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# Effect of tooth loss and nutritional status on outcomes after ischemic stroke

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ABSTRACT

*Objectives:* Tooth loss, closely associated with malnutrition, increases the risk for cardiovascular disease. The aim of this study was to examine the link between tooth loss, nutritional status, and stroke outcomes.
*Methods:* We retrospectively analyzed 195 consecutive patients with acute ischemic stroke who were evaluated for tooth loss. Tooth loss was classified as mild or severe. Nutritional status was evaluated using the Controlling Nutritional Status (CONUT) score. A poor neurologic outcome was defined as a score of 3 to 6 on the modified Rankin Scale at 3 mo post-stroke onset; a score of 0 to 2 was defined as a good outcome.
*Results:* A significant correlation was observed between tooth loss and the CONUT score at admission ($\rho = 0.156$; $P = 0.034$). Patients with poor outcomes had higher CONUT scores ($P < 0.001$) and a greater frequency of severe tooth loss ($P = 0.025$). On multivariate analysis, severe tooth loss (odds ratio [OR], 3.93; 95% confidence interval [CI], 1.31–11.8) and the CONUT score (OR, 1.33; 95% CI, 1.02–1.74) were independently associated with poor stroke outcomes.
*Conclusions:* Nutritional status was associated with tooth loss among patients with acute ischemic stroke. Severe tooth loss and a higher CONUT score were independently associated with poor stroke outcomes.


## Introduction

The prevalence of malnutrition has been reported to range from 8% to 34% among patients with acute ischemic stroke [1–4]. Nutritional status is strongly associated with poor stroke outcomes. The maintenance of adequate nutrition is essential in patients with acute stroke. A recent meta-analysis showed that malnutrition in stroke patients is associated with a higher frequency of dysphagia, previous stroke, diabetes mellitus, tube feeding, and reduced level of consciousness [5].

Oral health is important to consider in improving the status of nutrition. Impaired oral health status, including periodontal disease and tooth loss, may have an adverse effect on systemic health [6,7]. Periodontal disease is associated with chronic systemic inflammation and may lead to progressive atherosclerosis and cardiovascular disease (CVD) [8]. Tooth loss also has been considered a risk factor for cerebral disease and CVD [9]. Furthermore, tooth loss is closely associated with malnutrition and the risk for pneumonia, as it results in a decline in oral health and mastication deficiencies [10–12]. Hence, it is important to evaluate the nutritional and oral health status of patients with acute ischemic stroke.

We previously reported that malnutrition was independently associated with a poor functional outcome at 3 mo after stroke onset among patients with acute ischemic stroke [13]; however, we did not evaluate oral health, including tooth loss in that study. A few studies have reported that tooth loss is associated with high mortality among patients with tumors or CVD [14–16]. However, the association between tooth loss and stroke outcome is unclear. Additionally, few studies have investigated the link between tooth loss, nutritional status, and stroke outcome. In this study, we examined this relationship in patients with acute ischemic stroke.

## Methods

### Participants

This was a single-center, hospital-based, retrospective study involving consecutive patients with acute stroke hospitalized at the Hiroshima University. Between

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March 2011 and March 2017, 274 patients with acute ischemic stroke were admitted to our hospital. Participants were considered eligible if they were hospitalized within 1 wk of stroke onset. Ischemic stroke was defined as the sudden onset of acute neurologic deficits, with evidence of acute infarction on brain computed tomography or magnetic resonance imaging. The severity of the event was assessed according to the National Institutes of Health Stroke Scale (NIHSS) score. Stroke subtypes were classified according to the criteria laid down by the trial of ORG 10172 in Acute Stroke Treatment classification [17]. The following clinical characteristics were reported at admission: age; sex; body mass index (BMI); classical vascular risk factors, including hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, chronic heart failure (CHF), chronic kidney disease (CKD), daily alcohol intake >40 g, and smoking habit. Smoking habit was defined as current or past smoking. Hypertension was defined as a history of antihypertensive medication use before admission or a confirmed blood pressure of ≥140/90 mm Hg at rest, measured within 2 wk after stroke onset. Diabetes mellitus was defined as a glycated hemoglobin level of ≥6.5%, fasting blood glucose level of ≥126 mg/dL, or the use of antidiabetes medication. Dyslipidemia was defined as a total cholesterol (TC) level of ≥220 mg/dL, low-density lipoprotein cholesterol level of ≥140 mg/dL, high-density lipoprotein cholesterol level of <40 mg/dL, triacylglycerol levels of ≥150 mg/dL, or the use of antihyperlipidemia medication. Atrial fibrillation (AF) was defined as previous history of sustained or paroxysmal AF or AF detected at hospital arrival, or onset at any time during hospital stay. A diagnosis of CHF was made based on the judgment of the attending physician. CKD was defined as a reduction in the estimated glomerular filtration rate to <60 mL/min. This study complied with the Declaration of Helsinki for investigations involving humans, and the study protocol was approved by the Ethics Committee of the Hiroshima University Hospital. The requirement for informed consent was waived by the Ethics Committee considering the retrospective, non-interventional nature of the study.

*Estimation of tooth loss*

The number of teeth lost was evaluated by a dentist within 7 d after hospital admission. Of the 28 teeth, excluding the third molars, a loss of zero to seven teeth was classified as mild tooth loss and a loss of eight or more was classified as severe tooth loss. These categories are consistent with Dye et al.'s classification of functional dentition [18].

*Assessment of nutritional status*

Nutritional status was evaluated using the Controlling Nutritional Status (CONUT) score, calculated from the serum albumin concentration, the total peripheral lymphocyte count, and the TC level [13,19]. CONUT scores were calculated as described in Supplementary Table 1. The CONUT score ranges from 0 to 12; an individual with a normal nutritional status is awarded a score of 0, with higher scores indicating worse nutritional status. We obtained blood samples to determine the CONUT score within 2 d after admission. Additionally, Geriatric Nutritional Risk Index (GNRI) [20], which is calculated from serum albumin levels, and BMI were also assessed.

*Assessment of stroke outcome*

The primary outcome was evaluated from the 3-mo functional status. A poor outcome was defined as a score of 3 to 6 on the modified Rankin Scale (mRS); a score of 0 to 2 was defined as a good outcome.

*Statistical analysis*

Categorical variables are presented as numbers and percentages, and continuous variables as means with SD or median (interquartile range [IQR]). The statistical significance of intergroup differences was assessed using $\chi^2$ tests for categorical variables and Student's $t$ tests or Mann–Whitney U tests for continuous variables. Correlation analyses between age and the number of teeth lost or the CONUT score were performed using Spearman's rank correlation coefficient. The Cochran–Armitage test for trend was used to examine changes in poor outcome based on the number of teeth lost (0–7, 8–14, 15–21, and >22). Multivariate logistic analysis was performed to identify the indicators (age, sex, BMI, hypertension, diabetes mellitus, dyslipidemia, AF, CHF, CKD, daily alcohol intake, smoking habit, history of stroke, and NIHSS score at admission) for poor stroke outcome at 3 mo using a backward selection procedure with a $P > 0.10$ as the exclusion criterion for the likelihood ratio test (model 1). Next, multivariate logistic analysis was performed by adding the CONUT score and severe tooth loss to the indicators extracted from model 1, to elucidate the influence of nutritional status or severe tooth loss for poor stroke outcome (model 2). $P < 0.05$ was considered statistically significant. Statistical analysis was performed using JMP version 14 (SAS Institute, Inc., Cary, NC, USA).

## Results

We excluded 79 patients from the cohort because they were not evaluated for tooth loss. The patients who were not evaluated were younger, had a higher frequency of diabetes mellitus, and had lower NIHSS scores at admission (Supplementary Table 2). The remaining 195 patients were included in the final analysis. Baseline characteristics of these patients are presented in Table 1. Patients with severe tooth loss (n = 80) were significantly older, had a lower BMI, and a lower frequency of dyslipidemia than those with no tooth loss or mild tooth loss (n = 115). Patients with severe tooth loss had somewhat, although not significantly, higher CONUT scores than those with no tooth loss or mild tooth loss (median [IQR], 2 [1–4] versus 2 [1–3], $P = 0.171$). However, a significant correlation was observed between the number of teeth lost and the CONUT score by the Spearman's rank coefficient correlation ($\rho = 0.156$; $P = 0.034$).

*Indicators for stroke outcome*

Of the 195 patients included in the analysis, 38 were excluded because of lack of data on functional outcomes 3 mo after onset of ischemic stroke; 23 patients were excluded because their premorbid mRS score was ≥3. Of the remaining 134 patients, 45 (33.6%) had a poor outcome. Patients with a poor outcome were significantly

**Table 1**
Baseline characteristics at admission and univariate analysis to determine the factors associated with the severity of tooth loss

| | All (N = 195) | No tooth loss or mild tooth loss (0–7) (n = 115) | Severe tooth loss (≥8) (n = 80) | *P*-value |
|---|---|---|---|---|
| Age, y | 72.5 ± 10.5 | 69.9 ± 11.1 | 76.3 ± 9.69 | <.001 |
| Female, n (%) | 71 (36.4) | 37 (32.2) | 34 (42.5) | 0.173 |
| Body mass index, kg/m$^2$ | 22.5 ± 3.91 (n = 194) | 23 ± 4.34 (n = 114) | 21.9 ± 3.24 | 0.033 |
| Hypertension, n (%) | 145 (74.4) | 80 (69.6) | 65 (81.3) | 0.070 |
| Diabetes mellitus, n (%) | 57 (29.2) | 31 (27) | 26 (32.5) | 0.427 |
| Dyslipidemia, n (%) | 107 (54.9) | 71 (61.7) | 36 (45) | 0.028 |
| Daily alcohol intake, n (%) | 57 (31.7) (n = 180) | 38 (34.9) (n = 109) | 19 (26.8) (n = 71) | 0.325 |
| Current or past smoking, n (%) | 97 (54.2) (n = 179) | 57 (52.8%) (n = 108) | 40 (56.3) (n = 71) | 0.649 |
| Atrial fibrillation, n (%) | 57 (29.5 (n = 193) | 31 (27.2) (n = 114) | 26 (32.9) (n = 79) | 0.425 |
| Chronic heart failure, n (%) | 43 (22.1) | 22 (19.1) | 21 (26.3) | 0.292 |
| Chronic kidney disease, n (%) | 82 (42.1) | 44 (38.3) | 38 (47.5) | 0.238 |
| Previous stroke, n (%) | 43 (22.2) (n = 194) | 25 (21.9 (n = 114) | 18 (22.5%) | 1.000 |
| NIHSS score at admission, median (IQR) | 5 (2–15) | 4 (2–13) | 5 (2–17) | 0.589 |
| CONUT score, median (IQR) | 2 (1–4) (n = 185) | 2 (1–3) (n = 107) | 2 (1–4) (n = 78) | 0.171 |
| Ischemic stroke subtype, n (%) | | | | 0.194 |
| Cardioembolism | 65 (33.3) | 33 (28.7) | 32 (40) | |
| Large-artery atherosclerosis | 35 (17.9) | 23 (22) | 12 (15) | |
| Small-vessel occlusion | 29 (14.8) | 15 (13) | 14 (17.5) | |
| Others | 66 (33.8) | 44 (38.3) | 22 (27.5) | |

CONUT, Controlling Nutritional Status; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

**Table 2**
Baseline characteristics at admission and univariate analysis to determine the factors associated with 3-mo functional outcome

| | All (n = 134) | mRS 0–2 (n = 89) | mRS 3–6 (n = 45) | *P*-value |
|---|---|---|---|---|
| Age, y | 71.9 ± 10.8 | 70.3 ± 10.9 | 75.2 ± 10.5 | 0.013 |
| Female, n (%) | 46 (34.3) | 26 (29.2) | 20 (44.4) | 0.087 |
| Body mass index, kg/m$^2$, n (%) | 22.6 ± 4.33 | 23.2 ± 4.68 | 21.4 ± 3.54 | 0.047 |
| Hypertension, n (%) | 101 (75.4) | 69 (77.5) | 32 (71.1) | 0.525 |
| Diabetes mellitus, n (%) | 36 (26.9) | 23 (25.8) | 13 (28.9%) | 0.837 |
| Dyslipidemia, n (%) | 78 (58.2) | 58 (65.2) | 20 (44.4) | 0.027 |
| Daily alcohol intake, n (%) | 39 (31) (n = 126) | 28 (32.9) (n = 85) | 11 (26.8) (n = 41) | 0.542 |
| Current or past smoking, n (%) | 70 (55.6) (n = 126) | 56 (65.1) (n = 86) | 14 (35) (n = 40) | 0.002 |
| Atrial fibrillation, n (%) | 36 (27.1) (n = 133) | 15 (16.9) | 21 (47.7) (n = 44) | <0.001 |
| Chronic heart failure, n (%) | 28 (20.9) | 15 (16.9 | 13 (28.9) | 0.119 |
| Chronic kidney disease, n (%) | 52 (38.8) | 33 (37.1) | 19 (42.2) | 0.579 |
| Previous stroke, n (%) | 24 (18.1) (n = 133) | 20 (22.7) (n = 88) | 4 (8.9) | 0.058 |
| NIHSS score at admission, median (IQR) | 4 (2–14) | 3 (1–5) | 16 (4.5–24) | <0.001 |
| CONUT score, median (IQR) | 2 (1–4) (n = 124) | 1 (1–3) (n = 84) | 3 (2–5) (n = 43) | <0.001 |
| Number of teeth lost, median (IQR) | 5 (1–16) | 5 (1–12.5) | 8 (4–21) | 0.008 |
| Severe tooth loss, n (%) | 53 (39.6) | 29 (32.6) | 24 (53.3) | 0.025 |
| Ischemic stroke subtype, n (%) | | | | 0.024 |
| Cardioembolism | 42 (31.3) | 23 (25.8) | 19 (42.2) | |
| Large-artery atherosclerosis | 24 (17.9) | 19 (21.4) | 5 (11.1) | |
| Small-vessel occlusion | 23 (17.2) | 20 (22.5) | 3 (6.7) | |
| Others | 45 (33.6) | 27 (30.3) | 18 (40.0) | |

CONUT, Controlling Nutritional Status; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale.

older, had a lower BMI, a lower incidence of smoking and dyslipidemia, a higher frequency of AF, and more severe neurologic deficits than those with more favorable outcomes (Table 2). Patients with poor outcomes had a higher CONUT score (3 [2–5] versus 1 [1–3], $P$ <0.001), more tooth loss (8 [4–21] versus 5 [1–12.5], $P$ = 0.008), and a higher frequency of severe tooth loss (53.3% versus 32.6%, $P$ = 0.025) than those with more favorable outcomes. The proportion of patients with a poor functional outcome significantly increased with more severe tooth loss ($P$ = 0.027; Fig. 1).

Multivariate logistic regression analyses revealed that lower BMI and higher NIHSS score at admission were independently associated with poor outcomes 3 mo after stroke (Table 3, model 1). When including the additional indicators (CONUT score and severe tooth loss) in model 1, multivariate logistic regression analyses showed that severe tooth loss (odds ratio [OR], 3.93; 95% confidence interval [CI], 1.31–11.8; $P$ = 0.015), higher NIHSS score at admission (OR, 1.26; 95% CI, 1.14–1.39; $P$ < 0.001), and higher CONUT score (OR, 1.33; 95% CI, 1.02–1.74; $P$ = 0.036) were independently associated with poor outcomes 3 mo after stroke (Table 3, model 2). The number of teeth lost was also independently associated with the 3-mo functional outcome after adjustment for BMI, diabetes mellitus, NIHSS score at admission, and CONUT score (OR, 1.07; 95% CI, 1.01–1.13; $P$ = 0.016).

## Discussion

In the present study, we found that the nutritional status assessed using the CONUT score was associated with the number of teeth lost among patients with acute ischemic stroke. Additionally, severe tooth loss and a higher CONUT score were independently associated with a poor functional outcome.

Tooth loss is one of the common measures for the assessment of oral health status, and it leads to a decrease in chewing ability. In patients with severe tooth loss, food intake decreases and the serum vitamin C and carotene levels decrease as fruits and vegetables, which are hard to chew, are avoided [21]. These nutrients have an antioxidant effect [22], and adequate intake is necessary for the prevention of many non-communicable diseases (NCDs) including CVDs [23]. In fact, it is reported that having a greater number of present teeth (≥20) was associated with higher intake of fiber and

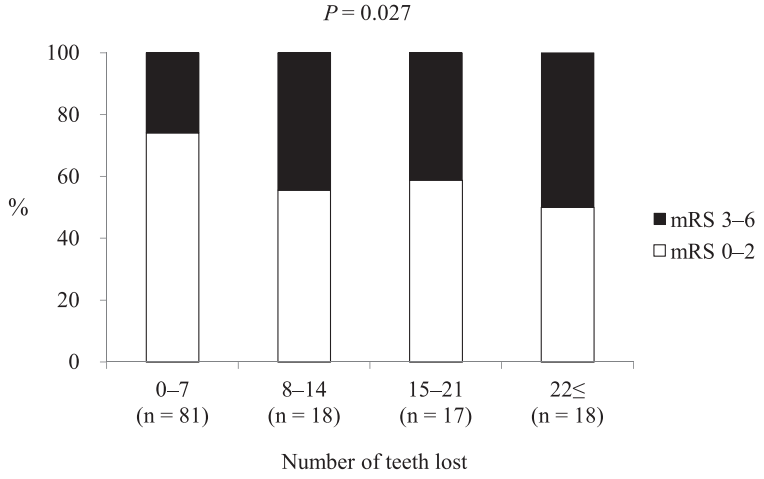


**Fig. 1.** Distribution of poor stroke outcome (mRS score 3–6) at 3 mo according to number of teeth lost. mRS, modified Rankin Scale.

**Table 3**
Indicators associated with poor outcome at 3 mo

| | Model 1* | | | Model 2† | | |
|---|---|---|---|---|---|---|
| | Odds ratio | 95% CI | *P*-value | Odds ratio | 95% CI | *P*-value |
| BMI | 0.82 | 0.70–0.96 | 0.014 | 0.88 | 0.74–1.06 | 0.173 |
| Diabetes mellitus | 3.19 | 0.94–10.7 | 0.061 | 2.34 | 0.63–8.70 | 0.204 |
| NIHSS score at admission | 1.27 | 1.16–1.38 | <0.001 | 1.26 | 1.14–1.39 | <0.001 |
| CONUT score | – | – | – | 1.33 | 1.02–1.74 | 0.036 |
| Severe tooth loss | – | – | – | 3.93 | 1.31–11.8 | 0.015 |

BMI, body mass index; CONUT, Controlling Nutritional Status; NIHSS, National Institutes of Health Stroke Scale.
*Model 1: Multivariate logistic analysis was performed to identify the indicators (age, sex, BMI, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, congestive heart failure, chronic kidney disease, daily alcohol intake, smoking habit, history of stroke, and NIHSS score at admission) for poor stroke outcome at 3 mo using a backward selection procedure with $P > 0.10$ as the exclusion criterion for the likelihood ratio test.
†Model 2: Multivariate logistic analysis was performed to identify the indicators (CONUT score and severe tooth loss added to the indicators extracted from model 1) for poor stroke outcome at 3 mo.

total calories in patients with stable coronary artery disease [24]. Therefore, tooth loss, nutrition, and NCDs are closely related.

The CONUT score, an index calculated from the serum albumin concentration, total peripheral lymphocyte count, and TC concentration, is a screening tool for nutritional evaluation that has been validated in hospital population [19]. Initial assessment of the nutritional status can be carried out using the CONUT score within a short period when these laboratory findings are available. The CONUT score has been evaluated for correlation and sensitivity with the Subjective Global Assessment, a gold standard index for nutritional assessment in hospitalized patients [19,25]. In the present study, we found that among patients with acute ischemic stroke, nutritional status assessed by the CONUT score was associated with the number of teeth lost. Findings that severe tooth loss was closely associated with malnutrition on admission might indicate that premorbid oral care is an important factor that determines the nutritional status of patients with acute ischemic stroke. Studies support that tooth loss is closely associated with malnutrition [26–28]. On the other hand, obesity that is caused by overnutrition or poor self-care practices, is also identified as a risk factor for tooth loss [29]. Although it is beyond the scopeof this study to further discuss the relationship between tooth loss and weight status, further longitudinal prospective studies are needed to investigate the causal relationship among tooth loss, malnutrition, and overnutrition.

Several studies have found that malnutrition is associated with poor stroke outcomes [3,30–32]. In the present study, we found an independent association between tooth loss and poor stroke outcomes after adjusting for several confounding factors including nutritional status on admission. There are several possible reasons for the association between severe tooth loss and poor outcomes after stroke. First, the effect of periodontal disease and caries should be considered. Periodontal disease is one of the causes of tooth loss. Periodontal disease is thought to be associated with chronic systemic inflammation [7,33]. It has been reported that high-sensitivity C-reactive protein levels increase in the peripheral blood of patients with periodontitis. These levels decrease with appropriate periodontal therapy [34]. Hence, it is considered that the enhancement of the systemic inflammatory response due to periodontal disease is involved in the onset and progression of vascular disorders. Furthermore, it has been shown that *Porphyromonas gingivalis*, a periodontopathogenic bacterium, can enter the vascular endothelial cells and is detected from atherosclerotic lesions [35]. These findings might indicate that tooth loss and periodontal disease are associated with stroke recurrence, leading to poor outcomes. Indeed, several large cohort studies have shown a correlation between periodontal disease and CVD, including stroke [36,37]. Similarly, tooth loss also has been associated with CVD [38] and cerebrovascular disease [39,40].

Another possible reason for the association between severe tooth loss and poor stroke outcomes may be the influence of dysphagia. Tooth loss is associated with oral-stage dysphagia and may predispose to aspiration pneumonia leading to a reduction in the level of activity [41]. Additionally, the severity of tooth loss in chronic stroke patients had an association with the level of oral intake and the degree of oropharyngeal dysphagia [42]. Malnutrition status during hospitalization leads to decline in functional status, resulting in poor ability to perform activities of daily living following discharge [43]. Malnutrition might cause poor oral health and poor oral health might indirectly cause malnutrition, as mentioned earlier. We speculate that the bidirectional relationship between severe tooth loss and malnutrition results in this vicious circle, leading to poor outcomes through some complications that may include aspiration pneumonia, incidence of cardiovascular events, and recurrence of stroke.

In the present study, we used the CONUT score as a nutritional parameter. However, the CONUT score might not be a comprehensive measure of nutritional status because it is calculated from only laboratory findings. GNRI, which is calculated from serum albumin levels and the BMI, also has been proposed for assessment of nutritional status [20,44]. In the present study, the number of teeth lost was also positively correlated with the GNRI. Additionally, the GNRI also was independently associated with poor outcomes at 3 mo after adjusting for severe tooth loss, similar to the CONUT score (data not shown). There may be some controversy regarding the appropriate assessment of nutrition for patients with acute ischemic stroke. We hav previously reported that the CONUT score is more useful for predicting functional outcomes than the GNRI score in patients with acute ischemic stroke [13]. Therefore, we adopted the CONUT score in this study. Apart from that, according to the American Society for Parenteral and Enteral Nutrition and the Academy of Nutrition and Dietetics criteria, evaluation of physical findings (muscle and fat loss) is needed to diagnose malnutrition [45]. We could not evaluate these parameters in the present study. Further studies using other more comprehensive measures of nutritional assessments, muscle or fat loss, are needed to better assess these relationships with tooth loss and functional stroke outcomes.

This study had several limitations. First, this was a single-center study with a small sample size. We could not evaluate tooth loss and functional outcomes in all patients, which may have led to a selection bias. However, baseline characteristics of the studied patients did not significantly differ from those previously reported in a large Japanese stroke registry-based study [46]. Therefore, we believe that the present study was not significantly influenced by selection bias. Second, being a retrospective study, detailed information on dental health status, including the severity of periodontal

disease, was unavailable. Thus, we could not evaluate the dental status more comprehensively by using indicators such as probing pocket depth. Additionally, we could not evaluate the chewing ability or occlusal force that might be associated with tooth loss. Third, detailed information was not available on the nutritional status and complications during the acute stage including delayed commencement of oral intake, nasogastric tube feeding, and the presence of aspiration pneumonia; however, usual dental and nutritional management were provided to all patients. Finally, the CONUT score may not be a real comprehensive score for assessments of nutritional status, as mentioned earlier. Other assessments of nutritional parameters, including physical findings, also are important to confirm the present findings.

## Conclusion

Assessment of the number of teeth and the CONUT score could be a useful prognostic marker of functional outcomes in patients with acute ischemic stroke. We believe that poor nutritional status and/or severe tooth loss on admission might be indicators that suggest poor stroke outcomes. Larger prospective studies are required to investigate whether active dental and nutritional interventions could contribute to favorable stroke outcomes.

## Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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## Disclosures

Hirofumi Maruyama reports grants from Daiichi Sankyo Co., Ltd., which are unrelated to the submitted work. All other authors declare that they have no conflicts of interest.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.nut.2019.110606.

## References

[1] Unosson M, Ek AC, Bjurulf P, von Schenck H, Larsson J. Feeding dependence and nutritional status after acute stroke. Stroke 1994;25:366–71.
[2] Choi-Kwon S, Yang YH, Kim EK, Jeon MY, Kim JS. Nutritional status in acute stroke: undernutrition versus overnutrition in different stroke subtypes. Acta Neurol Scand 1998;98:187–92.
[3] Collaboration FT. Poor nutritional status on admission predicts poor outcomes after stroke: observational data from the food trial. Stroke 2003;34:1450–6.
[4] Crary MA, Humphrey JL, Carnaby-Mann G, Sambandam R, Miller L, Silliman S. Dysphagia, nutrition, and hydration in ischemic stroke patients at admission and discharge from acute care. Dysphagia 2013;28:69–76.
[5] Chen N, Li Y, Fang J, Lu Q, He L. Risk factors for malnutrition in stroke patients: a meta-analysis. Clin Nutr 2019;38:127–35.
[6] Furuta M, Fukai K, Aida J, Shimazaki Y, Ando Y, Miyazaki H, et al. Periodontal status and self-reported systemic health of periodontal patients regularly visiting dental clinics in the 8020 promotion foundation study of Japanese dental patients. J Oral Sci 2019;61:238–45.
[7] Pihlstrom BL, Michalowicz BS, Johnson NW. Periodontal diseases. Lancet 2005;366:1809–20.
[8] Orlandi M, Suvan J, Petrie A, Donos N, Masi S, Hingorani A, et al. Association between periodontal disease and its treatment, flow-mediated dilatation and carotid intima-media thickness: a systematic review and meta-analysis. Atherosclerosis 2014;236:39–46.
[9] Cheng F, Zhang M, Wang Q, Xu H, Dong X, Gao Z, et al. Tooth loss and risk of cardiovascular disease and stroke: a dose-response meta analysis of prospective cohort studies. PLoS One 2018;13:e0194563.
[10] Müller F, Shimazaki Y, Kahabuka F, Schimmel M. Oral health for an ageing population: the importance of a natural dentition in older adults. Int Dent J 2017;67(suppl 2):7–13.
[11] Felton DA. Complete edentulism and comorbid diseases: an update. J Prosthodont 2016;25:5–20.
[12] Suma S, Naito M, Wakai K, Naito T, Kojima M, Umemura O, et al. Tooth loss and pneumonia mortality: a cohort study of japanese dentists. PLoS One 2018;13:e0195813.
[13] Naito H, Nezu T, Hosomi N, Aoki S, Kinoshita N, Kuga J, et al. Controlling nutritional status score for predicting 3-mo functional outcome in acute ischemic stroke. Nutrition 2018;55−56:1–6.
[14] Abnet CC, Qiao YL, Dawsey SM, Dong ZW, Taylor PR, Mark SD. Tooth loss is associated with increased risk of total death and death from upper gastrointestinal cancer, heart disease, and stroke in a chinese population-based cohort. Int J Epidemiol 2005;34:467–74.
[15] Ansai T, Takata Y, Yoshida A, Soh I, Awano S, Hamasaki T, et al. Association between tooth loss and orodigestive cancer mortality in an 80-year-old community-dwelling japanese population: a 12-year prospective study. BMC Public Health 2013;13:814.
[16] Vogtmann E, Etemadi A, Kamangar F, Islami F, Roshandel G, Poustchi H, et al. Oral health and mortality in the golestan cohort study. Int J Epidemiol 2017;46:2028–35.
[17] Adams HP, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. Toast. Trial of org 10172 in acute stroke treatment. Stroke 1993;24:35–41.
[18] Dye BA, Weatherspoon DJ, Lopez Mitnik G. Tooth loss among older adults according to poverty status in the united states from 1999 through 2004 and 2009 through 2014. J Am Dent Assoc 2019;150:9–23. e23.
[19] Ignacio de Ulíbarri J, González-Madroño A, de Villar NG, González P, González B, Mancha A, et al. Conut: a tool for controlling nutritional status. First validation in a hospital population. Nutr Hosp 2005;20:38–45.
[20] Bouillanne O, Morineau G, Dupont C, Coulombel I, Vincent JP, Nicolis I, et al. Geriatric nutritional risk index: a new index for evaluating at-risk elderly medical patients. Am J Clin Nutr 2005;82:777–83.
[21] Nowjack-Raymer RE, Sheiham A. Association of edentulism and diet and nutrition in us adults. J Dent Res 2003;82:123–6.
[22] Rock CL, Jacob RA, Bowen PE. Update on the biological characteristics of the antioxidant micronutrients: vitamin c, vitamin e, and the carotenoids. J Am Diet Assoc 1996;96:693–702. quiz 703−694.
[23] Knekt P, Ritz J, Pereira MA, O'Reilly EJ, Augustsson K, Fraser GE, et al. Antioxidant vitamins and coronary heart disease risk: s pooled analysis of 9 cohorts. Am J Clin Nutr 2004;80:1508–20.
[24] Mendonça DD, Furtado MV, Sarmento RA, Nicoletto BB, Souza GC, Wagner TP, et al. Periodontitis and tooth loss have negative impact on dietary intake: a cross-sectional study with stable coronary artery disease patients. J Periodontol 2019;90:1096–105.
[25] González-Madroño A, Mancha A, Rodríguez FJ, Culebras J, de Ulibarri JI. Confirming the validity of the conut system for early detection and monitoring of clinical undernutrition: comparison with two logistic regression models developed using sga as the gold standard. Nutr Hosp 2012;27:564–71.
[26] Nakamura M, Ojima T, Nagahata T, Kondo I, Ninomiya T, Yoshita K, et al. Having few remaining teeth is associated with a low nutrient intake and low serum albumin levels in middle-aged and older Japanese individuals: findings from the nippon data2010. Environ Health Prev Med 2019;24:1.
[27] Ioannidou E, Swede H, Fares G, Himmelfarb J. Tooth loss strongly associates with malnutrition in chronic kidney disease. J Periodontol 2014;85:899–907.
[28] Wu LL, Cheung KY, Lam PYP, Gao XL. Oral health indicators for risk of malnutrition in elders. J Nutr Health Aging 2018;22:254–61.
[29] Nascimento GG, Leite FR, Conceição DA, Ferrúa CP, Singh A, Demarco FF. Is there a relationship between obesity and tooth loss and edentulism? A systematic review and meta-analysis. Obes Rev 2016;17:587–98.
[30] Dávalos A, Ricart W, Gonzalez-Huix F, Soler S, Marrugat J, Molins A, et al. Effect of malnutrition after acute stroke on clinical outcome. Stroke 1996;27:1028–32.
[31] Gariballa SE, Parker SG, Taub N, Castleden M. Nutritional status of hospitalized acute stroke patients. Br J Nutr 1998;79:481–7.
[32] Kubo S, Hosomi N, Hara N, Neshige S, Himeno T, Takeshima S, et al. Ischemic stroke mortality is more strongly associated with anemia on admission than with underweight status. J Stroke Cerebrovasc Dis 2017;26:1369–74.
[33] Lockhart PB, Bolger AF, Papapanou PN, Osinbowale O, Trevisan M, Levison ME, et al. Periodontal disease and atherosclerotic vascular disease: does the evidence support an independent association?: a scientific statement from the American Heart Association. Circulation 2012;125:2520–44.
[34] Nakajima T, Honda T, Domon H, Okui T, Kajita K, Ito H, et al. Periodontitis-associated up-regulation of systemic inflammatory mediator level may increase the risk of coronary heart disease. J Periodontal Res 2010;45:116–22.
[35] Yamatake K, Maeda M, Kadowaki T, Takii R, Tsukuba T, Ueno T, et al. Role for gingipains in porphyromonas gingivalis traffic to phagolysosomes and survival in human aortic endothelial cells. Infect Immun 2007;75:2090–100.

[36] Holmlund A, Holm G, Lind L. Number of teeth as a predictor of cardiovascular mortality in a cohort of 7,674 subjects followed for 12 years. J Periodontol 2010;81:870–6.
[37] Xu F, Lu B. Prospective association of periodontal disease with cardiovascular and all-cause mortality: NHANES III follow-up study. Atherosclerosis 2011;218:536–42.
[38] Bahekar AA, Singh S, Saha S, Molnar J, Arora R. The prevalence and incidence of coronary heart disease is significantly increased in periodontitis: a meta-analysis. Am Heart J 2007;154:830–7.
[39] Joshipura KJ, Hung HC, Rimm EB, Willett WC, Ascherio A. Periodontal disease, tooth loss, and incidence of ischemic stroke. Stroke 2003;34:47–52.
[40] Elter JR, Offenbacher S, Toole JF, Beck JD. Relationship of periodontal disease and edentulism to stroke/TIA. J Dent Res 2003;82:998–1001.
[41] Furuta M, Komiya-Nonaka M, Akifusa S, Shimazaki Y, Adachi M, Kinoshita T, et al. Interrelationship of oral health status, swallowing function, nutritional status, and cognitive ability with activities of daily living in japanese elderly people receiving home care services due to physical disabilities. Community Dent Oral Epidemiol 2013;41:173–81.
[42] Mituuti CT, Bianco VC, Bentim CG, de Andrade EC, Rubo JH, Berretin-Felix G. Influence of oral health condition on swallowing and oral intake level for patients affected by chronic stroke. Clin Interv Aging 2015;10:29–35.
[43] Sato M, Ido Y, Yoshimura Y, Mutai H. Relationship of malnutrition during hospitalization with functional recovery and postdischarge destination in elderly stroke patients. J Stroke Cerebrovasc Dis 2019;28:1866–72.
[44] Yamada K, Furuya R, Takita T, Maruyama Y, Yamaguchi Y, Ohkawa S, et al. Simplified nutritional screening tools for patients on maintenance hemodialysis. Am J Clin Nutr 2008;87:106–13.
[45] Fischer M, JeVenn A, Hipskind P. Evaluation of muscle and fat loss as diagnostic criteria for malnutrition. Nutr Clin Pract 2015;30:239–48.
[46] Kamouchi M, Matsuki T, Hata J, Kuwashiro T, Ago T, Sambongi Y, et al. Prestroke glycemic control is associated with the functional outcome in acute ischemic stroke: the Fukuoka Stroke Registry. Stroke 2011;42:2788–94.

Supplement table 1.

Scoring system for the CONUT score [11]

| Parameter | None | Light | Moderate | Severe |
|---|---|---|---|---|
| Serum albumin (g/dL) | ≥3.50 | 3.00–3.49 | 2.50–2.99 | <2.50 |
| score | 0 | 2 | 4 | 6 |
| Total lymphocyte count (/$mm^3$) | ≥1600 | 1200–1599 | 800–1199 | <800 |
| score | 0 | 1 | 2 | 3 |
| Total cholesterol (mg/dL) | ≥180 | 140–179 | 100–139 | <100 |
| score | 0 | 1 | 2 | 3 |

Supplemental Table 2. Baseline chracteristics at admission and univariate analysis to determine the factors associated with evaluated the number of teeth loss

| | All (n = 274) | Evaluated the number of teeth loss (n = 195) | Non-evaluated (n = 79) | P |
|---|---|---|---|---|
| Age (y) | 71.2 ± 11.8 | 72.5 ± 11.0 | 67.8 ± 13.6 | 0.008 |
| Female | 96 (35.0%) | 71 (36.4%) | 25 (31.7%) | 0.487 |
| Body mass index, kg/m$^2$ | 22.6 ± 3.9 (n = 273) | 22.5 ± 3.9 (n = 194) | 23.0 ± 3.8 | 0.296 |
| Hypertension | 206 (75.2 %) | 145 (74.4 %) | 61 (77.2 %) | 0.647 |
| Diabetes mellitus | 96 (35.2 %) (n = 273) | 57 (29.2 %) | 39 (50.0 %) (n = 78) | 0.002 |
| Dyslipidemia | 154 (56.4 %) (n = 273) | 107 (54.9 %) | 47 (60.3 %) (n = 78) | 0.500 |
| Daily alcohol intake | 83 (32.8%) (n = 253) | 57 (31.7%) (n = 180) | 26 (35.6%) (n = 73) | 0.557 |
| Current or past smoking | 132 (52.2%) (n = 253) | 97 (54.2%) (n = 179) | 35 (47.3%) (n = 74) | 0.336 |
| Atrial fibrillation | 73 (26.8 %) (n = 272) | 57 (29.5 %) (n = 193) | 16 (20.3%) | 0.133 |
| Chronic heart failure | 55 (20.1%) | 43(22.1%) | 12(15.2%) | 0.245 |
| Chronic kidney disease | 113 (41.2%) | 82 (42.1%) | 31 (39,2%) | 0.687 |
| Previous stroke | 64 (23.4%) (n = 273) | 43 (22.2%) (n = 194) | 21(26.6%) | 0.490 |
| NIHSS score at admission | 4 [2−12] | 5 [2−15] | 3 [1−6] | <.001 |
| CONUT score | 2 [1−3] (n = 258) | 2 [1−4] (n = 185) | 2 [0−3] (n = 73) | 0.184 |

CONUT, Controlling Nutritional Status; NIHSS, National Institutes of Health Stroke Scale.
Data are presented as the means ± SD for age and body mass index; as median (interquartile range) for baseline NIHSS score and CONUT score; and as number of patients (%) for others.