RESEARCH ARTICLE

Early computed tomography-based scores to predict decompressive hemicraniectomy after endovascular therapy in acute ischemic stroke

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Abstract

Background

Identification of patients requiring decompressive hemicraniectomy (DH) after endovascular therapy (EVT) is crucial as clinical signs are not reliable and early DH has been shown to improve clinical outcome. The aim of our study was to identify imaging-based scores to predict the risk for space occupying ischemic stroke and DH.

Methods

Prospectively derived data from patients with acute large artery occlusion within the anterior circulation and EVT was analyzed in this monocentric study. Predictive value of non-contrast cranial computed tomography (ncCT) and cerebral blood volume (CBV) Alberta Stroke Program Early CT score (ASPECTS) were investigated for DH using logistic regression models and Receiver Operating Characteristic Curve analysis.

Results

From 218 patients with EVT, DH was performed in 20 patients (9.2%). Baseline- (7 vs. 9; p = 0.009) and follow-up ncCT ASPECTS (1 vs. 7, p<0.001) as well as baseline CBV ASPECTS (5 vs. 7, p<0.001) were significantly lower in patients with DH. ncCT (baseline: OR 0.71, p = 0.018; follow-up: OR 0.32, p = <0.001) and CBV ASPECTS (OR 0.63, p = 0.008) predicted DH. Cut-off ncCT-ASPECTS on baseline was 7-, ncCT-ASPECTS on follow-up was 4- and CBV ASPECTS on baseline was 5 points.

Conclusions

ASPECTS could be useful to early identify patients requiring DH after EVT for acute large vessel occlusion.
Introduction

Endovascular therapy (EVT) with stent-retriever devices in acute ischemic stroke involving the anterior circulation has been shown to be superior compared to standard medical treatment in recent randomized trials [1–5]. A meta-analysis of these trials showed benefits of endovascular therapy in almost all patient subgroups, while overall recanalization rates of 71% have been reported [6]. These studies suggest a decrease in rates of decompressive hemicraniectomy (DH) in the future, which has already been reported in a retrospective study by Sporns et al, who found a significant reduction in rates of DH after introduction of EVT between 2009 and 2013 in 497 patients with proximal arterial occlusion (17.4 vs 8.2%) [7].

DH has been shown to improve clinical outcome, shortens in-patient stay and mortality of patients with space occupying ischemic stroke [8, 9]. There is evidence that DH should be performed early and clinicians should not wait for clinical deterioration (e.g. decrease in consciousness) or radiological signs (e.g. midline-shift) [8, 10]. Patients at risk should be identified reliably and as early as possible, because there are neither validated clinical signs nor every patient can be extubated promptly and judged adequately after EVT (e.g. due to aspersion, pulmonary co-morbidities or postinterventional delirium).

The recent meta-analysis of the five thrombectomy trials showed that even patients with lower baseline Alberta Stroke Program Early CT score (ASPECTS), which quantifies infarct demarcation, can benefit from EVT [6]. However, not only patients with unsuccessful EVT, but also patients with low ASPECTS at baseline and follow-up are at risk of developing space-occupying infarctions. The extent of pretreatment infarction at baseline is a predictor for clinical outcome in patients with EVT [11, 12]. In addition, poor collateralization might also increase the risk for space occupying stroke. Therefore, we investigated the predictive value of non-contrast cranial computed tomography (ncCT) ASPECTS, cerebral blood volume (CBV) ASPECTS and baseline Menon score, a collateral score which can be used to determine extent of cerebral collateralization, for DH after EVT.

Materials and methods

Patient population

Clinical and neuroradiological data were analyzed from a prospectively derived, monocentric database including neuroradiological and neurological information of interventional treatment and clinical outcome. Ethics approval was sought from the ethics committee of the University Medical Center Goettingen and all patients gave informed written consent for the anonymized use of disease-related data on hospitalization. Patients were included in the analysis when presenting with acute ischemic stroke of the anterior circulation and receiving EVT between January 2013 and November 2016. Periprocedural factors were recorded by a stroke-experienced senior neuroradiologist and clinical data has been evaluated by an experienced, stroke-trained neurologist.

Imaging based scores

ASPECTS were separately assessed by two neuroradiologists (one with more than 5 years of experience). If ASPECTS differed between the raters, the neuroradiologists reviewed the imaging together and sought consensus. They separately rated ncCT and CT-perfusion (CTP) scans with the ASPECTS, a 10-point scoring system of the middle cerebral artery (MCA) territory. For every MCA region with acute ischemic signs, 1 point is subtracted from 10, resulting in an ASPECTS of 0 for a scan without ischemic lesions and an ASPECTS of 0 for complete MCA infarction [13]. The Menon collateral score (CS) quantifies pial collateral filling on single
phase CT angiography comparing the symptomatic- and asymptomatic hemisphere. It ranges from 0 (no vessels visible within the ischemic territory) to 5 (increased or normal prominence and extent of pial vessels within the ischemic territory). In our study, we used this score in its recent description, which quantifies the pial arterial filling from the anterior and posterior circulation, respectively, and adds the values to a 0 (no collaterals) to 10 (increased or normal collaterals) ordinal score [14].

Multidisciplinary stroke treatment

EVT was performed if patients presented within 6 hours after symptom onset, large vessel occlusion was found in CT-angiography (CTA), significant cerebral blood flow (CBF)/CBV-mismatch on multimodal stroke imaging (defined as difference of ≥ 2 points between CBF ASPECTS and CBV ASPECTS) and intracranial hemorrhage had been ruled out. Decision to perform EVT was based on a standard operating procedure [15] after January 2015 while being based on the judgement of the treating senior neurologist and neuroradiologist before January 2015. I.v.-recombinant tissue plasminogen activator was administered right after the ncCT if contraindications had been ruled out (0.9 mg/kg over 1 hour with 10% of initial bolus) and EVT has been performed without delay (bridging therapy). Following stroke imaging, patients were transferred to the angiography suite (Artis Zee (until 2015) and Artis Q (since 2015), Siemens Healthcare, Forchheim, Germany) where they underwent mechanical thrombectomy either with an aspiration catheter or with a combination of aspiration catheters and retrievable stents (Aperio, Acandis, Pforzheim, Germany; Trevo, Stryker, Mountain View, California; 3D Separator, Penumbra).

In the present study, baseline ASPECTS on ncCT was determined in all patients. ASPECTS on whole-brain CTP and CS could be evaluated in a subgroup (due to missing data, technical or procedural problems). These patients presented with occlusion of the proximal-, distal internal carotid- or medial cerebral artery (MCA) in the M1 or M2-segment, which was diagnosed on initial CT-angiogram. Vessel occlusion was confirmed on subsequent digital subtraction angiography and defined as modified thrombolysis in cerebral infarction score (mTICI) of 0 or 1. Successful recanalization was defined as mTICI 2b-3 on the final angiogram [16]. Patients were excluded if baseline imaging showed ICH or if DH had to be performed because of symptomatic ICH instead of space occupying cerebral infarction.

Indication for DH was based on an interdisciplinary case-to-case decision including the following factors: (suspected) patient will, co-morbidity, age, ischemic stroke within 48 h before admission, (anticipated) infarct-demarcation in more than two-thirds of the MCA territory, ncCT ASPECTS ≤ 4, space occupying edematous infarct-swelling and clinical deterioration. All patients with DH received a follow-up ncCT before surgery either as regular control ncCT 24 hours after EVT or earlier if clinical deterioration had been noted.

Imaging

Stroke imaging was acquired with a 128-slice multidetector CT scanner (Siemens Definition AS+; Siemens Healthcare Sector, Forchheim, Germany) and included a ncCT, followed by near whole-brain CTP and single phase CTA of extra- and intracranial arteries. The scan-protocol has been described in detail elsewhere [17].

Statistical analysis

Statistical analysis was performed using SPSS 21 (IBM SPSS Statistics, Armonk, NY, USA). Characteristics of all patients are shown as mean ± standard deviation (SD) if normally distributed and as median interquartile range (IQR) if not. Comparisons of imaging-based stroke
scores between patients with- and without DH were performed using the Mann-Whitney-U-test and Fischer’s exact-test as appropriate. To assess the predictive value of imaging-based stroke scores, logistic regression models including success of recanalization, symptom-to-final angiogram time, age and National Institute of Health Stroke Scale (NIHSS) have been used. Area under the receiver operator curve (AUROC) and confidence intervals (CI) were calculated for every imaging-based stroke score for the endpoint DH. AUROC vary from 0.5 for a model that correctly predicts outcome no better than chance to 1.0 for a model that perfectly discriminates between endpoints. Cut-off scores were defined as scores with maximal Youden-Index. P-values below 0.05 were considered statistically significant.

Results

From 218 included patients with EVT for large vessel occlusion in the anterior circulation, DH was carried out in 20 (9.2%) patients within a mean period from baseline imaging to surgery of 40.5 ± 37.4 hours (mean ± standard deviation; Table 1). Patients in the DH-group were significantly younger (63 vs 76 years; p = <0.001), had a lower rate of hyperlipoproteinemia (20% vs 50%; p = 0.029) and tended to have a higher NIHSS (18 vs 16 points; p = 0.095). Concerning periprocedural factors of EVT, patients in the DH-group had a lower rate of successful recanalization (40% vs 72%; p = 0.005) and a longer symptom-to-final angiogram time (270 vs 228 min; p = 0.036). A representative case of a patient with successful recanalization requiring DH is presented in Fig 1.

As shown in Table 2, baseline- (7 vs 9; p = 0.009), follow-up ncCT-ASPECTS (1 vs 7, p<0.001) as well as CBV ASPECTS (5 vs 7, p<0.001) were significantly lower in patients with DH. Time to follow-up ncCT was not significantly different between groups (29.5 vs 26 hours; p = 0.186).

Based on the group-differences shown in Table 1, we created logistic regression models including one imaging-based stroke score respectively in combination with the confounding factors age, successful recanalization, time-to-final angiogram and baseline NIHSS (Table 3). Patients with high baseline ncCT- and follow-up ncCT-ASPECTS as well as CBV-ASPECTS

| Table 1. Baseline characteristics of patients with- and without hemicraniectomy |
|---------------------------------|-----------------|----------------|
| **Age (years, IQR)**           | Hemicraniectomy (n = 20) | No-hemicraniectomy (n = 198) | p-value * |
| Sex (male, %)                   | 63 (48–67.5)     | 75.5 (64–80)     | <0.001 |
| Hypertension (n, %)             | 14 (70)          | 162 (81.8)       | 0.233  |
| HLP (n, %)                      | 4 (20)           | 98 (49.5)        | 0.029  |
| Diabetes mellitus (n, %)        | 6 (30)           | 52 (26.3)        | 0.596  |
| Atrial fibrillation (n, %)      | 6 (30)           | 87 (43.9)        | 0.339  |
| IV-thrombolysis (n, %)          | 11 (55)          | 141 (71.2)       | 0.131  |
| Successful recanalization (n, %)| 8 (40)           | 143 (72.2)       | 0.005  |
| NIHSS baseline (points ± SD)    | 18 ± 8           | 16 ± 6           | 0.095  |
| Symptom to admission time (min, IQR)| 129 (45, 210) | 80 (57.25, 155) | 0.480  |
| Groin puncture to final angiogram time (min, IQR) | 64 (46.75, 90.25) | 53 (36, 76.5) | 0.086  |
| Symptom to final angiogram time (min, IQR) | 270 (210–362) | 228 (175–283.5) | 0.036  |

IQR: Interquartile range, HLP: hyperlipoproteinemia, IV: intravenous, NIHSS: National Institute of Health Stroke Scale, SD: Standard deviation

*Mann-Whitney-U-test and Fischer’s exact test as appropriate

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Fig 1. Multimodal stroke imaging from a patient with endovascular therapy and decompressive hemicraniectomy CT-slices are shown in insular (left), ganglionic (middle) and supraganglionic levels.
had a decreased risk for DH. ncCT-ASPECTS after a median follow-up period of 27 hours (IQR, 18–48) was the strongest predictor for DH (OR 0.32; CI 95%, 0.17–0.59; p < 0.001), followed by CBV- (OR 0.63; 0.45–0.89; p = 0.008) and baseline ncCT-ASPECTS (OR 0.71; 0.47–1.07; p = 0.018). This association was not significant for the CS and DH (OR 0.63; 0.45–0.89; p = 0.100).

Table 4 shows the receiver operating characteristic analysis, which revealed that ncCT-ASPECTS at follow-up had excellent predictive value for DH (AUROC 0.95, CI 95%, 0.90–0.98) with a cut-off score of 4 points, followed by a moderate predictive value of the baseline ncCT- (AUROC 0.74, 0.68–0.80) and CBV-ASPECTS (AUROC 0.74, 0.67–0.81) with a cut-off score of 7 and 5 points respectively. Predictive value of the CS was poor (AUROC 0.68, 0.59–0.77) with a cut-off score of 5 points.

**Discussion**

In the present study, we investigated the prognostic value of imaging-based stroke scores to identify patients likely to require DH after EVT for large vessel occlusion in acute ischemic stroke. While there are no validated clinical signs indicating the need for DH after large, hemispheric stroke, internal carotid occlusion, female sex and age < 60 years have been identified as risk factors [18–19]. A study by Kasner et al showed an association between fatal brain edema and a history of hypertension or heart failure, increased white blood cell count, involvement of multiple vascular territories and early hypodensities on ncCT in ≥ 50% of the medial cerebral artery territory [20], which was already shown in the placebo arm of a randomized study investigating the effect of lubeluzole in patients with acute major stroke [21]. In our study, we found evidence for the predictive value of ncCT- and CBV-ASPECTS to identify patients at risk to develop space occupying ischemic stroke, which could be used to more exactly quantify ischemic areas and to accompany the previously described risk factors. ASPECTS are determined early after the ischemic event and represent a quantification of tissue in which cytotoxic and vasogenic edema will occur. This edema usually develops within the first 2 and 4 days, but can develop more rapidly in the first 24 hours after stroke [22]. Therefore, early findings on stroke

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**Table 2. ncCT-, CBV-ASPECTS and collateral score in patients with- and without hemicraniectomy**

|                      | Hemicraniectomy (n = 20) | No-hemicraniectomy (n = 198) | p-value* |
|----------------------|--------------------------|-----------------------------|----------|
| ncCT-ASPECTS at baseline (median, IQR) | 7 (5–8.75)               | 9 (7–9)                     | 0.009    |
| ncCT-ASPECTS follow-up (n = 173; median, IQR) | 1 (0–3)                  | 7 (5–8)                     | <0.001   |
| Time of follow-up CT (hours, IQR) | 29.5 (26.5–53)           | 26 (18–51)                  | 0.186    |
| CBV-ASPECTS (n = 171; median, IQR) | 5 (3.25–7)               | 7 (6–8)                     | <0.001   |
| Collateral score (n = 116; mean ± SD) | 4.56 ± 2.6               | 6.04 ± 2.16                 | 0.054    |

IQR: Interquartile range, SD: standard deviation, ncCT: non-contrast computed tomography, CBV: cerebral blood volume, ASPECTS: Alberta Stroke Program Early CT score; *Mann-Whitney-U-test or T-Test as appropriate

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imaging like attenuation changes within the grey matter resulting in the loss of grey-white matter differentiation at the cortex, loss of distinction of basal ganglia and of the insular ribbon, which are included in the ASPECTS, can guide therapeutic decisions. It has been shown, that if these changes have been found in more than 50% of the MCA territory, this predicts malignant infarction with a sensitivity of 61% and a specificity of 94% [23, 24]. ASPECTS represents a more standardized approach to identify irreversibly damaged brain tissue compared to volumetric measurements of ischemic brain tissue on ncCT. In this respect, a study by MacCallum et al. already showed that an ASPECTS <7 predicts a malignant course of ischemic stroke with increase of neurological deficit and decrease in consciousness in a population of patients with territorial ischemic stroke in the MCA circulation [25]. The cut-off ncCT-ASPECTS on baseline imaging in our study as well as the sensitivity and specificity (66% and 70%

|                | Odds ratio (95% CI) | p-value |
|----------------|--------------------|---------|
| ncCT-ASPECTS baseline | 0.71 (0.47–1.07) | 0.018   |
| Recanalization successful | 0.28 (0.08–0.95) | 0.041   |
| Symptom-to-groin time | 1 (0.99–1.01) | 0.186   |
| Age | 0.93 (0.89–0.97) | 0.001   |
| NIHSS baseline | 1.05 (0.96–1.14) | 0.317   |
| ncCT-ASPECTS follow-up | 0.32 (0.17–0.59) | <0.001  |
| Recanalization successful | 1.01 (0.16–6.42) | 0.988   |
| Symptom-to-final angiogram time | 1 (0.99–1.01) | 0.999   |
| Age | 0.87 (0.79–0.96) | 0.004   |
| NIHSS baseline | 0.936 (0.81–1.08) | 0.371   |
| CBV-ASPECTS baseline | 0.63 (0.45–0.89) | 0.008   |
| Recanalization successful | 0.27 (0.06–1.22) | 0.089   |
| Symptom-to-final angiogram time | 1.01 (0.06–2.22) | 0.081   |
| Age | 0.92 (0.87–0.97) | 0.004   |
| NIHSS baseline | 1.03 (0.92–1.16) | 0.560   |
| Collateral score | 0.63 (0.45–0.89) | 0.100   |
| Recanalization successful | 0.25 (0.05–1.35) | 0.108   |
| Symptom-to-final angiogram time | 1.01 (0.99–1.01) | 0.455   |
| Age | 0.96 (0.91–1.02) | 0.961   |
| NIHSS baseline | 1.13 (1–1.28) | 0.045   |

ncCT: non-contrast computed tomography; CBV: cerebral blood volume; ASPECTS: Alberta Stroke Program Early CT score; NIHSS: National Institute of Health Stroke Scale

Table 4. Predictive value of imaging parameters for hemicraniectomy

|                | AUROC (95% CI) | Cut-off score (sens, spec) |
|----------------|----------------|---------------------------|
| ncCT-ASPECTS at baseline (median, IQR) | 0.74 (0.68–0.80) | 7 (66.67, 70.68) |
| ncCT-ASPECTS follow-up (n = 173; median, IQR) | 0.95 (0.90–0.98) | 4 (100, 79.22) |
| CBV-ASPECTS (n = 171; median, IQR) | 0.74 (0.67–0.81) | 5 (57.14, 81.08) |
| Collateral score (n = 116; mean ± SD) | 0.68 (0.59–0.77) | 5 (77.78, 59.05) |

IQR: Interquartile range, SD: standard deviation, ncCT: non-contrast computed tomography, CBV: cranial blood volume, ASPECTS: Alberta Stroke Program Early CT score
vs 50% and 86%) are comparable between the study by MacCallum et al. and our study, indicating that the ASPECTS is likely to be a robust tool for risk stratification in patients with major stroke in the MCA territory.

However, the study by McCallum et al. does not report recanalization rates and did not include patients with EVT, while 27% of included patients received intravenous thrombolysis [25]. Successful recanalization is associated with improved outcome, however patients undergoing successful EVT with low baseline ASPECTS are at risk to develop space occupying infarctions anyway. In our study 8 (40%) from 20 patients in the DH-group were successfully recanalized, but required DH after all. Consequently, clinicians should not rely on successful recanalization alone as a predictor for good clinical outcome, but should include the ASPECTS for risk stratification. Moreover, showing even a higher predictive value of ncCT-ASPECTS on follow-up, our study stresses the need for regular follow-up ncCTs 24 hours after EVT, and maybe even earlier in patients showing an ASPECTS < 7 on baseline ncCT. The latest generation of flat detector CT allows for ASPECTS evaluation of the supratentorial brain within the angio suite [26] and patients with low ASPECTS on the flat detector CT or large contrast agent extravasation could benefit from earlier follow up ncCT, especially if the patents neurological status can’t be judged adequately (e.g. caused by sedative drugs and/or intubation).

Our study could also demonstrate that CBV-ASPECTS is useful for risk stratification concerning the requirement for DH. The lower cut-off at baseline compared to ncCT-ASPECTS (5 vs 7) could indicate that CBV-ASPECTS earlier identifies patients at risk for DH, as cut-off ncCT-ASPECTS at follow-up (with the highest predictive value) was comparable to CBV-ASPECTS at baseline (5 vs 4). Therefore, CBV indicates the core infarction which can’t be rescued by reperfusion therapies while changes in ncCT are more dynamic during the first 24 hours after stroke. However, our findings have to be interpreted with caution, as a recent study by Geuskens et al. [27], including patients from the MR-CLEAN trial [1], showed a significant proportion of patients with misclassification of ischemic core region and as different processing software packages include different thresholds of perfusion parameters, which again have been shown to produce different results [28, 29].

The CS described by Menon et al. is also likely to be useful for the prediction of DH-requiring [14]. In our study, there was a trend towards a lower CS in patients with DH and predictive value was lower compared to the ASPECTS. On the one hand, this could be explained by the lower patient number, in which the Menon score had been determined (n = 116) and thus a problem of statistical power; on the other hand, this score could be more variable concerning inter rater reliability and susceptibility to fluctuations of systemic blood pressure, as the autoregulation of cerebral arteries fails and perfusion (of the penumbra) is depends on mean arterial pressure [30].

Considering both the overall longer pre- and intra-clinical periods of multidisciplinary stroke treatment and lower CS in the DH-group, it is likely that collateralization as well as time from symptom onset to final angiogram and EVT influence the extent of cerebral infarction. As difference between symptom onset to admission was not significant different between the DH- and non-DH group, one could speculate that in-hospital delays of treatment and time of EVT influences the risk for DH more than pre-hospital delay, which is in line with a recent meta-analysis on periprocedural factors in the large randomized thrombectomy trials [31].

Strength of our study is the inclusion of prospectively derived patient data and the use of the robust outcome parameter DH in contrast to a clinical outcome construct like malignant infarction, which varies in its definition. The limitations of our study the monocentric design and low number of patients quantified with the CS.

In conclusion, our study provides additional evidence for the predictive value of ASPECTS obtained by initial, multimodal stroke imaging and underlines the importance of regular
follow-up ncCT. Imaging information seems to bear important information for the clinician for risk stratification besides known clinical risk factors like age and large vessel occlusion. Other studies with a multicenter design are needed to confirm our findings and to further determine the best timepoint for follow-up imaging in patients at risk for the development of space-occupying infarction.

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References

1. Berkhemer OA, Fransen PS, Beumer D, van den Berg LA, Lingsma HF, Yoo AJ, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med. 2015; 372:11–20. doi: 10.1056/NEJMoA1411587 PMID: 25517348
2. Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med, 2015; 372:1019–1030. doi: 10.1056/NEJMoA1414905 PMID: 25671798
3. Campbell BC, Mitchell PJ, Kleining TJ, Dewey HM, Churilov L, Yassi N, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2015; 372:1009–1018. doi: 10.1056/NEJMoA1414792 PMID: 25671797
4. Jovin TG1, Chamorro A, Cobo E, de Miquel MA, Molina CA, Rovira A, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med. 2015; 372:2296–2306. doi: 10.1056/NEJMoA1503780 PMID: 25882510
5. Saver JL, Goyal M, Bonafe A, Diner HC, Levy EI, Pereira VM, et al. Stent retriever thrombectomy after intravenous tPA vs tPA alone. N Engl J Med. 2015; 372:2285–2295. doi: 10.1056/NEJMoA1415061 PMID: 25882376
6. Goyal M, Menon BK, van Zwan WH, Dippel DW, Mitchell PJ, Demchuk AM, et al., Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet 2016; 387:1723–1731. doi: 10.1016/S0140-6736(16)00163-X PMID: 26888852
7. Sporns PB, Minnerup J, Warneke N, Dziewas R, Hanning U, Berkmeyer S, et al. Impact of the Implementation of Thrombectomy with Stent Retrievers on the Frequency of Hemicraniectomy in Patients with Acute Ischemic Stroke. Clin Neuroradiol 2015 [Epub ahead of print].

8. Schwab S, Steiner T, Aschoff A, Schwarz S, Steiner HH, Jansen O, Hacke W. Early hemicraniectomy in patients with complete middle cerebral artery infarction. Stroke 1998; 29:1888–1893. PMID: 9731614

9. Mori K, Nakao Y, Yamamoto T, Maeda M. Early external decompressive craniectomy with duroplasty improves functional recovery in patients with massive hemispheric embolic infarction: timing and indication of decompressive surgery for malignant cerebral infarction. Surg Neurol. 2004; 62:420–429. doi: 10.1016/s0039-128x(03)00175-9 PMID: 15518850

10. Vaheki H, Hofmeijer J, Juettler E, Vicaut E, George B, Algra A, et al. Early decompressive surgery in malignant infarction of the middle cerebral artery: a pooled analysis of three randomised controlled trials. Lancet Neurol 2007; 6:215–222. doi: 10.1016/s1474-4422(07)70036-4 PMID: 17303527

11. Jovin TG, Yonas H, Gebel JM, Kanal E, Chang YF, Grauovac SZ, et al. The cortical ischemic core and not the consistently present penumbra is a determinant of clinical outcome in acute middle cerebral artery occlusion. Stroke. 2003; 34:2426–2433. doi: 10.1161/01.STR.000012323.81947.C9 PMID: 14500935

12. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. ASPECTS Study Group. Alberta Stroke Programme Early CT Score. Lancet 2000; 355:1670–1674. PMID: 10905241

13. Pexman JH, Barber PA, Hill MD, Sevick RJ, Demchuk AM, Hudon ME, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. Am J Neuroradiol. 2001; 22:1534–1542. PMID: 11595901

14. Vagal A, Menon BK, Foster LD, Livorine A, Yeatts SD, Qazi E, et al. Association between ct angiogram collaterals and ct perfusion in the interventional management of stroke iii trial. Stroke. 2016; 47:535–538. doi: 10.1161/STROKEAHA.115.011461 PMID: 26658448

15. Schregel K, Behme D, Tsogkas I, Krauth M, Maier I, Karch A, Nikolajczyk R, Hinz J, Liman J, Psychogiou MN. Effects of Workflow Optimization in Endovascularly Treated Stroke Patients—A Pre-Post Effectiveness Study. PLoS One. 2016; 11:e0169192. doi: 10.1371/journal.pone.0169192 PMID: 28036401

16. Zaidat OO, Yoo AJ, Khatri P, Tomsono TA, von Kummer R, Saver JL, et al. Recommendations on angiographic revascularization grading standards for acute ischemic stroke: a consensus statement. Stroke 2013; 44:2850–2863. doi: 10.1161/STROKEAHA.113.001972 PMID: 23920012

17. Tsogkas I, Krauth M, Schregel K, Behme D, Wasser K, Maier I, et al. Added value of CT perfusion compared to CT angiography in predicting clinical outcomes of stroke patients treated with mechanical thrombectomy. Eur Radiol. 2016; 26:4213–4219. doi: 10.1007/s00330-016-4257-y PMID: 26905866

18. Treadwell SD, Thanvi B. Malignant middle cerebral artery (MCA) infarction: pathophysiology, diagnosis and management. Postgrad Med J 2010; 86:235–242. doi: 10.1136/pgmj.2009.094292 PMID: 20354047

19. Wijdicks EF, Rabinstein AA. Absolutely no hope? Some ambiguity of futility of care in devastating acute stroke. Crit Care Med 2004; 32:2332–2342. PMID: 15640651

20. Kasner SE, Demchuk AM, Berrouschotet J, et al. Predictors of Fatal Brain Edema in Massive Hemispheric Ischemic Stroke. 2001; 32:2117–23. PMID: 11546905

21. Grotta J. Lubeluzole treatment of acute ischemic stroke. The US and Canadian Lubeluzole Ischemic Stroke Study Group. Stroke. 1997; 28:2338–46. PMID: 9412611

22. Qureshi AJ, Suarez JL, Yahia AM, Mohammad Y, Uzun G, Suri MF, et al. Timing of neurologic deterioration in massive middle cerebral artery infarction: a multicenter review. Crit Care Med 2003; 31:272–277. doi: 10.1097/01.CCM.0000044503.35843.BD PMID: 12545028

23. von Kummer R, Meyding-Lamade U, Forsting M, Rosin L, Rieke K, Hacke W, et al. Sensitivity and prognostic value of early CT in occlusion of the middle cerebral artery trunk. Am J Neuroradiol 1994; 15:9–15. PMID: 8141071

24. Krieger DW, Demchuk AM, Kasner SE, Jauss M, Hantson L. Early clinical and radiological predictors of fatal brain swelling in ischemic stroke. Stroke 1999; 30:287–292. PMID: 9933261

25. MacCallum C, Churilov L, Mitchell P, Dowling R, Yan B. Low alberta stroke program early CT score (ASPECTS) associated with malignant middle cerebral artery infarction. Cerebrovasc Dis 2014; 38:39–45. doi: 10.1159/000363619 PMID: 25228461

26. Leyhe JR, Tsogkas I, Hesse AC, Behme D, Schregel K, Papageorgiou I, et al. Latest generation of flat detector CT as a peri-interventional diagnostic tool: a comparative study with multidetector CT. J Neurointerv Surg. 2016 [Epub ahead of print]
27. Geuskens RR, Borst J, Lucas M, Boers AM, Berkhemer OA, Roos YB, et al. Characteristics of Misclassified CT Perfusion Ischemic Core in Patients with Acute Ischemic Stroke. PLoS One. 2015; 10: e0141571. doi: 10.1371/journal.pone.0141571 PMID: 26536226

28. Fahmi F, Marquering HA, Streekstra GJ, Beenen LFM, Velthuis BK, VanBavel E, et al. Differences in CT perfusion summary maps for patients with acute ischemic stroke generated by 2 software packages. Am J Neuroradiol. 2012; 33:2074–2080. doi: 10.3174/ajnr.A3110 PMID: 22555577

29. Kudo K, Sasaki M, Yamada K, Momoshima S, Utsunomiya H, Shirato H, et al. Differences in CT Perfusion Maps Generated by Different Commercial Software: Quantitative Analysis by Using Identical Source. Neuroradiology. 2010; 254:200–209.

30. Eames PJ, Blake MJ, Dawson SL, Panerai RB, Potter JF. Dynamic cerebral autoregulation and beat to beat blood pressure control are impaired in acute ischaemic stroke. J Neurol Neurosurg Psychiatry. 2002; 72:467–472. doi: 10.1136/jnnp.72.4.467 PMID: 11909905

31. Saver JL, Goyal M, Lugt A, et al. Time to Treatment with Endovascular Thrombectomy and Outcomes From Ischemic Stroke: A Meta-analysis. JAMA, 2016; 316:1279–1288. doi: 10.1001/jama.2016.13647 PMID: 27673305