Research Article

Blood Pressure Variability and Atrial Fibrillation in Patients with Acute ST Segment Elevation Myocardial Infarction: The Relation with Left Atrial Electromechanical Delay – A 1-Year Follow-Up Study

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Keywords

Blood pressure variability · Atrial fibrillation · ST segment myocardial infarction · Left atrial electromechanical delay

Abstract

Purpose: To investigate the association between 24-h blood pressure variability (BPV) and atrial electromechanical delay (EMD) in patients with ST segment elevation myocardial infarction (STEMI) who developed new-onset atrial fibrillation (NOAF). **Materials and Methods:** A total of 175 STEMI patients (age 56.6 ± 10.5 years) who underwent primary percutaneous coronary intervention were subjected to in-hospital 24-h ambulatory BP monitoring, comprehensive echocardiography, and assessment of atrial EMD. The parameters of BPV analyzed were: (a) 24-h standard deviation (SD), (b) the coefficient of variation, and (c) the average of the daytime and nighttime SDs weighted for the duration of the daytime and nighttime interval (SD_{dn}). **Results:** Based on the median of BPV index (SD_{dn}) = 9.5 mm Hg of all participants, patients were stratified into low and high variability groups (SD_{dn} : 7.1 ± 1.5 vs. 13.5 ± 2.9 ; $p < 0.001$). Of the 175 patients with STEMI, 29 (16.7%) patients developed NOAF; 26 (28.9%) were in the high variability group and 3.5% were in the low variability group ($p < 0.001$). Echocardiographic data showed that the left atrial volume index ($p < 0.01$) and E/e' ratio ($p < 0.001$) were significantly higher in patients with high BPV. Inter and intra-atrial EMD were significantly increased in the high variability group compared to the low variability group ($p < 0.001$). With multiple linear analysis, there was significant correlation between SD_{dn} and intra-left

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atrial and inter-atrial EMD ($p < 0.001$ and < 0.01 , respectively). Cox regression analysis revealed that SD_{dn} and intra-atrial EMD were independent predictors for NOAF in patients with STEMI (OR = 3.75 and 02.72, respectively; $p < 0.001$). ROC analysis revealed that $SD_{dn} \geq 12.8$ was the optimal cut-off value for predicting NOAF during follow-up. **Conclusions:** Short-term BPV was associated with NOAF during the 1-year follow-up in patients with STEMI. In addition, BPV was correlated significantly with atrial EMD. Herein, BPV was predicted to be an early predictor of NOAF in patients with STEMI.

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Introduction

New-onset atrial fibrillation (NOAF) is a frequent arrhythmia in the setting of ST segment elevation myocardial infarction (STEMI, and has a negative impact on clinical outcome [1]. The pathogenesis of the occurrence of atrial fibrillation following myocardial infarction is multifaceted. It may include the risk factors for ischemic heart disease themselves, associated comorbidities, hemodynamic instability, severity of the coronary lesion, and inadequate perfusion after thrombolytics or after primary percutaneous coronary intervention [2, 3].

Blood pressure variability (BPV) is usually stratified into short-term (minutes to hours) and long-term BPV (days to months), while beat-to-beat oscillation is termed very-short-term BPV [4]. It is thought to be associated with cardiac events in hypertensive patients and in STEMI cases [5–7].

Atrial electromechanical delay (EMD) is an important marker of an arrhythmogenic substrate in subjects with atrial fibrillation [8, 9]. EMD is the time interval from the start of the P wave on the surface ECG to the beginning of the A wave of the mitral annulus on tissue Doppler imaging (the PA interval). In our research, we investigated the relationship between 24-h BPV and atrial EMD, and their association with NOAF in STEMI patients.

Subjects and Methods

A total of 189 STEMI patients who underwent successful primary percutaneous coronary intervention were recruited for the study. STEMI was defined as ≥ 2 mm (0.2 mV) in males or ≥ 1.5 mm new ST elevation in V2–V3 leads, or ≥ 1 mm (0.1 mV) in any other contiguous leads [10]. In addition, we considered new or supposed new LBBB to be equal to STEMI [11]. We Successful myocardial infarction was considered as Thrombolysis in Myocardial Infarction (TIMI) grade 3 flow with less than 30% residual stenosis. Patients with known paroxysmal atrial fibrillation at any time before index event, cardiogenic shock (as they received inotropes which may trigger atrial fibrillation), history of previous revascularization, or poor echocardiographic window were excluded. Patients with inflammatory conditions, chronic kidney diseases, or stroke were also excluded. Fourteen patients who did not complete follow-up were excluded, leaving a final number of 175 patients included in the study analysis.

Ambulatory BP Monitoring

All patients underwent ambulatory BP monitoring (ABPM) for 24 h within 7 days of discharge, using Mobil-O Graph (IEM GmbH, Stolberg, Germany). Measurements were scheduled to be recorded at 30-min intervals during the day (6 a.m.–11 p.m.) and at 45-min intervals during the night (11 p.m.–6 a.m.) [12]. The mean 24-h systolic (SBP) and diastolic (DBP) BP were obtained. Short-term BP variability was used as the standard deviation (SD), coefficient of variation (CV), and the average of the daytime and nighttime SDs weighted for the duration of the daytime and nighttime interval (SD_{dn}). The SD_{dn} is the mean of the wake and sleep SD values corrected for the number of hours included in each of these two periods, according to the following formula: $SD_{dn} = ([\text{day SD} \times \text{hours included in the daytime}] + [\text{night SD} \times \text{hours included in the nighttime}]) / (\text{hours included in daytime} + \text{nighttime})$ [13].

Table 1. Baseline characteristics of the study population

	All patients (n = 175)	Low BPV (n = 85)	High BPV (n = 90)	p value
Age, years	56.6±10.5	54.5±11.3	57.8±10.5	0.34
Male	118 (67.4)	55 (64.7)	63 (70)	0.29
Body mass index, kg/m ²	24.8±0.9	24.3±0.9	25.1±1.1	0.57
Smoking	73 (41.7)	35 (41.2)	38 (42)	0.34
Diabetes mellitus	80 (45.7)	37 (43.5)	43 (47.8)	0.46
Hypertension	86 (49.1)	39 (45.9)	47 (55.6)	0.06
Dyslipidemia	54 (31)	29 (34)	25 (28)	0.41
Family history	40 (20)	15 (17.6)	20 (22)	0.30
Systolic BP, mm Hg	130±31	130±25	132±35	0.16
Diastolic BP, mm Hg	79±21	80±19	79±25	0.55
Pulse rate, beats/min	86±23	88±15	89±22	0.41
Site of infarction				
Anterior wall myocardial infarction	103	51	52	0.48
Inferior wall myocardial infarction	59	28	31	0.31
Anterior + inferior	13	7	6	0.35
Medications				
β-Blocker	99 (56.6)	46 (54)	53 (58.9)	0.57
Calcium channel blockers	41 (23.4)	19 (22.4)	22 (24.4)	0.54
ACEIs	35 (20)	16 (18.8)	19 (21)	0.78
ARBs	48 (27)	22 (25.9)	26 (28.9)	0.60
Diuretics	39 (22)	18 (21)	21 (23)	0.65
Nitroglycerines	34 (19.4)	15 (17.6)	19 (21)	0.51

Data are presented as mean ± SD or n (%), as appropriate.

Calculation of BPV Indices

BPV Index. BPV index was defined as the weighted SD of 24-h BP, the awake and sleep period BP for both SBP and DBP.

Dipping Status. Patients with an average night BP drop of 10–20% are considered normal dippers, whilst nondippers are defined as those with an average drop of BP <10%. Subjects with an average drop of BP >20% are considered extreme dippers. Extreme dippers are patients with an average night BP decrease of >20% of the average daytime BP, whereas reversed dippers are those with an average sleep period BP higher than the average awake period BP [14].

BP Morning Surge. Subjectively, the morning period is the duration from 6:00 a.m. to 10:00 a.m. BP morning surge was calculated as the average of BP obtained at the first 2 h after waking minus the average BP readings during the night (as the average BP of 3 readings [15]).

Transthoracic Echocardiography

All participants underwent transthoracic echocardiographic evaluation using a commercially available cardiac ultrasound scanner (System Five; GE Vingmed Ultrasound, Horten, Norway) and 2.5- to 3.5-MHz transducers. Left ventricular (LV) dimensions, LV mass index, relative wall thickness, and left atrial dimensions as well as all conventional and tissue Doppler parameters were obtained and recorded. LV ejection fraction (EF%), left atrial volume index (LAVi) was determined by dividing left atrial volume by estimated body surface area. E/A ratio, mean mitral annular wave velocity (é), and mean E/e' were calculated [16].

Estimation of Atrial EMD

The time interval from the onset of the P wave on the surface ECG to the beginning of the A wave was considered the atrial EMD (PA interval). A wave was recorded at the lateral mitral annulus, the septal mitral annulus as well as the tricuspid annulus. Three cycles were recorded and the mean was obtained [17].

- Intra-right atrial conduction time = septal mitral annular PA minus tricuspid annular PA.
- Intra-left atrial conduction time = lateral mitral annular PA minus septal mitral annular PA.
- Inter-atrial conduction time = lateral mitral annular PA minus tricuspid annular PA.

Table 2. Blood pressure variability indices in the study groups

ABPM parameters	All patients (n = 175)	Low BPV (n = 85)	High BPV (n = 90)	p value
SD of day systolic readings	11.5±4.3	8.3±2.5	13.9±5.1	<0.001*
SD of day diastolic readings	7.5±2.8	7.1±1.5	8.6±3.3	0.13
SD of night systolic readings	10.3±4.7	8.3±2.9	12.9±4.1	0.002*
SD of night diastolic readings	7.5±2.7	6.1±1.5	9.2±3.2	<0.01*
SD of total systolic readings	11.9±3.9	9.3±2.9	14.0±3.4	<0.001*
SD of total diastolic readings	8.2±2.7	6.5±1.4	9.1±2.5	<0.01*
CV SBP, %	9.8 ± 6.1	8.9 ± 3.3	11.5 ± 7.6	<0.003*
CV DBP, %	4.1±2.0	3.9±2.0	4.2±1.9	0.23
Nondippers	72 (41)	13 (15)	59 (65.5)	<0.01
SBP Morning surge, mm Hg	39±8	13±4	48±11	<0.001*
DBP Morning surge, mm Hg	13±4	10±3	28±7	<0.01*
BPV index				
Weighted systolic SD day-night	10.2±3.4	7.1±1.5	13.7±2.9	<0.001*
Weighted diastolic SD day-night	3.1±1.5	2.9±0.9	3.3±1.6	0.09

Data are presented as mean ± SD or n (%), as appropriate. APBM, ambulatory BP monitoring; BP, blood pressure; SD, standard deviation; CV, coefficient variability; BPV, blood pressure variability. * Significance between high and low BPV.

Statistical Analysis

Categorical variables are presented as medians or means ± SDs, as appropriate. Comparisons between groups were obtained using the χ^2 test or Fisher's exact test, while continuous and normally distributed variables were compared by two-tailed unpaired *t* tests. Correlation tests were performed using the Spearman correlation coefficient test. Based on the median of BPV index (SD_{dn}) = 9.5 mm Hg, participants were stratified into two groups: low variability group and high variability group. Patients were followed up for 14 ± 3 months and the end point was the occurrence of atrial fibrillation. Univariable and multivariable regression analyses were carried out to characterize predictors of NOAF during follow-up. A receiver operating characteristic (ROC) curve was used to characterize the cut-off value of BPV index that predicts the occurrence of NOAF. SPSS version 16.0 (SPSS Inc) was used to perform all statistical analyses.

Results

Of the 175 patients who completed follow-up, 29 (16.7%) patients developed NOAF. Importantly, patients with high BPV had higher prevalence compared to those with low BPV (26 [28.9%] vs. 3 [3.5%], $p < 0.001$). Table 1 presents the demographic characteristics and ABPM parameters of patients with low versus high BPV. All demographic data were comparable among both groups. Only hypertension was more common in the high variability group, but the difference was not significant.

As seen in Table 2, the results show that all ABPM parameters were significantly increased in the high variability group compared with the low variability group, except for CV DBP and weighted diastolic SD_{dn} . CV SBP was 11.5 ± 7.6 in the high variability group versus 8.9 ± 3.3 in the low variability group ($p < 0.003$), and weighted systolic SD_{dn} was 13.7 ± 2.9 versus 7.1 ± 1.5 , respectively ($p < 0.001$). In addition, SBP and DBP morning surges were increased ($p < 0.001$ and $p < 0.01$, respectively). Furthermore, the percentage of nondippers was higher in those with high BP variability ($p < 0.01$).

Table 3 illustrates the echocardiographic characteristics of patients with low versus those with high BPV index. As seen, LAVi ($p < 0.01$) and E/e' ($p < 0.01$) were significantly

Table 3. Echocardiographic data of patients with low versus high blood pressure variability

	Low variability (n = 85)	High variability (n = 90)	p value
LVMI, g/m ²	91.5±13.6	93.1±13.9	0.11
Relative wall thickness	0.41±0.05	0.43±0.05	0.09
Ejection fraction, %	61.5±2.3	62.3±2.5	0.42
LA volume index, mL/m ²	23.9±4.1	34.5±4.6	0.01
Mitral E velocity, cm/s	75±13	71±11	0.09
Mitral A velocity, cm/s	73±11	72±13	0.13
E/A ratio	1.1±0.3	0.9±0.1	0.07
Mean E/e'	7.5±1.3	11.3±2.0	<0.001
PA lateral-PA tricuspid, ms	31.5±9.8	43.5±12.0	<0.001
PA lateral-PA septum, ms	23.6±7.5	29.4±11.8	<0.001
PA septum-PA tricuspid, ms	11.3±5.2	14.5±4.4	<0.01

Data are presented as mean ± SD. LVMI, left ventricular mass index; LA, left atrial; PA, time interval from P wave in ECG to A wave in mitral flow velocity.

Table 4. Association between blood variability index (SD_{dn}) and echocardiographic variables in multiple linear analysis

	Correlation coefficient	p value
Ejection fraction, %	-0.028	0.53
LAVi, mL/m ²	0.139	<0.05
E/e' ratio	0.175	<0.03
Intra-LA EMD	0.392	<0.001
Inter-atrial EMD	0.261	<0.01
Intra-right atrial EMD	0.231	<0.01

LAVi, left atrial volume index; LA, left atrial; EMD, electromechanical delay.

Table 5. Cox regression analysis of weighted systolic blood pressure variability index (SD_{dn}) for predicting NOAF

Variable	HR	95% CI	p values
Age, years	0.97	0.91–1.02	0.79
Gender	0.95	0.17–1.81	0.38
Hypertension	0.98	0.65–1.33	0.09
Diabetes mellitus	1.13	0.09–2.11	0.21
Dyslipidemia	0.65	0.15–1.07	0.63
Smoking	1.25	0.39–2.16	0.60
Ejection fraction, %	0.68	(0.21–1.25)	0.45
LAVi, mL/m ²	1.15	(0.43–1.98)	0.17
E/e' ratio	1.30	(0.23–2.41)	0.11
BPV index (SD _{dn}) ≥12.8 mm Hg	3.75	(1.59–6.35)	<0.001
Atrial EMD	2.72	0.95–5.03	<0.001

LAVi, left atrial volume index; BPV, blood pressure variability; EMD, electromechanical delay.

Fig. 1. ROC curve of the optimal cut-off value to predict new-onset atrial fibrillation in patients with STEMI.

increased in the group with high BPV, whereas LV mass index, relative wall thickness, and EF% were comparable. Importantly, the parameters of atrial EMD were significantly increased in patients with high BVP compared with those with low BPV ($p < 0.001$ for all).

With correlation analysis (Table 4), there was significant positive correlation between SD_{dn} LAVi ($p < 0.05$), E/e' ($p < 0.03$), intra-LA EMD ($p < 0.001$) and inter-atrial EMD ($p < 0.01$). Cox regression analysis (Table 5) revealed that SD_{dn} of systolic BP and intra-atrial EMD were independent predictors for NOAF during follow-up in patients with STEMI (OR = 3.75 and 02.72; $p < 0.001$ for both).

Using ROC curves (Fig. 1), the BPV index (weighted SD_{dn}) value of 12.8 mm Hg was the optimal cut-off value to predict the development of NOAF in patients with STEMI; AUC = 0.87 (95% confidence limit, 0.79–0.95), with a sensitivity of 81% and specificity of 93%.

Discussion

Our study was designed to investigate the association between in-hospital short-term BPV in patients with STEMI and NOAF during a 1-year follow-up in relation to atrial EMD. The results confirmed that intra-left atrial and inter-atrial EMD were increased in STEMI patients with in-hospital short-term BPV. Furthermore, we found that systolic, not diastolic, BPV determines the development of NOAF during follow-up, in both hypertensive and nonhypertensive patients. Importantly, we found that systolic BPV index value ≥ 12.8 mm Hg is the best cut-off value to predict the incidence of NOAF during long-term follow-up.

Previous studies have clearly shown that enhanced fluctuation of BP induces more vascular stiffness and artery remodeling, and may be the spark for the initiation of arteriosclerotic disease [18]. Many clinical trials have demonstrated that short- and long-term BPV not only independently contribute to cerebrovascular events but also implicate prognostic significance [7, 19–21].

The pathogenesis of the independent arrhythmogenic effect of BPV in the setting of STEMI is not clear and it is not obvious whether BPV would help to predict NOAF.

In the setting of acute STEMI, patients may have autonomic instability, which could be associated with BP fluctuation. In addition, those patients may have left atrial remodeling due to diastolic dysfunction and increased left atrial wall tension. These factors may trigger the development of atrial fibrillation.

The mechanism by which BPV may be associated with atrial EMD in the setting of STEMI is not clearly understood. However, in STEMI patients, increased LAVi, diastolic dysfunction, and left atrial remodeling may be associated with elevated brain natriuretic peptide due to increased wall tension – a finding that may be associated with both atrial fibrillation [22] and BPV [23].

It is clearly thought that the autonomic nervous system has a significant role in both short-term BP regulation and long-term sympathetic overactivity. This is suggested to be a mechanistic link between coronary artery disease and atrial fibrillation [24].

It is suggested that autonomic instability, chronic left atrial remodeling, and diastolic LV dysfunction may have a significant impact on the occurrence of NOAF. Furthermore, STEMI patients usually have neurohumoral activation [25] and cardiovascular inflammation [26] – pathophysiologic changes that may play a significant role in both BPV and increased atrial EMD.

With multivariate analysis, the results indicated that BPV and atrial EMD were independent predictors of the occurrence of NOAF during follow-up.

Konstantinou et al. [27] demonstrated that in patients with acute coronary syndrome, in-hospital systolic BPV was associated with adverse cardiovascular events during the 6 months of follow-up. This finding could be related to autonomic dysfunctional status associated with the pathophysiology of acute coronary syndrome, linking BP regulation mechanisms to adverse events.

In our study, increased atrial EMD, a marker of delayed atrial conduction in STEMI patients, was associated with BPV. The delayed atrial conduction suggests that electrophysiological changes in STEMI patients is more evident in subjects with BPV.

Limitations

First, the sample size was small. Second, this was a single-center study. Third, and importantly, the ABPM study was limited to 24 h.

Conclusion

Our findings showed that short-term BPV is associated with NOAF in patients with STEMI. Short-term BPV is predicted to be a contributor factor for left atrial EMD. These findings may explain the development of atrial fibrillation during follow-up of patients with STEMI.

Statement of Ethics

All participants gave a written informed consent, and the study was approved by the faculty ethical and scientific committee according to the Helsinki Declaration.

Disclosure Statement

The authors declare that they have no conflict of interest.

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Author Contributions

Ragab A. Mahfouz: idea, design of the study, and final approval. Mohamed El-Shetry and Mohamed Safwat: conception, collection of the data, and preparing the manuscript. Abdelfattah Frere: analysis.

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