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Pre-Operative Masseter Area is an Independent Predictor of Long-Term Survival after Carotid Endarterectomy

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WHAT THIS PAPER ADDS

Masseter muscle area (MA) can be measured reliably from pre-operative computed tomography angiography and is a significant predictor of long-term mortality after carotid endarterectomy, independent of other risk factors, anthropometric measures, and dental status. To understand its potential in risk stratification and long-term mortality, the results need to be validated in independent cohorts and studies powered to stratify for different indication categories.

Objective/Background: Sarcopenia is a predictor of mortality in elderly patients. Masseter area (MA) reflects sarcopenia in trauma patients. It was hypothesised that MA and Masseter density (MD) could be evaluated reliably from pre-operative computed tomography angiography (CTA) scans and that they predict post-operative survival in carotid endarterectomy (CEA) patients.

Methods: This was an observational registry study. Patients ($n = 242$) were operated on for asymptomatic stenosis ($n = 32$; 13.2%), amaurosis fugax ($n = 41$; 16.9%), transient ischaemic attack ($n = 85$; 35.1%), or ischaemic stroke ($n = 84$; 34.7%). Internal carotid artery stenoses were graded angiographically. Intraclass correlation coefficient (ICC) was used to analyse measurement reliability by three independent observers. Cox regression analysis was used to study the effect of MA and MD on survival (hazard ratio [HR]).

Results: Median patient age was 71.0 years (interquartile range [IQR] 13.0) and follow up time was 68.5 months (range 3–163 months); at the end of follow up (1 October 2017), 104 (43.0%) patients had died according to the National Population Register. The average MA (MAavg, the mean of left and right MA [median 394.0 mm^2; IQR 110.1 mm^2]) and MD (MDavg, the mean of left and right MD [median 53.5 HU; IQR 16.5 HU]) could be measured with excellent reliability (ICC > 0.865, $p < .001$ for all). In multivariable analyses only body surface area (BSA) ($p < .001$) and dental status were associated with MAavg ($p = .021$). Increased MAavg predicted lower mortality (HR 0.76, 95% confidence interval [CI] 0.61–0.96; $p = .023$) independent of age (HR 1.05, 95% CI 1.02–1.07; $p = 0.001$), female sex, body mass index, renal insufficiency, ipsilateral stenosis, indication category, and presence of teeth. MDavg was not associated with mortality. After further adjustment, BSA (the most significant determinant of MAavg) did not alter the association between MAavg and mortality (0.75, 95% CI 0.58–0.97; $p = .031$).

Conclusion: Average MA but not MD measured from the pre-operative CTA scan provides a reliable estimate of post-operative long-term survival in CEA patients independent of other risk factors, anthropometric measurements, and dental status.

Keywords: Carotid endarterectomy, Cerebrovascular disease, Computed tomography angiography, Muscle
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INTRODUCTION

The net benefit from carotid endarterectomy (CEA) is critically dependent on length of post-operative survival,[1] which in turn is influenced by several factors. Such factors include age, cardiovascular risk factors, chronic obstructive

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pulmonary disease, renal disease, body mass index (BMI), absence of statin use, and contralateral carotid occlusive disease.[1–5]

The biological state of reduced physiological reserve and increased vulnerability associated with age, i.e., frailty, reflects subclinical cardiovascular disease and has been found to be better than traditional surgical risk scores in estimating post-operative survival.[6–10] Frailty is an independent predictor of post-operative mortality in cardiovascular patients, doubling the risk of mortality and morbidity in patients with stable cardiovascular disease, acute coronary syndromes, heart failure, and surgical and other interventions.[9] Frailty can be estimated by measuring loss of muscle mass, i.e., sarcopenia, walking speed, and daily activity.[9]

Paraspinal muscle mass evaluated from computed tomography (CT) images predicted survival in patients undergoing elective open and endovascular abdominal aortic aneurysm repair,[11,12] and in general surgery and vascular patients.[13] Similarly, masseter muscle area (MA) measured from CT images predicted mortality and correlated well with psoas muscle area in elderly patients experiencing blunt trauma and traumatic brain injury.[14,15] In line with this, masseter muscle tension, chewing ability, dental status, and physical fitness have been shown previously to be closely associated in elderly care home residents.[16]

Sarcopenia related to stroke differs from that related to ageing in that it is characterised by rapid loss of muscle mass, structural alterations in the muscle, and bilateral difference in physical and functional performance determined by the brain lesion, whereas ageing related sarcopenia occurs slowly without structural alterations or bilateral differences.[17] In stroke patients, imbalanced neurovegetative status may also induce a direct catabolic signal to the muscle.[17] Sarcopenia related to stroke is probably unilateral, while that related to ageing and frailty is reflected bilaterally.

At present, sarcopenia is not evaluated pre-operatively and evaluation is not easy to implement in clinical practice. Furthermore, to the best of the authors' knowledge, no data exist on the effect of sarcopenia on post-operative long-term survival after CEA, which is an important factor when considering the net benefit from carotid surgery. It was hypothesised that sarcopenia could be evaluated easily from routine digital pre-operative CT angiography (CTA) scans by measuring MA and masseter density (MD) and that it is an independent predictor of post-operative survival. The purpose of this study was, firstly, to ascertain the reliability of MA and quality measurements from pre-operative CTA scans of CEA patients. Secondly, the study sought to determine the association between sarcopenia represented by these parameters and long-term post-operative mortality in a cohort of patients treated for carotid stenosis.

MATERIALS AND METHODS

Consecutive patients from the prospective vascular registry of Tampere University Hospital (TAUH) subjected to CEA from 2004 to 2010 ($n = 382$) were retrieved, and those with available digital pre-operative CT and CTA scans ($n = 242$; 63.4%) comprised the final study population. CTA was implemented in the authors' clinical practice in 2004; therefore, the majority of excluded patients were operated on during the early years, from 2004 to 2006 ($n = 93$). The demographics, risk factors, indications, and degrees of carotid stenosis of excluded patients ($n = 140$; 36.7%) did not differ significantly from those that were included (Table S1; see Supplementary Material). As patient data were recorded in the prospective register during the operation and no patients died during the operation, the database comprises all patients operated on. These indications are in line with published guidelines.[18] Cardiovascular risk factors obtained from the vascular registry were defined based on previous diagnoses and current medication as follows: diabetes (diagnosis/insulin or oral hypoglycemic medication), arterial hypertension (diagnosis/antihypertensive medication), cardiac risk factor (diagnosis of myocardial infarction, coronary intervention, angina pectoris, ischaemia on electrocardiography, congestive heart failure), pulmonary risk factor (diagnosis of chronic obstructive pulmonary disease), renal risk factor (diagnosis of renal insufficiency), peripheral arterial disease (diagnosis/peripheral vascular intervention or amputation), and dyslipidaemia (diagnosis/antihyperlipidaemic medication). Smoking was defined as smoking within last five years or current smoking.

Standard protocol approvals

The study was approved by the TAUH ethics committee and was conducted adhering to the principles of the Declaration of Helsinki.

Radiological assessment

All study patients were routinely subjected to brain CT and CTA. Internal carotid artery stenoses were determined (NASCET criteria) and categorised (<50%, 50–69%, 70–99%, and 100%)[19] by a neuro-interventional radiologist (J.P.P.). In a pilot analysis of a random set of 30 patients by three independent observers before and after sagittal and coronal tilt adjustment, head tilt was found to have a significant effect on MA measurements. Therefore, tilt alignment of the CTA sections was made according to a tangent along the lower border of arcus zygomaticus in the sagittal plane and along the lowest point of the orbitae in the coronal plane, and measurements were made 20 ± 2 mm below the arcus by outlining the outer surface of masseter muscle along the fascia, after which the image analysis programme automatically calculated the area (mm^2) and mean density (Hounsfield Unit [HU]) across the region of interest (Fig. 1). Thereafter, 30 CTA scans were first randomly selected and the analysis performed in a random and blinded fashion by three independent observers and reliability was assessed by intraclass correlation coefficient analysis (ICC) for both MA and MD measurements. Consequently, after confirmation of excellent repeatability, a single rater proceeded with the rest of the scans. The presence

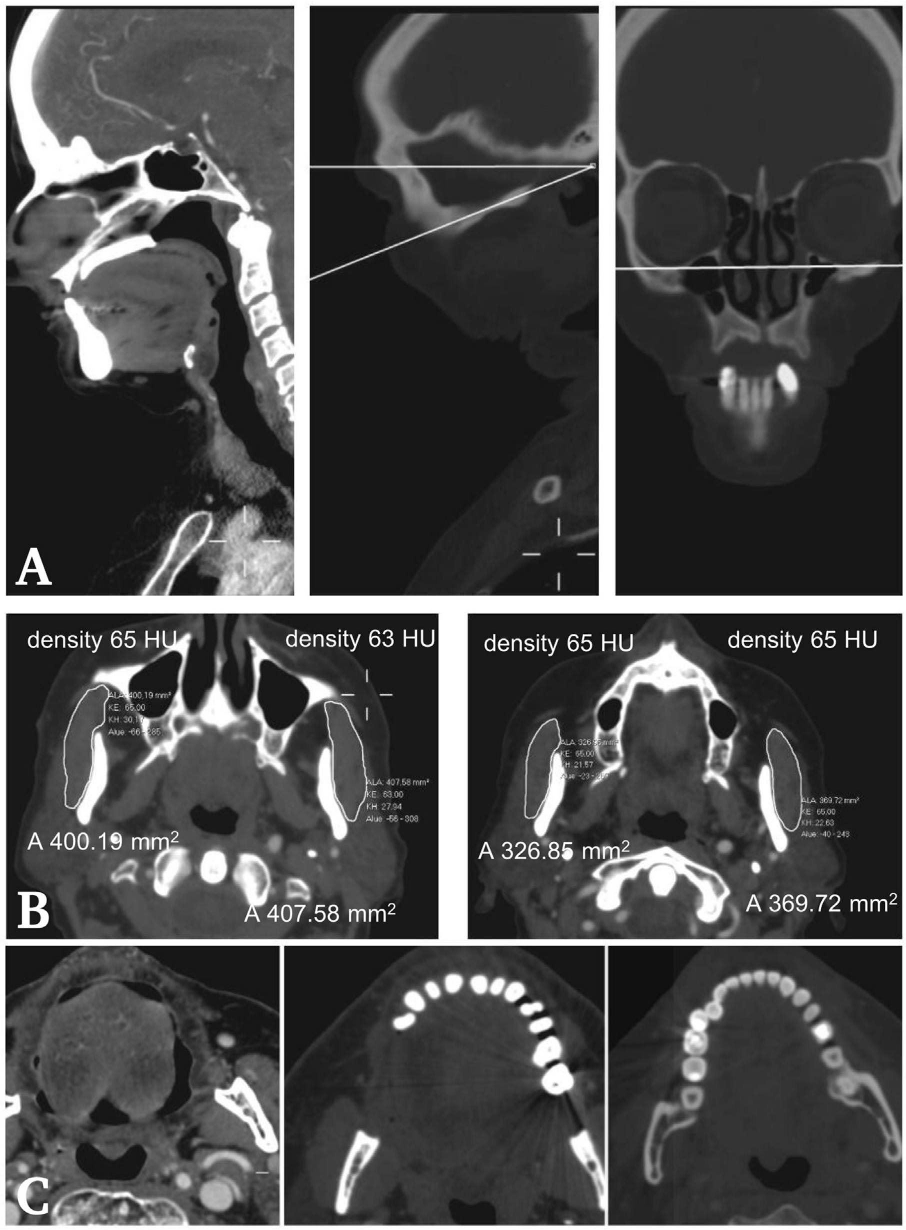

Figure 1. Representative pre-operative images of carotid endarterectomy patients demonstrating (a) the sagittal tilt and coronal tilt measurement, (b) the measurement of masseter area and density before and after tilt correction, where masseter area (A) and density is shown. (c) The grading of presence of teeth: no teeth any missing teeth, and no evidence of missing teeth. *Note.* HU = Hounsfield units.

of teeth was scored in three categories: (i) no teeth; (ii) any missing teeth; and (iii) no evidence of missing teeth (Fig. 1). Average MA (MAavg; mean of left and right MA) and MD (MDavg; mean of left and right MD) were calculated.

Survival and causes of death

Comprehensive long-term survival data on status of the patient (alive/dead) and date of death was obtained from the TAUH patient record database on 1 October 2017; the database is updated in a continuous fashion by the National Population Register. Patients were considered to be alive if there was no date of death available in the register on 1 October 2017, i.e., the last date known to be alive. The potential delay of data transfer from date of death to the National Population Register is between 1 − 3 weeks. Therefore, the register was reviewed on 1 November 2017 to ensure that all delayed information on deaths up to 1 October 2017 was recorded. This database provided full coverage of all the patients included in the study. In Finland, death certificates are mandatory and the data on deaths are without missing cases. The outcome event was all cause death. The causes of death based on International Statistical Classification of diseases and Related Health Problems (ICD-9 and ICD-10) classifications were obtained and divided further into cardiac (coronary artery disease, valvular heart disease, arrhythmia and congestive heart disease), cerebral (ischaemic or haemorrhagic stroke, cerebral bleeding, vascular dementia), peripheral vascular (peripheral arterial disease, aneurysms) cancer, infection, trauma, and other categories (Statistics Finland).

Statistical analysis

The statistical software used for analyses was SPSS 24 for Mac OS X (IBM, Armonk, NY, U.S.A.). Continuous variables were analysed with the Mann—Whitney *U*-test, and Kruskall—Wallis test for independent samples and the Wilcoxon signed rank test for related samples. Intraclass correlation coefficient (ICC) was utilised to analyse reliability, i.e., intra- and inter-observer variability of the measured parameters (areas, densities) measured by three independent observers. The two way random single measurement model was selected and both consistency and absolute agreement were calculated along with 95% confidence intervals (CIs). ICC was rated as poor (<0.40), fair (0.40—0.59), good (0.60—0.74), and excellent (0.75—1.00). Normal distribution of CT variables was ascertained visually and by Levene's test. The association between clinical characteristics and MA and MD was analysed with adjusted and unadjusted linear regression analysis. Predictors of survival were analysed using Cox regression proportional hazards analysis first as univariable analyses. The effect of age, sex, BMI, body surface area (BSA), and tooth loss on CT variables were examined, and included in the multivariable models owing to their strong a priori association with masseter parameters.[20] Testing of the proportional hazards assumption was based on log—log plots and the correlation of survival rankings with Schoenfeld residuals. All variables except for age fulfilled this assumption. Consequently, all multivariable models using Cox regression were performed with age as a time dependent covariate. Kaplan—Meier survival analysis was used to plot overall survival. Multivariable models testing the independent associations between risk factors and mortality were adjusted with factors associating nominally with mortality ($p < .1$) in univariable analysis. Missing values for ipsilateral stenosis ($n = 32$) and dental status ($n = 33$) were replaced by values calculated by multiple imputation (mice package for R).[21] Patients with a transient event as an indication (amaurosis fugax and transient ischaemic attack [TIA]) were pooled to a single category because the mortality risk attributable to these events was identical. Age, sex, BSA, and dental status were included in the multivariable models owing to their strong a priori association with masseter parameters.[20] For estimation of BSA (and BMI) body weight and height was available only for a subpopulation ($n = 158$; 65.3%). Owing to the large amount of missing data, BSA was included in the analyses separately and without replacing missing values. The reported hazard ratios (HRs) related to the main exposure variables (MAavg and MDavg) correspond to a 1 SD increase in exposure variables. Cox regression models with penalised splines were used to evaluate (plot) the relationship between MA and MD (psplines package for R). According to power analysis based on a pilot study of 100 patients, 242 patients were needed (power of 0.9) to detect a significant difference (alpha = 0.05) in post-operative survival between different MA and MD categories.

RESULTS

Patient characteristics

The median age of the patients was 71.0 years (interquartile range [IQR] 13.0). Less than one third of the patients were women (29.8%) and the majority of patients had hypertension (76.9%), a cardiac risk factor (52.9%), dyslipidaemia (55.8%), ipsilateral stenosis of 70—99% (85.7%), and contralateral stenosis of <50% (55.3%). The main indications for surgery were TIA (35.1%) and ischaemic stroke (34.7%), whereas a minority of the operations were due to asymptomatic stenosis (13.2%). The side of the operation was left in 55.0% and right in 45.0% of cases (Table 1). The majority of patients were on beta blockers (62.2%), statins (87.2%), antiaggregatory medication (73.1%), anticoagulants (37.8%), and

Table 1. Characteristics of carotid endarterectomy patients

Risk factor	$n = 242$	
Median (interquartile range [IQR]) age (y)	71.0	(13.0)
Median (IQR) body mass index (kg/m^2)	26.8	(5.6)
Median (IQR) body surface area	1.9	(0.3)
Female	72	(29.8)
Diabetes mellitus	71	(29.3)
Hypertension	186	(76.9)
Cardiac	128	(52.9)
Dyslipidaemia	135	(55.8)
Renal	5	(2.1)
Peripheral arterial disease	37	(15.3)
Pulmonary	25	(10.3)
Smoking	68	(28.1)
Ipsilateral stenosis (%)		
<50	2	(0.9)
50—69	28	(14.3)
70—99	180	(85.7)
100	0	(0)
Contralateral stenosis (%)		
<50	134	(55.3)
50—69	64	(26.4)
70—99	34	(14.0)
100	10	(4.1)
Indication		
Asymptomatic	32	(13.2)
Amaurosis	41	(16.9)
Transient ischaemic attack	85	(35.1)
Ischaemic stroke	84	(34.7)
Side[a]		
Right	109	(45.0)
Left	133	(55.0)

Note. Data are *n* (%) unless otherwise indicated. IQR = interquartile range.
[a] Side of the index operation.

antihypertensives (75.6%), whereas a smaller group received oral antidiabetic medication (25.6%) or insulin (16.0%).

Determinants of MA

In univariable analyses the strongest factors associated with MAavg were BSA, sex, age, and dental status ($p < .001$ for all; Table 2). In multivariable analyses, the only significant factors linked to MAavg were BSA ($p < .001$) and dental status ($p = .021$). For MDavg, the associating factors were sex, dental status, and age ($p < .01$ for all comparisons in univariable analyses, as well as in multivariable analysis; Table 2). Overall, BSA showed a clearly stronger association with MAavg than BMI. BMI did not correlate significantly with MDavg.

Inter- and intra-observer variability of the CT measurements

MAavg and MDavg demonstrated excellent reliability based on ICC analysis by three independent observers (ICC 0.865—0.971 and $p < .001$ for all) (Table 3).

Association between pre-operative MA and MD and long-term mortality

The median follow up was 68.5 months (range 3—163 months). During the follow up, 104 patients (43.0%) of the study population died. No patients were lost during follow up. A Kaplan—Meier survival plot is presented in Fig. 2.

In univariable analysis, MAavg was significantly associated with mortality with a 1 SD increase corresponding to a lower risk of death (HR 0.72, 95% CI 0.59—0.88; $p = .001$) (Table 4). MDavg was not significantly connected to mortality (HR 0.92, 95% CI 0.76—1.12; $p = .423$) (Table 4).

Factors associated significantly with the measured CT parameters (MAavg and MDavg) and factors nominally connected ($p < .1$) to mortality in univariable analyses (age, BMI, BSA, renal risk factor, ipsilateral stenosis, indication category, teeth) (Table 4) were selected for multivariable analysis. In the resulting multivariable Cox regression analysis, increased MAavg remained a predictor of lower mortality (HR 0.76, 95% CI 0.61—0.96; $p = .023$) independent of age (HR 1.05, 95% CI 1.02—1.07; $p = .001$), female sex, BMI, renal insufficiency, ipsilateral stenosis, indication category, and presence of teeth (Table 5). In a similar analysis, MDavg was not associated with mortality (HR 1.01, 95% CI 0.81—1.26; $p = .942$). The development of risk of death across the continuum of MAavg shows an inverse linear relationship between MAavg and mortality with a possible tendency for exponential growth in the risk of death when approaching the lowest end of the MAavg range (Fig. 3). The risk of death was linearly associated with age (Fig. S1; see Supplementary Material).

In order to verify that MA is associated with mortality, independently of BSA, which was the most significant determinant of MAavg, the same multivariable analysis was repeated in a subpopulation with available BSA measurement ($n = 182$, representing 63.6% of the entire study population). Despite the lower sample size, the association persisted (0.75, 95% CI 0.59—0.97; $p = .030$).

Table 3. Intraclass correlation coefficient (ICC) analysis of pre-operative computed tomography measurements of masseter muscles of carotid endarterectomy patients

Variable	ICC[a]	p	ICC[b]	p
Masseter area right side	0.785	<0.001	0.784	<0.001
Masseter density right side	0.940	<0.001	0.942	<0.001
Masseter area left side	0.880	<0.001	0.872	<0.001
Masseter density left side	0.974	<0.001	0.975	<0.001
Average masseter area	0.870	<0.001	0.865	<0.001
Average masseter density	0.970	<0.001	0.971	<0.001

[a] Model: two way random consistency.
[b] Model: two way random absolute.

Causes of death

Of the 104 dead patients, the causes of death were cardiovascular in 29.8%, subclassified further into cerebral (13.5%), cardiac (15.3%), and peripheral vascular (1.0%) causes. The remaining deaths were due to cancer (7.7%), infections (1.0%), trauma (1.0%), and other causes (5.8%).

DISCUSSION

According to the results, MAavg and MDavg can be easily and reliably measured after sagittal and coronal tilt adjustment below the zygomatic arch from routine pre-operative CTA images in CEA patients. The independent factors contributing to MAavg are BSA and dental status, whereas for MDavg these are sex, dental status, and age.

Table 2. Radiological characteristics of carotid endarterectomy patients

	Age					Body surface area				Sex			Teeth category			
	All	T1	T2	T3	p	T1	T2	T3	p	Male	Female	p	1	2	3	p
Masseter average area (mm^2)	395.0 (110.1)	423	404	362	<0.001	345	389	446	<0.001	420	349	<0.001	371	394	441	<0.001
Masseter average density (Hounsfield units)	53.5 (16.5)	59	53	49	<0.001	55	58	58	Non-significant	55	49	<0.01	48	57	59	<0.001

Note. Data are median (interquartile range), and as medians and tertiles indicated as T1, T2, and T3 according to age, body surface area and in different teeth categories (1 = no teeth; 2 = any missing teeth; 3 = no evidence of missing teeth according to computed tomography analysis). *P* values calculated for linear trend using linear regression analysis.

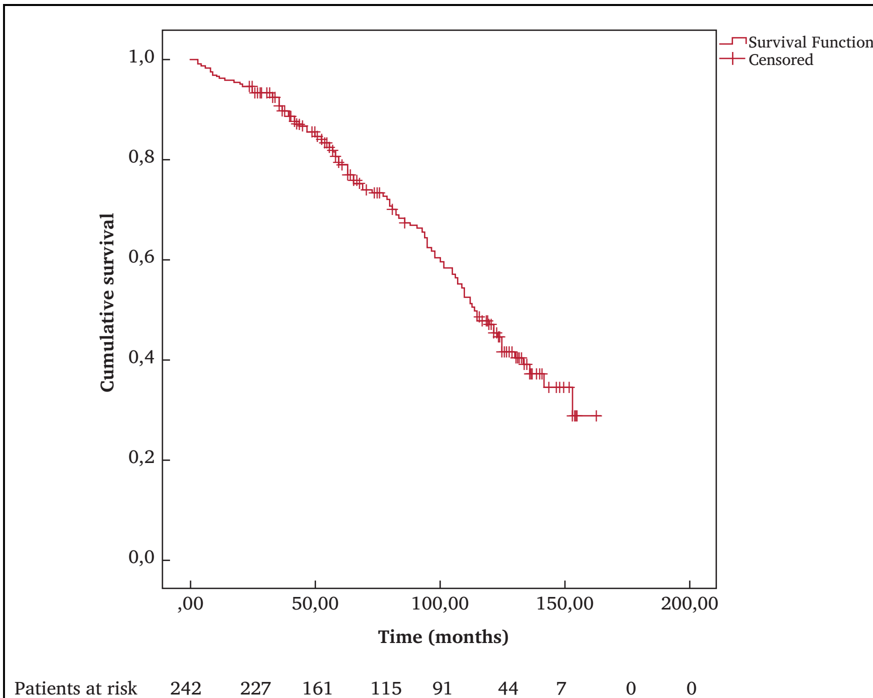

Figure 2. Kaplan–Meier survival plot of carotid endarterectomy patients.

Increased MAavg remains a predictor of lower mortality, independent of age, female sex, BMI, renal insufficiency, ipsilateral stenosis, indication category, and presence of teeth, whereas MD was not associated with mortality. This effect remains independent of BSA which is the most significant determinant of MA.

The finding of an inverse relationship between MAavg and mortality concurs with previous studies which found that MA predicted mortality in elderly patients suffering blunt trauma[14] or traumatic brain injury,[15] and this in turn suggests that MA could be used as a surrogate for sarcopenia. As in the present study, the association was mostly not influenced by age, suggesting that despite correlating with age, MA provides independent prognostic value when predicting death after trauma or CEA. In the study by Hu et al.,[15] sarcopenia was defined as a decrease in MA of $\geq$1 SD from the sex based mean. The mean MA in these sarcopenic patients was 281 mm^2 in men and 224 mm^2 in women, and they were at increased risk of 30 day mortality (80.0% vs. 50.6%) vs. those with greater MA.[15] This finding is in line with the current analyses, which showed an inverse association between MA and mortality, and suggests that there may be a different threshold for increased mortality according to sex. The present study was not powered to analyse sex differences and the association of MAavg with mortality persisted despite adjustment by sex. In addition to age and sex, other parameters with strong a priori association with masseter parameters (BMI, BSA, tooth loss) were also examined and included in the multivariable models.[20] In the present study, most of the significant risk factors previously associated with perioperative risk and long-term risk among CEA patients in large registry studies and clinical trials were also recorded and considered in the analyses.[22,23] Although some of the previously discovered risk factors were not associated with the risk of long-term mortality (contralateral stenosis and BMI) in the present study, these factors were recorded in the vascular registry online (i.e., at the time of the operation) by treating surgeons and thus with no information of the future outcomes. The smaller sample size in the present study compared with the previous large trials and registry studies most likely explains the lack of power to detect significant associations between these factors and mortality. The previous observation on the effect of age, sex, and dental status on MA and MD[20] was replicated in the present study, which supports the observations and methodology. There were no interactions between age and MA that would suggest the association between MA and mortality would be influenced by age. Age and MA were significantly associated but independent of death in the same model, which confirms that they provide information that is independent regarding survival. This exploratory analysis showed that there is no clear cut off for risk across the continuum of MA, which suggests that categorisation of masseter area would lead to better risk stratification results.

The primary shortcoming of the present study is that it was conducted retrospectively. However, the prospective vascular registry in use is audited annually for data loss and consistency. In addition, all data entries on surgical operations are done in the operation room to ensure all patients operated on are entered. All vascular patients are treated in a single centre, and the patient sample in this study was collected from a cohort comprising all consecutive CEA patients with CTA imaging available. No patients died within

Table 4. **Univariable Cox regression analysis of the effect of risk factors and pre-operative masseter area and teeth measured from computed tomography angiography images on long-term survival in carotid endarterectomy patients**

Risk factor	Univariable		
	Hazard ratio	95% confidence interval	*p*
Age	1.06	1.03–1.08	<0.001
Female sex	1.01	0.65–1.55	0.978
Body mass index	0.93	0.87–1.01	0.07
Body surface area	0.65	0.24–1.78	0.4
Diabetes mellitus	1.15	0.75–1.75	0.519
Hypertension	0.91	0.57–1.44	0.676
Cardiac[a]	1.32	0.89–1.97	0.17
Dyslipidaemia	0.74	0.50–1.10	0.137
Pulmonary	1.57	0.81–3.04	0.179
Renal[b]	2.60	0.95–7.09	0.063
Peripheral artery disease	1.47	0.89–2.42	0.133
Smoking	0.85	0.54–1.34	0.482
Ipsilateral stenosis	2.32	1.14–4.69	0.02
Contralateral stenosis	1.08	0.86–1.37	0.505
Indication	1.43	1.07–1.92	0.016
Teeth	0.67	0.49–0.92	0.012
Operated side (left/right)	0.70	0.46–1.10	0.1
Average masseter area	0.72	0.59–0.88	<0.001
Average masseter density	0.92	0.76–1.12	0.423

Note. Cox regression proportional hazards analysis. Indication category: (1) asymptomatic, (2) amaurosis fugax, (3) transient ischaemic attack, (4) stroke. The reported hazard ratios for masseter area and density parameters correspond to 1 standard deviation (SD) increase. The presence of teeth was scored in three categories: (1) no teeth, (2) any missing teeth and (3) no evidence of missing teeth.

[a] Diagnosis of myocardial infarction, coronary intervention, angina pectoris or ischaemia on electrocardiography and congestive heart failure.

[b] Diagnosed renal insufficiency.

Table 5. **Multivariable Cox regression analysis of the effect of risk factors and pre-operative masseter area and teeth measured from computed tomography angiography images on long-term survival in carotid endarterectomy patients**

Risk factor	Hazard ratio	95% confidence interval	*p*
Age	1.05	1.02–1.07	0.001
Sex	0.72	0.45–1.15	0.171
Renal	2.63	0.91–7.59	0.073
Indication	1.24	0.93–1.67	0.150
Ipsilateral stenosis	1.91	0.95–3.84	0.07
Teeth	0.74	0.53–1.05	0.093
Average masseter area	0.76	0.61–0.96	0.023

Note. Cox regression proportional hazards analysis. Indication category: (1) asymptomatic, (2) amaurosis fugax or transient ischaemic attack, (3) stroke. The reported hazard ratio for masseter area parameter corresponds to 1 standard deviation (SD) increase. The presence of teeth was scored in three categories: (1) no teeth, (2) any missing teeth, and (3) no evidence of missing teeth.

30 days of the operation. During the study period, carotid artery stenting was performed only rarely and these cases were excluded from the analysis. The present authors started using CTA for diagnostics in 2004. Therefore, the majority of excluded patients were those treated at the beginning of the study period. No differences were found in demographics, risk factors, or indications or degrees of carotid stenosis between those included and excluded in the study, which makes availability of CTA an unlikely source of bias. In Finland, determination of cause of death has been based on autopsy findings in approximately 30% of all deaths in the past two decades (www.tilastokeskus.fi), which is high compared with other European countries. The death certificates of all deceased, whether or not they underwent autopsy, are reviewed by the district forensic physician and therefore the number of patients with missing date or cause of death is negligible. The potential bias caused by delayed entry of date of death into the National Population Register was eliminated by re-checking the information one month after the end of follow up. The official cause of death has been demonstrated to be an accurate means of evaluating disease specific mortality in Finland.[24] This adds to the reliability of the present study. The patients were of Caucasian origin and with respect to cases of stroke, limited to those with mild to moderate strokes, which restricts the generalisability of the results. Finally, as post-operative CTA imaging was not routinely performed, the effect of the operative procedure itself on MA and MD could not be estimated, although it is an interesting future research topic.

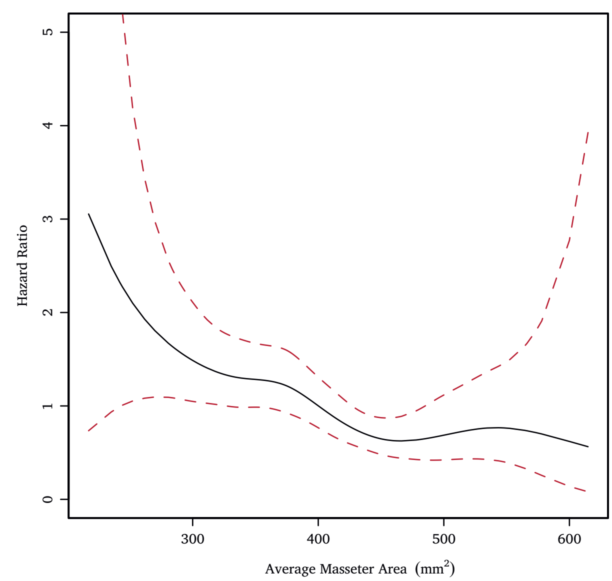

Figure 3. The development of risk of death (hazard rate) across the continuum of average masseter area (mm^2) in carotid endarterectomy patients. The model was adjusted by age, sex, body mass index, renal insufficiency, ipsilateral stenosis, indication category, and dental status.

SUMMARY AND CONCLUSIONS

After sagittal and coronal tilt correction, MA and MD can be reliably measured from pre-operative routine CTA images. MAavg but not MDavg provides long-term predictive value independently of age, female sex, BMI, renal insufficiency, ipsilateral stenosis, indication category, and presence of teeth, independently of BSA, which is the most significant determinant of MA. The results need to be validated in independent cohorts and studies powered to stratify for different indication categories.

MAavg but not MDavg measured from a pre-operative CTA scan provides a reliable estimate of post-operative long-term survival in CEA patients independently of other risk factors, anthropometric measures, and dental status.

CONFLICT OF INTEREST

None.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.11.011.

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