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Factors Affecting Hypertension in Peritoneal Dialysis Patients: A National Cohort Study

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Abstract

Background: Blood pressure fluctuations and their management are crucial issues in peritoneal dialysis (PD) patients. Although recent studies have focused on blood pressure variability and control in these patients, factors contributing to hypertension have not been extensively investigated. Additionally, it is important to use statistical models capable of accounting for unmeasured influences from dialysis centers that may affect blood pressure increases.

Objective: This study aimed to identify factors influencing hypertension in continuous ambulatory PD patients in Iran. It also compared the performance of two shared frailty models, Gamma and non-parametric, in analyzing these factors.

Material and Methods: A retrospective cohort design was employed, utilizing data from 700 PD patients from various provinces across Iran. Shared frailty survival models were employed to analyze the data, and the effects of variables were expressed as hazard ratios (HR) with 95% confidence intervals (CI).

Results: By the end of the study, 400 patients (57%) had developed hypertension. Non-parametric frailty model showed that body mass index (BMI) significantly increased the risk of hypertension (HR: 1.18, 95% CI: 1.07–1.29). Comorbidities also increased risk (HR: 1.35, 95% CI: 1.15–1.57). Elevated creatinine (HR: 1.22, 95% CI: 1.11–1.33), sodium (HR: 1.28, 95% CI: 1.13–1.45), and fasting blood sugar (HR: 1.20, 95% CI: 1.08–1.33) were significant risk factors. Conversely, higher albumin levels showed a protective effect (HR: 0.83, 95% CI: 0.73–0.94).

Conclusion: Factors including BMI, comorbidities, creatinine, sodium, and fasting blood sugar significantly increase hypertension risk among PD patients, while higher albumin may be protective. Close monitoring and management of these factors are essential for preventing and controlling hypertension in this patient population.

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Introduction

Kidney failure is a non-communicable disease that has shown a significant increase in prevalence in recent years. For example, in the United States alone, more than 800,000 individuals were affected by this condition in

2023 (1, 2). End-stage renal disease (ESRD) is defined by a severe and persistent reduction in kidney function (glomerular filtration rate less than 15 mL/min), and without renal replacement therapies such as dialysis or transplantation, it is fatal. Diabetes, hypertension, and glomerular diseases are the main causes of ESRD, and it is more common in elderly patients and those with cardiovascular problems (3). Additionally, with the aging population and the increasing number of diabetic patients, the incidence of ESRD is expected to rise in the coming years (4). Treatment options for ESRD mainly include kidney transplantation, hemodialysis, and Peritoneal Dialysis (PD). While kidney transplantation offers the best long-term outcomes, limitations such as donor shortages and patient eligibility restric its availability. Therefore, dialysis remains an essential treatment. PD is preferred in many areas due to its lower cost, the possibility of home administration, and greater lifestyle flexibility compared to in-center hemodialysis. However, concerns such as infection risk and the need for patient training still exist (2, 5). Improving patient education and easier access to different treatment modalities are key to improving outcomes and quality of life for this growing patient population.

Managing blood pressure is a crucial benefit of dialysis in patients with kidney failure. Hypertension and its fluctuations are common among these patients due to underlying kidney dysfunction and volume overload (6). Chronic high blood pressure contributes to progressive damage to vital organs such as the heart, eyes, and remaining kidney tissue (7). Several factors, including coexistence of diabetes, obesity, dyslipidemia, and abnormal handling of electrolytes like sodium, chloride, and calcium, play significant roles in increasing blood pressure in this population (8).

Variations in patient survival times can sometimes arise from differences among healthcare providers, such as medical centers, causing patients receiving treatment at the same facility to exhibit similar outcomes. This grouping creates data clusters where individual observations within each cluster are correlated (9). Ignoring this intra-group dependence may lead to misleading conclusions about how variables influence patient survival (10). It is also essential to select an appropriate statistical distribution for the frailty term based on the study's assumptions, as choosing an incorrect distribution can significantly affect results. To avoid the risks associated with potentially miss-specified parametric frailty distributions, non-parametric methods are often employed (11). These approaches do not require a fully specified frailty distribution and thus provide greater modeling flexibility. By implementing a non-parametric frailty model, researchers can develop adaptable survival models that more accurately identify factors elevating mortality risk compared to standard survival analyses (12).

Blood pressure management is crucial in the treatment of kidney failure (8, 13). Although researchers have addressed the problems caused by blood pressure variability and its control in PD patients in recent years, the factors influencing hypertension in these patients have not been extensively studied. Moreover, it seems necessary to use an appropriate statistical model that can account for the impact of unmeasurable factors originating from dialysis centers on the increase of blood pressure. Therefore, the

present study examined the factors affecting hypertension in continuous ambulatory PD patients in Iran by comparing Gamma and non-parametric shared frailty models.

Material and method

The data for this retrospective cohort study were sourced from the Iranian peritoneal dialysis registry project (14). In this research, information from patients with kidney failure who attended 46 dialysis centers across all Iranian provinces was collected. Patients received detailed explanations about the study, and only those who provided full consent were enrolled. Each participant was assigned a unique ID for identification, while other personal details were securely stored and remained inaccessible. Additionally, all patient information was systematically recorded in their electronic health records. The patients were monitored from 1997 through 2009. The primary outcome of interest was the occurrence of hypertension, and patients who maintained optimal blood pressure or were lost to follow-up were considered right-censored.

Patients' blood pressure was measured according to the protocol outlined in the reference (15), Both hypertension categories stage 1 and stage 2 were considered as hypertension. Hypertension stage I was defined as systolic blood pressure (SBP) between 130-139 mmHg or diastolic blood pressure (DBP) between 80-89 mmHg; Hypertension stage II was defined as SBP $\geq$ 140 mmHg or DBP $\geq$ 90 mmHg. Inclusion criteria consisted of individuals over 18 years old who were prescribed peritoneal dialysis treatment. Exclusion criteria included kidney transplantation or hemodialysis. Additionally, patients with incomplete electronic health records were excluded from the study. Therefore, a total of 700 patients with normal blood pressure at their first visit and complete records were examined. To identify factors influencing the occurrence of hypertension, two survival regression models with gamma and nonparametric frailties were used. These shared frailty models, by adjusting for the effect of dialysis centers in each province on the time to event occurrence, enhance the accuracy of the effects (16). Statistical analyses were conducted using R version 4.2.3, employing the nonparametric frailty model through the R package discfrail, with a significance threshold of 0.05.

Results

The baseline characteristics of 700 peritoneal dialysis patients with normal blood pressure showed a mean age of 50.28 years with a standard deviation of 16.74. The gender distribution included 33.66% males and 66.34% females. The mean body mass index (BMI) was 22.52 with a standard deviation of 5.42. Approximately 83.8% of patients had comorbid conditions. Additional baseline laboratory parameters and blood factor measurements for the patients are summarized in Table 1. The results indicated that 400 (57%) patients developed hypertension by the end of the study. The survival rates at 1, 5, and 10 years were 90%, 56%, and 40%, respectively. The median survival time for the patients, estimated using the Kaplan-Meier method, was 74 months with a standard error of 4.15.

Table 1. Baseline Characteristics of Peritoneal Dialysis Patients with Normal Blood Pressure at Study Entry

Variable	Value for Patients with Normal BP
Age (Mean±SD)	50.28 ± 16.74
Sex	
Male	236 (33.66%)
Female	464 (66.34%)
BMI (Mean±SD)	22.52 ± 5.42
Comorbidity	
Yes	586 (83.8%)
No	114 (16.2%)
FBS (Mean±SD)	124.23 ± 67.28
Trg (Mean±SD)	173.17 ± 97.43
K (Mean±SD)	4.62 ± 0.70
Na (Mean±SD)	139.19 ± 3.89
Cr (Mean±SD)	6.49 ± 2.64
Albumin (Mean±SD)	3.71 ± 0.44
BUN (Mean±SD)	77.56 ± 39.57

BMI: Body Mass Index; Cr: Serum Creatinine; Na: Serum Sodium; FBS: Fasting Blood Sugar; Trg: Triglycerides; Albumin: Serum Albumin; K: Serum Potassium; BUN: Blood Urea Nitrogen

Two shared frailty models, Gamma and non-parametric, were applied to assess the risk of hypertension in peritoneal dialysis patients, yielding similar results. The nonparametric model had lower AIC and BIC values, indicating better goodness-of-fit compared to the gamma model; therefore, the nonparametric model was preferred.

According to the findings, the variables significantly associated with increased risk of hypertension included BMI, presence of comorbidities, serum creatinine, and serum sodium. In the nonparametric model, the hazard ratio for BMI was 1.18 (95% CI: 1.07–1.29), indicating that each one-unit increase in BMI was associated with an 18% increase in the risk of hypertension. For comorbidities, the hazard ratio was 1.35 (95% CI: 1.15–1.57), suggesting that having comorbid conditions increased the risk by 35%. Serum creatinine showed a hazard ratio of 1.22 (95% CI: 1.11–1.33), reflecting a significant increase in risk with elevated creatinine levels. Additionally, serum sodium had a hazard ratio of 1.28 (95% CI: 1.13–1.45), demonstrating a strong association between increased serum sodium and higher hypertension risk.

Table 2: Shared Frailty Models for Risk Factors of Hypertension in Peritoneal Dialysis Patients

Variable	Gamma HR	Gamma 95% CI	Nonparametric HR	Nonparametric 95% CI
Age	1.02	0.98 - 1.06	1.01	0.97 - 1.05
Sex; male	1.10	0.85 - 1.40	1.08	0.83 - 1.38
BMI	1.15	1.05 - 1.25	1.18	1.07 - 1.29

Comorbidity	1.40	1.20 - 1.60	1.35	1.15 - 1.57
Cr	1.20	1.10 - 1.30	1.22	1.11 - 1.33
Na	1.25	1.10 - 1.40	1.28	1.13 - 1.45
FBS	1.18	1.05 - 1.30	1.20	1.08 - 1.33
Trg	1.12	0.98 - 1.25	1.10	0.96 - 1.25
Albumin	0.85	0.75 - 0.95	0.83	0.73 - 0.94
K	1.05	0.90 - 1.20	1.04	0.89 - 1.20
BUN	1.10	0.98 - 1.22	1.08	0.96 - 1.21
AIC	420.3		410.1	
BIC	435.7		425.5	

BMI: Body Mass Index; Cr: Serum Creatinine; Na: Serum Sodium; FBS: Fasting Blood Sugar; Trg: Triglycerides; Albumin: Serum Albumin; K: Serum Potassium; BUN: Blood Urea Nitrogen

Discussion

Hypertension is a common complication in advanced renal failure patients on peritoneal dialysis, affecting their survival and quality of life. Although patients initially had normal blood pressure, some developed hypertension over time, highlighting the importance of monitoring its onset and risk factors. Frailty survival models, especially the nonparametric type, provide a more accurate evaluation of biochemical factors influencing hypertension risk, with the nonparametric model showing better fit than the gamma model in this study. This underscores the value of choosing effective models for survival analysis in dialysis patients.

One of the findings of the present study is the positive association between increased BMI and the increased risk of hypertension in patients undergoing peritoneal dialysis. This result is consistent with existing evidence in the scientific literature; notably, a study investigating cardiovascular risk factors in peritoneal dialysis patients indicates that metabolic disorders, including obesity, play a significant role as modifiable factors in increasing the risk of cardiovascular diseases and hypertension complications in these patients. This review emphasizes that, besides non-modifiable factors such as age and gender, metabolic disorders and dialysis-related dysfunctions can contribute to elevated blood pressure and worsening cardiovascular status. Moreover, changes in glucose and lipid metabolism, common in peritoneal dialysis patients, may lead to increased BMI and subsequent development of hypertension (17). Therefore, the findings of your study regarding the role of BMI as an influential factor in predicting hypertension in peritoneal dialysis patients align with this known evidence and highlight the importance of weight management and metabolic factor control in this population.

In our study of PD patients with normal baseline blood pressure, comorbidity was associated with a higher risk of developing hypertension. This aligns with previous reports showing that comorbidity burden predicts adverse outcomes in dialysis populations. For example, Wu et al, observed that preexisting cardiovascular disease markedly increased mortality risk in PD patients (18), while Gómez et al, reported that higher comorbidity scores at dialysis initiation were linked to almost a twofold greater risk of death (19).

Although our outcome was incident hypertension rather than mortality, the consistent direction of association supports the role of comorbidity as a significant risk factor.
In present cohort study, higher baseline serum creatinine was linked to a greater hazard of developing hypertension. Evidence directly connecting creatinine to incident hypertension in peritoneal dialysis is limited. Previous studies have mainly treated creatinine as a marker of muscle mass and nutritional status rather than as a blood pressure predictor—for example, Park et al, found that higher creatinine reflected greater muscle mass and was associated with better survival among dialysis patients (20). Conversely, work on blood pressure regulation in dialysis has highlighted the dominant influence of fluid and sodium balance (8). More recent studies in PD have also shown that post-initiation blood pressure is closely related to residual kidney function and fluid status, underscoring the central role of volume pathways (21). Taken together, our finding may indicate that baseline creatinine does not act directly but instead captures indirect effects through nutritional, metabolic, and fluid-related mechanisms. Differences across studies in outcomes, measurement strategies, and confounder adjustment likely account for variability in reported associations. Further research using markers of fluid overload (e.g., NT-proBNP) or precise volume measurements is needed to clarify the pathways linking creatinine and hypertension in PD patients.
In our study, higher serum sodium (Na) was associated with a significantly increased risk of developing hypertension in PD patients. This finding is consistent with prior evidence. For example, Davies et al, showed that increasing the diffusive component of sodium removal using low-sodium PD fluids led to significant reductions in ambulatory blood pressure and improvements in fluid status (22). Also, in a retrospective cohort of 1,656 incident PD patients, Qiu et al, found that serum sodium ≥ 140 mmol/L modified the association between elevated systolic blood pressure (>130 mmHg) and increased mortality, suggesting high Na exacerbates risk associated with high BP (23).
In present study, fasting blood sugar (FBS) at baseline was significantly associated with increased risk of developing hypertension among patients. Although direct comparisons are limited, this finding aligns with several related observations. Vongsanim et al, suggested that chronic hyperglycemia may impair peritoneal sodium removal, which can contribute to increased systolic blood pressure (24). Selby et al, demonstrated that, in non-diabetic continuous ambulatory PD patients, dwells with high glucose concentration caused both rises in plasma glucose/insulin and in blood pressure compared to lower-glucose or amino acid solution dwells (25). Further, Najafimehr et al, found that higher FBS predicted increased mortality also in PD patients who did not initially have hypertension, indicating that elevated glucose has adverse effects even before hypertensive changes become clinically manifest (26). Together, these data support our finding that even among patients who begin with normal blood pressure, higher baseline FBS may predispose them to later development of hypertension. Particularly, mechanisms such as impaired insulin sensitivity, increased sodium retention, volume overload, and glucose-induced vascular dysfunction may mediate this effect.

One limitation of the present study was that for comorbidity, only information about the presence of this factor was available, and data regarding the type of disease or the medications used were not accessible to the authors. It was also possible that a patient with normal blood pressure at the beginning of the study already had hypertension and was using antihypertensive medication. However, the present study had the advantage of considering the worsening of blood pressure, as two stages of hypertension were taken into account.

The other strengths of the present research included the use of a nonparametric frailty survival model. The advantage of this model is considering the effect of treatment centers on the time to event, while information from those treatment centers to check the impact is not available. Such a powerful statistical model leads to increased validity of the results.

Conclusion

The factors including BMI, comorbidities, creatinine, sodium, and fasting blood sugar, play a significant role in increasing the risk of hypertension in peritoneal dialysis patients, while higher albumin levels may have a protective effect. These findings emphasize the importance of closely monitoring and managing these indicators to prevent and control hypertension in this patient population.

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