Frequency and predictors of decisions to change goals of care after acute ischemic stroke

Cover title: Ischemic stroke and change in goals of care

R. Hausammann*[1], E. Maslias*[2], M. Amiguet[3], R.J. Jox[4,5], G.D. Borasio[4], P. Michel[2]

[1] Private practice, Lenzerheide, Switzerland
[2] Stroke Centre, Neurology Service, Department of Clinical Neurosciences, Lausanne University Hospital and University of Lausanne, Switzerland
[3] Institute of Social and Preventive Medicine, University of Lausanne, Switzerland
[4] Palliative and Supportive Care Service, Lausanne University Hospital and University of Lausanne, Switzerland
[5] Institute of Humanities in Medicine, Department of Education and Research, Lausanne University Hospital and University of Lausanne, Switzerland

Supplementary Methods

The National Institutes of Health Stroke Scale (NIHSS) was performed or supervised by NIHSS-certified physicians at admission and at 24 hours and 7 days. Patients who died at any point during the evaluations were given a maximal NIHSS score of 42. In addition, vital signs, metabolic and hematologic parameters were measured usually in the emergency room and at 24-48 hours after admission. Stroke pathophysiology was classified according to TOAST criteria (1), with dissections, embolic stroke of undetermined etiology (ESUS) and multiple causes considered as separate mechanisms. Acute brain imaging at admission, mainly consisting of multimodal CT scans was assessed for early ischemic changes, ASPECTS (2) or pc-ASPECTS (3), and chronic vascular lesions. On the first arterial study of cervical and cerebral arteries obtained within 24 hours, stenosis ≥ 50% and occlusion were recorded for all intra- and extra-cranial arterial segments (4). Perfusion-CT was performed in most patients arriving ≤ 24 hours with a suspicion of supratentorial stroke. Repeat brain CT or MRI were performed at approximately 24 hours in patients receiving acute recanalization treatments. Imaging was also done again when clinically indicated, such as ≥2 NIHSS points-worsening, unless the patient already had a change in goals of care (CGC). The images were assessed for ischemic changes, mass effect, and hemorrhagic transformations according to ECASS-II (5). In patients with initial arterial occlusions, recanalization was reassessed whenever possible at 12-48 hours using angio-CT, angio-MRI or Doppler imaging. Recanalization of initially occluded arteries was classified as absent, partial or complete, according to our previous work (4).

Acute recanalization treatments including intravenous thrombolysis (IVT) and endovascular treatment (EVT) were performed according to international and national guidelines (6). Admission to the intensive care unit before transfer to the stroke unit was decided by the treating physician based on the severity of neurological and cardiorespiratory needs, and recorded in ASTRAL.

Supplementary table 1: Additional baseline data of the study population. Results are displayed as absolute counts and percentages for categorical variables and median with interquartile range (IQR) for continuous variables.

Variable	Overall population included	Patients with CGC (N = 440)	Control group (N =3824)	OR (95% CI)
Private health insurance	770 (18.3%)	57 (13.1%)	713 (18.9%)	0.65 (0.49 – 0.87)*
Ethnicity: non-Caucasian	140(3.3%)	8(1.8%)	132(3.5%)	0.52(0.25–1.06)
Vascular risk factors				
Prosthetic heart valves	148 (3.5%)	17 (3.9%)	131 (3.4%)	1.13 (0.68 – 1.9)
Dyslipidemia	3131 (73.6%)	255 (58.5%)	2876 (76.4%)	0.46 (0.38 – 0.57)*
Coronary artery disease	787 (18.6%)	124 (28.4%)	663 (17.4%)	1.88 (1.51 – 2.36)*
Low ejection fraction ≤35%	233 (5.5%)	47 (10.8%)	186 (4.9%)	2.36 (1.68 – 3.3)*
Obesity	2040 (48.1%)	150 (34.3%)	1890 (49.7%)	0.53 (0.43-0.65)*
Comorbidities				
Congestive heart failure	775 (18.2%)	117 (26.6%)	658 (17.3%)	1.73 (1.38 – 2.18)*
Other neurological disease	328 (7.7%)	31 (7.1%)	297 (7.8%)	0.9 (0.61 – 1.32)
Metastatic cancer	100 (2.4%)	17 (3.9%)	83 (2.2%)	1.8 (1.06 – 3.07)*
Peripheral artery disease	270(6.4%)	44(10%)	226(5.9%)	1.76(1.25–2.47)*
Current alcohol abuse	425(10%)	29(6.7%)	396(10.4%)	0.61(0.41–0.9)*
Body mass index (kg/m2)	25(5)	25(6)	25(5)	0.99(0.96–1.02)
Dementia	458(10.8%)	73(16.7%)	385(10.1%)	1.78(1.35–2.34)*
Previous cerebrovascular event	1160 (27.4%)	120 (27.5%)	1040 (27.4%)	1.01 (0.81 – 1.26)
In-hospital stroke	366 (8.6%)	78 (17.7%)	288 (7.54%)	2.64 (2.01- 3.47)*
Therapy at stroke onset				
Antiplatelets	1613 (38%)	193 (44.2%)	1420 (37.2%)	1,33 (1.09 – 1.63)*
Anticoagulants	507 (12%)	72 (16.6%)	435 (11.4%)	1.54 (1.17 – 2.02)*
Antihypertensives	2524 (59.4%)	297 (68.4%)	2227 (58.4%)	1.54 (1.25 – 1.91)*
Lipid-lowering drugs	1224 (28.8%)	119 (27.1%)	1105 (28.9%)	0.91 (0.73 – 1.14)
Antidiabetics	538 (12.7%)	53 (12.1%)	485 (12.7%)	0.94 (0.7 – 1.28)
Contraceptives or hormonal replacement therapy	96 (2.3%)	6 (1.4%)	90 (2.4%)	0.58 (0.25 – 1.34)
New neurological deficits				
Paresis	3336 (79%)	413 (95.8%)	2923 (77.1%)	6.83 (4.23 – 11.01)*
Aphasia	1462 (34.8%)	239 (54.5%)	1232 (32.6%)	2.48 (2.03 – 3.04)*

Variable	Overall population included	Patients with CGC (N = 440)	Control group (N =3824)	OR (95% CI)
Hemineglect	997 (23.8%)	165 (39.4%)	832 (22.1%)	2.29 (1.85 – 2.82)*
Dysarthria	2186 (52%)	339 (79.3%)	1847 (48.9%)	4.02 (3.15 – 5.13)*
Sensory	2079 (49.7%)	312 (74.64%)	1767 (46.9%)	3.33 (2.65 – 4.19)*
Visual field	1526 (36.6%)	309 (74.8%)	1217 (32.4%)	6.21 (4.92 – 7.84)*
Optic nerve or retina	19 (0.5%)	1 (0.2%)	18 (0.5%)	0.5 (0.07- 3.72)
Eye deviation	1057 (25.2%)	261 (62%)	796 (21.1%)	6.09 (4.93- 7.53)*
Oculomotor brainstem symptoms	467 (11.2%)	40 (9.6%)	427 (11.3%)	0.83 (0.59- 1.17)
Cerebellar/Ataxia/Vestibular/Cochlear	1305 (31.2%)	46 (11.1%)	1259 (33.7%)	0.25 (0.18 – 0.34)*
Other cognitive symptoms	394 (9.4%)	71 (17%)	323 (8.6%)	2.18 (1.65 – 2.88)*
Vital parameters				
Acute temperature (°Celsius)	36.3 (0.7)	36.2 (0.8)	36.3 (0.7)	0.81 (0.69 – 0.94)*
Acute blood glucose (mmol/L)	6.6 (2.2)	7.4 (2.9)	6.5 (2)	1.09 (1.06 – 1.12)*
Subacute temperature (°Celsius)	36.6 (0.9)	36.9 (0.9)	36.6 (0.8)	2.15 (1.81 – 2.56)*
NIHSS at 24 hours	4 (9)	21 (11)	3 (6)	1.21 (1.19 – 1.23)*
NIHSS at 7 days	2(7)	30(22)	2(5)	1.2(1.18–1.22)*
Way of hospital arrival				
Direct	3369 (79.1%)	324 (73.6%)	3045 (79.7%)	0.71 (0.57- 0.89)*
Via other emergency room	524 (12.2%)	38 (8.6%)	486 (12.7%)	0.65 (0.46 – 0.92)*
Prehospital and in-hospital treatment delays				
Onset of symptoms known	3083(72.4%)	298(67.7%)	2785(72.9%)	0.78(0.63–0.96)
Onset-to-needle time (min)	142.5 (85)	142.5 (90)	142.5 (85)	1 (1-1)
Door-to-needle time (min)	43 (36.8)	48.5 (42.3)	42 (36)	1 (1-1)
Onset-to-puncture (min)	240 (146.3)	279 (144)	235 (140)	1 (1-1)
Door-to-puncture (min)	103 (79.5)	112 (112)	99.5 (76.5)	1 (1-1)*
Arterial territory involved				
Posterior circulation	1062 (23.4%)	60 (13.8%)	1002 (26.7%)	0.44 (0.33- 0.58)*
Anterior circulation	2834(67.8%)	359(82.7%)	2475(66%)	2.46(1.9–3.19)*

Variable	Overall population included	Patients with CGC (N = 440)	Control group (N = 3824)	OR (95% CI)
Anterior and posterior circulation	81 (1.9%)	12 (2.8%)	69 (1.8%)	1.52 (0.81 – 2.82)
Undetermined	206 (4.9%)	3 (0.7%)	203 (5.4%)	0.12 (0.04 – 0.38)*
Acute ischemic lesion present	1525 (38.3%)	255 (62.5%)	1270 (35.5%)	3.03 (2.45-3.74)*
Chronic or subacute ischemic lesion (CT)	1293 (33.9%)	153 (38.7%)	1149 (33.3%)	1.27 (1.02 – 1.57)*
Leukoarariosis (CT)	1244 (32.6%)	159 (40.3%)	1085 (31.7%)	1.45 (1.17 – 1.8)*
Perfusion Imaging				
Focal hypoperfusion on CTP	2119(51.2%)	249(58.9%)	1870(50.3%)	1.41(1.15–1.73)*
No hypoperfusion	760 (18.4%)	15 (3.6%)	745 (20.1%)	0.15 (0.09 – 0.25)*
Not performed	1260 (30.4%)	159 (37.6%)	1101 (29.6%)	1.43 (1.16- 1.76)*
CTA clot burden score	9 (5)	4 (7)	9 (4)	0.76 (0.73 – 0.8)*
Acute recanalization treatment				
No recanalization treatment	2902(68.1%)	275(62.5%)	2627(68.8%)	0.78(0.62–0.93)*
IV thrombolysis only	987(23.2%)	114(25.9%)	873(22.9%)	1.18(0.94–1.48)
Endovascular treatment (+/- IV thrombolysis)	370(8.7%)	51(11.6%)	319(8.5%)	1.44(1.05–1.97)*
Recanalization on DSA if acute endovascular treatment	257 (81.85%)	27 (60%)	230 (85.5%)	0.25 (0.13- 0.51)*
Recanalization of intracranial arteries at 24 hours (if initially occluded)	493/1273(38%)	28/162(17.3%)	465/1111(41.8%)	0.29(0.18–0.44)
Stroke mechanism				
Atherosclerosis (with ≥50% stenosis)	571 (13.8%)	53 (12.2%)	518 (13.9%)	0.88 (0.65 – 1.19)
Cardiac	1309 (31.5%)	195 (45.7%)	1114 (29.9%)	1.97 (1.61 – 2.42)*
Lacunar	488 (11.8%)	4 (0.9%)	484 (13%)	0.06 (0.02 – 0.17)*
Dissection	170 (4.1%)	13 (3%)	157 (4.2%)	0.71 (0.4 – 1.27)
Embolic stroke of unknown source / Undetermined / incomplete work-up	1162 (28%)	80 (18.7%)	1082 (29%)	0.56 (0.44 – 0.73)*
Other determined/rare	206 (5%)	38 (9%)	168 (4.5%)	2.07 (1.43-2.99)*
Multiple/coexisting causes	248 (6%)	44 (10.3%)	204 (5.5%)	1.98 (1.41 – 2.79)*

Variable	Overall population included	Patients with CGC (N = 440)	Control group (N =3824)	OR (95% CI)
Acute vital parameters and laboratory exams				
Systolic blood pressure (mmHg)	152 (35)	154 (44)	152 (34.5)	1 (1 – 1)
Diastolic blood pressure (mmHg)	84 (22)	80 (24)	84 (23)	0.99 (0.99 – 1)*
Creatinine (µmol/L)	87 (32)	95 (41.5)	86 (30)	1 (1 – 1)*
Total cholesterol (mmol/L)	5.1 (1.7)	4.8 (1.5)	5.2 (1.6)	0.8 (0.73 – 0.88)*
C-reactive protein (mg/dl)	3 (9)	9 (25.25)	3 (8)	1.01 (1.01 – 1.02)*
WBC count (G/L)	8.1 (3.7)	8.8 (4.85)	8 (3.5)	1.06 (1.04 – 1.09)*
Hemoglobin (g/L)	139 (23)	130 (25)	140 (21)	0.97 (0.97 – 0.98)*
Platelet count (G/L)	223 (84)	220 (101.5)	223 (82)	1 (1-1)
Subacute vital parameters and laboratory exams				
Systolic blood pressure (mmHg)	137 (26)	140 (31.5)	136 (26)	1.01 (1 – 1.01)*
Diastolic blood pressure	70 (20)	69 (16.75)	70 (20)	0.99 (0.98- 0.99)*
Blood glucose (mmol/L)	5.7 (1.6)	6.6 (2.25)	5.7 (1.4)	1.22 (1.15 – 1.28)*
Creatinine (µmol/L)	80 (31)	89 (41.5)	79 (29)	1 (1 – 1)*
Any radiological hemorrhagic transformation within 7 days				
No	2554 (61.6%)	216 (50.7%)	2338 (62.8%)	0.61 (0.5 – 0.74)*
Any	425 (10.3%)	92 (21.6%)	333 (8.9%)	2.8 (2.17 – 3.62)*
Not checked	1168 (28.2%)	118 (27.7%)	1050 (28.2%)	0.97 (0.78 – 1.22)*
Length of hospital stay	9(7)	8(12)	9(7)	-1(-1.82– -0.17)*
mRS 4 or 5 in patients alive at 3 months	477(13%)	18(50%)	459(12.7%)	3.94(2.22–6.99)*
Death at 3 months	585(13.7%)	404(91.8%)	181(4.7%)	225.87(155.68–327.7)*

* Significant OR

CTA = Computed Tomography Angiography. DSA = Digital subtraction angiography. WBC = white blood cell.

Supplementary table 2: Causes of death in patients with and without a CGC split into in-hospital and post-hospital death. Results are displayed as absolute counts and percentages.

Causes of in-hospital death	Patients with CTG (N=337)	Control group (N=39)

Neurovascular	151 (44.8%)	13 (33.4%)
Stroke-related, non-neurovascular	138 (40.9%)	12 (30.8%)
Other vascular	8 (2.6%)	3 (7.7%)
Other non-vascular	12 (2.4%)	2 (5.1%)
Unknown	28 (8.3%)	9 (23.1%)
Causes of post-hospital death	**Patients with CTG (N=77)**	**Control group (N=354)**
Neurovascular	24 (31.2%)	57 (16.1%)
Stroke-related, non-neurovascular	25 (32.5%)	52 (14.7%)
Other vascular	3 (3.9%)	43 (12.2%)
Other non-vascular	12 (15.6%)	128 (36.2%)
Unknown	13 (16.9%)	74 (20.9%)

Supplementary table 3: Disposition of patients with a CGC alive at discharge from the acute stroke center. Results are displayed as absolute counts and percentages.

Total N	**103**
Home	5 (4.9%)
Rehabilitation	4 (3.9%)
Nursing home	36 (35.0%)
Other acute care hospital	30 (29.1%)
Specialized palliative care institution	28 (27.1%)

Supplementary references

1. Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of Subtype of Acute Ischemic Stroke - Definitions for Use in A Multicenter Clinical-Trial. Stroke. 1993;24(1):35-41.
2. Puetz V, Dzialowski I, Hill MD, Demchuk AM. The Alberta Stroke Program Early CT Score in clinical practice: what have we learned? 2. International journal of stroke : official journal of the International Stroke Society. 2009;4(5):354-64.
3. Puetz V, Sylaja PN, Coutts SB, Hill MD, Dzialowski I, Mueller P, et al. Extent of hypoattenuation on CT angiography source images predicts functional outcome in patients with basilar artery occlusion. Stroke. 2008;39(9):2485-90.
4. Vanacker P, Lambrou D, Eskandari A, Maeder P, Meuli R, Ntaios G, et al. Improving prediction of recanalization in acute large-vessel occlusive stroke. J Thromb Haemost. 2014;12(6):814-21.

5. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet. 1998;352(9136):1245-51.

6. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. Cerebrovascular diseases (Basel, Switzerland). 2008;25(5):457-507.