

A comparative study of oxidative stress, vascular calcification, and volume status in non-dippers and dippers receiving maintenance hemodialysis

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Background: Hypertension is a leading cause of cardiovascular mortality in patients with end-stage kidney disease, with 80% to 90% of dialysis patients affected. Many patients with hypertension exhibit a non-dipper blood pressure pattern that is influenced by various factors. This study investigated the relationship between blood pressure patterns, volume status, vascular diseases, and oxidative stress markers.

Methods: Forty-nine hemodialysis patients underwent 24-hour ambulatory blood pressure monitoring and were classified into “dipper” and “non-dipper” blood pressure groups. Laboratory tests, bioimpedance analysis, carotid ultrasound, and ankle-brachial index (ABI) measurements were performed, including baseline myeloperoxidase (MPO) and fetuin-A level assessments.

Results: Eleven patients were classified as dippers and 38 as non-dippers. The non-dipper group exhibited higher nighttime systolic blood pressure, consistent with their lack of nocturnal blood pressure decline. Further, this group had significantly elevated MPO levels (2.5 ng/mL vs. 1.5 ng/mL, $p = 0.03$) and accounted for all recorded deaths. No significant differences were found between the two groups regarding volume status, intima-media thickness, carotid artery calcification, or ABI.

Conclusion: Most hemodialysis patients exhibited a non-dipper pattern, which was significantly associated with increased MPO levels, suggesting a role of oxidative stress. There was no significant association with fluid overload, peripheral arterial disease, or vascular calcification. Further research is needed to explore the impact of oxidative stress on the non-dipper pattern in the hypertensive hemodialysis population.

Keywords: Ambulatory blood pressure monitoring, Renal dialysis, Hypertension, Peroxidase, Oxidative stress, Vascular calcification

Introduction

Hypertension, a risk factor for cardiovascular disease, is

prevalent among patients undergoing hemodialysis and significantly impacts mortality and morbidity rates [1]. It is estimated that 70% to 90% of hemodialysis patients have

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hypertension. Therefore, blood pressure (BP) measurement is essential in determining the prognosis of hemodialysis patients, and ambulatory BP monitoring (ABPM) has emerged as a powerful tool for assessing hypertension. ABPM has proven to be more effective in predicting the risk of cardiovascular disease than office BP measurements [2,3].

The non-dipping pattern is characterized by a lack of decline in BP during the night based on ABPM. This pattern is strongly associated with an increased risk of cardiovascular disease and higher mortality rates [4,5], and up to 70% to 80% of dialysis patients exhibit a non-dipping pattern [6,7]. The increased occurrence of hypertension and dipping patterns among patients with end-stage kidney disease can be attributed to several factors, including an imbalance due to dialysis, which results in fluid retention, atherosclerosis, vascular disease, left ventricular hypertrophy, and increased oxidative stress and inflammation. Patients with dialysis often exhibit vascular calcification, which has been linked to higher mortality from cardiovascular diseases [8]. In association with dialysis, hypertension and non-dipping BP pattern can be attributed to various factors. The prevalence of cardiovascular disease is well-documented to be markedly high among dialysis patients, necessitating the consideration of several related conditions, such as inflammation and oxidative stress, as well as vascular calcification and arteriosclerosis [9]. This study investigated the association of BP patterns with volume status, vascular calcification, and oxidative stress markers in hemodialysis patients.

Methods

Study population

Fifty-five patients undergoing maintenance hemodialysis for over three months were screened at Chung-Ang University Hospital and Sungae Hospital. Six patients were excluded: one lacked baseline laboratory data, two withdrew consent, and three did not complete ABPM. This study enrolled stable patients who received long-term hemodialysis at two centers. This study was conducted after informed consent was obtained from the participants and the subjects received sufficient explanation. It was approved by the Clinical Research Ethics Review Commit-

tee of Chung-Ang University Hospital (C2011128 [578]). The ABPM results were used to divide the 49 patients into dipper and non-dipper groups. The follow-up period for the study lasted from March 2014 to July 2017 and was conducted prospectively. Each patient was evaluated every 3 months during the first year and then annually thereafter. The median duration of follow-up was 32 months, with an interquartile range of 28 to 33 months.

Demographic and clinical data of the study patients

Age, sex, underlying kidney disease, and hemodialysis duration were investigated. Vascular access, dialysis session, dry weight, height, and body mass index were also recorded. Laboratory tests were performed, and dialysis adequacy, blood myeloperoxidase (MPO), and fetuin-A levels were measured.

Laboratory data

Venous blood was collected before dialysis in vacutainers (Becton-Dickinson) containing K₂EDTA. The samples were centrifuged for 15 minutes at 3,000 rpm, and the plasma was separated and stored at -20 °C until analysis. All other data, including hematological and biochemical parameters, were obtained from the patient's dialysis records. The data used for this study were anonymized and kept confidential. Serum fetuin-A (Biovender Research and Diagnostic Products) and MPO levels (ab119605; Abcam) were performed via the enzyme-linked immunosorbent assay kit.

Ambulatory blood pressure measurements and blood pressure during dialysis

BP was measured using office (during dialysis) BP and ABPM. Office BP was measured in a sitting position before and after hemodialysis using a validated automatic sphygmomanometer. The average of three measurements taken on the non-fistula arm after a 5-minute rest was used for analysis. After completion of hemodialysis, ABPM was measured using a TM-2430 ambulatory BP monitor (A&D Co.), and the machine was returned the day after hemodialysis. Daytime was defined as 06:00–22:00 and nighttime as 22:00–06:00, in accordance with standard ABPM proto-

cols. The mean systolic (SBP) and diastolic BPs (DBP) over 24 hours were calculated, and the nocturnal BP drop was measured. A decrease of $\geq 10\%$ in nocturnal BP compared with daytime BP was defined as a dipper pattern, and a decrease of $< 10\%$ was defined as a non-dipper pattern.

Bioimpedance analysis

Bioimpedance analysis was performed before dialysis after the patient rested for at least 30 minutes in the supine position using InBody S10 (InBody Co., Ltd.). Intracellular fluid volume, extracellular fluid volume (extracellular water, ECW), and total body water (TBW) were calculated through bioimpedance analysis. The edema index was defined as the value obtained by dividing the ECW by TBW. The appendicular skeletal muscle mass index (ASMI) was determined based on segmental body composition and skeletal muscle mass, using the formula: $ASMI = \text{total limb lean mass} / \text{height}^2$. In line with the recommendations from the Asian Working Group for Sarcopenia, we classified ASMI values of less than 7.0 kg/m^2 for males and less than 5.7 kg/m^2 for females as indicating “low skeletal muscle mass” in our study [10].

Measurement of carotid artery calcification and intima-medial thickness via carotid ultrasound

The presence of intima-medial thickness (IMT) and carotid plaque and calcification was assessed by an experienced ultrasound specialist. High-resolution B-mode ultrasound (iU22; Philips Ultrasound) was used to evaluate the common carotid artery (CCA)-IMT and carotid plaques at the CCA, CCA bifurcation, and proximal internal carotid artery (ICA). Carotid artery plaque was defined as a focal structure that encroached into the arterial lumen by $\geq 0.5 \text{ mm}$ or 50% of the surrounding IMT value or demonstrated a thickness $> 1.5 \text{ mm}$ as measured from the media-adventitia interface to the intima-lumen interface [11].

Measurement of the ankle-brachial index

At baseline, SBP in the bilateral arms (brachial artery) and bilateral ankles (posterior tibial artery or dorsalis pedis artery) were measured three times in the supine position using a hand-held Doppler device (BIDOP ES-100V3; Ha-

deco, Inc.). The ankle-brachial index (ABI) value was determined by taking the higher pressure of the two arteries at the ankle and dividing it by the higher brachial arterial systolic pressure. The mean of the three ABI measurements was then calculated for each individual.

Statistical analysis

Descriptive statistics are presented as numbers (percentages) or means and standard deviations. The Mann-Whitney U test and Fisher exact test were used to analyze continuous or categorical variables. Logistic regression analysis was conducted to determine the odds ratio (OR) and 95% confidence interval (CI) for the non-dipper pattern. The multivariate analysis utilized variables with $p < 0.10$ in the univariate analysis; the clinical variables assessed included age, sex, presence of diabetes mellitus, hypertension, hyperlipidemia, dialysis duration, body mass index, pre- and post-dialysis BP, and laboratory findings including levels of hemoglobin, glucose, albumin, creatinine, uric acid, calcium, phosphorous, total cholesterol, and intact parathyroid hormone [12,13]. Ultimately, the multivariate model was adjusted for age and post-dialysis SBP. To explore the relationships among variables, Spearman rank correlation analysis was performed and visualized as a heatmap. Additionally, overall survival and cardiovascular event-free survival were compared using Kaplan-Meier curves, and differences between groups were assessed using the log-rank test ($p < 0.05$). IBM SPSS version 19 (IBM Corp.) was used for all statistical analyses. All tests were two-tailed, and the threshold for statistical significance was set at $p < 0.05$.

Results

The study included 49 patients (mean age, 62.9 ± 10.4 years), and 57.1% of them were male (Table 1). The primary cause of kidney disease was diabetes mellitus (67.3%), followed by hypertension, glomerulonephritis, and other causes. Among the 49 patients who underwent hemodialysis, 38 (77.5%) belonged to the non-dipper group and 11 were in the dipper group. There were no significant differences in weight, dialysis adequacy, duration of dialysis, or basic blood test results between the two groups.

Naturally, nocturnal hypertension was more prevalent in

Table 1. Baseline characteristics

Characteristic	Dipper (n = 11)	Non-dipper (n = 38)	Total (n = 49)	p-value
No. of patients	11	38	49	
Age (yr)	67.9 ± 7.8	61.4 ± 10.7	62.9 ± 10.4	0.09
Male sex	7 (63.6)	22 (57.9)	28 (57.1)	0.62
Dialysis vintage (wk)	190 ± 166	237 ± 175	226 ± 172	0.44
Primary kidney disease				0.87
Diabetes mellitus	8 (72.7)	25 (65.8)	33 (67.3)	
Hypertension	3 (27.3)	9 (23.7)	12 (24.5)	
Glomerulonephritis	0 (0)	1 (2.6)	1 (2.0)	
Others	0 (0)	3 (7.9)	3 (6.1)	
Comorbidities				
Diabetes mellitus	8 (72.7)	25 (65.8)	33 (67.3)	>0.99
Hypertension	7 (63.6)	26 (68.4)	33 (67.3)	>0.99
Hyperlipidemia	2 (18.2)	10 (26.3)	12 (24.5)	0.71
Dry weight (kg)	58.6 ± 5.3	57.5 ± 9.1	57.7 ± 8.4	0.70
BMI (kg/m ²)	22.7 ± 2.0	23.1 ± 3.1	23.0 ± 2.9	0.64
Ultrafiltration (kg)	1.7 ± 0.9	2.1 ± 0.7	2.0 ± 0.8	0.44
Kt/V	1.64 ± 0.2	1.60 ± 0.3	1.61 ± 0.3	0.66
Vascular access				0.17
Arteriovenous fistula	3 (27.3)	18 (47.4)	21 (42.9)	
Arteriovenous graft	8 (72.7)	16 (42.1)	24 (49.0)	
Catheter	0 (0)	4 (10.5)	4 (8.2)	
Session per week				0.06
2 times	1 (9.1)	0 (0)	1 (2.0)	
3 times	10 (90.9)	38 (100)	48 (98.0)	
Hemoglobin (g/dL)	10.7 ± 1.3	10.4 ± 1.2	10.5 ± 1.3	0.77
Protein (g/dL)	6.6 ± 0.5	6.4 ± 0.5	6.5 ± 0.5	0.57
Albumin (g/dL)	3.8 ± 0.4	3.8 ± 0.3	3.8 ± 0.3	>0.99
Calcium (mg/dL)	9.0 ± 3.0	10.4 ± 2.4	10.1 ± 2.6	0.68
Phosphorus (mg/dL)	4.7 ± 1.8	4.8 ± 1.6	4.8 ± 1.6	0.74
Cholesterol (mg/dL)				
Total	138.3 ± 45.1	138.7 ± 30.8	138.6 ± 34.0	0.40
HDL	34.9 ± 8.2	43.9 ± 13.6	41.9 ± 13.1	0.049
LDL	74.3 ± 17.4	77.4 ± 27.0	76.7 ± 25.0	0.69
Triglyceride (mg/dL)	163.1 ± 180.5	116.4 ± 82.1	126.9 ± 111.2	0.69
hs-CRP (mg/L)	1.6 ± 2.4	2.7 ± 6.6	2.5 ± 5.9	0.52

Data are expressed as number only, mean ± standard deviation, or number (%).

BMI, body mass index; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein.

the non-dipper group (73.7%, $p < 0.001$). The SBP and DBP measured before dialysis in the dialysis room were 138.0 ± 28.4 and 66.7 ± 14.3 mmHg, respectively, in the dipper group and 148.6 ± 29.9 and 71.1 ± 17.0 mmHg, respectively, in the non-dipper group ($p = 0.15$ and $p = 0.34$, respectively) (Fig. 1). Although the non-dipper group showed a higher trend, there was no significant difference.

The average SBP and DBP measured with ABPM were

126.4 ± 9.3 and 70.9 ± 8.4 mmHg, respectively, in the dipper group and 135.6 ± 17.7 and 78.6 ± 10.3 mmHg, respectively, in the non-dipper group ($p = 0.03$ and $p = 0.02$, respectively). The SBP during sleep was significantly different between the dipper and non-dipper groups, with values of 111.0 ± 11.9 mmHg and 136.0 ± 19.5 mmHg, respectively (both $p < 0.001$). While there was no significant difference in SBP between the two groups during the day ($p = 0.28$),

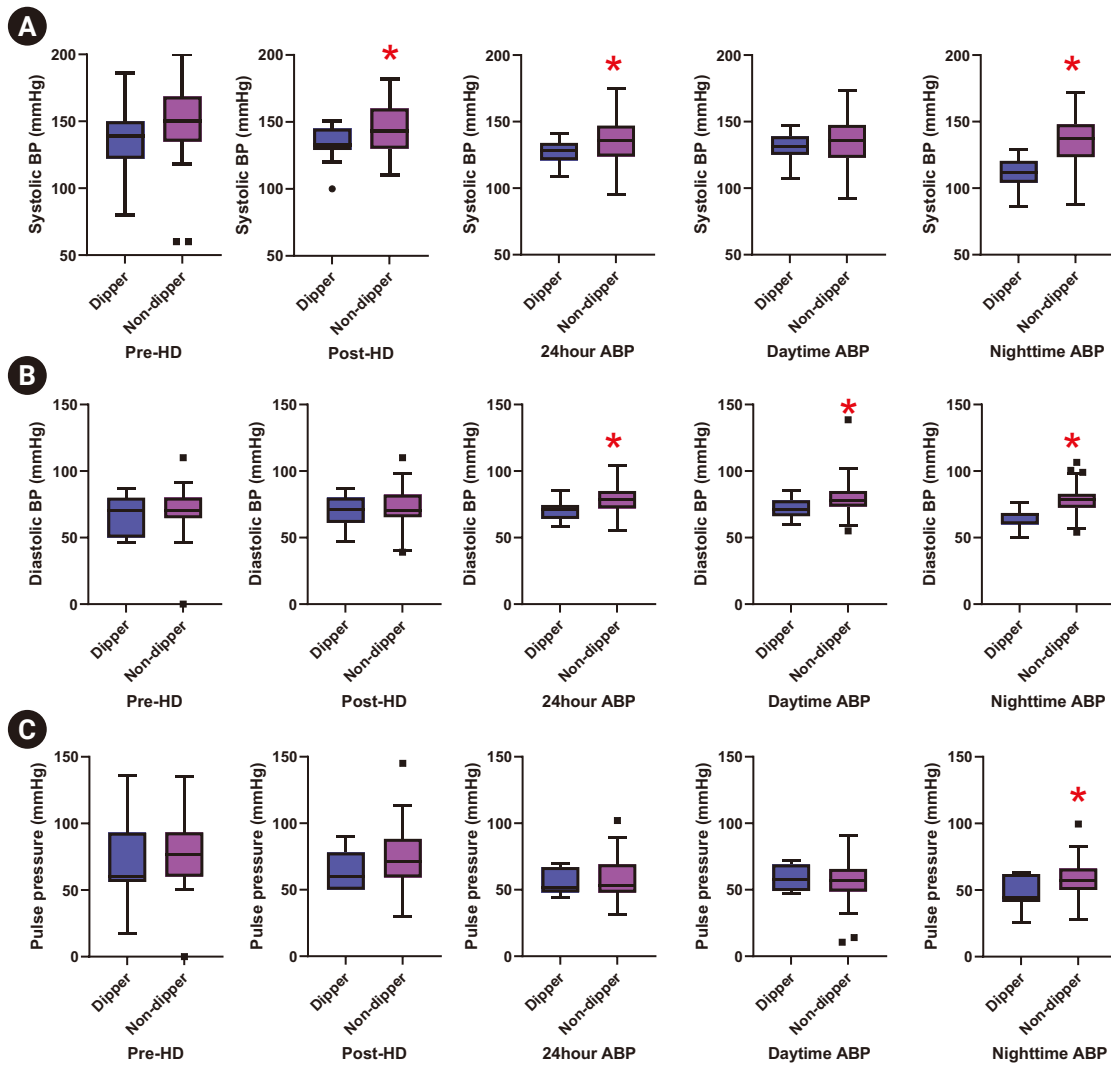


Figure 1. A comparative analysis of systolic and diastolic BPs between the dipper and non-dipper groups before and after HD and the 24-hour, daytime, and nighttime average BPs. This comparison provides insights into the differences in BP patterns in these two groups, which may have implications for cardiovascular risk.

ABP, ambulatory blood pressure; BP, blood pressure; HD, hemodialysis.

* $p < 0.05$, statistically significant.

the DBP showed a statistically significant difference ($p = 0.045$).

In terms of edema and skeletal muscle mass, edema (ECW/TBW, >0.4) was observed in six participants (54.5%) in the dipper group and 25 participants (65.8%) in the non-dipper group, though this difference was not statistically significant ($p = 0.50$) (Table 2). The non-dipper group also had a higher proportion of individuals with low skeletal muscle mass (26.3%) compared to the dipper group (18.2%), but this difference was similarly not statistically

significant ($p = 0.71$).

In this study, 42.9% of hemodialysis patients had carotid plaques, and 57.1% exhibited carotid artery calcification (Table 3). No significant differences between the dipper and non-dipper groups were observed in IMT measurements or carotid artery plaques. The mean IMT at the distal CCA was 5.8 ± 2.6 mm in the dipper group and 5.5 ± 0.8 mm in the non-dipper group ($p = 0.67$). Similarly, no significant differences were found in IMT measurements at the bifurcation ($p = 0.46$) or proximal ICA ($p = 0.80$). The

Table 2. Results of bioimpedance in non-dipper and dipper patients

Variable	Dipper (n = 11)	Non-dipper (n = 38)	p-value
Soft lean mass (kg)	43.0 ± 6.5	42.9 ± 8.5	0.99
Fat-free mass (kg)	45.6 ± 6.8	45.5 ± 8.9	0.99
Skeletal muscle mass (kg)	24.4 ± 4.0	24.2 ± 5.3	0.94
Appendicular skeletal muscle mass index (kg/m ²)	7.3 ± 1.0	7.3 ± 1.2	0.99
Low skeletal muscle mass	2 (18.2)	10 (26.3)	0.71
Percent body fat (%)	25.4 ± 9.5	23.6 ± 9.5	0.58
Phase angle	4.5 ± 1.1	4.8 ± 2.5	0.66
Edema index (ECW/TBW)	0.399 ± 0.012	0.403 ± 0.010	0.39
ECW/TBW >0.4	6 (54.5)	25 (65.8)	0.50

Data are expressed as mean ± standard deviation or number (%).

ECW, extracellular water; TBW, total body water.

Table 3. Comparison of carotid artery calcification and plaques between the dipper and non-dipper groups

Area of calcification	Dipper (n = 11)	Non-dipper (n = 38)	Total (n = 49)	p-value
IMT measurement				
Distal CCA (mm)	5.8 ± 2.6	5.5 ± 0.8	5.7 ± 0.3	0.67
CCA bifurcation (mm)	10.4 ± 6.9	12.2 ± 8.0	10.8 ± 1.0	0.46
Proximal ICA (mm)	6.2 ± 2.1	6.0 ± 3.5	6.1 ± 0.4	0.80
Carotid plaque	5 (45.5)	16 (42.1)	21 (42.9)	0.90
Carotid artery calcification	6 (54.5)	22 (57.9)	28 (57.1)	0.77
Right distal CCA	0 (0)	3 (7.9)	3 (6.1)	0.33
Right bifurcation	4 (36.4)	14 (36.8)	18 (36.7)	0.93
Right proximal ICA	0 (0)	7 (18.4)	7 (14.3)	0.12
Left distal CCA	0 (0)	3 (7.9)	3 (6.1)	0.33
Left bifurcation	6 (54.5)	17 (44.9)	23 (46.9)	0.62
Left proximal ICA	1 (9.1)	7 (18.4)	8 (16.3)	0.42

Data are expressed as mean ± standard deviation or number (%).

CCA, common carotid artery; ICA, internal carotid artery; IMT, intima-medial thickness.

prevalence of carotid artery plaques was 45.5% in the dipper group and 42.1% in the non-dipper group ($p=0.90$), and carotid artery calcification occurred in 54.5% and 57.9% of patients in the dipper and non-dipper groups, respectively, which was also not statistically significant ($p = 0.77$). Plaques at specific sites, such as the right and left bifurcation, similarly showed no significant differences between the two groups ($p > 0.05$).

A total of 12.5% of the patients had an ABI <0.9, and there was no discernible difference between the two groups ($p = 0.61$). In the non-dipper group, one patient exhibited arterial occlusive disease; however, none with a significantly reduced ABI showed clinical symptoms, such as claudication, rest pain, or ulcer. In contrast, two patients in the non-dipper group displayed intermittent claudication.

MPO levels were higher in the non-dipper group (2.5 ± 1.5 ng/mL) than in the dipper group (1.5 ± 0.9 ng/mL, $p = 0.03$) (Fig. 2). This association persisted after the adjustment for age and post-dialysis SBP (OR, 3.1; 95% CI, 1.1–8.7; $p = 0.03$). Fetuin-A levels were 116.1 ± 37.0 ng/mL in the dipper group and 112.3 ± 27.6 ng/mL in the non-dipper group, showing no significant difference between the two groups ($p = 0.44$). When divided by the median value of fetuin-A, the non-dipper group had a higher proportion of patients with lower fetuin-A levels than the dipper group (52.6% vs. 36.4%); however, this difference was still not statistically significant ($p = 0.496$).

A Spearman correlation analysis was performed to assess the associations between BP parameters (pre-/post-hemodialysis SBP, 24-hour/daytime/nighttime SBP),

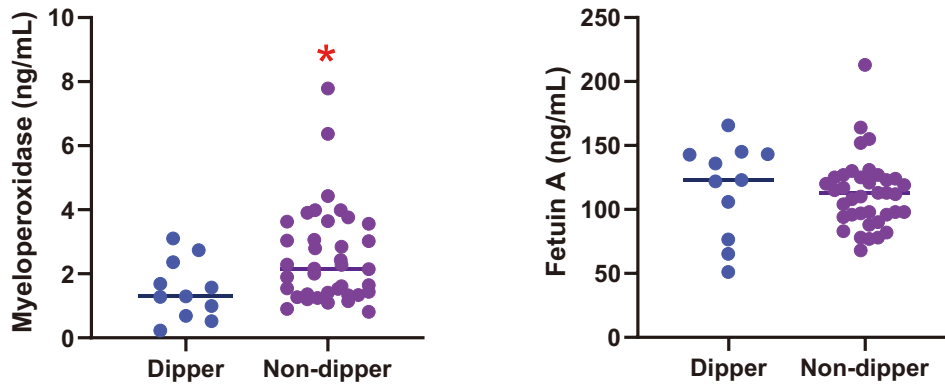


Figure 2. Comparison of myeloperoxidase and fetuin-A levels between the dipper and non-dipper groups. Myeloperoxidase, an oxidative stress and inflammation marker, was significantly higher in the non-dipper group. In contrast, fetuin-A, a biomarker of vascular calcification, showed no statistically significant difference between the two groups.

* $p < 0.05$, statistically significant.

bioimpedance indices (ECW/TBW, skeletal muscle index, phase angle), vascular measurements (distal CCA, CCA bifurcation, proximal ICA, ABI), and oxidative markers (MPO, fetuin-A). As shown in Fig. 3, most pairs exhibited weak or nonsignificant correlations. However, phase angle and ECW/TBW demonstrated a strong inverse relationship ($r = -0.81$), suggesting that higher ECW load was accompanied by reduced phase angle values. Overall, no other robust associations were observed that could imply meaningful clinical interactions.

Although five recorded deaths occurred exclusively in the non-dipper group, this difference was not statistically significant. Specifically, mortality occurred in 10.5% of the non-dipper group and did not occur in the dipper group ($p = 0.10$) (Fig. 4A). Of the five deaths, two were due to cardiovascular events, while three were related to non-cardiovascular infections. In addition, the overall incidence of cardiovascular events did not differ significantly between the two groups ($p = 0.78$) (Fig. 4B).

Discussion

This study investigated the prevalence of the non-dipping pattern using ABPM and its correlation with various cardiovascular and oxidative stress markers in 49 hemodialysis patients. Consistent with previous studies, most (77.5%) displayed a non-dipping pattern [6,7]. Although the mortality rate was higher in the non-dipper group, this difference was nonsignificant.

In patients with hypertension, the non-dipping pattern is associated with several clinical conditions, including obesity, diabetes mellitus, metabolic syndrome, and increased activity of the sympathetic nervous system; however, the precise pathophysiologic mechanisms remain unclear [14–16]. Among dialysis patients, the non-dipping pattern is primarily related to left ventricular hypertrophy, which could indicate volume overload, chronic inflammation evidenced by elevated levels of interleukin-6 and C-reactive protein, or cardiovascular diseases [17,18]. Both chronic kidney disease and hypertension predispose patients to conditions that favor vascular damage via inflammatory and oxidative stress pathways, contributing to greater arterial stiffness and atherosclerosis. These factors are closely intertwined with the non-dipping BP pattern observed in these patients.

Volume overload is closely related to the development of arterial stiffness, and studies using the ECW/TBW ratio (>0.4), commonly used as a measure of volume overload in dialysis patients, have also suggested this possibility [18–20]. In general, the prevalence of hypertension in hemodialysis patients is observed in approximately 80% to 90% of cases. However, in a study of transplant patients, the prevalence of hypertension decreased to 50.4% after transplantation, while non-dipping BP patterns were observed in 65.8% of cases [19]. The relationship between non-dipping patterns and volume status has been speculated, as volume overload tends to improve after kidney transplantation in patients with chronic kidney disease. However, in

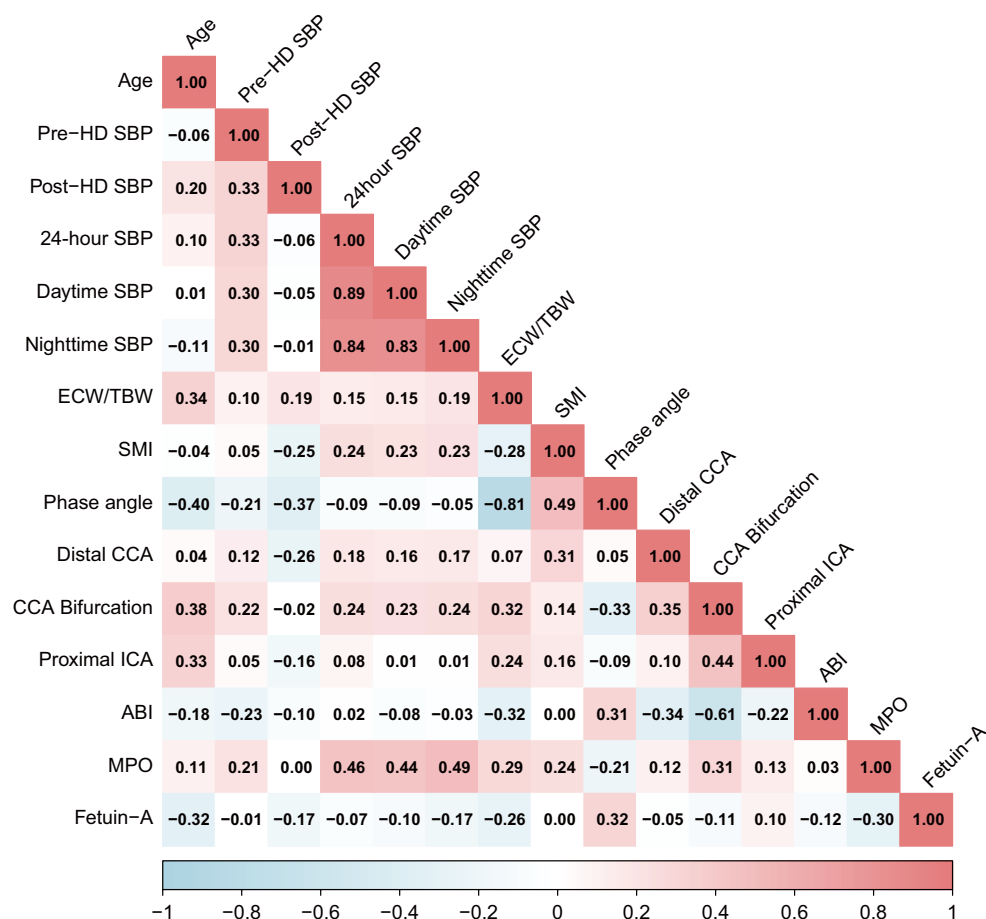


Figure 3. Spearman correlation matrix. This triangular heatmap shows Spearman correlation coefficients between clinical and biochemical variables. Positive correlations are in red, and negative correlations are in blue, with stronger colors indicating stronger relationships. Diagonal values represent self-correlations (1.0).

ABI, ankle-brachial index; CCA, common carotid artery; ECW, extracellular water; HD, hemodialysis; ICA, internal carotid artery; MPO, myeloperoxidase; SBP, systolic blood pressure; SMI, skeletal muscle mass index; TBW, total body water.

this study, the indicators representing the volume overload status in patients with non-dipping patterns were high (>0.4), but no statistical significance was found. This finding is consistent with that of Agarwal [21], suggesting that while there is a relationship between volume status and BP, controlling volume overload does not necessarily improve non-dipping patterns.

This study investigated the relationship between dipping patterns, the presence of plaques, and IMT in the carotid artery. Carotid plaque and calcification are common and serious issues in hemodialysis patients, particularly in the abdominal aorta and peripheral muscular arteries [22]. Studies have indicated that vascular calcification can predict mortality in these patients [23]. Interestingly, no major

differences were observed between the two groups, suggesting that traditional indicators of vascular disease may not be strongly linked to a non-dipper pattern. Although measures such as IMT and the high prevalence of carotid artery plaques are commonly used to assess cardiovascular risk in the general population, their effectiveness in distinguishing different BP patterns among hemodialysis patients may be limited.

ABI, commonly used to assess peripheral vascular disease, is crucial in predicting mortality and cardiovascular events in hemodialysis patients. Research consistently shows that a low ABI is associated with a high risk of mortality and cardiovascular complications [24]. The prevalence of peripheral arterial occlusive disease is high in

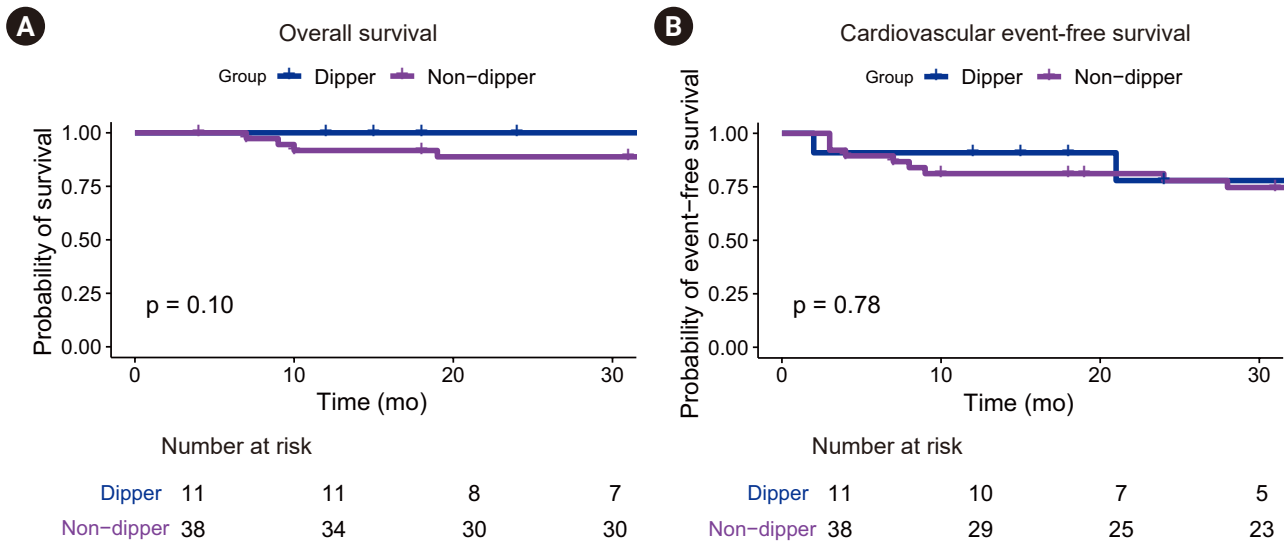


Figure 4. Survival analysis between the dipper and non-dipper groups. (A) Kaplan-Meier curves for overall survival in dipper and non-dipper groups. Although the dipper group showed a trend towards a higher mortality rate compared to the non-dipper group, the difference was not statistically significant. (B) Kaplan-Meier curves for cardiovascular event-free survival. No significant difference was found between the two groups.

hemodialysis patients (15.6%) [25]. While the positivity rate of other vascular markers was very high, the proportion of patients with an ABI ≤ 0.9 was not high in our group (12.5%). Additionally, there was no correlation with the non-dipping patterns. The recruited patient group did not have clinically significant peripheral vascular disease, which could have influenced the results. Further studies are needed to investigate the potential relationship between the non-dipping pattern and advanced peripheral vascular disease.

The non-dipper group exhibited elevated levels of MPO, an oxidative stress marker. In hemodialysis patients, MPO levels are often elevated and have been associated with both endothelial dysfunction and atherosclerosis [26]. Furthermore, the hemodialysis procedure itself can amplify MPO activity [27,28], partly due to increased neutrophil apoptosis and subsequent microinflammation [29].

In individuals with a non-dipping BP pattern, the insufficient decline in nocturnal BP results in persistent hemodynamic stress, potentially stemming from inadequate suppression of the sympathetic nervous system and relatively greater fluid retention [30]. This sustained stress can further elevate MPO levels. These observations align with the findings of prior studies that have established a link between non-dipping hypertension and oxidative stress

[31,32]. Although we did not observe significant differences in vascular calcification or fluid overload between the dipper and non-dipper groups, the elevated MPO levels suggest the involvement of an additional oxidative stress pathway in the non-dipper population.

In contrast, fetuin-A levels did not differ between the two groups. Whereas MPO is closely linked to acute oxidative stress and inflammation, fetuin-A may reflect biomarker of vascular calcification, potentially requiring larger samples or longer follow-ups to detect meaningful differences [33]. Further investigations are needed to clarify the role of fetuin-A in the non-dipping pattern observed in hemodialysis patients.

Finally, mortality rates within each group were analyzed. Although the non-dipper group had a higher number of recorded deaths, the disparity was not statistically significant. Nevertheless, the documented fatalities only transpired within the non-dipper cohort, underscoring the potential clinical significance of this BP pattern in prognosticating unfavorable consequences. However, several other BP parameters (e.g., post-hemodialysis SBP, 24-hour SBP/DBP, daytime DBP) were higher in non-dippers, suggesting that elevated BP itself may confound the relationship between non-dipping and outcomes. Consequently, the non-dipping pattern cannot be concluded to independently impact

prognosis without adequately adjusting for these BP differences.

This study had some limitations. The sample size was relatively small, and long-term follow-up was infeasible. Moreover, the study predominantly focused on Korean patients at the two hospitals, potentially restricting the generalizability of the findings to a broader population. Additionally, the study may have selection bias because no patients had advanced peripheral arterial occlusive disease. Furthermore, detailed information on BP medication usage and cardiovascular disease history, including echocardiography data, was not available, which may limit the interpretation of the findings.

However, this study significantly contributes to our knowledge of the complex associations among BP patterns, vascular diseases, inflammation, and oxidative stress. Although certain promising factors, such as nocturnal hypertension and MPO levels, show potential as predictive markers, it is crucial to conduct studies with larger groups of participants and extended observation periods for more definitive results. In conclusion, our findings suggest that the non-dipping BP pattern is common in hemodialysis patients and may be linked to elevated oxidative stress, as indicated by higher MPO levels. Nevertheless, no significant differences were observed in vascular calcification or fluid overload variables between dipper and non-dipper groups. Although the non-dipper group accounted for all recorded deaths, this difference did not reach statistical significance, leaving the prognostic impact of non-dipping patterns inconclusive. These results underscore the importance of larger, long-term studies to determine whether non-dipping patterns exert an independent effect on clinical outcomes beyond that of traditional risk factors such as elevated BP levels.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available from the corresponding author upon reasonable request.

Authors' contributions

Conceptualization: HK, JHH, CHM, SHK

Funding acquisition: SHK

Investigation: HK, JS, JHH, HRK, CHM, SHK

Methodology: HK, JS, JHH, HRK, SHK

Visualization: HES, SC, JMC, SK, SHK

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