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Investigating cognitive function in patients with endstage kidney disease under hemodialysis or peritoneal dialysis; a cross-sectional study



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ARTICLEINFO	A B S T R A C T		
<i>Article Type:</i> Original	Introduction: Studies have shown that patients with chronic kidney failure and patients under dialysis have a significantly augmented risk of developing cognitive damage compared		
Article History: Received: 13 Apr. 2025 Revised: 29 May 2025 Accepted: 4 Jun. 2025 Published online: 10 Jun. 2025	to the general population. Objectives: The purpose of this study was to explore cognitive function in people with end- stage kidney disease (ESKD) under hemodialysis or peritoneal dialysis who were referred to the dialysis center of Imam Reza Hospital in 2024. Materials and Methods: This cross-sectional study included 200 patients (100 patients under		
<i>Keywords:</i> End-stage kidney disease Cognitive function Hemodialysis Peritoneal dialysis	hemodialysis and 100 patients under peritoneal dialysis). Through a standardized MMSE (mini-mental state examination) questionnaire, the cognitive function of the patients was examined and compared between the two groups. Results: In this study, all variables of cognitive function including awareness of time ($P < 0.001$), awareness of place ($P < 0.001$), recall ($P < 0.001$), attention and calculation ($P < 0.001$), drawing ($P = 0.003$), and MMSE total score ($P < 0.001$) were significantly higher in patients under peritoneal dialysis in compared to patients under hemodialysis. Conclusion: Cognitive function appears to be significantly better in patients with ESKD under peritoneal dialysis than in those under hemodialysis. Given the high prevalence of cognitive impairment and its association with adverse outcomes, routine cognitive screening and individualized management strategies should be considered, regardless of dialysis modality.		

Implication for health policy/practice/research/medical education:

Cognitive function was significantly better in patients with end-stage kidney disease (ESKD) under peritoneal dialysis than in those under hemodialysis.

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Introduction

Chronic kidney disease is very common worldwide. Many people with this condition need renal replacement therapy. This therapy can be done through hemodialysis or peritoneal dialysis. These patients are susceptible to various diseases, including cognitive impairments, which can be particularly severe. Cognitive decline progresses more rapidly and intensely in these patients in comparison to others in the same age group within the general population (1). This greatly increases the burden of disease on patients, their families, and the healthcare system, while also driving up medical costs (2). Recent studies revealed that the occurrence of cognitive impairment among patients with chronic kidney disease is 40%, with 53% of affected patients undergoing hemodialysis and 40% receiving peritoneal dialysis, whereas 32% of individuals with untreated end-stage kidney disease (ESKD) and 26% of kidney transplant recipients demonstrate cognitive impairment (3). Successful kidney transplant patients show significant cognitive improvement, which is likely a consequence of enhanced white matter integrity following normalization of volume and osmotic status (4,5).

A recent systematic review classified the risk factors for cognitive disorders in such patients into three

Niknafs B et al

categories: Traditional risk factors, including advanced age, low literacy and physical activity levels, depression, poor sleep quality, and atherosclerosis. Non-traditional risk factors connected to ESKD such as inflammatory processes, vascular disease, anemia, and fluid overload. Dialysis-related risk factors like recurrent hypotensive episodes during dialysis, decreased cerebral blood flow, and cerebral hemorrhagic events in association with the use of heparin (6). Cognitive impairment has been stated to be three times more common in hemodialysis patients compared to the general population (7). Some studies described that peritoneal dialysis patients may have a lower risk of cognitive impairment and dementia compared to hemodialysis patients. This may be attributed to the stable physiological peritoneal dialysis effects on the brain and along with reduced hemodynamic stress as well as less pronounced volume reduction in certain brain regions (8,9).

Objectives

Theoretically, fewer hypotensive events and greater hemodynamic stability with peritoneal dialysis should result in fewer cerebral adverse events than hemodialysis because it does not involve heparin use daily (10). Additionally, since it is a continuous procedure and more effective at removing medium molecular weight molecules such as beta-2 microglobulin, peritoneal dialysis may be able to stabilize cognitive function more, especially in comparison to hemodialysis with low-flux filters. Therefore, in this controlled cross-sectional study, we sought to compare, retrospectively, the cognitive ability of peritoneal dialysis and hemodialysis patients, matching them by sex, age, and relevant risk factors.

Materials and Methods

Study design and participants

This research was a cross-sectional study that included patients under hemodialysis and peritoneal dialysis in the dialysis center of Imam Reza hospital in 2024-2025, and they were matched for demographic characteristics like age, weight, gender, and literacy level before the study. A total sample size of 200 people (100 patients under hemodialysis and 100 patients under peritoneal dialysis) was considered in this study.

Inclusion and exclusion criteria

Inclusion criteria were end-stage chronic renal failure under hemodialysis or peritoneal dialysis for more than three months, being between 18 and 80 years, and willingness to participate in the study. Patients who had an active infection, history of stroke within the previous six months, history of major depression, known dementia patients, or a history of dementia or cognitive impairment before dialysis, repeatedly experience hypotension during hemodialysis, or history of cognitive impairment due to other diseases such as multiple sclerosis was excluded from the study.

Data collection

To determine the cognitive function of ESKD patients, a previously validated and widely used standardized questionnaire (mini mental state examination [MMSE]) was conducted. This questionnaire contains five sections, including time awareness (score = 0-5), place awareness (score = 0-5), recall (score = 0-3), attention and calculation (score = 0-16), and drawing (score = 0,1) that was recorded by a physician directly from the ESKD patients. After adding up the obtained scores, the total score was considered from 0 to 30 for each patient in both groups (11). Finally, the results were compared between the two groups.

Statistical analysis

Data analysis was performed using SPSS software (version 26). Normality of the data distribution was evaluated using the Shapiro-Wilk test. All quantitative variables had normal distribution, thereby, they reported as the mean \pm standard deviation. Meanwhile, the independent T-test was conducted to analyze quantitative variables between the two groups. The frequency (percentage) was used to report qualitative variables, and the chi-square test was employed to compare the groups. In this study, a statistical significance level of less than 5% was considered.

Outcomes

The primary outcome of this study is to determine MMSE score in patients with end-stage renal disease undergoing hemodialysis or peritoneal dialysis. The secondary outcome will compare different cognitive domains between the hemodialysis and peritoneal dialysis groups

Results

Demographic data

In this study, which was conducted on patients under hemodialysis and peritoneal dialysis who referred to the dialysis center of Imam Reza hospital in 1403 who met the inclusion criteria and were the same in terms of demographic characteristics (e.g., age, gender, weight, and literacy level), 200 patients were studied in two groups of hemodialysis patients (n=100) and peritoneal dialysis patients (n=100). Their mean age in the hemodialysis and peritoneal dialysis groups was 57.96 ± 9.2 and 56.96 ± 4.7 years, respectively (P=0.335). The highest gender frequency in the two groups of patients under hemodialysis and peritoneal dialysis was males, with 56 cases (0.56%) and 52 cases (0.52%) respectively (P=0.670; Table 1).

Cognitive function of ESKD patients

Comparison of results related to cognitive function variables between hemodialysis patients and peritoneal dialysis patients is shown in <u>Table 2</u>. In this study, the

Table 1. Demographic data of end-stage kidney disease patients

Variables	Hemodialysis patients (n= 100)	Peritoneal dialysis (n= 100)	P value*
Gender			
Men	56 (56%)	52 (52%)	0.670
Women	44 (44%)	48 (48%)	0.670
Age (y)	57.96±9.21	56.96±4.72	0.335

* For qualitative variables, the chi-square test was applied to obtain results as frequencies (percentages). For quantitative variables, the independent samples T-test was applied to obtain the results as mean \pm standard deviation. The *P* < 0.05 was considered statistically significant.

Table 2. Comparison of cognitive function between patients

Variables	Hemodialysis patients (n = 100)	Peritoneal dialysis (n = 100)	P value*
Time awareness	3.02±1.31	4.34±0.93	<0.001
Place awareness	3.50±1.02	4.24±0.74	<0.001
Recall	3.86±1.31	4.72±0.87	<0.001
Attention and calculation	8.68±2.50	10.44±1.47	<0.001
Drawing	0.28±0.45	0.48±0.50	0.003
Overall MMSE score	19.34±5.15	24.22±2.69	<0.001

MMSE: Mini-Mental State Examination.

* The Independent Samples T-test was applied to obtain the results as mean \pm standard deviation. The *P* < 0.05 was considered statistically significant.

mean score of the time awareness variable in the two groups of patients under hemodialysis and peritoneal dialysis was 3.02 ± 1.31 and 4.34 ± 0.93 , respectively, which was significantly lower in the hemodialysis patients (P < 0.001). Additionally, the mean score of the location awareness variable in the patients under hemodialysis was significantly decreased compared to the patients under peritoneal dialysis (3.50±1.02 versus 4.24±0.74, respectively, P < 0.001). The mean score of the recall variable in the patients under hemodialysis was also lower than that in the patients under peritoneal dialysis (3.86±1.31 versus 4.72 ± 0.87 , respectively, P < 0.001). Moreover, the mean score of the attention and calculation in patients under peritoneal dialysis was significantly higher in comparison to the mean score of the patients under hemodialysis $(10.44 \pm 1.47 \text{ versus } 8.68 \pm 2.50, \text{ respectively, } P < 0.001).$ The mean score of the drawing variable was lower in the patients under hemodialysis when compared to the mean score of patients under peritoneal dialysis, which was statistically significant $(0.28 \pm 0.45 \text{ versus } 0.48 \pm 0.50,$ respectively, P = 0.003). Finally, the mean of the MMSE total score variable in the study's two groups of patients under hemodialysis and peritoneal dialysis was calculated by adding up all five variables, that was 19.34 ± 5.15 and 24.22 ± 2.69 , respectively. The results showed that the total MMSE score was significantly higher in patients under peritoneal dialysis than in patients under hemodialysis (P < 0.001).

Discussion

Studies show that 70% to 80% of dialysis patients have cognitive impairment (12). The most affected areas are visuospatial skills, memory, processing speed, attention, and executive function. Vascular disease, particularly microvascular brain injury, plays a major role. There is a robust linkage between cardiovascular disease and poor cognitive function in these patients (13). Both hemodialysis and peritoneal dialysis are renal replacement therapies, but their impact on cognitive outcomes can vary due to alterations in treatment modalities, such as frequency, duration, and physiological effect (14). Cognitive impairment is a major problem among patients receiving dialysis, contributing to reduced quality of life and increased rates of hospitalization (15). Despite its clinical importance, the precise prevalence, risk factors associated with cognitive impairment in this population have not been fully elucidated. This study contributes to the increasing body of evidence signifying that dialysis modality may impact cognitive outcomes in patients with ESKD. Our findings determine that patients undergoing peritoneal dialysis generally exhibit superior cognitive performance through multiple domains-including orientation, recall, attention, calculation, and overall MMSE scores-compared to those on hemodialysis. All cognitive performance variables-including orientation to time (P < 0.001), orientation to place (P < 0.001), recall (P < 0.001), attention and calculation (P < 0.001), drawing (P=0.003), and total MMSE score (P<0.001)were meaningfully higher in patients receiving peritoneal dialysis compared to those undergoing hemodialysis These results make parallel with several large-scale cohort studies and meta-analyses, which constantly report a lower risk of cognitive impairment and dementia among peritoneal dialysis patients relative to hemodialysis patients (16). Multiple large-scale cohort studies and meta-analysis have consistently demonstrated that patients initiating peritoneal dialysis exhibit a lower risk of developing dementia compared to those starting hemodialysis (17,18).

Through a retrospective cohort study involving 121623 incident dialysis patients in the United States, the cumulative prevalence of dementia was meaningfully lower in the peritoneal dialysis group compared to the hemodialysis group at 1, 2, and 3 years of followup. Specifically, the hazard ratio (HR) for dementia in peritoneal dialysis patients was 0.46 in unadjusted analyses and 0.74 in propensity score-matched models, indicating a substantially reduced risk. These findings persisted after modification for demographic and clinical features, suggesting that the dialysis modality itself may influence cognitive outcomes (18). A synthesis of 15 cohort and cross-sectional studies revealed that peritoneal dialysis patients generally performed better on neuropsychological assessments, including the MMSE and Montreal Cognitive Assessment (MoCA), and had a

Niknafs B et al

lower risk of dementia than hemodialysis patients (17,19). The detected cognitive advantages in peritoneal dialysis patients may be credited to several factors essential to the modality. Peritoneal dialysis provides continuous solute clearance and hemodynamic stability, potentially decreasing cerebral ischemic insults and the accumulation of neurotoxic metabolites. This is supported by neurophysiological studies showing shorter P300 latency and better cognitive performance in peritoneal dialysis/ continuous ambulatory peritoneal dialysis patients compared to those on hemodialysis, indicating a relative protection of attention and memory circuits. Additionally, peritoneal dialysis's gentler and more continuous nature may contribute to more stable cognitive function over time (17).

However, some studies have noted that the apparent increased risk of dementia in hemodialysis patients may be mitigated after monitoring for confounding factors such as age and comorbidities. For instance, a nationwide cohort study in Taiwan found that, after comprehensive adjustment, the alteration in dementia risk between hemodialysis and peritoneal dialysis was not significant from a statistical standpoint (sub-distribution HR 1.086; 95% CI, 0.940-1.255) (20). On the other hand, some analyses reported that while peritoneal dialysis patients often display better cognitive performance overall, certain cognitive tests revealed no statistically significant differences between the two modalities. Specifically, tests such as the Symbol Digit Modalities Test (SDMT), Trail Making Test-B (TMT-B), Rey Auditory Verbal Learning Test (RAVLT), and Benton Visual Retention Test (BVRT) showed comparable results between hemodialysis and peritoneal dialysis groups without significant differences (21). The study by Radić et al results showed that both cognitive and motor functions were impaired in ESKD patients compared to healthy norms. However, there were no significant differences between the hemodialysis and continuous ambulatory peritoneal dialysis groups in most cognitive and motor test outcomes, suggesting that the choice of dialysis modality may not significantly influence these aspects of neuropsychological performance in ESKD patients (22). The study by Radić et al, reports no statistically significant change in cognitive function between hemodialysis and peritoneal dialysis patients. This finding is based on a relatively small sample (n=42), which may limit generalizability, but the use of validated tests like SDMT provides a vigorous assessment. The study's focus on well-nourished, medically stable patients without dementia or cognitive impairment suggests that patient characteristics may performance an important role in cognitive outcomes, potentially overwhelming dialysis modality effects.

Our findings must be interpreted in light of several limitations. First, baseline differences in cognitive function and potential selection bias-whereby patients with better cognitive reserve may be preferentially assigned to or choose peritoneal dialysis can confound results. Second, the cross-sectional design of most studies, including ours, limits causal inference and the ability to assess cognitive trajectories over time. Third, variation in cognitive assessment tools and definitions of impairment complicates direct comparison across studies.

Conclusion

In conclusion, peritoneal dialysis appears to be connected with improved cognitive performance and a lower risk of dementia compared to hemodialysis in numerous studies, the confirmation is not unequivocal. Patient selection, comorbidities, and methodological modifications likely contribute to the detected variability. Clinicians should remain vigilant for cognitive impairment in all ESKD patients, modifying care to optimize both renal and cognitive health.

Limitations of the study

Despite these limitations, our results reinforce the clinical relevance of cognitive assessment in dialysis populations. Considering the elevated occurrence of cognitive impairment in patients with kidney failure and its traditional association with adverse clinical outcomes, routine cognitive screening and the employment of individualized management strategies are warranted for all patients, regardless of the dialysis modality. Future large-scale, prospective studies with standardized cognitive testing and careful adjustment for confounders are needed to simplify the causal connection between dialysis modality and cognitive outcomes.

Authors' contribution

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Ethical issues

The research conducted in this study adhered to the principles outlined in the Declaration of Helsinki. This study was

approved by the Islamic Azad University of Medical Sciences, Tabriz branch, Tabriz, Iran (Ethical code# IR.AIU.TABRIZ. REC.1403.508). Written informed consent forms were signed by all participants. This study was extracted from M.D, thesis of Negin Khadem Haghighi at this university (Thesis #162671365). Additionally, the authors have completely observed the ethical issues including data fabrication, falsification, plagiarism, double publication misconduct, or submission and redundancy.

Conflicts of interest

The authors declare that they have no competing interests.

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