High Blood Pressure & Cardiovascular Prevention (2025) 32:543–552
https://doi.org/10.1007/s40292-025-00733-w

Online ISSN 1179-1985

ORIGINAL ARTICLE

A Practical Predictor for Identifying Reverse-Dipper Blood Pressure Patterns: Left Atrial Coupling Index

Ayca Arslan[1] · Dogan Ilıs[1] · Inanc Artac[1] · Muammer Karakayali[1] · Timor Omar[1] · Zihni Cagin[1] · Zulfiye Kuzu[2] · Yavuz Karabag[1] · Ibrahim Rencuzogullari[1]

Received: 12 May 2025 / Accepted: 14 July 2025 / Published online: 28 July 2025
© The Author(s) 2025

Abstract

Introduction Hypertension is a common and persistent disorder and mostly causes myocardial structural and functional abnormalities. As a subtype pattern of HT, the reverse-dipper blood pressure (BP) is associated with worse cardiovascular outcomes and early-phase subclinical myocardial damage compared to other patterns. The Left Atrial Coupling Index (LACI) is a novel echocardiographic parameter developed to assess the mechanical function.

Aim The aim of this study was to investigate the role of the LACI in predicting the reverse-dipper BP pattern in patients with hypertension.

Methods A total of 404 hypertensive patients who underwent 24-hour ambulatory blood pressure monitoring were prospectively enrolled. Patients were classified into dipper, non-dipper, and reverse-dipper groups based on their nocturnal BP profiles. Comprehensive echocardiographic evaluations were performed, and LACI was calculated for each patient.

Results A reverse-dipper BP pattern was observed in 26%($n=105$) of the 404 patients. Those with a reverse-dipper BP pattern exhibited higher mitral E/A ratio, E/Em means, left atrial volume index (LAVI), and LACI, along with lower Em septal, Am lateral mitral, and Am septal values. LACI (OR:3.837, 95% CI: 2.620–5.620, $p<0.001$), LAVI, and Am lateral mitral value were found to be independent predictors of the reverse-dipper BP pattern. ROC curve comparison demonstrated that LACI was a better predictor of the reverse-dipper BP pattern than LAVI.

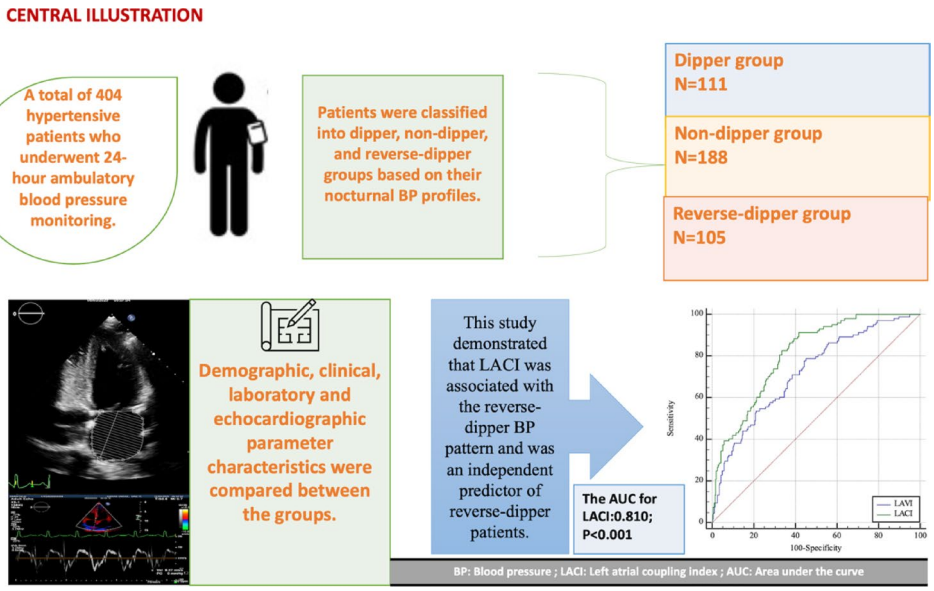
Conclusions Our study demonstrates that LACI, an easily accessible echocardiographic parameter, is a more robust predictor of the reverse-dipper BP pattern compared to traditional echocardiographic markers.

✉ Ayca Arslan
hivda.arslan@hotmail.com

[1] Department of Cardiology, M.D. Kafkas University School of Medicine, Kars, Turkey

[2] Department of Cardiology, M.D. Kayseri City Hospital, Kayseri, Turkey

Graphic abstract



Keywords Left Atrial Coupling Index · Reverse-dipper Blood Pressure Pattern · 24-hour Ambulatory Blood Pressure Monitoring · Hypertension · Nocturnal Blood Pressure Patterns

1 Introduction

Hypertension is a major risk factor for cardiovascular morbidity and mortality worldwide [1]. In addition to absolute blood pressure (BP) values, circadian BP patterns, particularly nocturnal BP behavior, have received increasing attention as a key determinant of cardiovascular risk [2]. In healthy individuals, a physiological decrease in BP occurs at night, known as the dipping pattern. However, some hypertensive patients exhibit altered nocturnal BP regulation, including non-dipper BP (reduced nocturnal BP decline) and reverse-dipper BP (nocturnal BP higher than daytime values). Reverse-dipper BP is associated with a higher risk of target organ damage and adverse cardiovascular events compared to other patterns [3, 4].

The pathophysiology of reverse-dipper BP is complex, involving autonomic dysfunction, arterial stiffness, and subclinical cardiac structural abnormalities [5, 6]. One emerging area of interest is the role of left atrial (LA) remodeling and dysfunction in contributing to abnormal nocturnal BP patterns. The LA plays a critical role in modulating left ventricular filling pressures and reflects chronic diastolic burden [7].

The Left Atrial Coupling Index (LACI) is a novel echocardiographic parameter designed to evaluate the mechanical function of the LA. A higher LACI suggests decreased LA contractile performance and increased atrial load, and it acts as an integrative measure for LA coupling. Elevated LACI values have been associated with diastolic dysfunction, heart failure with preserved ejection fraction, and reduced ejection fraction [8–10]. Despite the growing recognition of the importance of LA coupling in cardiovascular disease, its relationship with abnormal circadian BP patterns, particularly reverse-dippers, has not been fully elucidated. Given that reverse-dipper BP is frequently associated with subclinical cardiac remodeling, impaired LA coupling may play a central role in its pathogenesis.

In this prospective study, we aimed to investigate the relationship between LACI and nocturnal BP patterns, particularly the reverse-dipper BP pattern, in hypertensive patients.

2 Methods

2.1 Study Design and Population

This prospective observational study was conducted in a tertiary health center between January 1st and April 30th, 2025, and included 462 patients. Hypertensive patients who presented to the cardiology outpatient clinic and were referred for 24-hour ambulatory blood pressure monitoring (ABPM) were enrolled in the study. A total of 58 patients were excluded due to conditions that could potentially alter echocardiographic measurements and confound the assessment of hypertension-related cardiac changes. Patients with

atrial fibrillation or other significant arrhythmias, moderate to severe valvular heart disease, a history of myocardial infarction, ischemia-related wall motion abnormalities, and end-stage renal disease requiring dialysis were excluded. After exclusion, the remaining 404 patients were included in the study. The patients were classified into three groups based on their nocturnal BP patterns: dipper, non-dipper, and reverse-dipper (Fig. 1).

The study was approved by the local ethics committee and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

2.2 Ambulatory 24-Hour Blood Pressure Monitoring and Patient Classification

All patients underwent 24-hour ABPM using a validated oscillometric device (SpaceLabs Healthcare Model 90207, Snoqualmie, WA, USA). BP measurements were taken at 15–30-minute intervals during the daytime (07:00–23:00) and at 30–60-minute intervals during the night (23:00–07:00). According to nocturnal BP patterns, patients were classified into three groups: dipper ($n=111$): nocturnal systolic BP decrease of greater than or equal to 10%; non-dipper ($n=188$): nocturnal systolic BP decrease of less than 10%; reverse-dipper ($n=105$): nighttime systolic BP higher than daytime values [11].

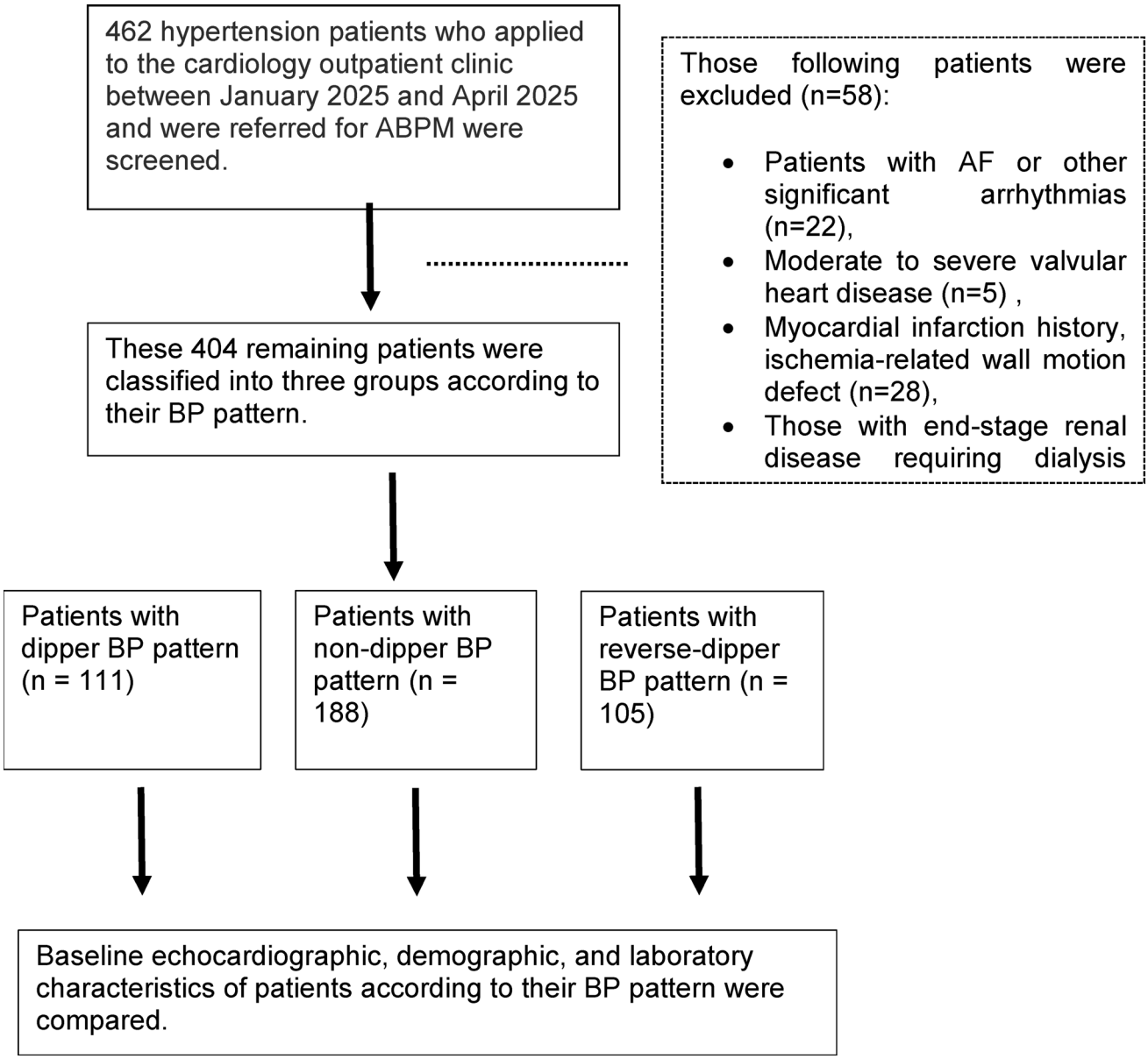


Fig. 1 Flowchart illustrating the study design and patient selection process

2.3 Echocardiographic Evaluation

All patients underwent transthoracic echocardiography (TTE) at their initial outpatient visit using a Philips EPIQ 7 C ultrasound system with an X5-1 matrix transducer. Standard 2D, M-mode, pulsed-wave Doppler, and tissue Doppler imaging (TDI) acquisitions were performed in accordance with American Society of Echocardiography (ASE) guidelines [12, 13].

LA volume was measured at the ventricular end-systole using the biplane area-length method from apical four-chamber and two-chamber views. The left atrial volume index (LAVI) was calculated by indexing the LA volume to body surface area (BSA). LACI was calculated as the ratio of LAVI to the septal Am velocity measured by tissue Doppler imaging (TDI) [8].

The left ventricular mass index (LVMI) was calculated using the Devereux formula and indexed to BSA. Left ventricular wall thickness (interventricular septum and posterior wall) was measured at the end-diastole. The left ventricular ejection fraction (LVEF) was calculated using the modified Simpson biplane method.

Transmitral inflow velocities (E and A waves) were obtained by pulsed-wave Doppler in the apical four-chamber view by placing the sample volume at the mitral leaflet tips. The TDI was performed at the septal and lateral mitral annulus, recording the early diastolic velocity (Em) and late diastolic velocity (Am). The E/ Em ratio was calculated using the mitral inflow E wave velocity divided by the average of the septal and lateral Em velocities.

2.4 Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) for normally distributed data or as median (interquartile range, IQR) for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. A one-way ANOVA was applied to compare variables across the three groups (dipper, non-dipper, and reverse-dipper). When significance was detected, Tukey's post-hoc test was used for pairwise comparisons. The Kruskal–Wallis test was used for non-normally distributed variables. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Relationships between LAVI, LACI parameters, and other echocardiographic/clinical variables were evaluated using Pearson's correlation coefficient (for normally distributed data) or Spearman's rank correlation coefficient (for non-normal data). Univariate logistic regression analysis was conducted to examine the association between clinical and echocardiographic variables and the reverse-dipper pattern. Variables with a p-value less than 0.05 and those considered clinically relevant were selected for multivariate analysis. A multivariate logistic regression analysis was performed to determine the independent predictors of the reverse-dipper BP pattern. The results were presented as odds ratios (OR) with 95% confidence intervals (CI). Septal Am velocity was excluded from the multivariate analysis due to its confounding interaction with other echocardiographic variables. The diagnostic performance of LAVI and LACI in predicting reverse-dipper hypertension was assessed by receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was calculated for each parameter. Optimal cut-off values were determined by the Youden Index, maximizing sensitivity and specificity. Sensitivity, specificity, positive predictive value, and negative predictive value were reported for the identified cut-offs. A p-value of less than 0.05 was considered statistically significant for all analyses.

3 Results

In this study, the mean age of the 404 patients was 59 ± 13 years, and 50.5% of them were female. Based on the pattern of hypertension, the patients were divided into the following three groups: dipper (n = 111, 27.5%), non-dipper (n = 188, 46.5%), and reverse-dipper (n = 105, 26%). Patients in the reverse-dipper group were older, had higher BNP levels, and exhibited higher sleep systolic BP, while lower hemoglobin and GFR levels were found in this group. Table 1 presents the baseline characteristics and laboratory parameters of the study population.

The reverse-dipper group had significantly higher left-sided metrics than the dipper and non-dipper BP pattern groups, including E/A ratio (0.85 ± 0.39 vs. 0.85 ± 0.24 vs. 0.79 ± 0.26, respectively; p = 0.028), LA max volume (55.0 ± 19.1 vs. 39.9 ± 12.8 vs. 44.3 ± 15.4, respectively; p < 0.001), E/Em mean (9.5 ± 4.4 vs. 8.3 ± 2.6 vs. 8.4 ± 3.4, respectively; p = 0.041), LACI (3.5 ± 1.9 vs. 1.9 ± 0.6 vs. 2.2 ± 0.9, respectively; p < 0.001), and LAVI (28.5 ± 9.1 mL/m² vs. 20.5 ± 6.2 vs. 22.6 ± 7.5 mL/m², respectively; p < 0.001). In addition, Em septal (6.2 ± 2.0 vs. 7 ± 1.7 vs. 6.8 ± 2.2, p = 0.001), Am septal (8.7 ± 2.0 vs. 10.9 ± 2.1 vs. 10.3 ± 2.1, respectively; p < 0.001), Em lateral (8.4 ± 2.8 vs. 9.7 ± 4.8 vs. 8.6 ± 3.3, respectively; p = 0.029), and Am lateral values (10.7 ± 2.7 vs. 12.0 ± 2.9 vs. 11.8 ± 2.7, respectively; p = 0.007) were all significantly lower in patients with the reverse-dipper pattern. Table 2 shows the distribution of the patients' echocardiogram results.

Table 1 Demographic, clinical, and laboratory characteristics of patients stratified by nocturnal BP pattern (dipper, non-dipper, and reverse-dipper), with p-values for intergroup comparisons

	Nocturnal BP Patterns				
Variable	Dipper (n=111)	Non-dipper (n=188)	Reverse-dipper (n=105)	Total (n=404)	p-value*
Age (years)	54±11	59±13§	64±12†‡	59±13	<0.001
Female gender, n (%)	58 (52.3)	88 (46.8)	58 (55.2)	204 (50.5)	0.350
BSA (kg/m²)	1.9±0.2	2±0.2	1.9±0.2	1.9±0.2	0.446
CAD, n (%)	12(10.8)	27 (14.4)	27 (25.7)†	66 (16.3)	0.008
DM, n (%)	16 (14.4)	42 (22.3)	27 (25.7)	85 (21.0)	0.106
Stroke, n (%)	2 (1.8)	9 (4.8)	3 (2.9)	14 (3.5)	0.369
CKD, n (%)	4 (3.6)	9 (4.8)	7 (6.7)	20 (5.0)	0.579
Smoking, n (%)	33 (29.7)	44 (23.4)	25 (23.8)	102 (25.2)	0.442
SBP (total) (mmHg)	139±16	140±17	138±18	140±17	0.654
DBP (total) (mmHg)	87±11	86±13	84±13	86±12	0.091
SBP (awake) (mmHg)	144±18	142±18	138±18†‡	142±18	0.032
DBP (awake) (mmHg)	90±13	87±13	84±13†‡	87±13	0.002
SBP (nocturnal) (mmHg)	129±18	136±17§	141±21†‡	135±19	<0.001
DBP (nocturnal) (mmHg)	79±13	82±12	83±14†	81±13	0.096
ASA, n (%)	20 (18.0)	43 (22.8)	35 (33.3)†	98 (24.2)	0.027
Clopidogrel, n (%)	4 (3.6)	12 (6.3)	8(7.6)	24 (5.9)	0.433
ACEi, n (%)	21 (18.9)	37 (19.7)	22 (21.0)	80 (19.8)	0.931
ARB, n (%)	32 (28.8)	61 (32.4)	31 (29.5)	124 (30.6)	0.771
Beta-blocker, n (%)	17 (15.3)	44 (23.4)	46 (43.8)†‡	107 (26.4)	<0.001
MRA, n (%)	2 (1.8)	0	4 (3.8)	6 (1.4)	0.034
DHP-CCB, n (%)	22 (19.8)	52 (27.6)	27 (25.7)	101 (25.0)	0.313
Non-DHP-CCB, n (%)	1(0.9)	3 (1.5)	0	4 (0.9)	0.415
Indapamide, n (%)	2 (1.8)	1 (0.5)	2 (1.9)	5 (1.2)	0.488
Thiazide, n (%)	23 (20.7)	49 (26.0)	29 (27.6)	101 (25.0)	0.454
Hemoglobin (g/dL)	14.9±1.7	14.7±2.0	14.3±1.8†	14.6±1.9	0.027
Na (mmol/L)	138±12	138±9	139±10	138±10	0.193
K (mmol/L)	4.2±0.3	4.2±0.4	4.2±0.4	4.2±0.4	0.299
LDL-C (mg/dL)	122±31	122±41	120±41	122±38	0.745
TG (mg/dL)	171±96	169±86	151±80	165±87	0.157
HDL-C (mg/dL)	51±12	50±12	50±12	50±12	0.827
eGFR (ml/dk/m²)	85±15	82±16	76±19†‡	81±17	0.007
BNP (pg/mL)	24 (14–45)	33 (17–58)	62 (26–105) †‡	33 (17–64)	<0.001
TSH (mIU/L)	1.5 (1.0-2.3)	1.6 (0.9–2.3)	1.8 (1.1–2.6)	1.6 (1.0-2.4)	0.529

BP: blood pressure; BSA: body surface area; CAD: coronary artery disease; DM: diabetes mellitus; CKD: chronic kidney disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; ASA: acetylsalicylic acid; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; MRA: mineralocorticoid receptor antagonist; DHP-CCB: dihydropyridine calcium channel blocker; non-DHP-CCB: non-dihydropyridine calcium channel blocker; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; eGFR: estimated glomerular filtration rate; BNP: brain natriuretic peptide, TSH: thyroid-stimulating hormone

*p values indicate differences between BP patterns. †$p<0.05$ versus dipper BP, ‡$p<0.05$ versus non-dipper BP, §$p<0.05$ versus dipper BP

In univariate analysis, age, coronary artery disease (CAD), hemoglobin, systolic BP (sleep), eGFR, BNP, Em septal, mitral (cm/s), Am lateral, mitral (cm/s), E/Em mean, mitral, LA max volume, LACI, and LAVI were significantly associated with the reverse-dipper pattern (Table 3).

Due to the potential correlation between LACI and LAVI (Variance Inflation Factor: 7.072), they were evaluated in separate multivariate logistic regression models, each adjusted for relevant covariates. In the model including LAVI, independent predictors of the reverse-dipper pattern group included LAVI (OR: 1.145, 95% CI: 1.095–1.197, $p<0.001$), systolic BP (awake) (OR: 0.821, 95% CI: 0.821–0.890, $p<0.001$), systolic BP (sleep) (OR: 1.145, 95% CI: 1.103–1.188, $p<0.001$), and Am lateral mitral (cm/s) value (OR: 0.882, 95% CI: 0.785–0.991, $p=0.034$). In the model including LACI, the following variables were independently associated with the reverse-dipper pattern group: LACI (OR: 3.837, 95% CI: 2.620–5.620, $p<0.001$), systolic BP (awake) (OR: 0.849, 95% CI: 0.814–0.886, $p<0.001$), and systolic BP (sleep) (OR: 1.154, 95% CI: 1.110–1.199, $p<0.001$). The independent predictors of the reverse-dipper BP pattern identified in these two separate multivariate models, including either LAVI or LACI, are summarized in Table 4.

A receiver operating characteristic (ROC) curve analysis was performed to compare the predictive performance of LAVI and LACI for identifying the reverse-dipper pattern. The AUC for LACI was higher than that for LAVI (0.810 vs. 0.724, respectively; $p<0.0001$), indicating that LACI had superior discriminative ability in predicting the reverse-dipper pattern. With a sensitivity of 91.3% and a specificity of 58.3%, the ideal cut-off value for LACI in predicting reverse-dipper BP was greater than 2.1769. The

Table 2 Echocardiographic parameters of dipper, non-dipper, and reverse-dipper groups, with p-values for intergroup comparisons

	Nocturnal BP Patterns				
Variable	Dipper ($n=111$)	Non-dipper ($n=188$)	Reverse-dipper ($n=105$)	Total ($n=404$)	p-value*
LA (cm)	3.5±0.4	3.6±0.4	3.8±0.4†‡	3.6±0.4	<0.001
E, mitral (cm/s)	66±16	63±15	64±20	64±17	0.198
A, mitral (cm/s)	81±19	82±15	79±18	81±17	0.257
E/A, mitral	0.85±0.24	0.79±0.26	0.85±0.39‡	0.82±0.29	0.028
Em septal, mitral (cm/s)	7±1.7	6.8±2.2	6.2±2.0	6.7±2.0	0.001
Am septal, mitral (cm/s)	10.9±2.1	10.3±2.1	8.7±2.0†‡	10.1±2.3	<0.001
Em lateral, mitral (cm/s)	9.7±4.8	8.6±3.3	8.4±2.8	8.8±3.7	0.029
Am lateral, mitral (cm/s)	12.0±2.9	11.8±2.7	10.7±2.7†‡	11.6±2.8	0.007
E/Em mean, mitral	8.3±2.6	8.4±3.4	9.5±4.4	8.7±3.5	0.041
LA maximum volume (mL)	39.9±12.8	44.3±15.4§	55.0±19.1†‡	45.9±16.8	<0.001
LA minimum volume (mL)	12 (9–18)	15 (10–22) §	22 (15–29) †‡	16 (11–23)	<0.001
LAVI (mL/m²)	20.5±6.2	22.6±7.5§	28.5±9.1†‡	23±8.2	<0.001
LACI	1.9±0.6	2.2±0.9§	3.5±1.9†‡	2.5±1.3	<0.001
PALS (2 C), %	29±10	26±10	22±10†‡	26±10	<0.001
PALS (4 C), %	26±10	24±9	21±10†	24±10	<0.001
IVSd (cm)	1.2±0.2	1.2±0.3§	1.2±0.2†	1.2±0.2	0.014
LVPWd (cm)	1.0±0.2	1.1±0.2§	1.1±0.2†	1.1±0.2	0.001
LVESD (cm)	3.3 (3-3.5)	3.2 (3-3.6)	3.3 (3-3.7)	3.3 (3-3.6)	0.716
LVEDD (cm)	4.4 (4.1–4.8)	4.4 (4-4.8)	4.3 (4-4.7)	4.4 (4-4.8)	0.739
LVMI (g/m²)	90 (71–128)	104 (84–161)	68 (0-160)	97 (64–160)	0.684
LVESV (mL)	30±10	30±13	29±13	30±12	0.490
LVEDV (mL)	72±20	73±22	73±24	73±21	0.867
LVEF, (%)	58.3±8.6	58.4±7.3	59.9±8.0	58.7±7.9	0.173
TAPSE (mm)	23 (21–25)	23 (20–26)	23 (20–26)	23 (20–26)	0.974

BP: blood pressure; LA: left atrium; E: peak early inflow velocity; A: peak late inflow velocity; Em: early diastolic tissue Doppler velocity; Am: tissue Doppler myocardial velocity at atrial contraction; LAVI: left atrial volume index; LACI: left atrial coupling index; PALS(2 C): peak atrial longitudinal strain measured from the apical 2-chamber view; PALS(4 C): peak atrial longitudinal strain measured from the apical 4-chamber view; IVSd: inter-ventricular septal thickness in diastole; LVPWd: left ventricular posterior wall thickness at end of diastole; LVESD: left ventricle end-systolic diameter; LVEDD: left ventricle end-diastolic diameter; LVMI: left ventricular mass index; LVESV: left ventricular end-systolic volume; LVEDV: left ventricular end-diastolic volume; LVEF: left ventricle ejection fraction; TAPSE: tricuspid annular plane systolic excursion

*p values indicate differences between BP patterns. †$p<0.05$ versus dipper BP, ‡$p<0.05$ versus non-dipper BP, §$p<0.05$ versus dipper BP

comparative predictive performance of LACI and LAVI is presented in Fig. 2.

4 Discussion

This study demonstrated that LACI was associated with the reverse-dipper BP pattern and was an independent predictor of reverse-dipper patients. Furthermore, LACI exhibited a superior discriminative ability compared to LAVI in identifying these patients.

Circadian BP variation has important clinical implications, and among its abnormal patterns, reverse-dipper BP is associated with the worst cardiovascular outcomes. Characterized by an abnormal nocturnal rise in BP, reverse-dipper BP has emerged as an independent predictor of adverse cardiovascular events, including myocardial infarction, stroke, heart failure, and all-cause mortality [14, 15]. While non-dipper BP also represents a deviation from the normal circadian rhythm, reverse-dipper BP appears to reflect a more profound disturbance in nocturnal autonomic and vascular regulation, which may underlie its stronger association with cardiovascular risk [14]. Consistent with previous studies [16, 17], our findings revealed that patients with a reverse-dipper pattern were significantly older and had a higher prevalence of CAD than those with dipper or non-dipper patterns. This may be attributed to age-related arterial stiffness, diminished baroreflex sensitivity, and a greater burden of vascular remodeling and endothelial dysfunction in CAD patients [18, 19]. In addition, we observed significantly higher BNP levels in patients with a reverse-dipper pattern compared to those with a dipper pattern, supporting the link between abnormal nocturnal BP patterns and subclinical cardiac stress. This observation aligns with previous reports

Table 3 Univariate logistic regression analysis of demographic, biochemical, and echocardiographic parameters for diagnosis of reverse-dipper BP pattern

Variable	Univariate		
	Odds ratio	95% CI	*p*-value
Age	1.049	1.028–1.069	<0.001
CAD	2.347	1.350–4.078	0.002
DM, n (%)	1.463	0.867–2.470	0.154
Stroke, n (%)	0.788	0.216–2.883	0.719
CKD, n (%)	1.593	0.618–4.108	0.335
SBP (awake) (mmHg)	0.983	0.970–0.997	0.014
DBP (awake) (mmHg)	0.972	0.954–0.990	0.002
SBP (nocturnal) (mmHg)	1.020	1.008–1.032	0.001
Hemoglobin (g/dL)	0.855	0.759–0.964	0.010
eGFR (ml/dk/m²)	0.978	0.966–0.991	0.001
BNP (pg/mL)	1.006	1.003–1.009	<0.001
LA (mm)	1.059	0.972–1.154	0.188
E/A, mitral	1.681	0.805–3.511	0.167
Em septal, mitral (cm/s)	0.828	0.731–0.937	0.003
Am lateral, mitral (cm/s)	0.856	0.784–0.933	<0.001
E/Em mean, mitral	1.105	1.031–1.185	0.005
LA maximum volume (mL)	1.046	1.030–1.062	<0.001
LA minimum volume (mL)	1.082	1.056–1.109	<0.001
LAVI (mL/m²)	1.110	1.075–1.146	<0.001
LACI	2.903	2.191–3.847	<0.001

BP: blood pressure; CAD: coronary artery disease; DM: diabetes mellitus; CKD: chronic kidney disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; eGFR: estimated glomerular filtration rate; BNP: brain natriuretic peptide; LA: left atrium; E: peak early inflow velocity; A: peak late inflow velocity; Em: early diastolic tissue Doppler velocity; Am: tissue Doppler myocardial velocity at atrial contraction; LAVI: left atrial volume index; LACI: left atrial coupling index

Table 4 Multivariate logistic regression models evaluating the association of LAVI and LACI with the reverse-dipper BP pattern

Variable	OR (LAVI model) (95% CI)	*p*-value	OR (LACI model) (95% CI)	*p*-value
SBP (awake) (mmHg)	0.821 (0.821–0.890)	<0.001	0.849 (0.814–0.886)	<0.001
SBP (nocturnal) (mmHg)	1.145 (1.103–1.188)	<0.001	1.154 (1.110–1.199)	<0.001
Am lateral, mitral (cm/s)	0.882 (0.785–0.991)	0.034		
LAVI (mL/m²)	1.145 (1.095–1.197)	<0.001		
LACI			3.837 (2.620–5.620)	<0.001

BP: blood pressure; SBP: systolic blood pressure; LAVI: left atrial volume index; LACI: left atrial coupling index

[20], indicating that even modest increases in nocturnal BP can independently predict higher BNP levels, potentially reflecting early myocardial strain and altered volume status [21]. Furthermore, in our study, patients with a reverse-dipper pattern had significantly lower hemoglobin and eGFR levels compared to those with a dipper pattern. Evidence regarding the association between reverse-dipper BP and anemia is limited and inconclusive; only one study found that patients with chronic kidney disease and a reverse-dipper BP pattern had significantly lower glomerular filtration rates and hemoglobin levels [22].

Structural and functional alterations in the heart are closely linked to circadian BP patterns. Transthoracic echocardiography (TTE) remains one of the most widely used noninvasive tool for assessing cardiac remodeling in this context. Although the echocardiographic features of the non-dipper pattern have been previously investigated [23], data specifically focusing on the reverse-dipper profile remain limited. In our study, patients with reverse-dipper BP had significantly larger LA dimensions, increased LAVI and LACI, and the presence of echocardiographic markers of diastolic dysfunction, such as a higher E/A ratio and E/Em mean, as well as reduced Em septal and Am lateral velocities. These findings reflect impaired myocardial relaxation and elevated LA filling pressures. Such changes may result from sustained nocturnal hypertension, which imposes chronic hemodynamic stress on the atrial and ventricular myocardium, leading to increased stiffness and impaired compliance. Previous studies have similarly reported a link between blunted nocturnal dipping and subclinical diastolic dysfunction or LA enlargement [24, 25]. The reverse-dipper pattern, as the most extreme variant of circadian BP disruption, may amplify these structural and functional changes due to persistent nocturnal pressure overload.

In the present study, both LACI and LAVI were found to be independent predictors of the reverse-dipper BP pattern. While LAVI presents structural remodeling through atrial enlargement, LACI provides a more comprehensive evaluation of atrial performance by incorporating both the volume and functional dynamics of LA. This dual nature may enable LACI to detect early or subtle abnormalities that LAVI alone might miss. In our ROC analysis, LACI demonstrated superior discriminative ability compared to LAVI in identifying reverse-dipper patterns. To the best of our knowledge, this is the first study to specifically evaluate LACI in relation to reverse-dipper BP. These findings suggest that LACI may serve as a more sensitive and functionally informative marker of atrial remodeling and altered hemodynamic states associated with this high-risk BP profile. These results are consistent with emerging evidence that LACI may outperform traditional structural markers in detecting subclinical cardiac dysfunction and predicting adverse outcomes [8, 9].

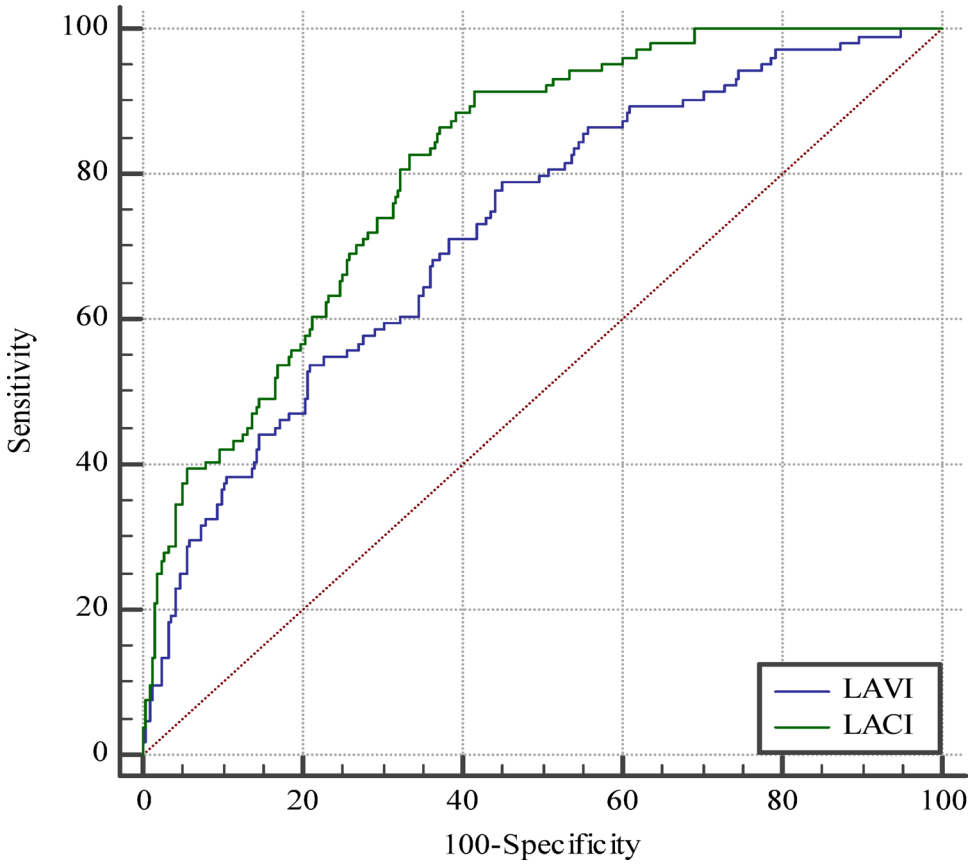


Fig. 2 Receiver operating characteristic (ROC) curves illustrating the predictive performance of LACI and LAVI in identifying the reverse-dipper blood pressure pattern. LACI: Left Atrial Coupling Index; LAVI: Left Atrial Volume Index

Ambulatory blood pressure monitoring is considered the gold standard for detecting circadian BP patterns; however, it has several limitations in clinical practice. The requirement to wear the device for 24 h can cause patient discomfort, and the procedure often necessitates multiple visits for device application and data interpretation, resulting in time inefficiencies and increased costs. In contrast, TTE is widely available, non-invasive, and can be performed in a single outpatient visit. In our study, echocardiographic evaluation was the best at predicting the reverse-dipper BP pattern among all parameters assessed. However, among the echocardiographic parameters, LACI emerged as the strongest independent predictor of reverse-dipper BP. By incorporating both structural and functional atrial parameters, LACI seems to offer a practical alternative to risk stratification. These findings suggest that TTE, a commonly used and accessible tool, may provide a time-efficient and cost-effective approach for identifying reverse-dipper patients in routine clinical care.

5 Conclusion

Although this study does not directly evaluate clinical outcomes, it focuses on predicting the reverse-dipper blood pressure pattern, which has been consistently associated with adverse prognoses. Therefore, the identification of this pattern remains clinically important. LACI reflects both anatomical and functional atrial characteristics and may serve as a useful marker for the detection of patients with reverse-dipper BP.

5.1 Limitations

This study has several limitations that should be acknowledged. First, this was a single-center study, which may limit the generalizability of our findings to other populations. Second, although 24-hour ABPM was used to classify dipping patterns, patient activity and adherence during the monitoring period may have influenced the BP measurements. Third, external validation in an independent cohort was not performed, which limits the generalizability and reproducibility of our findings.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40292-025-00733-w.

Author Contributions Ayca Arslan, Dogan Ilis, and Zulfiye Kuzu have given substantial contributions to the conception or the design of the manuscript. Timor Omar, Muammer Karakayali, and Zihni Cagın have given substantial contributions to the collection of the data. Inanc Artac and Yavuz Karabag have participated mostly in statistical data analysis. Ayca Arslan and Ibrahim Rencuzogullari have participated in the design, analysis, and drafting of the manuscript. All authors have participated in data analysis and drafting the manuscript. All authors contributed to the manuscript and read and approved the final version of the manuscript. All contributors are responsible for the overall content as guarantors.

Funding No funding.

Declarations

Conflict of interest The authors declare that they have no conflicts of interest to disclose.

Ethical Approval Ethical approval for the study was obtained from the local ethics committee, approval number 80576354-050-99/634. The study protocol was approved by the local ethics committee (Ethics Committee of the Dean of the Faculty of Medicine of Kafkas University—80576354-050-99/634 numbered ethics committee approval).

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. GBD 2019 Risk Factors Collaborators. Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of disease study 2019. Lancet. 2020;396(10258):1223–49. https://doi.org/10.1016/S0140-6736(20)30752-2.
2. Kario K. Nocturnal hypertension: new technology and evidence. Hypertension. 2018;71(6):997–1009. https://doi.org/10.1161/HYPERTENSIONAHA.118.10971.
3. Cuspidi C, Tadic M, Sala C, Carugo S, Mancia G, Grassi G. Reverse dipping and subclinical cardiac organ damage: a meta-analysis of echocardiographic studies. J Hypertens. 2021;39(8):1505–12. https://doi.org/10.1097/HJH.0000000000002836.
4. Parati G, Pengo MF, Avolio A, Azizi M, Bothe TL, Burnier M, Cappuccio FP, Sierra A, Fava C, Gironacci MM, Hoshide S, Kario K, Kollias A, Lombardi C, Maiolino G, Maule S, Narkiewicz K, Ohkubo T, Palatini P, Pepin J. L.,.ESH working group on blood pressure monitoring and cardiovascular variability. Nocturnal blood pressure: pathophysiology, measurement and clinical implications. Position paper of the European society of hypertension. J Hypertens. 2025. https://doi.org/10.1097/HJH.0000000000004053. 10.1097/HJH.0000000000004053. Advance online publication.
5. Kario K. Morning surge in blood pressure and cardiovascular risk: evidence and perspectives. Hypertension. 2010;56(5):765–73. https://doi.org/10.1161/HYPERTENSIONAHA.110.157149.
6. Huart J, Persu A, Lengelé JP, Krzesinski JM, Jouret F, Stergiou GS. Pathophysiology of the nondipping blood pressure pattern. Hypertension. 2023;80(4):719–29. https://doi.org/10.1161/HYPERTENSIONAHA.122.19996.
7. Nagueh SF, Smiseth OA, Appleton CP, Byrd BF, Dokainish H, Edvardsen T, Flachskampf FA, Gillebert TC, Klein AL, Lancellotti P, Marino P, Oh JK, Popescu BA, Waggoner AD Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the ASE and EACVI. J Am Soc Echocardiogr. 2016;29(4):277–314. https://doi.org/10.1016/j.echo.2016.01.011.
8. Benfari G, Essayagh B, Nistri S, Maalouf J, Rossi A, Thapa P, Michelena HI, Enriquez-Sarano M. Left atrial volumetric/mechanical coupling index: a novel predictor of outcome in heart failure with reduced ejection fraction. Circ Cardiovasc Imaging. 2021;14(1):e011608.
9. Vidula MK, Chirinos JA. Left atrial coupling index and its prognostic value in heart failure with reduced ejection fraction. Circ Cardiovasc Imaging. 2021;14(1):e012221.
10. Zheng R, Kusunose K. Linkage of left atrial function to heart failure with preserved ejection fraction. Int Heart J. 2023;64(1):4–9. https://doi.org/10.1536/ihj.22-659.
11. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYH, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I, ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J. 2018;39(33):3021–3104. https://doi.org/10.1093/eurheartj/ehy686. PMID: 30165516.
12. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ, Chamber Quantification Writing Group; American Society of Echocardiography's Guidelines and Standards Committee; European Association of Echocardiography. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr. 2005;18(12):1440-63. https://doi.org/10.1016/j.echo.2005.10.005. PMID: 16376782.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American society of echocardiography and the European association of cardiovascular imaging. J Am Soc Echocardiogr. 2015;28(1):1–39. https://doi.org/10.1016/j.echo.2014.10.003.
14. Cuspidi C, Sala C, Tadic M, Gherbesi E, De Giorgi A, Grassi G, Mancia G. Clinical and prognostic significance of a reverse dipping pattern on ambulatory monitoring: an updated review. J Clin Hypertens. 2017;19(7):713–21. https://doi.org/10.1111/jch.13023.
15. Kartaler F, Şahin M, Turan OE, Kutlu M. Relationship between dipping pattern and coronary artery disease severity in hypertension. Cureus. 2023;15(3):e36057. https://doi.org/10.7759/cureus.36057.
16. Satoh M, Asayama K, Kikuya M, Inoue R, Tsubota-Utsugi M, Obara T, Murakami K, Matsuda A, Murakami T, Nomura K, Metoki H, Imai Y, Ohkubo T. Nocturnal blood pressure decline and long-term cardiovascular risk: the Ohasama study. Clin Exp Hypertens. 2018;40(1):1–7. https://doi.org/10.1080/10641963.2016.1259324.
17. Yan B, Peng L, Han D, Sun L, Dong Q, Yang P, Zheng F, Ong H, Zeng L, Wang G. Blood pressure reverse-dipping and early carotid plaque formation in senior hypertensives. Med (Baltim). 2015;94(10):e604.

18. Laurent S, Boutouyrie P. Arterial stiffness and hypertension in the elderly. Front Cardiovasc Med. 2020;7:544302. https://doi.org/10.3389/fcvm.2020.544302.
19. Ghiadoni L, Taddei S, Virdis A, Sudano I, Di Legge V, Meola M, Di Venanzio L, Salvetti A. Endothelial function and carotid wall thickening in essential hypertension. Hypertension. 1998;32(1):25–32. https://doi.org/10.1161/01.hyp.32.1.25.
20. Tabara Y, Igase M, Miki T, Ohyagi Y, Matsuda F, Kohara K. J-SHIPP study group B-type natriuretic peptide and nocturnal blood pressure rise. J Hypertens. 2016;34(12):2393–401. https://doi.org/10.1097/HJH.0000000000001104.
21. Hirata Y, Matsumoto A, Aoyagi T, Yamaoki K, Komuro I, Suzuki T, Ashida T, Sugiyama T, Hada Y, Kuwajima I, Nishinaga M, Akioka H, Nakajima O, Nagai R, Yazaki Y. Plasma brain natriuretic peptide as a guide for cardiac overload. Cardiovasc Res. 2001;51(3):585–91. https://doi.org/10.1016/s0008-6363(01)00320-0.
22. Wang C, Zhang J, Liu X, Li C, Ye Z, Peng H, Chen Z, Lou T. Reversed dipper pattern and severe organ damage in chronic kidney disease. PLoS ONE. 2013;8(2):e55419. https://doi.org/10.1371/journal.pone.0055419.
23. Ermiş N, Otlu YÖ, Afşin A, Hidayet Ş, Açıkgöz N, Cansel M, Yağmur J, Çolak MC. Left atrial volume and function in non-dipper versus dipper hypertensives: 3D echocardiography. Anatol J Cardiol. 2016;16(6):428–33. https://doi.org/10.14744/AnatolJCardiol.2015.6569.
24. Tadic M, Cuspidi C, Pencic B, Mancia G, Grassi G, Kocijancic V, Quarti-Trevano F, Celic V. Impact of dipping patterns on left atrial function in hypertension. J Hypertens. 2020;38(11):2245–51. https://doi.org/10.1097/HJH.0000000000002542.
25. Możdżan M, Wierzbowska-Drabik K, Kurpesa M, Trzos E, Rechciński T, Broncel M, Kasprzak J. D. LV hypertrophy and diastolic function in dippers vs non-dippers. Arch Med Sci. 2013;9(2):268–75. https://doi.org/10.5114/aoms.2013.34534.