Review Article

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Enhancing the clinical value of single-phase computed tomography angiography in the assessment of collateral circulation in acute ischemic stroke: A narrative review

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Abstract:

Acute ischemic stroke (AIS) condition assessment and clinical prognosis are significantly influenced by the compensatory state of cerebral collateral circulation. A standard clinical test known as single-phase computed tomography angiography (sCTA) is useful for quickly and accurately assessing the creation or opening of cerebral collateral circulation, which is crucial for the diagnosis and treatment of AIS. To improve the clinical application of sCTA in the clinical assessment of collateral circulation, we examine the present use of sCTA in AIS in this work.

Keywords:

Acute ischemic stroke, collateral circulation, single-phase computed tomography angiography, vascular segmentation

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Introduction

Acute ischemic stroke (AIS) is a type of acute cerebrovascular event characterized by high lethality and high disability caused by unknown factors causing disorders in the blood supply to brain tissue, followed by local necrosis due to insufficient blood perfusion and oxygen flow to brain tissue, and ultimately causing neurological dysfunction of limbs.[1] The first-line therapy approach for controlling the gradual worsening of AIS at this time is early revascularization within the time or tissue window.[2,3] A thorough and precise evaluation of the patient's cerebral collateral circulation is one of the requirements for customized endovascular treatment of AIS.[4] A healthy collateral circulation plays a crucial role in the effective recanalization of the relevant arteries and the perfusion of the ischemic tissue by contributing to an increase in the ischemic semidark zone and a decrease in the infarct volume.[5-9] This makes determining the compensatory condition of the collateral circulation extremely important.

The assessment modalities for collateral circulation at this point are primarily taken from neuroimaging techniques, such as magnetic resonance angiography, digital subtraction angiography (DSA), computed tomography angiography (CTA), and perfusion imaging, of which DSA is the accepted gold standard.[10] However, in the real world, most hospitals are limited by the need to meet the requirements of completing advanced imaging screening and minimizing the time from onset to femoral artery puncture; in addition, the examination is expensive and can only be performed in an emergency, which limits its widespread

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clinical popularity. CT is the recommended technique for the clinical assessment of AIS, as opposed to DSA, because to its noninvasiveness and comparatively fast scanning and postprocessing times. With the development of postimage reconstruction technology and the upgrading of CT scanning gear, CTA technology is essentially on par with DSA testing. The purpose of this paper is to discuss the clinical significance of single-phase CTA (sCTA) as the preferred acquisition phase for practical assessment of the cerebral collateral circulation. We also summarize and analyze the current application of sCTA for the assessment of the collateral circulation in ischemic stroke.

Establishment of Cerebral Collateral Circulation

A network of tiny arteries connecting neighboring arterial groups is known as cerebral collateral circulation. Reverse blood perfusion is provided by creating bypass arteries or in the form of an arterial anastomosis network when the original intracranial blood supply arterial pathway is narrowed or occluded. This ensures that the ischemic region is compensated by blood supply and prevents ischemic necrosis of brain tissue.[11] Assessing the collateral circulation's compensation status can provide insight into the state of cerebral tissue blood flow reperfusion and clinical functional prognosis, as the blocked arteries supplying ischemic brain tissue must be kept open until they are cleared of blockage.[12] One unique physiological mechanism that the human body uses to maintain blood perfusion is collateral circulation. The purpose of creating intracranial collateral circulation is to make sure that, in the event of a severe narrowing or occlusion of the original blood supply artery, there is still enough blood supply available to ischemic tissues through alternative pathways to counteract the ischemic changes in tissues and preserve blood perfusion in the ischemic semidark zone. As a stroke develops, the cerebral collateral circulation opens. When a stroke happens, the vascular wall is mechanically stimulated to produce proangiogenic substances, which results in vasodilation. This remodeling of the vascular morphology opens the collateral circulation.[13] Genetic variations and individual basal conditions influence the collateral circulation's compensatory degree.[14-17]

Step-by-step Classification of the Collateral Circulation

The three levels of the human cerebral collateral circulation are as follows: [18] the primary collateral circulation, the most significant circulatory pathway, is primarily made up of the circle of Willis (CoW), the arterial ring at the base of the brain, which is made up of the bilateral anterior cerebral arteries, middle cerebral arteries, posterior cerebral arteries, anterior communicating arteries, and posterior communicating arteries. When intracranial vascular stenosis or occlusion occurs, the CoW can quickly connect the left and right cerebral hemispheres as well as the anterior and posterior circulation for blood supply, but the prerequisite is dependent on the integrity of the CoW. Less than 50% of patients have a complete, symmetrical, and well-developed vascular ring, according to related studies, which has an impact on the prognosis of ischemic stroke patients.[19,20] The ophthalmic artery and the soft meningeal anastomosing branches make up the majority of the secondary collateral circulation. The most significant component of this circulation is the blood supply to the middle cerebral cortex through the soft meningeal anastomosing arteries, which also provide cortical surface perfusion.[21] An alternate perfusion channel to the ischemic area can be quickly provided by recruiting preexisting arterial vasculature. It primarily relates to the network of soft meningeal arteries, which refill extremely quickly. Research has shown that in an ICA-blocked rat model, maximal vasodilatation can be reached in as little as 12 s.[22] Neovascularization makes up the tertiary collateral circulation, which opens up when the primary collateral circulation's blood flow is insufficient to supply the distal ischemic area following the ischemia interval. The tertiary collateral circulation opens and creates neovascularization, which includes the development of new blood vessels around the ischemia focus or the maturation of existing vessels, when both the primary and secondary collateral circulations are unable to satisfy the blood supply to the ischemic area.[23]

Single-phase Computed Tomography Angiography Assessment of Collateral Circulation Scores

A minimally invasive, noninvasive vascular imaging test is called a CTA. When a closer look at blood vessels in specific vascular diseases is required, spiral CT scanning of the contrast agent-filled vessels is required after an intravenous injection. The images are then processed by a computer to replicate the vessel body. Blood vessels are not specifically displayed during plain CT scanning. This method offers a good assessment of collateral circulation, dilatation, and stenosis or obstruction by displaying the vascular structure at various angles.[24] With its excellent resolution, a CTA examination can identify the vessels causing the focal area's stenosis, show occluded vessel sites and distal vessel filling, and rule out other vascular abnormalities such as arteriovenous malformations. Related research indicates that there is minimal variation between the collateral circulation data from DSA and the CTA scan, which is the most compatible.[25]

Conventional sCTA is the imaging test of choice for urgent detection of cerebrovascular status in patients with AIS, as it acquires images only during this period of the peak arterial phase. Its benefits include rapid imaging, noninvasive, and reasonably easy image postprocessing, as well as the ability to clearly show the precise location of vascular occlusion.[26,27] When determining the course of treatment and predicting the result for patients with AIS, sCTA is utilized to evaluate the state of the cranial collateral circulation. This allows for the potential avoidance of further imaging tests, such as multitemporal CTA and CT vascular perfusion. sCTA is frequently used to assess collateral circulation. Commonly used scores include (i) anterior circulation collateral scores, which are primarily quantitative scores by assessing the number of filling collateral vessels (e.g. regional soft cerebral score, regional leptomeningeal collateral, rLMC Miteff score, Maas score, and Tan score) and (ii) posterior circulation collateral scores (PC-CSs).

Anterior circulation side branch score

The anterior circulation, which includes the anterior choroidal artery, anterior cerebral artery, and middle cerebral artery in the frontal, temporal, and parietal lobes as well as the basal ganglia, is the internal carotid artery system that supplies blood to the anterior three-fifth of the cerebral hemispheres. The contralateral artery's collateral circulation can compensate for the main trunk of the anterior circulation when it is occluded, but when the two arteries originate from the same anterior cerebral artery trunk, it can cause anterior and medial infarction of the two cerebral hemispheres; obstruction of the distal artery can result in the contralateral foot and lower extremity's sensory-motor impairment; obstruction of the cortical branch can cause paralysis of the central lower extremities; obstruction of the deep penetrating branch can cause the contralateral side's central facial and tongue paralysis, etc., The rLMC score, which is based on the extension of the healthy vascular artery to the internal carotid artery or the middle cerebral artery of the damaged side of the brain, is currently used to evaluate the anterior circulation collateral branches.[28]

The rLMC score was used by Tang *et al*.[29] to assess patients with AIS; the lower the score, the worse the prognosis for patients undergoing thrombolysis, suggesting that rLMC predicted the clinical prognosis of AIS. Menon *et al*.'s[30] confirmation of the rLMC score's predictive value in cerebral infarction patients also showed that the score was related to prognosis. He *et al*.[31] showed that there was a strong agreement between the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) scales of the DSA and the visual collateral score scale of the sCTA and the rLMC scales. According to Wang *et al*.,[32] the rLMC score was able to predict both the occurrence of cognitive impairment (OR < 1) and the result of intravenous thrombolysis of AIS. The Quantification of pial collateral pressure (QPCP) ratio (QPCP/systemic mean arterial blood pressure) and ischemic brain tissue soft meningeal collateral pressure (QPCP) values were discovered by Araki *et al*.[33] to have a statistically significant correlation and good agreement with the sCTA-Maas score on the ASITN/SIR binary grading scale. According to Yu *et al*.'s assessment[34] of arterial side branches using the modified Tan and Miteff scores, patients who have adequate arterial side branch circulation in sCTA are more likely to have a positive outcome following mechanical thrombectomy (MT). In assessing the intracranial collateral circulation before thrombolysis, Yeo *et al*.[35] used the Miteff score and Maas score; they were able to predict adverse outcomes and bleeding risk after AIS receiving tissue plasminogen activator (tPA) thrombolysis with significant correlation. Jin[36] found that when the Maas score (lateral fissure + cerebral convexity) was compared to the Tan score (middle cerebral artery region) to predict the value of cerebral infarction recurrence, Tan had a higher predictive efficacy than Maas. The combined assessment of the two scales had the best predictive effect. According to research by Xia,[37] the Tan score was more predictive of the likelihood of a re-induced cerebral infarction in older stroke patients than the Maas score. According to Liu Song *et al*.'s evaluation[38] of the likelihood of re-induced cerebral infarction in elderly patients who had experienced an acute cerebral infarction, Tan scores were more predictive than Maas scores. The evaluation of Tan and Maas in the collateral circulation of patients with middle cerebral artery occlusive stroke was conducted by Zhang *et al*.;[39] the findings demonstrated that Tan score had higher sensitivity and specificity than Maas score, and both scores were negatively correlated with diffusion-weighted imaging (DWI) infarct volume (rs = –0.886, –0.713, $P < 0.001$). In addition, DWI infarct volume and CTA collateral circulation score were prognostic factors for patients with middle cerebral artery occlusive stroke ($P < 0.05$).

Posterior circulation side branch score

The vertebrobasilar artery system, which includes the vertebral artery, the basilar artery, and the posterior cerebral artery, supplies the posterior two-fifths of the brain, which includes the brain stem, cerebellum, posterior regions of the cerebral hemispheres, and a portion of the mesencephalon. Many foci of posterior circulation ischemia are difficult to find based only on signs and symptoms, and not all cases of the condition have a typical expression in clinical practice. There are several reasons why posterior circulation ischemia can present with different clinical symptoms. First, collateral circulation provides abundant compensation for the posterior circulation. Second, the brain stem contains a greater concentration of cranial nerve nuclei and afferent and efferent nerve levels than the anterior circulation's blood-supplying region. As a result, even a minor lesion can result in a major loss of nerve-level function. The symptoms with the highest diagnostic value in posterior circulatory ischemia were cross-sensory deficit, cross-motor deficit, kinesiophobia→dysphagia; monochronic CTA→sCTA, and quadrant blindness, according to a large registry of patients with anterior and posterior circulatory ischemia in China.[40] However, the sensitivity of these symptoms ranged from 1.3% to 4%. Assessing the collateral vasculature of the posterior circulation is more challenging than that of the anterior circulation due to its complexity, variability, and high inter-individual variability. The impact of collateral circulation on the functional prognosis of patients with acute basilar artery occlusion was not statistically significant, according to a single-center retrospective research.[41]

In patients with AIS brought on by basilar artery occlusion, Goyal *et al*.[42] assessed the collateral circulation before and following endovascular thrombectomy (EVT) with endovascular reperfusion therapy, with 0 denoting no posterior communicating artery (PCOM), 1 denoting unilateral PCOM, and 2 denoting bilateral PCOM. Patients treated with EVT for basilar artery blockage had better outcomes when they had bilateral PCOM. Using the PC-CS of single-phase CTA, which concentrates on the primary vascular branches of the vertebrobasilar artery and the posterior communicating artery, van der Hoeven *et al*.[43] conducted a semi-quantitative evaluation of posterior circulation collateral flow. A multifactorial analysis revealed that patients with at least one thicker PCOM had a better clinical prognosis, and that patients with good collateral branches (PC-CS: 6–10), moderate collateral branches (PC-CS: 4–5), and poor collateral branches (PC-CS: 0–3) had better prognoses. Alemseged *et al*.[44] discovered that revascularization is linked to a favorable result even more than 6 h beyond the anticipated start time in patients with basilar artery blockage who had less severe occlusion and good PC-CS status.

Clinical Value of Enhancing Single-phase Computed Tomography Angiography to Assess Collateral Circulation

The assessment of collateral circulation is currently primarily based on the acquisition speed and time; the hemodynamic information of collateral circulation is not available and cannot be shown for collateral vessels that are filling slowly; as a result, conventional sCTA is limited to the period of peak arterial phase during image acquisition, which means that collateral circulation will be understated. Luo *et al*.'s findings[45] demonstrated that the ASPECTS quantitative grading score, which was based on multitemporal CTA for collateral circulation, outperformed the sCTA maximum intensity projection (MIP) score ($P = 0.000$). This difference in performance could be attributed to the artificial control of the sCTA image acquisition time, as well as the underrepresentation of some collateral vessels with slow blood flow on the sCTA, which caused an overestimation of the lesion extent. In contrast, all patients in a study from the MR CLEAR registry who had large vessel occlusion in the anterior circulation and were undergoing endovascular therapy underwent sCTA, and the findings indicated that the association between functional independence and collateral function status in patients with early imaging was comparable to that in patients with late imaging. Thus, this research indicates that the link between collateral circulation and functional results is not significantly affected by the duration of image acquisition, thereby confirming the imaging efficacy and extensive accessibility of sCTA.[46,47] In a study conducted by Kim and Kim,[48] preoperative examinations for 157 patients having mechanical thrombectomy (MT); isCTA-MIP→is sCTA MIP(maximal intensity projection, MIP) and noncontrast CT + magnetic resonance imaging (MRI) were compared. The results verified that sCTA had adequate predictive value as a single preliminary examination before MT, resulting in a shorter examination-to-operation procedure time and a favorable prognosis. In addition, the results demonstrated that sCTA outperformed the MRI group on the modified Thrombolysis in the Cerebral Infarction Scale or mRS score. According to Yu *et al*.,[34] monophasic CTA images can be used as an imaging marker with evaluation reliability as long as they demonstrate enough arterial collateral branches – rather than enough venous turbidity – to indicate that a MT will be successful. As a result, increasing the number of arterial collateral branches that are adequately visible during the unit time phase may help improve the accuracy of sCTA assessment.

These days, computed tomography perfusion (CTP), a continuous CT scan carried out during a rapid intravenous contrast injection and reconstructed by computerized postprocessing, is combined with a "one-stop" examination to increase the sensitivity of sCTA for the assessment of collateral circulation in many hospitals. Through the parameters of cerebral blood flow, cerebral blood volume, mean passage time (MTT), and time to peak, it gives changes in local tissue perfusion information following computerized postprocessing reconstruction and so efficiently evaluates collateral circulation.[49] The MTT of the CTP observations is the amount of time it takes for the contrast agent to enter the body, progressively deteriorate, and reach half of its peak – a measure of how long it takes for the agent to travel through the capillaries. Research has shown that MTT can accurately reflect intracranial collateral circulation perfusion, which is a crucial marker for predicting when a cerebral infarction will occur. When CTP is paired with CTA data, it can enhance the functional and anatomical variations in collateral circulation, contributing to a more thorough and precise assessment.[50,51] Voleti *et al*.'s research[52] found that a smaller CTP core, a smaller penumbra, a greater mismatch, and a lower perfusion intensity ratio are all necessary to get a high Tan score (sCTA) in patients with major artery blockage that occurs during the delayed time frame (6–24 h). It is anticipated that collateral circulation evaluation with sCTA may prove to be a useful substitute

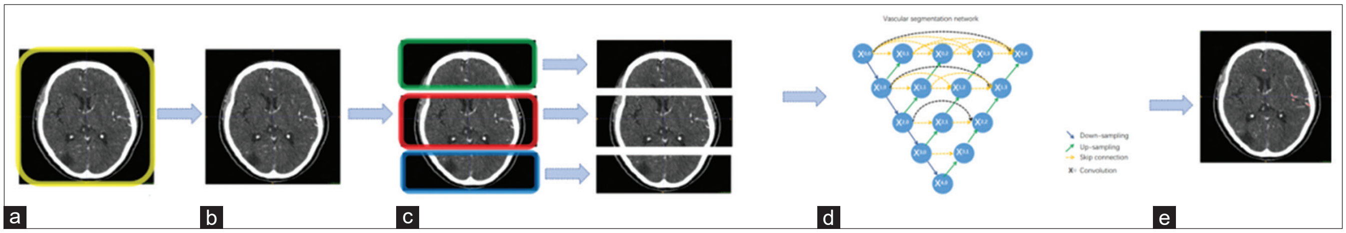

Figure 1: Vascular segmentation postprocessing simplified process. (a) Select cerebrum-ROI, (b) Normalization, (c) Intercepting data module, (d) Neural network algorithm prediction, (e) Segmentation results

for CTP, particularly in stroke centers where CTP cannot be implemented.

The viability of collateral circulation assessment through enhanced sCTA hinges on the advanced postprocessing methods of image segmentation, enhancement, visualization, data compression, and alignment fusion. These methods identify, classify, segment, and analyze the images and subsequently identify the features to be extracted or enhanced areas to help physicians provide an unbiased and precise diagnosis of the patient's condition.[53] Precise segmentation of CTA pictures can be utilized for various analysis activities such as 3D reconstruction of blood vessels, in addition to providing a quantitative description of various anatomical aspects of blood vessels and extracting region of interest for targeted observation. Vascular segmentation images can display low contrast, blurry, and various morphological vascular structures; nevertheless, they are limited by imaging noise, complex vascular structures, imaging angles, and imaging distances. By using a multimodal convolutional neural network CNN to segment cerebral blood vessels, smoothing and sharpening the original CTA images with Gaussian and Laplace filtering techniques, and fusing the CNN segmentation processed images with the original images, the accuracy of cerebral vascular segmentation is increased.[54] Sharpening the fine vascular structures to a Laplace operator centered at -8 improves both the spatial characteristics of the vascular points and the gray values of the pixel points at the image's edges. The original CTA images contain fine vascular structures that are challenging to identify.[55] When it comes to segmenting cerebral vessels, most assessments of cerebral vascular disease only require the acquisition of intracranial vessels without taking extracranial vessels into consideration. However, the actual segmentation results also contain some extracranial vessels, so it is worthwhile to investigate how to use additional spatial connections to exclude extracranial vessels in order to improve the vessel segmentation algorithm problem.[54] Spatial location information is an extremely important priori knowledge in the diagnosis of brain CTA image analysis. In the post-processing of cerebral vascular CTA images, in addition to segmenting and extracting blood vessels, removing bones is also a crucial step. Studies have shown that subtractive debridement technique performs significantly better than computerized automatic bone removal.[56,57] By entering the data from the head scan and the enhanced scan twice into the workstation for subtraction, using the arterial phase image to subtract the scan phase image, and subtracting the bone information (absorption coefficient remains unchanged) from the two sets of data before and after enhancement to obtain the data of vascular information (absorption coefficient changes), the subtractive debridement technique significantly improves the speed and quality of cerebrovascular CTA image postprocessing. To produce a complete head vasculature, the pictures acquired from the aforementioned processes are reassembled using vascular 3D reconstruction; the 3D image effect may be similar to DSA.[58,59] The enhancement of diagnostic value has been facilitated by the advancement of image postprocessing technology, and the superior quality of postprocessed images guarantees the high diagnostic value of CTA.[60] For our current experimental study, the segmentation of CTA vasculature using neural networks is simplified as follows [Figure 1]. The process entails first performing a straightforward postprocessing of the source images obtained by sCTA. Next, the middle cerebral artery is automatically extracted using a neural network. This is combined with an independently researched AIS collateral circulation assessment system to obtain a more accurate AIS collateral circulation result quickly and easily.

Summary

When it comes to evaluating the collateral circulation in AIS, sCTA continues to be the clinician's first choice when time and medical resources are scarce. Through sophisticated picture postprocessing techniques and a proven scoring system, sCTA offers a quick, precise, clear, and easy-to-understand depiction of the patient's intracranial collateral circulation. In addition, it can enhance decision-making for collateral circulation assessment. Maintaining blood perfusion in the ischemic semidark zone and lowering the eventual infarct volume in AIS patients need accurate monitoring of the collateral circulation. Improving the clinical utility of sCTA as a measure of AIS collateral circulation can support the advancement of primary precision medicine, fortify the identification and management of high-risk stroke conditions, and enhance the development of an integrated system for the prevention and treatment of strokes. Even though there are currently many objective conditions that limit sCTA examination, such as limitations on acquisition time phases and image gray value noise clarity, as neuroimaging technology advances, factors that influence images, such as acquisition mode, parameter settings, and noise level, will become less significant due to advances in artificial intelligence deep learning algorithms and intelligent image segmentation processing technology. This will enable the clinic to provide intelligent diagnosis and treatment.

Author contributions

M.D Yunqiu Yang wrote the manuscript, Dr. Zhen Wang and Prof. Qingmao Hu guided the article writing, Libo Liu and DR. Guorui Ma organized the information, and DR. Chen Yang proofreading of the manuscript.

Ethics committee approval and declaration of Helsinki

In accordance with the Declaration of Helsinki, the study protocol passed the ethical review of the Ethics Committee for Human Experiments of the Shenzhen Institute of Advanced Technology, Chinese Academy of Sciences (Grant No. SIAT-IRB-221015-H0614) and the Ethics Committee of Zhongshan Hospital of Traditional Chinese Medicine (Grant No. 2023ZSZY-LLK-252).

Data availability statement

Data sharing not applicable to this article as no datasets were generated and/or analyzed during the current study.

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Conflicts of interest

There are no conflicts of interest.

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