

Inverse association between number of teeth and left ventricular mass in women

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Objectives Recently, we have demonstrated a sex-specific inverse association between the number of teeth and hypertension. Left ventricular hypertrophy is a major cardiac sequel of hypertension. With the present study we sought to investigate whether there is also an inverse association between the number of teeth and left ventricular mass (LVM).

Methods We used data from 1913 subjects (1036 women and 877 men) who were recruited for the population-based Study of Health in Pomerania (SHIP). The number of teeth, with the exception of the third molars, was counted in the full mouth. LVM was determined echocardiographically. Multivariable analyses were adjusted for major confounders.

Results Women with fewer teeth had higher values for LVM than women with more teeth. This association was stable when controlled for major confounders. In the full model, edentulous women had an adjusted LVM of 178.4 g [95% confidence interval (CI) 170.4, 186.3 g] while women with 24–28 teeth had an adjusted LVM of 164.8 g (95% CI 156.8, 172.9 g; $P < 0.01$). In men, no such differences were observed.

Introduction

Hypertension is one of the leading risk factors for preventable deaths worldwide. High blood pressure and hypertension-related end organ damage account for 26% of the total mortality in Germany [1]. Hypertension has an inflammatory component; elevated levels of inflammatory serum markers are strong predictors of the progression of systolic blood pressure and incident hypertension [2]. There is current debate on the specific mechanisms responsible for the elevated levels of inflammatory serum markers. Overweight, diabetes and smoking may activate or promote inflammatory processes [3,4] and are major determinants of hypertension [5,6]. Sub-clinical chronic infections may further contribute to activated inflammatory processes. Among oral disorders, periodontal disease causes a measurable systemic inflammation [7]. In adults, periodontal disease represents the major cause of tooth extraction [8]. In cross-sectional studies, the number of teeth is thus a good approximation with respect to the history of periodontal disease.

Two recent studies [9,10] have investigated possible relations between the number of teeth and hypertension.

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Conclusions We conclude that there is an association between the number of teeth and LVM in women aged 45 years or older. In women, these findings further explain why poor oral health predicts all-cause and circulatory mortality. Further research in young, low-risk populations is needed to explore this association in men. *J Hypertens* 25:2035–2043 © 2007 Lippincott Williams & Wilkins.

Journal of Hypertension 2007, 25:2035–2043

Keywords: hypertension, left ventricular mass, oral health, tooth loss

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Received 24 January 2007 Revised 24 April 2007
Accepted 21 May 2007

A Japanese investigation [9] found an inverse relation between the number of teeth and hypertension in post-menopausal women. From recent analyses of the population-based Study of Health in Pomerania (SHIP) we replicated this inverse association in men but not in women [10].

Left ventricular hypertrophy is a major cardiac sequel of hypertension and represents a powerful predictor of morbidity and mortality from myocardial infarction, stroke and congestive heart failure [11]. Since inflammation is also a risk factor for left ventricular hypertrophy, we decided to test the hypothesis that there is an inverse association between number of teeth and left ventricular mass (LVM). Until now, this question has not received much attention, although precise epidemiological data on the association between the number of teeth and LVM may help explain the role of poor oral health as an important predictor for all-cause and cardiovascular mortality [12,13]. Existing studies on the association between oral health and left ventricular hypertrophy are limited by highly selected populations [14,15] or by ECG-derived definition of left ventricular hypertrophy [16]. With the present study we sought to overcome these limitations and to investigate whether there is an

inverse association between the number of teeth and echocardiographically measured LVM using data from a population-based sample of older adults.

Methods

Study population

SHIP is a cross-sectional epidemiological survey in West Pomerania, the north-eastern area of Germany. Study details including sampling methods and non-response analyses are given elsewhere [17,18]. In brief, a representative sample from the West Pomeranian population aged 20–79 years was taken. A sample comprising 7008 persons was selected using population registries where all German inhabitants are registered. Only individuals with German citizenship and main residency in the study area were included. The net sample (without migrated or deceased persons) comprised 6267 eligible subjects. The SHIP population finally comprised 4310 participants (response proportion 68.8%). All participants gave informed written consent. The study protocol is consistent with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of the University of Greifswald.

Echocardiography was *a priori* only performed in subjects aged 45 years or older (1274 women and 1304 men). Thirty-three subjects (11 women and 22 men) were excluded from the analyses because of a history of aortic valve replacement or current aortic stenosis, as evidenced by calcification of the leaflets with a reduced systolic opening and a Doppler gradient of at least 15 mmHg. Among the remaining, readable echocardiograms were available from 1938 subjects (1043 women and 895 men). A further 25 subjects were excluded from the analyses for refusing dental examinations (three women and three men) and missing interview data (four women and 15 men). This resulted in a study population of 1913 subjects (1036 women and 877 men) who were available for complete case analyses.

Measurements

Sociodemographic and medical characteristics were assessed by computer-assisted personal interviews, which were administered by trained and certified staff. Education was categorized into three levels [low (< 10 years), medium (10 years), high (> 10 years), categories based on the Eastern German three-level school system]. Smoking habits were divided into seven categories (never-smoker; ex-smoker: < 10, 10–19, \geq 20 cigarettes/day; current smoker < 10, 10–19, \geq 20 cigarettes/day). Diabetes mellitus was defined as a self-reported history of diabetes. Height and weight were measured for the calculation of the body mass index [BMI = weight (kg)/height² (m²)].

After a 5 min resting period, systolic and diastolic blood pressure was measured three times on the right arm of seated participants, using a digital blood pressure monitor

(HEM-705CP; Omron Corporation, Tokyo, Japan) with each reading being followed by a further resting period of 3 min. One of two differently sized cuffs was applied according to the circumference of the participant's arm. The mean of the second and third measurement was calculated and used for the present analyses. To avoid multicollinearity in the multivariable models, pulse pressure rather than systolic and diastolic blood pressure was used as a covariable in the multivariable analyses. Hypertension was defined as systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg or use of antihypertensive medication.

Two-dimensional and M-mode echocardiography was performed by certified physicians using a Vingmed CFM 800A system (GE Medical Systems, Waukesha, Wisconsin, USA). All data and measurements were stored digitally. M-mode images of the left ventricle were recorded at the papillary level. Left ventricular dimensions (interventricular septum thickness, posterior wall thickness and left ventricular end-diastolic diameter) were measured using the leading-edge convention, and LVM was calculated from the three dimensions [19]. Comparison of all intra-reader, intra-observer, inter-reader, and inter-observer LVM measurements revealed Spearman correlation coefficients of > 0.85 and differences in mean (\pm 2 SD) of < 5% (< 25%). LVM index was calculated by LVM/body surface area. Left ventricular hypertrophy was defined by a LVM \geq 215 g in men and \geq 156 g in women.

Trained and certificated dentists examined the dental status of participants [20]. The number of teeth was counted in the full mouth with the exception of the third molars, which tend to be impacted, congenitally missing, or removed surgically because of anticipated pericoronitis [21]. The maximum number of teeth was therefore 28. The inter-observer agreement of the tooth count was 100%.

Statistical analyses

The study population was divided into five groups using the quintiles of the number of teeth (0, 1–10, 11–18, 19–23 and 24–28 teeth). All analyses were sex-stratified. Categorical data are presented as numbers and percentages; continuous data are presented as mean (\pm SE). Multivariable analyses using LVM as the dependent variable were performed as linear regressions, and as logistic regressions using left ventricular hypertrophy. The coefficient β and its 95% confidence interval (95% CI) were calculated in the case of linear regressions and the odds ratio and its 95% CI in the case of logistic regressions. A value of $P < 0.05$ was considered statistically significant. Regression analyses were performed with SPSS software, version 14.0.1 (SPSS GmbH Software, Munich, Germany).

Multiple imputations

Multiple imputations of missing echocardiographic data have been recommended to reduce potential bias due to

missing values in complete case analysis [22]. As for the complete case analyses, we also excluded all 33 subjects with a history of aortic valve replacement or current aortic stenosis from analyses with imputed data, resulting in an imputed data set from 2545 subjects (1263 women and 1282 men).

In the present study, there were no missing values for gender and age. Among the 2545 subjects the proportion of missing values was $\leq 1\%$ for school education, smoking, diabetes, BMI, systolic and diastolic blood pressure, use of antihypertensive medication, and number of teeth. The proportion of missing values for LVM was 24%. For the imputation of missing echocardiographic data, we used additional information on correlates to LVM from the SHIP data set: history of myocardial infarction, ultrasound evidence of carotid artery stenosis [23], carotid artery intima–media thickness [18], and ECG findings of left ventricular hypertrophy (Sokolov index) [24].

We applied methods developed for incomplete data containing both continuous and categorical variables which were implemented in S-PLUS software (Insightful Corporation, Seattle, Washington, USA) [25]. As recommended, we investigated different imputation models. We chose gender, school education (three categories) and smoking status (seven categories) as categorical variables of the saturated log-linear model; all other variables were log-transformed or dichotomized. The multivariate normal regression model was designed by the 42 cells of the categorical variables. For each cell at least three observations for each of the continuous variables were available. In alternative models, we used smoking status with three categories (never-, ex-, or current smoking) to increase the number of observations per cell. In addition, we stratified according to use of antihypertensive medication. In further analyses, we applied a separate imputation model to each gender [22,26]. For all analysis we used a non-informative prior [22,25,26] to generate five imputations.

For the combined analyses in women, the worst fraction of missing information was 72% and was observed for smoking ≥ 20 cigarettes/day. The relative efficiency of the estimate for smoking of ≥ 20 cigarettes/day from the combined imputations in women was 87%. For the other variables in the model the corresponding percentages were $\leq 48\%$ and $\geq 91\%$. In men, the worst fraction of missing information was 68% and was observed for BMI. The relative efficiency of the estimate for BMI from the combined imputations in men was 88%. The alternative models and the separate imputations for each gender yielded similar results compared with the analyses presented in Tables 3–5 below.

Results

In both women and men, subjects with fewer teeth were older and less educated than subjects with more teeth

Table 1 Selected characteristics according to the number of teeth

Number of teeth	Women (n = 1036)					Men (n = 877)				
	0	1–10	11–18	19–23	24–28	0	1–10	11–18	19–23	24–28
n	187	211	212	244	182	142	183	179	174	199
Age (years)	68.6 (0.6)	64.4 (0.6)	59.4 (0.6)	56.1 (0.5)	54.0 (0.5)	70.2 (0.6)	64.2 (0.6)	62.0 (0.7)	57.2 (0.6)	54.7 (0.5)
School education (%)										
< 10 years	86.6	74.9	59.4	45.5	25.3	79.6	71.0	60.3	50.6	34.7
10 years	12.3	17.5	33.0	41.4	45.6	13.4	20.2	24.6	29.9	38.7
> 10 years	1.1	7.6	7.5	13.1	29.1	7.0	8.7	15.1	19.5	26.6
Cigarette smoking (%)										
never-smoker	62.6	67.8	65.1	59.8	61.5	7.7	14.8	18.4	23.0	28.6
ex-smoker <10 cpd	14.4	9.5	12.3	17.6	13.7	18.3	18.6	21.2	17.8	20.6
ex-smoker 10–19 cpd	4.8	6.2	3.3	5.7	4.9	21.1	10.4	12.8	16.1	12.1
ex-smoker >20 cpd	2.7	0.9	0.9	2.9	2.2	27.5	27.9	26.3	19.0	18.1
current smoker <10 cpd	9.1	6.6	7.5	7.0	9.3	9.2	7.7	4.5	5.2	5.0
current smoker 10–19 cpd	5.9	6.6	8.0	5.3	6.0	10.6	10.4	6.7	7.5	6.5
current smoker ≥ 20 cpd	0.5	2.4	2.8	1.6	2.2	5.6	10.4	10.1	11.5	9.0
Diabetes mellitus (%)	21.4	17.5	6.6	4.9	4.4	12.7	19.1	10.6	10.9	8.0
Body mass index (kg/m ²)	29.0 (0.4)	29.2 (0.4)	27.9 (0.3)	28.2 (0.3)	26.9 (0.4)	27.7 (0.3)	28.1 (0.3)	28.7 (0.3)	27.7 (0.3)	27.8 (0.2)
Systolic blood pressure (mmHg)	145.4 (1.6)	139.6 (1.4)	137.7 (1.5)	135.6 (1.2)	133.7 (1.4)	149.7 (1.6)	149.3 (1.5)	148.0 (1.5)	145.1 (1.4)	144.0 (1.4)
Diastolic blood pressure (mmHg)	82.5 (0.8)	82.8 (0.7)	84.6 (0.7)	84.6 (0.6)	83.6 (0.7)	84.6 (0.9)	86.3 (0.8)	88.5 (0.9)	89.0 (0.8)	89.9 (0.9)
Pulse pressure (mmHg)	62.9 (1.3)	56.8 (1.0)	53.3 (1.1)	51.0 (0.9)	50.1 (1.0)	65.1 (1.3)	63.0 (1.3)	59.5 (1.1)	56.1 (1.0)	54.0 (0.9)
Use of antihypertensive medication (%)	50.3	42.7	36.3	28.7	25.3	39.4	37.2	38.5	31.6	32.2
Hypertension (%)	75.9	65.9	59.4	52.9	44.5	79.6	79.8	79.9	70.7	68.3

Data are given as percentages and percentage or mean (standard error). cpd denotes cigarettes per day.

(Table 1). Among men with fewer teeth, there were lower proportions of never-smokers and higher proportions of former smokers compared to men with more teeth. In women no such trends were found. Women with fewer teeth more frequently had diabetes mellitus than women with more teeth. In men, there was also a difference in the diabetes prevalence between subjects with ≤ 10 teeth and subjects with ≥ 11 teeth, but this trend was not stable over all exposure groups. While women with fewer teeth had higher BMI values than women with more teeth, the mean BMI in men was relatively constant over all exposure groups. Systolic blood pressure and pulse pressure were higher in subjects with fewer teeth compared to subjects with more teeth. Men with fewer teeth had lower diastolic blood pressure than men with more teeth. The latter difference was not present in women. Women and men with fewer teeth received antihypertensive medication more frequently; this difference was greater in women than in men. The proportion of hypertensives continuously increased over decreasing number of teeth in women. In men, this increase was also present but blunted in subjects with ≤ 10 teeth. Overall, hypertension was more frequent in men (76.7%) than in women (61.4%) (Table 1).

With regard to echocardiographic characteristics, women with fewer teeth had higher values of LVM and LVM index as well as more frequently left ventricular hypertrophy than women with more teeth (Table 2). In men, these associations were less pronounced (Table 2).

Multivariable linear regression analyses in subjects with complete variables revealed that the inverse association between the number of teeth and LVM remained stable after adjustment for age in the female population (Table 3). Further inclusion of pulse pressure and use of antihypertensive medication did not materially affect the regression coefficients. The trend remained, but was attenuated when BMI was also considered as covariable. The full model, which included further potential confounders such as smoking behaviour and diabetes, only marginally altered this result (Table 3, Fig. 1).

In contrast, no clear trend between the number of teeth and LVM was observed in men (Table 3). Complete case analyses adjusted for age, pulse pressure and use of antihypertensive medication revealed a statistically significant difference in LVM between men with 11–18 teeth compared to men with 24–28 teeth, but this result was not maintained when analyses were further adjusted for BMI and other potential confounders (Table 3, Fig. 1).

Analyses using LVM index as alternative dependent variable revealed similar results (Fig. 2). While in women an inverse relation between the number of teeth and LVM index was corroborated ($P_{\text{trend}} = 0.007$), no such relation was present in men ($P_{\text{trend}} = 0.746$).

Table 2 Echocardiographic variables according to the number of teeth

Number of teeth	Women (n = 1036)				Men (n = 877)					
	0	1–10	11–18	19–23	24–28	0	1–10	11–18	19–23	24–28
n	187	211	212	244	182	142	183	179	174	199
IVS (mm)	10.4 (0.2)	9.9 (0.2)	9.5 (0.1)	9.0 (0.1)	8.9 (0.2)	10.6 (0.2)	10.7 (0.2)	11.1 (0.2)	10.4 (0.2)	10.5 (0.2)
LVEDD (mm)	49.5 (0.4)	49.1 (0.3)	49.4 (0.4)	49.6 (0.3)	48.3 (0.3)	53.3 (0.5)	53.7 (0.5)	54.0 (0.4)	54.0 (0.4)	52.9 (0.4)
PWD (mm)	9.9 (0.1)	9.9 (0.1)	9.3 (0.2)	9.1 (0.1)	9.0 (0.1)	10.4 (0.2)	10.5 (0.2)	10.5 (0.2)	10.0 (0.1)	10.0 (0.1)
LVM (g)	188.2 (3.9)	178.7 (3.1)	168.8 (3.1)	162.5 (2.5)	152.5 (3.0)	223.7 (4.9)	227.9 (4.6)	235.1 (4.6)	218.7 (4.3)	213.0 (3.5)
LVM index (g/m ²)	109.4 (2.1)	101.9 (1.6)	96.8 (1.6)	92.3 (1.3)	87.0 (1.5)	118.5 (2.5)	116.8 (2.3)	119.7 (2.3)	110.1 (1.9)	108.1 (1.6)
Left ventricular hypertrophy	69.5	65.9	59.9	50.8	39.6	51.4	53.0	53.1	48.3	46.2

Data are given as numbers and percentage or mean (standard error). IVS, interventricular septum thickness; LVEDD, left ventricular end-diastolic diameter; LVM, left ventricular mass; PWD, posterior wall thickness.

Table 3 Relation between the number of teeth and left ventricular mass (LVM)

Number of teeth	Women					Men				
	0	1–10	11–18	19–23	24–28 (reference)	0	1–10	11–18	19–23	24–28 (reference)
Complete case (women: $n = 1036$; men: $n = 877$)										
β (SE), adjusted for age	25.0 (5.3) [†]	18.6 (4.9) [†]	12.3 (4.6) [*]	8.6 (4.4) [*]	121.3 (9.9) const. $P_{\text{trend}} < 0.001$	1.4 (7.4)	9.2 (6.4)	17.8 (6.2) [†]	4.2 (6.0)	180.2 (14.3) const. $P_{\text{trend}} = 0.457$
β (SE), adjusted for age, pulse pressure, and use of antihypertensive medication	22.8 (5.1) [†]	18.6 (4.6) [†]	12.2 (4.4) [†]	8.8 (4.2) [*]	114.1 (9.8) const. $P_{\text{trend}} < 0.001$	3.3 (7.3)	9.1 (6.3)	17.9 (6.1) [†]	4.7 (5.9)	178.5 (14.5) const. $P_{\text{trend}} = 0.379$
β (SE) adjusted for the full model	13.5 (4.9) [†]	8.7 (4.4) [*]	7.1 (4.1)	3.8 (3.9)	13.8 (12.2) const. $P_{\text{trend}} = 0.011$	-1.0 (7.1)	4.4 (6.1)	10.3 (5.8)	3.6 (5.5)	-5.0 (21.4) const. $P_{\text{trend}} = 0.926$
Combined imputation (women: $n = 1263$; men: $n = 1282$)										
β (SE), adjusted for age	23.7 (5.4) [†]	19.4 (5.0) [†]	11.8 (4.5) [†]	8.6 (4.2) [*]	116.2 (10.6) const. $P_{\text{trend}} < 0.001$	8.6 (6.5)	9.1 (5.8)	15.0 (5.5) [†]	4.9 (5.4)	189.4 (13.9) const. $P_{\text{trend}} = 0.112$
β (SE), adjusted for age, pulse pressure, and use of antihypertensive medication	21.6 (5.1) [†]	19.0 (4.9) [†]	11.2 (4.4) [*]	8.4 (4.0) [*]	117.7 (10.2) const. $P_{\text{trend}} < 0.001$	8.0 (6.4)	8.2 (5.8)	14.1 (5.4) [†]	4.3 (5.3)	180.7 (14.1) const. $P_{\text{trend}} = 0.134$
β (SE) adjusted for the full model	12.0 (4.9) [*]	9.4 (4.7) [*]	6.4 (4.1)	3.2 (3.8)	12.9 (11.8) const. $P_{\text{trend}} = 0.014$	3.7 (6.3)	3.5 (5.4)	7.2 (5.1)	2.7 (4.9)	5.7 (26.4) const. $P_{\text{trend}} = 0.451$

Linear regression analysis, dependent variable: LVM. The full model included age, pulse pressure, use of antihypertensive medication, school education (three categories), smoking behaviour (seven categories), diabetes and body mass index. * $P < 0.05$, [†] $P < 0.01$, [‡] $P < 0.001$.

Logistic regression analyses were performed by using left ventricular hypertrophy as the dependent variable (Table 4). These analyses arrived at results similar to the findings from the linear regressions. Again, there was an inverse association between the number of teeth and the dependent variable in women, but not in men (Table 4).

Additional analyses were performed using different categorizations of age, BMI, and pulse pressure. Alternative models included hypertension instead of pulse pressure and use of antihypertensive medication as independent variables. Moreover, we tested further potential confounding factors such as alcohol consumption and healthcare utilization in the models. All these analyses confirmed the main result of an inverse association of the number of teeth with LVM, LVM index and left ventricular hypertrophy.

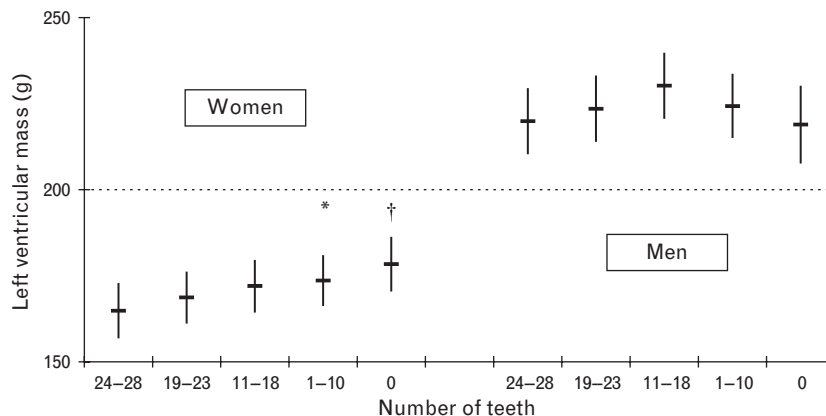
The characteristics of subjects who were included in and excluded from the complete case analysis are outlined in Table 5. Women were more likely than men to be included in the analysis. Subjects included were younger and better educated than subjects excluded. The proportions of current and ex-smokers were no different in women who were included or not, while in men more smokers were among those included compared to those excluded. Included women were less likely to have a history of diabetes mellitus, had lower BMI, systolic blood pressure and pulse pressure values, and were less likely to be hypertensive than excluded women. Included men had higher BMI and pulse pressure values and received antihypertensive medication less frequently than excluded men. Participants who were included had more teeth than those excluded. The imputed LVM values in excluded subjects were higher than the observed values in included subjects. Consequently, included subjects had left ventricular hypertrophy less commonly than excluded subjects (Table 5). Compared to the complete case analyses, all multivariable models using the imputed values arrived at similar results for the association between number of teeth and LVM, LVMI and left ventricular hypertrophy (Tables 3 and 4).

Discussion

In the present paper we demonstrate an association between the number of teeth and LVM in women aged 45–79 years. These results were stable in analyses using alternative end points and different sets of covariables. Although the subjects who had to be excluded from the study due to missing echocardiographic values differed considerably from subjects with complete data, multiple imputations did not suggest that such selection had severely biased our major findings.

Findings in women are partly in concordance with a Japanese population-based study [16], which revealed an inverse association between the number of teeth

Fig. 1



Relation between the number of teeth and left ventricular mass ($n = 1036$ women and 877 men). Data are adjusted means (95% confidence interval). Analyses were controlled for age, pulse pressure, use of antihypertensive medication, school education (three categories), smoking behaviour (seven categories), diabetes and body mass index. * $P < 0.05$, † $P < 0.01$ (reference group: 24–28 teeth).

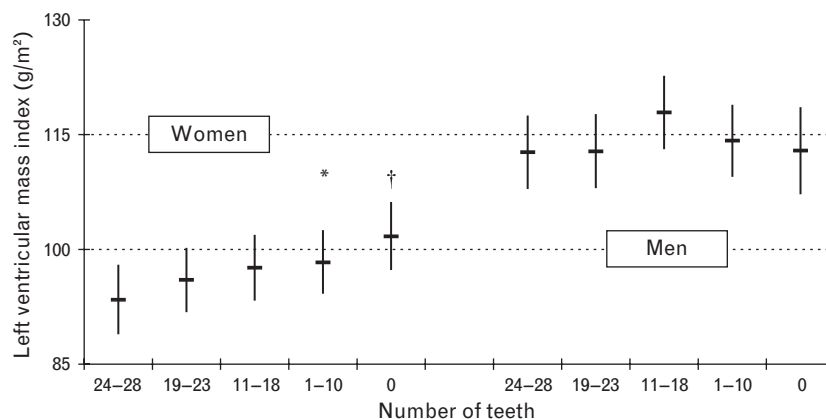
and ECG abnormalities, including left ventricular hypertrophy. Unfortunately, the Japanese study [16] used an aggregated end point for statistical analyses and did not specifically investigate left ventricular hypertrophy as a separate dependent variable.

Given that periodontal disease is the most common cause of tooth extraction in adults [8], the results in women are also in line with two other studies [14,15]. The first study [15] investigated 104 untreated subjects with essential hypertension. Patients with higher extents of periodontal disease had higher values for echocardiographically determined LVM index in multivariable analyses, which were controlled for body surface area as well as systolic and diastolic blood pressure. The second study [14]

analysed data from 99 recipients of kidney transplants and found similar results. Unfortunately, none of these studies [12–14] analysed the relation between oral health and LVM separately for women and men.

The most striking result of our study is the gender difference in the relation between the number of teeth and LVM. While there was a stable trend over all exposure categories in women, a blunted trend was found in men. This gender difference may be explained by several factors. First, it may reflect the generally higher susceptibility of female hearts for hypertrophic changes. Not only is the prevalence of left ventricular hypertrophy higher in women than in men, but women also respond with concentric hypertrophy following hypertension

Fig. 2



Relation between the number of teeth and left ventricular mass index ($n = 1036$ women and 877 men). Data are adjusted means (95% confidence interval). Analyses were controlled for age, pulse pressure, use of antihypertensive medication, school education (three categories), smoking behaviour (seven categories), diabetes and body mass index. * $P < 0.05$, † $P < 0.01$ (reference group: 24–28 teeth).

Table 4 Relation between the number of teeth and left ventricular hypertrophy

Number of teeth	Women					Men				
	0	1-10	11-18	19-23	24-28 (reference)	0	1-10	11-18	19-23	24-28 (reference)
Complete case (women: n = 1036; men: n = 877)										
OR (95% CI), adjusted for age	2.6 (1.6-4.2) [‡]	2.4 (1.5-3.7) [‡]	2.0 (1.4-3.1) [‡]	1.5 (1.0-2.2)*	1.0 P _{trend} < 0.001	1.0 (0.6-1.6)	1.1 (0.7-1.7)	1.2 (0.8-1.8)	1.0 (0.7-1.6)	1.0 P _{trend} = 0.774
OR (95% CI), adjusted for age, pulse pressure, and use of antihyper-tensive medication	2.5 (1.5-4.2) [‡]	2.6 (1.6-4.0) [‡]	2.2 (1.4-3.3) [‡]	1.6 (1.1-2.4)*	1.0 P _{trend} < 0.001	1.0 (0.6-1.7)	1.1 (0.7-1.7)	1.2 (0.8-1.8)	1.1 (0.7-1.6)	1.0 P _{trend} = 0.747
OR (95% CI), adjusted for the full model	1.9 (1.1-3.4)*	1.9 (1.1-3.1)*	2.0 (1.3-3.2) [†]	1.3 (0.9-2.1)	1.0 P _{trend} = 0.027	1.0 (0.6-1.7)	1.1 (0.6-1.7)	1.0 (0.6-1.6)	1.1 (0.7-1.7)	1.0 P _{trend} = 0.908
Combined imputation (women: n = 1263; men: n = 1282)										
OR (95% CI), adjusted for age	2.4 (1.5-3.7) [‡]	2.3 (1.4-3.7) [‡]	1.9 (1.3-2.9) [†]	1.5 (1.0-2.2)*	1.0 P _{trend} < 0.001	1.2 (0.8-2.0)	1.2 (0.8-1.8)	1.2 (0.8-1.7)	1.1 (0.7-1.6)	1.0 P _{trend} = 0.242
OR (95% CI), adjusted for age, pulse pressure, and use of antihyper-tensive medication	2.3 (1.4-3.7) [‡]	2.4 (1.5-4.0) [‡]	2.0 (1.3-3.0) [†]	1.5 (1.0-2.3)*	1.0 P _{trend} < 0.001	1.2 (0.7-2.0)	1.1 (0.7-1.7)	1.2 (0.8-1.7)	1.1 (0.7-1.6)	1.0 P _{trend} = 0.318
OR (95% CI), adjusted for the full model	1.8 (1.0-3.0)*	1.8 (1.0-3.2)*	1.9 (1.2-3.0) [†]	1.3 (0.8-2.1)	1.0 P _{trend} = 0.042	1.1 (0.6-2.1)	1.1 (0.7-1.7)	1.0 (0.6-1.5)	1.0 (0.7-1.6)	1.0 P _{trend} = 0.518

Logistic regression analysis, dependent variable: left ventricular hypertrophy. The full model included age, pulse pressure, use of antihypertensive medication, school education (three categories), smoking behaviour (seven categories), diabetes and body mass index. CI, confidence interval; OR, odds ratio. * P < 0.05, † P < 0.01, ‡ P < 0.001.

more frequently than men [27]. Since in our female population the inverse relation between the number of teeth and LVM was independent of pulse pressure and the use of antihypertensive medication, our data may suggest that female hearts also respond more intensely to inflammatory stimuli caused by poor oral health. Second, the gender difference may be explained partly by varying distributions of LVM determinants such as smoking and hypertension. Women were more frequently never-smokers and had hypertension less commonly than men. It is conceivable that second-order risk factors are more important in the female subpopulation that is at low risk with respect to left ventricular hypertrophy, than in the male high-risk population. Finally, survival bias may have contributed to the gender differences. Also, against the background of our previous report on an inverse association between number of teeth and hypertension [10], men with very few (≤ 10) teeth may be at a very high risk of LVH and may have died as a result of cardiovascular disease at a young age. This suggestion is supported by the finding of the present study that the proportion of male hypertensives increased with decreasing number of teeth as long as the number of teeth was ≥ 11 , but that this relation was blunted in men with ≤ 10 teeth. We cannot exclude from our data that an association between tooth loss and left ventricular hypertrophy might be present in younger men. In this context, the *a priori* restriction of echocardiography to subjects aged 45 years or older in our analyses might have yielded a false-negative result in the male subpopulation. This notion is supported by studies that found stronger associations between periodontal and cardiovascular disease in younger than in elderly men [28-30].

The inverse relation between the number of teeth and LVM may be explained by several mechanisms. First, it is conceivable that hypertension is an intermediate step between poor oral health and LVM in men but not necessarily in women, and that we may have underestimated the relation between the number of teeth and LVM in men by adjusting for pulse pressure and antihypertensive medication in our analyses. Second, systemic inflammatory mediators may exert direct effects on the heart muscle. Examples include pro-inflammatory cytokines activating intracellular signalling [31] and high-sensitivity C-reactive protein upregulating angiotensin II type 1 receptors [32]. Both mechanisms are known to lead to hypertrophy of myocytes. Third, poor oral health is associated with insulin resistance [33], which in turn is an important determinant of LVM [34]. Although we adjusted our multivariable models for BMI and diabetes mellitus, direct measures of insulin resistance were unfortunately not available for the present study. We therefore cannot unequivocally exclude residual confounding by insulin resistance.

Tooth loss has been demonstrated repeatedly to predict all-cause and circulatory mortality [12,13]. This associ-

Table 5 Variables in the left ventricular mass model for participants who were either included in or excluded from complete case analysis

	Women			Men		
	Excluded (n = 227)	Included (n = 1036)	P	Excluded (n = 405)	Included (n = 877)	P
Age (years)	62.7 (0.7)	60.3 (0.3)	0.003	64.8 (0.5)	61.2 (0.3)	< 0.001
School education (%)			0.009			0.024
<10 years	69.2	58.2		65.9	57.9	
10 years	21.6	30.3		21.5	26.1	
>10 years	9.3	11.5		12.6	16.0	
Cigarette smoking (%)			0.898			0.009
Never-smoker	62.9	63.3		12.4	19.2	
Ex-smoker <10 cpd	15.4	13.6		18.3	19.4	
Ex-smoker 10–19 cpd	5.4	5.0		15.7	14.1	
Ex-smoker ≥20 cpd	2.7	1.9		27.7	23.5	
Current smoker <10 cpd	6.3	7.8		6.1	6.2	
Current smoker 10–19 cpd	5.0	6.4		12.7	8.2	
Current smoker ≥20 cpd	2.3	1.9		7.1	9.5	
Diabetes mellitus (%)	17.1	10.8	0.011	14.5	12.3	0.279
Body mass index (kg/m ²)	29.9 (0.3)	28.3 (0.2)	< 0.001	29.1 (0.2)	28.0 (0.1)	< 0.001
Systolic blood pressure (mmHg)	142.4 (1.5)	138.3 (0.6)	0.008	149.0 (1.1)	147.1 (0.7)	0.113
Diastolic blood pressure (mmHg)	84.3 (0.8)	83.6 (0.3)	0.371	87.2 (0.6)	87.8 (0.4)	0.326
Pulse pressure (mmHg)	58.1 (1.2)	54.6 (0.5)	0.007	61.8 (0.8)	59.2 (0.5)	0.005
Use of antihypertensive medication (%)	42.9	36.4	0.077	41.7	35.6	0.042
Hypertension (%)	70.0	59.6	0.004	79.6	75.4	0.100
Number of teeth	11.9 (0.7)	13.7 (0.3)	0.011	10.8 (0.5)	14.2 (0.3)	< 0.001
Left ventricular mass (g)	–	170.0 (1.4)		–	223.5 (2.0)	
Imputation 1	181.2 (3.4)		0.001	237.1 (3.2)		< 0.001
Imputation 2	176.2 (3.5)		0.073	230.1 (2.7)		0.053
Imputation 3	182.7 (3.4)		< 0.001	237.7 (2.9)		< 0.001
Imputation 4	181.8 (3.7)		0.001	234.0 (3.0)		0.003
Imputation 5	177.9 (3.1)		0.019	232.5 (3.0)		0.011
Left ventricular hypertrophy (%)	–	57.1		–	50.3	
Imputation 1	64.8		0.037	60.7		< 0.001
Imputation 2	59.9		0.459	57.8		0.014
Imputation 3	67.4		0.005	59.0		0.004
Imputation 4	61.2		0.266	57.0		0.026
Imputation 5	64.3		0.053	57.0		0.026

The imputations 1 to 5 represent the five repetitions of the filled-in data set obtained from the multiple imputations of the missing values. Please see methods section for detailed information.

ation might be partly explained by an increased risk of atherosclerotic end points including endothelial dysfunction, stroke, myocardial infarction and aortic valve sclerosis in individuals with periodontal disease [23,35–37]. Other studies, however, did not confirm these findings [38,39]. Since left ventricular hypertrophy is a strong predictor of mortality [40,41], the inverse association between the number of teeth and LVM further explains the relation between poor oral health and mortality, at least in the female population.

We conclude that there is an association between the number of teeth and LVM in women aged 45 years or older. In women, these findings further explain why poor oral health predicts all-cause and circulatory mortality. Further research in young, low-risk populations is needed to explore this association in men.

Acknowledgements

SHIP is part of the Community Medicine Research net (CMR) of the University of Greifswald, Germany, which is funded by the Federal Ministry of Education and Research (grant no. ZZ9603) and the Ministry of Cultural Affairs as well as the Social Ministry of the Federal State of Mecklenburg-West Pomerania (<http://www.community-medicine.de>). This work was further sup-

ported by the BMBF Competence Network Heart Failure (Kompetenznetz Herzinsuffizienz).

There are no conflicts of interest associated with this work.

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