disease (SVD)-related cognitive decline. By severity, VCI can be divided into vascular dementia and VCI without dementia, which has not yet reached dementia but has already shown cognitive impairment in different cognitive domains.[54]

5.2. The application of CTA in VCI

CTA can provide detailed information on the structure of cerebral blood vessels, including stenosis, occlusion, and plaque formation in vessels such as the internal carotid artery (ICA) and the middle cerebral artery (MCA). This information is crucial for identifying and assessing the severity of cerebral vascular lesions and can serve as a diagnostic reference for cognitive impairments caused by LVO. As exemplified in MCA-related cognitive impairment, the MCA—a direct continuation of the ICA—serves as a critical vascular supply to important cognitive structural areas of the brain. It is mainly responsible for the blood supply to the dorsolateral cerebral hemisphere, including the frontal lobe, parietal lobe, temporal lobe, insular cortex, and basal ganglia region. Stenosis or occlusion of the MCA induces CBF dysregulation, leading to white matter lesions (WMLs) that manifest as cognitive deficits in visuospatial, executive, attention, language, and memory domains.[55,56]

Furthermore, cognitive impairment secondary to SVD, recognized as a distinct subtype of vascular dementia, has garnered increasing attention because it has an insidious onset and affects a broad population. Pathophysiological mechanisms encompass WMLs, lacunar infarcts, cerebral microbleeds, and enlarged perivascular spaces, which collectively contribute to cognitive deficits by disrupting neurovascular coupling and structural network integrity. CTA can reveal subclinical cerebrovascular pathologic risk and show not only the vascular structure but also the degree of early-stage stenosis and plaque formation in the aortic arch, ICA, and MCA. If these pathologic findings are detected early, further analysis can be performed to

assess their risk for cognitive impairment. For example, some studies have found that aortic arch plaque (AAP) is a risk factor for ischemic stroke. Its severity is significantly correlated with the volume of WMLs, an association that is independent of other risk factors. Importantly, the research suggests that the mechanism underlying the AAP–WML relationship is not thromboembolism, but may involve arterial stiffness exacerbated by aortic arch atherosclerosis, which damages the cerebral microcirculation through a "water hammer effect" or "tsunami effect," ultimately leading to WMLs. Therefore, early detection of AAP via CTA can serve as a sensitive indicator of individuals at high risk of WMLs, enabling further follow-up and early intervention.[57]

Similarly, high-risk features of carotid artery plaques, such as intraplaque hemorrhage (IPH) and ulceration, are strongly associated with the presence of covert brain infarctions (CBIs).[58] Although "covert," CBIs are significantly associated with cognitive decline and represent a critical mediator between vascular disease and cognitive impairment.[59,60] In addition, when proximal vascular pathologies are detected by CTA, distal small vessels may exhibit "tandem" pathologies in series, leading to lacunar infarcts and WMLs, further contributing to cognitive dysfunction.

Therefore, by non-invasively detecting plaque formation and the degree of stenosis in extracranial and intracranial arteries, CTA provides a temporal window for understanding the overall burden of systemic vascular disease affecting the brain. This capability aids in the early identification of individuals at high risk not only for overt stroke but also for subclinical vascular brain injury, which underlies a significant proportion of VCI. In summary, CTA has clinical significance because it can detect subclinical vascular injuries, which are atherosclerosis-related and precursors to the structural brain changes that lead to cognitive decline.

5.3. The application of CTP in VCI

CTP can quantify CBV and CBF. A decrease in these parameters reflects cerebral hypoperfusion and hypoxia, both of which induce WMLs and disrupt higher-order neural networks, thereby exacerbating cognitive deficits. In some patients with VCI, compensatory mechanisms such as collateral circulation recruitment and vasodilation initially preserve cerebral perfusion during ischemic challenges. However, as ischemia progresses, these compensatory mechanisms cannot maintain the stability of CBF and CBV, resulting in a decrease in parameter values. Notably, the magnitude of hemodynamic parameter decline correlates with the severity of cognitive impairment, demonstrating a relatively linear relationship between hypoperfusion and neurodegenerative progression.[16,61] In addition, TTP and MTT can be used to evaluate CBF perfusion. Their delayed occurrence in MCA stenosis patients may be related to slower blood flow velocity after compensatory mechanisms such as collateral circulation and vasodilation are established.

Notably, TTP/MTT changes occur prior to detectable CBF reduction and can serve as sensitive neuroimaging biomarkers for early identification of cognitive impairment. Cognitive impairment attributed to SVD is predominantly characterized by prolonged MTT in the frontal cortex and subcortical white matter, as shown on CTP. The quantitative parameters of CTP mentioned above can be applied to evaluate regional cerebral perfusion deficits, offering critical neuroimaging biomarkers for identifying early-stage cognitive deficits.[16,62]

It is noteworthy that, pathophysiologically, lacunar cerebral infarction is a heterogeneous disease with multiple underlying mechanisms. While lipohyalinosis is the most prominent cause, other less frequent causes include atherosclerotic disease and cardioembolism. This pathophysiological diversity leads to different assessment approaches and treatment strategies compared to non-lacunar infarcts, and therefore to different functional outcomes.[63] However, with regard to post-stroke cognitive impairment, the rate of patients developing mild cognitive impairment or dementia within four years after stroke onset is similar between lacunar ischemic stroke and non-lacunar stroke (OR: 0.72, 95% CI: 0.43–1.20).[17] That means that despite the generally smaller infarct volume in lacunar strokes, the incidence of cognitive impairment is relatively high. This might be related to concomitant cerebral SVD.[17]

Current research has found that the efficacy of CTP in distinguishing lacunar strokes varies depending on the ischemic region (cortical, subcortical, or posterior fossa). For example, the automated core–penumbra map of CTP demonstrates better discrimination for cortical ischemia (area under the curve [AUC] = 0.82), but poorer performance for subcortical (AUC = 0.55) and posterior fossa (AUC = 0.66) ischemia. The incorporation of delay time and MTT maps significantly enhances discrimination of subcortical ischemia (AUC increased to 0.80). Among clinically diagnosed lacunar syndromes identified by CTP, only 50–60% are ultimately confirmed as lacunar strokes, with the remainder potentially being cortical or posterior fossa strokes, thus necessitating further differentiation via MRI.[64]

For non-lacunar strokes, CTA alone exhibits a sensitivity of 94.2% and specificity of 74.7% in detecting LVO, while its combination with CTP improves sensitivity

to 98% and specificity to 84.4%.[65] However, in non-lacunar strokes, the integration of CTA and CTP significantly enhances the accuracy of arterial occlusion identification. Therefore, standardized diagnostic criteria for CTA and CTP applicable across all scenarios of cognitive function assessment have not yet been established. Future research on CTA and CTP should focus on the identification of differences in evaluation strategies for lacunar and non-lacunar strokes to develop targeted and precise evaluation protocols.

6. Application of 3D printing technology in CTA

In the modern medical tide of pursuing precision and individuality, 3D printing technology, with its powerful physical model-construction capability, is integrated into the entire process of ischemic stroke diagnosis and treatment. Through its close integration with CTA, this technology has opened new paths for clinical decision-making, surgery planning, and prognosis evaluation.

CTA-based 3D printing provides physicians with a highly accurate vascular map, offering a 1:1 replica of intricate anatomical details, such as plaque morphology and vascular stenosis. This modality serves as an intuitive preoperative planning tool for neurosurgical procedures and EVT.[18,66,67] Such models not only facilitate the planning of optimal interventional pathways[68] but also allow for the assessment of key parameters through the simulation of hemodynamic environments (e.g., carotid artery stenosis models). Their results are highly consistent with conventional CTA measurements,[18] effectively mitigating the inherent deficiency of 2D imaging, which lacks in-depth information. Concurrently, 3D-printed models can become powerful instruments for validating clinical conjectures. By constructing models with specific vascular curvatures, researchers can delve into and compare the efficacy of techniques such as contact aspiration and stent retrieval, thereby furnishing experimental evidence for the management of acute LVOs.[69] Moreover, the intervention of artificial intelligence further enhances efficiency, with applications such as the "focused view CTA" generated by deep learning and the CA-UNet model-based automated segmentation of the carotid artery, paving the way for swift and precise intelligent diagnosis.[70,71]

In addition, 3D-printed models also offer unique advantages in prognostic management. By precisely recreating the characteristics of carotid artery plaques, the models can assist in distinguishing between embolic strokes of undetermined source (ESUS) and non-ESUS.[72] The study found that up to 25% of patients in the ESUS group had mild stenosis (<30% vs. 0% in the non-ESUS group), with significantly higher rates of IPH (80.0% vs. 37.8%), plaque calcification (70.0% vs. 29.7%), and adventitial calcification (70.0% vs. 37.8%), along with greater maximum calcified plaque thickness (1.79 mm vs. 1.52 mm). These data demonstrate that this modeling approach can effectively differentiate ESUS from non-ESUS patients by identifying a characteristic pattern of non-severe stenosis (0–49%) with highly vulnerable plaque composition. This pattern is characterized by high IPH burden, significant calcification with adventitial involvement, and increased calcified plaque thickness. It is envisaged that this technology can be an important tool for predicting the risk of stroke recurrence based on the 3D analysis of perivascular fat density around the carotid artery in conjunction with CTA.[73,74]

Despite the promising outlook, current fusion-based applications are facing multiple challenges: the clinical promotion scale is limited, primarily restricted by the differences in the resolution of original images, the time-consuming and high cost of model making,[75,76] and the seamless fusion of CTA with other imaging data remains challenging. Nevertheless, the personalized, visualized, and tangible diagnosis and treatment paradigm represented by 3D printing combined with CTA is expected to profoundly change the diagnosis and treatment of ischemic stroke. With the intervention of artificial intelligence algorithms to address the problems of efficiency and accuracy,[75] as well as the continuous breakthroughs in materials science and multimodal fusion technology, this approach is bound to break through the bottlenecks. It has the potential to extend beyond precise surgery planning to encompass the entire chain of prevention and early warning, real-time treatment, and intelligent rehabilitation assistance, ultimately paving a more transparent and more efficient way for the prevention and treatment of ischemic stroke.

7. Limitations and future perspectives

Nonetheless, many challenges remain in the field. One of them is that there is no standardized assessment protocol. Variations in CTP parameter thresholds and post-processing software across studies hinder widespread clinical adoption and result in poor comparability of findings. In addition, for cognitive impairment assessment, specific CTA/CTP diagnostic criteria tailored to different stroke subtypes (e.g., lacunar vs. non-lacunar infarcts) are yet to be established. The reliability and generalizability of predictive models in real-world settings require further validation.

Future work should include large, multicenter efforts to develop and validate comprehensive standards for the acquisition, processing, and parameterization of

CTA/CTP data to provide strong evidence for the development of clinical guidelines. Building on current evidence, future work should delineate the clinical utility of CTA/CTP for differentiating post-stroke cognitive impairment across etiologies and subtypes, particularly its role in identifying cognitive decline following lacunar infarcts to inform more targeted image-based assessment workflows. In addition, further clarification is needed regarding the relationship between the types of large-vessel pathologies and the degree of stenosis identified by CTA, their associated distal "tandem" small-vessel involvement, and their correspondence with impairments in specific cognitive domains (e.g., executive function and processing speed). Therefore, close integration of artificial intelligence technology is essential to develop intelligent prognostic models that can automatically combine multimodal imaging and clinical data. The current focus should be on solving problems related to image processing speed, standardization, and deep feature mining using artificial intelligence algorithms. These algorithms can automatically identify subtle imaging features related to cognitive impairment and develop intelligent risk-stratification models for cognitive decline. At the same time, it is also encouraged to integrate CTA/CTP with multimodal information from other sources, including MRI and serum biomarkers, to develop comprehensive predictive systems. Meanwhile, it is crucial to further explore the physiological mechanisms underlying prognosis, particularly the interaction between collateral circulation and venous outflow. These concerted efforts will collectively advance the assessment of stroke prognosis and cognitive impairment toward standardization, precision, and systematization.

8. Conclusion

This review comprehensively summarizes the multifaceted value of CTA and CTP for assessing functional prognosis and cognitive impairment after ischemic stroke. However, the detailed interpretation of specific technical parameters in CTP and CTA imaging—such as tube voltage/tube current, field of view, scan range, and slice thickness—has not been exhaustively enumerated. Furthermore, an in-depth analysis of the specific applications of artificial intelligence in assisting CTA and CTP interpretation has not been thoroughly addressed. Accumulated evidence demonstrates that CTP, by quantifying the infarct core and penumbra, has become a cornerstone for decision-making in reperfusion therapy within extended time windows. Objective parameters, such as rCBF (<30%), provided by automated analysis software (e.g., RAPID) significantly enhance the precision of prognostic prediction. At the same time, assessment of collateral circulation on CTA (including mCTA) and tissue-level perfusion evaluation derived from CTP parameters (e.g., HIR) constitute powerful tools for the prediction of neurological outcomes. In addition, the ability of CTA to identify subclinical vascular pathologies (e.g., vulnerable plaques and aortic arch atherosclerosis) and the application of CTP in characterizing cerebral hypoperfusion patterns provide imaging biomarkers for the early prediction of VCI. The combination of CTA and 3D printing technology provides a basis for personalized surgical planning. This review will provide some reference for further research on the application of CTA and CTP in ischemic stroke, thereby providing more clinical evidence for optimizing treatment strategies and improving patient prognosis.

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Conflict of interest

De-Qin Geng serves as an Editorial Board Member of this journal, but was not in any way involved in the editorial and peer-review process conducted for this paper, directly or indirectly. Separately, other authors declared that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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