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# The Relationship Between Pulse Pressure and Hypervolemia in Hemodialysis Patients

## Hemodiyaliz Hastalarında Hipervolemi ile Nabız Basıncı Arasındaki İlişki

**Sami EVİRGEN[1], Alaattin YILDIZ[2]**

[1]Kastamonu University, Faculty of Medicine, Department of Internal Medicine, Kastamonu, Turkey
[2]Istanbul University, Istanbul Faculty of Medicine, Department of Nephrology, Istanbul, Turkey

**ORCID ID:** Sami Evirgen 0000-0001-6920-777X, Alaattin Yıldız 0000-0002-4066-929X

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**Corresponding Author**
Sami Evirgen

**E-mail**
samievirgen@yahoo.com

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### ABSTRACT

**Aim:** Hypervolemia is a common problem in hemodialysis (HD) patients. Because reaching to optimal dry weight (DW) is difficult. Chronic volume overload causes left ventricular hypertrophy. Therefore, risk of cardiovascular events is very high. High pulse pressure is an indicator of aortic stiffness, an independent risk factor for cardiovascular mortality. Pulse pressure has a strong correlation with systolic blood pressure and thus with myocardial infarction in hypertensive HD patients. Aim of this study is to investigate the relationship between pulse pressure (PP) and hypervolemia.

**Material and Methods:** Seventy (28 male (40%), 42 (60%) female) chronic HD patients with an average of age 48 ± 12 were enrolled. All patients underwent HD 3 times weekly were included. Fluid status [Total Body Water (TBW), ECW and Intracellular Water (ICW) values] was assessed twice (beginning and end of the HD) in HD patients with the body composition monitor (BCM). And blood pressure was measured simultaneously. Before and after hemodialysis, the weight of the patients was measured and recorded.

**Results:** At the beginning of HD, Extracellular Water (ECW) / body weight (BW) (%) was associated systolic blood pressure (SBP) and PP measured simultaneously (P=0.021, P=0.057 respectively). There was no association between diastolic blood pressure with hypervolemia and PP.

**Conclusion:** If patients have hypervolemia especially in the interdialitic period, they have prolonged exposition to cardiovascular risk factors, because hypervolemia is corralated with SBP and PP as well. Both of them are strongly associated with cardiovascular events. Removal of adequate fluid to obtain optimal dry weight causes decrease of systolic and pulse pressure proportionally.

**Keywords:** Pulse pressure, Hypervolemia, Hemodialysis

### ÖZ

**Amaç:** Hipervolemi hemodiyaliz hastalarında yaygın bir problemdir. Çünkü optimal kuru ağırlığı belirlemek zordur. Kronik volüm yüklenmesi sol ventrikül hipertrofisine yol açar. Bu yüzden kardiyovasküler hastalık görülme oranı yüksektir. Yüksek nabız basıncı aortik sertleşmenin bir göstergesi ve kardiyovasküler mortalite için bağımsız bir risk faktörüdür. Hipertansif hemodiyaliz hastalarında nabız basıncı tek başına sistolik kan basıncına göre miyokard infarktüsü oluşum riski için daha güçlü bir risk faktörüdür. Bu çalışmanın amacı her ikisi de kardiyovasküler hastalık için risk faktörü olan hipervolemi ile nabız basıncı arasındaki ilişkiyi incelemektir.

**Gereç ve Yöntemler:** Ortalama yaşları 48 ± 12 olan 70 (28 erkek (%40), 42 kadın (%60)) kronik hemodiyaliz hastası çalışmaya dahil edildi. Tüm hastalar haftada 3 gün hemodiyalize giriyordu. Vücut kompozisyonu monitörü (BCM) ile HD hastalarında sıvı durumu (Total Vücut Sıvısı, Ektrasellüler sıvı ve intrasellüler sıvı değerleri) iki kez (HD'nin başlangıcı ve bitişi) değerlendirildi ve aynı anda kan basınçları ölçüldü. Diyaliz öncesi ve sonrası kilo ölçümleri yapıldı ve kayıt edildi.

**Bulgular:** Diyalizin girişindeki Ekstrasellüller Sıvı (ESS) / Vücut Ağırlığı (VA) (%) ile sırasıyla giriş sistolik kan basıncı ve nabız basıncı arasında anlamlı korelasyon bulundu (P=0.021,P=0.057 ). Diyastolik kan basıncı ile nabız basıncı ve hipervolemi arasında bir ilişki saptanmadı.

**Sonuç:** İnterdiyalitik periyotta hastaların hipervolemik olması kardiyovasküler risk faktörlerine uzamış maruziyete neden olur. Çünkü hipervolemi ile nabız basıncı ve sistolik kan basıncı arasındaki ilişki bilinmektedir. Bu yüzden hastaların kuru ağırlığının doğru hesaplanması ile yeterli sıvının ultrafiltrasyonla çekilmesi sağlanabilir ve NB ile SKB'da orantılı azalmaya yol açarak kardiyovasküler olaylar azaltılabilir.

**Anahtar Sözcükler:** Nabız basıncı, Hipervolemi, Hemodiyaliz

## INTRODUCTION

Cardiovascular diseases are the most important and common cause of mortality and morbidity in end-stage renal disease (ESRD) patients (1). Vascular changes, including atherosclerosis and arteriosclerosis, contribute to increased cardiovascular mortality in this population (2,3). Atherosclerosis is associated with increased arterial intima-media thickness leading to luminal obstruction with ischemic events. Arteriosclerosis results in arterial stiffening, increased pulse wave velocity (PWV), systolic blood pressure (SBP), and pulse pressure (PP), leading to left ventricular hypertrophy (LVH) and reduced coronary perfusion (4,5). Hypertension (HT) is an important issue in CVD. ECW increase plays a role in the pathogenesis of HT, which is closely related to body sodium. In addition, the significant relationships have been found between hypervolemia and left ventricular hypertrophy (LVH) in ESRD patients. Compared to Chronic Renal Failure (CRF) patients receiving antihypertensive drugs, cardiovascular mortality and morbidity was found to be reduced when tight volume control was performed. It is known that 60-80% of chronic HD patients are hypertensive. (6). Blood pressure cannot be controlled with antihypertensive drugs in most of these patients. (7,8). In most HD patients, hypertension occurs due to volume burden, and this situation can be corrected by ultrafiltration (UF).

PP have been associated with high risks of cardiovascular events, all-cause mortality, and cardiovascular death in patients on Maintenance Hemodialysis (MHD) (9,10). In another study, reduction in PP with HD was shown to be associated with improved survival (11).

In this study, we aimed to evaluate the relationship between hypervolemia and pulse pressure (PP), which contributes to cardiovascular mortality in HD patients exposed to chronic hypervolemia, since DW could not be determined clearly.

## MATERIAL and METHODS

In this study, 70 patients who were on a standard chronic HD program 3 times a week for a total of 12 hours were examined. Exclusion criteria are as follows: People under 18 and over 65 aged, those with pacemakers or prostheses placed in any part of the body, Those who have amputation in any of their limbs, malnourished patients ( ≤ 15 kg/m2 ), Patients who do not sign the informed consent form, Those who are pregnant, those with AV fistula in both extremities, Those with end-stage liver and lung failure. Twenty-eight of the patients were men and 42 were women. Patients were on dialysis with the 4008S series Fresenius Medical Care dialysis machine. Average dialysate sodium was 133 mmol / L, dialysate flow rate was 500 ml / min, and blood flow rate was 300-400 ml / min. Electrodes were placed on the dorsal side of the wrist and metacarpophalangeal joints of the non-fistula arm of the patients lying on the dialysis bed, and on the dorsal faces of the ipsilateral ankle and metatarsophalangeal joints. The same electrodes were used in each measurement.

After examining the arterial tension of the patients, age, height, gender, entrance weight, entrance tension and targeted UF amounts are entered on the BCM (Body Composition Monitor Fres. Med. Care, Germany 50 frequency 5 kHz-1 MHz) and TBW, ECW and ICW values were measured before dialysis. At Thirty minutes after dialysis, the patients' arterial tension and body weights were measured, and TBW, ECW, ICW values were measured again with BCM. The duration of the study was three weeks.

### Statistical Analysis

All analyzes were performed using the SPSS 16.0 statistical software package. Continuous variables in group data were expressed as mean ± standard deviation (mean ± SD). Categorical variables were given with numbers and percentages. Parametric tests were used in the analysis of continuous variables, since the distribution of all continuous variables was normal. Student t test and analysis of variance were used for continuous variables in paired comparisons between groups. Paired samples t test was used to compare the values of within-group variables before and after dialysis. Chi-square test was used for comparison of categorical variables. Pearson correlation analysis was used to examine the relationship between continuous variables. The Statistical significance level was set to $p < 0.05$.

## RESULTS

The demographic characteristics of 70 patients included in the study are presented in Table 1. The mean age was 48 ± 12 (years). Seventy (28 male (40%), 42 (60%) female). Distribution of ESRD in terms of etiology; hypertension 20

**Table 1:** Demographic characteristics of patients

| Demographic, clinical and laboratorial parameters | HD group (n=70) |
|---|---|
| Age (years) | |
| Mean±SD | 48 ± 12 |
| Gender (M/F) [n (%)] | 28 (40) / 42 (60) |
| BMI (kg/m$^2$) | |
| Mean±SD | 28 ± 6 |
| Median (min-max) | 27.2 (18-46.4) |
| Dialysis time (months) | |
| Mean±SD | 57 ± 42 |
| Median (min-max) | 59 (12-102) |
| Hypertension [n (%)] | 33 (47) |
| Diabetes Mellitus [n (%)] | 12 (17.1) |
| Sistolic BP (mmHg) | |
| Mean±SD | 142 ± 26 |
| Median (min-max) | 140 (90-205) |
| Diastolic BP (mmHg) | |
| Mean±SD | 81 ± 14 |
| Median (min-max) | 80 (50-120) |
| Pulse Pressure (mmHg) | |
| Mean±SD | 61 ± 21 |
| Median (min-max) | 59.5 (20-119) |
| Kt/V | |
| Mean±SD | 1.76 ± 0.35 |
| Median (min-max) | 1.78 (1.14-3) |
| Hemoglobin (g/dL) | |
| Mean±SD | 12.2 ± 1.29 |
| Median (min-max) | 12.2 (9.67-15.4) |
| Hematocrit (%) | |
| Mean±SD | 35.3 ± 3.8 |
| Median (min-max) | 35.1 (28.3-46.3) |
| BUN (mg/dL) | |
| Mean±SD | 123 ± 26 |
| Median (min-max) | 124 (62-187) |
| Creatinine (mg/dL) | |
| Mean±SD | 8.3 ± 2.0 |
| Median (min-max) | 8.3 (4.9-14.3) |
| Sodium (mmol/L) | |
| Mean±SD | 137 ± 2.5 |
| Median (min-max) | 137 (132-143) |
| Calcium (mg/dL) | |
| Mean±SD | 9.1 ± 0.7 |
| Median (min-max) | 9.1 (6.5-10.8) |
| Phosphorus (mg/dL) | |
| Mean±SD | 4.9 ± 1.3 |
| Median (min-max) | 5 (2.1-8.2) |
| Albumin (g/dL) | |
| Mean±SD | 4.14 ± 0.31 |
| Median (min-max) | 4.1 (3.6-4.8) |
| hs-CRP ( mg/L ) | |
| Mean±SD | 6 ± 1.1 |
| Median (min-max) | 5.9 (3.4-8.8) |

**BMI:** Body mass index, **BP:** Blood pressure, **BUN:** Blood urea nitrogen, **hs-CRP:** High sensitivity C reactive protein, **Kt/V:** K: Urea clearance of dialyzer, **t:** time, **V:** Volume of distribution of urea.

**Table 2**: Comparison of HD input and output values of variables associated with hemodialysis

| | Pre-dialysis | Post-dialysis | P |
|---|---|---|---|
| Weight (kg ± ss) | 71 ± 16 | 67 ± 15 | <0.001 |
| SBP (mmHg ± ss ) | 142 ± 26 | 114 ± 21 | 0.001 |
| DBP (mmHg ± ss) | 81 ± 14 | 67 ± 14 | <0.001 |
| PP (mmHg ± ss) | 61 ± 21 | 47 ± 13 | 0.018 |
| TBW (litre ± ss) | 31.8 ± 7.2 | 29.3 ± 6.8 | <0.001 |
| ECW (litre ± ss) | 15.5 ± 3.2 | 12.8± 2.7 | <0.001 |
| İCW (litre ± ss) | 16.3 ± 4.3 | 16.5 ± 4.5 | <0.001 |
| TBW / BW (% ± ss) | 45.7 ± 7.6 | 44.1 ± 7.6 | <0.001 |
| ECW / BW (% ± ss) | 22.2 ± 2.9 | 19.2 ± 2.5 | <0.001 |
| İCW / BW (% ± ss) | 23.4 ± 5.1 | 24.9 ± 5.6 | <0.001 |

**SBP:** Systolic blood pressure, **DBP:** Diastolic blood pressure, **PP:** Pulse pressure, **TBW:** Total body water, **ECW:** Extracellular fluid, **ICW:** Intracellular fluid, **BW:** Body weight.

(28.5%), glomerulonephritis 12 (17.1%), diabetes mellitus 9 (12.8%), chronic stony pyelonephritis 3 (4.28%), polycystic kidney disease 2 (2.85%), and 24 (34.2%) with unknown etiology. A total of 33 patients were hypertensive (> 140/90 mmHg or using antihypertensive drugs). Eleven of them were using antihypertensive drugs (7 beta-blockers, 3 ACE inh. And 1 calcium channel blocker). Twelve patients (17.1%) were diabetic. Average dialysis time was 57 ± 42 months. The mean dialysis entry SBP of the patients was 142 ± 26 mmHg and the mean entry NB was 61 ± 21 mmHg.

The average input and output values of the variables associated with is presented in Table 2.

As shown in Figure 1, there was a significant correlation between the percentage of the patients' ECW input value to pre-dialysis body weight (BW) (ECW input / BW input (%)) and SBP input (p=0.021). But the relationship between the ECW input / BW input (%) value and the PP input value was found to tendency towards significant (p = 0.057). This was a finding proving the relationship between hypervolemia and SBP and PP. The significant relationships between TBW / BW (%) and ICW / BW (%) to SBP input and PP input were not be found respectively (p=0.172-p=0.508, p=0.466,p=0.922). There was a significant relationship between SBP input and change of PP (ΔPP) (p <0.001) (Figure 2).

## DISCUSSION

HD is the most commonly used renal replacement therapy in our country and in the world. One of the most common problems encountered in HD patients is that DW cannot be calculated precisely. As a result, inadequate UF can cause chronic hypervolemia in HD patients (12-16). This leads to an increase in blood pressure, which is an independent

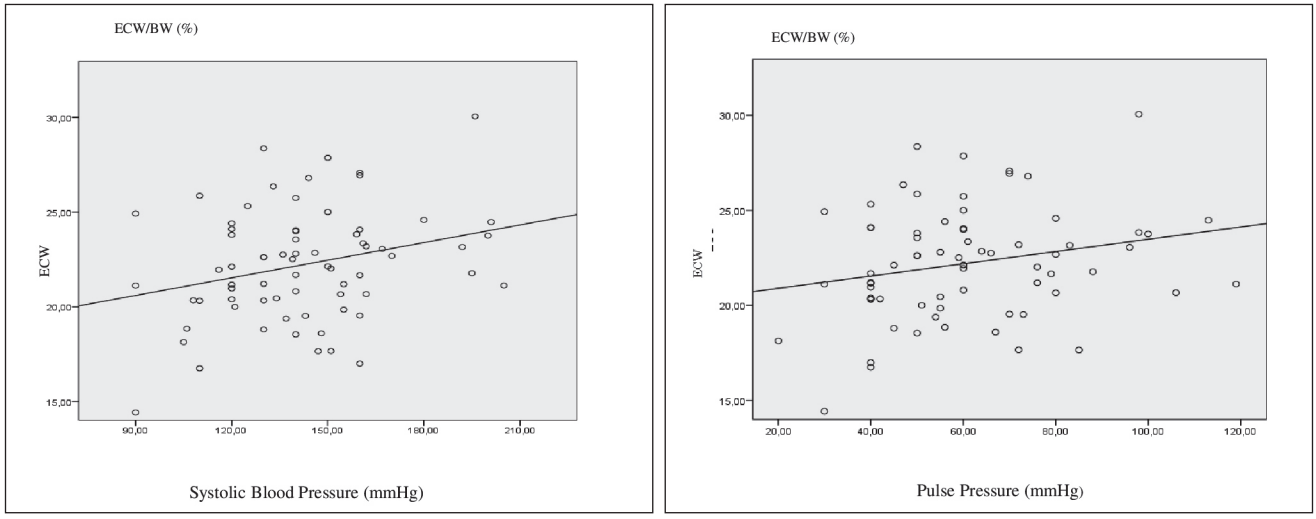


**Figure 1:** Relationship between ECW input / BW input (%) and SBP input and PP input (p=0.021, r=0.275, p=0.057, r=0.228, respectively).

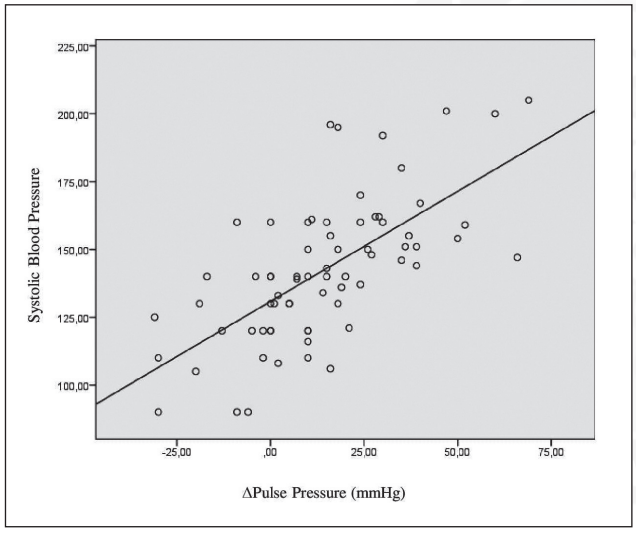


**Figure 2:** Relationship between SBP input and PP change (ΔPP) (p<0.001, r=0.666).

risk factor for CVD in patients. (17-19). In this study, we assessed the clinical relevance of BIA in hemodialysis and found that hypervolemia assessed by BIA was associated with ECW input / BW input (%) and SBP input and PP input. Another evidence of these findings that in this study, we have shown that there is a statistically significant difference between the ΔPP and SBP input as a result of removal of fluid from patients with hemodialysis.

In previous studies, the BIA method has been recommended for the assessment of the amount of fluid in body compartments (20-29). Fagugli et al. (30) examined the relationship between hypervolemia and HT and LVH using BIA measurements. They reported a strong correlation between hypervolemia and BP, and more importantly, a positive correlation between ECW and left ventricular mass index.

In a multicenter study conducted by Klassen et al. on 44,069 patients in HD patients, they found a very significant relationship between increased pulse pressure and increased mortality risk (31). Calculation of optimal DW is important to reduce CVE rates in HD patients. However this goal is not achieved in most dialysis centers beause the clinical parameters used to estimated DW are subjective and often unreliable. Kalainy et al. (32) reported that fluid volume expansion or contraction could not be reliably identified by clinical parameters, except that edema predicted fluid volume expansion. This study shows that BIA can assist to determine volume status. Many studies mention the benefits of using BIA in calculating dry weight in HD patients (33-38). In one study, it has been shown that positive results can be obtained on long-term surveillance in HD patients by preventing hypervolaemia and keeping PP at optimal levels after HD (39). Hong et al. (40) showed that strict volume control based on repeated measurements of bioimpedance spectroscopy allow to control hypervolemia and could reduce overhydration-related morbidity and mortality. In a study from our center, Erdan et al. (41), showed that volume control may improve not only the aortic blood pressure measurements but also arterial stiffness in hemodialysis patients.

In this study, the proportion of diabetic patients in the patients is less than expected. there may be criticism about this. However, since this study is a single-center study, the data of this population are presented.

In conclusion, despite technological advances in dialysis therapy, cardiovascular instability is still a major problem. In

recent years, new strategies such as hemofiltration, hemodiafiltration, sodium and UF that can provide good hemodynamic tolerance have been developed in controlling ECW. The increased PP is due to an increase in volume and SBP. In this case, sufficient UF should be done by accurately determining the dry weight of HD patients who may be hypervolemic, even if they are asymptomatic. Thus, they should be protected from the volume load caused by sodium and fluid intake in the pre-dialysis period, and thus from the negative effects of PP and SBP, which are independent risk factors of cardiovascular mortality. Due to the close relationship between sodium and water, restricting the sodium intake of patients is important in preventing increases in SBP and PP during interdiallytic and prediatric periods.

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This study produced from the thesis.

## Author Contributions

Planning of the study: **Sami Evirgen, Alaattin Yıldız,** Data collection: **Sami Evirgen,** Introduction: **Sami Evirgen,** Results: **Sami Evirgen,** Discussion and Conclusion: **Sami Evirgen, Alaattin Yıldız.**

## Conflicts of Interest

The authors did not declare any conflict of interest related to this article.

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## Ethical Approval and Informed Consent

Approval was obtained with the decisions of the Istanbul University non-invasive clinical research ethics committee. Date: 26.06.2009 issue: 2009/1979.

## Review Process

Extremely peer-reviewed and accepted.

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