**Original Article**

# The Determinants of Detrimental Changes in Pulse Pressure During Maintenance Hemodialysis Treatments

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**ABSTRACT**

***Background:*** Studies indicate that large fluctuations in pulse pressure during hemodialysis are associated with cardiovascular events, cardiovascular mortality, and all-cause mortality.

***Objective:*** We investigated the determinants of detrimental changes in pulse pressure (ΔPP) during hemodialysis.

***Methods:*** This prospective, observational cohort study was conducted from 1 to 30 April 2023 at Dr. Sardjito Hospital Yogyakarta, involving maintenance hemodialysis patients for ≥ 6 months. Patients were categorized into group 1 (detrimental ΔPP, ΔPP >5 mmHg or <−25 mmHg) and group 2 (stable ΔPP, −25 to 5 mmHg). Mann-Whitney, independent-t, chi-square, Fisher exact tests, and logistic regression were applied to evaluate associations between ΔPP groups and clinical variables.

***Results:*** This study involved 136 patients, 75 males (55.1%) with a mean age of 52 (18-87). The most common comorbid was hypertension, present in 85 patients (62.5%). The mean hemodialysis vintage of patients was 47.2 (6.5-330.7) months. We found significant difference between group in post-dialysis systolic blood pressure (SBP) (p=0.003), pre-dialysis diastolic blood pressure (DBP) (p=0.015), post-dialysis DBP (p=0.007), ultrafiltration (p=0.041), pre-dialysis mean-arterial-pressure (MAP) (p=0.013), post-dialysis MAP (p=0.002), and alpha-blocker treatment (p=0.037). Multivariate logistic regression analysis shows a significant association between groups of ΔPP with pre-dialysis DBP (p=0.035; OR=1.153; OR=$Exp^{(10x\mathcal{B})}$ =4.137) and post-dialysis SBP (p=0.007; OR=1.052; OR=$Exp^{(10x\mathcal{B})}$ =1.6487).

***Conclusion:*** Our study demonstrates that group 1, with detrimental changes in pulse pressure during hemodialysis, was found to have higher post-dialysis DBP, pre-dialysis DBP, post-dialysis SBP, pre-dialysis MAP, post-dialysis MAP, alpha-blocker treatment, and ultrafiltration, with significant association with post-dialysis SBP and pre-dialysis DBP.

***Keywords:*** Chronic Kidney Disease, Maintenance Hemodialysis, Detrimental Changes, **Δ** Pulse Pressure**.**

## Introduction

In Indonesia, hemodialysis is the most commonly used modality for renal replacement therapy. While essential, hemodialysis may lead to complications arising from changes in blood pressure during the procedure, including intra-dialytic hypotension and intra-dialytic hyper-tension, both of which may negatively impact

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patient outcomes. However, the extent to which blood pressure changes during hemodialysis affect or predict survival remains poorly understood.

Cardiovascular disease is a prevalent complication and the leading cause of mortality among patients with end-stage renal disease undergoing maintenance hemodialysis.[1] These patients frequently exhibit vascular changes, such as arteriosclerosis and atherosclerosis, contributing to increased pulse pressure.[2,3]

Pulse pressure, a recognized prognostic marker of vascular stiffness, is calculated by subtracting diastolic blood pressure (DBP) from systolic blood pressure (SBP).[4] Several key factors influence pulse pressure, including arterial wall compliance, stroke volume, vascular resistance, and patient-specific variables such as age, heart rate, height, underlying disease, endurance aerobic exercise, hormone replacement therapy, salt intake, and anti-hypertensive drugs.

Increased pulse pressure (PP) serves as an independent predictor of cardiovascular events, cardiovascular mortality, and all-cause mortality in both the general population and subgroups such as elderly individuals and those with hypertension.[5,6] Changes in pulse pressure are associated with factors including age, duration of hemodialysis, sex, blood flow rate, ultrafiltration, diabetes mellitus, inflammation, and albumin levels in patients undergoing maintenance hemodialysis.[7]

Compared to age-matched controls with normal renal function, patients on maintenance hemodialysis exhibit higher pulse pressure values, irrespective of mean arterial blood pressure (MAP).[7] Increased pulse pressure and arterial stiffness are associated with higher risks of cardiovascular events, cardiovascular mortality, and all-cause mortality in these patients.[8,9]

Hypervolemia may significantly contribute to changes in pulse pressure (ΔPP) in maintenance hemodialysis patients.[10] Volume overload has been linked to left ventricular hypertrophy and increased mortality.[11–13] Research suggests that decreased pulse pressure during hemodialysis is linked to a lower risk of hospitalization and mortality.[14] Regression models have limited these previous observations, assuming a linear relationship between pulse pressure changes and mortality. As a result, these models may be underpowered to detect a U-shaped association of high mortality with increases or decreases in pulse pressure.[14]

Some studies indicate that significant declines or increases in SBP during hemodialysis are linked to higher rates of cardiovascular events, cardiovascular mortality, and all-cause mortality.[15] Conversely, moderate pulse pressure reductions following hemodialysis are linked to improved survival outcomes. Large declines (>25 mmHg) or increases (>5 mmHg) in pulse pressure have been associated with higher mortality risks.[16] Moreover, increased pre- and post-dialysis pulse pressure have been identified as important predictors of all-cause mortality in hemodialysis patients.[9,17]

Despite various factors influencing pulse pressure changes in maintenance hemodialysis patients, the primary determinants of adverse pulse pressure changes in maintenance hemodialysis patients remain unclear. Therefore, this study aims to identify the factors contributing to detrimental changes in pulse pressure (ΔPP) during hemodialysis to identify the optimal blood pressure management strategies for these patients.

## Methods

### Design and participants

This prospective cohort study utilized data from patients 18 and older undergoing routine hemodialysis for more than 6 months at the Dr. Sardjito General Hospital hemodialysis center between April 1 and April 30, 2023. A total of 159 patients undergoing routine hemodialysis at Dr. Sardjito Hospital were considered for inclusion. Patient selection methods are illustrated in Figure 1 as a flowchart. After applying the exclusion criteria, the final sample comprised 136 patients.

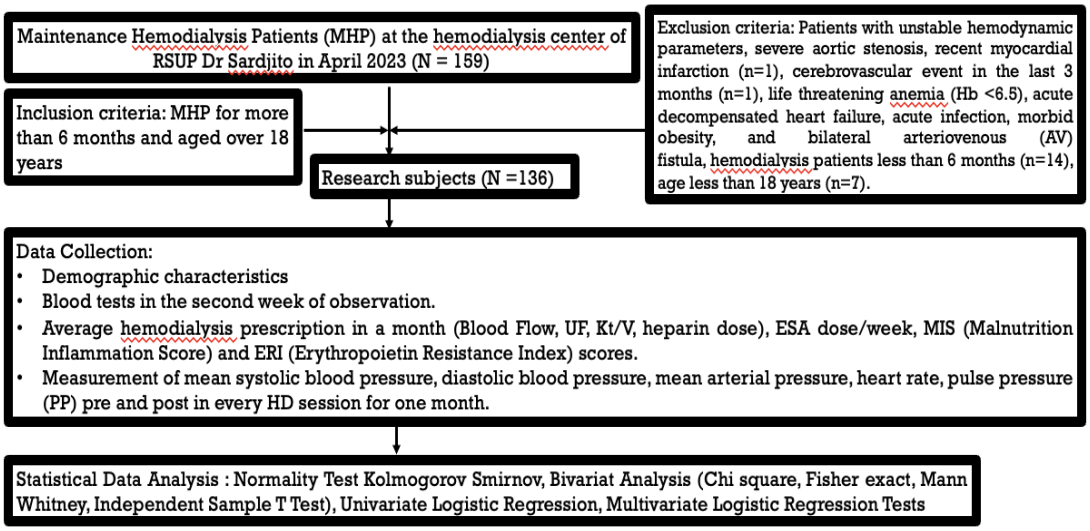


**Figure 1.** A flowchart of patient selection in our study

Demographic characteristics, including age, gender, duration of hemodialysis, body weight, height, body mass index (BMI), smoking status, causes of end-stage renal disease, routine blood tests, blood chemistry, average hemodialysis prescription over a month (blood flow, ultrafiltration volume, Kt/V, heparin dose), erythropoietin stimulating agents (ESA) dose/week, Malnutrition Inflammation Score (MIS), Erythropoietin Resistance Index (ERI) scores and measurement of mean systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, pulse pressure pre and post in every hemodialysis (HD) session for one month were recorded. All patients underwent an assessment of their hemodialysis records on April 1, 2023. The dialysis prescription lasts 3.5 to 5 hours, with blood flow rates between 120–300 ml/min, using standard bicarbonate dialysis concentrate (Sol-Cart® B-B.Braun) and polyethersulfone hemodialysis filter high permeability (Model SHM-DLPES-P1.6HF®–HOSPITECH®) with an effective surface area of 1.6 m2 and an ultrafiltration rate of 71 ml/h/mmHg. The erythropoiesis stimulant agents administered included Epoetin Alfa (Hemapo®–Kalbe Farma®) and Epoetin Beta (Recormon®-Roche®).

**Study Covariates**

The primary outcome of this study was to identify factors associated with detrimental changes in pulse pressure during hemodialysis. Detrimental changes in pulse pressure during hemodialysis are defined as significant declines (>–25 mmHg) or increases (>5 mmHg) in pulse pressure, both of which have been associated with higher cardiovascular and all-cause mortality.[16]

The inclusion criteria for this study were all patients aged 18 years and older who had been undergoing routine hemodialysis for more than 6 months at the hemodialysis center of Dr. Sardjito Hospital from April 1 to April 30, 2023. The exclusion criteria included patients with unstable hemodynamic parameters, severe aortic stenosis, recent myocardial infarction, cerebrovascular events in the past 3 months, life-threatening anemia (Hb <6.5), acute decompensated heart failure, acute infection, morbid obesity, bilateral arteriovenous (AV) fistula, those undergoing hemodialysis for less than 6 months, and those under 18 years of age.

The factors analyzed in this study included various demographic characteristics, blood tests, malnutrition status (assessed using the Malnutrition Inflammation Score (MIS) and body mass index (BMI)), iron deficiency

(evaluated based on transferrin saturation, blood iron levels/serum iron (SI) and total iron binding capacity (TIBC), Erythropoietin Resistance Index (ERI) score, dialysis prescription (include data of Kt/V values, blood flow, ultrafiltration volume and duration of hemodialysis) as well as hyper-parathyroid conditions (assessed by a simple examination of calcium levels and serum phosphorus levels) and measurement of mean systolic blood pressure, diastolic blood pressure, mean arterial pressure, heart rate, pulse pressure (PP) pre and post in every HD session for one month period.

**Statistical analysis**

Data processing was conducted using the SPSS 26.0 software package. Descriptive statistical methods measure central tendencies (mean, median) and summarize the numerical characteristics of the observed research variables. The results of data analysis were considered statistically significant if the p-value <0.05. The normality of data variables was analyzed using the Kolmogorov-Smirnov test. Continuous variables were summarized as mean±standard deviation (normal variables) or median and quartiles (non-normal variables). Categorical variables were presented as percentages.

Bivariate analyses, including Chi-square, Fisher exact, Mann-Whitney, and Independent Sample T-Test were used to determine the correlation significance between various independent factors and detrimental blood pressure changes during hemodialysis. The strength of the relationship between the independent factors and detrimental blood pressure changes during hemodialysis treatment was analyzed using univariate logistic regression, followed by multivariate logistic regression analysis to adjust for potential confounders.

## Results

Table 1 presents the basic characteristics of the study sample. Of the 136 patients, 75 (55.1%) were male, and the mean age was 52 years (range 18-87). Hypertension was the most prevalent comorbidity, affecting 85 patients (62.5%). The mean hemodialysis vintage was 47.2 months (6.5-330.7).

**Table 1.** Baseline characteristic

| | | Mean ± SD or Median (min-max) | n | % |
|---|---|---|---|---|
| Age (years) | | 52 (18-87) | | |
| Gender | Male | | 75 | 55.1 |
| | Female | | 61 | 44.9 |
| Dialysis Vintage (Months) | | 47.2 (6.5-330.7) | | |
| DM | Yes | | 29 | 21.3 |
| | No | | 107 | 78.7 |
| Hypertension | Yes | | 85 | 62.5 |
| | No | | 51 | 37.5 |
| Obstructive uropathy (stone/stricture urethra/prostate) | Yes | | 8 | 5.9 |
| | No | | 128 | 94.1 |
| GNC | Yes | | 11 | 8.1 |
| | No | | 125 | 91.9 |
| Others/unknown | Yes | | 2 | 1.5 |
| | No | | 134 | 98.5 |

| | |
|---|---|
| Weight (kg) | 60.53 ± 13.82 |
| Height (cm) | 160 (136-184) |
| BMI | 23.3 (14.8-35.1) |
| Albumin (mg/dl) | 4 (2.3-4.9) |
| EPO dose/weeks | 6000 (4000-8000) |
| SI | 52.5 (19-179) |
| TIBC | 195 (97-382) |
| Transferrin Saturation | 28.8 (8.8-99.4) |
| Hb | 9.5 (6.5-13,1) |
| AL | 6 (2.2-12.9) |
| AT | 200 (63-442) |
| Albumin (mg/dl) | 4 (2.3-4.9) |
| Calcium (mg/dl) | 8.9 (2.6-13) |
| Corrected calcium (calculator) | 8.9 (2.5-13.4) |
| Phosphorus (mg/dl) | 4.16 ± 1.58 |
| Corrected calcium x phosphorus (mg/dl) | 37.11 ± 14.49 |

| | | | |
|---|---|---|---|
| Malignancy | Yes | 3 | 2.2 |
| | No | 133 | 97.8 |
| Steroid | Yes | 2 | 1.5 |
| | No | 134 | 98.5 |
| Smoker | Yes | 1 | 0.7 |
| | No | 135 | 99.3 |
| Infection | Yes | 0 | 0.0 |
| | No | 136 | 100.0 |
| Transfusion | Yes | 2 | 1.5 |
| | No | 134 | 98.5 |
| Hepatitis B | Yes | 4 | 2.9 |
| | No | 132 | 97.1 |
| Hepatitis C | Yes | 0 | 0.0 |
| | No | 136 | 100.0 |
| HIV | Yes | 1 | 0.7 |
| | No | 135 | 99.3 |
| History of hemorrhage within 3 months | Yes | 7 | 5.1 |
| | No | 129 | 94.9 |
| ARB | Yes | 98 | 72.1 |
| | No | 38 | 27.9 |
| CCB | Yes | 98 | 72.1 |
| | No | 38 | 27.9 |
| Beta Blocker | Yes | 27 | 19.9 |
| | No | 109 | 80.1 |
| Statin | Yes | 7 | 5.1 |
| | No | 129 | 94.9 |
| Alpha Blocker | Yes | 21 | 15.4 |

| | | | |
|---|---|---|---|
| | No | 115 | 84.6 |
| Calcium Carbonate | Yes | 89 | 65.4 |
| | No | 47 | 34.6 |
| Amount of Anti-Hypertensive Drug Usage | 0 | 30 | 22.1 |
| | 1 | 10 | 7.4 |
| | 2 | 63 | 46.3 |
| | 3 | 25 | 18.4 |
| | 4 | 8 | 5.9 |

**Table 2.** Factors that influenced detrimental changes during hemodialysis treatment

| | Delta Pulse Pressure Category | | | | | | |
|---|---|---|---|---|---|---|---|
| | -24.99-4.99 | | | ≤-25 or ≥5 | | | P |
| | Median | Min | Max | Median | Min | Max | |
| Age (year) | 52.5 | 18 | 87 | 48 | 18 | 76 | 0,299* |
| Dialysis Vintage (months) | 47.40 | 6.5 | 330.75 | 46.65 | 6.60 | 205.75 | 0,553* |
| Height (cm) | 159.5 | 136 | 184 | 162 | 146 | 176 | 0,331* |
| BMI | 24.12 | 14.86 | 35.11 | 22.49 | 16.38 | 32.89 | 0,518* |
| Albumin (mg/dl) | 3.99 | 2.27 | 4.86 | 4.05 | 3.27 | 4.68 | 0,889* |
| EPO dose/week | 6000 | 4000 | 8000 | 6000 | 4000 | 6000 | 0,739* |
| SI | 53 | 27 | 179 | 52 | 19 | 135 | 0,724* |
| TIBC | 194.5 | 97 | 329 | 196 | 126 | 382 | 0,640* |
| Transferrin Saturation | 28.70 | 12.79 | 99.38 | 29.73 | 8.79 | 73.14 | 0.962* |
| Blood Flow | 225 | 130 | 300 | 230 | 150 | 300 | 0,053* |
| Hb | 9.45 | 6.50 | 12.40 | 9.55 | 6.50 | 13.1 | 0,752* |
| AL | 5.95 | 2.20 | 7.1 | 6 | 3.60 | 12.90 | 0,900* |
| AT | 202.5 | 63 | 442 | 196 | 94 | 442 | 0,662* |
| Albumin (mg/dl) | 3.99 | 2.27 | 4.86 | 4.05 | 3.27 | 4.68 | 0,889* |
| Calcium (mg/dl) | 8.94 | 2.60 | 13 | 8.78 | 6.92 | 12.64 | 0,392* |
| Post-dialysis Diastolic Blood Pressure (DBP) | 84.12 | 61 | 113 | 87.85 | 62.25 | 124.88 | 0,041* |
| Pre dialysis Pulse pressure | 64.72 | 33.12 | 116.89 | 67.74 | 30.5 | 100.5 | 0,539* |
| Time of Dialysis (hours) | 4.5 | 3 | 5 | 4.5 | 3 | 5 | 0,510* |
| Ultrafiltration Volume (ml) | 3000 | 300 | 5000 | 3500 | 300 | 5000 | 0,046* |
| ERI SCORE | 10.30 | 5.60 | 28.74 | 10.70 | 4.39 | 17.26 | 0,727* |
| MIS SCORE | 4 | 1 | 19 | 5 | 1 | 16 | 0,320* |

Cont.

| | Delta Pulse Pressure Category | | | | |
|---|---|---|---|---|---|
| | -24.99-4.99 | | ≤-25 or ≥5 | | P |
| | Mean | SD | Mean | SD | |
| Body Weight (kg) | 60.58 | 14.78 | 60.43 | 11.70 | 0,954** |
| KT/V | 1.75 | .31 | 1.73 | .34 | 0,795** |
| Phosphorus (mg/dl) | 4.29 | 1.53 | 3.88 | 1.65 | 0,151** |
| Corrected calcium x phosphorus (mg/dl) | 38.35 | 14.27 | 34.53 | 14.75 | 0,151** |
| Pre-Dialysis Systolic Blood Pressure (SBP) | 142.92 | 19.45 | 149.52 | 20.56 | 0,071** |
| Post Dialysis SBP | 143.76 | 21.75 | 159.48 | 35.23 | 0,002** |
| Pre-dialysis Heart rate | 79.55 | 11.44 | 79.92 | 11.76 | 0,864** |
| Post-dialysis Heart rate | 77.11 | 11.23 | 79.86 | 12.26 | 0,197** |
| Mean of peridialytic heart rate | 78.33 | 10.65 | 79.89 | 11.18 | 0,434** |
| Pre-dialysis Diastolic Blood Pressure (DBP) | 75.50 | 12.73 | 81.67 | 14.33 | 0,012** |
| Post-dialysis pulse pressure | 59.28 | 17.60 | 67.97 | 23.03 | 0,016** |
| Pre-dialysis MAP | 97.86 | 12.91 | 104.29 | 14.80 | 0,011** |
| Post-dialysis MAP | 104.27 | 12.99 | 114.15 | 22.23 | 0,001** |
| Hb | 9.30 | 1.46 | 9.37 | 1.57 | 0,795** |

*Independent T-test

| | | Delta Pulse Pressure Category | | | | |
|---|---|---|---|---|---|---|
| | | -24.99-4.99 | | ≤-25 or ≥5 | | P |
| | | N | % | N | % | |
| Gender | Male | 48 | 64.0 | 27 | 36.0 | 0,313# |
| | Female | 44 | 72.1 | 17 | 27.9 | |
| Others/unknown | Yes | 2 | 100.0 | 0 | 0.0 | 1,000$ |
| | No | 90 | 67.2 | 44 | 32.8 | |
| DM | Yes | 21 | 72.4 | 8 | 27.6 | 0,536# |
| | No | 71 | 66.4 | 36 | 33.6 | |
| Hypertension | Yes | 54 | 63.5 | 31 | 36.5 | 0,185# |
| | No | 38 | 74.5 | 13 | 25.5 | |
| Obstructive uropathy (stone/stricture urethra/prostate) | Yes | 7 | 87.5 | 1 | 12.5 | 0,437$ |
| | No | 85 | 66.4 | 43 | 33.6 | |
| Glomerulonephritis Chronic | Yes | 8 | 72.7 | 3 | 27.3 | 1,000$ |
| | No | 84 | 67.2 | 41 | 32.8 | |
| Vascular dialysis access | AV shunt | 85 | 68.0 | 40 | 32.0 | 0,747$ |
| | Others | 7 | 63.6 | 4 | 36.4 | |
| Heparin | Continue | 80 | 65.6 | 42 | 34.4 | 0,217# |
| | Mini | 7 | 77.8 | 2 | 22.2 | |
| | Free | 5 | 100.0 | 0 | 0.0% | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Ferrous Sulfate Injection | Yes | 10 | 58.8 | 7 | 41.2 | 0,406# |
| | No | 82 | 68.9 | 37 | 31.1 | |
| Malignancy | Yes | 3 | 100.0 | 0 | 0.0 | 0,551$ |
| | No | 89 | 66.9 | 44 | 33.1 | |
| Steroid | Yes | 1 | 50.0 | 1 | 50.0 | 0,544$ |
| | No | 91 | 67.9 | 43 | 32.1 | |
| Smoker | Yes | 1 | 100.0 | 0 | 0.0 | 1,000$ |
| | No | 91 | 67.4 | 44 | 32.6 | |
| Infection | Yes | 0 | 0.0 | 0 | 0.0 | - |
| | No | 92 | 67.6 | 44 | 32.4 | |
| Transfusion | Yes | 1 | 50.0 | 1 | 50.0 | 0,544$ |
| | No | 91 | 67.9 | 43 | 32.1 | |
| Hepatitis B | Yes | 3 | 75.0 | 1 | 25.0 | 1,000$ |
| | No | 89 | 67.4 | 43 | 32.6 | |
| Hepatitis C | Yes | 0 | 0.0 | 0 | 0.0 | - |
| | No | 92 | 67.6 | 44 | 32.4 | |
| HIV | Yes | 1 | 100.0 | 0 | 0.0 | 1,000$ |
| | No | 91 | 67.4 | 44 | 32.6 | |
| Bleeding History | Yes | 6 | 85.7 | 1 | 14.3 | 0,428$ |
| In 3 months | No | 86 | 66.7 | 43 | 33.3 | |
| ARB | Yes | 62 | 63.3 | 36 | 36.7 | 0,079# |
| | No | 30 | 78.9 | 8 | 21.1 | |
| CCB | Yes | 64 | 65.3 | 34 | 34.7 | 0,349# |
| | No | 28 | 73.7 | 10 | 26.3 | |
| Beta Blocker | Yes | 20 | 74.1 | 7 | 25.9 | 0,425# |
| | No | 72 | 66.1 | 37 | 33.9 | |
| Statin | Yes | 7 | 100.0 | 0 | 0.0 | 0,096$ |
| | No | 85 | 65.9 | 44 | 34.1 | |
| Alpha-blocker | Yes | 10 | 47.6 | 11 | 52.4 | 0,033# |
| | No | 82 | 71.3 | 33 | 28.7 | |
| Calcium carbonate | Yes | 60 | 67.4 | 29 | 32.6 | 0,937# |
| | No | 32 | 68.1 | 15 | 31.9 | |
| Amount of antihypertensive | 0 | 24 | 80.0 | 6 | 20.0 | 0,581# |
| drug treatment usage | 1 | 7 | 70.0 | 3 | 30.0 | |
| | 2 | 40 | 63.5 | 23 | 36.5 | |
| | 3 | 16 | 64.0 | 9 | 36.0 | |
| | 4 | 5 | 62.5 | 3 | 37.5 | |
| Corrected ca x phosphorus | <=55 | 82 | 66.7 | 41 | 33.3 | 0,547$ |
| | >55 | 10 | 76.9 | 3 | 23.1 | |

Notes:
*Mann Whitney test, **Independent T test, # Chi-Square test, $ Fisher exact test.

Bivariate analysis revealed significant mean differences between study groups, with the ultrafiltration volume, pre-hemodialysis diastolic blood pressure, post-hemodialysis systolic blood pressure, post-hemodialysis diastolic blood pressure, pre, and post-hemodialysis mean arterial pressure, post-hemodialysis pulse pressure and the use of alpha-blockers were found higher in the group 1 with detrimental pulse pressure changes ($\Delta PP = \leq -25$ or $\geq 5$) ($p < 0.05$).

**Table 3.** Factors that influenced detrimental changes during hemodialysis treatment

| | P | OR | CI 95% |
|---|---|---|---|
| Ultrafiltration Volume | 0,041 | 1,00 | 1,00-1,01 |
| Post-dialysis SBP | 0,003 | 1,02 | 1,01-1,04 |
| Pre-dialysis DBP | 0,015 | 1,04 | 1,01-1,06 |
| Post-dialysis DBP | 0,007 | 1,04 | 1,01-1,07 |
| Pre-dialysis MAP | 0,013 | 1,04 | 1,01-1,06 |
| Post-dialysis MAP | 0,002 | 1,04 | 1,01-1,06 |
| Alpha-blocker | 0,037 | 2,73 | 1,06-7,05 |

Notes: The analysis method uses univariate logistic regression

Univariate logistic regression analysis indicated that the incidence of detrimental PP changes was positively influenced by ultrafiltration volume, pre-HD diastolic blood pressure, post-HD systolic blood pressure, post-HD diastolic blood pressure, pre-HD MAP, post-HD MAP, and the use of alpha-blockers.

**Table 4.** Factors that influenced detrimental changes during hemodialysis treatment

| | | | | | 95% C.I. | |
|---|---|---|---|---|---|---|
| | B | P | OR | $Exp^{(\triangle \mathcal{B})}$ | Lower | Upper |
| Ultrafiltration Volume | 0.000 | .033* | 1.000 | 1 | 1.000 | 1.001 |
| Post-dialysis SBP | 0.050 | .007 | 1.052 | △=10 mmHg =(1.6487) | 1.014 | 1.091 |
| Pre-dialysis DBP | 0.142 | .035* | 1.153 | △=10 mmHg =(4.137) | 1.010 | 1.316 |
| Post-dialysis DBP | -0.067 | .113 | .935 | | .861 | 1.016 |
| Pre-dialysis MAP | -0.119 | .051 | .887 | | .787 | 1.000 |
| Alpha-blocker | 0.553 | .360 | 1.739 | | .532 | 5.687 |
| Constant | -2.960 | .111 | .052 | | | |

Notes: The analysis method uses multivariate logistic regression

Multivariate logistic regression analysis revealed ultrafiltration volume was not associated with detrimental pulse pressure changes (p = 0.33; OR = 1). However, higher pre-HD diastolic blood pressure (OR = 1.153; p = 0.035; OR = $Exp^{(10x\mathcal{B})}$ = 4.137) increased the odds of detrimental pulse pressure changes by 1.153 times for every 10 mmHg increase. Higher post-HD systolic blood pressure (OR = 1.052; p = 0.007; OR = $Exp^{(10x\mathcal{B})}$ = 1.6487) increased the likelihood of detrimental changes by 1.052 times for every 10 mmHg increase.

## Discussion

In this cohort of 136 maintenance hemodialysis patients, we observed that those with detrimental pulse pressure changes during hemodialysis exhibited higher post-dialysis DBP, pre-dialysis MAP, post-dialysis MAP, alpha-blocker treatment, and ultrafiltration volume. These patients also showed significant association with post-dialysis SBP and pre-dialysis DBP.

This study found that pre-HD diastolic blood pressure has a significant association with detrimental pulse pressure change during hemodialysis (p=0.035; OR=1.153; 95% C.I (1.010-1.316)) with OR 4.137 for every 10 mmHg increase. This finding is consistent with that of Hara M. et al., who demonstrated that higher pre-HD diastolic blood pressure increases the risk of cardiovascular disease and all-cause mortality in hemodialysis patients in Japan.[18]

Both increases and decreases in post-HD systolic blood pressure exceeding 5 mmHg were associated with the highest risk of cardio-

vascular events and all-cause mortality compared to patients with stable post-dialysis BP changes (within -5 to 5 mmHg).[19] Furthermore, an increase in post-dialysis systolic blood pressure is associated with subclinical volume overload.[19] In our study, post-HD systolic blood pressure also showed a significant association with detrimental pulse pressure changes during hemodialysis (p=0.07; OR=1.052; 95% C.I 1.014-1.091) with an OR of 1.6487 for every 10 mmH increase.

A study by Lertdumrongluk found that ultrafiltration volume per session and spKt/V were negatively correlated with delta pulse pressure changes (ΔPP).[16] In contrast, our study found no significant association between ultrafiltration volume (p=0.033; OR=1) and detrimental pulse pressure changes during hemodialysis. However, patients with detrimental pulse pressure changes post-hemodialysis underwent greater fluid removal during treatment (3500 cc vs 3000 cc).

Therefore, these findings suggest that appropriate therapeutic strategies could help mitigate the long-term complications associated with excessive pulse pressure changes during hemodialysis treatment. Such strategies may include:

1. Adjusting ultrafiltration volume by optimizing dry weight calculations, educating patients on nutrition, salt restriction, and fluid intake to reduce excessive inter-dialytic weight gain, and increasing the frequency and duration of hemodialysis in patients with large inter-dialytic weight gains.

2. Modifying hemodialysis prescriptions (e.g., atrium and ultrafiltration profiling, blood flow, and ultrafiltration volume) to prevent intradialytic hypertension or intradialytic hypotension.

3. Optimizing hypertension management to achieve appropriate blood pressure targets during hemodialysis (intradialytic and peridialytic hypertension) and inter-dialytic periods (<140/90 mmHg) while minimizing the use of alpha-blockers whenever possible.

## Conclusion

This study demonstrates that among the independent variables, pre-dialysis diastolic and post-dialysis systolic blood pressure have significant associations with detrimental changes in pulse pressure during hemodialysis. These factors may serve as key risk indicators for cardiovascular disease, arrhythmias, and both cardiovascular and all-cause mortality in maintenance hemodialysis patients. Future research employing more robust study designs and larger sample sizes must identify additional factors significantly contributing to detrimental pulse pressure changes during hemodialysis. Such studies will aid in developing targeted therapeutic strategies to modify pulse pressure responses during hemodialysis, potentially improving survival outcomes for maintenance hemodialysis patients.

## Limitations of the Study

Several limitations in this study should be considered. First, we did not measure intrinsic factors that could influence preload, afterload, and heart muscle contractility changes, which may affect changes in pulse pressure during hemodialysis. Additionally, the study's relatively short duration limits our ability to conclude causal relationships between the independent and dependent variables. Finally, since the study was conducted at a single hemodialysis center, the generalizability of our findings to the broader population of hemodialysis patients may be limited.

## Declarations

### Ethics approval and consent to participate

This article complied with all ethical rules at the research site.

### Competing interests

There are no conflicts of interest in writing this article.

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Not applicable.

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None.

**Author's Contribution**

Idea/concept: RD. Design: RD. Control/supervision: MP. Data collection/ processing: RD. Analysis/interpretation: RD. Literature review: RD. Writing the article: RD, Critical review: YW. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

## References

1. Collins AJ, Foley RN, Herzog C, Chavers BM, Gilbertson D, Ishani A. Excerpts from the US Renal Data System 2009 Annual Data Report. Am J Kidney Dis. 2010;55(1 Supll 1):S1– 420, A6– 7. doi:10.1053/j.ajkd.2009.10.009
2. London GM, Marchais SJ, Safar ME, Genest AF, Guerin AP, Metivier F. Aortic and large artery compliance in end-stage renal failure. Kidney Int. 1990;37(1):137–42. doi:10.1038/ki.1990.19
3. Barenbrock M, Spieker C, Laske V, Heidenreich S, Hohage H, Bachmann J, et al. Studies of the vessel wall properties in hemodialysis patients. Kidney Int. 1994;45(5):1397–400. doi:10.1038/ki.1994.182
4. Peng-Lin Y, Yue-Chun L. Pulse pressure index (pulse pressure/systolic pressure) may be better than pulse pressure for assessment of cardiovascular outcomes. Med Hypotheses. 2009;72(6):729–731. doi:10.1016/j.mehy.2008.12.041
5. Benetos A, Rudnichi A, Safar M, Guize L. Pulse pressure and cardiovascular mortality in normotensive and hypertensive subjects. Hypertension. 1998;32(3):560–564. doi:10.1161/01.hyp.32.3.560
6. Weiss A, Boaz M, Beloosesky Y, Kornowski R, Grossman E. Pulse pressure predicts mortality in elderly patients. J Gen Intern Med. 2009;24(8):893–896. doi:10.1007/s11606-009-1008-7
7. Tozawa M, Iseki K, Iseki C, Oshiro S, Yamazato M, Higashiuesato Y. Evidence for elevated pulse pressure in patients on chronic hemodialysis: A case-control study. Kidney Int. 2002;62(6):2195–2201. doi:10.1046/j.1523-1755.2002.00665.x
8. Amar J, Vernier I, Rossignol E, Bongard V, Arnaud C, Conte JJ. Nocturnal blood pressure and 24-hour pulse pressure are potent indicators of mortality in hemodialysis patients. Kidney Int. 2000;57(6):2485–2491. doi:10.1046/j.1523-1755.2000.00107.x
9. Tozawa M, Iseki K, Iseki C, Takishita S. Pulse pressure and risk of total mortality and cardiovascular events in patients on chronic hemodialysis. Kidney Int. 2002;61(2):717–726. doi:10.1046/j.1523-1755.2002.00173.x
10. Yazici H, Oflaz H, Pusuroglu H, Tepe S, Dogan C, Basci A, et al. Hypervolemia rather than arterial calcification and extracoronary atherosclerosis is the main determinant of pulse pressure in hemodialysis patients. Int Urol Nephrol. 2012;44(4):1203–1210. doi:10.1007/s11255-011-0024-9
11. Innes A, Charra B, Burden RP, Morgan AG, Laurent G. The effect of long, slow haemodialysis on patient survival. Nephrol Dial Transpl. 1999;14(4):919–922. doi:10.1093/ndt/14.4.919
12. Ozkahya M, Ok E, Cirit M, Aydin S, Akçiçek F, Başçi A, et al. Regression of left ventricular hypertrophy in haemodialysis patients by ultrafiltration and reduced salt intake without antihypertensive drugs. Nephrol Dial Transpl. 1998;13(6):1489–1493. doi:10.1093/ndt/13.6.1489
13. Ozkahya M, Ok E, Toz H, Asci G, Duman S, Basci A, et al. Long-term survival rates in haemodialysis patients treated with strict volume control. Nephrol Dial Transpl. 2006;21(12):3506–3513. doi:10.1093/ndt/gfl487

14. Inrig JK, Patel UD, Toto RD, Reddan DN, Himmelfarb J, Lindsay RM, et al. Decreased pulse pressure during hemodialysis is associated with improved 6-month outcomes. Kidney Int. 2009;76(10):1098–1107. doi:10.1038/ki.2009.340

15. Park J, Rhee CM, Sim JJ, Kim YL, Ricks J, Streja E, et al. A comparative effectiveness research study of the change in blood pressure during hemodialysis treatment and survival. Kidney Int. 2013;84(4):795–802. doi:10.1038/ki.2013.237

16. Lertdumrongluk P, Streja E, Rhee CM, Sim JJ, Gillen D, Kovesdy CP, et al. Changes in Pulse Pressure during Hemodialysis Treatment and Survival in Maintenance Dialysis Patients. Clin J Am Soc Nephrol. 2015;10(7):1179–1191. doi:10.2215/cjn.09000914

17. Klassen PS, Lowrie EG, Reddan DN, DeLong ER, Coladonato JA, Szczech LA. Association between pulse pressure and mortality in patients undergoing maintenance hemodialysis. JAMA. 2002;287(12):1548–1555. doi:10.1001/jama.287.12.1548

18. Hara M, Tanaka S, Taniguchi M, Fujisaki K, Torisu K, Masutani K, et al. Prognostic value of pre-dialysis blood pressure and risk threshold on clinical outcomes in hemodialysis patients: The Q-Cohort Study. Med. 2018;97(51):e13485. doi:10.1097/md.0000000000013485

19. Yang CY, Yang WC, Lin YP. Postdialysis blood pressure rise predicts long-term outcomes inchronic hemodialysis patients: a four-year prospective observational cohort study. BMC Nephrol. 2012;13:12. doi:10.1186/1471-2369-13-12