

Multimodal CT pc-ASPECTS in infratentorial stroke: diagnostic and prognostic value

Paola Caruso¹  · Mariana Ridolfi¹ · Carlo Lugnan¹ · Milos Ajčević^{1,2} · Giovanni Furlanis¹ · Giulia Bellavita¹ · Roberta Antea Pozzi Mucelli³ · Adrian Zdjelar³ · Maja Ukmar³ · Marcello Naccarato¹ · Alex Buoite Stella¹ · Paolo Manganotti¹

Accepted: 18 January 2021

Abstract

Background and purpose Diagnosis of posterior circulation stroke may be challenged. National Institutes of Health Stroke Scale (NIHSS) and brain imaging (non-contrast brain computed tomography-CT) are used for diagnosis; evaluation on posterior circulation stroke remains a limit of NIHSS, and the value of non-contrast CT (NCCT) is limited due to artifacts caused by the bones of the base of the skull. We tested the validity and prognostic value of posterior circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) in patients with posterior circulation stroke.

Methods Pc-ASPECTS allots the posterior circulation 10 points. We studied 50 patients with posterior circulation stroke. We applied pc-ASPECTS to NCCT, CT angiography, and CT Perfusion. We evaluated the correlation of pc-ASPECT with outcome parameters for stroke.

Results Out of 50 patients, CTP showed abnormalities in 34 cases. The pc-ASPECT score calculated on brain CT and on the brain CT + angio CT had a sensibility of 24%, calculated on brain CT, angio CT and CTPerfusion gain a sensibility of 72%. Pc-ASPECT MTT resulted to be the more reliable parameter: outcome given by NIHSS score at discharge, mRS at discharge, and at 3 months was more severe in patients with Pc-ASPECT MTT alteration. Outcome given by NIHSS score at discharge and mRS at discharge and 1 at 3 months was more severe in patients with higher NIHSS score at admission.

Conclusion We evaluated the usefulness of pc-ASPECTS on CTP in predicting functional outcome in acute posterior circulation stroke that appears to be a powerful marker for predicting functional outcome.

Keywords Posterior circulation stroke · Neuroimaging · CT Perfusion · pc-ASPECT · Functional outcome · Reperfusion therapy

Introduction

Stroke affecting the posterior circulation territory accounts for 20% or more of all acute ischemic stroke cases [1]. Due to a wide range of clinical features, usually characterized by mild

and unspecific symptoms, including vertigo and reduced level of consciousness, the diagnosis of posterior circulation stroke can be challenging [2, 3]. Patients with posterior circulation stroke may exhibit a delayed time to presentation, compared with patients with anterior circulation stroke, and the functional outcome of posterior circulation ischemic stroke is often severe [4–8].

Routine examinations for the diagnosis of posterior circulation stroke include clinical assessment using the National Institutes of Health Stroke Scale (NIHSS) and neuroimaging, generally, non-contrast brain computed tomography (NCCT). The NIHSS is the most widespread clinical scale used in patients presenting acute ischemic stroke symptoms. NIHSS at admission in anterior circulation ischemic stroke has been shown to be correlated with hypoperfused volume [9, 10] and with neurophysiological alterations [11], as well as powerful predictor of clinical outcome [12, 13].

✉ Paola Caruso
caruso.paola1983@libero.it

¹ Clinical Unit of Neurology, Department of Medicine, Surgery and Health Sciences, University Hospital and Health Services of Trieste, University of Trieste, Strada di Fiume, 447, 34149 Trieste, Italy

² Department of Engineering and Architecture, University of Trieste, Via Alfonso Valerio, 10, 34127 Trieste, Italy

³ Radiology Unit, Department of Medicine, Surgery and Health Sciences, University Hospital and Health Services of Trieste, University of Trieste, Strada di Fiume, 447, 34149 Trieste, Italy

This scale is simply to apply and rapid to perform and makes agreement between clinicians. However, the clinical evaluation on posterior circulation stroke remains still a limit of NIHSS [14].

Anterior circulation Stroke extent can be evaluated on NCCT by using a quantitative score called ASPECT [15]. The ASPECT (Alberta Stroke Program Early CT Score) is systematic approach to quantification of early CT ischemic changes (EIC) [16], in which the territory of the middle cerebral artery is analyzed assigned 10 points. Values are given from 10 down to 0: a normal CT scan has an ASPECTS value of 10 points. 1 point is subtracted for each area of early ischemic change, such as focal swelling, or parenchymal hypo attenuation. A score of 0 marks diffuse ischemia throughout the territory of the middle cerebral artery. The ASPECT score has been devised to evaluate the anterior circulation stroke, in the study of the posterior circulation stroke is more reliable to use pc-ASPECT. The pc-ASPECT was first introduced in 2008, the original study involved patients with suspected vertebra-basilar ischemia and patients with basilar artery occlusion in order to find a semi-quantitative score applicable on NCCT and angio CT source images (CTA-SI). The pc-ASPECT assigns the posterior circulation 10 points: two points each are subtracted for EIC in midbrain or pons and 1 point each for EIC in left or right thalamus, cerebellum or PCA-territory, respectively [17].

The value of non-contrast CT (NCCT) is limited by its capacity to detect ischemic changes in this vascular territory due to small lesion size and artifacts caused by the bones of the base of the skull [18]. Beside non contrast CT scan, CT angiography is increasingly performed and can be rapidly obtained, allowing the identification of the main vessel of the posterior circle. The pc-ASPECT evaluated on CTA-SI has been found to give information on clinical disability and mortality after a PC stroke. However, may present several limitations mainly due to wide operator interpretation [17, 19, 20].

In the past years, great research interest was shown towards CT perfusion (CTP), which is becoming increasingly widespread in emergency departments allowing the assessment of the extent of the salvageable tissue and the ischemic core on CBF CBV and MTT maps [21–24], thus, allowing the identification of patients who can most benefit the reperfusion treatment [10, 22, 25–28], wake-up stroke cases included [13, 29]. Only few studies have investigated and proved the additional diagnostic value of CTP compared with direct CT for posterior circulation stroke [30–32].

Nowadays advanced neuroimaging techniques have been studied for a better recognition of PC stroke in the acute phase, thus data from literature are controversial, the posterior circulation has not been evaluated in all its component (most of the studies regard the vertebral and basilar arteries), and imaging acquisition not always involve the whole brain circulation. The CTP in association to NCCT and CTA is a rapid and reliable tool for the evaluation of anterior circulation stroke,

although its diagnostic value in suspected posterior circulation is still unconfirmed [33].

The aim of our study was to evaluate diagnostic and prognostic value of multimodal CT pc-ASPECTS in infratentorial stroke and investigate the correlation between multimodal CT pc-ASPECTS and functional and morphological outcome.

Materials and methods

Study population

We analyzed clinical and processed neuroimaging data of patients with acute ischemic stroke admitted to the Stroke Unit of the University Medical Hospital of Trieste (Italy) between April 2016 and July 2019. The patients included in the study showed acute focal neurologic symptoms compatible with ischemic stroke of the posterior circulation. In the study were included all patients with acute PC ischemic stroke that were admitted to our emergency department within 4.5 h from symptom onset, and also patients with wake up stroke involving posterior circulation were included. No age limit was applied. Both genders were included in the study sample. Exclusion criteria were: hemorrhagic stroke, patients with stroke mimics (stroke mimics were excluded by a complete diagnostic work-up including anamnestic details, clinical and instrumental evaluation of patients), previous stroke, brain malignancy, and anterior circulation stroke.

For all included patients the following data were collected: demographic information (age, sex); stroke risk factors (hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, ischemic cardiopathy, atrial fibrillation); stroke etiology by TOAST classification [34]; neurological evaluation parameters using the National Institutes of Health Stroke Scale (NIHSS) score and Rankin score mRS at admission; neuroimaging data at admission (radiological examination through NCCT, CTA, CTP) and and follow-up NCCT 24-48 h after admission; reperfusion therapy applied at admission; and neurological outcome at discharge (NIHSS, mRS) and after 3 months (mRS). Intra-hospital mortality and length of hospitalization were detected.

Neuroimaging data acquisition, processing, and analysis

CT, CTA-SI, and CTP neuroimaging data were acquired and processed as described in previous studies [10, 27]. Briefly, all neuroimaging data were acquired by a 256 slice CT scanner (Brilliance iCT 256 slices, Philips Medical Systems, Best, Netherlands) at the Radiology Department of the University Medical Hospital of Trieste (Italy). NECT was acquired with 120 kV, 400-450 mAs, at a slice thickness of 0.9 and reconstructed at 5 mm. Angio CT acquisition protocol involved the

intravenous injection of 90–120 ml of contrast medium in an injection rate of 3–5 ml/s. The acquisition was performed with 120 kV, 375–400 mAs, at a slice thickness of 0.9. CTP acquisition protocol involved IV injection of 50 ml contrast medium, followed by 40 ml of saline bolus, both administered at an injection rate of 4 ml/s. The exposure parameters used were 80 kVp and 150 mAs, and three-dimensional axial acquisitions of 14 cm of the brain volume with a reconstruction of the slices set to 5 mm were performed using a series of repeated movements of the scanner table. Mean transit time (MTT), cerebral blood volume (CBV), and cerebral blood flow (CBF) perfusion maps were calculated by processing of CTP raw data by deconvolution-based method as described previously [10, 27, 35, 36].

Early ischemic changes were assessed using the 10-point posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) on NCCT, CTA source images, and on parametric CTP maps. pc-ASPECTS were evaluated by two radiologists and one neurologist blinded for clinical information, including follow-up and clinical outcome. The final decision was made by consensus. Puetz criteria were tailed [17]. pc-ASPECTS allots the posterior circulation 10 points. Two points each are subtracted for EIC in midbrain or pons and 1 point each for EIC in left or right thalamus, cerebellum, or PCA territory, respectively. Vessel occlusions were documented. We applied 3 different evaluation model A (only NCCT), model B (joint NCCT and CTA-SI pc-ASPECTS evaluation), and model C (joint NCCT, CTA-SI and CTP pc-ASPECTS evaluation). Israeli Vertebrobasilar Stroke Scale (IVBSS) was calculated for each case [37, 38]. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Statistical analysis

We performed all statistical analysis using SPSS Statistics 23 (IBM, Armonk/NY, USA). Kolmogorov-Smirnov test was used to evaluate the normal distribution of variables. Continuous variables with a normal distribution are presented as mean and standard deviations (SDs), non-continuous variables as percentages (%). Kendall tau test was used to investigate the possible relationship between pc-ASPECTS and baseline and outcome clinical and radiological parameters. A value of $p < 0.05$ was considered as significant. Multiple regression analysis was subsequently adopted on pc-ASPECT and outcome parameters.

Results

Sample characteristics and clinical outcome

Out of 1253 patients admitted to our Stroke Unit during the study period for a sudden onset of an ischemic stroke, 435

patients underwent CTP. Finally, 50 patients (33 M/17F) with a stroke of the posterior circulation and CTP fulfilled our inclusion criteria. Mean age was 67.40 ± 15.42 years old. For 44 patients, symptom onset was well known, and in 6 cases, a WUS was detected. Median and main baseline NIHSS score was 6 (0–30), 8.34 ± 6.92 . The Expanded National Institutes of Health Stroke Scale was applied; this is a standardized scale derived from NIHSS to which it adds specific elements to existing items to explore signs and symptoms of posterior circulation stroke [14]. Thirty-one patients received reperfusion therapies (62%), and in 19 cases standard treatment with antiplatelet therapy was started (38%). Reperfusion therapies involved intravenous thrombolysis alone in 44% of cases, thrombectomy alone in 6% of subjects, and the combination of the two reperfusion treatments in 12% of cases. Mean time from symptoms onset and neuroimaging acquisition was 207.8 ± 210.2 min, while the mean time from door to therapy was 215.71 ± 110.3 min. In 28 patients (56%) a vessel occlusions was observed: mainly vertebral and basilar artery were involved each in the 22% of cases, and more involved was the posterior cerebral artery (24%), while less involved were the posterior inferior cerebellar artery (8%) and the superior cerebellar artery (10%). In 66.7% of cases, good reperfusion was observed with mTICI 2b or 3 (Thrombolysis in Cerebral Infarction scale, [39]). Concerning patient's main risk factors for stroke, in 76% of cases, hypertension was detected, 48% of patients were affected by dyslipidemia, and atrial fibrillation was found in 30% of subjects, and diabetes mellitus was diagnosed in 18%. Thirty percent of patients were current smokers; in 18% of cases, an ischemic cardiopathy was seen. The genesis of stroke was cardio embolic in 32% of cases and atherothrombotic in 28% of patients. Lacunar stroke was seen in 15% of patients, in 22% of cases a cryptogenic stroke was determined, and ischemic stroke from rare causes was detected in 6% of cases. After all, in 10% of cases, a hemorrhagic infarction was seen, but only in 1 case it was symptomatic. Brain CT scan at 24 h was negative for focal ischemia in 40% of patients and showed a cerebral ischemia in different areas of the posterior circulation in the remaining cases: cerebellum 26%, occipital lobe 24%, pons 20%, mesencephalon 14%, and thalamus in 10% of cases. Functional outcome at 3 months was good (mRS 0–2) in 52% of patients (mRS 2.4 ± 2.01); and 4 patients (8%) were deceased. At discharge median NIHSS was 3.32 ± 7.23 , with a mRS of 2.72 ± 1.91 . Patient's demographical and clinical characteristics and clinical outcome are summarized in Table 1.

Multilodal pc-ASPECT baseline assessment

The pc-ASPECT applied on NCCT scan showed a value < 10 in 12 patients: 1 patient showed a score of 6, 1 a score of 7, 3 a score of 8, and 7 a score of 9; score inferior at 6 was not

Table 1 Demographical and clinical characteristics of patients, radiological evaluation of cerebral infarct, stroke etiology, reperfusion treatment, and clinical outcome.

Sex (M:F)	33:17
Age	67.40 ± 15.42
NIHSS baseline (median and main values)	6 (0–30) 8.34 (± 6.92)
e-NIHSS (Expanded National Institutes of Health Stroke Scale) (median and main values)	7 (0–30) 8.68 (± 6.96)
IVBSS (<i>Israeli Vertebrobasilar Stroke Scale</i>) (median and main values)	10 (0–40) 13.30 (± 10.9)
Symptoms onset—brain TC (min) (median and main values)	151 (41–1080) 207.8 (± 210.2)
Symptoms onset—treatment (min) (median and main values)	199.50 (75–660) 215.71 (± 110.3)
Vessel occlusion n(%)	
<i>Vertebral A</i>	11 (22%)
<i>Basilar A</i>	11 (22%)
<i>ACP (posterior cerebral artery)</i>	12 (24%)
<i>PICA (posterior inferior cerebellar artery)</i>	4 (8%)
<i>SCA (upper cerebellar artery)</i>	5 (10%)
Treatment n(%)	
<i>Conservative treatment</i>	19 (35%)
<i>Thrombolysis</i>	22 (8%)
<i>Thrombectomy</i>	3 (9.7%)
<i>Thrombolysis/Thrombectomy</i>	6 (19.4%)
Thrombectomy tools n(%)	
<i>Aspiration</i>	2 (22.2%)
<i>Stent</i>	4 (44.4%)
<i>Aspiration+ Stent</i>	3 (33.3%)
Comorbidity n(%)	
<i>Hypertension</i>	38 (76%)
<i>Diabetes</i>	9 (18%)
<i>Atrial fibrillation</i>	15 (30%)
<i>Dislipidemia</i>	24 (48%)
<i>Ischemic cardiopathy</i>	9 (18%)
<i>Smoke</i>	15 (30%)
Stroke Classification TOAST n(%)	
<i>Cardioembolic</i>	16 (32%)
<i>Atherothrombotic</i>	14 (28%)
<i>Small vessel disease</i>	0
<i>Cryptogenic</i>	17 (34%)
<i>Rare causes</i>	3 (6%)
Brain CT scan 24 h n(%)	
<i>No lesion</i>	16 (32%)
<i>Cerebellum</i>	13 (26%)
<i>Pons</i>	10 (20%)
<i>Mesencephalon</i>	7 (14%)
<i>Occipital</i>	12 (24%)
<i>Talamus</i>	5 (10%)
Ricanalization n(%) (TICI: Thrombolysis in Cerebral Infarction scale)	
<i>mTICI 3</i>	3 (33.3%)
<i>mTICI 1/2b</i>	3 (33.3%)
<i>mTICI 0</i>	3 (33.3%)

Table 1 (continued)

Sex (M:F)	33:17
Bleeding evolution n(%)	5 (10%)
NIHSS at discharge (median and main values)	2 (0–47) 3.32 (\pm 7.23)
mRS at discharge (median and main values)	3 (0–6) 2.72 (\pm 1.91)
Length of stay (median and main values)	10 (1–35) 12.08 (\pm 8.7)
mRS at 3 months (median and main values)	2 (0–6) 2.4 (\pm 2.01)
Mortality n(%)	4 (8%)

registered. The pc-ASPECT applied on CTASI was < 10 in 7 cases: 4 subjects presented a pc-ASPECT of 9, 2 of 8, and 1 of 6; score inferior of 6 was not registered. The pc-ASPECT applied on CTP was < 10 in 70% of patients, and main alterations were seen on cerebellum (30%) and occipital lobe (36%). Evaluation model A (only NCCT) and model B (joint NCCT and CTA-SI pc-ASPECTS evaluation) was able to detect an early hypoattenuation in 24% of cases, while model C (joint NCCT, CTA-SI and CTP pc-ASPECTS evaluation) detected in 72% of cases. In particular, early ischemic alterations were observed in 24% on NCCT and 14% on CTA-SI. In the same time, the alterations on CTP were observed in 38% on CBV, in 28% CBF, and in 58% on MTT maps. Considering pc-ASPECT on CBV, 2 patients presented a score of 6, 4 of 8, and 13 of 9. Pc-ASPECT on CBF was 6 in 1 subject, 8 in 2, and 9 in 11 patients. pc-ASPECT MTT resulted the more reliable parameter: 2 patients had a score of 2, 4 of 6, 3 patients a score of 7, 7 of 8, and finally score was 9 in 13 cases. pc-ASPECT on follow-up NCCT was altered in 60% of cases, particularly in 61.3% of subjects that received reperfusion treatment and 57.9% of cases with conservative treatment. A representative case of pc-ASPECTS assessment on NCCT, CTA-SI, and CTP maps is reported in Fig. 1.

Neurological deficit at baseline and on discharge

A significant negative correlation was observed between NIHSS score at baseline and pc-ASPECT MTT ($\tau = -0.46$; $p < 0.001$), showing that a more severe stroke at admission correspond to a lower pc-ASPECT MTT value. NCCT, CTA-SI, CBV, and CBF pc-ASPECTS did not correlate with neurological deficit at baseline. No correlation was observed between multimodal pc-ASPECTS and pre-morbid mRS, age, or time from onset to admission. The results of our study show that the pc-ASPECTS MTT is able to predict the clinical and functional outcome in the short term and at 3 months in patients not undergoing reperfusion therapy. The lower the pc-ASPECTS MTT score, the less favorable the outcome will be (Table 2).

In patients who did not receive reperfusion treatment, more severe NIHSS score at discharge, mRS at discharge, mRS at 3 months and follow-up ischemic lesion was significantly

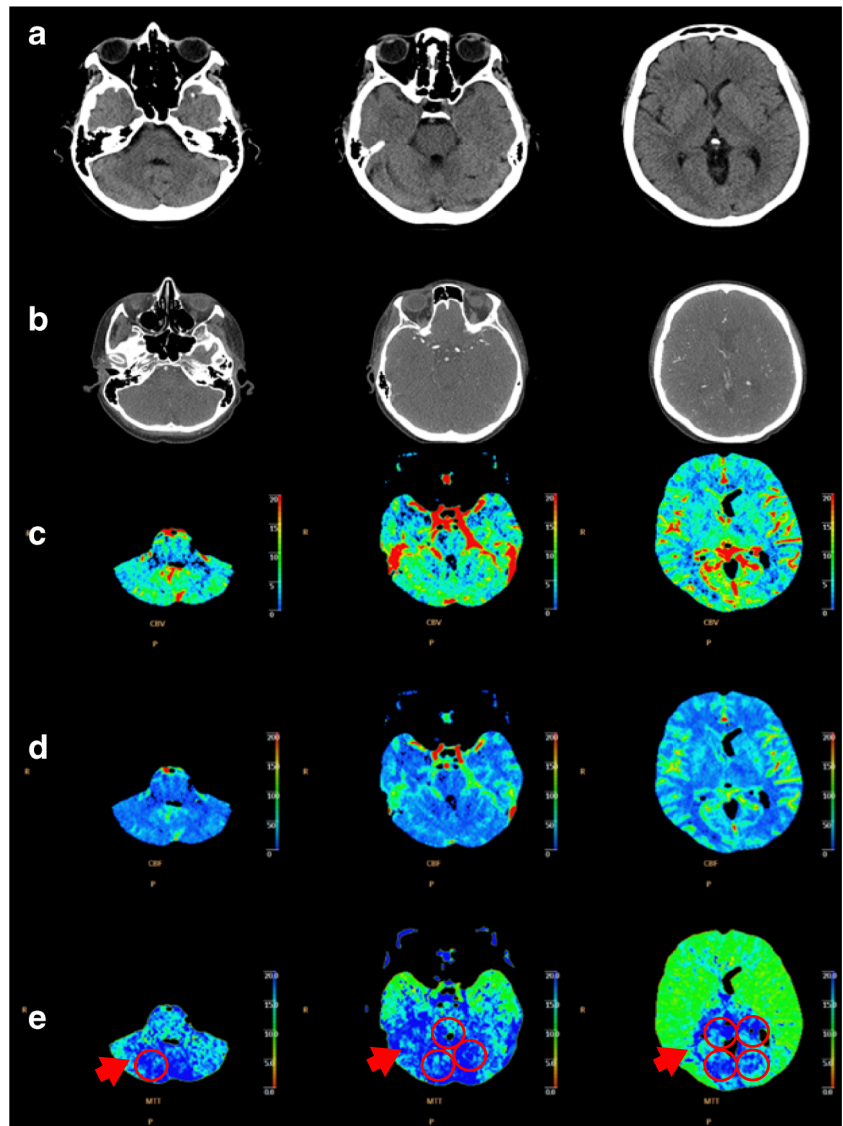
related with pc-ASPECT MTT alteration ($\tau = -0.63$; $p = 0.001$, $\tau = -0.62$; $p = 0.001$; $\tau = -0.56$; $p = 0.003$, $\tau = 0.451$; $p = 0.025$, respectively) (Table 3) (Fig. 2). NIHSS score at discharge, mRS at discharge, and mRS at 3 months was more severe in patients with higher NIHSS score at admission ($p < 0.001$, $p = 0.001$, $p < 0.001$, respectively). Atrial fibrillation relates with a worsen outcome in terms of NIHSS score at discharge, mRS at discharge, and mRS at 3 months ($p = 0.020$, $p = 0.011$, $p = 0.021$, respectively). A multivariate analysis showed a significant relation between mRS score at 3 months and basal NIHSS ($p = 0.004$).

In patients that underwent thrombolysis and thrombectomy, a relationship between NIHSS at discharge and pc-ASPECT CTA-SI has been found ($\tau = -0.38$; $p = 0.026$); similarly a correlation of pc-ASPECT CTASI and mRS at discharge was seen ($\tau = -0.39$; $p = 0.013$). Patients with higher mRS score at 3 months presented a lower value of pc-ASPECT on direct brain CT ($\tau = -0.31$; $p = 0.044$), on pc-ASPECT CTA-SI ($\tau = -0.43$; $p = 0.006$) and pc-ASPECT CBV ($\tau = -0.34$; $p = 0.029$), more often those subjects were older ($p = 0.044$) and affected by hypertension ($p = 0.001$) and ischemic cardiopathy ($p = 0.004$). A multivariate analysis showed a significant relation between pc-ASPECT CTASI and NIHSS at discharge ($p = 0.026$). pc-ASPECT evaluated on brain CT scan at 24 h showed a positive relation with pc-ASPECT on direct brain CT scan, CTASI, and CTP respectively ($p = 0.037$, $p = 0.007$, $p = 0.005$) (Fig. 3). A multivariate analysis showed a significant relation between pc-ASPECT CBV and the final extension of the ischemic lesion ($p = 0.001$) (Table 2).

Discussion

The main result of our study is that the use of extended neuroimaging protocol (direct brain CT scan, CTASI and CTP) in the acute phase of a PC stroke has a high sensibility and may be a practice prognostic and diagnostic tool for physicians. The pc-ASPECT score calculated on the direct brain CT and on the brain CT + angio CT had a sensibility of 24%, while calculated on brain CT, angio CT and CT Perfusion gain a sensibility of 72%.

Fig. 1 Example of imaging acquisition analysis: patient admitted to our stroke unit with dizziness, dysarthria, ataxia, and gait disorder (NIHSS: 5). No focal lesion or vessel abnormalities were seen at brain CT and CTASI (PC-ASPECT 10), and the analysis of CTP sequences showed cerebellar, mesencephalic, thalamus, and occipital hypoperfused areas in the MTT maps (PC-ASPECT 2). The evaluation of PC-ASPECT consists in removing 1 point for lesion/hypoperfusion area in the thalamus, occipital, and cerebellar regions (bilaterally) and 2 points for pons and mesencephalic areas involvement. **a** brain CT scan, pc-ASPECT 10. **b** CTASI, pc-ASPECT 10. **c** CTP CBV maps, no abnormalities, pc-ASPECT 10. **d** CTP CBF maps, no abnormalities, pc-ASPECT 10. **e** CTP MTT maps, 6 hypoperfused area, pc-ASPECT 2



About one fifth of all ischemic strokes affect the posterior circulation territory. Our data show that quantification of

hypoattenuation on CT perfusion source images predicts functional outcome in patients with posterior circulation stroke [2].

Table 2 Data relative at outcome parameters in patients that did not underwent reperfusion treatment

A		pc-ASPECTS TC	pc-ASPECTS CTASI	pc-ASPECTS CBV	pc-ASPECTS CBF	pc-ASPECTS MTT	NIHSS basale	mRS- pre
NIHSS at discharge	τ	-0.214	-0.040	-0.082	-0.128	-0.625	0.658	0.124
	p	0.300	0.849	0.687	0.534	0.001*	0.0002*	0.537
mRS at discharge	τ	-0.158	0.079	0.072	0.042	-0.623	0.609	0.226
	p	0.445	0.709	0.725	0.839	0.001*	0.001*	0.263
mRS 3 months	τ	-0.195	0.058	0.105	0.072	-0.563	0.708	0.385
	p	0.339	0.781	0.601	0.724	0.003*	0.00007*	0.052
Iachemic lesion	τ	-0.025	-0.051	0.420	0.292	0.451	-0.335	0.321
	p	0.919	0.835	0.046	0.173	0.025*	0.073	0.124

*significant correlation ($p < 0.005$)

bold data indicate significant results considering the p -value

Table 3 Reported analysis of patients treated with thrombolysis and thrombectomy

B		pc-ASPECTS TC	pc-ASPECTS CTASI	pc-ASPECTS CBV	pc-ASPECTS CBF	pc-ASPECTS MTT	NIHSS basale	mRS- pre
NIHSS at discharge	τ	-0.278	-0.380	-0.358	-0.160	-0.073	0.065	0.032
	p	0.097	0.026*	0.061	0.346	0.646	0.742	0.851
mRS at discharge	τ	-0.252	-0.393	-0.454	-0.179	0.082	0.188	0.066
	p	0.106	0.013*	0.010*	0.258	0.581	0.172	0.682
mRS 3 months	τ	-0.313	-0.432	-0.339	-0.100	0.057	0.188	0.119
	p	0.044*	0.006*	0.029*	0.524	0.701	0.169	0.455
Iachemic lesion	τ	0.335	0.437	0.449	0.186	0.078	-0.191	0.081
	p	0.037*	0.007*	0.005*	0.254	0.610	0.177	0.624

In patients who did not receive reperfusion treatment, more severe NIHSS score at discharge, mRS at discharge, mRS at 3 months and follow-up ischemic lesion was significantly related with pc-ASPECT MTT alteration. NIHSS score at discharge, mRS at discharge, and mRS at 3 months was more severe in patients with higher NIHSS score at admission. In patients that underwent thrombolysis and thrombectomy, a relationship between NIHSS at discharge and pc-ASPECT CTA-SI has been found, similarly a correlation of pc-ASPECT CTASI and mRS at discharge was seen. Patients with higher mRS score at 3 months presented a lower value of pc-ASPECT on direct brain CT, on pc-ASPECT CTA-SI and pc-ASPECT CBV.

bold data indicate significant results considering the *p*-value

CT with CT Perfusion (CTP) approximately doubles the detection rate of acute ischemia compared with plain CT [40]. The arterial supply to the cerebral hemispheres is derived from

the anterior circulation (AC) provided by the bilaterally paired internal carotid arteries, as well as by the posterior circulation (PC) provided by the bilateral vertebral arteries. About 20 % of cerebral blood flow is converged toward posterior circulation (PC), in line with the rate of PC strokes observed among ischemic strokes. According to TOAST classification, its main causes are cardio embolism and lacunas. About 30 % of the posterior circulation strokes remains of unknown etiology. Recognizing PC stroke can be insidious as it may simulate AC strokes clinically in a significant proportion of patients [41–44] although there is evidence of higher rate of visual field defects, cerebellar or (central) vestibular signs and symptoms, associated to decreased level of consciousness. Previous studies did not find any differences in functional outcome between PCS and ACS, although this finding is still debated. Several studies have evaluated the value of MRI DWI in predicting functional outcome in acute posterior and anterior ischemic stroke; however, the results are controversial particularly for posterior stroke [45–49].

Pallesen et al analyzed the prognostic value of pc-ASPECT applied on CTP (CBV, CBF and MTT maps), and they found that the early evaluation of hypoperfused ischemic areas was more reliable and sensitive on CTP MTT maps compared with the other maps of CTP and compared with the same evaluation on CTA-SI [32].

We sought to explore clinical and imaging parameters on acute CTP in patients with posterior circulation stroke and hypothesized that pc-ASPECTS score on CTP is an independent predictor of clinical outcome in such patients. Our results show that approximately 70% of patients with acute vertebrobasilar stroke had focal hypoperfusion on CTP, despite often incomplete CTP coverage of the posterior fossa. Focal hypoperfusion on CTP was a predictor of functional outcome at 3 months in this study population. In non-treated

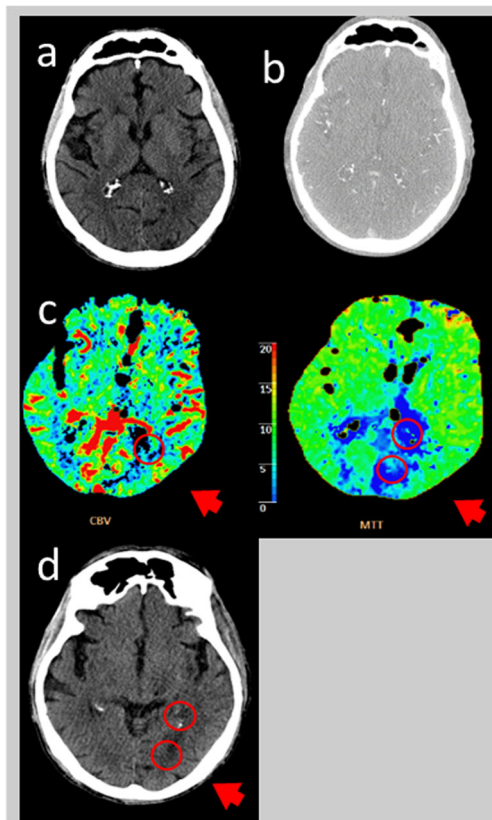


Fig. 2 a Brain CT scan showing no abnormalities, pc-ASPECT 10. b CTASI showing no abnormalities, pc-ASPECT 10. c CTP with evaluation of CBV and MTT maps showing hypoperfused areas (left thalamus and occipital areas), pc-ASPECT 9 and 8, respectively. d 24-h brain CT scan showing ischemic lesions in the same areas of MTT alteration in patients with conservative treatment

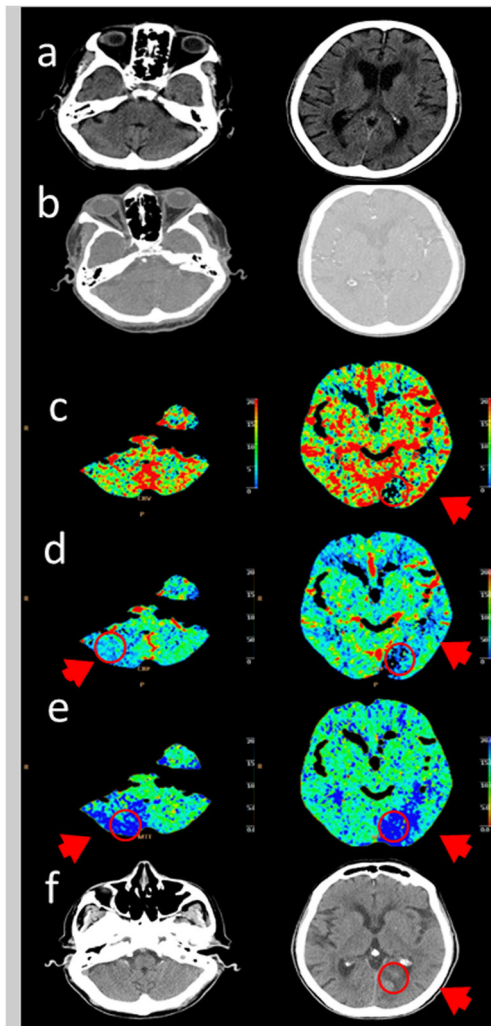


Fig. 3 a Brain CT scan showing no abnormalities, pc-ASPECT 10. b CTASI showing no abnormalities, pc-ASPECT 10. c CTP with evaluation of CBV maps showing hypoperfused areas, pc-ASPECT 9 (left occipital area). d CTP with evaluation of CBF maps showing hypoperfused areas, pc-ASPECT 8 (right cerebellar and left occipital areas). e CTP with evaluation of MTT maps showing hypoperfused areas, pc-ASPECT 8 (right cerebellar and left occipital areas). f 24-h brain CT scan showing ischemic lesions limited at only one area in patients treated with reperfusion therapy (left occipital area)

patients pc-ASPECTS MTT relate with stroke severity and NIHSS at admission; Pc-ASPECTS MTT relate with the extension of the final ischemic lesion on control CT scan. In 2008, Puetz et al. [17] proposed a new semi-quantitative grading system for PC (pc-ASPECTS) that is relatively simple and easy to apply and is based on previous findings that the numbers of territories involved and involvement of the pons and midbrain have a critical bearing on functional outcome in PC [50, 51]. The management of acute posterior circulation stroke is still a matter of debate.

Point of strength of our work include the assessment with the TCP of the whole brain with a more precise identification of the hypo perfused areas; the evaluation of all types of

ischemic stroke, with the inclusion of lacunar strokes, and the involvement of all the vessel of the posterior circulation. Thus, our study has some limitations. The sample size is limited. Clinical outcomes were identified retrospectively based on informatics research. Furthermore, the reliability for pc-ASPECTS on CTP was good but not excellent in several case. In conclusion, we evaluated the usefulness of newly developed pc-ASPECTS on CTP in predicting functional outcome in acute posterior circulation ischemic stroke, and found that this appears be a powerful marker for predicting functional outcome. More data are required in order to help clinicians in a better selection of patients suitable of reperfusion treatment.

Declarations

Conflict of interest The authors declare that there is no conflict of interest regarding the publication of this article. This manuscript is not under consideration for publication elsewhere.

Ethical approval The study was approved by Institutional Review Board of ASUITs and by the regional ethics board of Friuli-Venezia Giulia, Italy (CEUR), in respect of the declaration of Helsinki. All authors have read and approved the submitted manuscript, and the manuscript has not been submitted elsewhere nor published elsewhere in whole or in part.

Informed consent All patients gave the informed consent statement in order to treat their data.

Consent to participate All participants released their informed consent for treatment of clinical data after all procedures had been fully explained, as for standard institutional procedure. Figures are original and not previously published.

References

1. De Marchis GM, Kohler A, Renz N, Arnold M, Mono ML, Jung S, Fischer U, Karameshev AI, Brekenfeld C, Gralla J, Schroth G, Mattle HP, Nedeltchev K (2011) Posterior versus anterior circulation strokes: comparison of clinical, radiological and outcome characteristics. *J Neurol Neurosurg Psychiatry* 82:33–37
2. Markus HS, van der Worp HB, Rothwell PM (2013 Oct) Posterior circulation ischaemic stroke and transient ischaemic attack: diagnosis, investigation, and secondary prevention. *Lancet Neurol* 12(10): 989–998
3. Nouh A, Remke J, Ruland S (2014 Apr 7) Ischemic posterior circulation stroke: a review of anatomy, clinical presentations, diagnosis, and current management. *Front Neurol* 5:30. <https://doi.org/10.3389/fneur.2014.00030>
4. Caplan LR, Wityk RJ, Glass TA, Tapia J, Pazdera L, Chang HM, Teal P, Dashe JF, Chaves CJ, Breen JC, Vemmos K, Amarenco P, Tettenborn B, Leary M, Estol C, Dewitt LD, Pessin MS (2004) New England medical center posterior circulation registry. *Ann Neurol* 56:389–398
5. Bogousslavsky J, Van Melle G, Regli F (1988) The Lausanne Stroke Registry: analysis of 1,000 consecutive patients with first stroke. *Stroke*. 19(9):1083–1092
6. Flossmann E (2003) Prognosis of vertebrobasilar transient ischaemic attack and minor stroke. *Brain*. 126(9):1940–1954

7. Dewey HM, Sturm J, Donnan GA, Macdonell RAL, McNeil JJ, Thrift AG (2003) Incidence and Outcome of Subtypes of Ischaemic Stroke: Initial Results from the North East Melbourne Stroke Incidence Study (NEMESIS). *Cerebrovasc Dis* 15(1-2):133–139. <https://doi.org/10.1159/000067142>
8. Caplan LR (1979) Occlusion of the vertebral or basilar artery. Follow up analysis of some patients with benign outcome. *Stroke* 10(3):277–282. <https://doi.org/10.1161/01.STR.10.3.277>
9. Tong DC, Yenari MA, Albers GW, O'Brien M, Marks MP, Mosley ME (1998) Correlation of perfusion- and diffusion-weighted MRI with NIHSS score in acute (6.5 hour) ischemic stroke. *Neurology* 50:864–870
10. Furlanis G, Ajčević M, Stragapede L, Lugnan C, Ridolfi M, Caruso P, Manganotti P (2018) Ischemic volume and neurological deficit: correlation of computed tomography perfusion with the National Institutes of Health Stroke Scale Score in acute ischemic stroke. *J Stroke Cerebrovasc Dis* 27(8):2200–2207
11. Ajčević, M., Furlanis, G., Stragapede, L., Ridolfi, M., Caruso, P., Naccarato, M., ... & Manganotti, P. (2019). Brain Oscillatory Activity and Neurological Deficit in Hyper-acute Ischemic Stroke: Correlation of EEG Changes with NIHSS. In: Mediterranean Conference on Medical and Biological Engineering and Computing. Springer, Cham, pp. 133-141
12. Frankel MR, Morgenstern LB, Kwiatkowski T, Lu M, Tilley BC, Broderick JP, Libman R, Levine SR, Brott T (2000) Predicting prognosis after stroke: a placebo group analysis from the National Institute of Neurological Disorders and Stroke rt-PA Stroke Trial. *Neurology* 55:952–959
13. Furlanis G, Ajčević M, Stella AB, Cillotto T, Caruso P, Ridolfi M et al (2019) Wake-up stroke: thrombolysis reduces ischemic lesion volume and neurological deficit. *J Neurol* 267(3):1–8
14. Olivato S, Nizzoli S, Cavazzuti M, Casoni F, Nichelli PF, Zini A (2016) e-NIHSS: an Expanded National Institutes of Health Stroke Scale Weighted for Anterior and Posterior Circulation Strokes. *J Stroke Cerebrovasc Dis* 25(12):2953–2957. <https://doi.org/10.1016/j.jstrokecerebrovasdis.2016.08.011>
15. Schröder J, Thomalla G (2017) A Critical Review of Alberta Stroke Program Early CT Score for Evaluation of Acute Stroke Imaging. *Front Neurol* 7:245. <https://doi.org/10.3389/fneur.2016.00245>
16. Barber PA, Demchuk AM, Zhang J, Buchan AM, for the ASPECTS Study Group (2000) Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. *Lancet* 355:1670–1674
17. Puetz V, Sylaja PN, Coutts SB, Hill MD, Dzialowski I, Mueller P, Becker U, Urban G, O'Reilly C, Barber PA, Sharma P, Goyal M, Gahn G, von Kummer R, Demchuk AM (2008 Sep) Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. *Stroke* 39(9):2485–2490. <https://doi.org/10.1161/STROKEAHA.107.511162>
18. Hwang DY, Silva GS, Furie KL, Greer DM (2012) Comparative sensitivity of computed tomography vs. magnetic resonance imaging for detecting acute posterior fossa infarct. *J Emerg Med* 42:559–565
19. Sharon M, Boyle K, Yeung R, zhang L, Symons SP, Boulos MI, Aviv RI (2016) The predictive value of a targeted posterior fossa multimodal stroke protocol for the diagnosis of acute posterior ischemic stroke. *Neurovascular Imaging* 2(1):3. <https://doi.org/10.1186/s40809-016-0013-6>
20. Alemseged F, Shah DG, Bivard A, Kleinig TJ, Yassi N, Diomedes M, di Giuliano F, Sharma G, Drew R, Yan B, Dowling RJ, Bush S, Sallustio F, Caltagirone C, Mercuri NB, Floris R, Parsons MW, Levi CR, Mitchell PJ, Davis SM, Campbell BCV (2019) Cerebral blood volume lesion extent predicts functional outcome in patients with vertebral and basilar artery occlusion. *Int J Stroke* 14(5):540–547. <https://doi.org/10.1177/1747493017744465>
21. Lev MH, Segal AZ, Farkas J, Hossain ST, Putman C, Hunter GJ, Budzik R, Harris GJ, Buonanno FS, Ezzeddine MA, Chang Y, Koroshetz WJ, Gonzalez RG, Schwamm LH (2001) Utility of perfusion-weighted CT imaging in acute middle cerebral artery stroke treated with intra-arterial thrombolysis: Prediction of final infarct volume and clinical outcome. *Stroke*. 32:2021–2028
22. Perfusion CT PMW (2008) Is it Clinically Useful? *Int J Stroke* 3(1): 41–50. <https://doi.org/10.1111/j.1747-4949.2008.00175.x>
23. Wintermark M, Rowley HA, Lev MH (2009) Acute Stroke Triage to Intravenous Thrombolysis and Other Therapies with Advanced CT or MR Imaging: Pro CT. *Radiology*. 251(3):619–626. <https://doi.org/10.1148/radiol.2513081073>
24. d'Este CD, Roversi G, Padroni M, Bernardoni A, Tamborino C, de Vito A, Azzini C, Marcello O, Saletti A, Ceruti S, Lee TY, Fainardi E (2015) CT perfusion cerebral blood volume does not always predict infarct core in acute ischemic stroke. *Neurol Sci* 36(10):1777–1783. <https://doi.org/10.1007/s10072-015-2244-8>
25. Vilela P, Rowley HA (2017) Brain ischemia: CT and MRI techniques in acute ischemic stroke. *Eur J Radiol* 96:162–172
26. Caruso P, Furlanis G, Ridolfi M, Ajcevic M, Naccarato M, Manganotti P (2019) Safety of Early Repeated Thrombolysis: A Case Report. *Neurologist* 24(5):143–145
27. Manganotti P, Furlanis G, Ajčević M, Polverino P, Caruso P, Ridolfi M, Pozzi-Mucelli RA, Cova MA, Naccarato M (2019) CT perfusion and EEG patterns in patients with acute isolated aphasia in seizure-related stroke mimics. *Seizure* 71:110–115
28. Stragapede L, Furlanis G, Ajčević M, Ridolfi M, Caruso P, Naccarato M, Ukmar M, Manganotti P (2019) Brain oscillatory activity and CT perfusion in hyper-acute ischemic stroke. *J Clin Neurosci* 69:184–189
29. Caruso P, Naccarato M, Furlanis G, Ajčević M, Stragapede L, Ridolfi M, Polverino P, Ukmar M, Manganotti P (2018) Wake-up stroke and CT perfusion: effectiveness and safety of reperfusion therapy. *Neurol Sci* 39(10):1705–1712
30. Van der Hoeven EJ, Dankbaar JW, Algra A, DUST investigator, et al. (2015) Additional diagnostic value of computed tomography perfusion for detection of acute ischemic stroke in the posterior circulation. *Stroke* 46:1113–1115
31. Pallesen LP, Lambrou D, Eskandari A et al (2018) Perfusion computed tomography in posterior circulation stroke: predictors and prognostic implications of focal hypoperfusion. *Eur J Neurol* 25(5):725–731. <https://doi.org/10.1111/ene.13578>
32. Pallesen L-P, Gerber J, Dzialowski I et al (2015) Diagnostic and Prognostic impact of pc-ASPECTS Applied to Perfusion CT in the Basilar Artery International Cooperation Study. *J Neuroimaging* 25(3):384–389. <https://doi.org/10.1111/jon.12130>
33. Sporns P, Schmidt R, Minnerup J, Dziewas R, Kemmling A, Dittrich R, Zoubi T, Heermann P, Cnyrim C, Schwindt W, Heindel W, Niederstadt T, Hanning U (2016) Computed tomography perfusion improves diagnostic accuracy in acute posterior circulation stroke. *Cerebrovasc Dis* 41:242–247
34. Ma H, Campbell BCV, Parsons MW, Churilov L, Levi CR, Hsu C, Kleinig TJ, Wijeratne T, Curtze S, Dewey HM, Miteff F, Tsai CH, Lee JT, Phan TG, Mahant N, Sun MC, Krause M, Sturm J, Grimley R, Chen CH, Hu CJ, Wong AA, Field D, Sun Y, Barber PA, Sabet A, Jannes J, Jeng JS, Clissold B, Markus R, Lin CH, Lien LM, Bladin CF, Christensen S, Yassi N, Sharma G, Bivard A, Desmond PM, Yan B, Mitchell PJ, Thijs V, Carey L, Meretoja A, Davis SM, Donnan GA (2019) Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke. *N Engl J Med* 380: 1795–1803
35. Wintermark M, Flanders AE, Velthuis B, Meuli R, van Leeuwen M, Goldsher D, Pineda C, Serena J, van der Schaaf I, Waaijer A, Anderson J, Nesbit G, Gabriely I, Medina V, Quiles A, Pohlman S,

- Quist M, Schnyder P, Bogousslavsky J, Dillon WP, Pedraza S (2006 Apr) Perfusion-CT assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. *Stroke*. 37(4):979–985
36. De Lucas EM, Sanchez E, Gutierrez A (2008) CT protocol for acute stroke: tips and tricks for general radiologists. *Radiographics* 28: 1673–1687
 37. Leiva-Salinas C, Provenzale JM, Kudo K, Sasaki M, Wintermark M (2012) The alphabet soup of perfusion CT and MR imaging: terminology revisited and clarified in five questions. *Neuroradiology* 54(9):907–918
 38. Gur AY, Lampl Y, Gross B, Royter V, Shopin L, Bornstein NM (2007 May) A new scale for assessing patients with vertebrobasilar stroke—the Israeli Vertebrobasilar Stroke Scale (IVBSS): inter-rater reliability and concurrent validity. *Clin Neurol Neurosurg* 109(4): 317–322
 39. Higashida RT, Furlan AJ, Roberts H (2003) et-al. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. *Stroke*. 34(8):e109–e137
 40. Bill O, Faouzi M, Meuli R, Maeder P, Wintermark M, Michel P (2017 Jan) Added value of multimodal computed tomography imaging: analysis of 1994 acute ischaemic strokes. *Eur J Neurol* 24(1): 167–174
 41. Schonewille WJ, Wijman CA, Michel P et al (2009) Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. *Lancet Neurol* 8(8):724–730. [https://doi.org/10.1016/S1474-4422\(09\)70173-5](https://doi.org/10.1016/S1474-4422(09)70173-5)
 42. Carpenter MB (1972). *Core Text of Neuroanatomy*. Williams & Wilkins.
 43. Thierfelder KM, Baumann AB, Sommer WH, Armbruster M, Opherk C, Janssen H, Reiser MF, Straube A, von Baumgarten L (2014) Vertebral Artery Hypoplasia. *Stroke*. 45(5):1363–1368. <https://doi.org/10.1161/STROKEAHA.113.004188>
 44. Perren F, Poggia D, Landis T, Sztajzel R (2007) Vertebral artery hypoplasia: A predisposing factor for posterior circulation stroke? *Neurology*. 68(1):65–67
 45. Tei H, Uchiyama S, Usui T, Ohara K (2010) Posterior circulation ASPECTS on diffusion-weighted MRI can be a powerful marker for predicting functional outcome. *J Neurol* 257:767–773
 46. Engelter ST, Wetzel SG, Radue EW, Rausch M, Steck AJ, Lyrer PA (2004) The clinical significance of diffusion-weighted MR imaging in infratentorial strokes. *Neurology* 62:574–580
 47. Engelter ST, Wetzel SG, Bonati LH, Fluri F, Lyrer PA (2008) The clinical significance of diffusion-weighted MR imaging in stroke and TIA patients. *Swiss Med Wkly* 138:729–740
 48. Baird AE, Dambrosia J, Janket SJ, Eichbaum Q, Chaves C, Silver B, Barber PA, Parsons M, Darby D, Davis S, Caplan LR, Edelman RE, Warach S (2001) A three-item scale for the early prediction of stroke recovery. *Lancet* 357:2095–2099
 49. Wardlaw JM, Keir SL, Bastin ME, Armitage PA, Rana AK (2002) Is diffusion imaging appearance an independent predictor of outcome after ischemic stroke? *Neurology* 59:1381–1387
 50. Glass TA, Hennessey PM, Pazdera L, Chang H-M, Wityk RJ, Dewitt LD, Pessin MS, Caplan LR (2002) Outcome at 30 days in the New England Medical Center Posterior Circulation Registry. *Arch Neurol* 59:369–376
 51. Nagel S, Herweh C, Köhrmann M, Huttner HB, Poli S, Hartmann M, Hähnel S, Steiner T, Ringelb P, Hacke W (2012) MRI in Patients with Acute Basilar Artery Occlusion – DWI Lesion Scoring is an Independent Predictor of Outcome. *Int J Stroke* 7(4):282–288. <https://doi.org/10.1111/j.1747-4949.2011.00705.x>