Acta Clin Croat (Suppl. 1) 2021; 60:57-63
doi: 10.20471/acc.2021.60.s1.09

Original Scientific Paper

CORRELATION OF SARCOPENIA AND PERIODONTITIS IN PATIENTS ON CHRONIC HEMODIALYSIS

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SUMMARY – *Aim:* Hemodialysis patients present with signs of chronic systemic inflammation. Periodontitis can also trigger systemic inflammation and thus affect sarcopenia. The aim of the study was to examine the presence of sarcopenia and periodontitis in patients on chronic hemodialysis and see whether there is a correlation between them. *Methods:* The study included 53 patients on hemodialysis. Oral status and routine laboratory parameters, as well as body composition and handgrip strength, were measured. *Results:* 20.8% of patients had sarcopenia, while 69% had stage 4. periodontitis. No statistically significant correlation was found between sarcopenia and periodontitis, but fat mass (FM%) correlated positively with tooth loss (rho = 0.313, p = 0.027), as well as muscle fat (IMAT) (rho = 0.393, p = 0.005). Percentage of skeletal muscle in relation to body weight (wSMI) correlated negatively with tooth loss (rho = -0.393, p = 0.005), as well as the grip strength of the dominant hand (rho = -0.294, p = 0.043). *Conclusion:* In this pilot study, the correlation between sarcopenia and periodontitis in patients on HD 'was not determined, but a significant correlation of body composition parameters with tooth loss was found, which should be tested in a larger cohort of patients.

Key words: *periodontitis, sarcopenia, hemodialysis*

Introduction

In patients on chronic hemodialysis, muscle atrophy and impaired functional capacity are more likely to occur, as opposed to the rest of the same age population[1]. Moreover, patients on hemodialysis have greater muscular atrophy and reduced functional capacity, unlike patients with chronic renal failure who are not treated with hemodialysis[2].

Also, observational studies have confirmed frequent oral health problems in hemodialysis patients, especially periodontal disease, an inflammatory disease affecting the supporting tissues of the teeth[3-5]. The most common periodontal diseases result from the interaction of specific bacterial species with the components of the host immune response in patients prone to these diseases. Plaque-induced gingivitis and periodontitis leading to tooth loss are the most common[6]. Other conditions in patients on HD which cause poor oral health include uremic stomatitis, gingival bleeding due to platelet dysfunction or anticoagulant therapy, enamel hypoplasia and erosion of the tooth surface due to gastric acid regurgitation and vomiting caused by uraemia, changes in the maxillary bone and an increased risk of bone fractures[7].

In recent decades, research linking oral health and other systemic diseases have been conducted[8,9]. Although some studies have confirmed an association between oral status and sarcopenia in the elderly[10-13],

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there is currently no research linking these parameters in the chronic hemodialysis patient population.

Methods

Subjects

The study involved 53 patients of both sexes who are on a chronic hemodialysis program at the Department of Nephrology and Dialysis of the Clinic for Internal Diseases at the Sestre milosrdnice Clinical Hospital Center. Inclusion criteria were adulthood and dialysis vintage of 6 months or longer. Excluding criteria were history of limb amputation, implanted cardiac pacemaker or subdiaphragmatic electrical device, prescribed immunosuppressive therapy, and acute illness during the previous month. The study was conducted after approval of the Ethics committee of the Institution and in concordance with the Declaration of Helsinki. All patients signed informed consent prior to the study start.

Body composition analysis and hand grip strength

In the first part of the study, the body composition was determined by the multifrequency bioelectrical impedance method (BIA-ACC) (BioTekna, Marcon-Venice, Italy). Measurement was performed with participants in a supine position. Two electrodes were positioned on the hand at about 10 cm distance from each other, and two electrodes were placed on the foot at the same distance. The parameters of measurement were: Skeletal muscle mass expressed as % of fat-free mass (kg) (SM%); Skeletal muscle mass expressed as % of total body weight (kg) (wSMI); Skeletal muscle mass expressed as % of total body height (cm) (hSMI); Fat mass expressed as % of total body weight (kg) (FM%); and Intramuscular adipose tissue (IMAT) expressed as % of total body weight. The handgrip strength was measured by a hydraulic dynamometer (Hydraulic Hand Dynamometer, "SAEHAN SH5001", Rehaforum Medical). The measurement was performed in a sitting position, with the forearm and upper arm at an angle of 90 degrees. It was done three times with each hand, and resting pauses between measurements. The mean result of the dominant hand was taken into consideration.

Based on the results of body composition analysis and handgrip strength, we concluded which patients have sarcopenia according to the criteria of the European Working Group on Sarcopenia in Older People (EWGSOP)[14] - cut off results for the evaluation of sarcopenia: handgrip strength– male < 27kg, women < 16kg; ASM (appendicular skeletal muscle mass) - male < 20kg, women < 15 kg or ASM / height^2, male < 7.0 kg/m^2, women < 5.5 kg/m^2.

Monitored parameters

The parameters that were monitored were body mass, height, body mass index (BMI), and comorbidities. From routine laboratory blood tests, C- Reactive Protein (CRP) and serum albumin were isolated.

Dental examination

In the second part of the study, participants were examined by a single dentist at the Department of Nephrology and Dialysis. Periodontal status was evaluated at the bedside during HD sessions. The dental examination included the measurement of: approximate plaque index (API), probing depth (PD), papilla bleeding index (PBI), bleeding on probing (BOP), gingival recessions, clinical attachment loss (CAL)[15,16]. All indices were taken using a graduated periodontal probe with Williams marks on every millimeter. This dental examination confirmed which subjects had periodontitis[17].

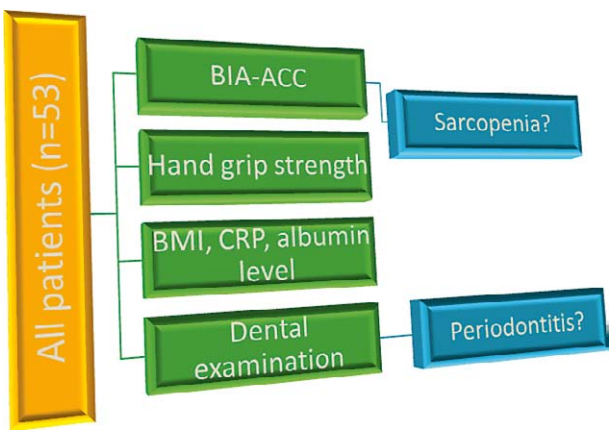

Figure 1. The overall flow-chart of study design

BIA-ACC= multifrequency bioelectrical impedance method; BMI= Body Mass Index; CRP= C- Reactive protein

The overall flow-chart of the study design is shown in Figure 1.

Statistical methods

Kolmogorov-Smirnov test has been used to assess continuous data normality distribution, and according to the results, appropriate non-parametric tests were used in the following analyses.

Categorical variables were represented as frequencies and percentages while continuous variables through medians and interquartile ranges (25th and 75th percentile – IQR). Spearman's coefficient, rho, was used to analyse the correlation between clinical variables API score and the number of lost teeth. Multivariate OLS regression models in predicting the API score and number of lost teeth were made to assess multivariate influence. All P values below 0.05 were considered significant. IBM SPSS Statistics version 25.0 has been used in all statistical procedures.

Results

Descriptive statistics of included participants are shown in Table 1. The median age of all participants was 69 (61-75) years, and there were 28 (53%) males. Severe periodontitis (stage 4) was found in 34 (69%) participants and defined sarcopenia in 11 (21%) patients. The correlation of clinical parameters with the number of lost teeth and API level is shown in Table 2. Number of lost teeth significantly positively correlates with age (rho=0.342; P=0.015), percentage of fat mass (FM%) (rho=0.313; P=0.027), IMAT (rho=0.393; P=0.005), while negatively with wSMI (rho=-0.393; P=0.005) and grip strength of dominant hand (rho=-0.294; P=0.043). API score significantly correlates with FM (rho=0.332; P=0.020) and IMAT (rho=0.314; P=0.028).

Multivariate Ordinary Least Square (OLS) regression model in predicting the number of lost teeth is shown in Table 3. and in predicting higher API score in Table 4. Dependent variables were: number of lost teeth and API score, respectively, while predictor variables included age, gender, sarcopenia, and grip strength. Regression models were statistically significant (P <0.05) and explained 26.1% and 25.2% of the dependent variable variance. In predicting the number of lost teeth, older age was the only significant predictor (adjusted to the influence of the other predictor variables in the model) with standardised coefficients β=0.59 and P=0.003 (Table 3). The presence of sarcopenia was the only negative significant predictor for higher API score, also adjusted to the influence of the other predictor variables used in the model (Table 4) with β=-0.37 and P=0.045. Participants with sarcopenia have more chance to have lower API scores.

Table 1. Descriptive statistics of included participants (N=53)

Characteristic	N = 53
Age (years)	69 (61-75)
Male gender	28 (53%)
BMI (kg/m^2)	26 (23-32)
FM (%)	33 (29-42)
IMAT (%)	2.50 (2.20-2.80)
wSMI (%)	22.0 (17.0-25.0)
hSMI (kg/m^2)	6.20 (5.10-7.10)
Skeletal Muscle (%)	34 (30-38)
Sarcopenia	11 (21%)
Number of lost teeth	13 (9-21)
PBI	0.92 (0.50-1.55)
API	100 (53-100)
BOP	77 (50-100)
Severe periodontitis (stage 4)	34 (69%)
Grip strength: dominant hand	26 (18-31)
Grip strength: non-dominant hand	20 (16-26)
Albumin level (g/L)	38.7 (36.3-40.5)
CRP (mmol/L)	4 (2-10)
S-score	-0.60 (-1.80-0.70)
ALST(kg)	15.2 (12.0-18.0)

[1] Statistics presented: median (IQR); n (%)
BMI= Body Mass Index; FFM= Fat-Free Mass; FM= Fat Mass; IMAT= Intermuscular Adipose Tissue; wSMI= Skeletal Muscle Mass expressed as a percentage in comparison to total body weight; hSMI= Skeletal Muscle Mass expressed as a percentage in comparison to height; PBI=Papilla Bleeding Index; API= approximate Plaque Index; BOP= Bleeding On Probing; CRO= C-Reactive Protein; ALST= Appendicular Lean Soft Tissue

Discussion

Severe chronic conditions of patients on hemodialysis, frequent protein-energy malnutrition but also chronic inflammation lead to decreased muscle mass[18], which contributes to poor physical performance and a sedentary lifestyle. This ultimately leads to cardiovascular damage and increased mortality in patients on

Table 2. Correlation of clinical parameters with number of lost teeth and API level: Spearman correlation coefficient

		Number of lost teeth	API
Age (years)	Correlation Coefficient	**0.342**	0.067
	P	**0.015**	0.649
BMI (kg/m^2)	Correlation Coefficient	0.100	0.192
	P	0.490	0.186
FM (%)	Correlation Coefficient	**0.313**	**0.332**
	P	**0.027**	**0.020**
IMAT (%)	Correlation Coefficient	**0.393**	**0.314**
	P	**0.005**	**0.028**
wSMI (%)	Correlation Coefficient	**-0.393**	-0.236
	P	**0.005**	0.103
hSMI (kg/m^2)	Correlation Coefficient	-0.199	0.029
	P	0.167	0.842
Skeletal Muscle (%)	Correlation Coefficient	-0.245	-0.069
	P	0.087	0.639
Grip strength: dominant hand	Correlation Coefficient	**-0.294**	-0.121
	P	**0.043**	0.418
Grip strength: non-dominant hand	Correlation Coefficient	-0.233	-0.203
	P	0.111	0.172
Albumin level (g/L)	Correlation Coefficient	0.010	-0.155
	P	0.946	0.289
CRP (mmol/L)	Correlation Coefficient	0.172	0.081
	P	0.233	0.580
S-score	Correlation Coefficient	-0.141	0.086
	P	0.330	0.558
ALST(kg)	Correlation Coefficient	-0.233	-0.015
	P	0.104	0.916

BMI= Body Mass Index; FM= Fat Mass; IMAT= Intramuscular Adipose Tissue; wSMI= Skeletal Muscle Mass expressed as a percentage in comparison to total body weight; hSMI= Skeletal Muscle Mass expressed as a percentage in comparison to height; CRP= C-Reactive Protein; ALST= Appendicular Lean Soft Tissue

Table 3. Multivariate OLS regression model in predicting the number of lost teeth

	Standardized Coefficients	95,0% Cl		P
	Beta	Lower Bound	Upper Bound	
Age (years)	0.59	0.13	0.58	0.003
Gender	-0.01	-6.21	5.86	0.954
Sarcopenia	-0.13	-8.62	3.81	0.439
Grip strength: dominant hand	-0.38	-0.85	0.20	0.219
Grip strength: non-dominant hand	0.40	-0.14	0.81	0.166

Table 4. Multivariate OLS regression model in predicting the higher API score

	Standardized Coefficients	95,0% Cl		P
	Beta	Lower Bound	Upper Bound	
Age (years)	0,26	-0,39	1,79	0,203
Gender	0,17	-16,80	41,59	0,396
Sarcopenia	-0,37	-61,62	-0,77	0,045
Grip strength: dominant hand	0,12	-2,08	2,99	0,720
Grip strength: non-dominant hand	-0,10	-2,67	1,92	0,742

chronic hemodialysis[19]. Thus, loss of muscle mass with a decrease in muscle strength indicates a condition of sarcopenia. Moreover, if worsening of physical performance also occurs, severe sarcopenia can be diagnosed[14]. Muscle decline in patients with chronic renal failure has been the subject of numerous studies, and inflammation has been shown to stimulate cellular signaling pathways that activate myostatin (a negative regulator of skeletal muscle growth), accelerating muscle catabolism[20,21].

Patients with chronic kidney disease (CKD) have a high prevalence of the periodontal disease, with leading gingivitis and periodontitis, which is linked with CKD progression through chronic inflammation[6,22]. In this study, 69% of patients had periodontitis stage IV, while 20.8% had sarcopenia. This coincides with previ-

ous researches, confirming that patients on hemodialysis have problems both with oral health and sarcopenia. But there is no significant correlation between periodontitis and sarcopenia, probably because of a too-small sample size.

However, it was found that tooth loss had a significant role in body composition. Fat mass (FM) correlated positively with tooth loss, as well as intramuscular fat (IMAT). Percentage of skeletal muscle in relation to body weight (wSMI) correlated negatively with tooth loss.

In a research done by McIntyre et al., 134 nephrological patients were examined with multi-slice CT scan of a 6 cm long section of the thigh so that the cross-sectional area (CSA) of muscle and fat was measured as well as some functional tests. They noticed that patients on hemodialysis had more significant muscle atrophy and functional capacity loss than CKD stage 4 patients who weren't on hemodialysis[2].

Another important predictor of muscle atrophy and later sarcopenia is intramuscular adipose tissue (IMAT), which is defined as ectopic adipose tissue accumulation between muscle groups beneath the muscle fascia and intramuscular adipose tissue, which is visible on Magnetic Resonance Imaging (MRI) images[23]. In our study, IMAT was measured with a dual-frequency bioimpedance device, and a significant positive correlation between a number of lost teeth and IMAT was found, meaning that probably due to teeth loss, patients had problems with nutrient intake, which eventually caused muscle quality decline, because of fat deposition in muscles. Another explanation could be that inflammatory state, due to bad oral health and other concomitant chronic comorbidities, caused adipose tissue accumulation in muscles. But further investigations with a bigger sample size are required.

In a study provided by Takahashi et al., 279 older patients in an outpatient dental clinic were examined for sarcopenia and oral status. They confirmed that participants who had sarcopenia had worse oral status and oral health-related quality of life compared to those without sarcopenia[12].

During a prospective study on 193 older participants, Hämäläinen et al. found that the ones with periodontitis at baseline had a higher decline in grip strength after 5 years than those who had healthy gingiva at baseline[11]. Similarly, in our study, there was a negative correlation between tooth loss and handgrip strength of the dominant hand, which also suggests an important link between oral health and sarcopenia.

Since sarcopenia affects all muscle groups, the relationship between masticatory muscles and sarcopenia has also been examined[24], which further inhibits sufficient nutrient intake and worsens sarcopenia.

Previous research has observed a positive correlation between periodontitis and serum CRP levels[6,25]. Furthermore, the number of teeth was negatively associated with serum CRP level in patients on HD[3]. On the other hand, one study showed that CRP levels significantly decreased after periodontal treatment in 41 patients on HD[26], while another showed that CRP levels in periodontitis treated patients were similar to non-treated patients[27]. In our study, there was not a significant link between CRP and oral health, maybe due to the small sample size or because of the influence of other comorbidities on CRP levels. In research conducted by Yazdi et al., there was also no significant correlation between CRP levels and periodontitis severity[28], as well as in a study by Kshirsagar et al.[29].

Hypoalbuminemia has been linked with higher mortality[30]. It is known that albumin levels decrease in inflammatory diseases due to pro-inflammatory cytokines blockage of the production of hepatic albumin[31]. That is mostly the reason why it has been the subject of many studies in recent years. In a study made by Rodriguez et al., there was a positive correlation between hypoalbuminemia and periodontitis[32]. Moreover, Chen et al. have shown that serum albumin levels negatively correlated with parameters of periodontal health status[6]. On the other hand, Cholewa et al. found no difference in albumin levels between dentate and edentulous patients on HD or patients with healthy periodontium or gingivitis and those with periodontitis[3], which was the case in our study, as well, where we found no correlation between albumin levels and periodontitis or sarcopenia.

This study has its limitations. First of all, small sample size, which was limited by inclusion and exclusion criteria, as well as with the willingness of patients to participate in a study. Secondly, we evaluated only one dialysis center, which from the start limits the variety of participants. Another limitation is the lack of a control group.

Opposite to that, the vital strength of this study is its originality in establishing a new link between oral status and body composition in the population of he-

modialysis patients, who are a very fragile and sensitive group. It is important to emphasize that a novel multi-frequency bioelectrical impedance device (BIA- ACC) was used, which measures body composition in detail, including intramuscular adipose tissue (IMAT), in comparison to other studies which mostly used computed tomography or MRI to measure IMAT. So one can conclude that our way of measuring is ethically more acceptable and affordable.

This study did not show a correlation between sarcopenia and periodontitis in patients on hemodialysis, according to sarcopenia definition by EWGSOP. What we did confirm is a significant link between tooth loss and body composition (FM, wSMI, IMAT) in patients on HD. This is new information that emphasizes the importance of oral health and its influence on adipose tissue deposition, especially intramuscular adipose tissue (IMAT), because it causes muscle dysfunction and favors the development of sarcopenia. Additional research with larger sample size is needed.

Acknowledgments

The authors sincerely thank everyone who participated in this research, particularly Siniša Šefer, MD and all dialysis personnel from Clinical University Hospital Sestre milosrdnice.

Conflicts of interest and source of funding: none declared.

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Sažetak

POVEZANOST SARKOPENIJE I PARODONTITISA U BOLESNIKA NA KRONIČNOJ HEMODIJALIZI

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Cilj: Bolesnici na hemodijalizi imaju prisutne znakove kronične sistemne upale. Parodontitis također može potaknuti sistemnu upalu i na taj način utjecati na sarkopeniju. Cilj istraživanja bio je ispitati prisutnost sarkopenije i parodontitisa u bolesnika na kroničnoj hemodijalizi te istražili postoji li njihova povezanost. *Metode:* U studiju su uključena 53 bolesnika koji su na hemodijalizi te im je učinjen oralni status, procjena stupnja parodontitisa, rutinska laboratorijska obrada, mjerenje sastava tijela i procjena snage stiska šake. *Rezultati:* Od ukupnog broja ispitanika 20,8 % je imalo sarkopeniju, dok je 69 % imalo 4. stadij parodontitisa. Nije pronađena statistički značajna povezanost između sarkopenije i parodontitisa (Z= -0,401, p=0,689), no utvrđena je pozitivna povezanost postotka masti u tijelu (FM%) s gubitkom zubi (rho= 0,313, p= 0,027), kao i intramuskularnog masnog tkiva s gubitkom zubi (IMAT) (rho=0,393, p=0,005). Postotak skeletnih mišića u odnosu na tjelesnu težinu (wSMI) korelira negativno s gubitkom zubi (rho= -0,393, p=0,005), isto kao i snaga stiska šake desne ruke (rho= -0,294, p= 0,043). *Zaključak:* Ovim pilot istraživanjem nismo utvrdili povezanost sarkopenije i parodontitisa kod ove skupine bolesnika, no otkrili smo značajnu povezanost parametara sastava tijela s brojem ispalih zubi, što bi dodatno trebalo ispitati na većem broju ispitanika.

Ključne riječi: *parodontitis, sarkopenija, hemodijaliza*