PERIODONTITIS AND EARLY MORTALITY AMONG ADULTS TREATED WITH HEMODIALYSIS: A MULTINATIONAL PROPENSITY-MATCHED COHORT STUDY

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Background Periodontitis, a multifactorial disease that involves inflammation of the structures supporting teeth, is common, treatable, and may be associated with mortality in the general population and adults with chronic diseases. However, it is unclear whether periodontitis is associated with survival in the setting of kidney failure.

Methods ORAL-D was a multinational cohort study involving 3338 dentate adults with end-stage kidney disease treated in a hemodialysis network in Europe and South America. ORAL-D was designed to examine the associations between oral health and all-cause and cardiovascular-related mortality in people on long-term hemodialysis. Propensity score methods were used to assemble a matched cohort of participants with moderate to severe periodontitis with characteristics similar to patients with no or mild periodontitis. Periodontal disease was assessed using the World Health Organization Community Periodontal Index. A random-effects Cox proportional hazards model was fitted with shared frailty to account for clustering of mortality risk within countries

Results Among the 3338 dentate participants, 1355 (40.6%) had moderate to severe periodontitis at baseline. Participants with moderate or severe periodontitis were older, more likely to be men, were more often married, unemployed or retired, had higher serum albumin levels, and had survived treated with dialysis for longer (**Table 1**).

Participants with moderate to severe periodontitis had evidence of deeper periodontal probing depths, more severe clinical attachment loss, increased distance between the cementum-enamel junction and free gingival margin, and more extensive bleeding on probing as expected (**Table 2**).

Moderate to severe periodontitis was associated with a lower risk of all-cause (9.1 versus 13.0 per 100 person years, hazard ratio 0.74, 95% confidence interval 0.61 to 0.90) and cardiovascular (4.3 versus 6.9 per 100 person years, hazard ratio 0.67, 0.51 to 0.88) mortality (**Table 3**). These associations were not changed substantially in sensitivity analyses restricted to participants with 12 or more natural teeth or when analyses accounted for competing causes of cardiovascular death.

Table 1 Baseline characteristics of study participants according to periodontal status in unmatched and matched cohorts

	Full cohort			After propensity score matching		
Variables	None or mild periodontitis (n=1983)	Moderate to severe periodontitis (n=1355)	Standardized difference†	None or mild periodontitis (n=1355)	Moderate to severe periodontitis (n= 1355)	Standardized difference†
Demographics						
Age (years)‡	57.3 (16.3)	61.7 (14.5)	0.23	61.8 (14.5)	61.7 (14.5)	0.005
Country						
Argentina	1304 (65.8)	177 (13.1)	0.99	846 (62.4)	177 (13.1)	0.91
France	28 (1.4)	11 (0.8)	0.05	27 (2.0)	11 (0.8)	0.08
Hungary	182 (9.2)	233 (17.2)	-0.20	141 (10.4)	233 (17.2)	-0.17
Italy	97 (4.9)	312 (23.0)	-0.49	89 (6.6)	312 (23.0)	-0.42
Poland	200 (10.1)	39 (2.9)	0.22	119 (8.8)	39 (2.9)	0.19
Portugal	169 (8.5)	464 (34.2)	-0.58	131 (9.7)	464 (34.2)	-0.55
Spain	3 (0.2)	119 (8.8)	-0.42	2 (0.2)	119 (8.8)	-0.42
Men‡	1116 (56.3)	852 (62.9)	-0.10	838 (61.9)	852 (62.9)	-0.02
European race	1899 (96.4)	1246 (91.9)	0.17	1297 (95.7)	1246 (91.9)	0.13
Socioeconomic characteristics						
Current or former smoker‡	381 (31.2)	408 (34.6)	-0.06	352 (26.0)	408 (34.6)	-0.15
Married	859 (60.7)	835 (68.0)	-0.12	583 (61.2)	835 (68.0)	-0.12
Secondary education	466 (39.4)	460 (40.4)	-0.02	331 (38.7)	460 (40.4)	-0.03
Employed	218 (18.1)	148 (12.9)	0.12	149 (16.7)	148 (12.9)	0.09
Family income above domestic average‡	132 (7.4)	106 (8.2)	-0.02	98 (7.6)	106 (8.2)	-0.02
Body mass index (kg/m^2)	26.9 (5.2)	26.7 (5.2)	0.04	26.9 (5.2)	26.7 (5.2)	0.04
Comorbid medical conditions						
Myocardial infarction	112 (10.0)	138 (13.3)	-0.09	95 (11.7)	138 (13.3)	-0.04
Stroke	88 (7.8)	125 (12.0)	-0.12	70 (8.6)	125 (12.0)	-0.12
Diabetes mellitus	338 (30.3)	335 (29.4)	0.02	238 (29.7)	335 (29.4)	0.005
Laboratory variables						
Serum albumin (g/dL)	3.7 (0.4)	3.9 (0.4)	-0.41	3.7 (0.4)	3.9 (0.4)	-0.41
Serum phosphorous (mmol/L)	1.6 (0.5)	1.5 (0.5)	0.16	1.5 (0.5)	1.5 (0.5)	0
Serum calcium (mmol/L)	2.2 (0.2)	2.2 (0.2)	0	2.2 (0.2)	8.8 (0.8)	0
Hemoglobin (g/dL)	11.0 (1.4)	11.2 (1.3)	-0.12	11.1 (1.4)	11.2 (1.3)	-0.06
Dialysis characteristics						
Time treated with dialysis (months)‡	75.1 (54.9)	84.6 (66.4)	-0.13	82.5 (59.1)	84.6 (66.4)	-0.02
Kt/V*	1.7 (0.3)	1.7 (0.3)	0	1.6 (0.3)	1.7 (0.3)	-0.27
Mean arterial pressure (mmHg)	89.0 (13.7)	91.7 (13.7)	-0.16	88.8 (13.5)	91.7 (13.7)	-0.17
Oral health practices and dental health						
Number of teeth‡	16.5 (9.4)	17.1 (8.3)	-0.05	16.5 (9.2)	17.1 (8.3)	-0.05
Number of decayed, missing, filled teeth	19.4 (8.9)	19.2 (8.1)	0.02	19.3 (8.8)	19.2 (8.1)	0.01
Use of dental floss	153 (7.8)	115 (8.6)	-0.02	90 (6.7)	115 (8.6)	-0.06
Brushing teeth twice or more often per day	1310 (67.1)	854 (64.2)	0.05	874 (65.2)	854 (64.2)	0.05

*Data are expressed as mean (SD) or number (%). *Kt/V refers to the clearance of urea and is a measure of the amount of dialysis received. Proportions do not always correspond to overall numbers of participants due to missing data. †Standardized differences of 0.2, 0.5 and 0.8 can be considered to represent small, medium and large differences, respectively. These differences do not denote statistical significance. To convert serum phosphorus from mmol/L to mg/dL, divide by 0.323. To convert calcium from mmol/L to mg/dL, multiply by 0.25. ‡Used in propensity score matching*

Table 2 Baseline periodontal characteristics defined by the World Health Organization Community Periodontal Index in unmatched and matched cohorts

	Full cohort			After propensity score matching		
Variables	None or mild periodontitis (n=1983)	Moderate to severe periodontitis (n=1355)	Standardized difference*	None or mild periodontitis (n=1355)	Moderate to severe periodontitis (n= 1355)	Standardized difference*
Periodontal probing depth, mm	0.68 (0.38)	1.53 (0.70)	-1.36	0.70 (0.38)	1.53 (0.70)	-1.33
Clinical attachment loss, mm	2.03 (1.56)	3.15 (1.55)	-0.59	2.12 (1.55)	3.15 (1.55)	-0.54
Distance between cementum-enamel junction and free gingival margin, mm	1.35 (1.49)	1.62 (1.49)	-0.15	1.42 (1.50)	1.62 (1.49)	-0.11
Bleeding on probing, % sites per person	13.1 (22.3)	20.7 (27.4)	-0.26	12.7 (21.7)	20.7 (27.4)	-0.28

Data are mean (SD). The periodontal pocket depth measurements were made at three sites on the vestibular and lingual aspects of each tooth and the periodontal probing depth (PPD) score was calculated as a mean value divided by the number of sites examined. The Bleeding on Probing (BOP) index evaluated the buccal, lingual, mesial and distal sulci of all teeth based on the tendency to bleed after a standard stimulus. The four surfaces of each tooth were tested to provide a maximum total of 128 sites and the index is the percentage of sites positive for bleeding on probing for each participant. The Clinical Attachment loss score was calculated as the sum of the mean PPD (sum of all values divided by the number of sites examined (6 per tooth)) and the mean (free gingival margin [GM]-cementum-enamel junction [CEJ]) (sum of all values divided by the number of sites examined (3 per tooth)).
**Standardized differences of 0.2, 0.5 and 0.8 can be considered to represent small, medium and large differences, respectively. These differences do not denote statistical significance.*

Table 3 Mortality outcomes with moderate to severe periodontitis among the whole cohort, propensity-weighted analyses and propensity-score matched patients with end-stage kidney disease treated with hemodialysis

		No (events per 100 person years)		
	Number of participants included in analyses	Moderate to severe periodontitis	No or mild periodontitis	Hazard ratio (95% CI)
All-cause mortality				
Whole cohort	3338	242 (9.1)	408 (11.7)	0.94 (0.73 to 1.21)
Propensity-weighted	3338	242 (9.1)	408 (11.7)	0.83 (0.68 to 1.00)
Propensity-matched	2710	242 (9.1)	314 (13.0)	0.74 (0.61 to 0.90)
Cardiovascular mortality				
Whole cohort	3338	113 (4.3)	212 (6.1)	0.91 (0.64 to 1.29)
Propensity-weighted	3338	113 (4.3)	212 (6.1)	0.76 (0.58 to 1.00)
Propensity-matched	2710	113 (4.3)	167 (6.9)	0.67 (0.51 to 0.88)

Hazard ratios are reported for moderate to severe periodontitis (no or mild periodontitis is the reference group). CI denotes confidence interval. Hazard ratios are controlled for age, sex, income, smoking, serum phosphorus, myocardial infarction, diabetes mellitus, mean arterial pressure, time on dialysis and number of teeth using a Cox proportional hazards regression model. Clustering by country was accounted for by random effects Cox proportional hazards regression fitted using a shared frailty model.

Conclusion Periodontitis does not appear to be associated with an increased risk of all-cause and cardiovascular mortality in adults treated with hemodialysis.

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