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How to predict the affected circulation in Large Vessel Occlusive Stroke?

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Abstract

INTRODUCTION: Acute large vessel occlusive, ischaemic strokes may benefit from endovascular recanalisation strategies. A delayed diagnosis of an acute large vessel occlusion could be avoided if it was possible to identify clinical and radiological data predictive of large vessel occlusions and the affected vascular circulation (anterior vs. posterior circulation). METHODS: All consecutive patients (2003–2011) in ASTRAL, a prospective single-centre registry of acute ischaemic strokes, were selected if a symptomatic, large vessel occlusion was found on CTA performed <12 h after stroke onset. Stroke was localised to anterior and posterior circulation using acute and follow-up radiological information. RESULTS: In 757 of 1523 patients with a large vessel occlusion (56 % anterior and 33 % posterior circulation strokes), multiple logistic regression analysis showed an association of anterior circulation occlusion with aphasia (OR 53.1, 95 %CI 16.1-175.9), hemineglect (32.2, 10.4-99.8), hemiparesis (4.8, 1.3-17.4) and hemisensory deficits (6.3, 2.6-15.3); and of posterior circulation occlusion with cerebellar (0.1, 0.0-0.1), visual field (0.1,0.0-0.2) and posterior-fossa-type oculomotor deficits (perfect prediction). Anterior circulation strokes had shorter onset-to-door interval (0.9, 0.9-1.0), higher admission diastolic blood pressure (1.1, 1.0-1.1) and more often early ischaemic signs on non-contrast CT (0.7, 0.5-0.9). ROC analysis showed an area under the ROC curve of 0.98. CONCLUSIONS: In acute large vessel occlusive strokes, posterior circulation localisation can be inferred by later presentation to the hospital, fewer cognitive, fewer sensory-motor and more cerebellar deficits, lower blood pressure and normal non-contrast CT. Clinical implementation may help to guide future recanalisation strategies.

Keywords: stroke, cerebrovascular occlusion, brain infarction - posterior circulation, brain infarction – anterior circulation, predictors.

Abbreviations

AIS	acute ischaemic stroke
AC	anterior circulation
AUC-ROC	the area under the curve – receiver operator characteristics
BP	blood pressure
CTA	CT-angiography
M1	middle cerebral artery
IQR	interquartile range
LVO	large vessel occlusion
mRs	modified Rankin scale
NCCT	acute non-contrast CT
PC	posterior circulation
T-ICA	terminal occlusion of the intracranial internal carotid artery

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Introduction

Careful selection of patients who are mostly likely to benefit from endovascular recanalisation is mandatory despite the current uncertainty about its clinical value [1-2]. Approximately half of posterior circulation (PC) and of anterior circulation (AC) patients have significant large vessel pathology (large vessel stenosis and/or occlusion) in the ischaemic territory [3] and are therefore candidates for endovascular treatments. Roughly 20 % of the ischaemic strokes are situated in the PC.

In order to determine the most appropriate acute treatment and prevention strategy in acute ischaemic stroke (AIS) patients likely having a large vessel occlusion (LVO), it is important to identify the affected circulation for several reasons: 1) in patients unable to undergo acute vascular imaging, the affected circulation should be identified before recanalisation treatment; 2) PC strokes with LVO may simulate middle cerebral artery infarction; 3) stroke severity (measured by NIHSS scale or FAST scale) may be used in AC but not PC to identify the presence or absence of a LVO; and 4) in case time windows for treatment of AC and PC stroke will be confirmed to be different in future clinical trials [4-11].

Therefore, we aimed to identify clinical and non-vascular radiological variables predictive for large vessel occlusions and the affected vascular circulation (AC vs. PC). Implementation of these predictors in pre-hospital phase and in stroke-receiving institutions who have no access to advanced neuroimaging capabilities such as CT-angiography (CTA) or MRI/MR-angiography, may be beneficial.

Materials and Methods

The ASTRAL registry is a prospective, observational single-centre registry of all consecutive ischaemic strokes admitted to the stroke unit and/or intensive care unit within 24 h after stroke onset or last well time, as published previously.[3] For this analysis, we selected all patients from 2003–2011 with AIS who had LVO occlusion on CTA performed <12 h of stroke onset or last well time. This time window was selected since acute endovascular recanalisation treatments may be beneficial in certain patients selected by tissue viability imaging, which may be beyond the currently recommended 6 to 8 h time window. [2,12,13] Stroke etiology was based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification, with three additional categories: dissection, rare and multiple. Clinical outcome at 3 months was considered favourable if the modified Rankin scale (mRs) scored 0-2 by mRs-certified medical personnel in person or by telephone. Clinical data were prospectively retrieved for each patient including demographic data, history of pre-existing cardiovascular risk factors, co-morbidity and presence of clinical symptoms or signs. Nystagmus, dissociated eye movements and vertical gaze palsies were classified as posterior-fossa-type oculomotor deficits. Blood pressure (BP), heart rate, temperature and serum glucose level at admission were assessed. On acute non-contrast CT (NCCT), early ischaemic changes were considered present on CT if the acute ASPECTS was <10. [14] For PC strokes, the pc-ASPECTS was used.[15] Hyperdense MCA sign, presence of leukoaraiosis were assessed on NCCT. In our stroke centre, all AIS patients who arrive within 24 h after symptom onset and have no contraindication for contrast imaging will undergo cervical and cranial arterial imaging as soon as possible, usually based on CT. Analysis of CTA was done by both a neurologist and neuro-radiologist aware of the clinical examination, using continuous axial and reformatted 3D MIP pictures of extra- and intracranial arteries. In case of discordance, an agreement was reached. Large vessel occlusions in ischaemic territory were defined as an occlusion in the trunk of the middle cerebral artery (M1), intermediate middle cerebral artery (M2), terminal occlusion of

the intracranial internal carotid artery (T-ICA), siphon of the internal carotid artery without distal T-occlusion, anterior cerebral artery (A1 or A2 segments), basilar artery occlusion, posterior cerebral artery (P1 or P2 segments) and intracranial part vertebral artery (V4). Occlusion was defined as absent filling of the examined arterial segment during the initial acquisition of contrast medium images. Occlusions were categorised as being within or outside the ischaemic territory, or both. Localisation of ischemia was based on radiological signs of acute ischemia on admission CT (including CT-perfusion in 81.4 % of the patients) and subacute or chronic CT or MRI-based imaging. Patients were excluded in case of inability to localize the stroke or if simultaneous AC and PC ischemia was diagnosed. Collection, analysis and publication of data in ASTRAL was approved by the Ethics Commission for Research on Humans of the Canton of Vaud (ECCV), Subcommission III.

Univariate logistic regression was performed to determine potential predictors of arterial occlusion with all relevant clinical, radiological and biological data included in ASTRAL. Significant predictors at 90 % level of significance were used to fit a multivariate model (Pearson or Spearman correlations) in a backward procedure selection. In the multivariate logistic regression analysis, the level of significance was set at 95 %, and the area under the curve – receiver operator characteristics (AUC-ROC) were calculated and graphically depicted. Interactions between significant or clinically relevant variables were tested. Statistical analysis was performed with STATA software (Version 11, 2009; College Station, Texas, USA).

Results

Of 1645 patients analyzed, 94 (6 %) were excluded because of the inability to localise the infarct and 28 (2 %) because of simultaneous AC and PC strokes. The remaining 1523 patients had a median age of 70 (IQR:21), were 41 % female and 387 (25 %) patients had vertebro-basilar ischemia. The median time from onset to hospital arrival was 128 min (IQR 170). LVO was seen in 56 % (630/1136) of AC and 33 % (127/387) of PC strokes. An acute basilar artery occlusion was detected in 46 (12 %) patients with a PC stroke. Overall, 506 patients (33 %) were treated with IV thrombolysis within 4.5 h (3 h before 10/2008), 47 (3 %) with endovascular treatment within 6 h and 56 (5 %) with recanalisation methods outside these time limits or with research protocols (neuroprotection trials, interventional trials).

Results of the univariate comparison between AC and PC strokes in patients with LVO are shown in Table 1. Patients with a posterior occlusive stroke were in general younger (66.2 vs. 71.2 years), male (67 % vs. 54 %) and had more often a history of a previous cerebrovascular event (33 % vs. 23 %). Both the NIHSS (4 vs. 10) and the BP on admission (150/80 vs. 158/90 mmHg) were significantly lower. The presence of clinical signs, assessed by the NIHSS subitems, differed significantly between both groups (Figure 1): posterior-fossa type oculomotor deficits (53 %), cognitive symptoms (13 %), ataxia (71 %) and decreased vigilance (31 %) were more frequently present in the PC strokes.

On multivariate analysis, a specific pattern of clinic-radiological signs appears with respect to the affected circulation in patients with LVO (Table 2). A statistical model based on circumstantial features (onset-to-door time), neurological signs (hemiparesis, sensory deficits, hemineglect, visual field defects, cerebellar defects and aphasia), diastolic BP and absence of early ischaemic signs on CT imaging ((pc-)ASPECTS=10) could differentiate between anterior and posterior circulation, occlusive strokes. The multivariate analysis showed an AUC-ROC of 0.98 (Figure 2).

Discussion

Determining the vascular territory of an acute ischaemic clinical syndrome on purely clinical grounds can be difficult, but this knowledge may be needed to determine the most appropriate acute treatment and prevention strategy. We found that in patients with acute large vessel occlusive strokes, readily available clinical and NCCT-based parameters allows localising a large vessel occlusion in the AC or PC with very high reliability (AUC 0.98). NCCT, the standard brain imaging modality in hyperacute stroke, has limited sensitivity in posterior circulation stroke. In patients not undergoing additional acute vascular imaging, the affected circulation could be identified. An important determinant of therapeutic efficacy is the speed and safety with which the occlusion can be detected, localised and the recanalisation and reperfusion can be achieved [12,16].

Regarding the clinical predictors of stroke localisation, hemispheric signs were highly discriminating for AC stroke, despite their occasional occurrence in supratentorial PC lesions. Sensory and motor (hemi) syndromes are also more frequent in AC strokes with LVO, but discriminate less well (Figure 1). Tao et al. recently demonstrated that clinical symptoms and signs considered typical of PC ischemia occur far less often than expected. He stated that localisation based on clinical neurological deficits is often inaccurate [4]. Compared to the recently published cohorts on the prevalence of consciousness disturbances in PC ischemia (<10->20 %), our patients with PC occlusions were more likely to have altered level of consciousness (31 %), but this was not significant in the multivariate analysis. The conflicting results are mainly based on the use of different criteria, distribution of stroke subtypes and age groups used in the different studies. Comparable data for posterior circulation strokes with a LVO and for other sites than the basilar artery is currently not available. Despite the presence of a symptomatic LVO in all our patients, the NIHSS score remained lower in the PC strokes, highlighting the probable insufficiency of this scale to describe PC strokes [4,17] These NIHSS scores may not mirror the severity of the stroke as patients with a stroke in the same brain territory may present with different levels of neurological deficit severity. Further, the stroke severity measured by NIHSS does not reliably predict the presence of arterial occlusions in posterior circulation strokes [11].

Early ischaemic changes were less frequently seen in PC strokes despite systematic use of validated CT-based scores for the AC and PC circulation [14-15], and despite the longer time to imaging in PC patients (median of 276 min vs. 170 min). It is well known that the ability of NCCT and MRI to depict early ischaemic signs in posterior circulation strokes is unsatisfactory (19 % false negative rate in early MRI), and that this independent of the presence of a LVO [5,8]. The longer time from stroke onset to hospital arrival and to stroke imaging may be a result of poorer stroke recognition in vertebro-basilar ischemia due to its highly variable clinical picture [18]. This may decrease the proportion of patients eligible for acute recanalisation treatment or delays its application, contributing to poorer outcome in PC strokes. Interestingly, knowledge of demographic data, pre-existing cardiovascular risk factors, co-morbidities or pre-existing treatment had no additional value in predicting the site of occlusion in our cohort.

Limitations of this study are several. First, the main limitation of our study is that currently it is rare to perform an endovascular reperfusion treatment without a previous vascular non-invasive imaging (CTA, MRA). Second, the study does not address the value of hyperdense artery signs on NCCT, for example, in the M1 or basilar artery; we decided not to analyse this because of the known, high interrater variability, mainly in the basilar artery [18]. And finally, we did not analyse the impact of our model on patient selection for revascularisation.

In conclusion, the use of clinico-radiological predictors localising a LVO to AC and PC is possible using simple parameters and may accelerate and individualise treatment decisions, in particular regarding endovascular recanalisation therapies. This model can select a subgroup of ischaemic stroke patients needing additional arterial imaging and, if possible, endovascular revascularisation therapies.

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Conflict of interest

We declare that we have on conflict of interest.

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Figures

Figure 1 - Presence of neurological deficits according to the localisation of the LVO.

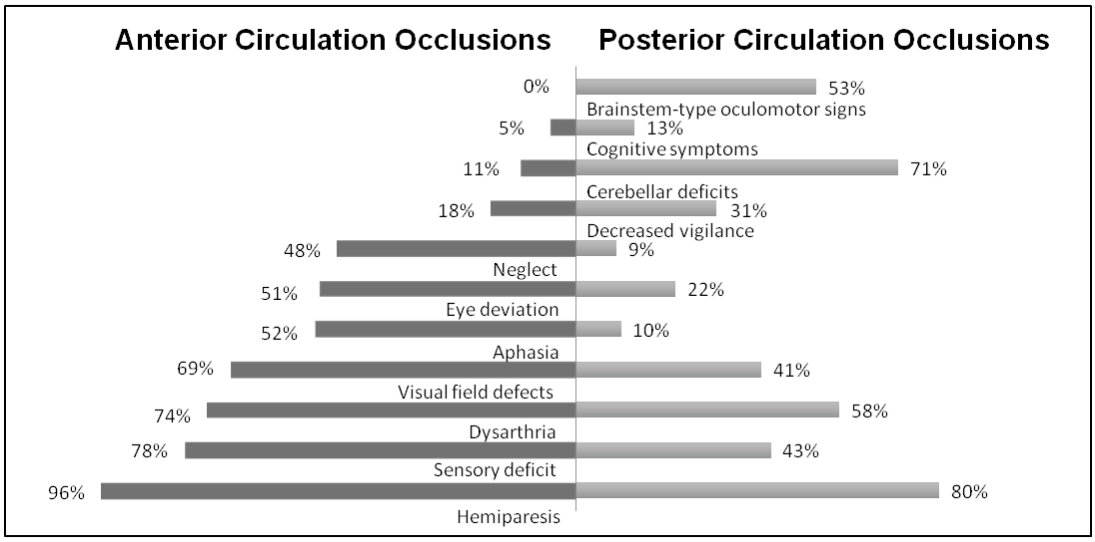
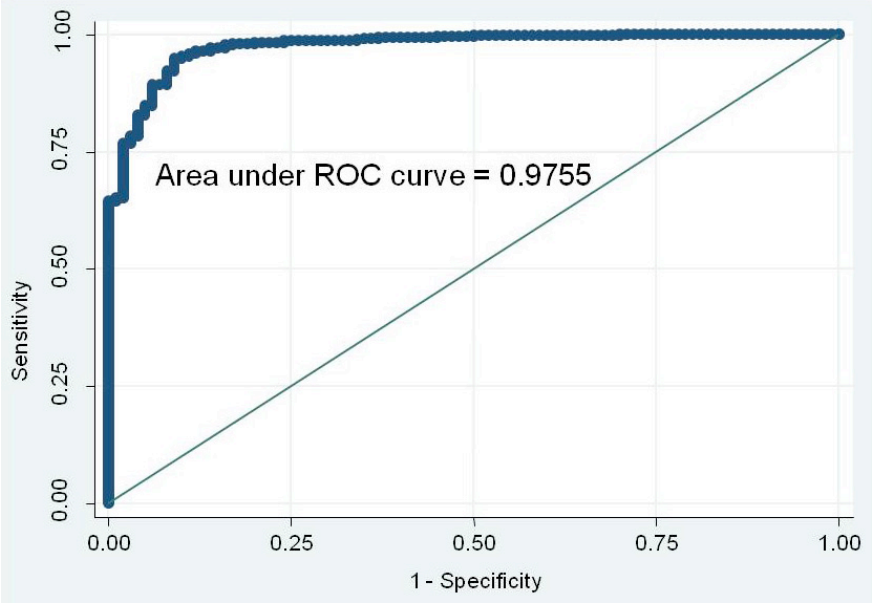


Figure 2 - AUC-ROC curve of the multivariate logistic regression analysis.



Tables

Table 1 - Univariate analysis on clinico-radiological factors associated with anterior circulation (n=630) and posterior circulation occlusions (n=127). For significant p values, 95 % confidence interval is added after odd ratio. Level of significance was set at 95 %. Continuous variables are described by the median and interquartile range (IQR); non-continuous variables by number and percentage.

	Anterior Circulation occlusion in ischaemic territory	Posterior Circulation occlusion in ischaemic territory	OR (95% CI)	p-value
Number	630	127		
Demographic				
Age (years)	71.2 (19.5)	66.2 (21.7)	1.02 (1.00-1.03)	<0.01
Male sex	54 %	67 %	1.74 (1.16-2.62)	<0.01
Medical history				
Previous cerebrovascular events	23 %	33 %	0.61 (0.40-0.93)	0.02
Pre-existing handicap (mRS3-5)	8 %	2 %	5.08 (1.22-21.16)	0.03
Atrial fibrillation	36 %	21 %	2.13 (1.30-3.49)	<0.01
Congestive heart failure	23 %	10 %	2.80 (1.36-5.76)	<0.01
Cancer	11 %	3 %	3.63 (1.11-11.9)	0.03
Presentation on arrival				
NIHSS on admission	10 (13)	4 (6)	1.06 (1.03-1.09)	<0.01
Acute metabolic data				
Temperature (°C)	36.4 (0.8)	36.2 (0.6)	1.40 (1.03-1.89)	0.03
Systolic BP (mmHg)	158 (38)	150 (39)	1.01 (1.01-1.02)	<0.01
Diastolic BP (mmHg)	90 (21)	80 (22)	1.03 (1.02-1.04)	<0.01
Etiology (modified TOAST criteria)				
Cardiogenic	45 %	25 %	2.03 (1.56-2.64)	<0.01
Atherosclerotic	15 %	15 %	1.01 (0.73-1.39)	0.96
Lacunar	3 %	17 %	0.16 (0.11-0.25)	<0.01
Dissection	6 %	7 %	0.88 (0.55-1.47)	0.60
Rare etiologies	3 %	4 %	1.32 (0.69-2.52)	0.85
Multiple causes	6 %	3 %	2.18 (1.11-4.31)	0.02
Undetermined	25 %	31 %	0.77 (0.60-0.99)	0.05
Acute CT imaging				
Time to imaging (min)	170 (194)	276 (313)	1.00 (1.00-1.00)	<0.01
Early ischaemic changes	56 %	27 %	3.47 (2.25-5.36)	<0.01
ASPECTS CT (adapted to the circulation)	8 (3)	10 (1)	0.61 (0.52-0.73)	<0.01
Acute treatment				
IV thrombolysis	39 %	15 %	0.30 (0.23-0.40)	<0.01
Endovascular treatment	3%	4 %	3.70 (2.73-5.01)	<0.01
Recanalisation treatment outside guidelines	5 %	3 %	0.80 (0.42-1.51)	0.49
Outcome				
Favourable (mRS 0-2) at 3 months	45 %	28 %	2.05 (1.58-2.67)	<0.01
Favourable (mRS 0-2) at 12 months	45 %	26 %	2.32 (.76-3.06)	<0.01

Table 2 - Independent predictors of LVOs to the anterior vs posterior circulation in acute ischaemic stroke. Variables with an odds ratio between 0 and 1 are in favour of posterior circulation occlusions, variables with an odds ratio higher than 1 are positively correlated with anterior circulation occlusions.

	OR (95 % CI)	**p-value**
Circumstantial features		
Onset-to-door time (per min)	0.9 (0.9-1.0)	0.02
Neurological examination		
Hemiparesis	4.8 (1.3-17.4)	0.02
Sensory deficits	6.3 (2.6-15.3)	<0.01
Hemineglect	32.2 (10.4-99.8)	<0.01
Visual field defects	0.1 (0.0-0.2)	<0.01
Cerebellar defects	0.05 (0.0-0.1)	<0.01
Aphasia	53.1 (16.1-175.9)	<0.01
Physiological findings		
Diastolic BP (per mmHg)	1,1 (1,0-1,1)	<0.01
Imaging findings		
Normal ASPECTS (adapted to circulation)	0.7 (0.5-0.9)	0.02