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Research Article

The Effect of Circadian Blood Pressure in The Development of Lacunar Infarcts, Together with Other Possible Factors

Gökhan KESKİN[1,*], Abdülkadir ÇAKMAK[2]

[1]Faculty of Medicine, Amasya University, Amasya, Turkey
***Corresponding Author**: **Email:** gokhan.keskin@amasya.edu.tr **ORCID:** 0000-0002-1695-5624

[2]Faculty of Medicine, Amasya University, Amasya, Turkey
Email: abdulkadir.cakmak@amasya.edu.tr - **ORCID:** 0000-0001-7427-3368

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Abstract:

This study was carried out in Amasya University S.S.R.E. Hospital Department of Neurology and Cardiology between 2021 and 2022. Total number of 58 patients (29 lacunar infarct patients and 29 control subjects, 42 females and 16 males) over the age of 45 (mean age 57.1+-6.8) were recruited to the study. All patients underwent 24-hour blood pressure monitoring. The patients with a history of stroke, malignancy, renal or endocrinal disease were excluded from the study. According to the systolic blood pressure measurements, twenty-seven patients were 'non-Dipper' and thirty-one patients were 'Dipper'. Diastolic blood pressure measurements revealed that twenty-one patients were 'non-Dipper' and thirty-seven patients were 'Dipper'.Mean daytime and night-time systolic blood pressure values were higher in patients with lacunar infarction (p:0.02). There was no difference in the diastolic BP and variability (p > 0,05). The clinical importance of the alteration in the reduction of blood pressure is still controversial. Understanding the alterations in blood pressure rhythmicity will be helpful to prevent and treat the lacunar infarctions.

1. Introduction

Lacunar infarcts are defined as small subcortical infarcts normally located in the basal ganglia brainstem etc. that result from occlusion of a single penetrating artery of the brain [1,2] and they account for about a quarter of all ischemic strokes [3]. With development using of magnetic resonance (MR) and computed tomographic (CT), silent lacunar infarction shown to occur among the elderly and patients with stroke [4,5]. Besides of age and other cardiovascular risks, lacunar infarction is related to arterial hypertension [6]. The major risk factor of the development of lacunar infarct is hypertension. Dipper is someone who shows a reduction in BP of 15% mm Hg; those who have less than a 15% reduction in BP during sleep are defined as non-dippers [7]. In patients with lacunar infarction, a reduced night-time blood pressure decreased as seen before [8]. On the other hand limited knowledge regarding the possible pathogenic role of circadian blood pressure changes for the occurrence of lacunar infarction is possible [9]. In this study we evaluated the association of the CBP alterations.

2. Materials and Methods

The study was carried out in Amasya University S.Ş.R.E. Hospital Department of Cardiology/Neurology between 2021 and 2022. Total number of 58 patients (29 lacunar infarct patients and 29 control subjects, 42 females and 16 males) over the age of 45 (mean age 57.1+-6.8) were enrolled to the study. Patients with a history of stroke, malignancy, renal or endocrinal disease were excluded from the study. Patients' clinical risk factors were determined and the occurrence of lacunar ınfarction was analysed. All patients underwent detailed physical examination after enrolment to the study. Presence of lacunar infarction risk factors, together with the presence of diabetes mellitus, hypertension, coronary artery disease and smoking was determined. Blood chemistries and complete blood count were analysed in the whole study population. Carotid and vertebral artery Doppler ultrasonography, electrocardiography (EKG), computerized tomography of brain and magnetic resonance

imaging were evaluated in patients with lacunar infarction (n=29) and in control subjects (n=29).

2.1 Blood Pressure Measurements

Non-invasive ambulatory blood pressure (ABP) monitoring and CBP monitoring were carried out with MAPASYS4 by using SYS-SAVE-33 software program. According to some population-based studies, for average daytime values, recordings between 6 AM and 10 PM and for average night-time values, recordings between 10 PM and 6 AM were used [8].
Holter recordings were accepted as successful if 80% or above of the measurements were valid. Successful Holter recordings were taken into consideration.
Blood pressure was obtained in daytime and in deep sleep with 15-minute intervals. Total, nocturnal and daytime systolic, diastolic, and mean BP and heart rate values were determined. MBP was calculated using SBP-DBP/3+DBP formula. Circadian blood pressure difference was determined as the difference between daytime and nocturnal measurements.
If the difference between the diurnal BP and nocturnal BP was equal to or greater than 10 mmHg, then the patient was accepted to be a dipper, whereas those who had less than a 10% reduction in BP during sleep were defined as non-dippers [10]. At least two measurements were performed for both systolic and diastolic BP.

2.2 Lacunar Infarct Classification

Evaluation of lacunar infarction was performed using MRI or CT imaging. Lacunar infarct is expressed as low-signal intensity areas on CT and/or T1-weighted MR images.

3. Results

3.1 Demographic Features

The number of patients with lacunar infarct and control patients are 29 and the results were evaluated in 3 stages:
1- evaluating patients with lacunar infarct and healthy controls
2-Comparison of ‘dipper’ and ‘non-dipper’ patients
3-Determination of the factors that can cause the occurrence of lacunar infarct

According to the SBP measurements, there were 27 non-dipper patients and 31 dipper patients. DBP measurements showed that there were 21 non-dippers and 37 dippers. Mean daytime and nocturnal SBP values were higher in patients with lacunar infarct (p:0,02). Reduced SBP variability was demonstrated. There was no difference in the variability of DBP measurements (p> 0.05).
History of hypertension (p: 0.001 OR, 4.84; 95% Cl, 1.47-15.97), night-time SBP values (p<0.001 OR, 1.11, 95% Cl, 1.05- 1.17) and reduced circadian SBP variability (p<0.001, OR: 15.1 95% Cl, 4.2-54.5) were significant factors in the development of lacunar infarct.

4. Discussions

Hypertension stands out as a very relevant risk factor for lacunar infarction [11,12]. The underlying pathophysiological mechanism of circadian BP variability causing lacunar infarct is unclear. In our study, presence of hypertension was found to be higher in the patients with lacunar infarct. Mean daytime and night-time systolic blood pressure values were higher and reduction in the alteration of systolic BP values was detected in patients with lacunar infarction. There was no difference in the Diastolic BP and its alterations. Hypertension, night-time systolic BP values and the reduction of the circadian systolic BD variability were effective factors in the development of lacunar infarction. A risk factors besides age, hypertension, and pathologic changes of circadian rhythmicity may cause multiple lacunar infarctions [8]. rolonged hypertension can produce hypertensive, atherosclerotic, and arteriosclerotic cerebrovascular changes (Figure 1) [13].

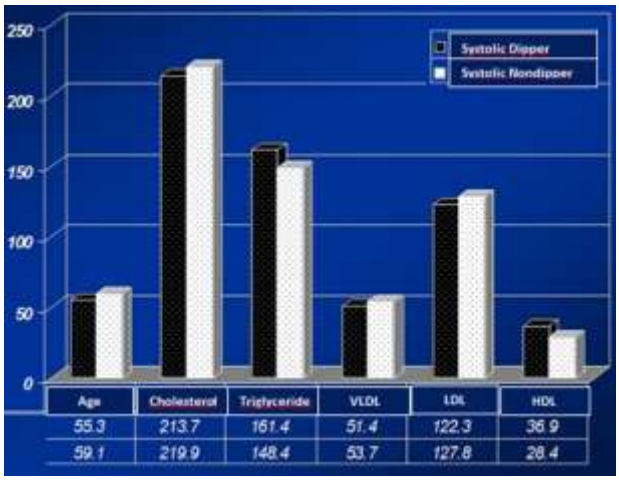

Figure 1. *Hypertensive, atherosclerotic, and arteriosclerotic cerebrovascular changes in long-term hypertension*

Circadian blood pressure patterns are the major impact factor on the development of early carotid atherosclerosis [14].
Systolic daytime blood pressure variability is most closely related to the extent of intima media thickness [15], which is generally considered as an early marker of atherosclerosis (Figure 2) [16]. The

lacunar infarction was due to the changes of systolic circadian blood pressure patterns. The diastolic component of blood pressure is the major determinant of cardiovascular risk, systolic hypertension (Figure 3) [8].

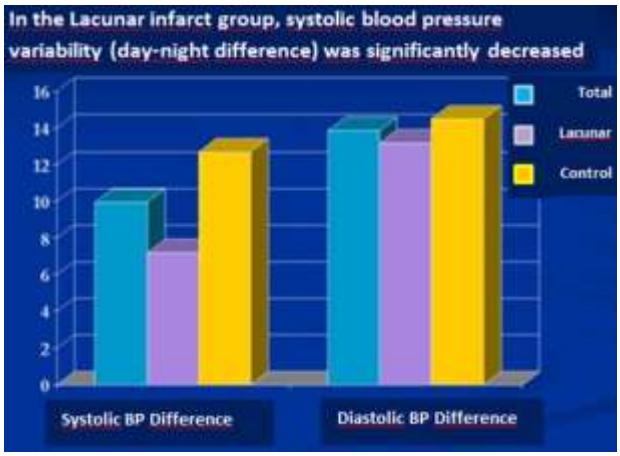

Figure 2. *Lacunar infarct group, systolic blood pressure*

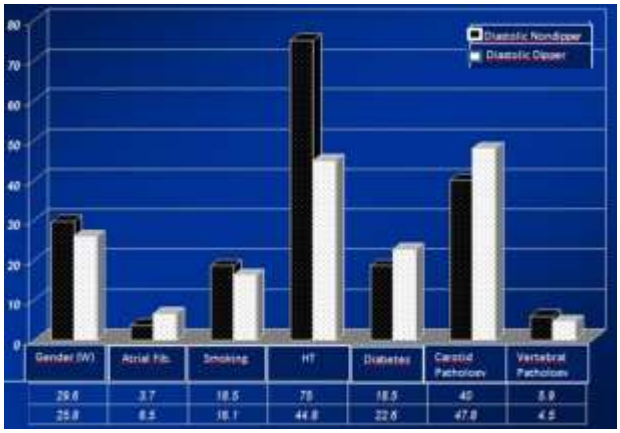

Figure 3. *Lacunar infarct group, diastolic blood pressure*

In recent studies it has been shown that daytime BP variability is more strongly related to organ damage than sudden BP changes (Figure 4) [17]. We used MAPASYS4 in our study to monitor ambulatory BP. The studies with lacunar infarct patients showed that reduced nocturnal BP dipping were associated with the development of lacunar infarct [18]. Most authors have reported that non-dippers, tended to have more severe target organ damage, including cerebrovascular and cardiovascular disease (Figure 5) [19,29]. Nocturnal pressure dip is frequently encountered in patients with hypertension and vascular disease and could be a risk factor for stroke [20]. An absent or lower

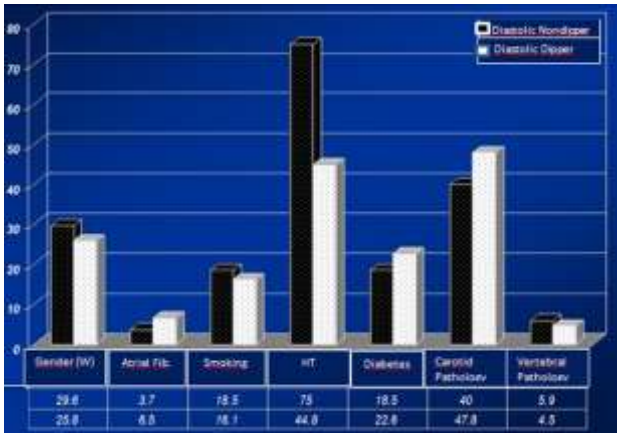

Figure 4. *Lacunar infarct group, diastolic blood pressure*

nocturnal blood pressure fall in elderly hypertensive patient is associated with silent cerebrovascular damage. In contrast, the presence of a nocturnal blood pressure fall could prevent progression of hypertensive vascular damage (Figure 6) [21]. The incidence in symptomatic (recurrent) and/or asymptomatic (silent) brain lesions was higher in non-dippers than in nocturnal dippers [20]. In dipper patients being treated with antihypertensive medications, who had additional new silent ischemic lesions, stenosed arterial lesions were demonstrated (Figure 7) [20]. Controlling high blood pressure is effective in preventing stroke recurrence [22] and preserving cerebral blood flow [23]. The diurnal change of autonomic nervous system activity is closely involved in the diurnal BP variation pattern [24]. A diurnal pattern of BP change, with morning values being higher than those recorded in the evening is well known and it decreases during night-time [20]. Diurnal SBP change was significantly reduced in patients with cortical infarcts and primary intracerebral haemorrhage, but the change in SBP was not prominent in those with subcortical infarcts compared with control subjects [20].

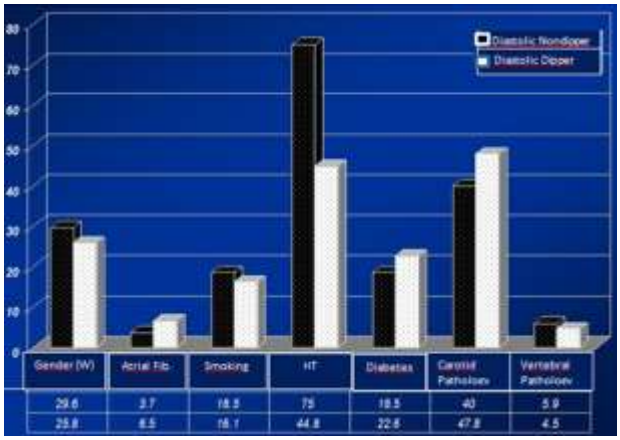

Figure 5. *Lacunar infarct group, diastolic blood pressure*

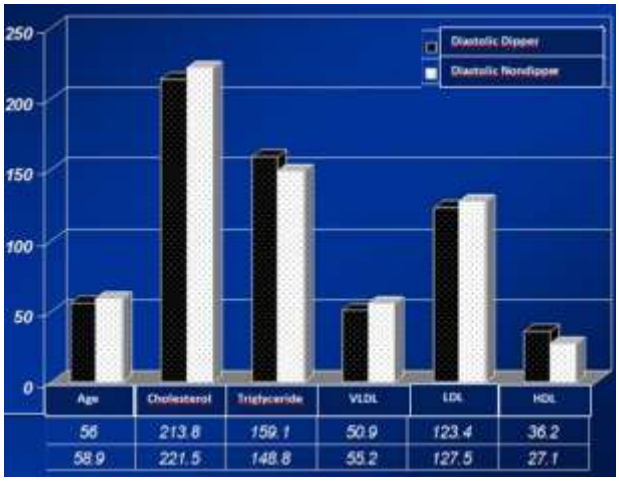

Figure 6. *Lacunar infarct group, diastolic blood pressure*

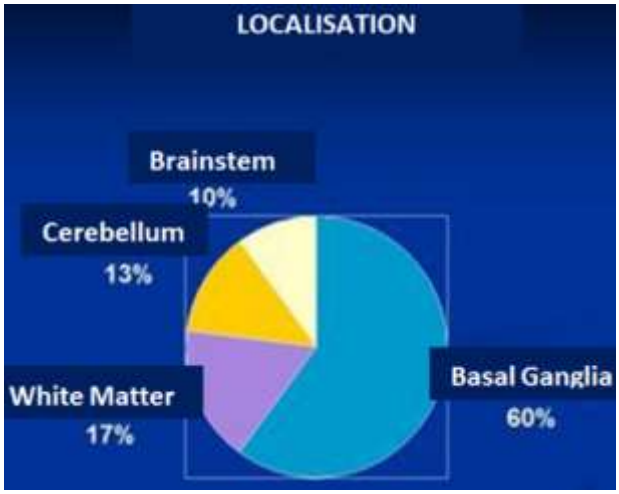

Figure 7. *Lacunar infarct localisation*

The clinical importance of reduced blood pressure variability is still controversial. Further studies with long term follow up are needed to understand/reveal/disclose the importance of circadian blood pressure alterations.

Author Statements:

- **Ethical approval:** As this work related to human issue required processes for permission has been done. (ethical report info: dated on 27.12 2021 Amasya University, E-76988455-044-49467).
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- **Data availability statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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