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ASSOCIATION OF MASSETER AREA AND RADIODENSITY WITH THREE-MONTH SURVIVAL AFTER PROXIMAL ANTERIOR CIRCULATION OCCLUSION

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ABSTRACT

BACKGROUND. Masseter area (MA), a surrogate for sarcopenia, appears to be useful when estimating postoperative survival, but there is lack of consensus regarding the potential predictive value of sarcopenia in acute ischemic stroke (AIS) patients. We hypothesized that MA and density (MD) evaluated from pre-interventional computed tomography angiography (CTA) scans predict postinterventional survival in patients undergoing mechanical thrombectomy (MT).

MATERIALS AND METHODS. 312 patients treated with MT for acute occlusions of the internal carotid artery (ICA) or the M1 segment of the middle cerebral artery (M1-MCA) between 2013 and 2018. Median follow-up was 27.4 months (range 0-70.4). Binary logistic (alive at 3 months, OR<1) and Cox regression analyses were used to study the effect of MA and MD averages (MAavg and MDavg) on survival.

RESULTS. In Kaplan-Meier analysis, there was a significant inverse relationship with both MDavg and MAavg and mortality (MDavg p<.001, MAavg p=.002). Long-term mortality was 19.6% (n=61) and three-month mortality 12.2% (n=38). In multivariable logistic regression analysis at three months, per 1-SD increase MDavg (OR 0.61, 95% CI 0.41-0.92, p=.018:) and MAavg (OR 0.57, 95% CI 0.35-0.91, p=.019) were the independent predictors associated with lower mortality. In Cox regression analysis, MDavg and MAavg were not associated with long-term survival.

CONCLUSIONS. In acute ischemic stroke patients, MDavg and MAavg are independent predictors of three-month survival after MT of the ICA or M1-MCA. A 1-SD increase in MDavg and MAavg was associated with a 39-43% decrease in the probability of death during the first three months after MT.

INTRODUCTION

Acute ischemic stroke (AIS) continues to be a significant cause of disability and mortality worldwide.[1] Several randomized trials have demonstrated that mechanical thrombectomy (MT) is the treatment of choice in patients with acute proximal anterior circulation ischemic stroke.[2–6] The number of patients receiving MT is increasing as this treatment is recommended by clinical practice guidelines, the time window from symptom onset to treatment has been widened, and the overall stroke treatment chain has been enhanced.[7] Optimising patient selection is crucial in order to efficiently allocate resources and to continue to improve the overall clinical outcome, especially survival, after AIS.

Recognized predictors of survival after a large vessel ischemic stroke include stroke severity, good collateral circulation, age, sex, diabetes, atrial fibrillation, renal insufficiency, frailty, and intracranial hemorrhage. The Alberta stroke program early computed tomography (CT) score (ASPECTS) has also been validated as a risk assessment tool in this cohort.[8–10] Muscle loss, i.e. sarcopenia, is a major component of frailty. In elderly patients, masseter muscle area correlates with psoas muscle area,[11] which has previously been verified to predict mortality in vascular surgical patients.[12–14] Additionally, masseter area measured from CT scans has been used in evaluating sarcopenia in carotid endarterectomy[15] and elderly blunt trauma patients[11] as well as after severe traumatic brain injury.[16,17] In addition to muscle area, radiodensity has also been ascertained as a marker of sarcopenia.[18] Furthermore, masseter muscle tension and chewing ability correlate with physical fitness and quality of life in the elderly.[19] Sarcopenia can be reliably diagnosed from CT scans by a clinician by measuring muscle area and density from a representative slice.[18,20] The advantages of this method include little or no additional costs, as CT imaging is routinely performed in AIS patients, as well as objectivity and reproducibility. Extensive data on the prevalence of sarcopenia after stroke is available in other studies,[21] but the potential predictive value of sarcopenia in AIS patients treated with MT remains unknown, to the best of our knowledge. We hypothesized that masseter area (MA) and density (MD) measured from standard preoperative CT angiography (CTA) images could predict mortality in a cohort of acute stroke patients undergoing MT.

MATERIALS AND METHODS

Patients

Patients were treated with MT at Tampere University Hospital (TAUH) between January 2013 and February 2018 (n=453). We retrospectively collected the patient data and the times of death from the TAUH patient record database, which is linked to the National Population Register, results of the blood tests from the Fimlab Laboratories Ltd database and CTA images from a picture archiving and communication system (PACS). The initial imaging protocol of stroke patients consisted of non-contrast-enhanced computed tomography (NCCT), CTA, and frequently also CT perfusion (CTP) scanning. The selection of patients as candidates for MT was conducted in a multidisciplinary team consisting of a stroke neurologist and a neurointerventional radiologist, and it was based on the absence of extensive irreversible ischemic changes and hemorrhage in NCCT, a proximal clot position in the internal carotid artery (ICA) or the M1 or M2 segments of the middle cerebral artery, and the amount of salvageable tissue in CTP imaging when available. There were no exclusion criteria for MT based on age, but patients with a history of moderate or severe dementia were treated conservatively. Patients referred to our institution from other hospitals were re-evaluated with at least NCCT and CTA upon arrival before proceeding to the angiographic suite. In line with the results of recent studies, we also treated patients within a longer timeframe, that is, patients presenting after 6 hours from symptom onset or suffering from a wake-up stroke provided that no large infarct could be detected in NCCT and there was still salvageable tissue based on the CTP maps.[22,23] Thrombolysis in cerebral infarction scale (TICI) was used to describe the technical outcome and TICI > 2a was set as a threshold for good outcome.

We included patients presenting with a M1- or ICA-thrombus and available digital preoperative CT and CTA scans (n=312, 68.8%) in the analyses. Position of the clot elsewhere in the cerebral circulation resulted in exclusion from the study (n=141, 31.1%). The excluded patients did not significantly differ from the study subjects with respect to age, sex, or a history of diabetes, hypertension, coronary artery disease, or atrial fibrillation (Supplementary table 1), an ASPECT-score of ≤7 at 0 and/or 24 hours was less common in the excluded patients. Data on dental status, serum creatinine, hemoglobin (Hb), or serum c-reactive protein (CRP) were not available for the excluded patients. Thrombus locations in the excluded cohort were as follows: M2-segment in 73, M3-segment in 14, basilar artery in 24, P1-segment in 8, A1-segment in 1, A2-segment 1, A3-segment 4, and major venous thrombi in 7 cases. 9 patients with ICA or M1 thrombus were excluded due to the artifacts in CTA caused by metallic dental fillings. Furthermore, 15 patients were excluded due to major space intracranial hemorrhages detected after the procedure: 11 patients had parenchymal hemorrhage (PH2), one patient had parenchymal hemorrhage remote (PHr2) and three patients had combination of both.

Imaging parameters and radiological assessment

CT scans were obtained using a 64-row multidetector CT scanner (General Electric LightSpeed VCT, GE Healthcare, Milwaukee, WI, USA). Brain NCCT was performed using the parameters 120 kV with AUTO mA and SMART mA technic, noise index 3.3, collimation 4x5 mm, 40% adaptive statistical iterative reconstruction (ASIR), and rotation 0.5 s. Images were obtained axially (0.625 mm thick slices) and then contiguous axial slices were reconstructed to the thickness of 5 mm and coronal slices to the thickness of 2 mm. CTA was performed with helical technique using a scanning range from the aortic arch to the vertex of the skull. The imaging parameters were 100 kV, AUTO mA and SMART-mA, noise index 9, 40% ASIR, collimation 40 x 0.625 mm, rotation 0.5 s, pitch factor 0.984. The contrast agent (iomeprol, 350 mg I/ml, IOMERON, Bracco, Milan, Italy) was administered via an antecubital vein with an 18-gauge cannula using a double-piston power injector with a flow rate of 5 ml/s using 70 ml of contrast agent followed by a 50 ml saline flush. Automatic bolus triggering from the aortic arch was used.

CTA images were used to measure the area (mm^2) and mean radiodensity (Hounsfield Unit, HU) across the region of interest of the masseter muscle. The measurements were performed after sagittal and coronal tilt adjustment, since in our previous study head tilt was found to have a significant effect on MA measurements.[15] The area and mean radiodensity were calculated from the CTA sections according to tangents along the lower borders of the zygomatic arches in sagittal planes and along the lowest points of the orbitae in coronal planes. Measurements were then made 20 ± 2 mm below the arches by outlining the outer surface of the masseter muscles along the fasciae. We have demonstrated excellent inter-observer reliability of masseter area and density measurements by three independent observers in our previous article.[15] In order to confirm intra-observer reliability, 30 CT scans in this study population were randomly selected and rated by a independent clinician in a repeated manner. Intraclass correlation coefficient (ICC) was determined for MA and MD measurements. The presence of teeth was scored in three categories: 1) no teeth, 2) any missing teeth, and 3) no evidence of missing teeth. Average MA (MAavg, mean of left and right MA) and MD (MDavg, mean of left and right MD) were calculated.

Statistical analysis

The statistical analyses were performed with SPSS 25 for Mac OS X. Reliability of radiological measurements was estimated by intraclass correlation coefficient (ICC) using two-way random single measurement with both consistency and absolute agreement. ICC over 0.75 was classified as excellent reproducibility. Normality distributions of parameters were observed using histograms and Levene's test. Means along with standard deviations were reported for normally distributed variables and medians with interquartile ranges for variables with skewed distributions. Based on normality, parametric or non-parametric tests were selected. The Mann-Whitney U-test was selected for non-Gaussian variables for two independent samples and the Kruskal-Wallis test for three or more independent samples. The Pearson correlation coefficient analysis was used to evaluate the pairwise association between the risk factors or other clinical variables and muscle parameters, and statistically significant ($p<.05$) correlations were checked with the multivariable Cox regression analysis using backward selection algorithm. Kaplan-Meier survival analysis was used to evaluate overall survival using tertiles of MAavg and MDavg. When studying three-month mortality in multivariable binary logistic regression analysis patients were classified as being alive or dead at the three-month fixed time-point. Cox regression was first carried out as univariable analyses, and the proportional hazards assumption was tested by log-minus-log plots. This was followed by a multivariable Cox regression analysis that included parameters associated with mortality ($p<0.1$) in univariable analyses as covariates. Both models, Cox and logistic regression, were adjusted for age, diabetes, local intracranial hemorrhage, and hemoglobin (Hb) level and in addition to these, dental status, atrial fibrillation, and serum creatinine level, which were significant in univariable Cox regression, were included in multivariable analysis. Increased CRP correlated inversely with Hb, but only the highest Hb value was selected for multivariable analysis in order to avoid confounding. Criteria for cerebral edema and local intracranial hemorrhage were determined by The Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST). Interactions between covariates and muscle parameters were tested by bivariate correlation. Age, sex, and dental status were examined and included in separate multivariable models because of their strong *a priori* association with masseter parameters.[24] Due to the emergency nature of AIS patients undergoing MT treatment, weight and height data were missing in the majority of the study cohort and NIH stroke scale in 25 patients (8.0%). We were able to calculate BSA only for 39.1% (n=122) of the patients and it was therefore not included in the multivariable analyses. MDavg did not correlate linearly with weight, height, or BSA in this subpopulation. However, in a subpopulation with the 3-month modified rankin scale (mRS) available (n=267, 85.6% of the population), MDavg and MAavg correlated equally with mRS 3-month in Pearson coefficient analysis (p=.002). The association of age with mortality was analyzed as a time-dependent covariate in all the Cox survival analyses. The main muscle parameters (MAavg and MDavg) were z-scored and reported hazard ratios (HRs) or odds ratios (ORs) correspond to a one standard deviation increase in the muscle parameter.

Ethical considerations

The study was conducted adhering to the ethical principles of the Declaration of Helsinki and was approved by the Pirkanmaa Hospital District Science Center.

RESULTS

Patient characteristics

The study included 312 patients (Table 1 shows the demographic data). The median age of the patients was 69.2 years (IQR 15.3) and 61.1% of the patients were male. Among these, 198 (63.5%) patients had an M1-thrombus, 74 patients (23.7%) an ICA-thrombus, and 40 patients (12.8%) had both an M1- and an ICA-thrombus in the preoperative CTA. TICI scale was > 2a in 283 patients (90.7%) indicating a good technical outcome of MT.

Table 1. Characteristics of acute stroke patients subjected to mechanical thrombectomy.

Risk factor	n=312
Age, median (IQR)	69.2 (15.3)
Female (%)	115 (36.9)
DM (%)	45 (14.4)
HT (%)	132 (42.3)
CAD (%)	43 (13.8)
FA (%)	157 (50.3)
M1-thrombus, n (%)	198 (63.5)
ICA-thrombus, n (%)	74 (23.7)
M1- and ICA-thrombus, n (%)	40 (12.8)
Cerebral edema, n (%)	122 (39.1)
Collateral Score, median (IQR)	2 (2)
NIH Stroke Scale, median (IQR)	16 (7)
ASPECTS 0h ≤ 7, n (%)	91 (29.2)
ASPECTS 24h ≤ 7, n (%)	99 (31.7)
TICI ≥ 2b (%)	283 (90.7)
Arrival Hb (g/l), median (IQR)	133 (22)

Arrival CRP(mg/l), median (IQR)	3 (7)
Creatinine level (µmol/l), median (IQR)	77 (29)
Teeth, n (%)	
No teeth	55 (17.6)
Any missing teeth	184 (59.0)
No evidence of missing teeth	73 (23.4)
MDavg (HU), (SD)	63.7 (12.4)
MAavg (cm^2), (SD)	4.3 (1.16)

DM, Diabetes mellitus; HT, hypertension; CAD, Coronary artery disease; FA, atrial fibrillation; M1, M1 segment of the middle cerebral artery; ICA, internal carotid artery; Hb, hemoglobin; CRP, c-reactive protein; ASPECTS, the Alberta stroke program early CT score; TICI, Thrombolysis in cerebral infarction scale; MDavg, Masseter density average; MAavg, Masseter area average.

Determinants of masseter area

Table 2 presents the MAavg and MDavg values of the cohort. Age, dental status, and sex were strongly associated with MAavg and MDavg ($p<.001$ for all). More specifically, advanced age, female sex, and poor dental status were linked to decreased MAavg and MDavg.

Table 2. Radiological parameters of acute stroke patients subjected to mechanical thrombectomy.

		Age tertiles				Teeth category				Gender		
	All (IQR)	T1	T2	T3	p	1	2	3	p	M	F	p
MAavg	4.1 (1.6)	4.7	3.9	3.6	<.001[a]	3.3	4.1	4.8	<.001[a]	4.5	3.6	<.001[b]
MDavg	63.8 (15.9)	70.3	63.5	59.0	<.001[a]	55.5	62.5	72.5	<.001[a]	65.5	61.0	<.001[b]

Masseter average area (MAavg, cm^2) and masseter average density (MDavg, Hounsfield Units) are presented as medians (interquartile range) in all patients and as medians and tertiles indicated as T1, T2 and T3 according to age, in different teeth categories (1=no teeth, 2=any missing teeth and 3=no evidence of missing teeth according to computed tomography analysis) and in male (M) and female (F) genders. [a] Statistically significant difference between the oldest and the youngest tertile and teeth categories ($P<.05$, Kruskal-Wallis test). [b] Statistically significant difference compared to males ($P<.05$, Mann-Whitney-U test).

Reproducibility of the CT measurement

Intraobserver variability of the MDavg and MAavg were excellent as tested by ICC analysis (ICC .839-.981, p< 0.001) (Supplementary table 2).

Association of preoperative masseter area and density with mortality

The follow-up lasted until December 31th, 2018 with the median duration being 27.4 months (IQR 30.2, range 0-70.4 months). According to the Kaplan-Meier survival analysis, most of the deaths occurred within the first 3 months (n=38, 62.3% of all deaths, 3-month mortality 12.2%) and, in line with this, the tertiles of MDavg and MAavg were almost parallel after three months of follow-up. Overall, there was an inverse relationship between both MDavg and MAavg and mortality in the log-rank test (p<.001 to p=.002) (figure 1). Long-term mortality was 19.6% (n=61) and no patients were lost to follow-up. The risk of death across the full range of MDavg showed an inverse linear relationship between standardized MDavg and mortality with a tendency for growth in the risk of mortality when approaching the lowest end of the MDavg range (Supplementary figure 1).

Univariable and multivariable binary logistic regression analyses were used to study the association of risk factors with three-month survival (Tables 3). MDavg and MAavg (OR 0.61, 95% CI 0.41-0.92, p=.018 and OR 0.57, 95% CI 0.35-0.91, p=.019; per 1-SD increase, respectively) as well as the Hb level (OR 0.98, 95% CI 0.96-1.00, p=.018 -.020) were independently associated with lower mortality. Furthermore, despite adding *a priori* risk factors (age, teeth, gender) strongly associated with MAavg and MDavg (Table 2) in multivariable analyses, increased MDavg and MAavg persisted as predictors of lower mortality (MDavg OR 0.58, 95% CI 0.39-0.86, p=.007; MAavg OR 0.52, 95% CI 0.32- 0.85, p=.009) (Supplementary table 3).

In multivariable Cox regression analyses of long-term survival, increased MDavg (HR 0.69, 95% CI 0.51-0.94, p=.017, per 1-SD increase) was independently associated with a 31% decrease in the probability of death, whereas MAavg was not statistically associated with long-term mortality (HR 0.74, 95% CI 0.53-1.03, p=.075) (Supplementary table 4). When multivariable Cox regression was performed only on patients surviving past the first three months after the intervention (n=274), MDavg and MAavg no longer showed a statistically significant association with survival (Supplementary table 5). Patients who died within the first three months postoperatively had smaller MAavg (4.33 vs. 3.68 cm^2, p=.001) and MDavg (64.6 vs. 57.3 HU, p=.001) compared to those alive after three months.

Table 3. Univariable and multivariable binary logistic regression on the association with 3-month postoperative mortality.

	Unadjusted		Adjusted with MDavg		Adjusted with MAavg	
Risk factor	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
Age (years)	1.0 (1.0-1.1)	.08*	1.00 (0.96-1.04)	.92	1.00 (0.97-1.04)	.97
Gender	1.5 (0.7-2.9)	.29	-		-	
DM	1.9 (0.9-4.7)	.09*	1.49 (0.60-3.07)	.39	1.74 (0.70-4.33)	.23
HT	1.0 (0.5-2.0)	.98	-		-	
CAD	2.2 (1.0-5.0)	.06*	1.77 (0.70-4.46)	.23	1.46 (0.58-3.64)	.42
AF	1.5 (0.7-2.9)	.28	-		-	
Cerebral edema	1.5 (0.7-2.9)	.27	-		-	
Unfavorable CS (0-1)	0.6 (0.3-1.3)	.19	-		-	
NIH Stroke Scale	1.0 (1.0-1.1)	.21	-		-	
ASPECTS 0h ≤ 7	1.0 (0.5-2.1)	.98	-		-	
ASPECTS 24h ≤ 7	0.9 (0.4-1.8)	.69	-		-	
Arrival Hb (per unit)	1.0 (0.9-1.0)	.001*	0.98 (0.96-1.00)	.020*	0.98 (0.96-1.00)	.018*
Arrival CRP (per unit)	1.0 (1.0-1.0)	.002*	-		-	
Creatinine (per unit)	1.0 (1.0-1.0)	.29	-		-	

Dental status (per category)	0.6 (0.4-1.1)	.10	-		-	
MDavg	0.5 (0.4-0.8)	.001*	0.61 (0.41-0.92)	.018*	-	
MAavg	0.5 (0.3-0.8)	.002*	-		0.57 (0.35-0.91)	.019*

Binary logistic regression analysis. A Multivariable model including parameters with P<.1 in univariable analysis. OR, Odds ratio; CI, Confidence interval; DM, diabetes mellitus; HT, hypertension; CAD, coronary artery disease; AF, atrial fibrillation; CS, collateral score; ASPECTS, the Alberta stroke program early CT score; Hb, hemoglobin (g/l); CRP, c-reactive protein (mg/l); MAavg, Masseter area average; MDavg, Masseter density average. Odds ratio (OR) estimated from binary logistic regression model with 3 months mortality after operation (cut-off 3 months). Odds ratios for MAavg and MDavg correspond to 1 standard deviation increase. * = statistical significance.

DISCUSSION

We found that MDavg and MAavg measured from preinterventional CTA scans are independent predictors of three-month mortality after MT of ICA or M1-MCA occlusions in patients with AIS and with a good initial technical outcome. During the first three months after the intervention, increases of 1SD in MDavg and MAavg were associated with a 39% and a 43% decrease in the probability of death, respectively. However, when analyzing only patients surviving past the initial three months no association of MDavg and MAavg with mortality could be demonstrated. We have previously reported the excellent feasibility and reliability of MDavg and MAavg measurements from routine CT images in clinical work.[15] This study demonstrates MAavg and MDavg to be independent predictors of three-month mortality in AIS patients treated with MT.

Wallace et al. and Hu et al. studied elderly trauma patients and found that MA correlates with survival.[11,16] Short- and long-term mortality were not analyzed separately in either study but similar to the present study, the majority of deaths occurred during the first months of follow-up. Our results may not be directly comparable to the findings in these earlier studies[11,16] due to differences in age and sex distributions, which according to our results can affect MA. In addition, the studies did not adjust for dental status, which has been demonstrated to be associated with MA in the present study and also in our previous study.[15] The association of dental status with the masseter muscle parameters has been proposed to be stronger than that of aging or skeletal muscle index in the elderly.[15,25,26] Dental status is also highly correlated with chewing ability, which, in turn, is associated with overall functional status.[27] In the study by Wallace et al., the patients were markedly older than in our study (mean age 80.0 years vs. median 69.2 years) and consequently the MA values were also smaller.[11] In the study by Hu et al. the proportion of males was higher than in our study (73.1% vs. 63.1%) and correspondingly the mean MA was larger.[16]

Muscle area and density are closely related, and in addition to muscle area, radiodensity has been demonstrated to be a marker of sarcopenia.[18] However, previous brain trauma studies[11,16] did not address MD which, like MA, is correlated to age, gender, and dental status.[15] Interestingly, we found that high mean MD value was the muscle parameter that best predicts survival. It is possible that fat infiltration in the masseter muscle is the first phase in the development of sarcopenia and signals frailty even before MA decreases, but further research is required to verify this.

The strong association between MAavg and MDavg with short-term mortality in AIS patients who received MT differs from our previous findings in patients treated with carotid endarterectomy for (mostly symptomatic) ICA stenoses in that the association with improved survival in the earlier study was evident only in long-term.[15] This may be due to differences in patient selection in the studies, since AIS patients eligible for MT are treated immediately, whereas those treated with carotid endarterectomy are operated mainly within 2 weeks from symptom onset. Additionally, patients with asymptomatic carotid stenoses or suffering from severe stroke are either denied operation or operated on a delayed schedule. Another notable difference between our studies was the lower mean/median MD in carotid endarterectomy patients compared to the MT patients (53.5 ± 16.5 vs. 63.7 ± 12.4 HU) despite comparable age and a higher proportion of males in the endarterectomy cohort. It is possible that this difference could be due to the common occurrence of stenosis also in the external carotid artery and the potential effect this has on the perfusion of the masseter muscles. The fact that in AIS patients the association of MAavg and MDavg with mortality was seen only in short-term follow-up can be correlated with the timing of significant changes in neuronal plasticity which might have its' most significant influence on recovery during the first 3 months after stroke.[28] Our results on the effect of Hb and creatinine values are in line with previous research.[29,30]

This was a single-center study focusing on AIS patients undergoing MT due to ICA or M1-MCA occlusions, which may limit the generalizability of the results. A further limitation is the retrospective nature of part of the data collection and measurements, which may introduce biases. Additionally, high quality data on the functional (as a rule the patients had pre-stroke mRS ≤2 to be eligible to MT) and nutritional status, or all relevant previous medications of the study subjects at the time of the MT was not available. However, our findings on the effect of advanced age, sex, and dental status on MA and MD are compatible with previous reports.[15,25,26] We consider our method of MA and MD measurement reliable according to excellent ICC values in the present and our previous study.[15]

SUMMARY AND CONCLUSIONS

MDavg and MAavg determined from routine pre-interventional CTA scans predict three-month survival in AIS patients suffering from ICA or M1-MCA occlusions treated with MT with a 1-SD increase in MDavg and MAavg corresponding to a 39-43 % decrease in short-term mortality.

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CONFLICTS OF INTEREST STATEMENT

The authors report no conflicts of interest.

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FIGURE LEGENDS

Figure 1. Kaplan-Meier survival plots. Kaplan-Meier survival curve comparing patients in different MDavg and MAavg tertiles in acute stroke patients subjected to mechanical thrombectomy. Patients in the lowest tertile had a significantly worse survival according to the log-rank test ($p<.001$).

ONLINE SUPPLEMENTS

Supplementary table 1. Demographics and computed tomography angiography findings between excluded and included patients.

Features	Sample N=312	Excluded N=141	p-value
Demographics			
Age median (years)	69.2 ± 16.0	69.5 ± 12.0	.815
Male (%)	197 (63.1%)	82 (58.2.0%)	.312
Risk factors			
DM, n	45 (14.4%)	22 (15.6%)	.743
HT, n	132 (42.3%)	65 (46.1%)	.451
CAD, n	43 (13.8%)	12 (8.5%)	.112
AF, n	163 (52.2%)	65 (46.1%)	.405
Procedural variables			
Cerebral edema, n	122 (39.1%)	57 (40.4.6%)	.790
ASPECTS 0h ≤7, n	91 (29.2%)	19 (13.5%)	.001
ASPECTS 24h ≤7, n	99 (31.7%)	25 (17.7%)	.002

DM, Diabetes mellitus; HT, hypertension; CAD, Coronary artery disease; AF, atrial fibrillation; ASPECTS, the Alberta stroke program early CT score. Statistically significant difference ($P<.05$, Kruskal-Wallis or chi-squared test).

Supplementary table 2. Intraclass correlation coefficient (ICC) analysis of masseter CT-measurements.

Variable	ICC[a]	95% CI	ICC[b]	95% CI	P-value
MAavg (cm^2)	.980	.959-.991	.981	.960-.991	< .001
MDavg (HU)	.841	.693-.921	.839	.692-.920	< .001

[a] Model: Intraclass correlation coefficient (ICC) two-way random consistency.

[b] Model: Intraclass correlation coefficient (ICC) two-way random absolute.

MAavg, Masseter area average; MDavg, Masseter density average; HU; Hounsfield Units.

Supplementary table 3. Multivariable binary log regression analysis of 3-month mortality and effect of *a priori* risk factors.

Risk factor	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Age (years)	1.01	(0.97-1.05)	.741	1.00	(0.97-1.05)	.703
Sex	1.16	(0.57-2.37)	.680	0.95	(0.46-1.99)	.898
Dental status (per category)	0.95	(0.49-1.83)	.950	0.95	(0.49-1.83)	.870
MDavg	0.58	(0.39-0.86)	.007*	-	-	-
MAavg	-	-	-	0.52	(0.32-0.85)	.009*

Cox regression proportional analysis. OR, Odds ratio; CI, Confidence of interval. MDavg, Masseter density average; MAavg, Masseter area average. Odds ratio (OR) estimated from binary logistic regression model with 3 month mortality after operation (cut-off 3 months). Odds ratios of MAavg and MDavg correspond to 1 standard deviation increase. * = statistical significance.

Supplementary table 4. Cox regression analysis of the effect of significant risk factors and masseter on long-term mortality.

Risk factor	HR	(95% CI)	p-value	HR	(95% CI)	p-value
Age	1.01	(0.98-1.04)	0.592	1.01	(0.98-1.04)	0.530
DM	1.77	(0.97-3.24)	0.063	1.81	(0.99-3.33)	0.054
AF	1.44	(0.84-2.47)	0.187	1.55	(0.90-2.65)	0.112
Arrival Hb	0.98	(0.97-0.99)	0.004*	0.98	(0.96-0.99)	0.001*
Creatinine level	1.00	(1.00-1.01)	0.166	1.00	(1.00-1.01)	0.061
Dental status	0.85	(0.53-1.36)	0.496	0.81	(0.51-1.30)	0.382
MDavg	0.69	(0.51-0.94)	0.017*	-	-	-
MAavg	-	-	-	0.74	(0.53-1.03)	0.075

Cox regression proportional hazards analysis. HR, Hazard ratio; CI, Confidence of interval; DM, diabetes mellitus; AF, atrial fibrillation; Hb, hemoglobin; CRP, c-reactive protein; MAavg, Masseter area average; MDavg, Masseter density average. Masseter area and density parameters hazard ratios correspond to 1 standard deviation increase. * = statistical significance.

Supplementary table 5. Survival analysis of the patients whose survival were over 3 months after operation (n=274).

Risk factor	HR	(95% CI)	p-value	HR	(95% CI)	p-value
Age	1.03	(0.98-1.09)	0.229	1.05	(0.99-1.10)	0.089
DM	2.17	(0.84-5.59)	0.107	2.11	(0.82-5.45)	0.124
AF	1.91	(0.78-4.70)	0.158	1.92	(0.78-4.70)	0.155
Arrival Hb	0.98	(0.96-1.00)	0.078	0.98	(0.96-1.00)	0.019*
Creatinine level	1.01	(1.00-1.02)	0.021*	1.01	(1.00-1.02)	0.026*
Dental status	0.82	(0.37-1.80)	0.618	0.68	(0.31-1.49)	0.332
MDavg	0.66	(0.39-1.11)	0.116	-	-	-
MAavg	-	-	-	1.02	(0.62-1.66)	0.953

Cox regression proportional hazards analysis. HR, Hazard ratio; CI, Confidence interval; DM, diabetes mellitus; AF, atrial fibrillation; Hb, hemoglobin; CRP, c-reactive protein; MAavg, Masseter area average; MDavg, Masseter density average. MAavg and MDavg hazard ratios correspond to 1 standard deviation increase. * = statistical significance.

Supplementary figure 1.

The development of risk of mortality. The risk of death (hazard ratio) across the full range of average masseter density (HU) in acute stroke patients treated with mechanical thrombectomy. The model was standardized by age, diabetes mellitus, atrial fibrillation, local intracranial hemorrhage, dental status, Hb and serum creatinine level at time of arrival.