Peritoneal dialysis (PD) patients are often volume-expanded and have higher-than-normal blood pressure (BP) levels. In the present study, we aimed to investigate the role of fluid balance and salt intake for BP control in our PD patients.

The study included 37 patients undergoing PD and having complete data for 3 consecutive months. Patients were allocated to one of two groups based on measured BP in the preceding 3 months: hypertensive patients (BP > 140/90 mmHg) and normotensive patients (did not meet the hypertensive BP criteria). Volume status was evaluated by bioimpedance analysis.

The 37 patients (18 women, 19 men) had a mean age of 46.4 years. The hypertensive and normotensive groups included 17 and 20 patients respectively. Sex, age, and time on PD were similar between the groups. Weight (77.3 ± 20.3 kg vs. 64.5±9.8 kg, \( p < 0.05 \)), total sodium load (2649.2 ± 621.9 mmol vs. 2272.4 ± 511.9 mmol, \( p < 0.05 \)), daily total sodium removal (160.5 ± 74.4 mmol vs. 112.1 ± 48.0 mmol, \( p < 0.05 \)), extracellular water (19.4 ± 4.3 L vs. 16.4 ± 3.5 L, \( p < 0.05 \)), and normalized extracellular water (11.6 ± 1.9 L vs. 10.1 ± 1.8 L, \( p < 0.05 \)) were all significantly higher in the hypertensive group.

Despite higher fluid and sodium removal, hypertensive patients were more hypervolemic than normotensive patients. Increasing fluid and salt removal by peritoneal ultrafiltration results in an increased financial burden and also causes serious clinical problems. Restricting fluid and salt intake is an alternative and safer strategy to maintain good fluid balance.

Key words
Bioimpedance analysis, hypertension, hypervolemia, salt intake, peritoneal sodium removal

Introduction
Cardiovascular disease is the leading cause of death in end-stage renal disease patients on peritoneal dialysis (PD), and hypertension is the major contributor to cardiovascular mortality and morbidity in these patients (1,2). Despite the fact that hypertension is multifactorial in cause, volume overload seems to be the most important causative factor in this population (3,4). Because of its nature as a continuous process, PD is believed to be better than hemodialysis for volume control (5). However, patients on PD are prone to develop hypertension and hypervolemia, especially after the first 2 or 3 years of dialysis, probably because of loss of residual renal function (6).

According to data from the renal registry of the Turkish Society of Nephrology, the prevalence of hypertension is clearly higher in PD patients (57.5%) than in hemodialysis patients (34.9%) in Turkey (7). In a single-center study, Koc et al. examined the relationships between blood pressure (BP), volume status, and cardiac hypertrophy in 74 prevalent PD patients. They reported that the prevalence of hypertension was 82% and that 56 of the 74 patients had uncontrolled hypertension despite the use of antihypertensive drugs (8).

Several factors cause hypervolemia and hypertension in PD patients. Excessive salt consumption is one of the main factors: it stimulates thirst and the subsequent water intake that contributes to volume overload and hypertension (9). Other factors that have been suggested to contribute to poor volume control in PD patients are ultrafiltration failure and decreased residual renal function (6,10). Although it is generally

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believed that hypervolemia is associated with inadequate fluid removal, a recent clinical trial showed that, compared with normotensive PD patients, hypertensive patients showed more fluid overload despite higher fluid and sodium removal (6,10,11).

In PD patients, reduced salt intake was found to be associated with a decline in BP (12). Günel et al. showed BP control in 47 hypertensive PD patients who were maintained on strict dietary sodium restriction after stopping antihypertensive medication (13). In most of the patients, body weight and BP were reported to have decreased significantly (13). Given that overhydration appears to be widely prevalent in PD patients, we aimed to investigate the role of hypervolemia and salt intake on BP control in our PD patients.

**Methods**

**Patient selection and classification**

This cross-sectional study was performed in 45 clinically stable patients who were undergoing PD therapy at Gazi University Hospital and who had not experienced peritonitis in the preceding 3 months. The inclusion criteria were PD treatment for at least 6 months, completion of monthly visits to our outpatient clinic, and the availability of complete data for 3 consecutive months (September, October, and November 2010). Of the 45 patients, 8 were excluded because of lack of data, leaving 37 patients for the investigation. The patients were allocated to one of two groups based on their office BP recordings in the preceding 3 months. Hypertensive patients [HT group (mean BP > 140/90 mmHg persistently or at least twice), n = 17] and normotensive patients [NT group (BP not meeting the HT group criteria), n = 20].

The study was conducted according to the Helsinki Declaration and approved by the Ethics Committee of Gazi University School of Medicine. All patients gave informed consent to participate in the study.

**BP measurements and bioimpedance analysis**

Brachial BP was measured twice in every patient, and the mean value was determined. Measurements were performed using a mercury sphygmomanometer with the patient in a sitting position after 10 minutes of rest. All patients usually taking an antihypertensive medication were asked to take their medication before the visit, and the number of antihypertensive drugs was also recorded.

To determine the volume status of the patients, bioelectric impedance analysis (BIA) was performed using a Quadscan 4000 multi-frequency bioimpedance spectrum analyzer (BodyStat, Douglas, Isle of Man). The measurement was performed at the right calf using 4 frequencies (5, 50, 100, and 200 kHz) in the supine position after patients had emptied their abdomen. Extracellular water (ECW), intracellular water (ICW), and total body water (TBW) were measured by BIA. The ECW was normalized to each patient’s height in meters (∆ECW).

**Evaluation of fluid and sodium removal**

Plasma sodium, urinary sodium removal, and peritoneal sodium removal were calculated for all patients. Urinary sodium removal was calculated as the 24-hour urine volume in liters multiplied by the sodium concentration in millimoles per liter of mixed urine. Peritoneal sodium removal was calculated as the sodium content in the total instilled dialysate minus the sodium content in total effluent. Total sodium removal was calculated as the sum of urinary sodium removal and peritoneal sodium removal. Daily urine output and ultrafiltration were recorded, and total fluid removal was calculated as the sum of those parameters. Plasma, dialysate, and urine sodium concentrations were measured by indirect ionometry. Total body sodium load was calculated as ECW multiplied by plasma sodium.

**Statistical analysis**

Statistical calculations were performed using the Statistical Package for the Social Sciences (version 13.0: SPSS, Chicago, IL, U.S.A.). Significance was defined as p < 0.05. Data are shown as mean ± standard deviation or percentage. Standard descriptive statistics, the two-tailed Student t-test, and the chi-square test were used, as appropriate, to compare characteristics between the groups. The Mann–Whitney U-test was used to compare non-normally-distributed values between the groups.

**Results**

Table I shows demographic and descriptive data for the 37 patients (19 men, 18 women). For all patients, mean age was 46.4 ± 15.7 years, and the mean time on PD was 40.5 ± 26.4 months. Of the 37 patients, 27 (73%) had a diagnosis of hypertension, and 5 (13.5%) had diabetes. According to the office BP recordings,
Of the 27 patients using antihypertensive medication (63%) had uncontrolled hypertension. Those 17 patients were allocated to the HT group; the remaining 20 patients (those without hypertension in their medical history or with a BP that was under control with antihypertensive medications) were allocated to the NT group.

The distribution of sex, age, time on PD, percentage of patients with diabetes, and body mass index were similar between the groups. The erythropoiesis-stimulating agent (ESA) prescription rate and the percentage of Extraneal (Baxter Healthcare Corporation, Deerfield, IL, USA) users were both higher in the HT group, but the differences were not statistically significant (Table I).

Body weight was higher in the HT group than in the NT group ($p < 0.05$). Total sodium load and total sodium removal were significantly higher in the HT group than in the NT group ($p = 0.04$ and $p = 0.05$, Table II). By BIA, ECW and TBW were significantly higher in the HT group than in the NT group (Table III). When ECW was normalized to the patient’s height in meters ($nECW$), the difference remained significant. The ICW and total fluid removal were also higher in the HT group, but the differences did not reach statistical significance.

**Discussion**

Hypertension is a common cardiovascular disease and leads to increased morbidity and mortality in PD patients (14). The impact of high BP on mortality in PD patients was well documented in a prospective study by Jager et al. (14), and those authors clearly defined mean arterial pressure as a prognostic factor for poor outcome. The results of older studies suggested that hypertension could be easily controlled by PD (15). However, later studies involving more patients and using 24-hour ambulatory BP monitoring techniques demonstrated that hypertension is a dramatic and unsolved problem in PD patients (16). Cocchi et al. (16) found that hypertension (defined according to World Health Organization and International Society of Hypertension criteria) was present in 88.1% of 504 patients and that 71% of the patients needed antihypertensive medications. In our study, 73% of patients were using antihypertensive medications, and 63% of those patients had uncontrolled hypertension.
One of the explanations for the dramatically high incidence of hypertension in PD patients might be the presence of latent hypervolemia in this population (17). Insufficient patient compliance to salt and fluid restriction might have major role. Also, health professionals might be inclined to support to a certain level of overhydration to maintain residual renal function (18). Although residual renal function is one of the most powerful predictors of outcome in PD patients, it should not allow those patients to have liberal fluid intake (19). The first step in maintaining renal residual function and avoiding hypervolemia should be salt restriction (19).

In the present study, body weight, TBW, ECW, and nECW were significantly higher in hypertensive PD patients, a result which can interpreted to mean that, compared with normotensive patients, patients with hypertension had more volume overload. It is now widely accepted that fluid and salt balance play a critical role in the regulation of BP and the success of PD therapy (7). Inadequate removal of fluid and sodium in PD is associated with increased mortality (20). There is growing evidence that PD patients are generally volume-overloaded and have high BP associated with left ventricular hypertrophy and dysfunction (7). Results of the recently published European Body Composition study, which is the first large multicenter study of hydration status in PD patients in Europe, also underlined the fact that fluid overload is a frequent problem in this group of patients (severe fluid overload was present in 25.2% of 639 PD patients) and that relying only on clinical parameters for its assessment might be misleading. In that study, mean TBW, ECW, and ICW were reported to be 35.8 L, 17.2 L, and 18.5 L respectively (21). The present study revealed even higher mean values for those parameters.

Consistent with the results of Chen et al. (11), hypertensive patients in our study were more hypervolemic, but also had higher fluid and sodium removal than did normotensive patients (Figures 1 and 2). The implication is that excess fluid and sodium intake leading to the development of fluid overload and hypertension deserves more attention in this group of patients (11). Our result is rather interesting because, in general, fluid overload is thought to be associated with insufficient fluid removal and decline in residual renal function (6,10). Given that fluid and salt removal usually reflect intake, higher fluid and salt removal likely mean that patients are ingesting more fluid and salt, which might have contributed to their higher BP (11,22).

Volume status is a balance between intake and removal, and so we should either restrict fluid and salt intake or increase their removal. However, increasing fluid and salt removal by peritoneal ultrafiltration results in an increased financial burden and also causes numerous clinical problems. The use of hypertonic glucose solution to increase the
amount of ultrafiltration can cause hyperglycemia, hyperlipidemia, and ultrafiltration failure (23).

The use of diuretics is another way to increase fluid and salt removal. It would be reasonable to prescribe a loop diuretic such as furosemide to patients with a daily urine volume of more than 100 mL starting on any form of PD therapy (6). That medication would help to preserve and enhance the urine volume and to maintain satisfactory fluid balance (6). But the effect of furosemide may decline over time as the glomerular filtration rate declines (6).

Restriction of fluid and salt intake is suggested as an alternative and better strategy to maintain good volume balance. In the literature, several studies confirm the beneficial effect of salt restriction on BP and volume control (12,13). Restriction of excess fluid intake and dietary salt ingestion will lower the dialysis dose, the need to use hypertonic solution, and BP. Consequently, such restriction will prevent the complications related to hypertonic dialysis solutions and will protect peritoneal membrane function (11). The Kidney Disease Outcomes Quality Initiative guideline recommends restricting dietary sodium intake to 100 mmol (6 g) salt daily for patients with chronic kidney disease (24). As far as PD patients are concerned, intake of salt should be recommended not to exceed approximately 5–6 g daily (6). However the recent SALTURK study on the relationship between hypertension and salt intake in the general Turkish population showed that daily salt consumption was approximately 18 g, with a daily urinary sodium excretion of 308.3 ± 143.1 mmol (25). In a recent study from Turkey in 373 chronic kidney disease patients (stages 1–5), the average daily salt intake was reported to be nearly 10 g (26). Despite continuous dietary reinforcement, our results were not much different. Average total sodium removal daily (which reflects daily salt consumption) in our study cohort was approximately 9.7 g for the HT group and 6.8 g for the NT group.

Use of ESAs has been reported to be associated with high BP in PD patients (27). In our study, the ESA prescription rate was higher in the HT group; however, it was not significantly different between the groups.

Our study is limited in being a cross-sectional analysis with a small number of patients. Strong conclusions cannot therefore be made from our results, because factors other than volume status might differ between the groups.

Conclusions
Our data showed that, although hypertensive PD patients had higher fluid and sodium removal, they were also more hypervolemic when compared with the normotensive patients. That result underlines the fact that dietary fluid and salt restriction should be a common strategy as an adjunct to the treatment of hypervolemia and hypertension in PD patients. In populations with a high salt consumption (such as the Turkish population), dietary salt restriction becomes much more crucial in achieving euolemic status.

Disclosures
The authors have no financial disclosures to declare and no conflicts of interest to report.

References

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