Penumbra salvage and infarct growth in acute ischemic stroke: Multiple factors explain high interindividual variability

G Sirimarco, MD, PhD¹, D Strambo, MD¹, S Nannoni, MD¹, C Cereda, MD^{1,2}, J Labreuche, BS³, G Saliou, MD, PhD⁴, R Meuli, MD⁴, A Eskandari, RN¹, M Wintermark, MD^{4,5}, P Michel, MD¹

¹Neurology Service and ⁴Department of Diagnostic and Interventional Radiology of the Lausanne University Hospital, Lausanne, Switzerland

²Stroke Center, Neurology Service, Ospedale Civico di Lugano, Lugano, Switzerland

³Department of Biostatistics, EA 2694-Santé publique : épidémiologie et qualité des soins, Univ. Lille, France

⁵Department of Diagnostic and Interventional Radiology of Neuroradiology Division, Stanford University and Medical Center, Stanford, USA

Background and aims

Effective treatment of ischemic stroke requires reperfusion of the penumbral brain tissue.
We aimed at investigating predictors of penumbra salvage and infarct growth.

Methods

In the Acute STroke Registry and Analysis of Lausanne (ASTRAL) from 2003 to 2016, we selected all middle cerebral artery (MCA) strokes with availability of a good quality CT-angiography <24h and thresholded CT-perfusion.
Penumbra salvage (PS) and infarct growth (IG) over 24 hours were correlated in multivariate analyses with clinical, radiological and biochemical variables, and in adjusted analysis with clinical outcome.

Results

In the 551 MCA strokes included, 49.2% were females, median age (±IQR) was 68.7±21, admission NIHSS 14±12, and onset-to-imaging time 169.5±283 minutes.
More PS was associated with higher BMI, hemineglect, absence of early ischemic changes, leukoaraiosis, other vascular territory involvement, larger baseline penumbra and a lower clot burden. Less IG was associated with current smoking, lower admission glycemia, larger baseline infarct core, absence of early ischemic changes, chronic vascular brain lesions, other territory involvement, absence of extracranial arterial pathology and hyperdense MCA sign, and lower clot burden. Adding subacute variables to these analyses, recanalisation were associated with more PS and less IG, and the absence of parenchymal haemorrhage with less IG (Table 1,2).
More PS and less IG were independently correlated with better 3 and 12 months functional outcome.

Independent predictors of penumbra salvage	Acute and subacute model	
	OR (95%CI) ¹	P Value
Acute variables		
Baseline penumbra (per 1 log SD increase)	18.05 (11.90 to 27.36)	<0.001
Leukoaraiosis	0.46 (0.27 to 0.77)	0.003
PCA and/or ACA involved	0.36 (0.17 to 0.77)	0.008
Neglect	1.66 (1.11 to 2.49)	0.013
Early ischemic changes	0.56 (0.36 to 0.85)	0.006
Clot burden score (per 1 point increase)	1.13 (1.04 to 1.22)	0.003
BMI (per 1 SD increase)	1.31 (1.04 to 1.65)	0.020
WBC (per 1 log SD increase)	0.82 (0.66 to 1.01)	0.056
Subacute variables		
Recanalisation		0.006 ²
No occlusion	1.00 (reference)	-
Recanalized	2.34 (1.27 to 4.29)	0.006
Non-recanalized	1.28 (0.64 to 2.56)	0.48
Parenchymal hemorrhage at 24h	0.56 (0.29 to 1.07)	0.078

Table 1. Independent predictors of penumbra salvage (categorized into tertiles). 1 Common odds ratio for higher tertiles in volume change of penumbra; 2 P-value for overall effect. Model 2 calculated using a backward-stepwise ordinal logistic model including all univariate acute and subacute predictors at P<0.10.

Independent predictors of infarct growth	Acute and subacute model	
	OR (95%CI) ¹	P Value
Acute variables		
Baseline infarct core (per 1 log SD increase)	0.44 (0.34 to 0.55)	<0.001
Early ischemic changes	2.27 (1.55 to 3.31)	<0.001
PCA and/or ACA involved	5.76 (2.75 to 12.05)	<0.001
Blood glucose (per 1 log SD increase)	1.33 (1.11 to 1.59)	0.002
Leukoaraiosis	2.05 (1.30 to 3.23)	0.002
Hyperdense MCA	1.91 (1.22 to 2.98)	0.004
Extracranial stenosis ≥50% or occlusion	1.55 (1.03 to 2.30)	0.032
Clot burden score (per 1 point increase)	0.87 (0.80 to 0.95)	0.001
Current smoking	1.54 (1.05 to 2.25)	0.027
Old infarct	1.66 (1.11 to 2.51)	0.015
Good Collaterals	Not selected	-
Subacute variables		
Recanalisation		<0.001 ²
No occlusion	1.00 (reference)	-
Recanalized	0.50 (0.31 to 0.83)	0.006
Non-recanalized	1.11 (0.64 to 1.90)	0.72
Parenchymal hemorrhage at 24h	2.61 (1.39 to 4.87)	0.003

Table 2. Independent predictors of infarct growth (into tertiles). 1 Common odds ratio for higher tertiles in change of Infarct core; 2 P-value for overall effect. Model 2 calculated using a backward-stepwise ordinal logistic model including all univariate acute and subacute predictors at P<0.10.

Conclusion

Penumbra salvage and infarct growth depend on multiple clinical, metabolic, parenchymal, and arterial variables. These findings may explain variability of treatment response and outcome, and may help select patients for late or more aggressive management.

References.

Lansberg MG, Lee J, Christensen S, Straka M, De Silva DA, Mlynash M, et al. RAPID automated patient selection for reperfusion therapy: a pooled analysis of the Echoplanar Imaging Thrombolytic Evaluation Trial (EPITHET) and the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) Study. Stroke. 2011; 42(6):1608–14; Bang OY, Saver JL, Kim SJ, Kim G-M, Chung C-S, Ovbiagele B, et al. Collateral Flow Predicts Response to Endovascular Therapy for Acute Ischemic Stroke. Stroke. 2011; 42(3):693–9; G Zhu, P Michel, A Aghaebrahim, J T. Patrie, W Xin, A Eskandari, W Zhang, M Wintermark. Prediction of Recanalization Trumps Prediction of Tissue Fate The Penumbra: A Dual-edged Sword. Stroke. 2013; 44:1014-1019.