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Electro-mechanical atrial and diastolic dysfunction in hypertensive patterns

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ABSTRACT

Objectives: Diastolic dysfunction (DD) remains a diagnostic challenge, particularly in hypertensive patients with non-dipping blood pressure profiles. Emerging evidence suggests that left atrial reservoir strain (LASr) and P-wave dispersion (Pd) may serve as sensitive, non-invasive markers for subclinical atrial dysfunction.

Patients and methods: This single-center, retrospective observational study included 176 individuals: 76 non-dipper hypertensive, 65 dipper hypertensive, and 35 normotensive controls. All subjects underwent transthoracic echocardiography and 12-lead electrocardiogram (ECG). LASr was measured via speckle-tracking echocardiography, and Pd was manually calculated from standard ECGs.

Results: Non-dipper patients exhibited significantly reduced LASr ($19.27 \pm 5.1\%$) and increased Pd (50.57 ± 8.1 ms) compared to dippers and controls ($p < 0.001$). A strong inverse correlation between LASr and Pd was observed. DD prevalence was highest among non-dippers (92.0%). Receiver operating characteristic analysis identified a Pd cut-off of 40.5 ms with 83% sensitivity, 80% specificity, and area under the curve 0.84 (95% confidence interval: 0.78-0.90) for detecting DD.

Conclusion: LASr and Pd provide complementary insights into atrial mechanical and electrical remodeling in hypertensive patients. Pd, as a simple and cost-effective ECG marker, may serve as a valuable tool for identifying DD, especially when advanced imaging is unavailable. These findings support integrating Pd into routine hypertensive patient evaluation.

Keywords: P-wave dispersion, left atrial reservoir strain, diastolic dysfunction, non-dipper hypertension, hypertension, ambulatory blood pressure monitoring.

Diastolic dysfunction (DD) remains a challenging clinical condition to diagnose, particularly in early stages and in the presence of chronic hemodynamic stressors such as hypertension.^[1] The development of left ventricular hypertrophy and increased myocardial stiffness impairs ventricular relaxation and raises filling pressures. Over time, this leads to volume overload and structural remodeling of the left atrium, including progressive atrial fibrosis.^[2] These histopathological changes disrupt both intra- and interatrial conduction continuity, ultimately resulting in atrial electromechanical discordance.^[2-4] In recent years, the use of advanced imaging parameters—such as left atrial reservoir strain (LASr) measured via speckle-tracking echocardiography—has gained attention for non-invasive assessment of this complex process.^[5,6]

In parallel, P-wave dispersion (Pd), a simple and widely accessible electrocardiogram (ECG) parameter, has emerged as a potential

surrogate marker of atrial conduction heterogeneity.^[7] In our study, we stratified hypertensive individuals into dipper and non-dipper groups and observed that the non-dipper blood pressure profile was associated with more pronounced DD. The significant and strong inverse correlation identified between LASr and Pd highlights the potential of Pd as a practical, low-cost marker that may reflect underlying atrial electromechanical imbalance. These findings suggest that Pd may serve as a complementary tool in the early detection and monitoring of DD, particularly in the hypertensive population.

PATIENTS AND METHODS

This single-center, retrospective observational study was conducted at the Department of Cardiology, Gazi University Faculty of Medicine, following approval by the University's Ethics Committee (approval no:



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2025-1408, date: 04.08.2025). All procedures adhered to the ethical standards of the Declaration of Helsinki, and required institutional permissions were obtained prior to data access.

Patient Selection

A total of 176 individuals who underwent both transthoracic echocardiography and 12-lead electrocardiography between January 2022 and June 2025 were evaluated retrospectively. Based on 24-hour ambulatory blood pressure monitoring, patients with hypertension were classified into dipper (n=65) and non-dipper (n=76) groups, while a normotensive group was included as the control cohort (n=35). The dipping pattern was defined according to current hypertension guidelines, with a nocturnal systolic blood pressure decline of $\geq 10\%$ accepted as dipper status.^[8,9]

Inclusion criteria encompassed adults aged 18 or older with a diagnosis of essential hypertension for the patient groups, presence of normal sinus rhythm, and complete clinical, echocardiographic, and electrocardiographic records of acceptable quality. Patients were excluded if they had a history of atrial arrhythmias, moderate or severe valvular heart disease, reduced left ventricular systolic function (LVEF $< 50\%$), congenital heart disease, prior cardiac surgery, or suboptimal imaging quality.

Echocardiographic Evaluation

All echocardiographic assessments were conducted by experienced cardiologists using standard imaging protocols and a commercially available ultrasound machine (GE Vivid E95). The evaluation was carried out according to the 2016 guidelines from the American Society of Echocardiography and the European Association of Cardiovascular Imaging.^[10,11] DD was diagnosed when at least three of the following four parameters were abnormal: septal e' velocity < 7 cm/s or lateral e' < 10 cm/s, E/e' ratio > 14 , left atrial volume index (LAVI) > 34 mL/m², or peak tricuspid regurgitation velocity ($TR V_{max}$) > 2.8 m/s.^[12]

Left Atrial Strain Analysis

LASr was assessed offline using two-dimensional speckle-tracking echocardiography. Apical four-chamber views were acquired at a frame rate between 60-90 fps, and endocardial borders were manually traced at end-systole using dedicated software (EchoPAC v206, GE Healthcare). LASr was defined as the peak positive longitudinal strain of the left atrium during ventricular systole. Measurements were performed by two independent observers blinded to clinical and ECG data.

Electrocardiographic Assessment

Standard 12-lead ECGs were recorded with a paper speed of 25 mm/s and calibration of 10 mm/mV, which corresponds to routine clinical practice. The ECGs were manually analyzed using handheld calipers and magnifying lenses by two experienced cardiologists blinded to the echocardiographic findings. P-wave duration was measured in all leads, from the onset of the P-wave (initial deflection from the isoelectric line) to the end (return to baseline). The maximum and minimum P-wave durations were identified, and Pd was calculated as their difference.^[13] All measurements were repeated by both observers, and average values were used. A random sample of 30 ECGs was reanalyzed to assess intra- and inter-observer reproducibility. Agreement was quantified using the intraclass correlation coefficient (ICC), which demonstrated excellent

reproducibility for Pd measurements (intra-observer ICC =0.93, inter-observer ICC =0.91).

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 26.0. The Shapiro-Wilk test was used to determine data distribution. Continuous variables were presented as mean \pm standard deviation or median with interquartile ranges, and analyzed using independent-samples t-test or Mann-Whitney U test where appropriate. Categorical data were expressed as frequencies and compared using the chi-square test. Correlations between Pd and LASr, as well as other echocardiographic parameters, were evaluated using Spearman or Pearson coefficients. Receiver operating characteristic (ROC) analysis was conducted to determine the optimal Pd cut-off for predicting DD. Statistical significance was set at a p-value < 0.05 .

RESULTS

A total of 176 individuals were included in the study, comprising 35 normotensive controls, 65 dipper hypertensive patients, and 76 non-dipper hypertensive patients. The three groups were similar in terms of age and sex distribution. Left ventricular ejection fraction was preserved in all groups, with no statistically significant difference observed ($p=0.074$). However, the left ventricular mass index progressively increased from the control group to the non-dipper group (88.5 ± 9.3 vs. 101.4 ± 10.6 vs. 112.8 ± 12.2 g/m²; $p < 0.001$) (Table 1).

Daytime and nighttime systolic blood pressures were significantly higher in both hypertensive groups compared to controls, with the highest values observed in the non-dipper group (daytime SBP: 145.5 ± 10.1 mmHg; nighttime SBP: 139.2 ± 9.3 mmHg; both $p < 0.001$). Estimated glomerular filtration rate showed a modest but statistically significant decline in the non-dipper group compared to controls (76.1 ± 12.4 vs. 84.2 ± 10.7 mL/min/1.73 m²; $p=0.022$).

Diastolic function parameters revealed significant deterioration in the non-dipper group. E/A ratio, E velocity, and E/e' values were significantly elevated in this group (E/e' : 20.71 ± 3.1 ; $p=0.004$), while e' velocities were reduced (5.58 ± 1.1 cm/s; $p=0.021$). Similarly, the LAVI and peak $TR V_{max}$ were significantly higher in the non-dipper group (LAVI: 45.8 ± 5.4 mL/m²; $TR V_{max}$: 3.50 ± 0.27 m/s).

Left atrial strain analysis revealed a marked reduction in LASr among non-dippers ($19.27 \pm 5.1\%$) compared to dippers ($26.72 \pm 4.8\%$) and controls ($32.22 \pm 4.5\%$), with a statistically significant difference ($p=0.002$). In parallel, Pd was significantly prolonged in the non-dipper group (50.57 ± 8.1 ms), compared to both dipper patients (42.15 ± 7.0 ms) and controls (35.70 ± 6.6 ms) ($p < 0.001$). DD was identified in 64.0% of dipper patients and 92.0% of non-dipper patients, while none of the control subjects met the diagnostic criteria ($p=0.001$) (Table 2).

A significant inverse correlation was observed between Pd and LASr, while positive correlations were noted between Pd and E/e' , LAVI, and $TR V_{max}$ (Table 3).

ROC analysis indicated that a Pd cut-off value of 40.5 ms predicted the presence of DD with 83% sensitivity and 80% specificity, yielding an area under the curve (AUC) of 0.84 (95% confidence interval: 0.78-0.90) (Figure 1).

Table 1. Baseline clinical and imaging characteristics of study participants

Parameter	Control (n=35)	Dipper (n=65)	Non-dipper (n=76)	p-value
Age (years), mean	58.9	58.9	61.9	0.065
Female, n (%)	16 (45.7%)	32 (49.2%)	40 (52.6%)	0.62
EF (%)	63.2±3.1	62.5±3.4	61.8±3.8	0.074
LVMI (g/m ²)	88.5±9.3	101.4±10.6	112.8±12.2	<0.001
Daytime SBP (mmHg)	121.6±7.4	138.9±8.6	145.5±10.1	<0.001
Nighttime SBP (mmHg)	111.4±6.5	121.8±6.9	139.2±9.3	<0.001
eGFR (mL/min/1.73 m ²)	84.2±10.7	79.5±11.1	76.1±12.4	0.022
E/A ratio	0.70±0.09	1.18±0.25	2.21±0.41	0.003
E (cm/s)	45.7±6.1	77.0±8.4	111.3±10.2	0.012
e' (cm/s)	8.07±1.0	6.33±1.2	5.58±1.1	0.021
E/e' ratio	5.78±1.1	12.62±2.3	20.71±3.1	0.004
LAVI (mL/m ²)	27.8±3.6	37.9±4.8	45.8±5.4	0.018
TR V _{max} (m/s)	2.43±0.22	3.00±0.24	3.50±0.27	0.047
LASr (%)	32.22±4.5	26.72±4.8	19.27±5.1	0.002
P-wave dispersion (ms)	35.70±6.6	42.15±7.0	50.57±8.1	<0.001
Diastolic dysfunction, n (%)	0 (0%)	42 (64%)	70 (92%)	0.001

Values are presented as mean ± standard deviation or number (percentage). P-values indicate comparisons among the three groups (control, dipper, and non-dipper) using One-Way ANOVA or chi-square test, as appropriate.

EF: Ejection fraction; LVMI: Left ventricular mass index; SBP: Systolic blood pressure; eGFR: Estimated glomerular filtration rate; E/A: Ratio of early (E) to late (A) mitral inflow velocity; e': Early diastolic mitral annular velocity; E/e': Ratio of mitral inflow velocity to mitral annular early diastolic velocity; LAVI: Left atrial volume index; TR V_{max}: Tricuspid regurgitation maximum velocity; LASr: Left atrial reservoir strain.

Table 2. Comparison of independent parameters according to the presence of diastolic dysfunction

Parameter	DD present (n=78)	DD absent (n=98)	p-value
P-wave dispersion (ms)	46.36±6.33	35.70±6.59	<0.001
LASr (%)	22.99±4.95	32.22±4.53	<0.001

Values are expressed as mean ± standard deviation. P-values indicate comparisons between patients with and without diastolic dysfunction. DD: Diastolic dysfunction; LASr: Left atrial reservoir strain.

Table 3. Correlation analysis between P-wave dispersion and echocardiographic parameters

Parameter	Spearman correlation	p-value
LASr (%)	-0.72	<0.001
E/e'	0.65	<0.001
LAVI (mL/m ²)	0.60	<0.001
TR V _{max} (m/s)	0.58	<0.001

Correlation coefficients were calculated using Spearman's rank correlation test.

LASr: Left atrial reservoir strain; E/e': Ratio of mitral inflow velocity to mitral annular early diastolic velocity; LAVI: Left atrial volume index; TR V_{max}: Tricuspid regurgitation maximum velocity.

Intra- and inter-observer reproducibility for Pd measurements was excellent, with ICC values of 0.93 and 0.91, respectively.

DISCUSSION

LASr and Pd have increasingly gained attention as sensitive and accessible markers for the detection of DD.^[14] In our study, we demonstrated that patients with a non-dipping hypertension pattern exhibit significant alterations not only in hemodynamic parameters but also in atrial mechanical and electrophysiological properties, particularly reflected by reduced LASr and increased Pd values.

LASr, derived from speckle-tracking echocardiography, has emerged as a reliable non-invasive index of left atrial compliance and reservoir function. In a 2022 study by Miljković et al.,^[1] a LASr cut-off of 24.27%

was reported to predict DD with a sensitivity of 78.9% and specificity of 84.6%. In our cohort, non-dipper patients demonstrated a substantially lower average LASr value (19.27%, p=0.002), clearly indicating a greater impairment in atrial functional reserve compared to dipper and control groups. This supports the notion that LASr is not only a marker of DD itself, but also a sensitive indicator of the deleterious impact of altered circadian blood pressure rhythms on atrial performance.

Similarly, Pd—a measure of atrial conduction heterogeneity—was found to be significantly elevated in the non-dipper group and was positively correlated with the presence of DD. While Pd has traditionally been associated with arrhythmia risk, our findings suggest that it may also reflect the burden of diastolic pressure and atrial structural remodeling.^[15] The mean Pd in non-dippers was 50.57 ms, a value approaching thresholds considered to be arrhythmogenic in prior

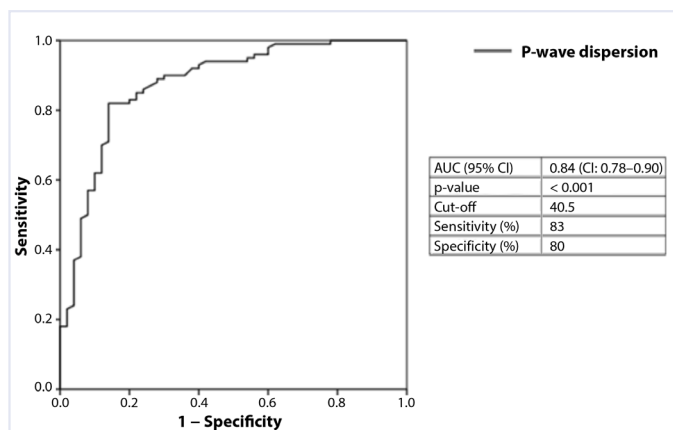


Figure 1. Receiver operating characteristic (ROC) curve of P-wave dispersion for predicting diastolic dysfunction.

ROC curve of P-wave dispersion for predicting diastolic dysfunction. The ROC analysis demonstrated the discriminatory performance of P-wave dispersion in identifying diastolic dysfunction. The area under the curve (AUC) was 0.84 (95% confidence interval [CI]: 0.78-0.90, $p < 0.001$). A cut-off value of 40.5 ms yielded a sensitivity of 83% and a specificity of 80%.

studies. Importantly, we identified a Pd cut-off value of 40.5 ms, which demonstrated 83% sensitivity and 80% specificity in predicting DD, with an AUC of 0.84. This level of diagnostic performance supports the potential of Pd as a simple yet clinically valuable tool in the early identification of DD.

In our cohort, non-dipper hypertensive individuals tended to demonstrate lower LASr values, suggesting a potentially higher cardiovascular risk. Moreover, the inverse relationship observed between LASr and Pd may reflect underlying atrial electromechanical disintegration, a mechanism that could link elevated diastolic load to impaired atrial conduction.

In summary, this study emphasizes the diagnostic value of LASr and Pd as non-invasive, accessible, and complementary parameters for detecting subclinical DD.^[16,17] The concurrent presence of reduced LASr and elevated Pd appears to reflect both mechanical and electrical atrial impairment, providing a more comprehensive assessment of atrial involvement in patients with disturbed circadian blood pressure profiles.^[14] These findings not only highlight the importance of evaluating atrial function in hypertensive patients, but also suggest that Pd may serve as a valuable screening tool in clinical practice when echocardiographic modalities are limited or unavailable.

This study has several limitations that should be acknowledged. First, its retrospective and single-center design may limit the generalizability of the findings. Second, although Pd measurements were carefully performed using manual calipers on standard 12-lead ECGs, the potential for inter-observer variability remains, despite internal validation. Third, although Pd is traditionally associated with arrhythmic risk, our study did not evaluate arrhythmic outcomes such as atrial fibrillation or other supraventricular arrhythmias; this limitation should be addressed in future prospective studies. Finally, prospective, multi-center studies with larger sample sizes and long-term follow-up are needed to further validate these results.

In conclusion, our study demonstrates that both Pd and LASr are strongly associated with DD, particularly in patients with a non-dipping hypertensive profile. The identification of a Pd cut-off value of 40.5 ms with high diagnostic accuracy supports its potential as a simple, cost-effective screening parameter. When combined with LASr, Pd may offer a more comprehensive, non-invasive approach to assessing atrial function and subclinical DD in clinical practice. These findings contribute to the growing body of evidence supporting atrial-focused assessment in the evaluation of hypertensive patients at risk for diastolic impairment.

Ethics

Ethics Committee Approval: This single-center, retrospective observational study was conducted at the Department of Cardiology, Gazi University Faculty of Medicine, following approval by the University's Ethics Committee (approval no: 2025-1408, date: 04.08.2025).

Informed Consent: Due to the retrospective nature of the study, written informed consent was waived by the local ethics committee.

Footnotes

Authorship Contributions

Surgical Medical Practices: Ö.S.; Concept: Ö.S., M.C.; Design: Ö.S., M.C.; Data Collection or Processing: Ö.S., S.Ü.; Analysis or Interpretation: Ö.S., M.C.; Literature Search: Ö.S.; Writing: Ö.S.

Conflict of Interest: No conflict of interest was declared by the authors.

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