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THE ASSOCIATION BETWEEN FRAGMENTED QRS ON ELECTROCARDIOGRAPHY AND BLOOD PRESSURE PATTERN IN PATIENTS WITH HYPERTENSION

HİPERTANSİYONU OLAN HASTALARDA KAN BASINCI PATERNİ VE EKG'DE FRAGMANTE QRS ARASINDAKİ İLİŞKİ

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ÖZ

AMAÇ: Fragmante QRS (FQRS) kompleksleri bölgesel mi-yokardiyal fibrozisi gösterir ve artmış kardiyovasküler mortalite ve morbidite ile ilişkilidir. Hipertansiflerde fQRS ve kan basıncı paterni arasındaki ilişkiyi araştıran bir çalışma yoktur. Bu çalışmanın amacı hipertansiflerde kan basıncı paterni ve fQRS arasındaki ilişkiyi araştırmaktır.

GEREÇVEYÖNTEM: Kliniğimizde ambulatuvar kan basıncı izlemi yapılmış olan hastalar geriye dönük olarak incelendi. Gündüz değerlerine göre gece sistolik kan basıncının %10-20 düşmesi "dipping patern", bu düşüşün olmaması ise "non-dipping patern" olarak gruplandırıldı. fQRS major koroner arter sulama bölgesi ile uyumlu ardışık iki derivasyonda, ilave bir R dalgasının varlığı, R/S dalgasının çentiklenmesi veya fragmantasyonu olarak tanımlandı.

BULGULAR: Dipping grubunda 98 hasta, non-dipping grubunda ise 89 hasta vardı. Her iki grup yaş, cinsiyet, beden kitle indeksi, lipit profili ve antihipertansif ilaç kullanımı yönünden benzerdi. EKG'de fQRS varlığı dipper grubunda 14 hastada (%14), non-dipper grubunda ise 27 hastada (%30) mevuttu (p=0.008). EGG'de fQRS varlığı non-dipper kan basıncı paterninin bir öngördürücüsüydü (p=0.046, odds oranı=2.27, %95 güven aralığı= 1.04-6.37).

SONUÇ: EKG'de fQRS varlığı non-dipper kan basıncı paternine sahip hastalarda daha fazla bulundu. Ayrıca, bu değişken non-dipper paterninin öngördürücüsüydü.

ANAHTAR KELİMELER: Kan basıncı izlemi, elektrokardiyografi, hipertansiyon, fragmante QRS

ABSTRACT

OBJECTIVE: Fragmented QRS (fQRS) complexes on electrocardiography (ECG) signify areal scar and fibrosis in the myocardium. Our aim was to investigate association between fragmented QRS and blood pressure pattern in hypertensive patients.

MATERIAL AND METHODS: Patients underwent ambulatory blood pressure were studied retrospectively. Patients whose systolic blood pressure was 10-20% lower during the night when compared to the day were grouped as "dipping group", while those who had a decrease less than 10% during the night were grouped as "non-dipping group". The fQRS was defined as the presence of a second R wave, notching of R or S wave or fragmentation in two contiguous leads on ECG corresponding to epicardial major coronary artery region.

RESULTS: The dipping group had 98 patients, while the non-dipping group had 89 patients. The groups were similar in terms of age, sex, body mass index, lipid profile and antihypertensive drugs. The fQRS was observed in 14 patients in the dipper group and 27 patients in the non-dipping group (p=0.008). The fQRS on ECG was found to be an independent predictor of non-dipping blood pressure pattern (p=0.046, odds ratio=2.27).

CONCLUSIONS: The presence of fQRS was more than in hypertensives with non-dipping pattern compared with dipping pattern and this variable was a predictor of non-dipping pattern.

KEYWORDS: Blood Pressure Monitoring, electrocardiography, hypertension, fragmented QRS

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INTRODUCTION

In healthy individuals, blood pressure decreases starting late in the evening and reaches the lowest level around midnight. It starts rising immediately after waking up in the morning. These typical changes in blood pressure are known as circadian rhythm. However, this normal circadian rhythm is impaired in some cardiac and extra-cardiac patients. Based on the observance of ambulatory blood pressure measurements, 10-20% decrease of average systolic blood pressure during the night when compared to that during the day in hypertensive patients is called a dipping pattern (dippers), while a lack of such a decrease in systolic blood pressure is called a non-dipping pattern (nondippers) (1). Non-dipping pattern is unfavorable situation in patients with hypertension and normotensive subjects. Growing evidence indicates that hypertensives with non-dipping pattern have worse cardiovasculary outcomes than hypertensives with dipping pattern. Non-dipping pattern is associated with elevated risk of all-cause mortality (2) and higher frequency of target organ damage in patients with hypertension (3-5).

Fragmented QRS (fQRS) complexes are described as notching or fragmentation of R or S wave on standard 12 lead surface ECG. Gardner et al. (6) have been shown that the fragmentation of QRS complexes is caused by slow speed and non-uniform activation of myofibrils by virtue of cardiac fibrosis. It has been demonstrated that patients with fQRS have a high incidence of unwanted cardiovascular events and sudden death (7, 8).

We designed this study to investigate the possible relationship between fQRS and blood pressure pattern in hypertensive patients. We hypothesized that fQRS may higher in non-dipper hypertensive patients compared with dipper ones.

MATERIALS AND METHODS

Patients: Patients whose ambulatory blood pressure was monitored in Balikesir University Faculty of Medicine Cardiology clinic in the period between March 2013 and February 2016 were studied retrospectively. Chronic hypertensive patients over the age of eighteen were included. Patients with the following conditions were excluded: overt coronary artery disease, previous myocardial infarction or coronary intervention, cardiomyopathy, moderate and serious valve disease, moderate and serious heart failure, history of cerebrovascular disease, transient ischemic attack, peripheral artery disease, diabetes, alcohol or narcotic use, creatinine >1.5 mg/dl, systemic diseases including inflammatory diseases, more than 20% fall of average systolic blood pressure during night, secondary hypertension, masked hypertension, sleep apnea syndrome, extreme obesity (body mass index ≥40 kg/m^2), chronic obstructive lung disease, atrial fibrillation, cardiac devices, serious arrhythmia, night workers, typical left or right bundle branch block (QRS duration more than 120 ms), and incomplete right bundle block (QRS duration <120 ms and RSR′ patterns in V1–2 precordial leads). Clinical data of the patients were obtained from electronic medical recordings and files.

Definition of hyperlipidemia: Hyperlipidemia was defined as the fasting blood total cholesterol level of more than 200 mg / dl or the hypolipidemic drug use.

Definition of Smokers: Smokers were defined as current smokers.

Ambulatory blood pressure monitoring: Twenty four-hour ambulatory blood pressure monitoring was carried out using a digital recorder (Mobil-O-Graph, PWA, 0044, Germany). Daytime was defined as the time interval between the hours of 07.00 and 23.00, and night-time was defined as the time interval between the hours of 23.00 and 07.00. The recorder was adjusted to take measurements in 15 minute intervals during the day and in 30 minute intervals during the night. The patients were instructed to perform their usual daily activities, but also to remain inactive during the measurements. When 80% of the raw data were valid, recordings were accepted.

Definition of dipping and non-dipping blood pressure pattern: Dipping pattern was defined as a night time reduction in mean systolic blood pressure lower 10% to 20% compared with day-time values. Non-dipping pattern was

defined as less than 10% fall in average systolic blood pressure at night compared with day-time values.

Electrocardiographic left ventricular hypertrophy: Left ventricular hypertrophy was investigated using Sokolow–Lyon voltage index (9). ECG criteria for fQRS: All ECGs were recorded at a filter range from 0.15 to 100 Hz. As defined by Das et al. (10), V1 to V5 leads were assigned as left anterior descending coronary artery region. DI, V5, V6 and aVL leads were assigned as left circumflex coronary artery territory. DII, DIII, aVF leads was assigned as right coronary artery region. The fQRS was defined as the presence of a secondary R wave (R′), notching of R or S wave, and the presence of fragmentation at least in two contiguous leads corresponding to a major coronary artery region. All electrocardiograms were reviewed by two skilled cardiologists. Two cardiologists were consistent for ECG signs of fQRS except one case (this case was excluded). The study was conducted in accordance with the principles of the Helsinki declaration.

STATISTICAL ANALYSES

Continuous data that fit normal distribution are shown as mean ± standard deviation, while those that do not fit the normal distribution are given as median and interquartile range. Categorical variables were expressed as frequency and percentage. Comparisons between categorical variables were made by chi-square test (when necessary, Fisher's exact test). The intergroup comparisons of continuous variables fitting normal distribution were made by t test, while those of non-normally variables were made by Mann-Whitney U test. Binary logistic regression analyses were made to determine for independently associated variables with non-dipping blood pressure pattern. In multivariate logistic regression analysis on age, gender, body mass index, smoking, use of antihypertensive medications, LVH, and the presence of fQRS on ECG were included as independent variables. A p value of less than 0.05 was considered significant.

Ethical Approval: The study protocol was approved by the Balikesir University ethics committee.

RESULTS

Seven hundred fifty four patient files and medical records were reviewed. One hundred ninety six patients with newly diagnosed hypertension, 51 patients with extreme dipper pattern, 126 patients with white coat hypertension, 21 patients with elevated night blood pressure, 34 patients with technically insufficient data, 27 patients with blood creatinine level> 1.5 mg / dL, 88 patients with known coronary artery disease or coronary intervention, and 24 patients due to other causes were excluded from the study. One hundred eighty-seven patients who met the criteria of our study were included in the study. Ninety-eight of the patients included in the study displayed the dipping pattern, while eighty-nine the non-dipping pattern. Both groups were similar in terms of age, gender, smoking frequencies, frequency of hyperlipidemia, creatinine levels, antihypertensive medications, and body mass index. The baseline clinical characteristics of the patients in both groups are shown in **(Table 1)**.

Table 1. Clinical characteristics of patients in dipping and nondipping groups

Variables\Group	Dipping Group (n=98)	Nondipping Group (n=89)	*P*
Age, years (mean ± SD)	53.52 ± 8.3	54.2 ± 5.9	0.525
Female, n (%)	56 (57)	42 (47)	0.175
Smoking, n (%)	31 (32)	39 (44)	0.086
Body mass index, kg/ m²	27.4 ± 2.5	28.1 ± 2.9	0.113
Clinic SBP, mmHg (mean ± SD)	127 ± 9	130± 11	0.102
Clinic DBP, mmHg (mean ± SD)	77 ± 7.8	78 ± 8.6	0.497
Hyperlipidemia, n (%)	31 (32)	32 (36)	0.533
Creatinine, mg/dl (mean ± SD)	0.79 (0.14)	0.82 (0.13)	0.248
ACEI-ARB plus diuretic, n (%)	45 (66)	59 (66)	0.996
Beta blocker, n (%)	22 (22)	29 (33)	0.121
Calcium channel blocker, n (%)	26 (27)	24 (17)	0.947
fQRS on ECG, n (%)	14 (14)	27 (30)	0.008
Electrocardiographic criteria of LVH, n (%)	19 (19)	33 (37)	0.007

ACEI: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, DBP: Diastolic blood pressure, fQRS: Fragmented QRS, SD: Standard deviation, SBP: Systolic blood pressure, LVH: Left ventricular hypertrophy

Number of patients with fQRS were 14 (14%) in the dipping group and in 27 patients (30%) in the non-dipping group (p=0.008). All patients with fQRS on ECG had notched at R or S wave.

Mean day-time systolic blood pressure was 127 ± 5 mmHg in non-dipping group and 125 ± 7 mmHg in the dipping group (p=0.127). The mean of the night-time systolic blood pressure measurements was 117±7 mmHg in the non-dipping group and 111±8 mmHg in the dipping group. Thus, mean night-time systolic blood pressure was higher in the non-dipping compared with the dipping group (p<0.001).

Mean night-time systolic blood pressure decline in the non-dipping group was less when compared with the dipping group (8±4 versus 16±5, p<0.001). Findings of 24-hour blood pressure monitoring are shown in **(Table 2)**.

Table 2: 24-h Ambulatory blood pressure monitoring results of patients in dipping and nondipping groups

Variable\Group	Dipping Group (n=98)	Nondipping Group (n=89)	*P*
Day-time SBP, mmHg (mean ± SD)	125 ± 7	127 ± 5	0.127
Day-time DBP, mmHg (mean ± SD)	79 ± 2	80 ± 6	0.142
Nighttime SBP, mmHg (mean ± SD)	111 ± 8	117 ± 7	<0.001
Nighttime DBP, mmHg (mean ± SD)	69 ± 4	70 ± 5	0.126
Nighttime SBP decrease, % (mean ± SD)	16 ± 5	8 ± 4	<0.001
Nighttime SBP decrease, mmHg (mean ± SD)	17 ± 4	7 ± 3	<0.001

DBP: Diastolic blood pressure, SBP: Systolic blood pressure, SD: Standard deviation

Age, gender, smoking, body mass index, use of antihypertensive medications, LVH, and the presence of fQRS on ECG were defined as independent variables in the logistic regression analysis. Based on logistic regression analysis, we found out that the presence of fQRS on ECG was a predictor of non-dipping blood pressure pattern (p= 0.046). Results of logistic regression analysis are shown in **(Table 3)**. In addition, we found that, in detection of non-dipping pattern, sensitivity of the fQRS on ECG was 30% and specificity 86%.

Table 3: Results of multivariate logistic regression analysis for non-dipping blood pressure patternresults of patients in dipping and nondipping groups

Variables	*P*	OR	95% CI
Age	0.345	1.02	0.97-1.06
Gender	0.146	1.61	0.84-3.07
Smoking	0.136	1.67	0.84-3.32
Body mass index, kg/ m²	0.083	1.11	0.98-1.26
ACEI-ARB plus diuretic	0.411	1.44	0.60-3.48
Beta blocker	0.170	1.82	0.77-4.32
Calcium channel blocker	0.503	1.3	0.58-3.02
fQRS	0.046	2.27	1.04-6.37
LVH	0.031	2.53	1.07-5.84

ACEI-ARB: Angiotensin converting enzyme inhibitor-Angiotensin receptor blocker, CI: Confidence interval, fQRS: Fragmented QRS, LVH: Left ventricular hypertrophy, OR: Odds ratio

DISCUSSION

The main finding of our study is that fQRS is higher in hypertensive patients with non-dipper blood pressure pattern compared with dipper ones. Further, presence of fQRS on ECG was a risk factor for non-dipping pattern in the logistic regression analyses. The precise mechanism of non-dipping status is not fully understood. Evidence from many studies signifies the important role of imbalance between sympathetic and parasympathetic nervous system. Researchers have shown that non-dippers had an increase in sympathetic nervous system activity and decrease in parasympathetic nervous system activity throughout the night (11,13). Consequently, hypertensives with non-dipping pattern are exposed to chronically increased catecholamine effect. It is a well-known fact that, chronically exposure to catecholamines is result in cardiac hypertrophy (14, 16). Therefore, it is a reasonable inference that increased sympathetic activity is cause of more extensive myocardial fibrosis in non-dippers compared to dippers. Thus, more extensive myocardial fibrosis may be responsible for the formation of fQRS on ECG in patients with non-dipping blood pressure pattern. Because, it has been revealed by nuclear cardiological methods (17, 18) and magnetic resonance imaging studies (19) that the fQRS on ECG indicates cardiac fibrosis. In a recent study, presence of fQRS on ECG has been associated with myocardial fibrosis in patients with hypertension (20). Furthermore, it has been shown that there is positively association between number of lead with fQRS and more extensive cardiac fibrosis (21). In present study, frequency of fQRS on ECG was higher in the non-dippers compared to the dippers. In addition, in detection of non-dipping pattern, the fQRS on ECG had low sensitivity but high specificity. Moreover, the presence of fQRS on ECG was a predictor for non-dipping blood pressure pattern. These findings may be evidences of extensive fibrosis in non-dipper hypertensives compared to dippers hypertensives.

It has been demonstrated with many studies that non-dippers have higher frequency of left ventricular hypertrophy compared to dippers in patients with treated (3) and untreated hypertension (22, 23). Although ECG has low sensitivity predicting of left ventricular hypertrophy, it is first-line diagnostic tool. But, the specificity of ECG is high for diagnosing left ventricular hypertrophy (24). In present study, we found that frequency of electrocardiographic criteria of left ventricular hypertrophy (Sokolow-Lyon criteria) were higher in the non-dippers. This finding may be an evidence of higher left ventricular hypertrophy in non-dippers compared to dippers.

Non-dipping pattern was associated with advanced age and obesity conditions that increase cardiovascular risk (25). In our study, age and obesity were not significantly higher in the non-dipping group in univariate analyses and these variables were not predictors of non-dipping pattern in logistic regression analyses. It may be due to our relatively low number of cases. Above all, in our study, the number of obese and elderly patients was very low.

The main limitation of this study is the lack of quantitative measurements of myocardial fibrosis such as cardiac magnetic resonance imaging or radionuclide imaging. Another limitation is relatively small number of patients. The presence of fQRS on ECG was higher in hypertensive patients with non-dipping blood pressure pattern compared to the ones with dipping pattern. Moreover, the presence of fQRS on ECG was a predictor of non-dipping blood pressure pattern in patients with hypertension. These findings may be explained by more extensive myocardial fibrosis and higher frequency of myocardial hypertrophy in the non-dippers compared to the dippers. Considering it is an easily applicable method, fQRS might suggest non-dipping blood pressure pattern in patients with hypertension.

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