Original research

Brain atrophy predicts mortality after mechanical thrombectomy of proximal anterior circulation occlusion

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ABSTRACT

Background Brain atrophy is associated with an inferior functional outcome in patients undergoing mechanical thrombectomy (MT) for acute ischemic stroke. We hypothesized that brain atrophy determined from pre-interventional non-contrast-enhanced CT scans would also be linked to increased mortality in this cohort.

Methods A total of 204 patients treated with MT for acute occlusions of the internal carotid artery (ICA) or the M1 segment of the middle cerebral artery (M1) at Tampere University Hospital, Finland between 2013 and 2017 were retrospectively studied. Brain atrophy index (BAI), masseter muscle surface area and density, chronic ischemic lesions, and white matter lesions were evaluated from pre-interventional CT studies. Logistic regression was applied in analyzing the association of BAI with 3-month mortality.

Results Median age at baseline was 69.9 years (IQR 15.6) and mortality at 3 months was 13.2% (n=27). BAI, measured with an excellent reproducibility (intraclass correlation coefficient ≥0.894, p<0.001), was significantly associated with age (r=0.54), white matter lesions (r=0.43), dental status (r=−0.31), masseter area (r=−0.24), masseter density (r=−0.28), and chronic ischemic lesions (r=0.24) (p<0.001 for all). In univariable analysis, BAI demonstrated a strong association with mortality (OR 2.02, 95% CI 1.34 to 3.05, per 1 SD increase), and none of the other factors associated with mortality remained as significant when included in the same multivariable model. The results remained similar when extending the follow-up up to 2.5 years.

Conclusions Brain atrophy predicts 3-month mortality after MT of the ICA or the M1 independent of age, masseter sarcopenia, chronic ischemic lesions, or white matter lesions.

INTRODUCTION

Mechanical thrombectomy (MT) is regarded as the treatment of choice for patients with acute ischemic stroke (AIS) due to proximal anterior circulation occlusion.1–4 Despite the introduction of this method as well as the overall development of interventional techniques, medical therapy, and preventive measures, there is still potential for improvement in the post-interventional survival of patients with AIS, whereby it is crucial to identify key prognostic markers applicable for clinical practice.

Identified predictors of mortality after a large vessel ischemic stroke include stroke severity, time to treatment after symptom onset, unsuccessful recanalization, poor collateral circulation, age, sex, diabetes, atrial fibrillation, renal insufficiency, frailty, and the presence of symptomatic intracranial hemorrhage. Furthermore, in the general stroke population, the presence of white matter lesions (WMLs) has been linked to poorer outcome, but a similar association has not yet been demonstrated in patients treated with MT.5–8 Chronic ischemic lesions (CILs), in turn, were linked to post-interventional outcome after MT in our previous study.9 The Alberta Stroke Program Early CT Score (ASPECTS) has also been established as a prediction tool in this cohort.10

Brain atrophy can be easily measured by determining the bicaudate index or brain atrophy index (BAI) from CT scans.11 It is independently associated with increased mortality in older individuals, patients with manifest arterial disease, and elderly trauma patients.11–14 Furthermore, in patients with AIS undergoing MT, cerebral atrophy has been linked to inferior functional outcome.15 Moreover, brain atrophy is associated with physical frailty,16–17 and in our previous study we showed that sarcopenia, represented by masseter muscle area and density, is associated with poor 3-month survival after MT.18 The potential predictive value of BAI and its dependence on sarcopenia as well as other risk factors in patients with AIS treated with MT remains poorly defined. We hypothesized that including BAI in multivariable models could improve the prediction of mortality after MT due to AIS.

METHODS

Patients

We retrospectively investigated patients treated with MT at Tampere University Hospital between January 2013 and December 2017 (n=432). Non-contrast-enhanced computed tomography (NECT), CT angiography (CTA), and in most cases, CT perfusion (CTP) scanning were included in the imaging protocol. Individuals transferred for treatment from other hospitals were re-evaluated on arrival. Patient selection for MT was conducted by a stroke neurologist and a neurointerventional radiologist. Absence of extensive irreversible ischemic changes and hemorrhage in NECT, the
presence of a proximal occlusion in the CTA, and a sufficient
amount of salvageable tissue in CTP imaging when available
were prerequisites for MT. Even patients arriving after 6 hours
from symptom onset or suffering from a wake-up stroke were
treated with MT on the condition that no large infarct could be
detected and there was salvageable tissue. In patients with a
history of moderate or severe dementia, MT was withheld.

Patients with a thrombus of the internal carotid artery (ICA)
or the M1 segment of the middle cerebral artery (M1), suffi-
cient quality digitally stored pre-interventional NECT and CTA
scans, an ASPECT score of >7 at the 24-hour CT, absence of
substantial parenchymal hematoma after MT, and surviving
a minimum of 24 hours after the intervention were analyzed.
Patients with main thrombus in a location other than ICA or M1
(n=100) were excluded. Seven patients, originally diagnosed
with an ICA thrombus, had a high-grade stenosis of the ICA or
the common carotid artery and were therefore left out of the
analyses. Furthermore, nine patients were excluded due to CT
artifacts caused by metallic dental fillings which inhibited muscle
measurements. Those with larger infarcts (n=102), parenchymal
hematoma 2, or remote parenchymal hematoma 2 (n=9) at
24 hours were excluded because of the high likelihood of having
a poor 3-month outcome, thus masking potential weaker predic-
tive signals. Additionally, one patient died within 24 hours
and was hence excluded from the study. Online supplementary
figure 1 shows the inclusion/exclusion criteria of study patients.
A total of 228 patients (52.8% of individuals treated with MT)
were excluded.

Thrombus locations in the excluded cohort were as follows:
ICA in 78, M1 segment in 111, M2 segment in 81, M3 segment
in 11, basilar artery in 24, P1 segment in 7, A1 segment in 1, A2
segment in 1, A3 segment in 3, and major vein thrombi in 7 cases.
Fifty-two of the excluded patients had occlusions in multiple
locations. The excluded patients did not differ significantly from
the study subjects with respect to age, sex, or a history of hyper-
tension, diabetes, or atrial fibrillation. Coronary artery disease
was significantly less prevalent and brain edema more prevalent
in the excluded patients compared with the included patients
(9.2% vs 16.2%, p=0.029 and 49.1% vs 28.9%, p<0.001,
respectively).

Imaging parameters and radiological assessment
CT imaging was conducted with a 64-row multidetector CT
scanner (General Electric LightSpeed VCT, GE Healthcare,
Milwaukee, Wisconsin, USA). The parameters 120 kV with
AUTO mA and SMART mA technic, noise index 3.3, 40%
adaptive statistical iterative reconstruction (ASIR), collimation
4×3 mm, and rotation 0.5 s were applied for NECT. Images
were obtained axially (0.625 mm slices). Subsequently, adja-
cent axial slices were reconstructed to the thickness of 5 mm
and coronal slices to the thickness of 2 mm. The CTA scanning
range extended from the aortic arch to the vertex of the skull
and a helical technique was used. The following imaging param-
eters were applied: 100 kV with AUTO mA and SMART-mA,
noise index 9, 40% ASIR, collimation 40×0.625 mm, rotation
0.5 s, and pitch factor 0.984. Automatic bolus triggering of the
contrast agent (iomeprol, 350 mg I/ml, IOMERON, Bracco,
Milan, Italy) from the aortic arch was used and it was admin-
istered with an 18-gauge cannula via an antecubital vein applying
a double-piston power injector with a 5 mL/s flow rate (70 mL of
contrast agent followed by a 50 mL saline flush).

One radiologist (SP) determined BAI from NECT images.
The measurements were performed at the same axial level as
the heads of the caudate nuclei: the shortest distance between

Figure 1  Representative preoperative non-contrast-enhanced
CT image of a patient treated with mechanical thrombectomy
demonstrating the measurement of brain atrophy index.

these (intercaudate distance) and the distance between the inner
skull surfaces (interskull distance) were measured in the same
coronal plane (figure 1). BAI values were obtained by dividing
the intercaudate distance by the interskull distance. Sarcopenia
was evaluated from CTA scans by measuring the masseter muscle
area (MA, mm²) and mean radiodensity (MD, Hounsfield Unit,
HU) as described in our previous study. The presence of teeth
was classified into three categories: (1) no teeth, (2) any missing
teeth, and (3) no evidence of missing teeth. Average masseter
area (MAavg, mean of left and right MA) and masseter density
(MDavg, mean of left and right MD) were calculated. The pres-
ence of WMLs was assessed from NECT images according to
the Fazekas scale and scored as follows: 0, absence of lesions,
1, small caps or pencil-thin lining in the periventricular white
matter or punctate foci in other white matter areas, 2, smooth
halo in the periventricular white matter or beginning confluence
of focal lesions, and 3, irregular periventricular hyperintensity
extending into deep white matter or large confluent lesions in
other white matter areas. Admission NECT was also evaluated
for the presence, region, and side of CILs entailing territorial
infarcts and lacunar infaracts (including branched atheromatous
disease-type lesions). The excellent inter- and intra-observer
reliability of masseter area and density measurements have been
demonstrated by independent observers in previous studies. The
same reproducibility analyses were performed for BAI and
Fazekas in order to confirm inter-observer reliability. Conse-
quentially, 30 CT scans of the MT patients were randomly selected
and evaluated by two independent radiologists. The technical
outcome was evaluated with the modified Thrombolysis In Cere-
bral Ischemia (mTICI) grading from digital subtraction angiog-
raphy studies at the end of the procedure. The modified Rankin

Figure 1  Representative preoperative non-contrast-enhanced
CT image of a patient treated with mechanical thrombectomy
demonstrating the measurement of brain atrophy index.
Scale (mRS) score was assessed by a neurologist 3 months after MT over the telephone or during a follow-up visit.

Statistical analysis
Statistical analyses were performed with SPSS 25 for Mac OS X. Normality distributions of parameters were observed using histograms and Kolmogorov–Smirnov test with Lilliefors Significance Correction. Medians with IQR were reported for non-categorical variables. For generalizability, BAI, MAavg, and MDavg were reported as means and SD. Counts with frequencies were used for categorical variables. The cohort was divided into three subgroups based on BAI tertiles and the risk factors were reported accordingly. Based on normality, parametric or non-parametric tests were selected for comparisons. For two independent groups, the Mann–Whitney U test was selected for non-gaussian continuous variables. For three independent groups, the Kruskall–Wallis test was used for non-gaussian and one-way ANOVA for normally distributed variables. The Chi-square test was used for categorical comparisons. The intraclass correlation coefficient (ICC) was applied to estimate reproducibility—that is, inter-observer variability of the BAI measurements and Fazekas scale. ICC >0.75 was classified as excellent reproducibility using two-way random single measurements with consistency and absolute agreements along with 95% confidence intervals.

 pairwise association between the risk factors or other clinical variables and BAI were evaluated with Pearson correlation coefficient analysis. The association between BAI and risk factors significantly correlated with it was further examined with multivariable linear regression analysis. Multicollinearity was also tested by calculating the variance inflation factor (VIF) values for the significantly correlating factors. Univariable and multivariable logistic regression analyses were used to investigate the associations between 3-month mortality and each risk factor. Parameters associated with mortality (p<0.1) in univariable analyses were selected as covariates in the multivariable analyses. Multivariable models with BAI were therefore created for age, WML, MAavg, and MDavg. Kaplan–Meier survival analysis was performed to describe the association between BAI tertiles and overall mortality. The Log rank test was used to compare the survival distributions between the tertiles. BAI, MAavg, and MDavg were z-scored and reported odds ratios (ORs) correspond to a 1 SD increase in the parameter value. A good technical outcome of treatment was defined as mTICI score ≥2b and a good clinical outcome as mRS 0–2 at 3 months. The sample size of the study is sufficient (80% power with a two-sided alpha value of 0.05) for detecting continuously distributed risk factors that correlate with r≥0.24 with mortality (effect size estimate medium by Cohen’s d value 0.483).

Ethical considerations
The study was conducted following the ethical principles of the Declaration of Helsinki and approved by the Pirkanmaa Hospital District Science Center. As this study was conducted retrospectively based on patient records, ethics committee approval or informed patient consent were not required.

RESULTS
Patient characteristics
The demographics of the study patients (n=204) are shown in table 1. Patients were predominantly male (61.3%) and median age was 69.9 years (IQR 15.6). Altogether 157 patients (77.0%) had M1 thrombus, 68 patients (33.3%) ICA thrombus, and 21 patients (10.3%) both. There were significant differences in age, WMLs, CILs, dental status, MAavg, and MDavg among the BAI tertiles. Patients within the highest tertile were older and had more WMLs and CILs than patients in the other tertiles. Furthermore, patients within the lowest tertile had fewer missing teeth than other patients. MAavg and MDavg values decreased as BAI increased. Good procedural success was achieved in 186 patients (91.2%). The 3-month mRS was available for 179 patients (87.7%) of which 114 (63.7%) experienced a good clinical outcome.

Determinants of BAI
Age (r=0.54, p<0.001), WMLs (r=0.43, p<0.001), dental status (r=−0.31, p<0.001), MAavg (r=−0.24, p<0.001), MDavg (r=−0.28, p<0.001), and CILs (CIL: r=0.24, p<0.001; lacunar: r=0.23, p<0.001; multiple: r=0.19, p=0.008) correlated significantly with BAI in Pearson coefficient analysis (online supplementary table 1). According to linear regression analysis adjusted with all significant correlating factors, only age, WMLs, and lacunar CILs were independently associated with BAI (p<0.01 for all).

Reproducibility of CT measurements
Inter-observer variability was determined for BAI measurement and Fazekas scale with excellent reproducibility as tested by ICC analysis (ICC 0.894–0.956, p<0.001) (online supplementary table 2).

Association of preoperative brain atrophy with 3-month mortality
The follow-up lasted until December 31, 2018 with a median duration of 30.8 months (IQR 28.9, range 0–70.4 months). Three-month mortality was 13.2% (n=27, 62.8% of all deaths) for all patients. The mortality at 3 months differed significantly between BAI tertiles: mortality was 4.9% (n=3) in the lowest tertile, 11.8% (n=9) in the middle tertile, and 22.4% (n=15) in the highest tertile (p=0.013). No patients were lost to follow-up.

In univariable analyses, BAI was significantly associated with increased 3-month mortality (OR 2.02, 95% CI 1.34 to 3.05, per 1 SD increase) (table 2). Other statistically significant predictors were age (OR 1.05, 95% CI 1.01 to 1.09, per 1 year increase), WMLs (Fazekas scale) (OR 1.66, 95% CI 1.15 to 2.41, per one grade increase), MAavg (OR 0.52, 95% CI 0.31 to 0.86, per 1 SD increase), and MDavg (OR 0.55, 95% CI 0.36 to 0.83, per 1 SD increase). Other demographic characteristics or comorbidities were not significantly associated with mortality.

In multivariable analyses, BAI persisted as a predictor of increased mortality (OR range 1.81–1.87, 95% CI 1.16 to 2.93, per 1 SD increase) independent of age or WMLs. In addition to BAI, both MAavg (OR 0.39, 95% CI 0.35 to 1.00, per 1 SD increase) and MDavg (OR 0.63, 95% CI 0.41 to 0.97, per 1 SD increase) were significantly associated with mortality. Further analyses indicated that multicollinearity was not a concern (age, Tolerance=0.57, VIF=1.76; WML, Tolerance=0.70, VIF=1.43; MAavg, Tolerance=0.68, VIF=1.47; MDavg, Tolerance=0.67, VIF=1.50). The association between arrival hemoglobin and 3-month mortality was evaluated in additional analyses showing significance both in the univariable (OR 0.95, 95% CI 0.92 to 0.98, per g/L increase) and multivariable models (OR 0.95, 95% CI 0.93 to 0.98, per g/L increase). Arrival hemoglobin did not weaken the odds ratio (OR=1.99) or statistical significance of BAI (95% CI 1.28 to 3.09) in the multivariable model. Overall mortality during follow-up was 21.1% (n=43). When extending...
Table 1 Characteristics of patients with acute ischemic stroke treated with mechanical thrombectomy

| Risk factor, n (%) | All (n=204) | BAI tertile | P value |
|-------------------|-------------|-------------|---------|
|                   | Lowest (n=61) | Middle (n=76) | Highest (n=67) |
| Age (years), median (IQR) | 69.9 (15.6) | 60.1 (18.9) | 70.4 (10.9) | 76.5 (12.8) | <0.001* |
| Male | 125 (61.3) | 36 (59.0) | 51 (67.1) | 38 (56.7) | 0.405 |
| Hypertension | 89 (43.6) | 21 (34.4) | 39 (51.3) | 29 (43.3) | 0.140 |
| Diabetes mellitus | 35 (17.2) | 8 (13.1) | 13 (17.1) | 14 (20.9) | 0.507 |
| Coronary artery disease | 33 (16.2) | 9 (14.8) | 10 (13.2) | 14 (20.9) | 0.427 |
| Atrial fibrillation | 113 (55.4) | 31 (50.8) | 41 (53.9) | 41 (61.2) | 0.474 |
| M1 thrombus | 157 (77.0) | 47 (77.0) | 57 (75.0) | 53 (79.1) | 0.844 |
| ICA thrombus | 68 (33.3) | 22 (36.1) | 28 (36.8) | 18 (26.9) | 0.389 |
| M1 and ICA thrombus | 21 (10.3) | 8 (13.1) | 9 (11.8) | 4 (6.0) | 0.394 |
| Edema | 59 (28.9) | 15 (24.6) | 24 (31.6) | 20 (29.9) | 0.655 |
| Collateral score <2 | 47 (23.0) | 17 (27.9) | 16 (21.1) | 14 (20.9) | 0.564 |
| ASPECTS 24 hours | 0.763 |
| 8 points | 49 (24.0) | 17 (27.9) | 16 (21.1) | 16 (23.9) |
| 9 points | 73 (35.8) | 21 (34.4) | 30 (39.5) | 22 (32.8) |
| 10 points | 82 (40.2) | 23 (37.7) | 30 (39.5) | 29 (43.3) |
| Arrival hemoglobin (g/L), median (IQR) | 133 (25) | 132 (18) | 133 (31) | 134 (23) | 0.628 |
| Creatinine level (μmol/L), median (IQR) | 77 (28) | 76 (27) | 77 (29) | 79 (32) | 0.421 |
| NIHSS 0 hour, median (IQR) | 15 (8) | 16 (6) | 15 (8) | 15 (8) | 0.655 |
| WMLs (Fazekas), median (IQR) | 0 (1) | 0 (0) | 0 (2) | 1 (1) | <0.001* |
| CILs | 64 (31.4) | 9 (14.8) | 25 (32.9) | 30 (44.8) | 0.001* |
| Multiple CILs | 46 (22.5) | 7 (11.5) | 18 (23.7) | 21 (31.3) | 0.026* |
| Lacunar CILs | 27 (13.2) | 3 (4.9) | 8 (10.5) | 16 (23.9) | 0.005* |
| Dental status | <0.001* |
| No teeth | 37 (18.1) | 4 (6.6) | 19 (25.0) | 14 (20.9) |
| Any missing teeth | 122 (59.8) | 31 (50.8) | 47 (61.8) | 44 (65.7) |
| No evidence of missing teeth | 45 (22.1) | 26 (42.6) | 10 (13.2) | 9 (13.4) |
| Masseter average area (mm²), mean (SD) | 429.7 (119.3) | 460.8 (117.2) | 435.5 (119.5) | 394.8 (113.6) | 0.006* |
| Masseter average density (Hounsfield units), mean (SD) | 64.1 (12.8) | 68.1 (11.8) | 65.0 (11.7) | 59.5 (13.5) | <0.001* |
| Brain atrophy index, mean (SD) | 0.143 (0.033) | 0.106 (0.015) | 0.140 (0.008) | 0.180 (0.022) | <0.001* |

*Statistically significant.

ASPECTS, Alberta Stroke Program Early CT Score; CIL, chronic ischemic lesion; ICA, internal carotid artery; M1, M1 segment of middle cerebral artery; NIHSS, NIH Stroke Scale; WML, white matter lesion.

The follow-up up to 2.5 years, the results of Kaplan–Meier analysis remained similar: patients in the highest and middle BAI tertiles had a significantly worse survival compared with the lowest tertile according to the log rank comparisons (p<0.01 for both) (figure 2).

**Discussion**

We found that BAI measured from admission NECT scans with excellent reproducibility is an independent predictor of 3-month mortality after MT in patients presenting with ICA or M1 occlusions. A 1 SD increase in BAI is associated with a twofold increase in 3-month mortality. None of the other parameters associated with mortality remained as significant as BAI in the multivariable analyses.

To the best of our knowledge, the association between brain atrophy and post-interventional survival in patients undergoing invasive procedures has not been thoroughly investigated. A recent study on trauma patients by Tanabe et al. demonstrated a 1.5 times higher risk of 1-year mortality per each 1 SD increase in BAI, which persisted after adjusting for covariates. Although Tanabe et al. did not find a significant difference in 30-day mortality, their Kaplan–Meier survival curves show a trend resembling our survival curves: most of the deaths occurred within the first 3 months, after which the curves continue to run more parallel. In the aforementioned study, masseter sarcopenia also had a cumulative effect on mortality. Similarly, in our previous work we showed that MDavg and MAavg are independent predictors of 3-month survival after MT of the ICA or M1. Masseter muscle parameters also remained as significant predictors of mortality when included as covariates in the model along with BAI in the present study. This finding suggests that both BAI and masseter sarcopenia are predictors of 3-month mortality in patients treated with MT.

Earlier studies have established that age is a predictor of survival after ischemic stroke and that brain atrophy increases mortality among elderly patients. In consensus with prior research, we also found age to be an important factor predicting mortality, but in the present study we additionally ascertained...
Figure 2  Kaplan–Meier survival curves of patients with acute ischemic stroke treated with mechanical thrombectomy: comparing different brain atrophy index (BAI) tertiles. Patients in the highest and middle BAI tertiles had a significantly worse survival compared with the lowest tertile according to the log rank test (p<0.01 for both comparisons).

Table 2  Unadjusted and adjusted associations between risk factors and 3-month mortality using logistic regression in patients with acute ischemic stroke treated with mechanical thrombectomy

| Risk factor | Unadjusted OR (95% CI) | P value | BAI adjusted OR (95% CI) | P value |
|-------------|------------------------|---------|--------------------------|---------|
| Age, per year increase | 1.05 (1.01 to 1.09) | 0.026* | 1.02 (0.98 to 1.07) | 0.375 |
| M1 thrombus | 0.55 (0.23 to 1.31) | 0.177 | | |
| ICA thrombus | 1.21 (0.52 to 2.80) | 0.662 | | |
| M1 and ICA thrombus | 0.30 (0.04 to 2.35) | 0.252 | | |
| Edema | 1.85 (0.80 to 4.26) | 0.150 | | |
| Collateral score <2 | 1.83 (0.76 to 4.40) | 0.177 | | |
| ASPECTS 24 hours, per point increase | 1.30 (0.76 to 2.21) | 0.341 | | |
| Creatinine level, per μmol/L increase | 1.00 (1.00 to 1.01) | 0.245 | | |
| NIHSS 0 hour, per point increase | 1.04 (0.96 to 1.12) | 0.401 | | |
| WMLs, per Fazekas grade increase | 1.66 (1.15 to 2.41) | 0.007* | 1.37 (0.91 to 2.06) | 0.137 |
| CILs | 1.34 (0.58 to 3.12) | 0.497 | | |
| Multiple CILs | 1.54 (0.63 to 3.79) | 0.347 | | |
| Lacunar CILs | 1.60 (0.55 to 4.66) | 0.388 | | |
| Dental status, per grade increase | 0.58 (0.30 to 1.11) | 0.101 | | |
| MAavg, per SD greater than mean | 0.52 (0.31 to 0.86) | 0.012* | 0.59 (0.35 to 1.00) | 0.050* |
| MDavg, per SD greater than mean | 0.55 (0.36 to 0.83) | 0.004* | 0.63 (0.41 to 0.97) | 0.036* |
| BAI, per SD greater than mean | 2.02 (1.34 to 3.05) | 0.001* | 1.81 to 1.87 (1.16 to 2.93)† | 0.004–0.009† |

*Statistically significant.
†Calculated by adjusting BAI with each significant risk factor individually. Reported as a range of point estimates.

ASPECTS, Alberta Stroke Program Early CT Score; BAI, brain atrophy index; CIL, chronic ischemic lesion; ICA, internal carotid artery; M1, M1 segment of middle cerebral artery; MAavg, masseter average area; MDavg, masseter average density; NIHSS, NIH Stroke Scale; WML, white matter lesion.

that age loses its significance as a predictor when considered together with BAI. Conversely, Tanabe et al found age to be significant even after adjusting for BAI and masseter area. This discrepancy could be explained by the differences in the study populations: the study by Tanabe et al included only patients aged 65 years or older and studied a wide range of trauma patients. Furthermore, Tanabe et al examined mortality over a 1-year period, in which the effect of age is likely to be greater. Our results suggest that both age and BAI are important prognostic factors for patients undergoing MT, although BAI appears to be more relevant in predicting short-term mortality.

In addition to age, our results showed that BAI is also strongly associated with the presence of WMLs and CILs. The association between WMLs and clinical outcome in patients treated with MT is contradictory in prior research. In our study we showed that the presence of WMLs does not persist as a significant predictor of 3-month mortality in the same model with BAI. Our results do not resolve the predictive value of WMLs on the clinical outcome at 3 months. However, they do suggest that BAI is a distinctly stronger predictor of mortality than WMLs in the same time frame. Moreover, WML evaluation is more reliable from magnetic resonance images compared with CT scans, whereas BAI measurements from CT images have shown excellent reliability. Hence, compared with WMLs, BAI could be a more useful prognostic tool for clinical practice. In earlier research, CILs have been associated with poor clinical outcome at 3 months after MT in sexagenarians and older. The study time frame may explain the lack of significant results between CILs and mortality in our analyses: even though the presence of CILs is associated with poor functional outcome at 3 months, its effect on mortality may appear after a longer period. Our analyses on overall mortality, however, suggest that BAI may also have a long-term predictive value. The associations between BAI and CILs and mortality in patients treated with MT in the long term would require additional research.

In our study, hemoglobin persisted as a significant predictor of mortality after adjusting for covariates whereas serum creatinine did not reach statistical significance at any point. Our results on the effect of hemoglobin and creatinine are in line and corroborated by previous studies in stroke patients. Mortality after MT is still relatively high considering the high reperfusion rates. The full picture of factors contributing to the higher mortality risk despite successful recanalization is unclear.
In our previous studies we have demonstrated the excellent feasibility and reliability of MAavg and MDavg measurements from routine CTA images in clinical work and their relation with survival in patients treated with carotid endarterectomy and MT. In the present study we found that brain atrophy is associated with an increased risk of 3-month mortality after MT. Although MRI is frequently used for detection of degenerative brain changes, unlike CT it is often not available in acute situations. BAI measured from routine CT images with excellent reproducibility, similar to masseter parameters, could therefore provide an additional prognostic tool in identifying which patients with a large vessel occlusion will benefit from MT. Identifying patients more susceptible to poor outcomes would enable, for example, better resource allocation for post-procedural rehabilitation. In future studies, severe brain atrophy would even be worth considering when assessing the appropriateness of MT for patients in poor condition.

Our study has some limitations. First, the population of the study only consists of patients with AIS at a single center undergoing MT due to ICA or M1 occlusions, which may limit the generalizability of the results. Second, the retrospective nature of part of the data collection and measurements may further limit the generalizability and expose the results to selection bias as well as potential non-evaluated confounders. Another potential source of confounding is the post hoc exclusion of patients with large strokes (ASPECTS ≤7) or large post-procedural parenchymal hematoma at 24 hours. Exclusion by such strong predictors will probably enhance the effect of BAI on mortality. In addition, high quality data on the pre-stroke functional and nutritional status or all relevant previous medications of the study subjects at the time of the MT were not available.

CONCLUSIONS
Brain atrophy determined from routine pre-interventional non-contrast-enhanced CT scans predicts mortality in patients with AIS with occlusions of the ICA or the M1 segment of the middle cerebral artery treated with MT independent of age, masseter sarcopenia, or the severity of chronic ischemic or white matter lesions.

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