

# Evaluation of the Relationship Between Postprandial Hypotension and Carotid Intima Thickness in Peritoneal Dialysis Patients

## Periton Diyaliz Hastalarında Postprandiyeal Hipotansiyon ve Karotid İntima Kalınlığının Arasındaki İlişkinin Değerlendirilmesi

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### Abstract

**Aim:** Postprandial hypotension is recognized as a common cause of syncope and falls. This study aimed to determine the frequency of postprandial hypotension in patients undergoing peritoneal dialysis and to investigate the relationship between postprandial hypotension and carotid intima thickness. **Materials and Methods:** The study was conducted at the Peritoneal Dialysis Unit of Hatay Training and Research Hospital and was designed as a retrospective study. A total of 28 patients on peritoneal dialysis were included. Inclusion criteria were patients older than 18 years of age who had been on peritoneal dialysis for at least three months. Patients wore an ambulatory blood pressure Holter device, and carotid Doppler ultrasonography was performed.

**Results:** The study included 28 patients with a mean age of  $48 \pm 14.04$  years (range: 18–68); 14 were male and 14 were female. The mean systolic blood pressure was  $131.2 \pm 23.4$  mmHg (range: 81–178), and the mean diastolic blood pressure was  $75.7 \pm 14.2$  mmHg (range: 48–99). Ambulatory blood pressure was normal in 12 patients, while 16 patients were hypertensive. Hypertension was present in 25 patients (89.3%). Carotid intima thickness was evaluated in 26 patients, and increased thickness was detected in 10 of them (35.7%). Postprandial hypotension was observed in six patients (21.4%), all of whom had a history of hypertension.

### Öz

**Amaç:** Postprandiyeal hipotansiyon, senkop ve düşmelerin yaygın bir nedeni olarak kabul edilmektedir. Bu çalışmada, periton diyalizi hastalarında postprandiyeal hipotansiyon sıklığını belirlemeyi ve karotid intima kalınlığı ile olan ilişkisini araştırmayı amaçladık.

**Gereç ve Yöntem:** Çalışma, Hatay Eğitim ve Araştırma Hastanesi Periton Diyalizi Merkezi'nde yürütülmüş olup, retrospektif tasarıma sahip bir araştırmadır. Çalışmaya toplam 28 periton diyalizi hastası dahil edildi. Çalışmaya 18 yaşından büyük ve en az üç aydır periton diyalizi yapılan hastalar dahil edildi. Hastalara ambulatuvar kan basıncı holter cihazı takıldı ve karotid doppler yapıldı.

**Bulgular:** Çalışmaya toplam 28 hasta dahil edildi. Hastaların yaş ortalaması  $48 \pm 14,04$  (18-68 arası) idi. Hastaların 14'ü erkek, 14'ü kadındı. Ortalama sistolik kan basıncı  $131,2 \pm 23,4$  mmHg (81-178 arası), ortalama diyastolik kan basıncı ise  $75,7 \pm 14,2$  mmHg (48-99 arası) idi. 12 hastada ambulatuvar kan basıncı normal, 16 hastada ise hipertansiyon saptandı. Hastaların 25'inde (%89,3) hipertansiyon mevcuttu. Toplam 26 hastada karotid intima kalınlığı incelendi ve hastaların %35,7'sinde (10 hasta) kalınlık tespit edildi. Postprandiyeal hipotansiyon altı hastada (%21,4) saptandı. Postprandiyeal hipotansiyon olan tüm hastaların hipertansiyon öyküsü vardı.

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**Conclusion:** In this study, the prevalence of hypertension was 89.3%, and the frequency of postprandial hypotension was 21.4%. Increased carotid intima thickness was identified in 35.7% of the patients. No significant correlation was observed between postprandial hypotension and carotid intima thickness.

**Keywords:** Carotid Intima Thickness; Hypertension; Peritoneal Dialysis; Postprandial Hypotension

**Sonuç:** Çalışmamızda hipertansiyon prevalansı %89,3 olarak bulundu. Postprandiial hipotansiyon sıklığı %21,4 idi. Hastaların %35,7'sinde (26 hastadan) karotid intima kalınlığı artışı saptandı. Postprandiial hipotansiyon ile karotid intima kalınlığı arasında bir ilişki tespit edilmedi.

**Anahtar Kelimeler:** Karotid İntima Kalınlaşması; Hipertansiyon; Periton Diyalizi; Postprandiial Hipotansiyon

## INTRODUCTION

Renal replacement therapies include hemodialysis (HD), peritoneal dialysis (PD), kidney transplantation and recently palliative care has been advised for some patients. Approximately 7-10% of chronic kidney failure patients worldwide receive PD as kidney replacement therapy. Hypertension is common in dialysis patients. Diagnosis, treatment and control of hypertension in dialysis patients is and remains difficult. The International Society of Peritoneal Dialysis recommends including blood pressure (BP) measurements at every clinic visit and weekly home measurements to assess blood pressure. Diagnostic performance of clinical and home BP recordings have been evaluated in a cohort of 81 stable patients on PD, using ambulatory blood pressure measurement (ABPM). In conclusion it has been shown that one week home systolic BP measurement results is similar to standard clinical systolic BP measurement (1, 2). Home BP measurements or ABPM (Ambulatory Blood Pressure Monitoring) measurements are recommended for the diagnosis of hypertension in PD patients. To diagnose hypertension in PD patients, BP of home measurements should be over the mean BP 135/85 mmHg in seven consecutive days. On the other hand, ABPM on PD patients should be over the mean BP 130/80 mmHg at a 24-hour follow-up. PD patients who have a white coat/office BP of 140/90 mmHg and higher values, can be diagnosed with hypertension (3). Recently, it has been shown that BP may decrease after a meal in elderly hemodialysis patients with autonomic failure. Postprandial hypotension (PPH) is defined as a 20 mmHg drop in systolic BP and a 10 mmHg drop in diastolic BP two hours after a meal. PPH is

recognized as a common cause of syncope and falls. The mechanism of postprandial BP reduction is not fully understood. PPH is likely the result of a change in compensatory mechanisms for meal-induced splanchnic blood accumulation and a decrease in peripheral vascular resistance after food intake. A decrease in BP is detected after oral glucose load in this type of patients. Vasoactive gastrointestinal peptides may play a role in glucose-induced splenic vasodilation. However, these have not been fully explained. The role of insulin in PPH is also not understood (4, 5).

## MATERIAL AND METHOD

### Participant and Data Collection

Patients on peritoneal dialysis in the Hatay Training and Research Hospital PD Center between February 1, 2022 and April 1, 2022 were included in the study. Patients older than 18 years of age and who had been on PD treatment for more than three months were included in the study. Demographic characteristics, previous diagnoses of the patients were noted and biochemical parameters were evaluated. Carotid intima thickness was measured by the same radiologist. A 24-hour ABPM was measured and all the patients were told to note the times they ate. Hypertension was diagnosed in patients with 24-hour ABPM mean blood pressure  $\geq 130/80$  mmHg and in patients who had previously been prescribed one or more antihypertensives. PPH was defined as a decrease in the systolic BP of more than 20 mmHg and diastolic BP of more than 10 mmHg within two hours after meals. Different threshold values have been used in studies of intima-media thickness. However, an intima-media

thickness of  $\geq 0,9$  mm is usually considered abnormal (6, 7). We used this value in our study as the threshold value.

### Ethical Consideration

Ethics committee approvals of the study were obtained in writing from Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee (October 12, 2023; number 19). The Declaration of Helsinki was adhered to throughout the study.

### Data Analysis

In statistical analysis, data was evaluated using the SPSS (Statistical Package for Social Sciences) 20.0 computer package program. In statistical analysis, while evaluating the difference between groups, the t-test was used in comparing the measurement means and the Mann-Whitney U test was used in comparing the measurement means where nonparametric conditions were provided. Chi square was used for comparison for normally distributed measurements.  $p < 0.05$  was considered statistically significant.

### RESULTS

A total of 28 patients were recruited into the study. The average age of the patients was  $48 \pm 14.04$  (range 18-68). Half of the patients were male and half were female. Mean systolic BP  $131.2 \pm 23.4$  mmHg (range between 81-178), mean diastolic BP  $75.7 \pm 14.2$  mmHg (range between 48-99) ABPM pressure was

normal in 12 patients and was high in 16 patients. Hypertension was present in 25 of the patients (89.3%), only three patients were found to be normotensive. BP was under control with antihypertensive treatment in nine of the patients with hypertension. Among the patients with hypertension, 12 had non-dipper hypertension and six had inverse hypertension. ABPM values are given in Table 1. Carotid intima media thickness was examined in a total of 26 patients, and. increased thickness was found in 35.7%,10 of the patients. PPH was detected in six patients (21.4%). All patients with PPH had hypertension. ABPM was normal in only two of these patients. Half of the patients with PPH had carotid intima thickness. A decrease of more than 10% in BP during sleep time compared to daytime measurements indicates a circadian change. The presence of this diurnal variation is defined as dipper normotensive or hypertensive, which is a normal finding, and its absence is defined as non-dipper normotensive or hypertensive. A non-dipper pattern was detected in two patients who have hypertension history.

The biochemical parameters of the patients are given in Table 2. 32.1% of the patients had diabetes mellitus. PPH was not detected in any of the diabetes mellitus patients. There was a positive correlation between PPH and high BP, but it was not statistically significant. No relationship was found between PPH and hemoglobin, serum albumin, vitamin D, C-reactive protein and parathormone levels.

**Table 1.** Ambulatory Blood Pressure of Patients

	24-hour Average	Daytime Average	Night Average
Systolic blood pressure (mmHg)	131.6 $\pm$ 23.1 (81-178)	132.8 $\pm$ 23.4 (84-179)	127.0 $\pm$ 24.9 (70-177)
Diastolic blood pressure (mmHg)	75.5 $\pm$ 14.5 (48-99)	77.0 $\pm$ 15.0 (48-106)	70.8 $\pm$ 14.6 (41-99)

**Table 2.** Biochemical Parameters of Patients

	Mean±Standard Deviation
Glucose (mg/dl)	143.3 ±65.0 (79-314)
Blood Urea Nitrogen (mg/dl)	44.1±12.0 (26-72)
Serum Creatinine (mg/dl)	7.7±2.2 (3.1-12.7)
Alanine Aminotransferase (IU/L)	17.6±9.0 (7.0-42)
Serum Albumin (gr/dl)	3.5±0.4 (2.9-4.5)
Calcium (mg/dl)	8.8±0.8 (6.8-10.5)
Phosphorus (mg/dl)	5.0±1.1 (3.4-8.0)
Potassium (mmol/l)	4.3±0.5 (3.6-5)
Bicarbonate (mmol/L)	25.0±3.5 (18-33)
C-reaktif protein (mg/dl)	12.6±14.4 (0.6-44)
Haemoglobin (gr/dl)	10.7±1.2 (7.8-14)
Vitamin D (ng/mL)	9.1±5.0 (3-22)
Parathyroid Hormone (µg/L)	464.8±422.3 (24-1859)

## DISCUSSION

Postprandial hypotension is a clinical situation thought to affect all elderly people with hypertension. It is equally common in patients with diastolic heart failure, Parkinson's disease, diabetes mellitus, and autonomic dysfunction. If patients have symptoms like postprandial dizziness, fatigue, syncope, and falls, care professionals should be aware of this situation. Although more common than orthostatic hypotension, PPH is less evaluated by physicians. The socio-economic results associated with falls require better screening of PPH in hospital and outpatient examinations (8).

Postprandial hypotension is a common occurrence in the elderly population. The frequency of this condition is higher in frail elderly individuals who may be more prone to complications such as syncope and falls than in the normal population. Although it is often easy to make the diagnosis, it is relatively difficult to determine the relationship between symptoms, decreases in BP, and satiety. The decrease in postprandial BP may occur due to the inadequacy of some or all of the previously discussed mechanisms to balance the situation created by the increase in intestinal blood volume. The disruption of one or more of these mechanisms may result in the failure to balance the situation that

causes hypotension. Whether symptoms occur or not depends on the ability of the patients to apply adequate autoregulation. (9).

In a study of elderly patients, PPH (34%) was found to be more common than orthostatic hypotension (24%). However, more symptoms are seen in orthostatic hypotension than in PPH. Both conditions have been found to be associated with morbidity and mortality. It has been emphasized that treatment measures should be taken in the presence of comorbidities such as carotid artery occlusion (10).

In our study, PPH was detected in 21.4% of the patients. Increased carotid intima thickness was detected in 35.7% of the patients. None of the patients who have increased carotid intima thickness had diabetes mellitus. In the study performed by Jang with 94 elderly individuals, the patients were followed for 36 months. PPH was detected in 47 patients and it was shown to develop in seven more patients during follow-up. While the rate of new cardiovascular disease development was 55.3% in the PPH group, it was 8.5% in the control group. In addition, PPH, high body mass index, hypertension, diabetes mellitus, and high systolic and diastolic BP were associated with the development of new cardiovascular diseases (11).

In one study (Aronow et al.), the decrease in postprandial systolic BP was associated with the increase in falls (40%), syncope (24%), new coronary events (28%), new stroke events (12%), and in all causes of death. (40%) (12).

In another study, it was shown that postpartum haemorrhage was an independent indicator of all-cause mortality over a five year period (13). In our study, the prevalence of hypertension in the entire patient group was 89.3%.

The prevalence of hypertension in the PD population is between 29% and 88%. Many factors and comorbidities are important in the pathogenesis of hypertension in PD patients. In dialysis patients, situations such as increased volume status, use of erythropoietin (which causes an increase in viscosity and has a vasoconstrictive effect), decreased renal residual functions, and hyperparathyroidism may trigger hypertension (14).

In the study of Vareta et al. (15), the prevalence of white coat/office and ambulatory hypertension was found to be 92,9% and 95%, respectively. 92.1% of the patients were using an average of 2,4 BP reducing drugs per day. White coat/office and ABPM elevations were detected in 52.% of the patients. Target BP was achieved in 38.3% of the patients. 31.% of the patients had controlled hypertension, 5% had white coat hypertension, 19,3% had masked hypertension and 39.3% had persistent hypertension. In addition, while isolated nocturnal hypertension was detected in 23.% of the patients, isolated daytime hypertension was not found in any of the patients (15).

Low sodium peritoneal solution has been shown not to be superior to standard sodium solution for BP control. However, the use of low sodium PD solution was found to be associated with more frequent hypotensive attacks (16).

In PD patients with high BP (>140/90 mmHg), it is recommended to optimize the treatment in order to keep systolic BP <140 mmHg and diastolic BP <90 mmHg. Studies have shown that mortality risk increases with increasing systolic BP in PD patients. On the other hand, an observational study reported

that systolic BP of 110 mmHg or lower may be associated with increased mortality risk in these patients and that this situation may have a protective effect in patients with systolic BP above 120 mmHg. When changing antihypertensive treatment in PD patients with hypertension, it is important not to make these arrangements without optimizing their volume status. The principle behind preventing or treating hypertension in PD is to protect residual renal function, maximize peritoneal ultrafiltration and urine output, and achieve euvolemia. Avoiding hypotension with keto acid supplementation and a low-protein diet preserves residual renal function. (17, 18).

The optimal target blood pressure level in PD patients is still unknown. Non-drug therapy is known as the first step in the treatment of PPH. Lifestyle changes such as increasing water intake before meals or eating six small meals a day instead of large meals can be effective treatment options. It has also been emphasized that changes such as slowing gastric emptying, drinking water (to increase stomach bloating), exercising after meals and changing the temperature of the meal may also be beneficial. The most commonly used in pharmacological therapy are  $\alpha$ -glucosidase (delaying disaccharide absorption), Somatostatin and vasopressin (by blocking/antagonizing the release of peptides potentially responsible for splanchnic vasodilation), antihypertensive agents (lowering pre-meal BP), and caffeine (direct) inhibition.

In general, patients with peripheral noradrenergic degeneration and low plasma norepinephrine levels tend to respond well to midodrine and droxidopa. This also applies to patients with low "sympathetic reserve". In contrast to these patients, in patients with relatively preserved "sympathetic reserve" and normal or slightly decreased plasma norepinephrine levels, "norepinephrine enhancers" (pyridostigmine, atomoxetine, and yohimbine) are more effective. In general, it should not be forgotten that treatment must be individualized for the patient. Also, fludrocortisone and octreotide are other treatments that can be used. (19, 21).

Clinicians should evaluate elderly patients, especially those with chronic diseases (diabetes,

end-stage renal disease, and heart failure) for PPH. Examining patients' postprandial findings and questioning them for symptoms of hypotension may prevent the diagnosis of PPH from being overlooked. Patients with symptoms consistent with hypotension should be monitored for blood pressure, and more care should be taken in this regard in groups at risk (22).

Our knowledge of how PPH changes throughout the day in the elderly is still insufficient. However, studies examining postprandial BP changes show that BP changes after a morning meal are greater than after other meals, and that BP changes that occur at other times of the day cause fewer symptoms than in the morning. This is important to consider, as measurements taken in the morning may be more effective for diagnosis. Furthermore, knowing this situation may be useful in determining

when to administer antihypertensive treatment and may reduce the risk of developing symptoms (23).

## CONCLUSION

In conclusion, PPH can often be overlooked due to its asymptomatic course. However, it is detected at a high rate in screening (especially in elderly patients and patients with hypertension). PPH can cause serious morbidity and mortality, especially in terms of cardiovascular diseases, and care should be taken in this regard. In addition, it can cause falls and cause significant harm and even death. Although carotid intima thickening is considered an early sign of atherosclerosis, no relationship was found between PPH and carotid intima thickening in our study. There was a positive correlation between high BP and PPH, but it was not statistically significant.

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## ETHICS COMMITTEE APPROVAL

The approval of the ethics committee for this study was obtained from the Ethics Committee of Mustafa Kemal University (Date and no: 12.10.2023; 19).

## DECLARATION OF CONFLICT OF INTEREST

Any financial or other interest related to the study there is no conflict.

## FINANCIAL SUPPORT

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## PEER REVIEW

External independent, double blind.

## AUTHOR CONTRIBUTIONS

Idea, design: CH, Uİ

Plan: CH, Uİ, AŞ

Data collection: CH, Uİ

Analysis: CH, Uİ, AŞ

Article writing: AŞ, Uİ

Critical review: Uİ

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