J Surg Med. 2021;5(12):1170-1173.
DOI: 10.28982/josam.1002516 Research article

Journal of Surgery and Medicine
e-ISSN=2602-2079

Fragmented QRS and blood pressure pattern in normotensive individuals with a history of preeclampsia

Kemal Göçer [1], Ekrem Aksu [2], Uğurkan Erkayıran [3]

[1] Department of Cardiology, Necip Fazıl State Hospital, Kahramanmaras, Turkey
[2] Department of Cardiology, Kahramanmaras Sutcu Imam University Faculty of Medicine, Kahramanmaras, Turkey
[3] Department of Obstetrics and Gynecology, Necip Fazıl State Hospital, Kahramanmaras, Turkey

ORCID ID of the author(s)
KG: 0000-0003-2673-1971
EA: 0000-0003-1939-1008
UE: 0000-0002-8519-1883

Corresponding Author
Kemal GÖÇER
Department of Cardiology, Necip Fazıl State Hospital, Dulkadiroglu, Kahramanmaras, Turkey
E-mail: k.gocer01@hotmail.com

Ethics Committee Approval
The ethics committee of Kahramanmaras Sutcu Imam University Faculty of Medicine approved the study on 22.07.2020 with decision number 3. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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

Financial Disclosure
The authors declared that this study has received no financial support.

Published
2021 December 20

Abstract

Background/Aim: Hypertension is well defined in preeclamptic individuals and those with a history of preeclampsia. However, the relationship between blood pressure pattern and fragmented QRS on electrocardiography (ECG) has not been elucidated in normotensive patients with a history of preeclampsia. This study aimed to investigate the frequency of non-dipper blood pressure (BP) patterns in normotensive individuals with a history of preeclampsia and to evaluate the relevance of this pattern to fragmented QRS (fQRS).
Methods: Sixty-three normotensive (office BP measurement) patients with a history of preeclampsia were included in this study between August 2020 and January 2021. These individuals underwent 24-hour ambulatory BP monitoring. The patients were divided into two groups as dipper and non-dipper, according to their BP patterns. The two groups were compared in terms of echocardiographic parameters, laboratory values, and QRS fragmentation on ECG.
Results: Left ventricular diastolic dysfunction (LVDD) diagnosed by echocardiography (P= 0.015) and fQRS on ECG (P=0.002) were significantly higher in the non-dipper group than in the dipper group. Tricuspid regurgitation velocity (P=0.004) and average E/e' ratio (P<0.001) were higher in the non-dipper group. Mitral E/A ratio (P=0.437) and left atrial volume index (P=0.439) were similar between the two groups in echocardiography. The fQRS, LVDD, triglyceride, and low-density lipoprotein were subjected to multivariate logistic regression analysis, and fQRS was found to be an independent predictor of the non-dipper BP pattern in women with a history of preeclampsia (P=0.023, OR=4.951, 95% CI:1.245-19.688).
Conclusion: The presence of an fQRS pattern on the ECG is associated with a non-dipper BP pattern in normotensive individuals with a history of preeclampsia.

Keywords: Preeclampsia, Fragmentation, Electrocardiography, Holter, Blood pressure

How to cite: Göçer K, Aksu E, Erkayıran U. Fragmented QRS and blood pressure pattern in normotensive individuals with a history of preeclampsia. J Surg Med. 2021;5(12):1170-1173.

Introduction

Preeclampsia is a multisystemic disease that occurs in women after the 20th week of pregnancy, characterized by new-onset hypertension and proteinuria or hypertension and multi-organ dysfunction [1]. The incidence of preeclampsia is 3-5% in all pregnancies [2]. The disease usually resolves after birth. However, even after delivery, an increased risk of developing cardiovascular (CV) events despite a normotensive course exists in individuals with a history of preeclampsia [3]. This suggests that it might be related to the blood pressure (BP) pattern. The BP is usually the highest during the daytime and lowest at night. A decrease of less than 10% in nighttime BP levels in 24-hour ambulatory blood pressure monitoring (ABPM) is defined as a non-dipper BP pattern. This pattern is associated with increased CV mortality [4]. Adverse cardiac outcomes caused by preeclampsia do not end with delivery and left ventricular diastolic dysfunction (LVDD), endothelial dysfunction, and atherosclerosis can be observed. It is reported that these adverse cardiac effects seen after preeclampsia is resolved [5]. This process, which is not precisely known, may be related to myocardial and vascular remodeling [6].

Fragmented QRS (fQRS) pattern on electrocardiography (ECG), which is an indicator of delayed and inhomogeneous ventricular conduction, was associated with myocardial fibrosis, scarring, and numerous CV diseases [7]. The fQRS, observed in approximately one-third of hypertensive patients, has a higher incidence than in normotensives even in the absence of left ventricular hypertrophy (LVH) [8]. Various studies consider the relationship between fQRS and non-dipper BP in hypertensive patients [9].

In this study, we investigated the frequency and relationship of non-dipper BP pattern and fQRS in normotensive individuals with a history of preeclampsia.

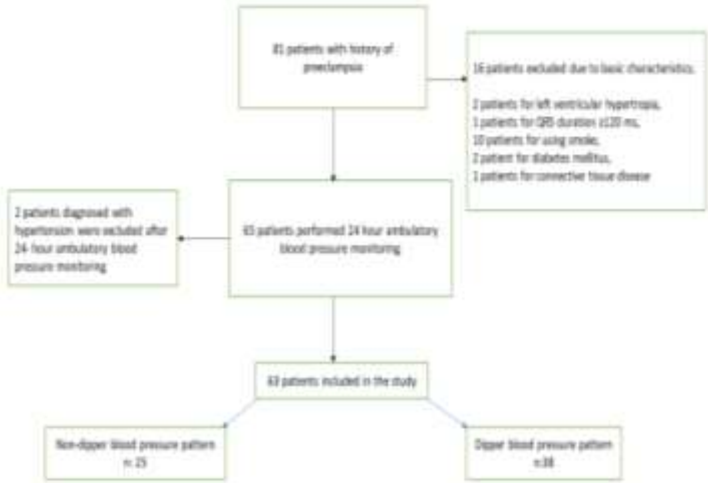
Materials and methods

Study design

This prospective cross-sectional study was conducted between August 2020 and January 2021 at the cardiology, obstetrics, and gynecology clinic. A total of 63 normotensives (according to office BP) consecutive individuals with a history of preeclampsia were included. Written informed consent was obtained from all individuals. The study was conducted per the principles of the Helsinki declaration and approved by the Ethics Committee of Kahramanmaras Sutcu Imam University Faculty of Medicine (22.07.2020, decision no:3).

Eighty-one individuals were examined. Ten smokers, two individuals with LVH, one individual with left bundle branch block, two individuals with diabetes mellitus (DM), one individual with collagen connective tissue disease, and two individuals with hypertension at 24-hour ABPM were excluded. The remaining 63 individuals constituted our study population (Figure 1). They were divided into two groups as dipper and non-dipper, according to their BP patterns. Demographic data and medical histories of all patients were recorded. Electrocardiography, echocardiography, and 24-hour ABPM were performed for all participants. The fQRS and echocardiographic measurements were blindly evaluated to prevent operator-induced bias without knowing the clinical status of the individuals. Laboratory routines consisting of glucose, blood urea nitrogen, creatinine, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG), and hemoglobin were noted.

Figure 1: Flow chart of the study protocol



Definition of preeclampsia

Preeclampsia was defined according to criteria issued by The American College of Obstetricians and Gynecologists in 2017, which include new-onset hypertension after 20 weeks of gestation (systolic ≥ 140 mmHg and/or ≥90 mmHg diastolic BP on two occasions at least 4 hours apart) in addition to proteinuria (≥300 mg in a 24-hour urine or spot urine protein/creatinine ≥30 mg/mmol or at least +1 in stick test), in the absence of proteinuria, new-onset hypertension with any complications, a platelet count of less than 100.000/microliter, pulmonary edema, cerebral or visual symptoms, elevated serum liver enzymes to twice of the normal range, and a serum creatinine concentration of greater than 1.1 mg/dL in the absence of other renal diseases.

Blood pressure measurements

The blood pressure of participants was measured at the time of admission to the hospital. The average office BP values were recorded by calculating the average of the last two BP values measured 2-3 times with an automatic BP measuring device, 1-2 minutes apart after a 5-minute rest. Hypertension and normal BP were determined by the office BP and 24-hour ABPM based on 2020 International Society of Hypertension Global Hypertension Practice guidelines. Normal BP, high-normal BP, and hypertension were defined as <130 and <85 mmHg, 130-140 and/or 85-90 mmHg, ≥140 and/or ≥90 mmHg for systolic and diastolic pressures, respectively.

A 24-hour ambulatory BP device (Mobil-O-Graph NG (I.E.M. Stolberg Germany)) was placed in all individuals to determine BP level and pattern. The cuff of the BP device was placed on the non-dominant arm and the blood pressure was measured automatically every 30 minutes. Participants were asked to continue their daily activities. ABPM was re-performed to individuals with more than 20 percent invalid registration. Mean daily (24 hours), daytime, and nighttime BP records were obtained from ABPM based on the sleep and waking periods. No change was observed in the sleep and wake-up periods while the device was attached. Dipper BP pattern was defined as a more than 10% decrease in systolic and diastolic BP at nighttime, while the non-dipper pattern indicated less than 10% reduction at nighttime in systolic and diastolic BP.

Electrocardiography

Standard 12-lead surface ECG (filter range, 0.15-100 Hz; AC filter, 60 Hz, 25 mm/s, 10 mm/Mv) was performed to all participants. ECGs were blindly interpreted by two independent cardiologists and fQRS morphology defined by Das was examined on the ECG. The fQRS was defined as the presence of various RSR' patterns or notching of the R or S waves in at least two consecutive leads corresponding to a major coronary artery region when the QRS duration was <120 ms.

Echocardiographic parameters

All measurements were performed with the Philips EPIQ 7C (Philips Healthcare, MA, USA) ECHO device in the left lateral decubitus position. Doppler echocardiography and m-mode parameters in two-dimensions were measured per the guidelines of the American Society of Echocardiology (ASE) and the European Association of Cardiovascular Imaging (EACVI). The ejection fraction (EF) was calculated with M-mode imaging. Peak early transmitral flow velocity (E), peak late transmitral flow velocity (A), isovolumic relaxation time (IVRT), and deceleration time (DT) were measured through pulsed doppler in all individuals. Pulsed-wave tissue doppler imaging recordings were obtained through a view of the lateral and septal sections of the mitral annulus from the apical four-chamber after the measurements of conventional echocardiography were completed. Normal diastolic function of LV (EF >50) was defined as the presence of only one or the absence of these parameters: Septal e' velocity < 7 cm/s or lateral e' velocity <10 cm/s, average E/e' >14, Left atrial volume index (LAVI) >34ml/m², tricuspid regurgitation (TR) velocity >2.8 m/s. The presence of two or more of these parameters was defined as LVDD.

Statistical analysis

The effect size (0.492) was calculated with the power analysis program according to the reference study at a test power of 0.80 and a significance level of 0.05. The minimum number of patients was determined as 53 before the study began. Statistical Package for Social Sciences (SPSS) for Windows 21 was used to analyze the data. Continuous variables were expressed as mean (standard deviation) and categorical variables, as a percentage. The participants were divided into two groups as non-dipper and dipper. Kolmogorov-Smirnov test, skewness, and kurtosis were used for the assessment of normal distribution. Independent Student's t-test was used for continuous variables with normal distribution. The Chi-square test was performed on categorical variables. Fragmented QRS, LVDD, TG, and LDL were entered into a multivariate logistic regression analysis. A 2-sided *P*-value of <0.05 was considered significant.

Results

Sixty-three individuals with a history of preeclampsia were included in the study. These individuals were divided into two groups as non-dipper (n=25) and dipper (n=38) according to their 24-hour ABPM. The two groups were compared in terms of basic characteristics (Table 1). There was no significant difference between the two groups' mean body mass indexes (*P*=0.841) and ages (*P*=0.731).

Table 1: Baseline characteristics and clinical findings of study groups

	Dipper (n=38)	Non-dipper (n=25)	*P*-value
Age, years	29.81 (4.63)	30.20 (3.78)	0.731
Body mass index (kg/m2)	36.42 (3.41)	36.27 (2.36)	0.841
Creatinine (mg/dl)	0.80 (0.14)	0.75 (0.14)	0.185
LDL (mg/dl)	108.13 (28.27)	116.51 (26.74)	0.244
HDL (mg/dl)	51.35 (6.33)	49.57 (7.30)	0.307
Triglycerides (mg/dl)	174.76 (64.87)	169.32 (64.33)	0.745
Blood pressure (mm Hg)			
Systolic			
Office	115.25 (10.19)	115.40 (9.67)	0.958
Daytime	115.13 (8.52)	111.24 (9.78)	0.1
Night-time	100.26 (7.99)	106.16 (8.35)	0.007
24-h	111.10 (8.19)	109.72 (9.19)	0.534
Night–day ratio	0.87 (0.02)	0.95 (0.03)	<0.001
Diastolic			
Office	75 (5.32)	72 (6.77)	0.054
Daytime	72.52 (8.33)	68.28 (6.73)	0.037
Night-time	61.97 (8.07)	63.20 (6.48)	0.527
24-h	67.92 (8.27)	66.56 (6.52)	0.491
Night–day ratio	0.85 (0.03)	0.92 (0.06)	<0.001
Fragmented QRS, n (%)	4 (10.5)	11 (44)	0,002
Diastolic dysfunction, n (%)	4 (10.5)	9 (36)	0,015

Abbreviations: LDL: low-density lipoprotein, HDL: high-density lipoprotein

Echocardiographic parameters of all individuals were noted and compared. There was no difference between the two groups in terms of mitral E/A ratio (*P*=0.437) and LAVI (*P*=0.439). TR velocity (*P*=0.004) and average E/e' ratio (*P*<0.001) were significantly higher in the non-dipper group. Table 2 shows the parameters in detail. fQRS (*P*=0.002) and LVDD (*P*=0.015) significantly differed between the two groups.

The presence of LVDD, TG, LDL, and having fQRS were included in the multivariate regression analysis (Table 3). We found that fQRS was an independent predictor of the non-dipper BP pattern (*P*=0.023, OR=4.951, 95%CI 1.245-19.688).

Table 2: Echocardiographic findings of dipper and non-dipper groups

	Dipper	Non-dipper	*P*-value
LVEF (%)	63.76 (2.86)	63.56 (2.46)	0.772
IVST, mm	9.68 (0.66)	9.68 (0.69)	0.981
Mitral E velocity, cm/s	87.81 (7.19)	92.36 (9.49)	0.035
Mitral A velocity, cm/s	73.23 (10.45)	81.08 (12.69)	0.010
Mitral E/A ratio	1.23 (0.25)	1.17 (0.28)	0.437
DT, ms	170.13 (7.51)	166.48 (6.97)	0.057
IVCT, ms	33.68 (2.89)	32.04 (3.85)	0.058
ET, ms	291 (7.95)	286.24 (8.68)	0.029
IVRT, ms	70.60 (5.92)	73.04 (6.49)	0.130
LAVI, mL/m2	20.34 (3.29)	21.08 (4.20)	0.439
TR velocity, cm/s	1.97 (0.15)	2.17 (0.28)	0.004
Tissue Doppler parameters			
Septal e′, cm/s	10.55 (2.03)	8.44 (2.78)	0.002
Lateral e', cm/s	12.31 (2.66)	9.36 (3.20)	<0.001
Average e', cm/s	11.43 (2.17)	8.90 (2.85)	<0.001
Septal A', cm/s	9.02 (1.44)	8.44 (1.73)	0.150
Lateral A', cm/s	10.57 (2.18)	9.12 (2.20)	0.012
Average E/e' ratio	8 (2)	11.29 (3.31)	<0.001

DT: Deceleration Time, ET: Ejection Time, IVCT: Isovolumetric Contraction Time, IVRT: Isovolumetric Relaxation Time, IVST: Interventricular Septal Thickness, LAVI: Left Atrial Volume Index, TR: Tricuspid Regurgitation

Table 3: Independent predictors of non-dipper blood pressure pattern

	B	OR	*P*-value	95%CI
Diastolic dysfunction	1.115	3.049	0.140	0.683-13.409
Triglycerides	-0,004	0.996	0.430	0.987-1.006
Low-density lipoprotein	0.004	1.004	0.727	0.983-1.025
Fragmented QRS, n (%)	1.600	4.951	0.023	1.245-19.688

Discussion

Preeclampsia occurs after the 20^{th} week of pregnancy and is accompanied by organ dysfunctions. The condition regresses with delivery and BP returns to normal levels. However, individuals with a history of preeclampsia have been associated with CV mortality in the future despite the disappearance of the disease [10]. This is the first study on the non-dipper BP pattern, which we think will cause adverse CV events in normotensive individuals with a history of preeclampsia. We investigated fQRS and echocardiographic parameters, which we assumed to affect this pattern.

Blood pressure follows a circadian rhythm throughout the day. Nighttime BP levels decrease more than 10% compared to daytime BP. A less than %10 decrease in BP at nighttime is defined as the non-dipper pattern. Individuals with non-dipper BP patterns had three times more adverse CV events than dipper individuals [11]. Non-dipper normotensive individuals have been associated with a decrease in LVDD and an increase in left ventricular mass. In addition, a few studies report that the non-dipper normotensive pattern was related to chronic kidney disease, high creatinine levels, DM, and metabolic syndrome, which are CV risk factors [12, 13]. In our study, no difference was found between creatinine values, body mass index, and lipid profiles in the non-dipper group compared to the dipper group. The emergence of CV adverse events takes a long time due to the low average age of these individuals. In addition, these patients were not compared with a healthy group and both groups had a history of preeclampsia.

Fragmented QRS is an indicator of ventricular conduction caused by myocardial scarring, ischemia, or fibrosis [14]. Eyuboglu et al. [15] reported that fQRS could be associated with impaired circadian BP changes in prehypertensive patients. The fQRS is more common in hypertensive patients compared to normotensives. In addition, the frequency of fQRS was increased in hypertensive individuals with non-dipper BP patterns compared to individuals with dipper BP patterns [8]. The fQRS pattern was also detected on ECG in normotensive healthy individuals, but the reason for this could not be revealed. It was observed that the frequency of fQRS increased in preeclampsia. In our study, the fQRS pattern was higher in non-dipper BP pattern in normotensive individuals with a history of preeclampsia compared to those with a dipper BP pattern. The increased sympathetic activity due to nighttime autonomic dysfunction in hypertensive patients may have a similar underlying mechanism in normotensive non-dipper individuals. The incidence of ventricular arrhythmia was increased in individuals with non-dipper hypertension and sudden death was observed. The fQRS, which affects the non-dipper BP pattern in our study, may be an indicator of ventricular arrhythmia. Individuals should be followed closely in terms of the fQRS pattern.

Left ventricular diastolic dysfunction often precedes deterioration in systolic function in hypertension and can lead to heart failure or pulmonary edema, both of which are highly common in patients with preeclampsia [16]. In a study, LVDD was seen in 1 out of 5 cases of preeclampsia and in 38.9% of individuals with severe preeclampsia. Muthyala et al. [17] reported that stage 2 LVDD was observed in two-thirds of the severe preeclampsia group. Left ventricular diastolic dysfunction, which is frequent in preeclampsia, was significantly higher in the non-dipper group. In our study, no difference was observed between dipper and non-dipper groups in terms of systolic dysfunction. There were numerically more significant differences in tissue Doppler parameters between the two groups compared to pulsed Doppler parameters. Tissue Doppler imaging may be a sensitive echocardiographic technique to detect diastolic dysfunction. In our study, the effect of diastolic dysfunction on non-dipper BP could not be demonstrated. This may be because our patients were normotensive or not hypertensive enough.

There were some limitations to our study. First, this study was small and scaled. Second, a filter setting of 40 or 60 Hz was not optimal to evaluate fQRS on ECG compared to a low-pass filter setting (100 or 150 Hz). Additionally, the effects of wearing the 24-hour ambulatory BP device on the emotional state, hence their reflection of the BP records, were not known.

Conclusion

The fQRS pattern may be a simple and reliable test for predicting future cardiovascular adverse events in individuals with a history of preeclampsia.

References

1. Atadağ Y, Aydın A, Kaya D, Öksüz A, Köşker HD. Risk assessments, pregnancy and birth processes of pregnant women at primary health care center: A retrospective study. J Surg Med. 2017;1(1):5-8.
2. Filipek A, Jurewicz E. Preeklampsja – choroba kobiet w ciąży [Preeclampsia - a disease of pregnant women]. Postepy Biochem. 2018 Dec 29;64(4):232-29. doi: 10.18388/pb.2018_146
3. McDonald SD, Malinowski A, Zhou Q, Yusuf S, Devereaux PJ. Cardiovascular sequelae of preeclampsia/eclampsia: a systematic review and meta-analyses. Am Heart J. 2008 Nov;156(5):918-30.
4. Tigen K, Karaahmet T, Fotbolcu H, Gürel E, Cevik C, Gecmen C, et al. The influence of dipper and nondipper blood pressure patterns on left ventricular functions in hypertensive patients: a tissue Doppler study. Turk Kardiyol Dern Ars. 2009;37(2):101-6. PMID: 19404031
5. Sánchez-Aranguren LC, Prada CE, Riaño-Medina CE, Lopez M. Endothelial dysfunction and preeclampsia: role of oxidative stress. Front Physiol. 2014 Oct 10;5:372.
6. Staff AC, Dechend R, Pijnenborg R. Learning from the placenta: acute atherosis and vascular remodeling in preeclampsia-novel aspects for atherosclerosis and future cardiovascular health. Hypertension. 2010 Dec;56(6):1026-34.
7. Eyuboglu M. Fragmented QRS as a Marker of Myocardial Fibrosis in Hypertension: a Systematic Review. Curr Hypertens Rep. 2019 Aug 26;21(10):73.
8. Tanriverdi Z, Eyuboglu M, Bingol Tanriverdi T, Nurdag A, Demirbag R. The relationship between fragmented QRS and non-dipper status in hypertensive patients without left ventricular hypertrophy. Clin Exp Hypertens. 2017;39(7):680-4.
9. Zhang R, Chen S, Zhao Q, Sun M, Yu B, Hou J. Fragmented QRS complex is a prognostic marker of microvascular reperfusion and changes in LV function occur in patients with ST elevation myocardial infarction who underwent primary percutaneous coronary intervention. Exp Ther Med. 2017 Jun;13(6):3231-3238.
10. Diehl CL, Brost BC, Hogan MC, Elesber AA, Offord KP, Turner ST, Garovic VD. Preeclampsia as a risk factor for cardiovascular disease later in life: validation of a preeclampsia questionnaire. Am J Obstet Gynecol. 2008 May;198(5):e11-3.
11. Verdecchia P, Porcellati C, Schillaci G, Borgioni C, Ciucci A, Battistelli M, et al. Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. Hypertension. 1994 Dec;24(6):793-801.
12. Hoshide S, Kario K, Hoshide Y, Umeda Y, Hashimoto T, Kunii O, et al. Associations between nondipping of nocturnal blood pressure decrease and cardiovascular target organ damage in strictly selected community-dwelling normotensives. Am J Hypertens. 2003 Jun;16(6):434-8.
13. Rodrigues TC, Canani LH, Viatroski RS, Hoffmann LH, Esteves JF, Gross JL. Masked hypertension, nocturnal blood pressure and retinopathy in normotensive patients with type 1 diabetes. Diabetes Res Clin Pract. 2010 Feb;87(2):240-5.
14. Das MK, Khan B, Jacob S, Kumar A, Mahenthiran J. Significance of a fragmented QRS complex versus a Q wave in patients with coronary artery disease. Circulation. 2006 May 30;113(21):2495-501.
15. Eyuboglu M, Akdeniz B. Association Between Non-Dipping and Fragmented QRS Complexes in Prehypertensive Patients. Arq Bras Cardiol. 2019 Jan;112(1):59-64.
16. Maurer MS, Spevack D, Burkhoff D, Kronzon I. Diastolic dysfunction: can it be diagnosed by Doppler echocardiography? J Am Coll Cardiol. 2004 Oct 19;44(8):1543-9.
17. Muthyala T, Mehrotra S, Sikka P, Suri V. Maternal Cardiac Diastolic Dysfunction by Doppler Echocardiography in Women with Preeclampsia. J Clin Diagn Res. 2016 Aug;10(8):QC01-3.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.