

Depression associated with higher all-cause mortality and infection-related adverse outcomes in patients undergoing dialysis

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Introduction and Aims:

Depression increases all-cause mortality, cardiovascular events, and infections in the general population. Dialysis patients with depression had a higher mortality risk, but the clinical impact of depression on cardiovascular and infection events is unclear. This population-based cohort study aimed to investigate the mortality, cardiovascular risks, and infection risks of depression among patients receiving dialysis.

Table 1. Baseline patient characteristics, comorbidities, and medication prescriptions for dialysis patients with and without depression

Characteristic	Dialysis patients with depression	Dialysis patients without depression	p value
	(n = 2475)	(n = 12,375)	
Characteristic	N (%)	N (%)	
Age (mean ± SD)	62.6 ± 12.3	62.6 ± 12.3	0.984
Age group			1.000
18–39	109 (4.4%)	545 (4.4%)	
40–59	870 (35.2%)	4350 (35.2%)	
60–85	1496 (60.4%)	7480 (60.4%)	
Sex			1.000
Male	901 (36.4%)	4505 (36.4%)	
Female	1574 (63.6%)	7870 (63.6%)	
Dialysis modalities			0.394
Hemodialysis	2326 (94.0%)	11570 (93.5%)	
Peritoneal dialysis	149 (6.0%)	805 (6.5%)	
Urbanization level			0.779
City area	1773 (71.7%)	8824 (71.4%)	
Rural area	699 (28.3%)	3531 (28.6%)	
Socioeconomic status			0.022
Low	944 (38.1%)	4638 (37.5%)	
Moderate	1088 (44.0%)	5226 (42.2%)	
High	443 (17.9%)	2511 (20.3%)	
Comorbidities			
Diabetes mellitus	1355 (54.7%)	6343 (51.3%)	0.002
Hypertension	2086 (84.3%)	10082 (81.5%)	0.001
Hyperlipidemia	587 (23.7%)	2504 (20.2%)	<0.001
Coronary artery disease	747 (30.2%)	3077 (24.9%)	<0.001
Heart failure	660 (26.7%)	3298 (26.7%)	1.000
Cerebrovascular disease	548 (22.1%)	1481 (12.0%)	<0.001
Autoimmune disease	61 (2.5%)	231 (1.9%)	0.061
Malignancy	207 (8.4%)	845 (6.8%)	0.007
Alcohol dependence	23 (0.9%)	86 (0.7%)	0.264
Psychotic disorder	76 (3.1%)	62 (0.5%)	<0.001
Anxiety disorder	375 (15.2%)	407 (3.3%)	<0.001
Sleep disorder	660 (26.7%)	1214 (9.8%)	<0.001
Medications use			
Antiplatelets/warfarin	1143 (46.2%)	5697 (46.0%)	0.912
Antihypertensive drugs	1880 (76.0%)	9224 (74.5%)	0.144
Statins	757 (30.6%)	3735 (30.2%)	0.707
Oral antidiabetic agents	791 (32.0%)	3739 (30.2%)	0.090
Insulin	667 (26.9%)	2967 (24.0%)	0.002
Antipsychotic agents	761 (30.7%)	1798 (14.5%)	<0.001
Benzodiazepines	1480 (59.8%)	5399 (43.6%)	<0.001
Hypnotics	1506 (60.8%)	4935 (39.9%)	<0.001
Comorbidities score*			
Median (IQR)	6 (3–9)	4 (2–7)	<0.001
First dialysis, year			<0.001
2000–2003	1025 (41.4%)	5667 (45.8%)	
2004–2007	1450 (58.6%)	6708 (54.2%)	
Follow-up, years			
Mean ± SD	3.2 ± 2.1	3.6 ± 2.2	<0.001
Median (IQR)	2.7 (1.5–4.6)	3.1 (1.7–5.1)	<0.001

*Comorbidities score was defined as Taiwan index for hemodialysis (From: Clin J Am Soc Nephrol 2014;9:513–519).

Reference

1. Sep 2013;62(3):493–505.
2. CJASN. Nov 2008;3(6):1752–1758.
3. Seminars in dialysis. Jan-Feb 2010;23(1):74–82.
4. Kidney international. Oct 2008;74(7):930–936.
5. CJASN. Jun 2009;4(6):1057–1064.
6. NEJM. Sep 23 2004;351(13):1296–1305.

Methods:

We identified hemodialysis patients from the National Health Insurance Database Registry for Catastrophic Illness with International Classification of Disease, ninth revision, codes and procedure codes identifying diseases from 2000 to 2007. We enrolled 2475 dialysis patients with depression and controls without depression and matched them by age and gender (1:5). Censor was defined as death, loss to follow-up, or the end of 2008. Cumulative incidences and hazard ratios of major cardiovascular events and severe infections were calculated after adjusting for competing mortality.

Results:

Dialysis patients with depression had a significantly higher cumulative incidence of mortality (45.29% vs. 39.52%; incidence rate ratio, 1.28; 95% confidence interval, 1.20–1.36) and severe infection events (46.06% vs. 40.32%; incidence rate ratio, 1.30; 95% confidence interval, 1.22–1.39) than those without depression. Multivariable Cox regression analysis showed depression as an independent risk factor for death (adjusted hazard ratio, 1.22; 95% confidence interval, 1.14–1.31) and severe infection events (adjusted hazard ratio, 1.14; 95% confidence interval, 1.06–1.22) in dialysis patients after adjusting for comorbidities and drugs prescribed during the follow-up period. Further stratified analyses and sensitivity analyses are needed to confirm the results.

Conclusion:

Depression in dialysis patients is associated with increased infection risks and all-cause mortality. Early detection of and intervention for depression are warranted for this population.

Table 2. Risks of mortality and related adverse outcomes for dialysis patients with and without depression

Variable	Overall events		Incidence rate ratio (95% CI)	Adjusted hazard ratio (95% CI)	
	Dialysis patients with depression	Dialysis patients without depression		Model 1†	Model 2‡
All-cause mortality§	1121	4890	1.28 (1.20–1.36)***	1.15 (1.07–1.23)***	1.24 (1.16–1.33)***
Severe infection events related mortality	513	2100	1.32 (1.20–1.46)***	1.19 (1.08–1.32)***	1.22 (1.09–1.35)***
Hospitalization for severe infection events	1140	4990	1.30 (1.22–1.39)***	1.16 (1.08–1.24)***	1.14 (1.06–1.22)***
Sepsis	592	2408	1.35 (1.24–1.48)***	1.20 (1.09–1.32)***	1.19 (1.08–1.31)***
Septic shock	183	637	1.54 (1.30–1.81)***	1.38 (1.16–1.65)***	1.36 (1.13–1.62)***
Pneumonia	465	1804	1.41 (1.27–1.56)***	1.25 (1.12–1.39)***	1.19 (1.07–1.33)**
Intensive care unit admission	1177	5176	1.29 (1.21–1.37)***	1.13 (1.06–1.21)***	1.13 (1.05–1.21)***
Respiratory failure with mechanical ventilator use	50	264	1.00 (0.74–1.35)	0.85 (0.62–1.17)	0.82 (0.60–1.13)

†Model 1: Adjusted for comorbid disorders (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, cerebrovascular disease, autoimmune disease, malignancy, alcohol dependence, psychotic disorder, anxiety disorder, sleep disorder) and competing risk of mortality.
‡Model 2: Adjusted for comorbid disorders, medications (antiplatelets/warfarin, antihypertensive drugs, statins, oral antidiabetic agents, insulin, antipsychotic agents, benzodiazepines, hypnotics) and competing risk of mortality. §Adjusted hazard ratio of all-cause mortality used the Cox proportional hazard model. *p<0.05, **p<0.01, ***p<0.001.

Table 3. Sensitivity analyses showing the impact of depression on death and infection in dialysis patients

Analyses	Adjusted Hazard Ratio (95% CI)†						
	All-cause mortality	Severe infection-related mortality	Hospitalization for severe infection events	Sepsis	Septic shock	Pneumonia	Intensive care unit admission
Main analysis	1.24 (1.16–1.33)***	1.22 (1.10–1.36)***	1.13 (1.06–1.22)***	1.19 (1.08–1.31)***	1.36 (1.13–1.62)***	1.20 (1.07–1.34)**	1.13 (1.05–1.21)***
Approach 1	1.34 (1.20–1.50)***	1.24 (1.04–1.49)*	1.17 (1.04–1.31)**	1.16 (0.98–1.36)	1.44 (1.06–1.94)*	1.18 (0.97–1.42)	1.20 (1.07–1.34)**
Approach 2	1.22 (1.13–1.32)***	1.22 (1.08–1.37)***	1.14 (1.05–1.23)***	1.15 (1.03–1.29)**	1.34 (1.09–1.64)**	1.19 (1.05–1.35)**	1.12 (1.04–1.21)**
Approach 3	1.24 (1.12–1.36)***	1.27 (1.10–1.48)***	1.16 (1.05–1.27)**	1.24 (1.09–1.42)**	1.42 (1.11–1.81)**	1.25 (1.07–1.46)**	1.12 (1.02–1.24)*
Approach 4	1.26 (1.16–1.38)***	1.22 (1.06–1.39)**	1.12 (1.03–1.22)*	1.17 (1.04–1.33)*	1.22 (0.97–1.54)	1.21 (1.05–1.39)**	1.07 (0.99–1.17)

†Adjusted for comorbidities (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, cerebrovascular disease, autoimmune disease, malignancy, alcohol dependence, psychotic disorder, anxiety disorder, sleep disorder), medications (antiplatelets/warfarin, antihypertensive drugs, statins, oral antidiabetic agents, insulin, antipsychotic agents, benzodiazepines, hypnotics), and competing mortality (except for the HR of all-cause mortality).
Approach 1: redefining depression diagnosis as the major depression diagnostic codes (ICD-9 codes 296.2 and 296.3).
Approach 2: redefining depression diagnosis as the presence of any depression diagnostic code in at least two outpatient claims or one inpatient claim and the use of any depression-related medication.
Approach 3: redefining depression diagnosis as the presence of any depression diagnostic code in at least two outpatient claims or one inpatient claim and psychiatrists outpatient visits.
Approach 4: propensity score-matched approach.
§Main analysis of all-cause mortality used the Cox-proportional hazard model.
*p<0.05, **p<0.01, ***p<0.001.

