ORIGINAL RESEARCH PAPER

Radiology

PERMEABILITY VALUES IN THE PCT MULTIMODE PROTOCOL AS PREDICTOR OF HEMORRHAGIC TRANSFORMATION AFTER THROMBECTOMY IN ACUTE STROKE

KEY WORDS: Thrombectomy; Stroke; Permeability; Perfusion; Hemorrhage; Acute.

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ABSTRACT

BACKGOURND AND PURPOSE: Permeability is altered in the acute stroke and related to hemorrhagic transformation. We aimed to compare the ischemic cerebral area in hemorrhage tissue after thrombectomy in comparisson with ischemic area with no haemorragic transformation.

MATERIAL AND METHODS: We retrospectively found 190 patients who underwent to mechanical thrombectomy, with occlusion of the M1 segment of the middle cerebral artery, the internal carotid artery or both completion of a stroke CT imaging work-up including non-contrast CT at admission and CT control at 24 hours post-ictus

RESULTS: 82 patients met the inclusion criteria. The average value for ischemic area in the hemorrhagic transformation was 2.63 and the non-hemorrhagic transformation was 2.74 with no statistical differences in the permeability values between the group with hemorrhagic transformation and the group without P=.766.

CONCLUSIONS: The values of permeability were not useful to predict hemorrhagic transformation after thrombectomy with intravenous thrombolysis as some studies have shown.

Abbreviations: CT: computed tomography; MRI: Magnetic Resonance Imaging; PCT: perfusion computed tomography; CBF: cerebral blood flow; CBV: cerebral blood volume; MTT: mean transit time.

Introduction

Nowaways, stroke is one of the most important causes of disability around the world. It is important to recognize that noninvasive studies such as TC and MRI have become tools for diagnosis and selection for fibrinolysis and endovascular treatment.

In the same time, we used perfusion CT for selection of patients whom have chance to be candidates for thrombectomy by finding the penumbra area and mismatch. We usually analyze CBF, CBV and MTT, but not permeability as routine. Some studies based on CT perfusion have described the association between high permeability score and probability to transformation hemorrhagic infarction[1,2].

Patients with acute stroke develop changes in the blood-brain barrier permeability, and these changes are considered as predictors of hemorrhagic transformation and could be measured indirectly by permeability in the CT o MRI perfusion[2,3].

We decided to find out if the information acquired in our multimode PCT for acute stroke could give us more information to decide what case to carry into the endovascular room for thrombectomy.

Materials and methods

We made a retrospective follow-up from january 2016 to december 2016 and found 190 patients underwent to mechanical thrombectomy in vall d´hebron´s Hospital. But only 92 patients were following the inclusion the inclusion criteria: 1) with occlusion of the M1 segment of the middle cerebral artery, the internal carotid artery or both 2) completion of a stroke CT imaging work-up including non-contrast CT, CT angiography (CTA), and CTP at admission in our protocol for stroke; 3) treatment involving intra-arterial thrombolysis with tPA and no response base on NIHSS (more than points compared to basal) 4) CT control at 24 hours post-ictus to make a comparison between non-hemorrhagic transformation and hemorrhagic transformation.

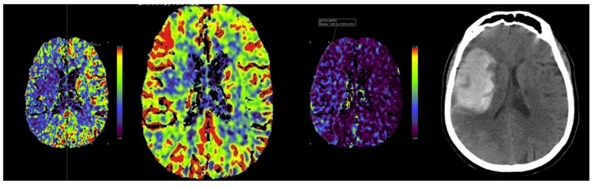
85 patients did not have perfusion CT or interpretable permeability maps at Vall d´Hebron Hospital in Barcelona, Spain. We excluded 3 patients with movement artefacts and 10 patients with no clear appearance of hemorrhagic transformation.

Radiographic characteristics in permeability were analyzed by two neuroradiologist.

Calculation of permeability

Permeability color maps was retrospectively rebuilt from PCT data using modified Patlak method based on our protocol for acute stroke in multimodal PCT. PCT was performed on a Siemens definition ASPLUS 128 slice scanner. After intravenous administration of 50 mL iodinated contrast at 5mL/s by an injector into an antecubital vein (Omnipaque, 350/40 mL), images are acquired. Imaging parameters of adquisition were 70 kVp, 150 mAs, and 1.25-mm section collimation. Slice thickness was 4.0 mm acquired at a time for 61 seconds. The modified Patlak model (calculated in Siemens Syngo Neuroperfussion) calculates vascular permeability (Flow product extract) with CT enhancement values after the peak contrast enhancement is reached. A 81 years old patient with left brachio-crural paresia, dysarthria, left central facial paresia with NIHSS 10. A) CBF color maps showing hypoperfusion with right MCA acute ischemic stroke. B) CBV color maps showing mismatch in MCA territory C) Admission permeability color maps showed permeability abnormality in right MCA territory. D) head CT after mechanical thrombectomy shows hemorrhagic transformation in the ischemic territory.

We processed the imaging and calculated the permeability maps using Syngo Neuroperfusion. We defined abnormality based in color maps and guided by the CBF. We traced an area in three different slice from, over and down the ganglia basal zone around the abnormality area and the the mean in the affected area is calculated. The area was measured by hand-drawn in the region of interest separately. Contralateral non ischemic hemisphere was used as a control.



(A) (B) (C) (D)

Results

Before the analysis the homogeneity of variance in the permeability values is tested by using Leven's test (F= 1.369 P=.245) for the assumption of homoscedasticity.

The Anova test did not show statistical differences in the permeability values between the group with hemorrhagic transformation and the group without P=.766

On the table below we show the descriptive data of the permeability values of the group with hemorrhagic transformation and the group without. As we can see, the difference between the means of both groups is very low, as the one-way ANOVA shows.

GROUP	N	MEAN	STANDARD DEVIATION	TYPICAL ERROR
WITH HEMORRHAGIC TRANSFORMATION	26	2.6304	1.79815	.35265
WITHOUT HEMORRHAGIC TRANSFORMATION	56	2.7443	1.51007	.20179
TOTAL	2.7082	1.59660	.17632	.17632

No statistical difference was found between the two groups.

Statistical Analysis

For the Statistical Analyses, a one-way ANOVA was performed to analyse the differences between the permeability values of the ischaemic area on a group of patients that had suffered hemorrhagic transformations and a group of patients who had not. Statistical analysis was carried out using SPSS version 23.0 (IBM SPSS statistics editor) A value of P<0.05 was considered statistically significant.

Discussion

Hemorrhagic transformation is a complication in the developing of ictus. Many factors have been associated to this, such as high ASPECTS, time to reperfusion[4], rTPA treatment[5], heparin and aspirin use[6,7].

Ischemic tissue in brain causes cytotoxic edema characterized by intracellular water accumulation, and later vasogenic, in which water moves accros the blood-brain barrier into the extracellular interstitial space[8]. Ischemia in rats has demonstrated disruption of the blood-brain barrier as early as 20 minutes after and occlusion has happened[8,9]. A loss of the blood-brain barrier is associated with hemorrhagic after an ictus[10]. Cerebral ischemia contributes to damage of the barrier[11], and iodized contrast do not cross the normal barrier, but when it is damaged, it is crossed by contrast and the measurement of the contrast is considered as an indicator of endothelial junction failure.

The alteration in the blood-brain barrier can be measured by CT[11] or MRI[12], but CT is the main imaging modality in the majority of clinical centers, because of its availability and fast use. Furthermore, it do not delay the endovascular treatment and the Patlak model is an adequate analytical tools to measure these values[13,14].

To apply this model is necessary to use arterial and parenchymal contrast enhancement in order to measure the rate of contrast passing from intravascular to extravascular compartment[15,16]; it behaves as an indirect measurement of microvascular permeability[17].

In our study, we used the information acquired in our multimode PCT for acute stroke. But our values under the area did not reveal correlation with hemorrhagic transformation. The average of permeability score were similar in both groups with no statistical difference, because some patients with high score did not develop hemorrhagic transformation and vice versa. This result disagree with studies that showed evidence of high permeability in cerebral ischemia/infarct tend to progress to hemorrhagic transformation[15,18].

Elevated permeability was predictive for hemorrhagic transformation after tissue plasminogen activator administration[19]. However, we did not found any study which correlates hemorrhagic transformation after thrombectomy and permeability values.

This study is limited by the design. We infer we may have variation in the size of thrombus with total ischemic area and time of evolution from the acute occlusion to time that the patients get in our center. These factors may sway in the permeability area, we made the measure in the area with ischemia and permeability map which were shown in the CT-perfusion, it may cause that small volume of infarcted area has low probability to develop hemorrhagic transformation. There is evidence that suggests that permeability increases from 2 to 4 hours when the stroke has happended[20-22]. The time between the onset of symptoms and the beginning of the exploration may condition a difference when comparison permeability values under the area.

Conclusion

The values of permeability was not useful to predict haemorragic transformation after thrombectomy as studies with intravenous thrombolysis have shown. Our study was limited because the extension of the infarct and the time of CT-perfusion were not considered. Further studies are needed to validate our findings.

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