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Original Paper

Dispersion of Ventricular Repolarization in Relation to Blood Pressure Values in Essential Hypertension

Ana Ciobanu[1], Andreea Simona Hodorogea[1,2], Mădălina Ababei[1], Gabriela Silvia Gheorghe[1,2], Adriana Mihaela Ilieșiu[1,2], Gabriela Uscoiu[1,2], Camelia Nicolae[1,2], I.T. Nanea[1,2]

[1]Cardiology Department, "Theodor Burghele" Clinical Hospital, Bucharest, Romania
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

REZUMAT

Dispersia repolarizării ventriculare în relație cu valorile presiunii arteriale în hipertensiunea arterială esențială

Obiective: Analiza parametrilor dispersiei repolarizării clasici (intervalul QT, dispersia QT (QTd)) și noi (intervalul Tpeak – Tend (Tpe), raportul Tpe/QT) în relație cu profilul tensional și valorile presiunii arteriale (TA) în hipertensiunea arterială esențială (HTAE).

Metodă: 62 de pacienți consecutivi cu HTAE gradele I și II, vârstă medie 55±11 ani, au fost incluși și evaluați simultan prin monitorizare Holter electrocardiografică și monitorizare ambulatorie a presiunii arteriale timp de 24 de ore. Parametrii dispersiei repolarizării au fost măsurați manual.În funcție de raportul TA sistolică diurnă/nocturnă, calculat după formula 100 x (media TA diurnă –media TA nocturnă)/ media TA diurnă, profilul tensional nocturn a fost clasificat în dipper (raport ≥ 10%) și non-dipper (raport<10%).

Rezultate: QTd, Tpe și Tpe/QT s-au corelat cu TA diastolică (TAD) pe 24 ore și cu valorile TAD în perioada de trezire. Tpe și Tpe/QT au prezentat o corelație inversă cu raportul TA sistolică diurnă/nocturnă și au avut valori semnificativ mai mari la non-dipperi față de dipperi. QT nu s-a corelat cu TA și a avut valori similare între dipperi și non-dipperi.

Concluzii: Corelațiile parametrilor dispersiei repolarizării în mod particular cu valorile TAD, explicate în contextul unui lot de studiu relativ tânăr, sugerează că TAD este mai utilă față de TAS în stratificarea riscului cardiovascular la vârste mai tinere.Tpe și Tpe/QT au valori mai mari la non-dipperi față de dipperi, în timp ce QT și QTd au valori similare între cele două grupuri.

Cuvinte cheie: interval QT, dispersie QT, interval T peak - T end, profil tensional nocturn, hipertensiune arterială

Corresponding author: Ana Ciobanu, MD, PhD Candidate
"Theodor Burghele" Clinical Hospital, Bucharest, Romania
20 Panduri Street, District 5, Bucharest, Romania e-mail: ana_ciobanu@outlook.com

ABSTRACT

Objectives: Analysis of classical parameters of dispersion of repolarization (QT interval, QT dispersion (QTd)) and the novel ones (T peak-end interval (Tpe), Tpe/QT ratio) in relation to blood pressure (BP) profile and values in essential hypertension.

Methods: 62 consecutive patients with mild to moderate hypertension, mean age 55±11 years, were included and evaluated simultaneously by Holter electrocardiography and ambulatory blood pressure monitoring for 24 hours. The parameters of the dispersion repolarization were measured manually. According to diurnal/nocturnal systolic BP (SBP) ratio, calculated as 100 x (mean diurnal BP- mean nocturnal BP)/mean diurnal BP, nocturnal blood pressure profile was classified into dipper (ratio ≥ 10%) and non-dipper (ratio < 10%).

Results: QTd, Tpe and Tpe/QT correlated with the values of 24 hour diastolic blood pressure (DBP) and morning DBP. Tpe and Tpe/QT showed significant reverse correlations with the diurnal/nocturnal BP ratio and had significantly higher values in non-dippers compared to dippers. QT did not show any correlation with BP values and was similar between dippers and non-dippers.

Conclusion: The correlation between dispersion of repolarization parameters particularly with the values of diastolic blood pressure, explained in the context of a relatively young study group, leads to the conclusion that DBP is more useful than SBP in cardiovascular risk stratification at a younger age. Tpe and Tpe/QT have higher values in non-dippers compared to dippers, while QT and QTd are similar between these groups.

Key words: QT interval, QT interval dispersion, T peak - T end interval, nocturnal blood pressure profile, hypertension

INTRODUCTION

Hypertension associates with sudden cardiac death, its relationship with ventricular arrhythmias being demonstrated by numerous studies (1). Multiple mechanisms were proposed in order to explain this association, involving both structural and electrophysiological myocardial changes. The electrical ventricular remodeling includes non-uniform prolongation of action potential and duration heterogeneity of refractory periods and conduction velocities of adjacent myocardial areas. All of these changes are referred to as increased dispersion of ventricular repolarization. As cellular basis for this important mechanism of arrhythmogenesis, 3 myocardial cell types were described, with distinct electrophysiological properties: epicardial, endocardial and midmiocardial M cells (2). Differences between their repolarization periods have as an electrocardiographic correspondence changes in T wave features (2). Subsequently, several non-invasive electrocardiographic (ECG) parameters were proposed for quantification of the repolarization dispersion such as QT interval duration, QT dispersion (QTd), T wave microalternans, and more recently, T peak – T end interval (Tpe), T peak - T end/QT ratio (Tpe/QT) and T peak – T end interval dispersion (dTpe).

Experimental studies showed that the peak of the T wave corresponds to the epicardial cell repolarization and that the end of the T wave corresponds to the end of M cells repolarization, so the T peak - T end interval is an index of dispersion of ventricular repolarization (3-5), being useful to stratify the arrhythmic risk (6-11).

There is evidence that the arrhythmic risk in hypertension increases with rises in blood pressure and that the circadian rhythm of blood pressure could play also a role in arrhythmogenesis (1).

In the light of these proofs our purpose is to analyze the classical parameters of repolarization dispersion (QT interval, QT dispersion) and the new ones (T peak-end interval, Tpe/QT ratio and Tpe dispersion) in relation to blood pressure values and profile, in essential arterial hypertension.

METHODS

We included consecutive patients with grades I and II essential hypertension diagnosed according to the European Guidelines for the Management of Hypertension (12), in sinus rhythm..

Exclusion criteria were: secondary hypertension, documented ischemic heart disease (positive ECG stress test, coronary angiography with significant stenosis, prior myocardial infarction), heart failure, severe valvular disease, chronic kidney disease stages III-V, diabetic autonomic neuropathy, atrial fibrillation, bundle branch blocks, pre-excitation syndromes, electrolyte disturbances, treatment with antiarrhythmic drugs.

The patients were evaluated simultaneously by Holter ECG and ambulatory blood pressure monitoring (ABPM) for 24 hours.

Holter ECG monitoring used a true 12 lead continuous recording device (CardioScan 12.4.0054a). On its traces we performed manual measuring of the repolarization dispersion parameters. QT interval was defined as the interval between the onset of the QRS complex and the end of the T wave and was measured in all leads. We took into account its maximal value. Tpe was defined as the interval between the peak and end of the T wave and was measured in the precordial leads. We have taken into account also the mean and maximum values of this interval. For both Tpe and QT intervals the end of the T wave was measured by convention using the method of the tangent to the steepest slope of the descending portion of the T wave. For each interval we performed 3 consecutive measurements in the same lead and then calculated the arithmetic mean. QTd and dTpe were defined as the difference between the highest and lowest value of QT and Tpe intervals. QT, QTd, Tpe and dTpe were corrected to heart rate using Bazett formula and their corrected values were taken into account.

ABPM was performed using a General Electric Tonoport V device. We noted the following parameters provided by ABPM: 24 hours systolic and diastolic blood pressure (BP24) and morning systolic and diastolic BP (defined as 2 hour average of four 30 minutes BP readings just after wake-up) (13).

The diurnal/nocturnal BP ratio was calculated as 100x (mean diurnal BP- mean nocturnal BP)/mean diurnal BP (14). The nocturnal blood pressure profile was classified using this ratio into dippers (ratio $\geq$ 10%) and non-dippers (ratio < 10%) (14).

Statistical analysis

The results are presented as mean ± standard deviation for numeric variables and as absolute numbers and percentages for categorical variables. For the analysis of numeric variables, parametric (Student's t-test, ANOVA) or non-parametric (Mann-Whitney, Kruskal-Wallis) tests were used. Bartlett's test was used for variances homogeneity verification. Categorical variables were compared using χ^2 or Fisher's exact test. Linear regression was used for correlation between different numeric variables. Statistical significance was considered for a p-value <0.05. Statistical analysis was performed using STATISTICA 8.0 and EpiInfo 3.5.3. Graphical representations were performed with STATISTICA 8.0.

Data collection was performed using a database created with Microsoft Access 2010, respecting patients' confidentiality.

RESULTS

The basic characteristics of the subjects are depicted in **Table 1**.

Ventricular repolarization dispersion parameters were evaluated in relation to the parameters derived from ABPM. Analyzing their correlations with the values of BP24 and morning BP, we observed the following (**Table 2**): QTd, Tpe in leads V1-V3, mean Tpe, maximal Tpe and Tpe/QT in leads V1 and V2 significantly correlated with DBP24; QTd, Tpe in leads V2-V4, mean Tpe, maximal Tpe, Tpe/QT in leads V2, V3, V5,mean Tpe/QT and maximal Tpe/QT correlated with morning DBP. The parameters did not correlate with the SBP24 or morning SBP.

At the same time, Tpe and Tpe/QT in leads V2 and V5 and mean Tpe and mean Tpe/QT showed significant reverse correlations with the diurnal/nocturnal BP ratio (**Table 3**).

Comparing ventricular repolarization dispersion parameters in relation to the patterns of nocturnal BP profile, we found significantly higher values of the following parameters for non-dippers compared to dippers (**Table 4**): Tpe in lead V2 (**Fig. 1**), Tpe/QT in lead V2 (**Fig. 2**), Tpe in lead V5 (**Fig. 3**) and mean Tpe (**Fig. 4**).

QT did not show any correlation with blood pressure values and was similar between dippers and non-dippers.

DISCUSSION

There are many controversies regarding which of the blood pressure values, systolic or diastolic, is a more useful predictor for cardiovascular risk stratification. DBP in the general population increases until the seventh decade (60 years for male and 70 years for female) (15) by increasing peripheral resistance (16), an effect that is

Table 1. Basic characteristics of the analyzed group

Parameters	Total (n=62)	Dippers (n=30;48.3%)	Non-dippers (n=32;51.7%)	p
Age (years)	55 ± 11	54 ± 11	56 ± 11	0.49
Male gender	26 (41.9%)	11 (36.6%)	15 (46.8%)	0.41
Body mass index (kg/m2)	29.2 ± 4.8	27.7±5.6	29.9±4.2	0.12
Left ventricular mass index* (g/m2)	92.10 ± 20.77	97.78±20.72	89.44±21.81	0.17
Risk factors				
Smoking	12 (19.3%)	6 (20%)	6 (18.7%)	0.84
Dislipidemia	33 (53.2%)	16 (53.3%)	17(53.1%)	0.98
Disorders of glucose metabolism†	30 (48.3%)	14 (46.6%)	16 (50%)	0.78
Obesity	29 (46.7%)	13 (43.3%)	16 (50%)	0.59
Blood pressure values				
SBP24	134.9±10.4	134.6±9.2	135.1±11.4	0.85
DBP24	82.1±9.0	82.1±8.8	82.1±9.4	0.99
Morning SBP	126.9±14.1	122.7±14.3	130.2±13.2	0.05
Morning DBP	73.6±10.3	70.5±11.1	76.0±9.0	0.05
Nocturnal blood pressure profile				
Diurnal/nocturnal BP ratio	8.3 ± 8.0	14.8±4.8	3.3±6.1	<0.0001
Extreme-dipper	4 (6.4%)			
Dipper	26 (42%)			
Non-dipper	22 (35.5%)			
Reverse-dipper	10 (16.1%)			

*calculated by Devreux formula

† include diabetes mellitus, impaired glucose tolerance and impaired fasting glucose

Table 2. Correlations between the dispersion of repolarization parameters and the 24 hour blood pressure, pulse pressure and morning blood pressure

Parameter	SBP24		DBP24		morning SBP		morning DBP	
	r	p	r	p	r	p	r	p
QT	0.07	0.61	0.11	0.43	0.08	0.53	0.01	0.92
QTd	0.14	0.30	0.36	0.009	0.15	0.27	0.30	0.03
Tpe V1	0.06	0.71	0.42	0.02	-0.07	0.70	0.20	0.27
Tpe/QTV1	0.02	0.88	0.40	0.03	-0.07	0.70	0.17	0.34
Tpe V2	0.02	0.85	0.30	0.03	0.12	0.37	0.44	0.0009
Tpe/QTV2	-0.06	0.65	0.28	0.04	0.07	0.62	0.39	0.003
Tpe V3	-0.16	0.23	0.30	0.03	-0.07	0.59	0.32	0.01
Tpe/QTV3	-0.23	0.09	0.09	0.52	-0.13	0.32	0.26	0.05
Tpe V4	-0.21	0.12	0.10	0.46	-0.14	0.30	0.28	0.04
Tpe/QTV4	-0.24	0.07	0.07	0.58	-0.20	0.14	0.24	0.09
Tpe V5	-0.04	0.75	0.12	0.37	0.00	0.97	0.30	0.03
Tpe/QTV5	-0.05	0.71	0.14	0.30	-0.03	0.82	0.22	0.11
Tpe V6	-0.15	0.27	0.12	0.38	-0.16	0.24	0.10	0.44
Tpe/QTV6	-0.20	0.14	0.08	0.54	-0.23	0.09	0.06	0.63
mean Tpe	-0.11	0.41	0.30	0.02	-0.08	0.56	0.32	0.01
mean Tpe/QT	-0.18	0.19	0.16	0.22	-0.13	0.35	0.27	0.04
maximum Tpe	-0.07	0.60	0.30	0.02	-0.01	0.92	0.32	0.01
maximum Tpe/QT	-0.16	0.23	0.10	0.45	-0.07	0.57	0.26	0.05
dTpe	-0.06	0.65	-0.02	0.85	-0.02	0.85	0.07	0.60

*r – Pearson correlation coefficient

Table 3. Correlations between dispersion of repolarization parameters and the diurnal/nocturnal BP ratio

Parameter	Diurnal/nocturnal BP ratio	
	r	p
QT	-0.01	0.90
QTd	-0.19	0.16
Tpe V1	0.08	0.64
Tpe/QTV1	0.00	0.99
Tpe V2	-0.30	0.03
Tpe/QTV2	-0.29	0.03
Tpe V3	-0.16	0.25
Tpe/QTV3	-0.14	0.30
Tpe V4	-0.08	0.55
Tpe/QTV4	-0.05	0.71
Tpe V5	-0.29	0.03
Tpe/QTV5	-0.29	0.03
Tpe V6	-0.05	0.68
Tpe/QTV6	-0.02	0.88
mean Tpe	-0.28	0.04
mean Tpe/QT	-0.27	0.05
maximum Tpe	-0.20	0.08
maximum Tpe/QT	-0.19	0.08
dTpe	-0.05	0.70

*r – Pearson correlation coefficient

Table 4. The mean values of the parameters of dispersion of repolarization between the types of nocturnal blood pressure profile

Parameter	Dippers (n=30;48.3%)	Non-dippers (n=32;51.7%)	p
QT (ms)	422.6±21.3	422.9±28.6	0.96
QTd (ms)	48.5±18.9	47.7±19.6	0.87
Tpe V1 (ms)	58.9±11.6	57.9±13.1	0.82
Tpe/QTV1	0.1490±0.0312	0.1533±0.0383	0.73
Tpe V2 (ms)	68.1±11.7	77.3±13.6	0.01
Tpe/QTV2	0.1747±0.0263	0.1924±0.0321	0.03
Tpe V3 (ms)	72.7±11.3	77.2±16.1	0.26
Tpe/QTV3	0.1817±0.0279	0.1891±0.0356	0.41
Tpe V4 (ms)	67.6±11.0	72.9±15.0	0.17
Tpe/QTV4	0.1706±0.0279	0.1795±0.0362	0.34
Tpe V5 (ms)	63.2±9.4	71.4±13.3	0.02
Tpe/QTV5	0.1590±0.0225	0.1726±0.0314	0.09
Tpe V6 (ms)	61.8±10.6	65.1±11.8	0.30
Tpe/QTV6	0.1530±0.0213	0.1577±0.0284	0.50
mean Tpe (ms)	65.9±7.2	71.2±10.8	0.04
mean Tpe/QT	0.1655±0.0176	0.1762±0.0265	0.10
maximum Tpe (ms)	76.4±9.2	83.8±14.2	0.08
maximal Tpe/QT	0.1918±0.0210	0.2061±0.0311	0.06
dTpe (ms)	22.5±8.9	25.5±13.7	0.36

attenuated with age (17). In contrast, SBP continuously rises with age, mainly by increase of vessels stiffness and of pulse wave reflection (16). Thus the association between SBP and cardiovascular risk becomes higher with age.

In the present study we found correlations between parameters exploring the dispersion of ventricular repolarization with the values of DBP.

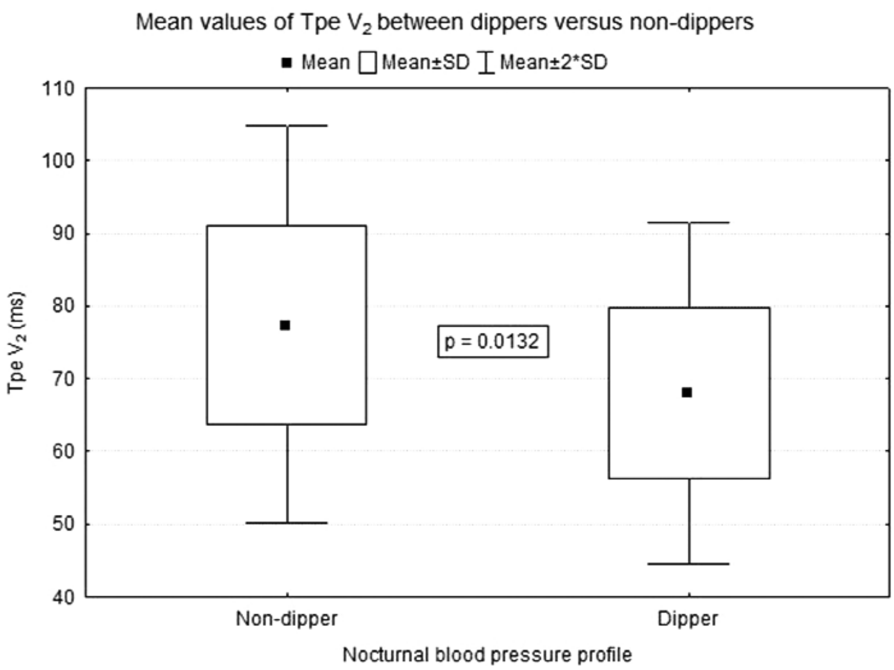

Figure 1. Mean values of Tpe V2 between dippers versus non-dippers

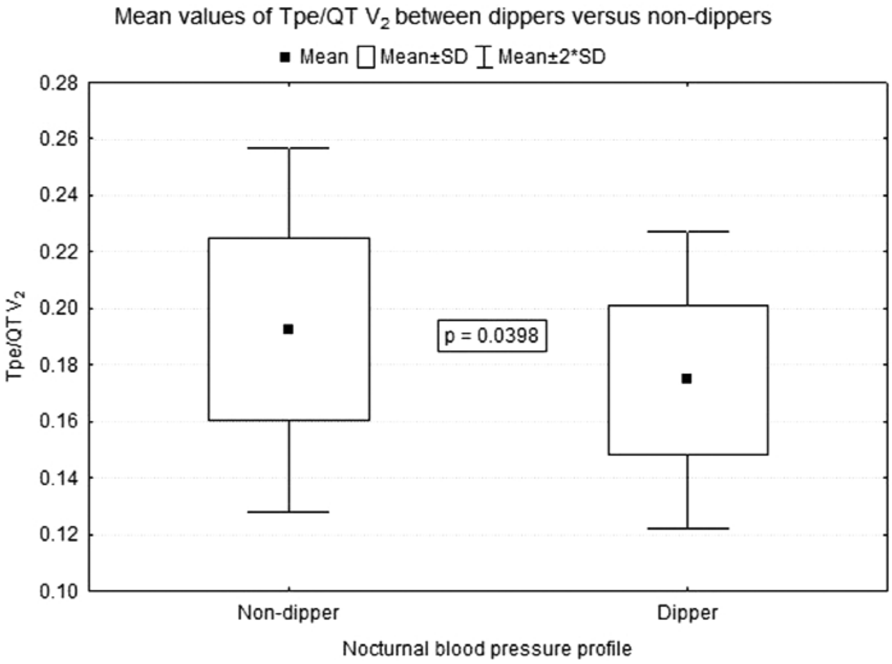

Figure 2. Mean values of Tpe/QT V2 between dippers versus non-dippers

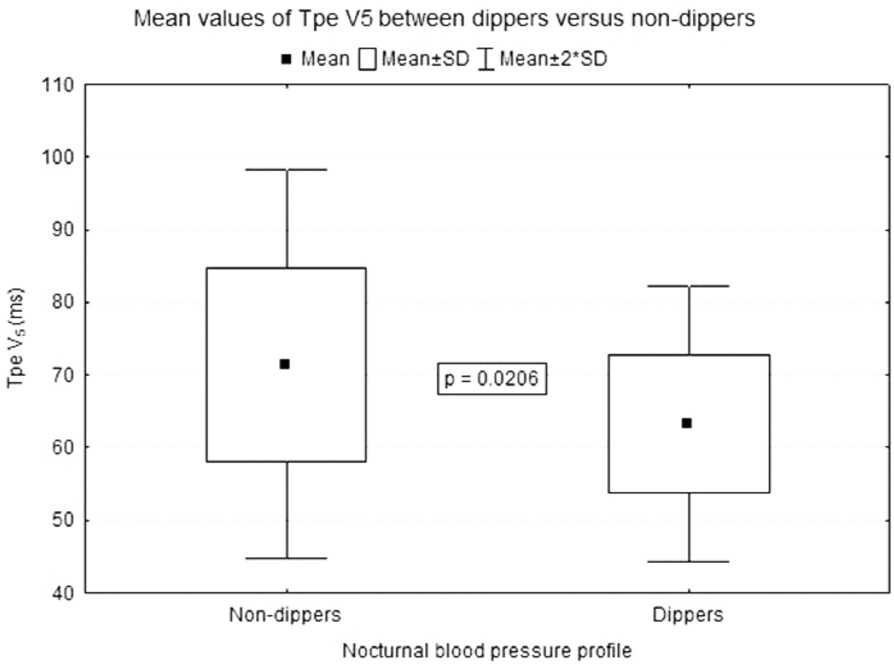

Figure 3. Mean values of Tpe V5 between dippers versus non-dippers

From the pathophysiological point of view the increase of DBP translates into increased afterload. Consequently, dispersion of repolarization seems influenced by changes in afterload. The correlation between dispersion of repolarization parameters particularly with the values of DBP might be explained in the context of a relatively young study group (mean age of 55 ±11 years). Thus we consider that DBP is more useful than SBP in cardiovascular risk stratification at a younger age.

Literature data report a higher incidence of ventricular arrhythmias in hypertensive versus normotensive patients. In patients with hypertension arrhythmias are particularly more frequent in those with higher values of morning BP (18,19), caused by the rises in serum catecholamines (20) and afterload

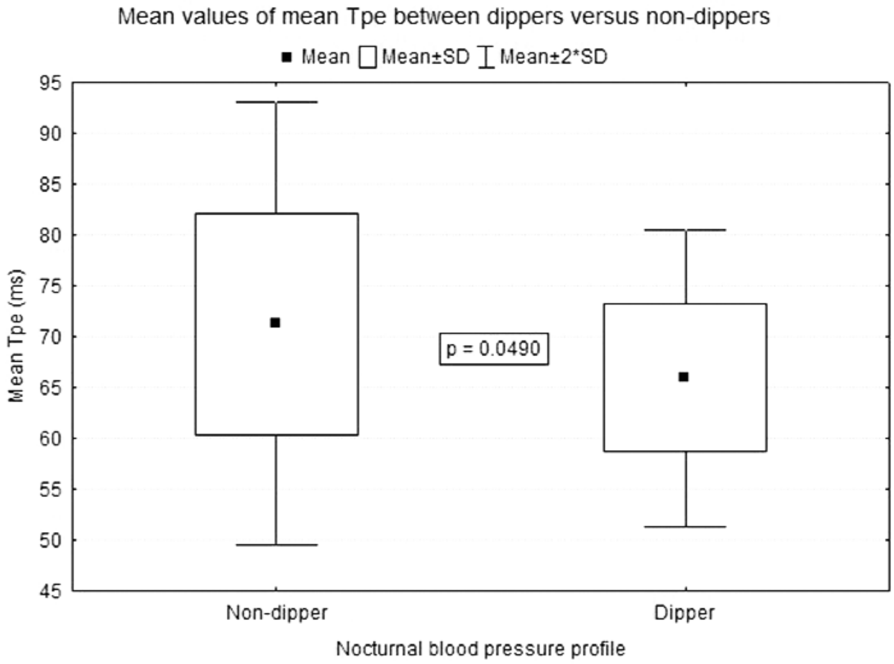

Figure 4. Mean values of mean Tpe between dippers versus non-dippers

(21). The increase in afterload was found to induce electrophysiological changes by influencing the duration of action potentials and ventricular repolarization (18,22). Thus, the present study revealed correlations between parameters of dispersion repolarization and values of DBP during the period of awakening (morning DBP).

The nocturnal blood pressure profile was also shown to influence the dispersion of ventricular repolarization, some studies reporting significantly higher values of QT interval duration and QT dispersion in non-dippers compared to dippers, with the mention that non-dippers had significantly higher left ventricular mass indexes than dippers (23-25). Regarding the new parameters of dispersion of repolarization, few studies on their relationship with the nocturnal BP profile exist. Demir et al. (26), studying a group of 80 hypertensive patients of which 30 with an absent dipping pattern, reported significantly higher QT, QTd, Tpe and Tpe/QT in non-dippers. It needs however to be mentioned that the two groups studied differed by severity of ventricular hypertrophy, the non-dipper subgroup showing significantly higher left ventricular mass index. Karaagac et al. (27) conducted a study on a group of 70 hypertensive patients with metabolic syndrome, half with an absent dipping pattern, with no significant differences between groups based on basic characteristics (demographics, cardiovascular risk factors, parameters of left ventricular remodeling and diastolic function). Values of Tpe and Tpe/QT were significantly higher in non-dippers, while the QT and QTd were similar between the two groups.

In our study Tpe and Tpe/QT (in leads V2 and V5 and their mean values in all precordial leads) were reverse correlated with diurnal/nocturnal BP ratio and were significantly higher in non-dippers versus dippers. In the light of the data presented, with significant differences of QT and QTd values between groups probably dependant on left ventricular mass index, we consider the absence of these differences in our study group due to the basic characteristics which are similar between dippers and non-dippers (**Table 1**).

CONCLUSIONS

The correlation between dispersion of repolarization parameters particularly with the values of diastolic blood pressure, explained in the context of a relatively young study group, leads to the conclusion that diastolic blood pressure is more useful than systolic blood pressure in cardiovascular risk stratification at a younger age.

Tpe and Tpe/QT have higher values in non-dippers compared to dippers, presenting also a reverse correlation with the diurnal/nocturnal BP ratio, while QT and QTd were similar between these groups.

QT did not show any correlation with blood pressure values.

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