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Clinical/perfusion CT CBV mismatch as prognostic factor in intraarterial thrombectomy in acute anterior circulation stroke

Marc Saake*, Lorenz Breuer, Philipp Gölitz, Martin Köhrmann, Stefan Schwab, Arnd Dörfler, Stephan Kloska

Department of Neuroradiology, University of Erlangen-Nuremberg, Schwabachanlage 6, 91054 Erlangen, Germany

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ABSTRACT

Objective: Contradictory results were reported for the outcome after endovascular recanalization (ERT) in acute anterior circulation ischemic stroke. We assessed whether a clinical/perfusion CT cerebral blood volume (CBV) mismatch concept (CPM) can identify patients who will benefit from reperfusion therapy.
Methods: Imaging and clinical data of 58 consecutive ERT cases with acute anterior circulation stroke (ICA, M1, proximal M2) undergoing intraarterial thrombectomy within 4.5 h after symptom onset were analyzed retrospectively. CPM was defined as NIHSS ≥ 8 and PCT CBV ASPECTS ≥ 7. Minor CBV lesion was defined as PCT CBV ASPECTS ≥ 7.
Results: All baseline characteristics other than blood glucose did not differ between the paired groups. Revascularization was achieved in 87.9% of all patients without significant difference between the paired groups. Favorable clinical outcome after 3 months (mRS ≤ 2) resulted in 29.3% of all patients, in contrast to 47.4% of the CPM positive and 52.2% of the minor CBV lesion groups.
Conclusion: CPM can identify patients who will benefit from reperfusion therapy in acute anterior circulation ischemic stroke.

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1. Introduction

Stroke is one of the leading causes of morbidity and mortality worldwide and a common cause of depression, epilepsy, and dementia in the elderly. 85% of strokes are ischemic, resulting from an arterial vessel occlusion. Depending on the site of occlusion, mortality rates reach 53–92%, with higher mortality rates in large vessel occlusion. The keystones of acute stroke treatment are fast and accurate detection of brain tissue at risk and time sensitive performance of reperfusion therapy in patients eligible. Beside factors like time from symptom onset, infarct demarcation on non-contrast CT (NCCT) and initial National Institute of Health stroke scale (NIHSS), a beneficial patient selection criterion for reperfusion therapy might be the size of the mismatch between the potentially salvageable tissue (penumbra) and the irreversibly damaged tissue (core) [1,2].

Reperfusion therapy is the only proven causal treatment for acute ischemic stroke. Currently intravenous thrombolysis (IVT) is the only FDA-approved reperfusion strategy. However, IVT has several limitations such as a limited time window and a weak effect in ischemic strokes caused by large vessel occlusions. In these cases, interventional procedures might improve recanalization rates and patient outcome [3]. Significant improvements have been made in the last years in the development of endovascular reperfusion therapies (ERT) [4]. By now, ERT has been demonstrated to be an effective means of achieving reperfusion in stroke patients with proximal cerebral artery occlusions [5]. However, favorable outcome after stroke intervention remains limited, with only 25–50% of patients achieving a modified Rankin Scale ≤ 2 at 90 days [6,7]. Moreover, recent reports suggested that outcome after ERT might be equal to IVT [8,9].

Combined clinical/imaging mismatch concepts compare the clinical symptoms to the imaging findings. Numerous studies have shown that the clinical/MRI diffusion mismatch between the NIHSS score and the infarct size on diffusion weighted imaging (DWI) may identify patients at risk of infarct growth and early neurological deterioration [10–12]. However, CT represents the most

Abbreviations: IVT, intravenous thrombolysis; ERT, endovascular reperfusion therapy; NCCT, non-contrast CT; PCT, perfusion CT; CBV, cerebral blood volume; CBF, cerebral blood flow; DWI, diffusion weighted imaging; NIHSS, National Institute of Health Stroke Scale; MMCT, multimodal CT; mRS, modified Rankin Scale; CTA, CT angiography; TTP, time to peak; DSA, digital subtraction angiography; ASPECTS, Alberta Stroke Program Early CT score; MCA, middle cerebral artery; ROC, receiver operating characteristics; PPV, positive predictive value; NPV, negative predictive value; CPM, clinical/PCT CBV mismatch.

* Corresponding author. Tel.: +49 91318539388.
E-mail address: marc.saake@uk-erlangen.de (M. Saake).

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frequently used imaging modality in acute stroke patients. Previous studies have reported poor sensitivity and poor interobserver agreement for the detection of early ischemic changes on NCCT [13]. Several mismatch concepts have been proposed to improve CT stroke detection. A clinical/NCCT approach did not reliably identify patients more or less likely to benefit from intravenous thrombolysis [14]. Perfusion CT (PCT) has been shown to be an accurate predictor of both thrombolytic therapy benefit and clinical outcome [15]. The most frequently used PCT-based approach compares the region of reduced cerebral blood volume (CBV, presumably representing irreversible infarction) and the area of reduced cerebral blood flow (CBF) that lies outside of the CBV abnormality (potentially representing reversible ischemia). The region of reduced CBV has been shown to most accurately describe the infarct core [16] and to correlate with MRI DWI lesions in hyperacute stroke [17].

We hypothesized that clinical/PCT CBV mismatch (CPM) between the patient's clinical stroke severity defined by the NIHSS score and the PCT CBV lesion size can identify patients who will benefit from reperfusion therapy in acute anterior circulation ischemic stroke.

2. Materials and methods

2.1. Study population

Institutional review board approval was obtained before the commencement of this retrospective study. Informed consent of the patient or next of kin was obtained according to local laws and regulations.

A total of 277 consecutive patients who underwent multimodal stroke CT (MMCT) in our department between June 2010 and July 2012 were analyzed retrospectively for the study. Inclusion criteria were acute anterior circulation stroke, use of MMCT for primary imaging, proximal anterior circulation vessel occlusion (i.e. occlusion of the internal carotid artery, M1, and/or proximal M2 segment of the middle cerebral artery) and performance of ERT due to clinical indication. Exclusion criteria were an age of less than 18 years, incomplete or non-diagnostic examinations, and signs of hemorrhage in the initial NCCT. Additional IVT was not considered an exclusion criterion, as IVT is the primary standard therapy in acute stroke.

2.2. Stroke therapy and follow-up

All stroke patients admitted to our hospital are treated at our local stroke unit. According to standard procedures the severity of clinical stroke symptoms is assessed in every patient by the National Institutes of Health Stroke Scale (NIHSS) [18]. All eligible stroke patients receive body weight adapted (0.9 mg tPA/kg) IVT according to standard guidelines [19].

As outcome measure we used the modified Rankin Scale (mRS), a 7-point scoring system that distributes patients from 0 (no symptoms) to 6 (death) [20]. The pre-stroke mRS score was determined by a structured questionnaire during the hospital stay of the patient. Three months after stroke onset, the structured questionnaire was performed again for all patients by telephone to assess the level of independence at home.

2.3. Imaging and endovascular recanalization therapy (ERT)

In all acute stroke patients a standardized MMCT protocol, consisting of NCCT, PCT with 9.6 cm whole brain coverage in the z-axis, and supra-aortic CT angiography (CTA) was performed according to hospital guidelines. All examinations were performed on a 128-section CT scanner (Somatom Definition AS+; Siemens, Forchheim, Germany). Image reconstruction parameters for NCCT were: section thickness, 5.0 mm; increment, 5.0 mm; reconstruction kernel, H31s. Primary PCT image reconstruction parameters were: section thickness, 5.0 mm; increment, 5.0 mm; reconstruction kernel, H20f. From this dataset PCT parameter maps (CBV, CBF, and time to peak (TTP)) were calculated using a CT workstation (Multimodality Workplace MMWP; Siemens, Forchheim, Germany) running standard software (Syngo VPCT Neuro; Siemens, Forchheim, Germany).

All digital subtraction angiographies (DSA) were performed on a biplane flat-detector angiography system (Axiom Artis dBA; Siemens, Forchheim, Germany) by staff neuroradiologists. Using standard angiographic procedures, the affected internal carotid artery was investigated. For ERT procedures the device vendor guidelines were followed. The selection of the used reperfusion catheter system was to the discretion of the neurointerventionalist. Generally, all ERT systems aim to remove the clot from the cerebral artery, but they differ in technical details.

NCCT was repeated at 24–72 h after symptom onset for follow-up.

2.4. Image analysis

All examinations were anonymized. Images were transferred to a workstation (MMWP, Siemens, Forchheim, Germany). Review and analysis of the MMCT and ERT images was performed by a senior neurology resident and a senior neuroradiology resident in consensus. For assessment of the NCCT images and the color-coded PCT parameter maps the Alberta Stroke Program Early CT Score (ASPECTS) was used. The ASPECTS is a semiquantitative approach to infarct sizing on NCCT that has been demonstrated to be both reliable and predictive of outcome following acute stroke treatment [21]. The ASPECTS ranges from 0 to 10. For signs of infarction in each of the 10 parts of the middle cerebral artery (MCA) territory one point is subtracted from 10. Thus, a minor infarction has a high, a major infarction a low ASPECTS. Meanwhile, the ASPECTS has been adapted to the similar assessment of PCT parameter maps [22]. ERT images were scored for recanalization success, using the primary arterial occlusive lesion (AOL) [23] and thrombolysis in cerebral infarction (TICI) [24] scores.

2.5. Data analysis

It has been suggested that an NIHSS score of ≥ 8 is associated with a high rate of neurological deterioration, a low frequency of spontaneous functional recovery, and cortical perfusion deficits [11,25]. So, we used this cut-off point as a clinical indicator of a large volume of ischemic brain tissue. Patients were dichotomized for favorable versus unfavorable outcome at 90 days, with favorable outcome defined as mRS ≤ 2. Receiver operating characteristics (ROC) analysis was performed for PCT CBV ASPECTS in regard of patient outcome. The optimal threshold level for dichotomization of PCT CBV ASPECTS was determined by maximizing the sum of sensitivity and specificity, and minimizing the Euclidean distance of (sensitivity, specificity) to the point (1, 1) of the ROC curve [26].

We divided the study population into the following groups:

1. minor stroke (NIHSS < 8) versus major stroke (NIHSS $\geq$ 8) groups (NIHSS approach),
2. minor CBV lesion (PCT CBV ASPECT score > threshold) versus major CBV lesion (PCT CBV ASPECT score < threshold) groups (CBV size approach),
3. clinical/PCT CBV matched (CPM negative) versus clinical/PCT CBV mismatched (CPM positive) groups (CPM approach).

We compared the paired groups with regard to the following variables: background characteristics including age, gender,

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