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## Mini Review

# The relationship between tooth loss and cerebral stroke

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## KEYWORDS

Tooth loss;  
Cerebral stroke;  
Prospective study

## Summary

**Objective:** Tooth loss has been suggested as a potential risk factor for cerebral stroke. This report reviews prospective studies investigating the association between tooth loss and stroke.

**Method:** The PubMed database was used to identify studies about the relationship between tooth loss and stroke including prospective, cohort, and follow-up studies reported from 2000 to 2010.

**Results:** Four prospective follow-up studies have been conducted on the relationship between tooth loss and stroke and three of four reports have suggested that tooth loss is related to incidence of both ischemic and hemorrhagic stroke.

**Conclusion:** The results of this review study support the hypothesis that there is an association between early tooth loss and the occurrence of stroke.

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## Introduction

A cerebral stroke results in damage to the brain due to a reduction in the blood supply. When a blood vessel that normally delivers oxygen and nutrients to the brain is obstructed, the condition is called an ischemic stroke, or cerebral ischemia. Hemorrhagic stroke occurs when a blood vessel supplying the brain bursts and causes bleeding into the brain. In any stroke, the nerve cells in the affected area of the brain may be deprived of oxygen and die within minutes of onset. As a result, the stroke may cause impairment of

bodily functions – such as speech, memory and movement – that are controlled by the affected portion of the brain [1]. Obviously, a stroke can be a debilitating event. Indeed, over the past two decades, stroke has been reported to be the third highest cause of death, and the top reason for need for long-term care. Prevention of stroke is an urgent theme for Japan as well as in other countries of the world.

Some cross-sectional studies have addressed the fact that stroke patients have fewer teeth [2,3], and our clinical data from Hiroshima City General Rehabilitation Center agrees with these findings [4]. At the time of our study, this center had 100 beds and 358 discharged patients who received a dental check between April 2008 and 31 December 2009. Comparing the number of teeth remaining in stroke patients with other patients, we found that stroke patients in their 50s and 60s had significantly fewer remaining teeth than did patients in the corresponding age groups who had been hospitalized for other conditions. Moreover, the number of teeth remaining was significantly lower among stroke

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**Table 1** Number of remaining teeth among stroke patients and patients with other conditions found in this study compared with the results of the Survey of Dental Diseases (2005).

Age (years)	Stroke patients		Other patients		p value	Survey of dental diseases
	Number of subjects	Number of remaining teeth	Number of subjects	Number of remaining teeth		
20–29	3	29.0 ± 2.6	12	28.3 ± 1.3	0.67	29.0 ± 1.8
30–39	4	27.8 ± 1.3	13	27.8 ± 3.0	0.99	28.3 ± 2.0
40–49	10	26.8 ± 2.7	10	26.7 ± 3.5	0.94	26.9 ± 3.5
50–59	28	18.4 ± 9.4*	26	24.5 ± 5.4	0.01 <sup>#</sup>	24.4 ± 6.1
60–69	49	18.3 ± 9.2	39	22.2 ± 7.2	0.03 <sup>#</sup>	19.7 ± 8.7
70–79	56	13.3 ± 10.9	41	13.3 ± 9.3	0.98	13.3 ± 10.1
≥80	31	9.2 ± 10.5	35	8.9 ± 8.8	0.92	8.0 ± 9.2

<sup>#</sup> Significant difference was seen between stroke patients and patients with other diseases ( $p < 0.05$ ).

\* Significant difference was seen compared to the Survey of Dental Diseases (2005) ( $p < 0.05$ ).

patients in their 50s than data reported for that age group in the Survey of Dental Diseases (2005) (Table 1). It can be hypothesized that issues leading to tooth loss are causally related to onset of stroke.

Several previous studies address this hypothesis. In this report, we review these cohort studies and also describe possible causal pathways for these associations.

## Methods

The PubMed database was searched for English-language reports, published over the period 2000–2010, on the topic of tooth loss and stroke including prospective, cohort, or follow-up studies. Hazard ratio (HR) and 95% confidence interval (CI) using Cox proportional hazards models were compared concerning common confounding factors such as age, sex, education and other sociodemographic factors. In addition, the citations listed in the references of the identified reports were also examined.

## Results

Four prospective follow-up studies [5–8] have been conducted on the relationship between tooth loss and cerebral stroke (Table 2). Joshipura et al. [5] assessed the incidence of ischemic stroke among 41,380 men who were free of cardiovascular disease and diabetes at baseline. During 12 years of follow-up, 349 ischemic stroke cases were documented and men who had fewer than 24 teeth at baseline were found to

be at a higher risk for stroke compared to men with 25 or more teeth (HR = 1.57; 95% CI: 1.24–1.98), adjusted for age, amount smoked, obesity, alcohol, exercise, family history of cardiovascular disease, multivitamin and/or vitamin E use, profession, baseline reported hypertension, and hypercholesterolemia.

Abnet et al. [6] evaluated the relationship between tooth loss and the causes of death associated with smoking such as cancer, heart disease, and stroke. The subjects were 29,584 healthy rural Chinese adults aged 40–69 at baseline who were categorized in terms of tooth loss as having less than or equal to or greater than the median number of teeth lost among other subjects of the same age at baseline. During the 10–15 year follow-up period, tooth loss significantly increased the risk of stroke death (HR = 1.11; 95% CI: 1.01–1.23) independently of smoking.

Heitmann and Gamborg [7] followed 2932 subjects (1474 men and 1458 women) aged 30, 40, 50, and 60 years at baseline noting the incidence of fatal and non-fatal cardiovascular disease, coronary heart disease or stroke over a 5–12 year period. During an average 7.5 years of follow-up, 38 women and 48 men developed stroke. Edentulous subjects had a >3-fold increased hazard (HR) of developing stroke (HR = 3.25; 95% CI: 1.48–7.14) compared to subjects with 26–32 teeth remaining. This association was similar for men and women, and for smokers and non-smokers, as well as for the more and less educated.

Choe et al. [8] evaluated the overall risk of stroke and the risk of different subtypes of stroke in relation to tooth loss among 867,256 Korean men and women, aged 30–95 years.

**Table 2** Summary of studies evaluating the relationship between tooth loss and cerebral stroke.

Study authors	Sample size	Lengths	Expose	Outcomes	Relative risk (95%CI)
Joshipura et al. [5]	41,380	12 years	<24 teeth versus 25 or more teeth	Ischemic stroke	Men: 1.57 (1.24–1.98)
Abnet et al. [6]	29,584	15 years	Less than the median number of teeth lost	Total stroke	Total: 1.11 (1.01–1.23)
Heitmann and Gamborg [7]	2,932	5–12 years	0 versus 28–32 teeth	Total stroke	Total: 3.25 (1.48–7.14)
Choe et al. [8]	867,256	14 years	≥7 lost teeth versus 0 during first 3 years	Total stroke	Men: 1.3 (1.2–1.4) Women: 1.2 (1.0–1.3)

During a 14-year follow-up period, a graded association between higher tooth loss and higher risk of total stroke was observed both in men [ $\geq 7$  lost teeth versus 0 (HR = 1.3; 95% CI: 1.2–1.4)] and in women (HR = 1.2; 95% CI: 1.0–1.3). The HRs for ischemic and hemorrhagic stroke were also similar in men and women.

## Discussion

This review study suggests that tooth loss may be related to both ischemic and hemorrhagic stroke.

Periodontal disease, one of the most common chronic infections, has been reported to be a risk factor for coronary heart disease [9–11] and many studies have evaluated the relationship between periodontal disease and/or tooth loss and subsequent stroke [12–17]. In this case, tooth loss could be used as a proxy measure for periodontal disease, or exposure to chronic infection because the main cause of tooth loss after age 40 years may be periodontal disease [18]. These studies addressed the assumption that tooth loss is associated with an increased risk of ischemic stroke. Several potential mechanisms have been proposed for such an association. Periodontal microorganisms have been found in atheromas [19]. The endotoxin in the microorganisms may damage endothelial cells and induce smooth muscle proliferation [20]. Periodontal disease may increase the production of inflammatory markers and clotting factors such as C-reactive protein [21] and fibrinogen and may increase platelet aggregation [22], thus contributing to atherosclerosis and thrombosis. It has been hypothesized that periodontal disease may cause coronary heart diseases and subsequent stroke through the above causal pathway. Two review studies conducted meta-analyses that included the above reports; Janket et al. [23] found that periodontal disease is associated with a 19% increase in risk of future cardiovascular disease (95% CI: 1.08–1.32) and Khader et al. [24] suggested that subjects with periodontitis had 1.15 times the risk of coronal heart disease as healthy subjects (95% CI: 1.06–1.25). These meta-analyses provide evidence for the existence of causal relationship between periodontal diseases and coronary heart disease, but it is unclear at this stage whether there is a causal relationship between periodontal disease and stroke.

A previous study [16] has indicated that ischemic stroke should be evaluated separately because its etiology is more consistent with an infection hypothesis, whereas hemorrhagic stroke is strongly associated with hypertension, and is not generally associated with dental or other infections. However, Choe et al. [8] suggests that tooth loss is independently associated with an increased risk of stroke and that hypertension does interact antagonistically. These diseases appear to have a number of characteristics in common. They are more likely to occur in older persons, males, smokers, people with lower educational status, those with fewer financial resources, and socially isolated or stressed subjects [25]. Stroke and its associated risk factors including arteriosclerosis, diabetes, hypertension, and hyperlipidemia have been described as lifestyle-related diseases, diseases that are closely related to such factors as diet, exercise, smoking habit, alcohol consumption, and stress. Oral diseases, such as dental caries and periodontal diseases, are also closely

related to individual lifestyle and are categorized as lifestyle-related diseases [26,27]. Considering this categorization, it is quite reasonable to expect that the oral health status of patients with stroke associated with lifestyle-related diseases may be worse than that of healthy adults. Recently, Starr and Hall [28] reviewed the literature on edentulism published from 2008 to 2009 and noted that peak or prior intelligence of an individual is an important predictor of a wide range of outcomes in later life including mortality and morbidity, social class and social mobility, smoking cessation, cardiovascular disease, hypertension, disability and C-reactive protein levels. It is interesting to consider the possibility that prior intelligence also influences edentulism as well as the incidence of stroke.

In conclusion, it is quite difficult to rule out all common risk factors as confounding variables, therefore, the exact mechanisms of the relationship between cerebral stroke and tooth loss are difficult to identify. However, it is encouraging that a simple measure like tooth loss, whether or not reflecting a chronic oral infection, may identify subjects at risk for stroke. This knowledge can be used to encourage early cardio-protective preventative initiatives as well as dental treatment.

## Conflict of interest

None declared.

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