Good Clinical and Radiological Correlation from Standard Perfusion Computed Tomography Accurately Identifies Salvageable Tissue in Ischemic Stroke

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Introduction: It has been debated whether the penumbral pattern, as identified using multimodal imaging, is a specific marker of tissue viability in ischemic stroke. We assessed whether perfusion computed tomography (PCT) accurately identifies salvageable tissue and helps predict postreperfusion outcomes. *Methods:* A retrospective study of patients with anterior circulation stroke undergoing reperfusion therapies who had a PCT before treatment and an assessment of vessel recanalization post treatment was conducted. Tissue at risk was considered as that with reduced cerebral blood flow, whereas the infarct core was the region of reduced cerebral blood volume, the mismatch region being salvageable tissue. The volume of hypodensity in slices corresponding to perfusion acquisition cage in 24-hour computed tomography (partial lesion volume [PLV]) was measured. Outcome variables were the amount of preserved tissue, that is, the difference between volumes of tissue at risk and PLV expressed as a percentage, and the modified Rankin Scale (mRS) score at 3 months. *Results:* Patients (n = 34) meeting the inclusion criteria were included. Vessel recanalization was associated with a larger amount of tissue at risk preserved from definite lesion (89% [interquartile range {IQR}: 76-94] versus 46% [IQR: 23-86], $P < .005$). The amount of preserved tissue correlated with clinical outcome at 24 hours: for each 10% of preserved tissue, the National Institutes of Health Stroke Scale score improved by 3 points (95% confidence interval [CI]: –4.9 to –.8, $P = .007$) and was the only predictor of independency (mRS score 0-2) following adjustment for covariates (odds ratio 1.15, 95% CI: 1.04-1.28, $P = .005$). *Conclusions:* PCT provides accurate markers of viability of tissue in acute ischemic stroke and could help predict the degree of improvement following reperfusion. **Key Words:** Perfusion computed tomography—ischemic stroke—ischemic penumbra—reperfusion—mechanical thrombectomy—thrombolysis—endovascular treatment.

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Introduction

The pathophysiological basis for reperfusion therapies following ischemic stroke relies on the presence of recoverable tissue, that is, ischemic penumbra,[1] and on the principle that the earlier the reperfusion, the higher the probability of good outcomes.[2] However, beyond the first few minutes of stroke onset, and especially at larger time windows, the ability to recover depends not only on the time delay but also on particular tissue susceptibility; both parameters may vary considerably between individuals. Hence, it is necessary to identify the persistence of recoverable tissue accurately to optimize patient selection for reperfusion therapies. Multimodal magnetic resonance imaging (MRI)[3] and perfusion computed tomography (PCT) images[4] are used in estimating irreversibly damaged and at-risk (but potentially recoverable) tissue following an ischemic stroke.[5-7] Favorable mismatch profiles in perfusion imaging have been proposed as surrogates for persistence of penumbra, the extent of which can predict good neurological outcomes in ischemic stroke. Some clinical trials have failed to demonstrate that selection based on the presence of a target mismatch can identify patients who might benefit from revascularization therapies, the penumbral pattern on its own being considered lacking in specificity as a marker of recoverable tissue.[8,9] However, more recent studies have demonstrated that, in patients with proximal arterial occlusion and PCT criteria of salvageable tissue, mechanical thrombectomy (MT) improved functional outcome.[10,11] Our aim, in the current study, is to determine whether data available to the clinician from PCT studies routinely performed in the emergency assessment of acute ischemic stroke, can accurately distinguish irreversibly damaged tissue from potentially salvageable tissue and, if so, whether PCT data on admission correlate with evolution of neurological function and would help predict the degree of improvement achievable after effective reperfusion.

Materials and Methods

Study Design and Patient Sample

This is a retrospective observational study conducted at the Stroke Unit of the Department of Neurology at the University Hospital Ramón y Cajal (Madrid, Spain). Included were those patients with acute ischemic stroke due to anterior circulation large-vessel occlusion, treated with reperfusion therapies, whether intravenous thrombolysis (IVT) or endovascular treatment such as MT. Treatment protocols followed current guidelines.[12] For the purpose of the present study, we selected patients who had a complete and readable PCT, together with a computed tomography angiography (CTA), demonstrating the vessel occlusion before treatment, and assessment of vessel recanalization using transcranial Doppler ultrasound monitoring (in every patient undergoing IVT) or digital subtraction angiography (the latter in cases undergoing MT) after treatment and within 8 hours from symptom onset. Every patient was followed up with a noncontrast cranial computed tomography (NCCT) at 24 hours.

A database was designed to include clinical and radiological data. Patients with incomplete radiological dataset, those without assessment of vessel recanalization after treatment and within 8 hours from symptom onset, and those with hemorrhagic transformation that impeded measurement of hypodense lesion in the 24-hour computed tomography (CT) were excluded from the present study.

Patients gave informed consent for the procedures and for the use of data for investigational purposes. The study had the approval from the Ethics Committee of our hospital and was conducted according to the recommendations of the Helsinki Declaration.

Image Acquisition and PCT Postprocessing

On admission, a complete multimodal CT scan including a cranial NCCT, PCT, and CTA using a 64-slice spiral CT scanner (Toshiba Aquilion 64, Toshiba Corporation, Tokyo, Japan) was obtained. A follow-up NCCT was performed at 24 hours. Acquisition and processing methodology followed current recommendations.[4,13]

NCCTs were obtained from the skull base to the vertex for every 40-mm slice. PCT was performed with the injection of 50 mL iodinated contrast medium (4-6 mL/second). Rapid cine scanning produced a series of sequential images of 4 sections each of 8-mm thickness with a total coverage of 32 mm of parenchyma. The area of interest (PCT cage) was selected in the region where early signs of ischemia can be identified in NCCT or, if these signs were not identified, an axial CT cut at the level of the thalamus and basal ganglion was chosen and the PCT cage extended 32 mm (4×8 mm slices) rostrally. CTA was performed from the aortic arch to the vertex with the injection of 50-60 mL of contrast medium (4 mL/second) using an automated system for image acquisition following the bolus (Sure Start, Toshiba Corporation, Tokyo, Japan). Acquisition was performed by slicing every .5 mm to permit subsequent multidimensional image reconstruction.

PCT maps were computed using the Vitrea Advanced 6.0 software from the dynamic contrast CT-scan acquisition (Vital Images; MediMark Europe, Grenoble, France). The arterial input function and the venous outflow from major vessels are automatically selected by the system, or manually selected if needed for a better definition of values. The processing is based on a singular-value deconvolution algorithm considering the arterial and venous time–intensity curves[4] to create color maps of cerebral blood flow (CBF) (mL/100 g/minute), cerebral blood volume (CBV) (mL/100 g), mean transit time (MTT) (seconds), and TTP (seconds).