Increased risk of death, cardiovascular and infection-related adverse outcomes in dialysis patients with dementia

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Introduction and Aims:

Dementia increases all-cause of mortality, cardiovascular events, and infection events in general population but the clinical impact of dementia on dialysis patients is unclear. This nationwide cohort study aimed to investigate the mortality, cardiovascular and infection risks of dementia on patients undergoing dialysis.

Methods:

We enrolled incident dialysis patients from the Catastrophic Illness Registry from National Health Insurance Database from 2000 to 2007. There were 1247 dialysis patients with dementia and non-depression controls with 1:5 matched by age and sex. Patients were followed to death, loss 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 dementia had a significantly higher cumulative incidence of mortality (66.16% vs. 53.63%; incidence rate ratio (IRR): 1.58; 95% confidence interval [CI]: 1.46 – 1.70]), cardiovascular events (37.53% vs. 34.44%; IRR: 1.29; 95% CI: 1.16 – 1.42) and severe infection events (60.55% vs. 46.89%; IRR: 1.65; 95% CI: 1.52 – 1.79) than those without dementia. Multivariable Cox regression analysis showed dementia as an independent risk factor for death (adjusted hazard ratio [aHR]: 1.38; 95% CI: 1.27 – 1.50), cardiovascular events (aHR: 1.16; 95% CI: 1.03 – 1.30), and severe infection events (aHR: 1.35; 95% CI: 1.24 – 1.48) in dialysis patients after adjusting for comorbidities and drugs prescribed during the follow-up period. Further stratified analysis and sensitivity analysis confirm the results.

Conclusion:

Dialysis patients with dementia are associated with increased all-cause mortality, cardiovascular and infection risks.

Table 1. Baseline patient characteristics, comorbidities, and medications prescriptions between dialysis patients with and without dementia

	Dialysis patients with dementia (n = 1247)	Dialysis patients without dementia (n = 6191)	p value
Characteristic	N (%)	N (%)	
Age (mean ± SD)	74.4 ± 8.5	74.2 ± 8.3	0.575
Age group			0.898
18 – 64	170 (13.6%)	850 (13.7%)	
65– 74	443 (35.5%)	2215 (35.8%)	
75– 84	527 (42.3%)	2635 (42.6%)	
≥85	107 (8.6%)	491 (7.9%)	
Sex			0.942
Male	541 (43.4%)	2676 (43.2%)	
Female	706 (56.6%)	3515 (56.8%)	
Dialysis modalities			0.706
Hemodialysis	1205 (96.6%)	5966 (96.4%)	
Peritoneal dialysis	42 (3.4%)	225 (3.6%)	
Urbanization level			0.450
City area	851 (68.4%)	4158 (67.3%)	
Rural area	393 (31.6%)	2024 (32.7%)	
Socioeconomic status			0.154
Low economics	547 (43.9%)	2617 (42.3%)	
Moderate economics	585 (46.9%)	2892 (46.7%)	
High economics	115 (9.2%)	682 (11.0%)	
Comorbidities			
Diabetes mellitus	744 (59.7%)	3032 (49.0%)	<0.001
Hypertension	1068 (85.6%)	5123 (82.7%)	0.014
Hyperlipidemia	222 (17.8%)	1036 (16.7%)	0.380
Coronary artery disease	379 (30.4%)	1974 (31.9%)	0.317
Heart failure	383 (30.7%)	1969 (31.8%)	0.470
Cerebrovascular disease	543 (43.5%)	962 (15.5%)	<0.001
Autoimmune disease	15 (1.2%)	81 (1.3%)	0.870
Malignancy	94 (7.5%)	573 (9.3%)	0.060
Alcohol dependence	10 (0.8%)	30 (0.5%)	0.236
Psychotic disorder	103 (8.3%)	22 (0.4%)	<0.001
Sleep disorder	202 (16.2%)	662 (10.7%)	<0.001
Parkinson's disease	113 (9.1%)	102 (1.6%)	<0.001
Medications use			
Antiplatelets/Warfarin	529 (42.4%)	2801 (45.2%)	0.072
Anti-hypertensive drugs	804 (64.5%)	4271 (69.0%)	0.002
Statins	204 (16.4%)	1359 (22.0%)	<0.001
Oral antidiabetic agents	340 (27.3%)	1656 (26.7%)	0.733
Insulin	302 (24.2%)	1240 (20.0%)	0.001
Antipsychotic agents	397 (31.8%)	807 (13.0%)	<0.001
Benzodiazepines	450 (36.1%)	2596 (41.9%)	<0.001
Hypnotics	476 (38.2%)	2378 (38.4%)	0.899
Comorbidities score*			
Median (IQR)	7 (4-10)	6 (3-9)	<0.001
First time dialysis year			<0.001
2000 – 2003	444 (35.6%)	2580 (41.7%)	
2004 – 2007	803 (64.4%)	3611 (58.3%)	
Follow-up years			
Mean ± SD	2.3 ± 1.7	2.9 ± 2.0	<0.001
Median (IQR)	1.8 (1.0-3.2)	2.4 (1.4-4.1)	<0.001

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

Table 2. Risks of mortality and related adverse outcomes between dialysis patients with and without dementia

Variable	Overall events		Incidence rate ratio (95% CI)	Adjusted Hazard Ratio (95% CI)	
	Dialysis patients with dementia	Dialysis patients without dementia		Model 1†	Model 2‡
All-cause mortality§	825	3320	1.58 (1.46 - 1.70)***	1.43 (1.31 - 1.55) ***	1.38 (1.27 - 1.50) ***
Major cardiovascular events	468	2132	1.29 (1.16 - 1.42)***	1.12 (1.00 - 1.26)*	1.16 (1.03 - 1.30)*
Severe infection events related mortality	438	1543	1.65 (1.48 - 1.83)	1.49 (1.32 - 1.68)***	1.40 (1.24 - 1.58)***
Hospitalization for severe infection events	755	2903	1.65 (1.52 - 1.79) ***	1.41 (1.29 - 1.54)***	1.35 (1.24 - 1.48)***
Sepsis	473	1610	1.76 (1.59 - 1.95) ***	1.53 (1.36 - 1.72)***	1.44 (1.28 - 1.62)***
Shock	146	434	1.89 (1.56 - 2.27) ***	1.80 (1.46 - 2.22)***	1.69 (1.36 - 2.10)***
Pneumonia	379	1224	1.86 (1.66 - 2.09) ***	1.53 (1.34 - 1.74)***	1.44 (1.27 - 1.64)***
Intensive care unit admission	728	3021	1.47 (1.35 - 1.59) ***	1.28 (1.17 - 1.40)***	1.26 (1.15 - 1.38)***

Major cardiovascular events were defined as composite endpoints of acute coronary syndrome, ischemic stroke, and hemorrhagic stroke.
†Model 1: Adjusted for comorbid disorders (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, cerebrovascular disease, autoimmune disease, malignancy, alcohol dependence, psychotic disorder, sleep disorder, parkinson's disease), and competing risk of mortality
‡Model 2: Adjusted for comorbid disorders, medications (antiplatelets/warfarin, anti-hypertensive drugs, statins, oral antidiabetic agents, insulin, antipsychotic agents, benzodiazepines, hypnotics), and competing risk of mortality
§Adjusted Hazard Ratio of all-cause mortality was used Cox-proportional hazard model.
*p<0.05, **p<0.01, ***p<0.001

Table 3. Sensitivity analyses showing the impact of dementia on deaths and infection events in dialysis patients

	Adjusted Hazard Ratio (95% CI)†		
	Main analysis	Approach 1	Approach 2
All-cause mortality	1.38 (1.27 - 1.50)***	1.39 (1.27 - 1.53) ***	1.38 (1.24 - 1.54) ***
Major cardiovascular events	1.16 (1.03 - 1.30)*	1.20 (1.06 - 1.37)**	1.16 (1.00 - 1.34)
Severe infection events related mortality	1.40 (1.24 - 1.58)***	1.40 (1.22 - 1.61)***	1.39 (1.18 - 1.62)***
Hospitalization for severe infection events	1.35 (1.24 - 1.48)***	1.34 (1.21 - 1.49)***	1.42 (1.26 - 1.60)***
Sepsis	1.44 (1.28 - 1.62)***	1.45 (1.27 - 1.65)***	1.44 (1.24 - 1.68)***
Shock	1.69 (1.36 - 2.10)***	1.69 (1.32 - 2.15)***	1.75 (1.32 - 2.32)***
Pneumonia	1.44 (1.27 - 1.64)***	1.44 (1.25 - 1.67)***	1.41 (1.19 - 1.67)***
Intensive care unit admission	1.26 (1.15 - 1.38)***	1.25 (1.13 - 1.39)***	1.21 (1.08 - 1.37)***

†Adjusted for comorbidities (diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, cerebrovascular disease, autoimmune disease, malignancy, alcohol dependence, psychotic disorder, sleep disorder, parkinson's disease), medications (antiplatelets/warfarin, anti-hypertensive drugs, statins, oral antidiabetic agents, insulin, antipsychotic agents, benzodiazepines, hypnotics), and competing mortality (except for the HR of all-cause mortality).
Approach 1: redefining dementia diagnosis as the presence of any dementia diagnostic code in at least two outpatient claims or one inpatient claim and neurologists or psychiatrists outpatient visits
Approach 2: propensity score-matched approach
§Main analysis of all-cause mortality was used Cox-proportional hazard model.
*p<0.05, **p<0.01, ***p<0.001

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