

ASSOCIATION OF PERIODONTITIS WITH ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN ADULTS WITH END-STAGE KIDNEY DISEASE: A MULTINATIONAL COHORT STUDY

DIIVERUM

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Background

Oral disease is highly prevalent in the general population and represents a potential and reversible determinant of poor health in dialysis patients. Periodontitis is associated with adverse cardiovascular events in healthy adults, but the link between periodontal disease and clinical outcomes in individuals with end-stage kidney disease is poorly understood. We aimed to evaluate the association between periodontitis and all-cause and cardiovascular mortality in dialysis patients.

Methods

We conducted a prospective multinational cohort study in 4205 adults with end-stage kidney disease treated with hemodialysis (the ORAL-D study) during 2010-2012 who had undergone a standardized oral examination to evaluate periodontitis according to the World Health Organization definition. The impact of periodontitis on mortality risk was studied in 3338 dentate participants (Table 1 and Table 2). The primary outcomes were all-cause and cardiovascular mortality. We used univariate and random-effects multivariable-adjusted Cox proportional regression analyses to examine the association of periodontitis with all-cause and cardiovascular mortality. We controlled for age, gender, race, smoking history, income, prior cardiovascular events (myocardial infarction; stroke), diabetes, patient time on dialysis, mean arterial blood pressure and serum phosphorus. We fitted regression analysis using a shared frailty model to account for clustering within countries.

Results

During 6150 person-years of follow-up, 650 deaths occurred of which 325 were cardiovascular. 1355 (40.6%) participants had moderate to severe periodontitis. In crude analyses (Figure 1), moderate to severe periodontitis was associated with lower risks of all-cause (HR 0.78, 95% confidence interval 0.67 to 0.92) and cardiovascular mortality (0.70, 0.56 to 0.89) and there was evidence of decreasing mortality risk with more severe periodontal disease (P=0.02 for trend). However, when analyses were adjusted for other prognostic clinical and socio-demographic factors, periodontitis was not associated with all-cause (0.86, 0.71 to 1.05) or cardiovascular mortality (0.77, 0.59 to 1.02) (Table 3). Similar results were observed when the Centers for Disease Control (CDC) definition for periodontitis was used (data not shown).

Conclusion

In adults treated with haemodialysis, periodontitis is not an independent risk factor for early mortality or cardiovascular death.

Table 1 Baseline characteristics of study participants

Variables	Severity of periodontitis		All dentate patients (N = 3338)	All participants (N = 4205)
	None or mild (N = 1983)	Moderate to severe (N = 1355)		
Demographics				
Age (years)	57.3 (16.3)	61.7 (14.5)	59.1 (15.8)	61.6 (15.6)
Country				
Italy	97 (4.9)	312 (23.0)	409 (12.3)	593 (14.1)
Spain	3 (0.2)	119 (8.8)	122 (3.7)	189 (4.5)
France	28 (1.4)	11 (0.8)	39 (1.2)	48 (1.1)
Portugal	169 (8.5)	464 (34.2)	633 (19.0)	762 (18.1)
Poland	200 (10.1)	39 (2.9)	239 (7.2)	319 (7.6)
Hungary	182 (9.2)	233 (17.2)	415 (12.4)	550 (13.1)
Argentina	1304 (65.8)	177 (13.1)	1481 (44.4)	1744 (41.5)
Men	1116 (56.3)	852 (62.9)	1968 (59.0)	2426 (57.7)
European	1899 (96.4)	1246 (91.9)	3145 (94.6)	3987 (94.8)
Socioeconomic characteristics				
Ever smoker	381 (31.2)	408 (34.6)	789 (32.9)	1029 (33.4)
Married	859 (60.7)	835 (68.0)	1694 (64.1)	2161 (64.6)
Secondary education	466 (39.4)	460 (40.4)	926 (39.9)	1139 (38.1)
Employed	218 (18.1)	148 (12.9)	366 (15.5)	387 (12.8)
Family income above domestic average	132 (7.4)	106 (8.2)	238 (7.7)	313 (8.0)
Comorbid medical conditions				
Myocardial infarction	112 (10.0)	138 (13.3)	250 (11.6)	348 (12.5)
Stroke	88 (7.8)	125 (12.0)	213 (9.8)	287 (10.3)
Diabetes mellitus	338 (30.3)	335 (29.4)	673 (29.9)	933 (32.0)
Laboratory variables				
Serum albumin (g/dl)	3.7 (0.4)	3.9 (0.4)	3.8 (0.4)	3.8 (0.4)
Serum phosphorus (mmol/l)	1.6 (0.5)	1.5 (0.5)	1.5 (0.5)	1.5 (0.5)
Serum calcium (mmol/l)	2.2 (0.2)	2.2 (0.2)	2.2 (0.2)	2.2 (0.2)
Haemoglobin (g/dl)	11.0 (1.4)	11.2 (1.3)	11.1 (1.4)	11.1 (1.3)
Dialysis characteristics				
Time on dialysis (months)	60 (36-96)	64 (41-104)	62 (39-100)	60 (38-98)
Kt/V	1.7 (0.3)	1.7 (0.3)	1.7 (0.3)	1.7 (0.3)
URR	0.8 (0.06)	0.8 (0.06)	0.8 (0.06)	0.8 (0.06)
Mean arterial pressure (mm Hg)	89.0 (13.7)	91.7 (13.7)	90.2 (13.7)	90.0 (13.5)

Data are expressed as mean (SD), number (%), or median (25th percentile, 75th percentile). 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.

Table 2 Baseline dental characteristics in patients with periodontitis defined by the World Health Organization Community Periodontal Index

	None or mild periodontitis (N=1983)	Moderate to severe periodontitis (N=1355)
No. of decayed, missing, filled teeth (mean, SD)	19.4 (8.9)	19.2 (8.1)
Periodontal probing depth, mm (mean, SD)	0.68 (0.38)	1.53 (0.70)
Clinical attachment loss, mm (mean, SD)	2.03 (1.56)	3.15 (1.55)
Distance between cementum-enamel junction and free gingival margin, mm (mean, SD)	1.35 (1.49)	1.62 (1.49)
Bleeding on probing, % sites per person	13.1 (22.3)	20.7 (27.4)
Use of dental floss (n, %)	153 (7.8)	115 (8.6)
Use of mouth wash (n, %)	494 (25.3)	722 (54.3)
Brushing teeth ≥ twice per day (n, %)	1310 (67.1)	854 (64.2)

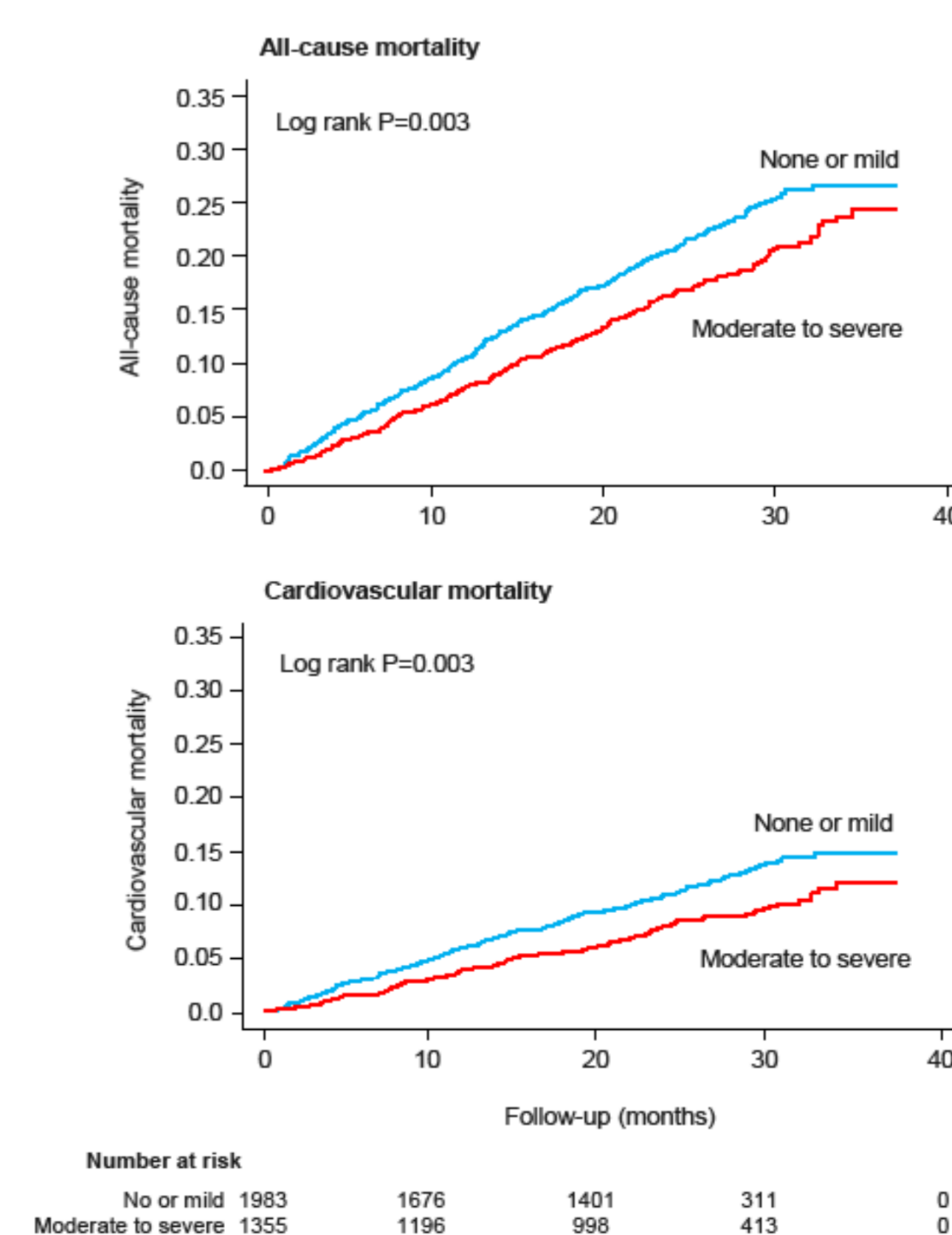
Data are mean (SD), or median (25th, 75th centiles) or number (proportion) where indicated.

Table 3 Distribution of mortality outcomes and hazard ratios for death according to periodontitis status

	No. of patients	No. of deaths (%)	Unadjusted hazard ratio (95% CI)	P value for trend	Age and country adjusted hazard ratio (95% CI)	P value for trend	Fully adjusted hazard ratio (95% CI)*	P value for trend
Deaths from all causes								
Moderate to severe periodontitis (reference: no or mild periodontitis)	1355	242 (17.9)	0.78 (0.67-0.92)		0.82 (0.68-0.99)		0.86 (0.71-1.05)	
Periodontitis severity				0.02		0.12		0.39
No periodontitis	460	97 (21.1)	Reference		Reference		Reference	
Mild periodontitis	1523	311 (20.4)	1.01 (0.80-1.27)		1.12 (0.89-1.40)		1.07 (0.85-1.35)	
Moderate periodontitis	678	128 (18.9)	0.84 (0.65-1.10)		0.95 (0.71-1.26)		0.95 (0.71-1.27)	
Severe periodontitis	677	522 (16.8)	0.74 (0.56-0.96)		0.84 (0.63-1.13)		0.87 (0.64-1.17)	
Deaths from cardiovascular disease								
Moderate to severe periodontitis (reference: no or mild periodontitis)	1355	113 (8.3)	0.70 (0.56-0.89)		0.75 (0.57-0.99)		0.77 (0.59-1.02)	
Periodontitis severity				0.02		0.16		0.29
No periodontitis	460	50 (10.9)	Reference		Reference		Reference	
Mild periodontitis	1523	162 (10.6)	1.02 (0.74-1.40)		1.14 (0.83-1.57)		1.08 (0.79-1.49)	
Moderate periodontitis	678	60 (8.9)	0.77 (0.53-1.12)		0.88 (0.58-1.32)		0.86 (0.57-1.30)	
Severe periodontitis	677	53 (7.8)	0.66 (0.45-0.98)		0.79 (0.52-1.19)		0.79 (0.51-1.20)	

*Fully adjusted hazard ratios have been controlled for age, gender, income, smoking, serum phosphorus, myocardial infarction and diabetes mellitus, mean arterial pressure, and time on dialysis using a random-effects Cox regression model fitted using shared frailty by country. P values are for the comparison with the reference values used in the model. CI denotes confidence interval.

Figure 1 Unadjusted Kaplan Meier curves for early survival according to severity of periodontitis.



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