THE NUMBER OF LOST TEETH - A POTENTIAL PREDICTIVE MARKER FOR THE CARDIOVASCULAR DISEASES IN A SAMPLE OF HOSPITALIZED ADULTS

Mirela Mihart[1], Veronica Mercuț[2], Sanda Mihaela Popescu[3], Mihaela Ionescu[4], Adina Dorina Glodeanu[5], Mihaela Jana Țuculină[6], Marcel Adrian Popescu[2], Marina Olimpia Amărăscu[2], Petre Costin Mărășescu[2] Diana Elena Vlăduțu[2], Monica Scrieciu[2]

[1]Doctoral School, University of Medicine and Pharmacy of Craiova, Emergency Dentistry Department, County Emergency Clinical Hospital, Drobeta-Turnu Severin, Romania
[2]Department of Prosthodontics, Faculty of Dental Medicine, University of Medicine and Pharmacy, Craiova, Romania
[3]Department of Oral Rehabilitation, Faculty of Dental Medicine, University of Medicine and Pharmacy, Craiova, Romania
[4]Department of Medical Informatics and Biostatistics, Faculty of Dental Medicine, University of Medicine and Pharmacy, Craiova, Romania
[5]Department of Cardiology, Faculty of Dental Medicine, University of Medicine and Pharmacy, Craiova, Romania
[6]Department of Endodontics, Faculty of Dental Medicine, University of Medicine and Pharmacy of Craiova, Romania

Corresponding author: Mihaela Ionescu, *e-mail*: mihaela.ionescu@umfcv.ro
Diana Elena Vlăduțu, *e-mail*: diana.vladutu@umfcv.ro

All the authors have equally contribution.

ABSTRACT

Aim of the study: to evaluate the degree of statistical association between the oral parameter represented by the total number of permanent lost teeth (NLT) on both arches, and a certain type of cardiovascular disease. **Materials and methods:** 84 hospitalized participants in the Cardiology Department from DrobetaTurnu-Severin County Emergency Clinical Hospital were evaluated in the Emergency Dentistry Department of the same hospital. The demographic and clinical data were collected and statistically analyzed using Chi-square and Kendall's tau-b, followed by two binomial regression models. **Results:** A strong, positive association between the NLT and the presence of heart valve diseases, respectively cardiomyopathy was highlighted by Chi-square tests ($\chi^2(2) = 8.774$, $p = 0.023$, respectively $\chi^2(2) = 19.137$, $p < 0.0005$) Also, NLT between 9 and 14 may be considered a statistically significant predictor of developing cardiomyopathy (unadjusted OR = 6.548, 95%CI = 1.764 – 24.304, $p < 0.0005$), and NLT between 15-27 for developing heart valve diseases (unadjusted OR = 7.886, 95% CI = 1.698 – 36.616, $p = 0.008$). **Conclusions:** For the group of participants included in the study**,** NLT had a statistically significant predictive value especially for heart valve diseases and cardiomyopathy.

Key words: number of lost teeth, cardiovascular diseases, oral status, statistical analysis

INTRODUCTION

Cardiovascular diseases (CVD) represent a group of disorders of the heart and blood vessels representing the most common non-communicable diseases and the main cause of death and disability worldwide, with dramatic socioeconomic impact [1]. Cardiovascular diseases affect millions of people in developed and developing countries, representing a public health problem [2]. Although a decrease in the mortality rate has been observed in developed countries in recent decades, cardiovascular diseases are still the main cause of death [3]. In Romania, 1 out of 2 people die due to a cardiovascular disease, representing a percentage of 52%, almost double the EU

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average. Standardized rates of mortality from cardiovascular diseases in Romania are two and a half times higher than the European average [4].

CVD develops gradually over time and manifests symptom sonly in the advanced stage [5]. It is estimated that by the year 2030, approximately 23.6 million people per year will die from CVD [6].

The relationship between oral and general health has been paying attention from clinicians and researchers, more and more [7]. The reason why oral health is gaining attention worldwide is explained by the fact that it has an impact on peoples 'overall health and quality of life [8]. Indeed, data from specialized literature show that oral health has an impact on general health and vice versa. This type of oral-general health interaction has been recognized by dentists and general practitioners [9].

In 2022, the WHO Report on the State of Global Oral Health estimated that oral diseases affect almost 3.5 billion people worldwide, with 3 out of 4 people in middle-income countries being affected. According to the WHO report, oral diseases of public health importance are dental caries, periodontal diseases, tooth loss, as well as oral cancers.

Tooth loss is generally the end point of an oral condition, mainly advanced tooth decay and severe periodontal disease, but can also be due to trauma or other causes. The estimated global mean prevalence of complete tooth loss is nearly 7% among people aged 20 years or older. For people aged 60 years or older, a much higher overall prevalence of 23% was estimated [10].

In Japan, 40% of people aged 40s and 60% of people aged 50s have lost at least one tooth [11]. In the United States, 26% of adults aged 65 or older have eight or fewer teeth left, and about 17% of them have lost all their teeth [12].

Tooth loss has been associated with various chronic systemic conditions [9], among them cardiovascular diseases [13]. In the last two decades, many studies have been carried out, indicating a close relationship between the oral cavity and cardiovascular diseases (CVD), although the pathological and physiological mechanisms have not been fully explained [14,15]. Studies have reported that the risks of CVD and stroke were increased in subjects with a reduced number of teeth at the time of examination or tooth loss during disease monitoring [16]. The fact that tooth loss has been considered a risk factor for brain diseases and CVD [2] has led to numerous studies that have analyzed the association between tooth loss and signs of CVD revealed by coronary angiography in coronary atherosclerosis, by ultrasound carotid or by self-report in the case of angina pectoris [17-19].

Tooth loss is one of the common markers for assessing oral health status [20]. Studies measuring the association between lost teeth and signs of CVD – such as coronary atherosclerotic burden with coronary angiography, carotid ultrasound, arterial stiffness, or self-reported angina pectoris as a simple and objective indicator of inflammation within oral disease – but were independently associated with cardiovascular events and mortality in many epidemiological studies [21-23].

The aim of the present study was to evaluate the degree of statistical association between the oral parameter represented by the total number of permanent teeth lost on both arches, and a certain type of cardiovascular disease, in a group of hospitalized subjects in the cardiology department, with various cardiovascular diseases. In this sense, for the subjects included in the study, it was investigated whether the number of lost teeth can be a predictive marker for a certain cardiovascular disease, taking other factors

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into account.

MATHERIALS AND METHODS

Study design

The study was conducted on 84 participants hospitalized in the Cardiology Department, in the period July - September 2022, within the Drobeta Turnu-Severin County Emergency Clinical Hospital, Romania. For those participants, the dental assessments and treatments were necessary in the Emergency Dentistry Department of the same hospital. For the analysis of the correlation of the number of lost teeth with a certain type of cardiovascular disease, only subjects hospitalized in the Cardiology Department were included in the study, because it was observed that oral health is frequently altered in case of hospitalized subjects [24]. Moreover, in some studies it is mentioned that 71.0% of the hospitalized subjects for various types of rehabilitation [25] and 91.0% of the hospitalized subjects for the care of acute conditions [26] present an altered oral status.

This study received Approval No. 06/14.07.2022 from the Ethical Council of the Drobeta Turnu-Severin County Emergency Clinical Hospital and Approva lNo.73/02.05.2022 from the University and Scientific Ethics and Deontology Commission of the University of Medicine and Pharmacy in Craiova, in accordance with the provisions of the Helsinki Declaration [27].

Selection of study participants

Study participants were selected according to the inclusion and exclusion criteria. According to the inclusion criteria, adult subjects were elected for the study, whowere over 21 years old, with cardiovascular disease confirmed by a specialist cardiologist, with at least one lost tooth, without fixed and removable dentures. According to the exclusion criteria, participants under the age of 21, with cardiovascular disease not confirmed by a cardiologist, with full dental arch or restored by fixed and removable dentures were not selected for the study. Each participant included in the study was informed about the purpose of the study and signed the informed consent.

Dental evaluation

The clinical dental examination of the participants included in the study was performed by a trained investigator, following WHO standards and the Helsinki Declaration [27]. For this purpose, each participant included in the study was seated in the chair of the dental unit in a sitting position, with the head in a normal position, using natural light, the light of dental operation lamp, the dental mirror (Mirror Rhodium Simple Stem Size:5-24MM, Germany) and dental probe (Goldman – Fox – Willams PA-Probe DE Germany) [28]. Both arches were considered to have a maximum number of 28 teeth, and the presence or absence of wisdom teeth, impacted teeth and residual deciduous teeth were not considered [29]. Each study participant had at least one lost tooth, considering both arches.

Data collection

For each subject included in the study, an observation sheet was drawn up during the hospitalization in the cardiology department. From the observation sheets of all study participants, the following data were collected: age, gender, residence, type of cardiovascular disease, presence of other systemic co-morbidities. Depending on these, the following categories of parameters were specified:

- the demographic parameters that included the following variables: a) age, for which the following age groups were established: 50-59 years, 60-69 years, 70-79 years, over 80 years; b) gender, with two categories: male and female; c) residence, with two categories:

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urban and rural;
- the cardiovascular parameters, representing the type of cardiovascular disease mentioned in the observation sheet; the following categories of variables were thus created: heart valve diseases, coronary heart diseases, cardiomyopathies, cardiac arrhythmias, arterial hypertension (AHT);
- the other systemic co-morbidities parameters, mentioned in the observation sheets, the following categories of variables being established: metabolic disorders, lung disorders, chronic renal failure, anasarca, others.

Through the dental assessment, the value of the oral parameter represented by the total number of lost teeth on both arches was noted, referred to below as the number of lost teeth (NLT). Based on this value, the study participants were divided into several categories: the group with 1–8 lost teeth, the group with 9–14 lost teeth, the group with 15–27 lost teeth [30]. Depending on the topography of the absent teeth and the location of the edentulous areas of the ridges, the study participants were distributed, according to the Kennedy system of edentation classification, into four classes: class I included subjects with edentulous areas on both half-arches, located posterior to the remaining natural teeth; class II included subjects with an edentulous area located on a single hemi-arch, posterior to the remaining natural teeth; class III included subjects with an edentulous area located laterally, with remaining natural teeth both anterior and posterior to it; class IV included subjects with a single edentulous area, located anterior to the remaining teeth, but encompassing both hemi-arches, crossing the midline [31]. The participants with 1–2 remaining teeth were included in the category of those with extended edentation [32], and those with 28 lost teeth on an arch in the category of those with complete edentulism [33].

Statistical analysis

Descriptive analysis of participants' data was performed using Microsoft Excel 365 (San Francisco, CA, USA). Statistical analysis was performed using Statistical Package for Social Sciences (SPSS), version 26 (IBM Corp., Armonk, NY, USA). Mean ± standard deviation (SD) was used for continuous variables; these variables were compared using Kendall's tau-b test. All categorical variables were defined as numerical values and percentages, and their associations were tested with the Chi-square test. Six binomial regression models were created to ascertain the effects of the studied parameters on the probability of participants having a certain cardiovascular disease. Three partial regression models (generic Model 1) included all categories of demographic variables (age, gender, residence) and each category of the NLT oral parameter. Three complete regression models (generic Model 2) included all categories of demographic variables (age, gender, residency), all categories of co-morbidities (metabolic diseases, lung diseases, kidney failure, and anasarca, others) and each category of the NLT oral parameter. Linearity of the continuous variables with respect to the logit of the dependent variable was assessed via the Box-Tidwell (1962) procedure. A Bonferroni correction was applied using all terms in the models, resulting in statistical significance being accepted when $p < 0.01$ (for Model 1) and $p < 0.00714$ (for Model 2). Based on this assessment, all continuous independent variables were found to be linearly related to the logit of the dependent variable.

Table 1. Distribution of the study participants according to specified parameters.

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1. Demographic parameters				
Age group	50 – 59 years	60 – 69 years	70 – 79 years	over 80 years
No. (%)	21 (25.00%)	19 (22.62%)	35 (41.67%)	9 (10.71%)
Gender	Males		Females	
No. (%)	40 (47.62%)		44 (52.38%)	
Residence	Urban		Rural	
No. (%)	34 (40.48%)		50 (52.59%)	

2. Cardiovascular parameters (type of cardiovascular disease)					
CVD	Diseases of the valves	Coronary diseases	Disorders of rythm	Cardiomyopathy	AHT
No. (%)	58 (59.05%)	44 (52.38%)	44 (52.38%)	60 (71.43%)	48 (57.14%)

3. Parameters: other general comorbidities				
Comorbidities	Metabolic	Lung	Chronic renal failure Anasarca	Comorbidities
No. (%)	36 (42.86%)	64 (76.19%)	30 (35.71%)	22 (26.19%)

RESULTS

The descriptive statistical processing of the recorded data revealed that the age of the participants included in the study varied between 50-89 years (average 69.49 ± 10.09).

Of the 84 participants included in the study, only 13.1% (n=11) were aged between 50-59 years and had NLT between 1-8, and 30.91% (n=27) were aged over 70 years and had NLT over 9. The distribution of study participants according to the defined parameters is shown in Table1.

Table 2. Study participants' distribution according to NLT and type of edentation.

No	**Oral parameter: NLT**					
1.	1-8 lost teeth		9-14 lost teeth		15-27 lost teeth	
No. (%)	27 (32.14%)		32 (38.10%)		25 (29.76%)	
2.	Type of maxillary edentation					
	Class I Kennedy	Class II Kennedy	Class III Kennedy	Fourth class Kennedy	Extended edentation	Complete edentulism
No. (%)	6 (7.14%)	28(33.33%)	35(41.67%)	0(0.0%)	13(15.48%)	2(2.38%)
3.	Type of mandible edentation					
	Class I Kennedy	Class II Kennedy	Class III Kennedy	Fourth class Kennedy	Extended edentation	Complete edentulism
No. (%)	22 (26.19%)	30 (35.71%)	24 (28.57%)	0 (0.0%)	6 (7.14%)	2 (2.38%)

The value of the oral NLT parameter ranged from 2 to 26 (mean 12.42 ± 5.52), and 41.67% (n=35) of the subjects presented maxillary Kennedy class III edentation and 35.71% (n=30) presented mandibular Kennedy class III edentation (Table 2).

Distribution of study participants is presented in Table 3 according to NLT group, demographic data, CVD category and type of co-morbidity.

Table 3. Distribution of study participants according to NLT, demographic data, CVD category and type of comorbidity.

NLT categories

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	1-8 lost teeth	9-14 lost teeth	15-27 lost teeth	Total
Total subjects	27	32	25	84
1. Demographic data				
a. Age (years old)				
50–59	11 (52.4%)	8 (38.1%)	2 (9.5%)	21(100%)
60–69	7 (36.8%)	6 (31.6%)	6 (31.6%)	19(100%)
70–79	9 (25.7%)	15 (42.9%)	11 (31.4%)	35(100%)
+80	0 (0%)	3 (33.3%)	6 (66.7%)	9 (100%)
b. Gender				
Males	16 (40.0%)	11 (27.5%)	13 (32.5%)	40(100%)
Females	11 (25.0%)	21 (47.7%)	12 (27.3%)	44(100%)
c. Residency				
Rural	15 (30.0%)	20 (40.0%)	15 (30.0%)	50(100%)
Urban	12 (35.3%)	12 (35.3%)	10 (29.4%)	34(100%)
2. CVD data				
Heart valve diseases	16 (27.6%)	19 (32.8%)	23 (39.7%)	58(100%)
Coronary heart diseases	17 (38.6%)	13 (29.5%)	14 (31.8%)	44(100%)
Cardiomyopathies	11 (18.3%)	29 (48.3%)	20 (33.3%)	60(100%)
Cardiac arrhythmias	13 (29.5%)	19 (43.2%)	12 (27.3%)	44(100%)
Arterial hypertension	12 (25.0%)	21 (43.8%)	15 (31.2%)	48(100%)
3. Comorbidities				
Metabolic comorbidities	9 (25.0%)	13 (36.1%)	14 (38.9%)	36(100%)
Lung comorbidities	19 (29.7%)	28 (43.8%)	17 (26.6%)	64(100%)
Kidney failure and anasarca	8 (28.6%)	12 (42.9.%)	8 (28.6%)	28(100%)
Other comorbidities	4 (18.2%)	13 (59.1%)	5 (22.7%)	22(100%)

A Chi-square test for association was conducted between the category of NLT and the presence of a specific CVD. All expected cell frequencies were greater than five. There was a statistically significant association between the NLT categories and the presence of heart valve diseases, $\chi^2(2) = 8.774$, $p = 0.023$, as well as the presence of cardiomyopathy, $\chi^2(2) = 19.137$, $p < 0.0005$. No association was identified in relation to the presence of coronary heart diseases, cardiac arrhythmia disorders, or AHT.

Also, a Kendall's tau-b correlation was run to determine the relationship between the NLT value and the presence of a specific CVD amongst the 84 participants. There was a strong, positive association between the NLT groups and the presence of heart valve diseases, which was statistically significant, $\tau_b = 0.183$, $p = 0.048$. Similar results were obtained in relation to the presence of cardiomyopathy, with $\tau_b = 0.262$, $p = 0.005$. No other associations were identified.

For each category of NLT, the odds ratio (OR) analysis for developing a specific CVD (unadjusted and independently adjusted with demographic and co-morbidities data) provided the results presented in Table 4.

Table 4. Unadjusted and independently adjusted odds ratio for the NLT categories according to CVD.

	Categories of subjects according to NLT OR (95% CI)

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Cardiac condition	1-8 lost teeth		9-14 lost teeth		15-27 lost teeth	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
No adjustment						
Heart valve diseases	0.519 (0.197–1.368)	0.185	0.487 (0.189 –1.253)	0.136	7.886 (1.698 –36.616)	0.008
Coronary heart diseases	1.889 (0.739–4.827)	0.179	0.463 (0.189 –1.137)	0.093	1.230 (0.480 –3.150)	0.666
Cardiomyo-pathies	0.112 (0.038–0.328)	<0.0005	6.548 (1.764 –24.304)	<0.0005	1.900 (0.619 –5.834)	0.262
Cardiac arrhythmias	0.779 (0.311–1.949)	0.593	1.578 (0.648 –3.847)	0.315	0.779 (0.305 –1.988)	0.601
Arterial hypertension	0.467 (0.184–1.183)	0.108	1.768 (0.712 –4.391)	0.220	1.182 (0.457 –3.059)	0.731
Adjustment with gender						
Heart valve diseases	0.502 (0.187–1.343)	0.170	0.480 (0.182–1.264)	0.137	7.883 (1.696–36.646)	0.008
Coronary heart diseases	1.657 (0.630–4.362)	0.306	0.543 (0.215–1.373)	0.197	1.169 (0.444–3.081)	0.752
Cardiomyopat hies	0.118 (0.040–0.346)	<0.0005	6.138 (1.632–23.081)	0.007	2.005 (0.64–6.245)	0.230
Cardiac arrhythmias	0.799 (0.315–2.023)	0.636	1.547 (0.623–3.843)	0.347	0.787 (0.308–2.012)	0.617
Arterial hypertension	0.471 (0.184–1.209)	0.117	1.746 (0.690–4.423)	0.240	1.195 (0.461–2.842)	0.690
Adjustment with age						
Heart valve diseases	0.605 (0.211–1.736)	0.350	0.459 (0.176–1.201)	0.113	7.628 (1.571–37.033)	0.012
Coronary heart diseases	1.642 (0.594–4.541)	0.340	0.473 (0.192–1.167)	0.104	1.583 (0.572–4.377)	0.376
Cardiomyopat hies	0.062 (0.016–0.245)	<0.0005	6.515 (1.753–24.210)	0.005	1.913 (0.585–6.251)	0.283
Cardiac arrhythmias	0.820 (0.302–2.230)	0.698	1.562 (0.640–3.816)	0.327	0.692 (0.254–1.887)	0.472
Arterial hypertension	0.544 (0.198–1.493)	0.237	1.720 (0.686–4.310)	0.247	0.942 (0.340–2.610)	0.908
Adjustment with residence						
Heart valve diseases	0.514 (0.195–1.357)	0.179	0.489 (0.19-1.259)	0.138	7.906 (1.702-36.736)	0.008
Coronary heart diseases	1.888 (0.738–4.833)	0.185	0.464 (0.189-1.138)	0.093	1.231 (0.481-3.152)	0.665
Cardiomyopat hies	0.102 (0.034–0.309)	<0.0005	6.868 (1.83-25.773)	0.004	1.916 (0.621-5.909)	0.258
Cardiac arrhythmias	0.793 (0316–1.994)	0.623	1.557 (0.637-3.809)	0.332	0.775 (0.303-1.987)	0.596
Arterial hypertension	0.462 (0.182–1.174)	0.105	1.781 (0.716-4.434)	0.215	1.183 (0.457-3.063)	0.729
Adjustment with metabolic comorbidities						
Heart valve diseases	0.454 (0.167-1.24)	0.124	0.466 (0.178-1.218)	0.119	10.517 (2.133-51.854)	0.004
Coronary heart diseases	2.353 (0.869-6.372)	0.092	0.458 (0.181-1.158)	0.099	1.021 (0.382-2.734)	0.967
Cardiomyopat	0.107 (0.036-0.32)	<0.0005	6.59 (1.773-24.494)	0.005	1.91 (0.613-5.956)	0.265

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hies						
Cardiac arrhythmias	0.603 (0.223-1.631)	0.319	1.581 (0.615-4.062)	0.342	1 (0.365-2.738)	1.000
Arterial hypertension	0.501 (0.195-1.288)	0.151	1.847 (0.731-4.665)	0.194	1.042 (0.392-2.772)	0.934
Adjustment with lung comorbidities						
Heart valve diseases	0.478 (0.178-1.286)	0.144	0.535 (0.204-1.404)	0.204	7.535 (1.614-35.168)	0.010
Coronary heart diseases	2.052 (0.785-5.369)	0.143	0.382 (0.149-0.983)	0.046	1.343 (0.513-3.516)	0.548
Cardiomyopathies	0.106 (0.034-0.329)	<0.0005	5.64 (1.489-21.36)	0.011	2.465 (0.738-8.238)	0.143
Cardiac arrhythmias	0.819 (0.323-2.075)	0.674	1.428 (0.573-3.557)	0.445	0.835 (0.322-2.165)	0.711
Arterial hypertension	0.49 (0.19-1.264)	0.140	1.535 (0.602-3.917)	0.370	1.339 (0.5-3.586)	0.561
Adjustment with other comorbidities						
Heart valve diseases	0.339 (0.114-1.012)	0.053	0.647 (0.236-1.772)	0.397	7.992 (1.646-38.798)	0.010
Coronary heart diseases	1.972 (0.758-5.13)	0.164	0.422 (0.165-1.082)	0.072	1.246 (0.484-3.204)	0.649
Cardiomyopathies	0.075 (0.022-0.261)	<0.0005	10.331 (2.35-45.407)	0.002	1.831 (0.593-5.66)	0.293
Cardiac arrhythmias	0.722 (0.283-1.843)	0.495	1.812 (0.709-4.632)	0.214	0.75 (0.291-1.93)	0.551
Arterial hypertension	0.283 (0.099-0.814)	0.019	3.842 (1.169-12.628)	0.027	1.024 (0.371-2.828)	0.964
Adjustment with kidney failure and anasarca						
Heart valve diseases	0.52 (0.198-1.383)	0.190	0.48 (0.181-1.244)	0.128	7.94 (1.713-36.941)	0.008
Coronary heart diseases	1.84 (0.702-4.841)	0.212	0.48 (0.196-1.195)	0.114	1.22 (0.464-3.215)	0.686
Cardiomyopathies	0.103 (0.036-0.321)	<0.0005	6.59 (1.741-24.952)	0.006	2.00 (0.636-6.312)	0.236
Cardiac arrhythmias	0.817 (0.318-2.124)	0.677	1.50 (0.591-3.794)	0.385	0.78 (0.292-2.073)	0.620
Arterial hypertension	0.466 (0.182-1.184)	0.108	1.77 (0.718-4.416)	0.219	1.18 (0.461-3.065)	0.731

The unadjusted OR for oral parameter NLT with values between 9 and 14 may be considered a statistically significant predictor of developing cardiomyopathy (OR = 6.548, 95%CI = 1.764 – 24.304, p < 0.0005), unlike the loss of less than 9 teeth, which seem to have a reversed role (OR = 0.112, 95% CI = 0.038 – 0.328, p < 0.0005). Also, the unadjusted OR for oral parameter NLT with values between 15-27 may be considered a statistically significant predictor of developing heart valve diseases (OR = 7.886, 95% CI = 1.698 – 36.616, p = 0.008). These two parameters maintain their role as statistically significant predictors even when associated with demographic parameters (gender, age, residence) or co-morbidities (metabolic or lung-associated co-morbidities, kidney failure, and anasarca) (Table 4). The adjustment with other co-morbidities confirms the role of the oral parameter NLT with values between 9 and 14, as a statistically significant predictor of

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developing cardiomyopathy (OR = 3.842, 95% CI = 1.169 – 12.628, p = 0.027), unlike the loss of less than 9 teeth, which seem to have a reversed role (OR = 0.283, 95% CI = 0.099 – 0.814, p = 0.019).

*Partial model analysis (**Model 1**)*

For coronary heart diseases, cardiac rhythm disorders and AHT, the three logistic regression models were not statistically significant, $p > 0.05$. No predictor variable (NLT, gender, age, or residence) was statistically significant.

For cardiomyopathy, two models were statistically significant. The first model included the first category of subjects with 1 – 8 NLT. There were two standardized residuals with values close to 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(4) = 23.204$, $p < 0.0005$. The model explained 34.6% (Nagelkerke R2) of the variance in cardiomyopathy and correctly classified 76.2% of cases. Of the four predictor variables, only NLT was statistically significant. Subjects with NLT ≤ 8 had smaller odds of exhibiting cardiomyopathy than subjects with NLT > 8.

The second model included the following category of subjects with NLT between 9 and 14. There were two standardized residuals with values close to 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(4) = 12.023$, $p < 0.017$. The model explained 34.6% (Nagelkerke R2) of the variance in cardiomyopathy and correctly classified 67.9% of cases. Of the four predictor variables, only NLT was statistically significant. Subjects with NLT between 9 and 14 had 6.466 higher odds to exhibit cardiomyopathy than the other subjects.

For heart valve diseases – the model including the third category of subjects with NLT between 15 and 27 – was statistically significant. There was one standardized residual, around 2.5 standard deviations, which was kept in the analysis. The logistic regression model was statistically significant, $\chi^2(4) = 10.392$, $p = 0.034$. The model explained 16.4% (Nagelkerke R2) of the variance in valvular disease and correctly classified 69% of cases. Of the four predictor variables, only NLT was statistically significant. Subjects with NLT ≥ 15 had 7.631 times higher odds to exhibit heart valve diseases than subjects with NLT < 15.

*Complete model analysis (**Model 2**)*

For cardiac rhythm disorders, the logistic regression models (for all three categories of lost teeth) were not statistically significant, $p > 0.05$. No predictor variable (NLT, gender, age, residence, metabolic co-morbidities, lung co-morbidities, kidney failure and anasarca, other co-morbidities) was statistically significant.

For heart valve and coronary heart diseases, the model corresponding to the category of subjects with NLT between 9-14 was also not statistically significant, $p > 0.05$. For coronary diseases and AHT, the model corresponding to the category of subjects with NLT between 15-27, was not statistically significant, $p > 0.05$.

For heart valve diseases – two models were statistically significant. For the model corresponding to subjects with 1-8 lost teeth, there was one standardized residual, around 2.5 standard deviations, which was kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 20.343$, $p = 0.009$. The model explained 30.3% (Nagelkerke R2) of the variance in valvular disease and correctly classified 72.6% of cases. Of the eight predictor variables, only two were statistically significant. The presence of co-morbidities (lung and other co-morbidities) and NLT ≤ 8 were associated with a reduction in the likelihood of exhibiting heart

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valve diseases. For the second model (15-27 NLT), there was one standardized residual, around 2.5 standard deviations, which was kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 22.810$, $p = 0.004$. The model explained 33.5% (Nagelkerke R2) of the variance in heart valve diseases and correctly classified 73.8% of cases. Of the eight predictor variables, only two were statistically significant. Subjects with NLT ≥ 15 had almost 10 times higher odds of exhibiting heart valve disorders than the others, while the presence of co-morbidities (other than lung and metabolic diseases) were associated with a reduction in the likelihood of exhibiting heart valve diseases.

For coronary disorders – the model corresponding to the first category of lost teeth (1-8 NLT) was statistically significant. For this model, there were two standardized residuals, around 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 20.811$, $p = 0.008$. The model explained 29.3% (Nagelkerke R2) of the variance in valvular disease and correctly classified 79.8% of cases. Of the eight predictor variables, only two were statistically significant. Subjects with metabolic diseases had almost 3 times higher odds of exhibiting coronary heart disorders than the others, while kidney failure and anasarca were associated with a reduction in the likelihood of exhibiting these diseases.

For cardiomyopathy – all three models were statistically significant. The first model included subjects with NLT between 1 – 8. There were three standardized residuals with values around 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 47.052$, $p < 0.0005$. The model explained 61.5% (Nagelkerke R2) of the variance in cardiomyopathy and correctly classified 84.5% of cases. Of the eight predictor variables, four were statistically significant. Subjects with associated lung diseases had 2.622 times higher odds to exhibit cardiomyopathy than subjects without lung diseases, while subjects with an increased age had 1.16 times higher odds to exhibit cardiomyopathy than the others. On the other hand, NLT ≤ 8 and the presence of kidney failure and anasarca were associated with a reduction in the likelihood of exhibiting cardiomyopathy.

The second model included subjects with NLT between 9 -15. There were three standardized residuals, around 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 26.764$, $p = 0.001$. The model explained 39.1% (Nagelkerke R2) of the variance in valvular disease and correctly classified 75.0% of cases. Of the eight predictor variables, three were statistically significant. Subjects with NLT ≤ 14 and the presence of kidney failure and anasarca had 11.813 times higher odds, respectively 7.186 times higher odds to exhibit cardiomyopathy than subjects without these diseases. On the other hand, co-morbidities (other than metabolic or lung) were associated with a reduction in the likelihood of exhibiting cardiomyopathy.

The third model included subjects with NLT between 15 and 27. There were three standardized residuals, around 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi^2(7) = 21.145$, $p = 0.007$. The model explained 31.9% (Nagelkerke R2) of the variance in valvular disease and correctly classified 81.0% of cases. Of the eight predictor variables, two were statistically significant. Subjects with kidney failure and anasarca, as well as subjects with lung co-morbidities had 6.017 times higher odds,

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respectively 6.767 times higher odds to exhibit cardiomyopathy than subjects without these diseases.

Table 5. Adjusted regression analyses on the association between clinical and dental variables and CVD.

	Oral parameter NLT OR (95% CI)					
Cardiac condition	1-8 lost teeth		9-14 lost teeth		15-27 lost teeth	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
NLT adjusted with demographic parameter data (partial model)						
Heart valve diseases	0.582 (0.2-1.695)	0.321	0.464 (0.174-1.24)	0.126	7.631 (1.565-37.212)	0.012
Coronary heart diseases	1.507 (0.528-4.298)	0.444	0.547 (0.216-1.389)	0.205	1.421 (0.496-4.069)	0.513
Cardiomyo-pathies	0.057 (0.014-0.235)	<0.0005	6.466 (1.702-24.564)	0.006	2.162 (0.652-7.169)	0.208
Cardiac arrhythmias	0.856 (0.311-2.351)	0.763	1.518 (0.608-3.787)	0.371	0.698 (0.253-1.926)	0.487
Arterial hypertension	0.538 (0.194-1.491)	0.234	1.747 (0.682-4.47)	0.245	0.953 (0.34-2.669)	0.927
NLT adjusted with demographic and comorbidities parameters data (complete model)						
Heart valve diseases	0.164 (0.038-0.701)	0.015	0.802 (0.259-2.484)	0.702	9.658 (1.752-53.249)	0.009
Coronary heart diseases	3.133 (0.845-11.624)	0.088	0.324(0.100-1.043)	0.059	1.226 (0.380-3.958)	0.734
Cardiomyopat hies	0.007 (0.001-0.087)	<0.0005	11.813 (1.869-74.670)	0.009	4.272 (0.978-18.652)	0.054
Cardiac arrhythmias	0.470 (0.135-1.639)	0.236	1.746 (0.559-5.446)	0.337	1.093 (0.340-3.515)	0.882
Arterial hypertension	0.303 (0.086-1.066)	0.063	3.957 (1.046-14.964)	0.043	0.802 (0.236-2.730)	0.725

For AHT – two models were statistically significant. The first model included the first category of lost teeth (1-8 NLT). There were two standardized residuals with values around 2.5 standard deviations, which were kept in the analysis. The logistic regression model was statistically significant, $\chi2(7) = 24.538$, $p = 0.002$. The model explained 34.0% (Nagelkerke R2) of the variance in cardiomyopathy and correctly classified 71.4% of cases. Of the eight predictor variables, one was statistically significant. Subjects with associated metabolic diseases had 3.445 times higher odds of exhibiting AHT than subjects without metabolic diseases. For the second model, the logistic regression model was statistically significant, $\chi2(7) = 25.652$, $p = 0.001$. The model explained 35.3% (Nagelkerke R2) of the variance in AHT presence and correctly classified 76.2% of cases. Of the eight predictor variables, three were statistically significant. Subjects with NLT $\leq$ 14 and the presence of metabolic co-morbidities had 3.957 times higher odds, respectively 1.934 times higher odds to exhibit AHT than subjects without these diseases. On the other hand, co-morbidities (other than metabolic or lung diseases) were associated with a reduction in the likelihood of exhibiting AHT. Overall results for NLT categories are present in Table 5.

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DISCUSSIONS

The investigation of the statistical association relationship between the oral parameter NLT and the types of cardiovascular conditions, present in a group of hospitalized subjects, highlighted the fact that the NLT correlates statistically with certain cardiovascular conditions, and the type of statistical correlation between the two parameters varies according to the variables' adjustment. In 2021, Beukers et *al.*, in a systematic review and meta-analysis of 75 prospective cohort studies from around the world, provided evidence that tooth loss is associated with an increased risk of events related to atherosclerotic cardiovascular diseases [34]. However, the relationship between oral health and cardiovascular diseases is complex and multifaceted, remaining a topic still under debate [35].

The main categories of cardiovascular diseases present in the subjects included in the study were varied: heart valve diseases, coronary diseases, cardiomyopathies, rhythm disorders, AHT. CVDs comprise various conditions that affect the heart and its blood vessels [36] often including the following types: (a) atherosclerotic cardiovascular diseases (coronary, cerebrovascular and peripheral vascular diseases), (b) valvular diseases of the heart, (c) heart failure and cardiomyopathies, (d) arrhythmias, (e) infectious and autoimmune conditions (including infective endocarditis), and (f) hypertension [37].

In the studied group, the NLT value increased with the age of the study participants. Borg-Bartolo et *al*. mentioned the fact that untreated carious lesions and tooth loss represent oral conditions with a high prevalence worldwide, however, with great variations from one country to another, from one age group to another and according to socio-economic status, although the research results were limited [38]. In 2015, Dye et *al*. reported that approximately 52% of US adults aged 20-64 have at least one lost tooth, and 19% of people aged 65 and over are completely edentulous [39]. Zhang et *al.* showed that tooth loss is highly associated with aging, showing that each 1-year increase in age is statistically associated with a 9% increase in the probability of becoming complete edentulism. The authors concluded that there is an approximately 2.5 times higher risk of becoming complete edentulous for every 10 years of aging [9]. The increase in the value of the oral NLT parameter with age is an important aspect of its predictive value, regarding cardiovascular diseases. In this sense, some authors specify that, especially in old age, the effect of tooth loss on cardiovascular diseases is causal. The same authors show that the effect of tooth loss on stroke was significant only for people aged ≥60 years [40].

The number of participants who belonged to the three value categories of the NLT varied according to the gender of the participants. If for the NLT category with value 1-8, the number of male participants was higher, for the NLT category with value 9-15 the number of female participants was double the number of male participants, and for the NLT category 15- 27, the number of participants of both genders was approximately equal. These data suggest that throughout life, female participants lose more teeth than male participants. These results are consistent with the results of other research, which states that partially edentulous dental arches were significantly more common in women [41-43]. On the contrary, other studies reported no statistically significant correlation between gender and partially edentulous dental arches [44, 45]. Also, several studies have shown that

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a statistically significant association between gender and tooth loss pattern was not achieved [46-48].

Class I is more frequent in the older age group as compared to the younger in which class III is more commonly present [41].

The data of the present study indicate that 50 out of 84 (almost 60%) of the participants came from rural areas. Considering that all the subjects included in the study were hospitalized in the cardiology ward, these data suggest the idea that for the geographical area studied, among those who had a cardiovascular disease and required hospitalization, most came from the rural area. The number of subjects included in one of the NLT oral parameter categories varied by residential area. For the NLT category with a value of 1-8, the number of subjects from the rural environment was 25% higher than the number of subjects from the urban environment, and for the NLT category with a value of 15-27, the difference was 50%. Instead, from the point of view of the residential area, of 32 subjects belonging to the NLT category with a value of 9-14, 62.5% came from the rural environment and 37.5% from the urban environment. Similar results have been reported in other studies, which stated that tooth loss was higher among rural adults compared to urban adults [49]. Also, other studies have noted that male participants living in rural areas are more likely to have fewer teeth than urban participants [50] and that tooth loss is essentially greater among rural smokers compared with counterparts from the urban environment [51].

The analysis of statistical correlations between the category of NLT and cardiovascular diseases revealed a significant association between the category of NLT, as well as the effective value of NLT, and heart valve diseases and cardiomyopathies, but not with coronary diseases, heart rhythm disorders or AHT.

The findings of the current study demonstrated using unadjusted and independently adjusted risk estimates with demographic parameter values (age, gender, residence) and co-morbidity parameter values (metabolic, lung, other, renal failure or anasarca) only a statistically significant association between NLT with 9-14 and cardiomyopathies and between NLT with value between 15-27 and heart valve diseases. For the oral NLT parameter with a value between 1-8, no associations were noted with any of the cardiovascular conditions studied, and for categories 9-14 and 15-27 of the NLT, no other types of associations were highlighted.

Lee et *al.* showed that oral health, as assessed by the number of lost teeth, is statistically consistently, strongly, and dose-dependently associated with myocardial infarction, heart failure, ischemic stroke, and mortality in a large population cohort, after adjustment for age, body mass index, other cardiovascular risk factors and socioeconomic status [29].

For heart valve diseases, both the partial model and the full model of statistical analysis by binomial logistic regression revealed that subjects belonging to the NLT category with a value between 15-27 had 7.631 times higher and 10 times higher odds, respectively to develop heart valve disease than subjects included in the first two NLT categories. The presence of co-morbidities such as renal failure, fluid overload, or other, except lung or metabolic, were associated with a reduction in the occurrence of heart valve disease. The results are consistent with other studies that also found that increased numbers of lost teeth were independently associated with the risk of heart valve disease, especially aortic valve atherosclerosis, further emphasizing the link between oral health and cardiovascular

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diseases [52]. Regarding the necessity and effectiveness of dental screening and treatments before heart valve surgical replacement, Kouwenberg et *al.* stated that these aspects remain unclear [53]. Also, Krasniqi et *al.* noted that mandatory preoperative dental screening with subsequent elimination of sources of dental sepsis before surgery was not associated with lower risk of infective endocarditis or all-cause mortality compared with mandatory preoperative dental screening targeted at surgical patients of aortic valve by trans-catheter techniques. However, medical guidelines recommend preoperative dental screening before heart valve surgery, although data from specialized literature are limited in this regard [54].

For coronary heart disease, results varied by logistic regression analysis model. In the case of the analysis through the partial logistic regression model, no correlation was revealed between the NLT categories and the categories of the demographic parameter variables. In the case of the analysis by the full logistic regression model, it was found that in subjects with NLT between 1-8 the probability of exposure to coronary heart disease was statistically significant. Also, subjects with metabolic diseases were almost 3 times more likely to have coronary heart disease than others, while renal failure and anasarca were associated with a reduced likelihood of having these conditions. Matsuyama et *al.* showed that the probability of coronary heart disease was significantly higher by 1.04 percentage points per lost tooth [40], and Dietrich et *al.* stated that there is a firm association between oral health assessed by the presence of periodontitis, the presence of carious lesions and tooth loss and atherosclerotic cardiovascular disease, represented by coronary heart disease, stroke and peripheral vascular disease [39]. Moreover, a stepwise and independent association was observed between tooth loss and several prognostic biomarkers of coronary heart disease, which suggested that tooth loss and its underlying mechanisms may be involved in several pathophysiological pathways also involved in the development and prognosis of coronary heart disease [55]. However, other authors considered that the relationship between tooth loss and coronary heart disease and stroke risk remains controversial, as some studies have shown that tooth loss is associated with an increased risk of coronary heart disease and stroke over time, while others did not find a relationship between them. Furthermore, the statistical dose-response relationship between tooth loss and the risk of coronary heart disease or stroke has not been described [2].

In the case of cardiomyopathy, statistically significant correlations with NLT, both in the partial logistic regression analysis and in the full model analysis. Partial model analysis showed that subjects with NLT between 9 and 14 were 6.466 more likely to have cardiomyopathy than other subjects. Full model analysis indicated that subjects with NLT between 1-8 and associated lung disease were 2.622 times more likely to have cardiomyopathy than subjects without lung disease, while subjects with an older age were more likely to have 1.16 times more likely to have cardiomyopathy than others. Also, subjects with NLT between 9 and 15 and the presence of renal failure and anasarca were 11.813 times and 7.186 times more likely to have cardiomyopathy than subjects without these diseases, respectively. Subjects with NLT between 15-27 and renal failure and anasarca, as well as subjects with lung comorbidities, were 6.017 times and 6.767 times more likely to have cardiomyopathy, respectively, than subjects without these diseases. It is observed that NLT represents a predictive variable for cardiomyopathy, especially in the case of association with

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another systemic condition. Studying the influence of oral health among people with diabetes, Gibson et *al.* demonstrated a high prevalence of non-functional dentition (<20 teeth) and poor oral health status, which were associated with a consistently increased risk of cardiovascular disease, including ischemic heart disease, transient ischemic attack, stroke, heart failure and diabetic cardiomyopathy [56]. It can be seen that the number of teeth represents a predictive variable for cardiomyopathy, especially in the case of association with another systemic condition. Worldwide, from 1990 to 2019, the number of cardiomyopathy cases increased substantially, and the condition remains an important global public health problem, with significant geographic variation in its prevalence. The highest standardized rates of cardiomyopathy related to age, alcohol consumption and mortality were observed in Eastern Europe [57].

For heart rhythm disorders, within the analyzed study group, statistical tests showed significant associations between NLT and the presence of this condition, but logistic regression models did not reveal significant statistical associations. These results are consistent with those obtained by Dietrich et *al.* who stated that there is little or no evidence to support any link between oral health and other forms of non-atherosclerotic cardiovascular disease such as hypertension, arrhythmias and heart failure [37]. Conversely, in a study on mice with experimentally induced open occlusion, Suita et *al.* showed that there is a correlation between occlusal disharmony and atrial fibrillation. In this research, occlusal disharmony was induced by tooth loss, which resulted in the vertical and horizontal migration of the remaining teeth to the edentulous space [58].

In the case of AHT, only the complete statistical analysis model by logistic regression highlighted significant results for the studied group. Subjects with NLT between 1-8, respectively 9-15 and metabolic disorders had a 3.445, respectively 3.957 higher probability of presenting AHT than those without associated metabolic disorders. Xu K et *al.* found that there was a bidirectional relationship between tooth loss and high blood pressure, meaning that people with tooth loss have a higher risk of high blood pressure and that hypertensive people have a higher risk of tooth loss. The authors demonstrated a positive association when severe tooth loss was set as the exposure and hypertension as the outcome. Using adjusted risk estimates, the risk of hypertension was increased by 12% in people with severe tooth loss. Edentulous subjects appeared to have a higher risk of hypertension. There was a linear dose-response relationship between the severity of tooth loss and the risk of hypertension. For every 7 lost teeth, the risk of hypertension increased by 11.9% [59]. Another systematic review and meta-analysis study also suggested that tooth loss is associated with an increased risk of hypertension and higher systolic blood pressure [60]. Chatzopoulos et *al.* showed people who self-reported anemia, bleeding disorders, cardiovascular disease, heart attack, high blood pressure, implanted defibrillator, had a significantly higher rate of incident tooth loss. The authors stated that future studies should further investigate the potential causal relationships between these systemic conditions, tooth loss, and periodontal disease [61].

Limitations of the study are determined by the small sample size, so the analysis of the predictive value of the NLT parameter on cardiovascular conditions may not have the necessary power. Another limit is represented by the fact that the loss of teeth represents the final stage of the evolution of several oral and dental conditions, being also involved socio-

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economic and behavioral factors [62]. Although the present study revealed statistically significant associations between tooth loss and cardiovascular disease, it is clear that the variables chosen did not capture the complexity and multiple facets of these correlations.

CONCLUSIONS

1. For the group of participants included in the study, NLT was statistically correlated with the presence of heart valve diseases and cardiomyopathies, in the unadjusted statistical analysis, in the analysis independently adjusted for age, gender and the presence of co-morbidities, and by partial statistical logistic regression models.
2. The full logistic regression model revealed the predictive value of NLT for heart valve disease in subjects without co-morbidities. In subjects with coronary diseases, the reduced number of missing teeth had predictive value especially in those with metabolic co-morbidities.
3. The full statistical logistic regression model showed that NLT had a statistically significant predictive value for cardiomyopathies especially in subjects with pulmonary co-morbidities, renal failure, or anasarca and for hypertension especially in subjects with metabolic co-morbidities.

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