

DEPRESSIVE SYMPTOMS AND EARLY ALL-CAUSE AND CARDIOVASCULAR MORTALITY IN HEMODIALYSIS PATIENTS: A MULTINATIONAL COHORT STUDY



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Background Depression is common in adults with kidney failure treated with dialysis. Approximately one-quarter of adults treated with dialysis have depression¹. Existing studies show a link between depression and total mortality, but the association between depression and cardiovascular death is less certain, since few trials of treatment for depression in adults with CKD are available²⁻³, despite patients with CKD citing depression as a key research priority⁴.

Methods We conducted a prospective multinational cohort study involving adults from France, Italy, Poland, Portugal, and Turkey who were treated with long-term hemodialysis within a single dialysis network between April and November 2010. Depression was considered present when patients reported a Beck Depression Inventory (BDI) II score ≥ 14 at baseline. Sensitivity analyses considered a BDI II score ≥ 20 to identify depression. Multivariable Cox proportional hazards regression was used to assess adjusted hazards for all-cause and cardiovascular mortality at 12 months.

Results 3086 participants received a BDI II questionnaire, and 2278 (73.8%) answered all of the 21 questions (complete respondents) and were included in the analyses. Baseline characteristics are reported in **Table 1**. Compared with respondents, incomplete respondents were older, less often men, experienced lower educational attainment, were less frequently employed, received lower dialysis doses and had lower serum albumin. The proportion of respondents prescribed antidepressant therapy (9.8%) was similar to that for non-responders (9.3%; $P=0.65$). 1047 (46%) of the complete respondents reported symptoms consistent with depression (BDI ≥ 14). Depressive symptoms were associated with being older or female, experiencing lower educational attainment, receiving a pension or being unemployed, lower physical activity, not being waitlisted for a kidney transplant, pre-existing diabetes, stroke or peripheral vascular disease, lower levels of blood pressure, hemoglobin, serum albumin, and phosphorus and more frequent prescription of neuroactive drugs including antidepressant, antipsychotic and hypnotic agents. During a follow up of 11 (SD 2.5) months on average (2096 person-years), we recorded 175 deaths, of which 66 were attributable to cardiovascular causes. The results of unadjusted analyses for all-cause and cardiovascular mortality are shown in **Figure 1**. Depression (BDI score ≥ 14) was not associated with all-cause mortality (adjusted hazard ratio 1.26 [95% confidence interval 0.93–1.71]) or cardiovascular mortality (0.82 [0.50–1.34]) (**Table 2**). When a higher BDI score (BDI score ≥ 20) was used in sensitivity analyses to identify moderate depression, depression was associated with total mortality (1.40 [1.02–1.93]) while an association with cardiovascular mortality was not evident (1.05 [0.63–1.77]).

Table 1 Demographic and clinical characteristics of hemodialysis patients according to the presence or absence of depression symptoms

Characteristic	BDI II score ≥ 14 (n=1047)	BDI II score < 14 (n=1231)	Overall (n=2278)	P value for difference based on BDI II score
Demographics				
Age	65.3 (14.3)	62.1 (15.2)	63.6 (14.9)	<0.001
Country				0.009
France	39 (3.7)	70 (5.7)	109 (4.8)	
Italy	232 (22.2)	218 (17.7)	450 (19.8)	
Portugal	505 (48.2)	635 (51.6)	1140 (50.0)	
Turkey	271 (25.9)	308 (25.0)	579 (25.4)	
Men	555 (53.0)	831 (67.5)	1386 (60.8)	<0.001
European	1011 (96.6)	1164 (94.6)	2175 (95.5)	0.07
Socioeconomic characteristics				
Living alone	104 (11.2)	114 (10.6)	218 (10.9)	0.66
Employment status				0.006
Employed	80 (9.0)	163 (15.5)	243 (12.5)	
Unemployed	129 (14.4)	134 (12.8)	263 (13.5)	
Retired	685 (76.6)	753 (71.7)	1438 (74.0)	
Secondary education	241 (27.1)	449 (42.8)	690 (35.6)	<0.001
Current or former smoker	223 (25.4)	361 (34.9)	584 (30.5)	<0.001
Wait-listed for transplant	29 (2.8)	58 (4.7)	87 (3.8)	0.02
Daily physical activity	39 (4.6)	72 (7.2)	111 (6.0)	0.003
Clinical characteristics at baseline				
Myocardial infarction	116 (11.1)	158 (12.8)	274 (12.0)	0.20
Stroke	85 (8.1)	61 (5.0)	146 (6.4)	0.02
Peripheral vascular disease	194 (18.5)	184 (15.0)	378 (16.6)	0.02
Diabetes	273 (33.6)	259 (27.4)	532 (30.3)	0.005
Dialysis characteristics				
Time on Dialysis, months	48.8 (25.5–87.0)	48.8 (26.4–86.1)	48.8 (26.1–86.3)	0.94
Kt/V	1.74 (0.33)	1.69 (0.31)	1.71 (0.32)	<0.001
Mean arterial pressure	89.5 (13.8)	91.3 (13.9)	90.5 (13.9)	0.002
Laboratory variables				
Serum albumin, g/l	38.9 (4.2)	40.2 (4.1)	39.6 (4.2)	<0.001
Serum phosphorus, mg/dl	4.37 (1.28)	4.47 (1.27)	4.43 (1.28)	0.06
Hemoglobin, g/dl	11.3 (1.3)	11.4 (1.3)	11.3 (1.3)	<0.001
Medications				
Antidepressant	120 (11.5)	104 (8.5)	224 (9.8)	0.02
Antipsychotic	19 (1.8)	9 (0.7)	28 (1.2)	0.02
Hypnotic	70 (6.7)	54 (4.4)	124 (5.4)	0.02

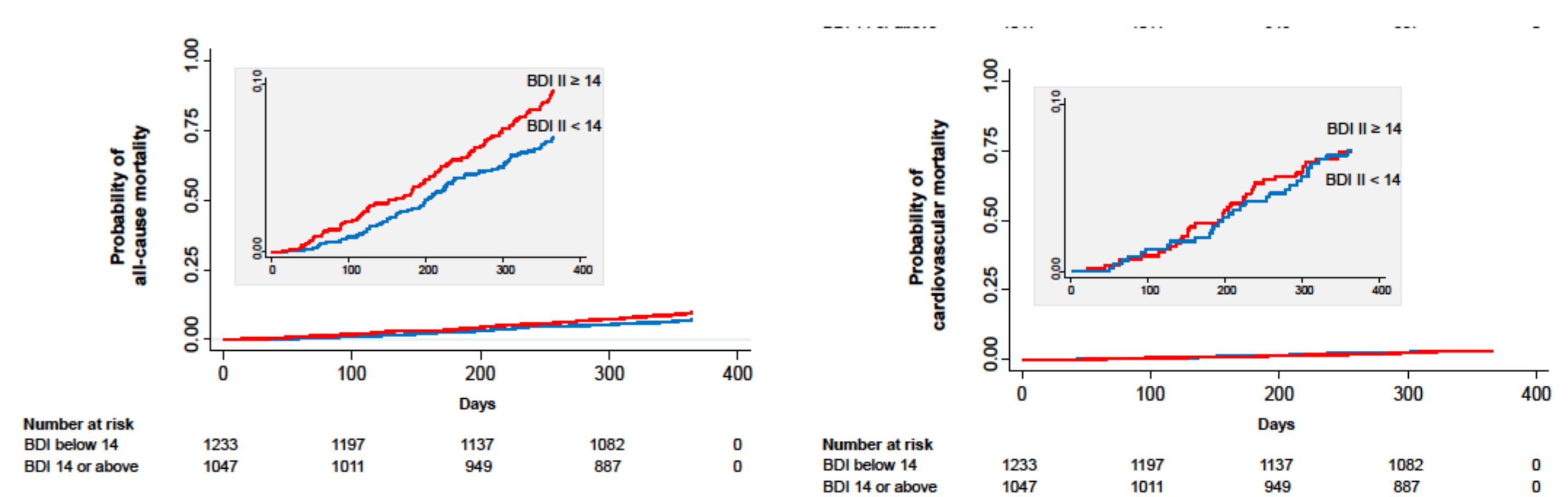
BDI II = Beck Depression Inventory II. Data are expressed as mean (SD), number (%), or median (25th percentile, 75th percentile). Kt/V refers to the clearance of urea and is a measure of the amount of dialysis received. Proportions do not always correspond to overall numbers of participants due to missing data.

Table 2 Cox proportional hazards model for all-cause and cardiovascular mortality

	All-cause mortality	Cardiovascular mortality
Unadjusted analysis		
BDI II score ≥ 14	1.44 (1.07–1.94)	0.99 (0.61–1.62)
Bivariate analysis stratified by country		
BDI II score ≥ 14	1.46 (1.08–1.97)	0.99 (0.61–1.61)
Multivariate analysis (stratified by country)		
BDI II score ≥ 14	1.26 (0.93–1.71)	0.82 (0.50–1.34)
Age, per year increase	1.05 (1.03–1.06)	1.07 (1.04–1.09)
Female	0.76 (0.55–1.06)	-
Former or current smoker (versus never)	0.69 (0.47–1.03)	-
Employed (versus unemployed)	0.57 (0.20–1.60)	0.51 (0.07–3.91)
Diabetes mellitus	1.56 (1.13–2.16)	2.08 (1.26–3.43)
Myocardial infarction	1.18 (0.79–1.77)	1.62 (0.90–2.91)
Mean arterial pressure >90 mmHg	0.59 (0.43–0.80)	-
Serum phosphorus >5.5 mg/dl	0.89 (0.57–1.38)	0.92 (0.46–1.83)

Multivariate analysis for all-cause mortality included adjustment for age, gender, smoking status, employment, diabetes mellitus, myocardial infarction, mean arterial pressure and serum phosphorus. Multivariate analysis for cardiovascular mortality included adjustment for age, employment status, diabetes mellitus, myocardial infarction, and serum phosphorus.

Figure 1 Unadjusted associations between depressive symptoms (Beck Depression Inventory) and all-cause and cardiovascular mortality



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Conclusion In this study, there was no evidence of an association between depression and cardiovascular mortality in adults with kidney failure treated with hemodialysis in this cohort. Previously reported associations between depression and cardiovascular death are potentially influenced by the diagnostic tool used to identify depression and the threshold score used to classify depression in people with end-stage kidney disease.

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