The Diagnostic Value of Combined 24-h BP and ECG Holter Monitoring in Detection of Cardiac Arrhythmias in Patients with Arterial Hypertension

Nabil Naser¹,², Esad Pepic³, Sevleta Avdíc⁴
¹Polyclinic „Dr. Nabil”, Sarajevo, Sarajevo, Bosnia and Herzegovina
²Faculty of Medicine, University of Sarajevo, Sarajevo, Bosnia and Herzegovina
³Institute for Pathophysiology, Faculty of Medicine, University of Sarajevo, Bosnia and Herzegovina
⁴Bayer Medical Institute, Tuzla, Bosnia and Herzegovina

Corresponding author: Assoc. Prof. Nabil Naser, MD. PhD. Polyclinic „Dr. Nabil”, Sarajevo, Bosnia and Herzegovina. Tel: +387 33 777 711, fax: +38733 777 710. E-mail: nabil@bih.net.ba. ORCID ID: http://www.orcid.org/0000-0002-278-8574.

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1. BACKGROUND
Arterial hypertension is a major cause of morbidity and mortality worldwide. Elevated BP is the leading global contributor to premature death, accounting for almost 10 million deaths in 2015, 4.9 million due to ischaemic heart disease and 3.5 million due to stroke. The global prevalence of hypertension was estimated to be 1.4 billion in 2019, with a prevalence of over 150 million in central and eastern Europe. The worldwide prevalence of hypertension will continue to rise towards 1.5 billion by 2025. Arterial hypertension is a major cardiovascular risk factor and underlies many cardiovascular conditions, including heart failure, coronary artery disease, peripheral artery disease, stroke, chronic renal failure and cognitive decline. Arrhythmias are common problems in hypertensive patients. The presence and complexity of both supraventricular and ventricular arrhythmias may influence morbidity, mortality, as well as the quality of life of patients.

ABSTRACT
Background: Arrhythmias are common problems in hypertensive patients. The presence and complexity of both supraventricular and ventricular arrhythmias may influence morbidity, mortality, as well as the quality of life of patients. Objective: The aim of this study was to assess the diagnostic value of combined 24h BP and ECG Holter monitoring in detection of cardiac arrhythmias in patients with arterial hypertension. Methods: We analyzed the simultaneous records of combined 24h BP and ECG Holter monitoring for 356 adult patients with diagnosed arterial hypertension in the period from January 2017 until January 2021 year. The cardiac arrhythmias were classified in three main groups as following: a) Supraventricular arrhythmias; b) Ventricular arrhythmias; c) Bradycardia’s. Standard transthoracic echocardiograms were performed in order to evaluate signs of hypertensive or structural heart disease with focus on left ventricle hypertrophy and LV function. Results: Patients had a mean age of 64 ± 11 years, 62% male. Average clinic BP was 153.4±18/87.5±14 mmHg. More than 46% of patients displayed a very high-risk profile. In all enrolled patients, cardiac arrhythmia was detected in 302 (84%) patients. The total number of patients with supraventricular arrhythmias was 153 (50.7%) patients. Ventricular arrhythmias were detected in 98 (32.5%) patients. Bradycardia’s were detected in 51 (16.9%) patients. Elevated resting heart rate in sinus rhythm was detected in 87 (31.6%) of 275 patients with sinus rhythm.

Conclusion: Most arrhythmias are related to longstanding arterial hypertension. Effective treatment of arterial hypertension plays important role in preventing structural and functional cardiac abnormalities which will contribute to the reduction of cardiac arrhythmias in hypertensive patients.

Keywords: Arterial hypertension, combined 24-h BP and ECG Holter monitoring, Cardiac arrhythmias.
scribed for the management of hypertensive patients can contribute to the manifestation of arrhythmias, mainly through electrolyte disturbances. The first non-invasive ambulatory blood pressure monitoring (ABPM) devices appeared in the 1960s, initially for experimental use only, and the first paper on the technique, by Kain et al., was published in the journal Circulation in 1964. Ambulatory blood pressure monitoring (ABPM) is being used increasingly in both clinical practice and hypertension research. It is now considered an essential part of standard clinical practice, both for diagnosis and for assessing response to therapy. After FDA approval in 2010, the use of device with combined blood pressure (BP) and ECG Holter monitoring have shown the advantages over office BP measurement, especially the fact that it provides a large number of readings taken in the patient's daily environment (including during sleep) as well as the simultaneously and continuously recording and storing ECG and blood pressure data for 24 hours side by side, gives the physician more useful information to evaluate the patient's cardiovascular status and detection of cardiac arrhythmias. The combined BP and ECG Holter also provides interactive blood pressure recording at times of certain cardiac abnormalities. This can enhance the diagnostic value of the recorded data, while increasing patient comfort and ease of use. It is also used for assessing response to pharmacological and non-pharmacological therapy.

2. OBJECTIVE
The aim of this study was to assess the diagnostic value of combined 24h BP and ECG Holter monitoring in detection of cardiac arrhythmias in patients with arterial hypertension.

3. PATIENTS AND METHODS
We analyzed the records of combined 24h BP and ECG Holter monitoring for 356 adult patients with elevated blood pressure in the period from January 2017 until January 2021 year. All patients underwent clinical and physical examination. Baseline examination included medical history, physical examination, 12-leads electrocardiogram, 24h BP and ECG Holter monitoring, transthoracic echocardiogram and estimation of other cardiovascular risk factors (family history, smoking, obesity, sedentary lifestyle, dyslipidemia, chronic stress). Arterial hypertension was defined according to the new 2018 ESC/ESH guidelines for the management of arterial hypertension.

24 hours recording of BP and ECG was performed using Labtech combined three-channel, full disclosure ECG Holter and ABPM system Cardiospy devices (ABPM patient monitor EC-3H/ABP). Equipped with clinically validated technology in all three internationally recognized standards (BHS, ESH and ANSI). The device computes accurate and comprehensive systolic and diastolic readings, heart rate, mean arterial pressure, BP load and pulse pressure. The QRS and PM can be detected with high precision, while template and rhythm analysis can be interactively modified by the user. This user-friendly software provides high-quality time-and frequency-based HRV, PQ, QT, ST, PM, Atrial Fibrillation, Flutter analysis, BBB and AV block detection and ABP results. The transparency and the interpretation of the results are aided by color-coded graphs and tables. The software offers a wide range of languages to choose from.

The cardiac arrhythmias were classified in three main groups as following: a) Supraventricular arrhythmias which include: atrial fibrillation (AF) and flutter, Atrial high-rate episodes (AHREs), paroxysmal supraventricular tachycardia (PSVT) and premature atrial or supraventricular beats (PAGs); b) Ventricular arrhythmias which include: premature ventricular beats (PVBs), ventricular tachycardia (VT) and ventricular fibrillation; c) Bradyarrhythmia’s which include: sick sinus syndrome and AV blocks. Also, we analyzed the elevated resting heart rate in sinus rhythm. Standard transthoracic echo-cardiograms were performed using commercially available equipment (Epic-7, Philips and Vivid 7, GE-Healthcare) in order to evaluate signs of hypertensive or structural heart disease with focus on left ventricle hypertrophy and LV function.

The recordings were programmed to measure blood pressure (BP) at 30-minute intervals from 7am to 10pm and at 1-hour intervals from 10pm to 7am, while the 3 channel ECG recording is simultaneously performed during the 24h monitoring. For all patients we incorporated a participant diary and used it to define sleep and awake periods. Maximum BP measurement time was limited to less than 140 seconds, and the monitors were set for a maximum pressure of 240 mmHg. Participants were given verbal instructions on wearing the monitor, including that they should try to leave the cuff on during the entire monitoring period, that they should try to hold their cuffed arm as still as possible during a reading to ensure that the monitor would get an accurate reading and that faulty readings would trigger a repeat measurement. The minimum number of readings we accepted as an adequate ABPM session was 18 for awake and 7 for sleep, the minimum hours of ECG recording we accepted as adequate ECG-3 channel recording for at least 20 hours.

The study population was categorized into 2 main groups: The first, patients with arterial hypertension and without cardiac arrhythmias, the second group of patients with arterial hypertension and cardiac arrhythmias. The second group was categorized into 3 subgroups according to the type of arrhythmias: a) Supraventricular arrhythmias: atrial fibrillation (AF) and flutter, atrial high-rate episodes (AHREs), paroxysmal supraventricular tachycardia (PSVT) and premature atrial or supraventricular beats (PAC). b) Ventricular arrhythmias: premature ventricular beats (PVBs), ventricular tachycardia (VT) and ventricular fibrillation. c) Bradyarrhythmia’s: sick sinus syndrome and AV blocks. Also, we analyzed the elevated resting heart rate in sinus rhythm patients.

4. RESULTS
In this study we enrolled consecutive 356 adult male and female patients with elevated blood pressure in the period from January 2017 until January 2021 year. Patients with newly diagnosed or previous history of hyper-
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All patients have simultaneously ambulatory blood pressure and ECG monitoring (ABPM) for at least 24h using Labtech combined three-channel, full disclosure ECG Holter and ABPM system devices. Arterial hypertension was defined according to the new 2018 ESC/ESH guidelines for the management of arterial hypertension. The collected study variables include age, gender, body duration of hypertension, known cardiovascular risk factors such as positive family history, obesity, dyslipidemia, tobacco smoking, sedentary lifestyle and chronic stress, comorbidities. The left ventricular hypertrophy (LVH), LV systolic function (EF) and LV diastolic dysfunction were estimated by Echocardiography. The patient’s demographic, risk factors, clinical and comorbidity characteristics are shown in Table 1.

Table 1. Patient demographic, risk factors, comorbidity and antihypertensive drugs characteristics

| Demographics                  |          |          |
|-------------------------------|----------|----------|
| Age, years                    | 64 ± 11  |          |
| Male gender                   | 189 (53%)|          |
| Female gender                 | 167 (47%)|          |
| Duration of hypertension, years | 12 ± 4.8 |          |

| Risk factors                  |          |          |
|-------------------------------|----------|----------|
| Family history for cardiovascular disease | 224 (63%)|          |
| Obesity                       | 203 (57%)|          |
| Dyslipidemia                  | 256 (72%)|          |
| Tobacco Smoking               | 167 (47%)|          |
| Sedentary lifestyle           | 210 (59%)|          |
| Chronic stress                | 157 (44%)|          |

| Comorbidity                   |          |          |
|-------------------------------|----------|----------|
| Coronary heart disease, n (%) | 122 (47%)|          |
| Diabetes Mellitus, n (%)      | 75 (21%) |          |
| Cerebrovascular disease, n (%)| 53 (15%) |          |
| Peripheral vascular disease, n (%) | 84 (24%) |          |

| Echocardiographic parameters  |          |          |
|-------------------------------|----------|----------|
| Left Ventricle Hypertrophy (LVH), n (%) | 167 (47%)|          |
| Enlargement of Left atrial size, n (%) | 117 (33%)|          |
| Normal LV Systolic Function, n (%) | 231 (65%)|          |
| LV Diastolic Dysfunction, n (%) | 192 (54%)|          |

| Antihypertensive drugs, n (%)   |          |          |
| ACEI/ARBs                      | 56 (15.7%)|          |
| ACEI/ARBs + Diuretic as single pill | 75 (21%)  |          |
| Calcium channel blockers (CCB) | 23 (6.5%) |          |
| ACEI/ARBs + CCB                | 31 (8.7%) |          |
| Beta-blockers (BB)             | 54 (15%)  |          |
| BB + diuretics                 | 52 (14.6%)|          |
| ACEI/ARBs + CCB + Diuretic as single pill | 29 (8.1%) |          |
| Alpha blockers                 | 36 (10.1%)|          |
| Nitrates                       | 146 (41%) |          |

Table 2. Type of cardiac arrhythmias detected by 24h ECG Holter monitoring

| Cardiac Arrhythmia                        | Patients | %    |
|------------------------------------------|----------|------|
| Hypertensive patients without cardiac arrhythmias | 54       | 16.2%|
| Hypertensive patients with cardiac arrhythmias | 302      | 84.8%|

|                  |          |      |
|------------------|----------|------|
| Supraventricular Arrhythmias               |          |      |
| Atrial fibrillation and Flutter             | 53       | 34.6 |
| AHRE                                         | 28       | 18.3 |
| Paroxysmal Supraventricular Tachycardia (SVFT) | 18        | 11.8 |
| Premature Atrial Contractions (PACs)        | 54       | 35.3 |

|                  |          |      |
|------------------|----------|------|
| Ventricular Arrhythmias                         |          |      |
| Premature Ventricular Beats (PVBs)              | 81       | 82.7 |
| Ventricular Tachycardia                         | 11       | 11.2 |
| Ventricular Fibrillation                         | 6        | 6.1  |

|                  |          |      |
|------------------|----------|------|
| Bradyarrhythmia’s | 51       | 16.9 |
| Sick sinus syndrome                                     | 17      | 33.3 |
| AV Blocks                                                 | 34      | 66.7 |

Elevated resting heart rate in sinus rhythm patients 87 31.6%

Figure 1. Type of cardiac arrhythmias detected by 24h ECG Holter monitoring in hypertensive patients.
5. DISCUSSION

Arterial hypertension constitutes a major risk factor and underlies many cardiovascular conditions, including heart failure, coronary artery disease, peripheral artery disease, stroke, chronic renal failure and cognitive decline. In addition, many epidemiological studies have highlighted the link of hypertension with a wide spectrum of cardiac arrhythmias, which can significantly affect prognosis through important implications on the morbidity and even the mortality of hypertensives.

When hypertension is suspected because of an elevated screening blood pressure, the diagnosis of hypertension should be confirmed either by repeated office BP measurements over a number of visits or by out-of-office blood pressure measurement using 24h ambulatory blood pressure monitoring (ABPM) or home blood pressure monitoring (HBPM). A 12-lead electrocardiogram (ECG) should
be part of the routine assessment in all hypertensive patients. 24h ECG Holter monitoring is recommended for detection and evaluation of cardiac arrhythmias in hypertensive patients with suspected arrhythmia. Trans-thoracic echocardiography may be useful to assess other signs of hypertensive or structural heart disease and left ventricular systolic function. Despite the overwhelming evidence of treatment benefit, in our study <30% of patients with treated hypertension achieve an BP target of <140/90 mmHg which is in which is in line with published studies and official data. Physician inertia (inadequate up titration of treatment, especially from monotherapy), intense modifying of risk factors and lifestyle and poor patient adherence to treatment (especially when based on multiple pills) are now recognized as the major factors contributing to poor BP control (1-6).

Hypertension is associated with left ventricular hypertrophy, impaired diastolic filling of the left ventricle, increased left atrial pressure, left atrial hypertrophy and enlargement, increased atrial fibrillation, increased atrial ectopic activity, and slowing of intra- and interatrial electrical conduction velocities (3). A significant association has been demonstrated between hypertension and arrhythmias. Arrhythmias are common problems in hypertensive patients. The presence and complexity of both supraventricular and ventricular arrhythmias may influence morbidity, mortality, as well as the quality of life of patients. Diastolic dysfunction of the left ventricle, size and function of the left atrium, and left ventricular hypertrophy (LVH) have been suggested as the underlying risk factors for supraventricular, ventricular arrhythmias and sudden death in hypertensive patients (1-5).

Left ventricular hypertrophy (LVH) is a common finding in patients with cardiovascular disease (CVD) and CVD risk factors. LVH has been associated with both ventricular and supraventricular arrhythmias. In the published studies there was a good correlation between left ventricular hypertrophy and left ventricular diastolic dysfunction. Also, left ventricular hypertrophy was found to correlate significantly with the arrhythmia score. Among patients affected by left ventricular diastolic dysfunction and left ventricular hypertrophy, the correlation with the arrhythmia score was even closer (4-8).

Hypertensive heart disease is known to be related to increased number of supraventricular premature beats (SVPBs). Uncontrolled hypertension, worse diastolic dysfunction, LVH, left atrial (LA) enlargement, increased sympathetic activity, caffeine and alcohol abuse, smoking, and electrolyte disturbances are all well-recognized factors associated with SVPBs. Chatterjee S et al. in the published meta-analysis of 10 eligible studies with 27,141 patients reports that the incidence of supraventricular tachycardia (SVT) in patients with LVH was 11.1% compared with 1.1% among patients without LVH. Patients with LVH had 3.4-fold greater odds of developing SVT than those without LVH. The incidence of ventricular arrhythmias was 5.5% compared with 1.2% in patients without LVH. The occurrence of ventricular tachycardia or fibrillation was 2.8-fold greater, in the presence of LVH. Presence of LVH in hypertensive patients is associated with a greater risk of sustained supraventricular/atrial and ventricular arrhythmias (9, 10).

Moreover, there are various paroxysmal supraventricular tachycardias (such as AV nodal re-entrant tachycardia, atrial tachycardias, or atrial flutter) which can occur in patients with hypertensive heart disease and, importantly, lead to severe symptoms, or even acute pulmonary edema, due to diastolic (and/or systolic) dysfunction and shortened diastolic filling time during those tachyarrhythmias (10-14).

Atrial fibrillation is one of the most frequent supraventricular arrhythmias in hypertensive patients. For men and women, the risk of AF increases by 1.5 and 1.4 fold, respectively, in the presence of hypertension. Its incidence is increasing with each decade of age, as does the risk of hypertension. The two entities have a bidirectional relationship, and they share similar predisposing factors. The main pathophysiological mechanisms of hypertension-related AF include hypertension-induced LVH and subsequent LA enlargement and remodeling, while activation of the sympathetic nervous system and the renin-angiotensin-aldosterone system (RAAS) also contribute to the development of AF (13). AF during hypertension increases the risk of thromboembolic complications and heart failure. The incidence of atrial fibrillation (AF) has increased progressively in the last decades, relating closely to the aging of the population and increasing prevalence of risk factors such as hypertension, obesity, dyslipidemia, cigarettes smoking, diabetes mellitus, heart disease, chronic obstructive pulmonary disease, and sleep apnea (11-14). In patients who have atrial fibrillation, the presence of hypertension increases the incidence of stroke by an additional 2 to 3 times. Atrial fibrillation should be considered as a manifestation of hypertensive heart disease. Atrial fibrillation and flutter (AF) increase the risk of cardiovascular morbidity and mortality and hypertensive patients have up to a 42% increased risk of developing AF. In patients with atrial fibrillation, aggressive treatment of hypertension may reverse the structural changes in the heart, reduce thromboembolic complications, and retard or prevent the occurrence of atrial fibrillation (11, 16, 18).

Patients with arterial hypertension may manifest a wide spectrum of ventricular arrhythmias. It has been long recognized that ventricular premature beats or non-sustained ventricular tachycardia (VT) can complicate the profile of hypertensive heart disease. On a pathophysiological basis, the presence of LVH is probably the most significant factor for the development of ventricular arrhythmias in hypertensives. The association between hypertension, ventricular arrhythmias and cardiac mortality has been well defined. The Framingham Study also indicated that the presence of ventricular premature contractions increased the risk of sudden death by a factor of 2-9 in men and 1-6 in women (18). Furthermore, it is known that LVH is a powerful risk factor for SCD, through malignant ventricular arrhythmias, such as runs of sustained VT and ventricular fibrillation, especially in hypertensives with coronary artery disease (CAD) (2, 10, 13, 15).
Bradyarrhythmia's in the setting of arterial hypertension can occur not infrequently and can have a different etiology, including drug-related arrhythmias, degenerative electrical disease, or the obstructive sleep apnea (OSA) syndrome. The association of LVH with bradyarrhythmia's, including complete atrioventricular block and symptomatic sick sinus syndrome requiring permanent pacemaker implantation, has been observed in several studies. Atrioventricular (AV) block is a common reason for pacemaker implantation, and the number of pacemaker implantations is increasing. Hypertension and higher fasting glucose level each predispose to conduction abnormalities. The fact that a higher systolic blood pressure was associated with AV block even after adjusting for baseline MI and time-updated MACE. Atrioventricular block is associated with multiple known cardiovascular risk factors and conditions. Postmortem studies of individuals with AV block and no other prevalent cardiovascular disease demonstrate fibrosis of the conduction system. The close link of LVH with degenerative electrical disease has been demonstrated in various studies. Thus, patients with hypertensive heart disease and LVH seem to manifest more often conduction disturbances, such as bundle branch block, AV block of various degrees, and especially infra-Hisian block. Sinus node dysfunction may also occur in such patients, as a result of accelerated fibrosis and calcification, which frequently accompany patients with LVH. Regardless of the mechanism, if the association between elevated systolic blood pressure and AV block was causal, the published data suggest that almost half of all AV blocks could be connected to an elevated systolic blood pressure. In our and in published studies, modifiable risk factors of an elevated systolic blood pressure and a higher fasting glucose level were independently associated with AV block. Effective treatment of hypertension and maintenance of normal blood glucose levels may be useful strategies in preventing AV block (2, 12, 13, 17).

A high resting heart rate >80-85 bpm has been associated with an adverse prognosis in patients with CAD and HF. In hypertensive patients free from other overt cardiac disease this is less clear, and an elevated resting HR in these patients seems to be more of a risk marker than a risk factor (2, 18, 19).

### 6. CONCLUSION

Hypertensive patients may manifest a wide range of cardiac rhythm disturbances, ranging from bradyarrhythmia's to supraventricular premature beats, atrial fibrillation, or other supraventricular and ventricular tachyarrhythmias. These cardiac arrhythmias may either cause symptoms or be completely asymptomatic, depending on the underlying cardiac function. Most arrhythmias related to longstanding arterial hypertension are either linked to left ventricular hypertrophy, to sympathetic overactivity, to the antihypertensive treatment, or to concomitant comorbidities. Effective treatment of arterial hypertension plays important role in preventing structural and functional cardiac abnormalities which will contribute to the reduction of cardiac arrhythmias in hypertensive patients.

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