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Ambulatory blood pressure variability and elevated non-specific inflammatory markers

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Abstract

Objective: In the age of the biomarkers, costly and unnecessary determinations are frequent. It has been observed that hypertension is associated with abnormalities of the erythrocyte series by increasing the level of red blood cell distribution width (RDW) and neutrophil-lymphocyte ratio (NLR). Blood pressure variability (BPV) seems to be a surrogate risk factor in hypertension. The goal was to test the relationship between BPV and "non-specific" markers of inflammation. **Method:** A number of 53 treated hypertensive patients were included. From the complete blood count (CBC) neutrophil-lymphocyte percentage ratio and red cell distribution width (RDW) were calculated. Based on 24 hour ambulatory BP monitoring (ABPM), BPV was calculated by the average real variability (ARV). Using the median of this value, the subjects were divided into low and high variability groups. The inflammatory status of the groups, the correlation between biomarkers of inflammation and BPV were analyzed. **Result:** The median ARV was 10.89 mmHg, the NLR in the low versus increased variability group was 2.83±0.14 vs. 2.32±0.2, p=0.04, and the RDW was 13.2±0.34% vs 12.52±0.20% in the high variability group, p=0.03. We found positive correlation between RDW and BP variability, p=0.00, r^2=0.19, CI 0.1220 to 0.6009. The correlation between NLR and ARV was statistically less significant, p=0.05, r^2=0.07, CI: 0.01101-0.5087. **Conclusions:** Increased blood pressure variability appears to be associated with more pronounced inflammatory status. The NLR and RDW as parts of the routine investigations are cost-effective and could be useful for screening of patients with high cardiovascular risk for specific investigations.

Keywords: neutrophil-lymphocyte ratio, red cell distribution width, average real variability

Introduction

The importance of blood pressure variability (BPV) over 24 hour and its relationship to target organ damage has been reported in several studies, but the underlying cause of BP variations is still a matter of debate. The gold standard to evaluate circadian

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BP profile is the 24-h BP monitoring which allows also an accurate evaluation of the 24-h BPV [1]. It has been hypothesized that chronic inflammation could be incriminated in the pathophysiology of hypertension and could alter BP profile [2]. In hypertensive subjects, elevated serum levels of inflammatory cytokines, high sensitive C-reactive protein (hs-CRP), adhesion molecules were found supporting the presence of inflammation [3].

Many inflammatory markers, such as cytokines, and adhesion molecules have been found elevated in HT, supporting the role of inflammation [4]. In latest studies the total blood count derived red cell distribution width (RDW) and neutrophil lymphocyte ratio (NLR) have been established as cost-efficient markers of inflammation. Higher values were recorded in hypertensive patients with altered circadian BP variability especially with non-dipper pattern [2,5]. The aim of this study was to evaluate the relationship between 24-h BP variability and hematological markers RDW and NLR.

Material and Methods

In this study 53 hypertensive subjects were included, 33.9% women / 66.03% men, fulfilling the inclusion criteria. All the patients gave written informed consent, the study was performed in line with the World Medical Association Declaration of Helsinki. Inclusion criteria were: history of HTN, or use of hypertension medication or daytime BP greater than 135/85 mmHg or nighttime BP > 120/70 mmHg or 24-h BP > 130/80 mmHg according to ESH/ESC guidelines [1]. Patients with diabetes mellitus, kidney or liver disease, pregnant women, younger than 18 years, presence of thrombosis, hematological disorders, tumors, inflammatory diseases that could alter white blood cells (WBC) were excluded from the study. The ambulatory BP monitoring (ABPM) was carried out for 24-hour for each patient starting between 8-10 am, measurements were performed at every 20 minutes at daytime as well as at nighttime. Blood pressure variability over 24 hour was calculated for each subject by using the formula of average real variability (ARV) [7]. By using the median of the recorded ARV values, subjects were divided in two groups, group 1 included subjects with high variability, group 2 comprised those with low variability. As part of routine laboratory tests, total blood count analysis was performed, blood samples were collected in the morning between 8-10 am, from brachial vein, after 8 hours of fasting. The inflammatory status of the groups were compared by analysing white blood cell count (WBC), red cell distribution width (RDW), neutrophil-lymphocyte ratio (NLR), obtained by dividing the percentage of neutrophils by those of lymphocytes. Data were collected as raw-data, the characteristics of the groups were compared by unpaired t-test, correlations were performed by using Pearson's test. The p value < 0.05 was considered statistically significant.

Results

The median value calculated for ARV was 10.89 mmHg. Therefore, in group 1 there were 22 subjects, 7 male, 15 female while in group 2 there were included 31 subjects, 15 male and 16 female. Mean age in group 1 was 69.64±12.02 years while in group with low variability 59.97±12.37 years. In group with high variability 45,4% of the subjects displayed dipper profile, while in group with low variability 71% were dippers. In group 1 mean systolic BP was 133.6±15.60 mmHg while in group 2 was 127.8±11.69 mmHg. Mean diastolic BP in group 1 was 73.05 mmHg vs 72.3 mmHg in group 2. Regarding inflammatory markers, the mean RDW values showed statistically significant difference among the groups, figure 1. The NLR was also higher in group 1 reflected in figure 2. By using Pearson's test, positive correlation was recorded between RDW values and ARV as well as between NLR and ARV defined by average real variability as shown in figure 3 and 4.

Discussion

In our study we aimed to evaluate the relationship between blood pressure variability and non-specific hematological markers of inflammation, RDW and NLR. We found that subjects with blood pressure variability values above 10.89

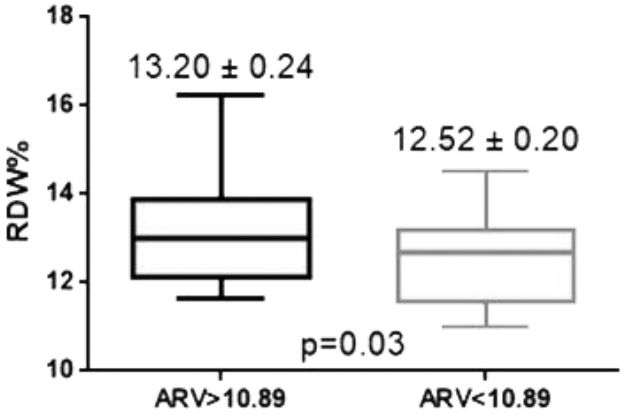

Figure 1. Mean RDW% values of group 1 and group 2 compared with t-test (RDW%- red cell distribution width, ARV- average real variability)

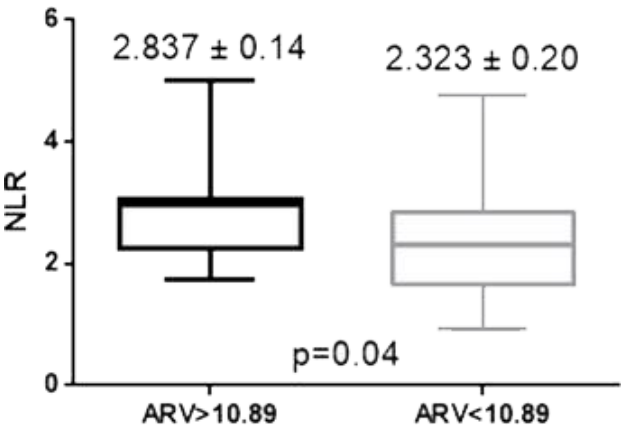

Figure 2. Mean NLR values of group 1 and group 2 compared with t-test (NLR- neutrophil lymphocyte ratio, ARV- average real variability)

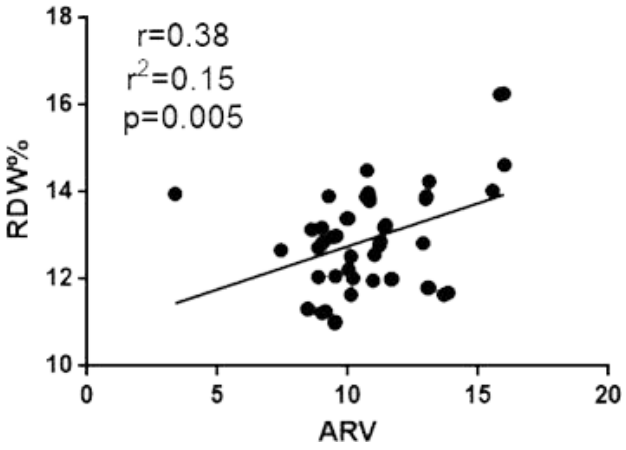

Figure 3. Pearson's correlation between ARV and RDW% (ARV- average real variability, RDW%- red cell distribution width)

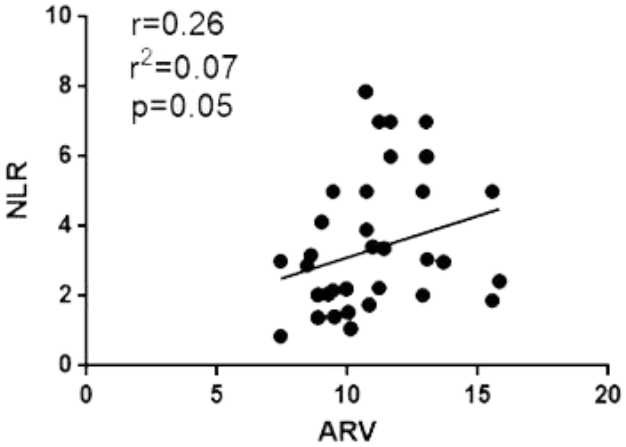

Figure 4. Pearson's correlation between ARV and NLR (ARV- average real variability, NLR- neutrophil lymphocyte ratio)

mmHg associate greater levels of inflammatory markers like RDW and NLR. These results are in range with data from large studies, but although BPV was assessed by 24-hour monitoring, variability was defined as dipper profile [6]. A difference between the groups was recorded also in terms of dipper/non-dipper profile, where dipper profile was significantly greater in subjects with low variability. In order to define BPV several parameters were suggested. Mena et al highlited the superiority of average real variability and proved that in contrast to other parameters this index adds prognostic information to 24-hour BP monitoring [7]. We found positive correlation between NLR values and ARV. In previous studies higher NLR levels were associated to higher risk of developing atherosclerotic disease. Nonetheless, elevated NLR levels may indicate subclinical inflammation which promotes atherosclerosis and plays crucial role in several diseases including hypertension. Therefore, we believe that elevated values of NLR associated with high BP variability could have a more pronounced negative impact in the progression of hypertension [8, 9]. Positive correlation was found also between the hematological marker RDW and elevated ARV values. The available studies found only correlations between elevated RDW values in hypertension and prehypertension, data regarding the association between BP variability and RDW values are very limited [10].

A possible explanation for this association could be the fact that oxidative stress as well as chronic inflammation may alter the production of red blood cells resulting in a rise of RDW values [11].

Also, there are some limitations of the study, like the relatively small sample size. We defined a cut-off value for ARV of 10.89 mmHg but there is no international limit defined and could be very different in large cohorts. We only assessed NLR and RDW and our study did not evaluate specific inflammatory markers like hs-CRP, interleukins which are linked to atherosclerotic diseases.

Conclusion

High blood pressure variability is associated to higher values of RDW and NLR. These non-specific low-cost inflammatory markers could be of importance by screening of high risk hypertensive patients for further specific investigations. Nonetheless, decreasing BPV below 10,89 mmHg could represent a new therapeutic target in the management of patients with hypertension. In order to define a correct cut-off value further populational studies are needed.

Conflict of interest

The authors confirm that there are no conflicts of interest

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