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The Association Between The Severity of Coronary Atherosclerosis and Abnormal Nocturnal Blood Pressure Variations in Hypertensive Patients

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ABSTRACT

It is well known that the hypertension and coronary artery disease show a strong cause and effect relationship, but the severity and complexity of atherosclerosis in non-dipper hypertensive patients is undefined yet.

We evaluated the association between dipper or non-dipper hypertension and the extent of coronary atherosclerosis by SYNTAX score, in patients with the chronic coronary syndrome referred for percutan coronary angiography.

Hypertensive patients that performed a percutan coronary angiography for the first time were included, and the SYNTAX score was computed. According to their ambulatory blood pressure measurements, the hypertensive patients were grouped as dippers and non-dippers.

One hundred and twenty-four patients were included. 87 hypertensive patients were accepted as dipper group, and 37 patients were in non-dipper hypertension group. The mean SYNTAX score for dipper group was 10.3±2.6 and 14.6±3.9 for non-dipper group (p<0.001). The number of diseased vessels is higher at the non-dipper group (1.5±1.1 versus 2.2±1.7, p<0.001). The hypertensive patients that have a high SS were more likely to be non-dipper.

In hypertensive patients, the non-dipper pattern of nocturnal blood pressure variations is associated with more complex and severe coronary artery lesions in chronic coronary syndrome.

Keywords: Coronary Artery Disease; Hypertension; Atherosclerosis; Coronary Angiography, Dipper, Non-Dipper

Introduction

The relationship between hypertension and atherosclerosis is well known, and the guidelines are listing hypertension as a major risk factor for coronary heart disease (1,2). Epidemiologic investigations have also confirmed this close etiological relationship. Hypertension can damage coronary arteries with different mechanisms. The coronary arterial endothelial dysfunction, impaired vascular wall permeability, altered properties of platelets and coronary vascular remodeling are proven mechanisms of CHD induced by hypertension (3,4,5). Hypertension is also accepted as independent risk factor for major adverse cardiovascular events and worse prognosis (6).

Recently, ambulatory blood pressure monitoring (ABPM) has gained importance for hypertension treatment management (7). ABPM has revealed that the circadian (day/night) blood pressure profile is variable in patients with hypertension. Some of hypertensive patients do not show a nocturnal decrease in blood pressure and they are called as "non-dippers," whereas other patients exhibit night-time BP fall and called as "dippers" (8). Non-dipper pattern of hypertension is a potent predictor of major adverse cardiovascular events and associated with increased end-organ damage (9,10).

The SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score quantifies the severity and complexity of coronary artery lesions in patients undergoing a coronary angiography (11). High syntax score (SS) means more complex coronary artery lesions and worse prognosis of treatment. Many studies confirmed that SS could predict clinical outcomes after coronary artery bypass grafting (CABG) or percutan coronary intervention (PCI) (12,13). This study aimed to examine the relationships between nocturnal blood pressure variations (dipper, non-dipper) and the complexity of coronary arterial lesions (CAL). Due to the absence of better indicators for assessing the coronary complexities, studies about

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the relationship between risk factors-for example hypertension- and the severity of CAL were not many. So we designed this study to determine this relationship.

Materials and Methods

Study Population: From January 2019 to October 2020, we screened all essential hypertension patients who applied to the Van training and research hospital and had 24-hour ambulatory blood pressure monitoring. There were 1764 hypertension patients in our database. We looked for patients with coronary angiography because of chronic coronary syndrome for the last two years. Previous coronary angiogram, history of myocardial infarction or acute coronary syndrome, previous percutan coronary intervention or coronary artery bypass grafting, heart failure, secondary hypertension and chronic kidney or liver diseases were the exclusion criteria of the study. We found 172 relevant patients and called them. Forty-eight of them are not available or did not give consent. One hundred twenty-four patients in the database included coronary angiography cases because of ischemia evidence in non-invasive stress tests. All included patients called and signed informed consent for data collection. Demographic parameters were recorded.

Measurements and Definitions: The latest ESC guideline on the subject has defined the hypertension limits as being above 140 mmHg systolic and / or 90 mmHg diastolic (15). Blood pressure values recorded with a portable device, Contec ABPM-50. The device recorded the blood pressure per 30 minutes while the patients continued their normal daily activities. Blood pressure recording data was loaded into a software. It was analyzed with Contec-ABPM program. Day-time, night time and all time blood pressure averages (systolic, diastolic and mean arterial blood pressures) were calculated. Mean artery blood pressure calculated with a formula of 'Diastolic BP+(Systolic BP-Diastolic BP)/3'. If the night-time mean artery pressure decrease over %10 occurs, it was defined as dipper pattern of hypertension. Otherwise if the nocturnal decrease remains under %10, it was called as non-dipper pattern of hypertension. Eighty-seven of patients showed dipping pattern in ambulatory blood pressure monitoring, and 37 of patients were non-dipper.

The SYNTAX score (SS) was calculated for all patients by the SS algorithm that is available in the

relevant website (14). Each coronary lesion more than a 50% diameter stenosis in vessels and at least 1.5 mm was separately score. Double investigators calculated the SS at a different time to reduce interpretations due to researchers and one week later each researcher recalculated the SS to minimalize inaccuracy. Patients also divided to two groups according to their SS scores. The patients with a SS above 22 were determined as 'high SS group', and the other lower SS patients were named 'low SS groups'.

Statistical Analysis: The gathered data were analyzed statistically by using SPSS version 18 (SPSS Inc., USA). Kolmogorov-Smirnov test was performed to detect the distribution of the variables. We observed that all the variables were distributed normally. Variables are presented as mean ± standard deviation. Categorical variables are expressed as number (%). Student-t test was used for comparing quantitative variables. Pearson chi-square tests were performed for categorical variables. A p-value < 0.05 was considered statistically significant.

Results

Of 124 patients, dipper group was predominant (n=87 and n=37). Table 1 summarizes patient demographics. Female patients were more than males in both groups (%59 of dippers and %54 of non-dippers), but it was not statistically significant (0.284). Age, body-mass index (BMI) and current smoker rates were similar between the groups. Among the patient groups, the proportions of patients with Type 2 Diabetes Mellitus and Dyslipidemia were similar (p-value 0.68 and 0.231, respectively). Non-dipper group patients had a slightly longer duration of hypertension than dippers (4.3±1.4 and 3.7±1.2) (p=0.322), and they were receiving more anti-hypertensive drugs (p=0,044). For all anti-hypertensive drug subgroups, non-dipper groups had a higher rate of drug use (Table 2).

First blood pressure measurements at the office were similar between groups but 24 hours mean systolic BP was higher at non-dipper patients (p=0.023). The systolic, diastolic, and mean arterial pressures were higher at the non-dipper group as the classification suggests (p<0.001). There was no difference for other daytime or 24-hour blood pressure measurements. Heart rate average differences were not statistically significant. Mean syntax score of dipper group's coronary angiograms was 10.3±2.6. Non-dipper hypertensive patients had a mean 14.6±3.9 syntax

Table 1. Patient Characteristics Results

	Total n=124	Group 1 (dipper) n=87	Group 2 (non-dipper) n=37	p
Age (mean±SD)	48.5±12.6	47.2±11.3	50.4±13.2	0.136*
Sex (female) (n,%)	72 (58)	52 (59)	20 (54)	0.284**
BMI (mean±SD)	26.1±4.6	25.6±3.4	27.2±4.1	0.164*
Current smokers, n(%)	61 (0.49)	44 (0.5)	17 (0.45)	0.124**
Diabetes Mellitus n(%)	27 (21,7)	19 (21,8)	8 (21,6)	0.68**
Dyslipidemia, n(%)	49 (39,5)	35 (40)	14(37,8)	0.231**
Hypertension duration, years (mean±SD)	3.9±2.0	3.7±1.2	4.3±1.4	0.322*
Number of drugs (mean±SD)	1.8±1.2	1.7±0.4	2.2±1.1	0.044*
Office SBP, mmHg (mean±SD)	151.7±22.4	152.4±21.4	149.8±23.8	0.381*
Office DBP , mmHg (mean±SD)	91.9±14.6	92.6±15.6	91.3±16.4	0.201*
24 h mean SBP , mmHg (mean±SD)	136.2±12.7	133.2±14.6	138.8±12.2	0.023*
24 h mean DBP , mmHg (mean±SD)	84.6±12.0	81.4±11.1	89.1±16.1	0.045*
24 mean HR (mean±SD)	77.6±9.9	76.1±11.4	80.8±8.1	0.396*
Daytime mean SBP , mmHg,(mean±SD)	137.5±18.2	136.8±14.1	138.6±15.2	0.404*
Daytime mean DBP, mmHg,(mean±SD)	88.7±14.9	88.5±12.5	89.1±12.1	0.766*
Daytime mean HR (mean±SD)	77.0±9.3	76.1±11.2	79.0±9.9	0.380*
Nighttime mean SBP, mmHg (mean±SD)	126.3±14.5	122.8±12.2	135.6±14.9	<0.001*
Nighttime mean DBP, mmHg (mean±SD)	81.9±14.4	76.4±11.1	89.1±11.1	<0.001*
Night time mean HR,(mean±SD)	67.7±9.1	66.1±11.2	70.1±6,3	0.056*
Daytime MAP , mmHg (mean±SD)	106.4±14.7	106.2±12.1	107.3±12.9	0.401*
Nighttime MAP , mmHg (mean±SD)	94.0±11.2	91.0±10.1	98.9±11.7	<0.001*
Syntax score (mean±SD)	12.7±4.4	10.3±2.6	14.6±3.9	<0.001*
Number of diseased vessels (mean±SD)	1.7±1.4	1.5±1.1	2.2±1.7	<0.001*

SD: Standart Deviation, *Student-T Test, **Pearson chi-square test

Table 2. Results Regarding Drugs Used By Patients

	Dipper n=87	Non-dipper n=37	p
CCB n(%)	20 (22.9)	12(32.4)	<0.001**
β-blockers n(%)	14(16.09)	11(29.7)	<0.001**
Anti-RAS n (%)	31(35.6)	24(64.8)	<0.001**
Diuretics n(%)	11(12.7)	7(18.9)	<0.001**

**Pearson chi-square test

Table 3. Treatment Methods of Patients According To Coronary Angiography Results

	Dipper n=87	Non-dipper n=37	p
PCI n(%)	49 (56,3)	23 (62,16)	0,042**
CABG n(%)	15 (17,2)	6 (16,21)	0,31**
MT n(%)	23 (26,4)	8 (21,62)	0,038**

**Pearson chi-square test
PCI: Percutan Coronary Intervention, **CABG:** Coronary Artery By-pass Grefting, **MT:** Medical Treatment

score, and this difference is statistically significant (p<0.001). Non-dipper group has also more diseased vessels (2.2±1.7 and 1.5±1.1) (p<0.001). Treatment types of patients, shown at Table 3. Non-dipper patient group had a higher rate of percutan coronary interventions (PCI) than dipper group (p:0.042).

The vast majority of patients were in the low SS group (n=101). In the 'High SS group' there were ten dipper patients and 13 non-dipper patients (%56 non-dippers rate). But the 'low SS group' had less non-dipper patients (24 non-dipper and 77 dippers). According to these results, the hypertensive patients who have undergone a coronary angiogram and have a high SS score are more likely to be non-dipper (p<0.001).

Discussion

Although the relationship between hypertension and coronary atherosclerosis is well described, there are not much data about correlation of hypertension and complexity or severity of coronary atherosclerosis. The pathogenesis of hypertension and coronary artery lesions are different from each other, but there are much interactions between two illnesses. The hypertension could accelerate the atherosclerosis in CHD patients by reducing coronary reserve because of microvascular disease (16, 17). In 2014, Im et al. used coronary CT angiography (CCTA) in asymptomatic hypertensive adults to investigate the relationship between the grade of blood pressure (BP) and plaque characteristics, severity and prevalence of coronary atherosclerosis (18). A grade-response relationship is founded according to grade of hypertension. Zhang et al. showed higher syntax score and more diseased vessels in

hypertensive coronary heart disease patients than non-hypertensive patients (19). Some independent risk factors were described for complexity of CAL's, such as old age, male gender, and diabetes mellitus, at the same time, smoking, dyslipidemia, and hypertension were not defined as independent risk factors (20).

It is known that non-dipper hypertensive patients have a higher risk of cardiovascular disease than dipper patients (21, 22). Non-dippers are also associated with adverse cardiac remodelling and dysfunction (23). The non-dipper pattern is considered to be a strong predictor of adverse events and associated with end-organ damage. The association between coronary artery lesion complexity and non-dipper hypertension pattern is not well-known. We aimed to investigate this relationship in patients with the chronic coronary syndrome. We used Syntax score system to evaluate the CAL's complexity and severity. When the non-dipper and dipper groups were compared, the mean SS was higher in the non-dipper group. As expected, we found a positive correlation between high SS and non-dipper hypertension pattern. The number of diseased vessels was higher at the non-dipper group. When the hypertensive patients with high SS were also examined, it was found that the non-dipper pattern was more frequent. These results were seen as another evidence that the non-dipper pattern leads to poor cardiovascular outcomes.

Another conclusion drawn from the study is that patients with non-dipper patterns have more advanced coronary artery disease, although they use more drugs. This result suggests that the use of multiple drugs may not prevent the progression of coronary artery lesions in patients with the non-dipper pattern.

This study suggests that the arterial hypertension and especially the non-dipper pattern of hypertension can be considered a risk factor for severity and complexity of coronary artery lesions in patients with chronic coronary syndrome. Therefore, hypertensive patients should be evaluated and classified with ABPM, and the patients with non-dipper pattern should be approached more carefully because of their higher risk.

References

1. Knuuti J, Wijns W, Saraste A et al. ESC Scientific Document Group, 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes: The Task Force for the diagnosis and management of chronic coronary syndromes of the European Society of Cardiology (ESC), *European Heart Journal*, Volume 41, Issue 3, 14 January 2020, Pages 407–477, https://doi.org/10.1093/eurheartj/ehz425

2. Lawes CM, Bennett DA, Lewington S, Rodgers A. Blood pressure and coronary heart disease: a review of the evidence. Semin Vasc Med 2002; 2: 355-368.

3. Sudano I, Roas S, Noll G. Vascular abnormalities in essential hypertension. Curr Pharm Des 2011; 17: 3039-3044.

4. Figueiredo VN, Yugar- Toledo JC, Martins LC, et al.. Vascular stiffness and endothelial dysfunction: correlations at different levels of blood pressure. Blood Press 2012; 21: 31-38.

5. Sipahi I, Tuzcu EM, Schoenhagen P, et al. Effects of normal, pre- hypertensive, and hypertensive blood pressure levels on progression of coronaryatherosclerosis. J Am Coll Cardiol 2006; 48: 833-838.

6. Turnbull F. Effects of different blood- pressure- lowering regimens on major cardiovascular events: results of prospectively- designed overviews of randomised trials. Lancet 2003; 362: 1527-1535.

7. Head GA, Mihailidou AS, Duggan KA, et al. Definition of ambulatory blood pressure targets for diagnosis and treatment of hypertension in relation to clinic blood pressure: prospective cohort study. BMJ 2010; 340: 1104.

8. O'Brien E, Sheridan J, O'Malley K. Dippers and non-dippers [letter].Lancet 1988; 2: 397.

9. Verdecchia P, Porcellati C, Schillaci G, et al. Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. Hypertension 1994; 24: 793-801.

10. Cuspidi C, Meani S, Salerno M, et al. Cardiovascular target organ damage in essential hypertensives with or without reproducible nocturnal fall in blood pressure. J Hypertens 2004; 22: 273-280.

11. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, *et al.* The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005; 1: 219-227.

12. Farooq V, Head SJ, Kappetein AP, Serruys PW Widening clinical applications of the SYNTAX Score. Heart 2014; 100: 276-287.

13. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary inter- vention in patients with three- vessel disease and left main coronary disease: 5- year follow- up of the randomised, clinical SYNTAX trial. Lancet 2013; 381: 629-638.

14. Serruys P.W, Onuma Y, Garg S, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009; 5: 50-56.

15. Williams, B.; Mancia, G.; Spiering, W.; Agabiti, R.E.; Azizi, M.; Burnier, M.; Clement, D.L.; Coca, A.; Simone, G.; Dominiczak, A.; et al. ESC/ESH Guidelines for the management of arterial hypertension. Eur. Heart J 2018; 39: 3021-3104.

16. Juhola J, Magnussen CG, Berenson GS, et al. Combined effects of child and adult elevated blood pressure on subclinical atherosclerosis: the International Childhood Cardiovascular Cohort Consor- tium. Circulation 2013; 128: 217-224

17. Delles C, Neisius U, Carty DM Proteomics in hypertension and other cardiovascular diseases. Ann Med 2012; 44: 55-64.

18. Im, T.S., Chun, E.J., Lee, M.S. et al. Grade-response relationship between blood pressure and severity of coronary atherosclerosis in asymptomatic adults: assessment with coronary CT angiography. Int J Cardiovasc Imaging 2014; 30: 105-112.

19. Zhang et al. Characteristics of coronary arterial lesions in patients with coronary heart disease and hypertension. Springer Plus 2016; 5: 1208.

20. Tanaka T, Seto S, Yamamoto K, et al. An assessment of risk factors for the complexity of coronary artery disease using the SYNTAX score. Cardiovasc Interv Ther (2013; 28: 16-21.

21. Kurpesa M, Trzos E, Drozdz J, Bednarkiewicz Z, Krzeminska-Pakula M. Myocardial ischemia and autonomic activity in dippers and nondippers with coronary artery disease: assessment of normotensive and hypertensive patients. Int J

Cardiol 2002; 83: 133-142.

22. Ohkubo T, Hozawa A, Yamaguchi J, et al. Prognostic significance of the nocturnal decline in blood pressure in individuals with and without high 24 hour blood pressure: the Ohasama study. J Hypertens 2002; 20: 2183-2189.

23. H.-S. Seo et al. Non-dippers are associated with adverse cardiac remodeling and dysfunction (R1). International Journal of Cardiology 2006; 171-177.