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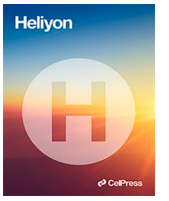

Research article

Association of tooth loss and periodontal disease with all-cause mortality in cancer survivors: A cohort study based on NHANES

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ABSTRACT

Background: Increasing evidence supports the association between impaired oral health and elevated mortality. However, there is currently a lack of research on the impact of tooth loss and periodontal disease on survival outcomes in cancer survivors. This study aims to clarify the effect of tooth loss and periodontitis on all-cause mortality on cancer survivors.

Methods: The clinical data of cancer survivors were collected from National Health and Nutrition Examination Survey (NHANES) 1999–2018. Mortality data were obtained by linking to records in the National Death Index until December 31, 2019. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal threshold for discriminating mortality based on the number of teeth lost. Kaplan–Meier survival curves and Cox regression analysis were performed to calculate hazard ratios (HRs) and 95 % confidence intervals (95 % CI) for tooth loss and periodontitis.

Results: A total of 3271 cancer survivors were assessed for tooth loss status, while 1267 patients were evaluated for periodontitis status. The prevalence of any tooth loss and CDC-AAP periodontitis was 83.5 % and 47.2 %, respectively. The ROC curve showed the cut-off point of tooth loss for predicting mortality is > 5. Cancer survivors with tooth loss>5 had significantly lower bone density (1.06 *vs.* 1.13 g/cm^2, $P < 0.001$), elevated C-reactive protein level (0.3 vs. 0.18 mg/dL, $P < 0.001$), and a trend of lower lean body mass (46.9 vs. 47.6 kg, $P = 0.093$). Besides, cancer survivors with severe periodontitis also exhibited elevated C-reactive protein level (0.34 vs. 0.21 mg/dL, $P = 0.033$). All-cause mortality significantly increased in cancer survivors with either tooth loss>5 (HR = 1.290, $P = 0.001$) or severe CDC-AAP periodontitis (HR = 1.682, $P = 0.016$) in the multivariate Cox regression analysis.

Conclusion: Tooth loss and periodontitis are strong risk factors for reduced overall survival in cancer survivors. Cancer survivors should emphasize diligent oral hygiene and consistent dental check-ups to optimize long-term oral health. The causal relationship between oral health and survival rates in cancer survivors requires further validation through randomized controlled trials.

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1. Introduction

Oral health is a fundamental aspect of overall well-being, and it undergoes inevitable physiological changes with age. Among all age demographics, the elderly are particularly vulnerable to oral diseases [1,2]. Tooth loss and periodontal disease are prevalent oral health issues among older adults, significantly affecting their quality of life. Studies indicate that around 40 % of American adults experience varying degrees of periodontal disease, with over 20 % of individuals aged 60 and above being edentulous [3,4]. Some investigations have explored the relationship between oral health and adverse outcomes, including an increased overall mortality rate [5], an elevated risk of cardiovascular disease [6], expedited cognitive decline [7], and a higher susceptibility to cancer [8].

Cancer treatments like radiation therapy and chemotherapy significantly impact oral tissues and structure. Additionally, the body's response to cancer and measures taken during cancer therapy make cancer patients susceptible to noticeable malnutrition and cachexia [9]. Oral issues can exacerbate these challenges, leading to inadequate nutritional intake by patients and impacting the recovery process [10]. Whether compromised oral health accelerates cancer patient mortality remains a subject of debate. A previous study showed that no discrepancy in cancer mortality was observed between cardiovascular disease patients with different periodontal status from the National Health and Nutrition Examination Survey (NHANES) [5]. However, another study discovered that periodontal disease or edentulism increased the risk of cancer-related mortality in participants aged 40 and older who had no prior cancer diagnosis [11].

To date, there is limited research on the relationship between oral health and mortality in cancer survivors, and it is unclear whether the impact of impaired oral health differs among various cancer types. This study aimed to assess the impact of tooth loss and periodontal disease on the mortality of cancer survivors, examining their impact on various cancer types and considering different degrees of tooth loss and periodontal disease through subgroup analysis.

2. Materials and methods

2.1. Study population

NHANES is a large-scale and ongoing nationally representative health survey of US population conducted by the National Center for Health Statistics (NCHS). The surveys have received approval from the institutional review board of the National Center of Health Statistics, and written informed consent has been obtained from all participants. In this study, data on tooth count were derived from NHANES 1999–2018, while the data on periodontitis were derived from NHANES 1999–2004 and NHANES 2009–2014. The analytic sample included all adults with a cancer history, and those with multiple cancer history, missing data on tooth count, periodontal examinations, and baseline characteristics were excluded in the analysis.

2.2. Sample collection

The following demographic variables were collected: age, sex, weight, height, body mass index (BMI), race/ethnicity, income level, health insurance, comorbidities, tooth count, gingival recession, pocket depth, diabetes, smoking history, alcohol usage history.

BMI is calculated by weight (kg) divided by height (m) squared. The race of all participants included Mexican American, other Hispanic, non-Hispanic White, non-Hispanic Black, and other race. Income level is defined by poverty income ratio (PIR), which is calculated by dividing household income in the survey year by the poverty threshold. Gingival recession (GR) is the distance from the free gingival margin to the cementoenamel junction, pocket depth (PD) is the distance from the free gingival margin to the bottom of the sulcus, and the periodontal attachment loss (AL) was calculated from GR and PD to represent the distance from the cementoenamel junction to the bottom of the sulcus. Smoking history is defined as having smoked at least 100 cigarettes in one's life. Alcohol usage history is defined as having consumed at least 12 alcohol drinks per year.

2.3. Measurement and classification and periodontitis

Two definitions were used for periodontitis: (1) according to the Centers for Disease Control and Prevention-American Academy of Periodontology (CDC-AAP) [12], no periodontitis is defined as no evidence of mild, moderate, or severe periodontitis; mild periodontitis is defined as $\geq$2 interproximal sites with AL$\geq$3 mm, and$\geq$2 interproximal sites with PD $\geq$ 4 mm (not on same tooth) or one site with PD $\geq$ 5 mm; moderate periodontitis is defined as $\geq$2 interproximal sites with AL$\geq$4 mm (not on same tooth), or $\geq$2 interproximal sites with PD $\geq$ 5 mm (not on same tooth); severe periodontitis is defined as $\geq$2 interproximal sites with AL$\geq$6 mm (not on same tooth) and $\geq$1 interproximal site with PD $\geq$ 5 mm; (2) according to previous studies based on NHANES data [11,13], one or more periodontal sites with both AL$\geq$3 mm and PD $\geq$ 4 mm were defined as periodontitis.

2.4. Follow-up

The NHANES-Linked Mortality File was created by the National Center for Health Statistics (NCHS) by linking NHANES respondents to the National Death Index (NDI). All participants were followed until the date of death or December 31, 2019. The survival time was calculated from the date of medical examination to either death or censoring.

2.5. Statistical analysis

Categorical data were represented as counts with percentages and compared using Pearson's chi-square test or Fisher's exact test. For non-normally distributed continuous data, median values along with the interquartile range (IQR) were utilized, and group comparisons were performed using the Mann–Whitney *U* test. Cox proportional hazard models were used to investigate the association of tooth loss and periodontitis with mortality. The results are shown as hazard ratios (HRs) together with 95 % confidence intervals. Three incremental models with increasing numbers of varieties were created. Model 0 was unadjusted; Model 1 was adjusted for age and sex; Model 2 was adjusted for Model 1 plus BMI, race/ethnicity, income level, health insurance, smoking history, and alcohol usage history; Model 3 was adjusted for Model 2 plus diabetes, hypertension, asthma, arthritis, thyroid diseases, cardiac diseases, pulmonary diseases, and liver diseases. Receiver operating characteristic (ROC) curve analysis is conducted to assess the optimal number of teeth loss to discriminate mortality. Adjusted survival curves is performed to assess the impacts of tooth loss and periodontitis on survival time.

3. Results

3.1. Demographic characteristics of the cancer survivors

A total of 3271 cancer survivors were assessed for tooth loss status, while 1267 patients were evaluated for periodontitis status. The

Table 1
Baseline characteristics of cancer survivors.

Factor	Overall[a]	Tooth loss (n = 3271)[a]		*P* value	Periodontitis defined by CDC/AAP (n = 1267)[b]		*P* value
		Tooth loss > 5	Tooth loss≤5		Yes	No	
Age, median (25th-75th), year	68 (58–77)	72 (63–80)	62 (51–73)	<0.001*	70 (60–78)	62 (50–72)	<0.001*
Sex, %				0.001*			<0.001*
Male	1575 (48.2)	899 (50.7)	676 (45.1)		321 (53.7)	253 (37.8)	
Female	1696 (51.8)	874 (49.3)	822 (54.9)		277 (46.3)	416 (62.2)	
Height, median (25th-75th), cm	167.1 (159.9–174.4)	166.7 (159.3–173.4)	167.6 (160.8–175.3)	<0.001*	168 (160.1–175)	166 (159.4–173.7)	0.066
Weight, median (25th-75th), kg	78.2 (67–92)	77.8 (66.8–90.8)	79 (67.5–92.9)	0.029*	78.8 (67.2–94.7)	77.1 (66.7–90.5)	0.196
BMI, median (25th-75th), kg/m^2	27.8 (24.4–32.1)	27.8 (24.6–32.1)	27.8 (24.3–32.1)	0.659	27.4 (24.1–32)	27.6 (24.5–31.6)	0.927
Race/ethnicity, %				<0.001*			0.005*
Mexican American	221 (6.8)	110 (6.2)	111 (7.4)		41 (6.9)	55 (8.2)	
Other Hispanic	150 (4.6)	89 (5)	61 (4.1)		28 (4.7)	28 (4.7)	
Non-Hispanic White	2309 (70.6)	1184 (66.8)	1125 (75.1)		404 (67.6)	498 (74.4)	
Non-Hispanic Black	460 (14.1)	321 (18.2)	139 (9.3)		101 (16.9)	68 (10.2)	
Other race/ethnicity	131 (4)	69 (3.9)	62 (4.1)		24 (4)	20 (3)	
Income level, %				<0.001*			<0.001*
PIR<1	439 (13.4)	318 (17.9)	121 (8.1)		72 (12)	69 (10.3)	
1 ≤ PIR<2	842 (25.7)	600 (33.8)	242 (16.2)		155 (25.9)	108 (16.1)	
2 ≤ PIR<3	556 (17)	340 (19.2)	216 (14.4)		95 (15.9)	117 (17.5)	
PIR≥3	1434 (43.8)	515 (29)	919 (61.3)		276 (46.2)	375 (56.1)	
Health insurance, covered (%)	3084 (94.3)	1681 (94.8)	1403 (93.7)	0.157	561 (93.8)	637 (95.2)	0.272
Comorbidity							
Diabetes, %	627 (19.2)	432 (24.4)	195 (13)	<0.001*	122 (20.4)	88 (13.2)	0.001*
Hypertension, %	1821 (55.7)	1109 (62.5)	712 (47.5)	<0.001*	338 (56.5)	321 (48)	0.002[a]
Asthma, %	504 (15.4)	286 (16.1)	218 (14.6)	0.213	75 (12.5)	97 (14.5)	0.310
Arthritis, %	1613 (49.3)	978 (55.2)	635 (42.4)	<0.001*	278 (46.5)	278 (41.6)	0.077
Thyroid diseases, %	600 (18.3)	313 (17.7)	287 (19.2)	0.268	97 (16.2)	163 (20.3)	0.060
Cardiac diseases, %	629 (19.2)	463 (26.1)	166 (11.1)	<0.001*	87 (14.5)	56 (8.4)	0.001*
Pulmonary diseases, %	485 (14.8)	346 (19.5)	139 (9.3)	<0.001*	73 (12.2)	57 (8.5)	0.031*
Liver diseases, %	174 (5.3)	109 (6.1)	65 (4.3)	0.022*	23 (3.8)	32 (4.8)	0.414
Smoking history[c], %	1839 (56.2)	1176 (66.3)	663 (44.3)	<0.001*	343 (57.4)	313 (46.8)	<0.001*
Alcohol usage history[d], %	2161 (66.1)	1070 (60.3)	1091 (72.8)	<0.001*	418 (69.9)	488 (72.9)	0.231

Abbreviations: BMI, body mass index; IQR, interquartile range; NHANES, National Health and Nutrition Examination Survey; PIR, poverty income ratio.

* Statistical significance.

[a] Data derived from NHANES 1999–2018.

[b] Data derived from NHANES 1999–2004 and NHANES 2009–2014.

[c] Smoked more than 100 cigarettes in life.

[d] Had at least 12 alcohol drinks/1 year.

flowchart of participant selection was shown in Supplementary Fig. 1. The prevalence of any tooth loss and CDC-AAP periodontitis was 83.5 % (2730/3271) and 47.2 % (598/1267), respectively. Demographic characteristics were shown in Table 1. To determine the optimal tooth loss threshold for distinguishing the mortality in cancer survivors, we conducted an ROC curve analysis. The results indicated that a tooth loss count>5 provided the best discrimination of mortality (Fig. 1).

Subsequently, the baseline characteristics of cancer survivors were compared based on whether the tooth loss count was >5 and whether they met the CDC-AAP periodontitis criteria (Table 1). The results indicated that, compared to cancer survivors with tooth loss≤5, those with tooth loss>5 were older ($P < 0.001$), more likely to be male ($P = 0.001$), have lower income level ($P < 0.001$), higher proportion of smoking history ($P < 0.001$), and higher prevalence of comorbidities, including diabetes, hypertension, arthritis, cardiac diseases, pulmonary diseases, and liver diseases. However, cancer survivors with tooth loss≤5 had higher proportion of alcohol usage history ($P < 0.001$). Similarly, the comparisons between cancer survivors with and without periodontitis showed that, cancer survivors with periodontitis were older ($P < 0.001$), more likely to be male ($P < 0.001$), have lower income levels ($P < 0.001$), higher prevalence of diabetes ($P < 0.001$), higher proportion with smoking history ($P < 0.001$), and higher prevalence of comorbidities, including diabetes, hypertension, cardiac diseases, and pulmonary diseases.

3.2. Associations of tooth loss and periodontitis with mortality in cancer survivors

With a mean follow-up of 86 months, 1122 out of 3271 (34.3 %) patients died. After the adjustment of baseline characteristics including age, sex, BMI, race, income level, health insurance, comorbidities, smoking history, and alcohol usage history, the adjusted survival curve showed that patients with tooth loss>5 and with periodontitis had a worse survival rate (Fig. 2).

The hazard ratio of tooth loss and periodontitis for all-cause mortality in cancer survivors was assessed by Cox regression (Table 2). After adjustment of baseline characteristics including age, sex, BMI, race/ethnicity, income level, health insurance, comorbidities, smoking history, and alcohol usage history, any tooth loss is strongly associated with increased mortality for cancer survivors (HR = 1.555, 95 % CI = 1.220–1.984). Furthermore, the impact of tooth loss on the survival rate of cancer survivors gradually increases with an increasing number of missing teeth. Although the impact of periodontitis defined by NHANES on mortality did not reach statistical significance in the final model (HR = 1.188, 95 % CI = 0.943–1.496), severe CDC-AAP-defined periodontitis is associated with mortality (HR = 1.684, 95 % CI = 1.081–2.625). In the multivariate Cox regression, both of tooth loss>5 and severe CDC-AAP periodontitis were independent risk factor for overall survival (Tables 3 and 4).

3.3. The impacts of tooth loss on mortality in subgroups

To investigate whether tooth loss at different locations is associated with differences in the mortality rate among cancer survivors, we conducted subgroup analyses based on the location of tooth loss (Supplementary Table 1). Interestingly, we found that once tooth loss begins, there is often the loss of multiple teeth. Among cancer survivors with tooth loss, only 10.3 % had lost a single tooth. Among these patients with the loss of a single tooth, the proportions of patients with the loss of central incisors, lateral incisors, canines, first bicuspids, second bicuspids, first molars, and second molars were 6.1 %, 2.3 %, 3.8 %, 4.6 %, 13.7 %, 35.1 %, and 34.4 %, respectively, indicating that the loss of molars is an early event in the overall tooth loss. Due to the limited number of patients with the loss of a single tooth, we conducted the Cox analysis based on the location of missing teeth. The results revealed that the loss of teeth in most locations (except for first bicuspids) were associated with an increased mortality rate after the adjustment of baseline characteristics. Among

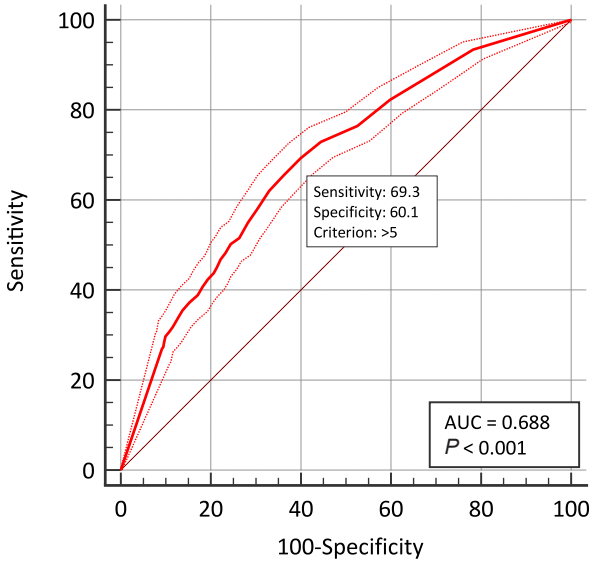

Fig. 1. The area under the receiver operating characteristic (ROC) curve for tooth loss in relation to mortality.

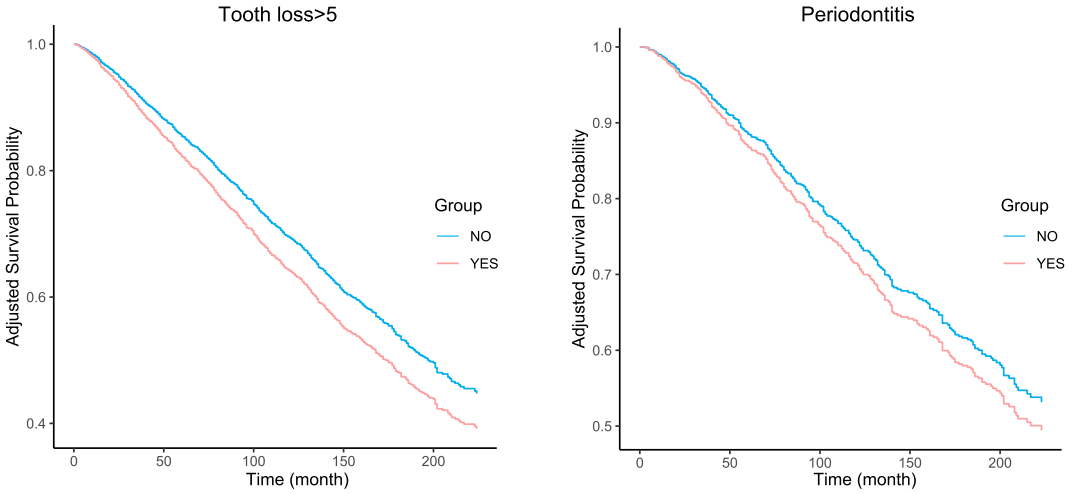

Fig. 2. Adjusted survival curve of overall survival stratified by tooth loss and periodontitis. The curve was adjusted by age, sex, BMI, race, income level, health insurance, comorbidities, smoking history, and alcohol usage history.

Table 2
Hazard ratio of tooth loss and periodontitis for all-cause mortality in cancer survivors adjusted by baseline characteristics.

Factor	HR (95 % CI)			
	Model 0	Model 1	Model 2	Model 3
Tooth loss (n = 3271)				
Any loss *vs.* 0	3.356 (2.651–4.249)[a]	1.944 (1.532–2.466)[a]	1.593 (1.250–2.031)[a]	1.555 (1.220–1.984)[a]
1–2 *vs.* 0	1.882 (1.412–2.509)[a]	1.318 (0.986–1.762)[a]	1.295 (0.964–1.739)	1.271 (0.940–1.720)
3–4 vs. 0	1.946 (1.445–2.620)[a]	1.498 (1.110–2.023)[a]	1.354 (0.988–1.855)	1.372 (0.993–1.895)
5–6 vs. 0	3.052 (2.230–4.177)[a]	1.761 (1.274–2.433)[a]	1.677 (1.175–2.395)[a]	1.719 (1.198–2.466)[a]
7–8 vs. 0	3.436 (2.513–4.698)[a]	1.793 (1.297–2.479)[a]	1.803 (1.273–2.555)[a]	1.746 (1.214–2.510)[a]
9–10 vs. 0	4.213 (3.041–5.835)[a]	2.209 (1.569–3.110)[a]	1.717 (1.170–2.519)[a]	1.581 (1.065–2.347)[a]
>10 vs. 0	4.848 (3.804–6.178)[a]	2.472 (1.926–3.173)[a]	1.972 (1.508–2.580)[a]	1.851 (1.413–2.424)[a]
Periodontitis (n = 1267)				
NHANES definition, yes *vs.* no	1.409 (1.129–1.759)[a]	1.364 (1.111–1.674)[a]	1.195 (0.950–1.502)	1.188 (0.943–1.496)
CDC/AAP definition, yes *vs.* no	1.795 (1.464–2.202)[a]	1.371 (1.118–1.680)[a]	1.209 (0.980–1.491)	1.171 (0.947–1.447)
Mild *vs.* no	1.224 (0.666–2.250)	0.871 (0.473–1.607)	1.025 (0.555–1.913)	1.012 (0.538–1.903)
Moderate *vs.* no	1.782 (1.439–2.207)[a]	1.181 (0.952–1.465)	1.170 (0.940–1.456)	1.136 (0.911–1.417)
Severe *vs.* no	2.556 (1.662–3.932)[a]	2.092 (1.359–3.221)[a]	1.803 (1.616–2.800)[a]	1.684 (1.081–2.625)[a]

Abbreviations: CDC/AAP, Centers for Disease Control/American Academy of Periodontology; CI, confidence interval; HR, hazard ratio.
Model 0 was unadjusted; Model 1 was adjusted for age and sex; Model 2 was adjusted for Model 1 plus BMI, race/ethnicity, income level, health insurance, smoking history, and alcohol usage history; Model 3 was adjusted for Model 2 plus diabetes, hypertension, asthma, arthritis, thyroid diseases, cardiac diseases, pulmonary diseases, and liver diseases.
[a] Statistical significance.

them, the loss of molars showed the highest hazard ratio.

Given that tooth loss or periodontitis may affect food intake, potentially leading to malnutrition, we compared bone density and lean body mass among different groups of cancer survivors. The results revealed that cancer survivors with tooth loss>5 had significantly lower bone density (1.06 *vs.* 1.13 g/cm^2, $P < 0.001$), and a trend of lower lean body mass (46.9 vs. 47.6 kg, $P = 0.093$), whereas these results were not observed in patients with periodontitis (Fig. 3). In term of inflammation level, cancer survivors with tooth loss>5 and severe periodontitis had significantly higher C-reactive protein level, although there was no significant difference in CRP levels between those with and without periodontitis.

4. Discussion

Oral health is an important part of overall health. For the first time, we investigate the impact of oral health on mortality in cancer survivors in the large nationally representative cohort. Our study reveals that tooth loss and periodontitis are prevalent among cancer survivors. Patients with tooth loss often have multiple missing teeth, and the absence of teeth, regardless of their location or quantity, significantly increases the risk of mortality. Patients with tooth loss exhibit significantly lower bone density and lower body weight. After the adjustment of baseline factors, tooth loss>5 and severe periodontitis remain independent risk factors for mortality in cancer survivors.

Table 3
Univariate and multivariate logistic regression analysis of the impact of tooth loss >5 on overall survival ($n = 3271$).

Factors	Univariate analysis		Multivariate analysis	
	HR (95 % CI)	*P* value	HR (95 % CI)	*P* value
Age, year	1.087 (1.079–1.094)	<0.001[a]	1.077 (1.069–1.085)	<0.001[a]
Sex		<0.001[a]	1.263 (1.116–1.430)	<0.001[a]
Female	1 (reference)			
Male	1.715 (1.523–1.931)			
BMI, kg/m^2	0.965 (0.955–0.975)	<0.001[a]	0.969 (0.958–0.981)	<0.001[a]
Race/ethnicity		<0.001[a]		<0.001[a]
Mexican American	1 (reference)		1 (reference)	
Other Hispanic	1.013 (0.626–1.637)		0.939 (0.579–1.521)	
Non-Hispanic White	1.776 (1.335–2.362)		1.167 (0.872–1.562)	
Non-Hispanic Black	2.050 (1.492–2.817)		1.667 (1.209–2.299)	
Other race/ethnicity	1.164 (0.710–1.909)		0.857 (0.520–1.413)	
Income level		<0.001[a]		<0.001[a]
PIR<1	1 (reference)		1 (reference)	
1 ≤ PIR<2	1.299 (1.080–1.562)		0.808 (0.667–0.978)	
2 ≤ PIR<3	1.021 (0.833–1.250)		0.668 (0.541–0.824)	
PIR≥3	0.571 (0.474–0.688)		0.538 (0.440–0.658)	
Health insurance	2.526 (1.767–3.609)	<0.001[a]		
Tooth loss >5	2.747 (2.408–3.134)	<0.001[a]	1.290 (1.114–1.494)	0.001[a]
Comorbidity				
Diabetes	1.664 (1.447–1.913)	<0.001[a]	1.299 (1.123–1.503)	<0.001[a]
Hypertension	1.602 (1.419–1.809)	<0.001[a]		
Asthma	0.925 (0.781–1.097)	0.371		
Arthritis	1.439 (1.279–1.619)	<0.001[a]		
Thyroid diseases	0.980 (0.839–1.144)	0.799		
Cardiac diseases	2.347 (2.064–2.668)	<0.001[a]	1.371 (1.198–1.569)	<0.001[a]
Pulmonary diseases	1.609 (1.383–1.871)	<0.001[a]	1.385 (1.184–1.621)	<0.001[a]
Liver diseases	1.208 (0.935–1.560)	0.149		
Smoking history	1.400 (1.241–1.580)	<0.001[a]	1.251 (1.100–1.422)	0.001[a]
Alcohol usage history	0.836 (0.739–0.944)	0.004[a]		

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Statistical significance.

Several meta-analyses have investigated the association between oral health and the risk of cancer, which consistently indicate that individuals with periodontal disease or tooth loss are at a higher risk of developing cancer [14]. Tooth loss may pose a risk for certain tumors by affecting dietary habits and disrupting the balance of oral microbiota [15]. Prolonged oral inflammation may also lead to a systemic inflammatory response, thereby increasing the risk of cancer [16]. Specifically, there is a certain association between periodontal disease and various cancers such as esophageal cancer, gastric cancer, pancreatic cancer, and oral cancer [17]. However, whether tooth loss and periodontitis directly impact the prognosis of cancer survivors remains unclear. Similar to our study findings, research on individuals with no prior cancer diagnosis showed that individuals with tooth loss had a higher risk of total cancer death. However, they did not find an association between periodontal disease and the risk of cancer mortality [11]. In our study, both tooth loss and severe periodontitis are independent factors of higher mortality risk.

Recent research suggests that periodontal disease and tooth loss may be associated with body composition, including bone density, muscle mass, and fat distribution [18]. Some studies have indicated a link between periodontal disease and reduced bone density [19]. Furthermore, tooth loss can lead to alterations in dietary patterns, potentially affecting nutritional intake. Some studies have found associations between tooth loss and weight loss, decreased muscle mass, and abnormal fat distribution [20–22]. In our study, we observed that patients with tooth loss>5 had significantly lower bone density, and a trend of lower lean body mass compared to cancer survivors with tooth loss≤5. However, inconsistently, our study did not observe differences in bone density and lean body mass between patients with periodontal disease and those without.

This study has some limitations. First, due to database limitations, we do not have information on the cancer treatment of these cancer survivors. However, their long follow-up time suggested that a considerable proportion of them were likely to be curatively treated patients. Second, periodontal examination methods in different years were different. The partial quadrant periodontal examination method in certain years might lead to an underestimation of the severity of periodontal disease. Nevertheless, our study confirmed that severe CDC-AAP periodontitis remained an independent risk factor for mortality in the multivariate Cox regression analysis. Third, although the NHANES database includes some patients' causes of death, the substantial amount of missing data prevents meaningful statistical analysis. Fourth, Charlson comorbidity index and detailed smoking status was not analysis in this study due to a lack of sufficient data. These details will be addressed in future prospective cohort studies. Fifth, the observational design of our study prevents us from making definitive conclusions about the causal relationship between oral health and survival in cancer survivors. The potential causal link between oral health and mortality in cancer survivors needs to be verified through randomized controlled trials.

In conclusion, our study represents the first investigation into the relationship between oral health and mortality in cancer

Table 4
Univariate and multivariate logistic regression analysis of the impact of severe periodontitis (CDC/AAP) on overall survival ($n = 1267$).

Factors	Univariate analysis		Multivariate analysis	
	HR (95 % CI)	*P* value	HR (95 % CI)	*P* value
Age, year	1.087 (1.075–1.098)	<0.001[a]	1.080 (1.067–1.869)	<0.001[a]
Sex		<0.001[a]	1.520 (1.235–1.869)	0.009[a]
Female	1 (reference)			
Male	1.912 (1.562–2.340)			
BMI, kg/m^2	0.956 (0.939–0.973)	<0.001[a]	0.967 (0.946–0.987)	0.002[a]
Race/ethnicity		0.162		
Mexican American	1 (reference)			
Other Hispanic	0.925 (0.458–1.867)			
Non-Hispanic White	1.216 (0.819–1.804)			
Non-Hispanic Black	1.513 (0.950–2.410)			
Other race/ethnicity	0.697 (0.303–1.603)			
Income level		<0.001[a]		0.019[a]
PIR<1	1 (reference)		1 (reference)	
1 ≤ PIR<2	1.248 (0.875–1.780)		0.645 (0.447–0.931)	
2 ≤ PIR<3	1.088 (0.753–1.572)		0.536 (0.366–0.786)	
PIR≥3	0.708 (0.508–0.988)		0.480 (0.340–0.678)	
Health insurance	2.822 (1.457–5.467)	0.002[a]		
Severe periodontitis	1.964 (1.296–2.976)	0.001[a]	1.682 (1.102–2.568)	0.016[a]
Comorbidity				
Diabetes	1.515 (1.177–1.949)	0.001[a]		
Hypertension	1.613 (1.316–1.976)	<0.001[a]	1.286 (1.042–1.586)	0.019[a]
Asthma	0.854 (0.626–1.165)	0.318		
Arthritis	1.301 (1.066–1.589)	0.010[a]		
Thyroid diseases	0.974 (0.747–1.270)	0.847		
Cardiac diseases	1.853 (1.414–2.429)	<0.001[a]		
Pulmonary diseases	1.255 (0.917–1.717)	0.157		
Liver diseases	0.911 (0.544–1.527)	0.724		
Smoking history	1.151 (0.942–1.406)	0.168		
Alcohol usage history	0.792 (0.641–0.979)	0.031[a]		

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Statistical significance.

survivors. Impaired oral health adversely affects all-cause mortality. This study represents a novel step in uncovering the associations between tooth loss, periodontitis, and mortality across various cancer types. These findings underscore the importance for oncologists and healthcare providers to integrate oral health assessments into routine care for cancer survivors. Collaborative efforts between dental and medical professionals can ensure comprehensive care, addressing both oncological and dental needs. Educating cancer survivors about the importance of maintaining good oral hygiene and regular dental check-ups should be a key component of survivorship care plans.

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Ethics declarations

Population of this study was enrolled form NHANES database, which is approved by the Ethics Review Board of National Center for Health Statistics (https://www.cdc.gov/nchs/nhanes/irba98.htm).

Data availability statement

All data used in this research were obtained from the public data available in the NHANES database (https://wwwn.cdc.gov/nchs/nhanes/).

CRediT authorship contribution statement

Yong-Jun Wu: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tian-Yu Lin:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Xiao-Fan Pu:** Writing – review & editing, Writing – original draft, Visualization,

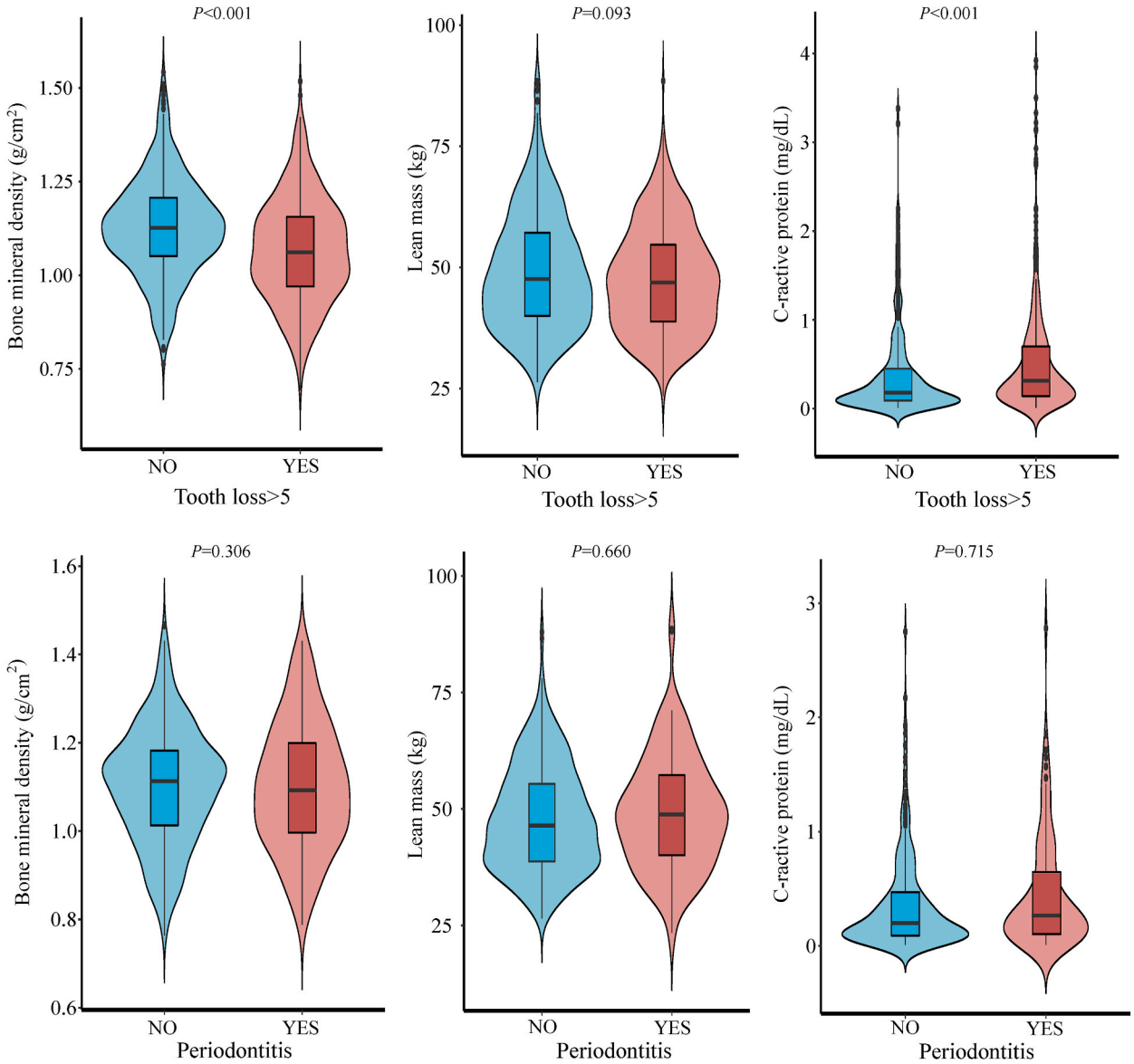

Fig. 3. Comparison of whole body bone mineral density, lean body mass, and C-reactive protein level between individuals with tooth loss>5 and tooth loss≤5, and between those with and without periodontitis.

Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chao-Lei Zhang:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36813.

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