Importance of Biochemical Investigations, Electrocardiography and Ambulatory Blood Pressure Monitoringin Primary Health in Hypertensive Elderly Patients Management

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According to SEPHAR studies I, II and III conducted in Romania the prevalence of hypertension increased, decreased and again increased in more than 10 years from 44.92 to 40.1% and than to 45.1%, expecting more good results in further years. Ambulatory blood pressure monitoring (ABPM) is the main method used by family doctors in primary health carefor detectingthe variability of blood pressure (BP), and treatment response. The goals of this study were to identify the electrocardiographic presence of the left ventricular hypertrophy(LHV)in elderly hypertensive patientsand analyze the differences between those who have controlled hypertension and those who have white-coat, masked or sustained hypertension so to highlight the importance of using ABPM in the primary care service in Romania.

Keywords: ambulatory blood pressure monitoring, left ventricular hypertrophy, hypertension, elderly, primary health care

According to SEPHAR studies I, II and III conducted in Romania the prevalence of hypertension increased in lastten years from 44.92% to45.1%, expecting to increase also in further years[1-3].Taking this into account and knowing as well that hypertension is increasing with age, and only 30.8% of hypertensive patients have blood pressure (BP) controlled [3], it is necessary for general practitioners to pay more attention especially to elderly hypertensives, conducting investigations that quickly reveal cardiac damage, and quantify cardiovascular risk.

Although clinic BP monitoring is the first method of detecting hypertension and further treatment results it may have some drawbacks especially with BP patterns that are so common in both treated and untreated hypertensive patients like masked hypertension(which means normal clinic BP and elevated ambulatory BP) and white-coat hypertension(which means elevated clinic BP and normal ambulatory BP)[4,5]. Therefore ambulatory blood pressure monitoring(ABPM) is the main method of detecting the variability of BP andtreatment response and furthermore, it is used toemphasize the correlation between BP patterns and cardiac damage like left ventricular hypertrophy(LVH)[6-10].

Several studies demonstrated a strong correlation between LVH and ABPM either determined echocardiographically or electrocardiographically[11-13], but we didn't find studies thatpresented this kind of correlation in hypertensive treated elderly in the medical family practice, in Romania.

The goals of this study were to identify the electrocardiographic presence of the LVH in hypertensive elderly, and the differences between those who have controlled hypertension and those who have white-coat, masked or sustained hypertension with the purpose to highlight the use of ABPM in the primary care service in Romania.

Experimental part

Material and methods

Study population and design

Data of this observational cross-sectional study were gathered by the participation of three primary health care practice from Timis County Romania. All participants at the study were known hypertensives for at least oneyear by their own general practitioner doctor. Period of study inclusion was from January 2017 until January 2018. Inclusion criteria were: patients aged 65 years or older, under antihypertensive treatment for at least one year, with optimal ABPM (more than 23 h recording, minimum two valid measurements/hour, equals more than 70% of the measures). Were excluded from the study newly discovered hypertensives and patients who exhibit technical difficulty with ABPM, meaning problems in the reading, or those who didn't tolerate the equipment because of anxiety orbecause of the discomfort given by wearing the cuff.

Categories according to age: young old (65-74 years), middle old(75-84 years) and oldest old ≥85 years.

BP targets were defined as normal clinic blood pressure ≤140/90 mmHg; normal ambulatory blood pressure: 24h BP <130/80mmHg; daytime systolic blood pressure (SBP) ≤130mmHg and diastolic BP ≤85mmHg; night-time systolic BP ≤120mmHg and diastolic blood pressure (DBP) ≤80mmHg[14];

For ABPM pattern BP was defined as:

-Controlled hypertension(CH)- normal clinic BP and normal ambulatory blood pressure;

-The white-coat effect in uncontrolled hypertension(WCEUH)- raised clinic BP and normal ambulatory blood pressure;

-The masking effect in uncontrolled hypertension(MEUH)- normal clinic BP and raised ambulatory blood pressure;

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-Sustained uncontrolled hypertension(SUH)- raised clinic BP and raised ambulatory blood pressure[15,16].

Pulse Pressure(PP) was defined as the difference between the systolic and diastolic blood pressure for the clinic and ambulatory blood pressure[14].

For 24h ambulatory blood pressure monitoring nocturnal dipping was defined as night-day blood pressure ratio with the following categories: extreme dippers >20, dippers between 10 and 20%, nondippers between 0% and 10% and reverse dippers ratio less than 0% [14,17].

Electrocardiographic LVH was identified when index Sokolow-Lyon: SV1+ RV5 >3.5 mV, index Sokolow-Lyon modified: larger S+ larger R ≥3.5mV, R in aVL ≥1.1 mV or index Cornell modified: product between voltage and duration of QRS ≥ 244 mV*ms[14].

Body mass index(BMI) was calculated as weight, in kilograms, divided by square height in square meters. Were defined three categories: BMI less than 25kg/m^2 as normal weight, BMI between 25kg/m^2 and 29.9 kg/m^2 as overweight, and BMI more or equal than 30 as obese.

Clinical data, anthropometric measurements, biochemical tests

At the visit to the office anthropometric measurements (body weight in kilograms, height in centimeters) were made after the measurement for clinic BP, and BMI was calculated.

Biochemical tests were done to asses lipid profile: total serum cholesterol(Total Cholesterol) in mg/dL, high-density lipoprotein cholesterol(HDL_C) in mg/dL, low-density lipoprotein cholesterol in mg/dl (LDL_C), Triglycerides in mg/dl.

Clinic BP was measured by the general practitioner, using a calibrated mercury sphygmomanometer, with the patient in the sitting position after 5 min of rest, using every time an adequate sized cuff. According to the auscultatory technique, systolic BP was defined by phase 1 Korotkoff sound and diastolic BP by phase 5 Korotkoff sound. The mean from three measurements made after 5min rest, at 3 min distance was taken as the value for clinic BP. Hypertension on the elderly was defined as BP ≥ 140/90mmHg [6]. Clinic pulse pressure was calculated.

ABPM technique was done by a trained assistant after the measurement for clinic BP. A calibrated twenty-four-hour Holter TA, with an adequate sized cuff, was used for the measurements. Twenty four hours BP was done by all participants. Measurement settings were made at 15 min during daytime(between 07:00 am and 11:00 pm) and 30 min during night-time(between 11:00 pm an 07:00 am). For each of the participants was taken into account mean of the following values 24h systolic BP, 24h diastolic BP, daytimeSBP, night-timeSBP, daytimeDBP, night-time DBP. Daytime, night-time pulse pressure, as well as nocturnal dipping for both systolic and diastolic blood pressure, were calculated.

*Ethics:*The study is in accordance with the World Medical Association Helsinki Declaration. The research protocol was approved by the Ethics Committee of the University of Medicine and Pharmacy Victor Babes Timisoara and all participants gave their informed consent at the beginning of the study.

Data analysis

Statistical analyses were done with SPSS version 20 with a significance level of p value<0.05. Using descriptive statistics continuous variables were reported as mean and SD and categorical variables were reported as frequency and percentage. The differences between BP pattern were evaluated with Pearson chi-square test.

Results and discussions

We identified two-hundred and forty-three elderly treated hypertensive aged more than 65 years, who met the inclusion criteria in the study. Descriptive clinical and anthropometric characteristics of the study population according to age are pointed out in table 1. The profile of the patients included in the study was young old(67.1%) female (58,.3% from total group), living in urban area (68.1%), with controlled hypertension(44.2%), past smokers (46%), occasionally alcohol consumption(46%), which is appropriate with the general profile of Romanian hypertensive patients from Sephar II study [18], only that in our study we included only elderly treated hypertensive patients age 65 years or more.

From our sample in the young-old category half of the cohort had controlled hypertension (44.2%), followed by those who had SUH and MEUH(21.5%),then from those who had WCEUH (12.5%).In the middle-old category, the percentage of patients who had CH is equal with those who had SUH(36.2%), but there was a change in the percentage of those with MEUH and WCEUH respectively less with MEUH(13%) and more with WCEUH(14.5%). In the oldest-old category, only 9.1% of them had SUH,many of them were instead with CH(45.5%), and then again the percentage of those with MEUH(18,2%) was smaller than the percentage of those with WCEUH(27.3%). If we take into account only these percentages we can say that the oldest-oldage group patients had the most frequent BP

		Age Groups			Total
		young-old 67.1%	middle-old 28.4%	oldest-old 4.5%	
Gender	Female	58.3%	56.5%	54.5%	57.6%
Region	Urban	68.1%	59.4%	90.9%	66.7%
Hypertension Patterns	CH	44.2%	36.2%	45.5%	42.0%
	WCEUH	12.9%	14.5%	27.3%	14.0%
	MEUH	21.5%	13.0%	18.2%	18.9%
	SUH	21.5%	36.2%	9.1%	25.1%
Smokers	Yes	19.6%	14.5%	36.4%	18.9%
	No	34.4%	39.1%	27.3%	35.4%
	Past smokers	46.0%	46.4%	36.4%	45.7%
Alcohol consumption	Yes	11.7%	10.1%	9.1%	11.1%
	No	42.3%	53.6%	36.4%	45.3%
	Occasional	46.0%	36.2%	54.5%	43.6%

*Note.*CH-Controlled hypertension, WCEUH-White-coat effect in uncontrolled hypertension, MEUH-Masked effect in uncontrolled hypertension, SUH-Sustained uncontrolled hypertension.

Table 1
BASELINE CHARACTERISTICS OF THE STUDY ACCORDING TO AGE.

pattern CH and WCEUH and youngest-old age group patients had the most frequent BP pattern CH, MEUH, and SUH. Mean age in all BP pattern category was 73.31±5.42 (table 2) meaning that most of the patientsare youngest-old. We also have to specify that the prevalence of masked effect is bigger than the prevalence of white-coat effect but smaller than the prevalence of sustained hypertension in treated elderly hypertensive patients which is appropriate with the results of other studies [15,19,20] where was proved that these BPpatterns are predictors for higher risk of LVH.Prevalence of smokers among BP patterns, presented in figure 1, was bigger in CH versus SUH and in MEUH versus WCEUH, but within these, we identified many past smokers than smokers with all reports above repeated.

Biochemical and anthropometric characteristics of the study group, pointed out in tabel 2, brings in front,thatour cohort is made from overweightpatients (BMI 32.63±5.37, kg/m2) withlipid profile not in good limits(Total cholesterol 219.55±29.15 mg/dL; LDL_C155.71±29.84 mg/dL; triglycerides 144.36±31.76 mg/dL;)but appropriate as values in all BP pattern category which differs from the

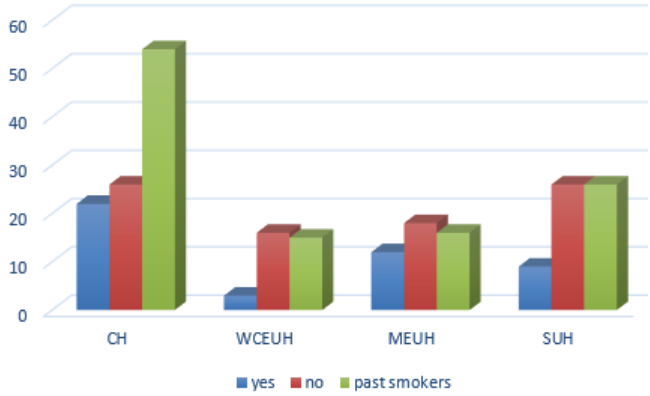

Fig. 1. Prevalence of smoking status among BP patterns

cohort of other studies where lipid profile was different among BP patterns e.g. Pierdomenico SD. et al. in his study [15]:LDL_C was lower in WCUCH than in CH and SUCH. $HDL_c$was higher at MEUH group and the differences between groups were statistically significant (p=0.01).

Table 2

BIOCHEMICAL AND ANTHROPOMETRIC CHARACTERISTICS OF THE STUDY GROUP

	CH n=106	WCEUH n=34	MEUH n=46	SUH n=61	TOTAL n=243	p
Gender,%	53.9%	41.2%	63.0%	68.9%	57.6%	0.86
Age, years	72.88±5.39	74.12±6,074	72.67±5.26	74.05±5.19	73.31±5.42	0.65
Body Mass Index, kg/m^2	32.47±5.36	33.02±5,66	33.49±5.96	32.03±4.76	32.63±5.37	0.21
Total Cholesterol, mg/dl	218.60±29.62	217.32±33.15	219.28±26.07	222.59±28.70	219.55±29.15	0.18
HDL_C, mg/dl	59.72±11.37	66.56±8.836	68.48±9.80	65.72±13.61	63.84±11.90	**0.01**
LDL_C, mg/dl	158.88±28.62	150.76±32.27	150.80±29.28	156.87±30.77	155.71±29.84	0.73
Triglycerides, mg/dl	146.01±33.37	139.71±32.21	140.80±29.28	146.87±30.77	144.36±31.76	0.62

*Note.*CH-Controlled hypertension, WCEUH-White-coat effect in uncontrolled hypertension, MEUH-Masked effect in uncontrolled hypertension, SUH-Sustained uncontrolled hypertension. HDL_C- High density lipoprotein cholesterol, LDL_C -Low density lipoprotein cholesterol.

Table 3

CHARACTERISTICS OF HYPERTENSION PATTERNS ACCORDING TO THE CLINIC AND AMBULATORY BLOOD PRESSURE MONITORING

	Hypertension Patterns				
	CH, n=102	WCEUH, n=34	MEUH, n=46	SUH, n=61	TOTAL, n=243
Clinic SBP, mmHg	127.27±6.22	161.86±10.73	127.43±5.36	163.95±13.36	141.35±19.74
Clinic DBP, mmHg	70.24±4.73	94.34±2.85	79.43±7.48	95.87±2.16	81.78±12.30
Clinic PP, mmHg	57.03±3.86	67.52±9.51	48.00±8.02	68.08±11.96	59.56±11.01
24h_SBP, mmHg	119.64±1.53	122.86±1.18	140.37±2.25	149.31±4.46	131.46±13.10
24h_DBP, mmHg	72.33±1.26	75.16±0.88	87.31±0.88	89.93±0.87	79.98±8.01
24h_PP, mmHg	47.32±0.32	47.70±0.37	53.05±1.38	59.38±3.61	51.48±5.40
ABP Daytime SBP, mmHg	120.73±1.69	124.30±1.46	143.11±2.81	153.36±5.29	133.66±14.40
ABP Daytime DBP, mmHg	72.95±1.52	75.81±1.39	88.39±1.05	91.39±1.02	80.90±8.39
ABP Daytime PP, mmHg	47.78±1.05	48.49±0.85	54.73±2.05	61.96±4.54	52.75±6.45
ABP Night-time SBP, mmHg	115.53±2.75	117.44±1.77	130.03±4.31	134.12±5.18	123.21±9.06
ABP Night-time DBP, mmHg	69.96±2.38	72.72±2.89	83.28±2.11	84,41±2,12	76.50±7.07
ABP Night-time PP, mmHg	45.57±3.73	44.72±3.15	46.76±4.56	49.71±5.65	46.72±4.73
Nocturnal SBP Dipping, %	4.29±2.47	5.50±1.88	9.10±3.77	12.46±4.13	7.42±4.64
Nocturnal DBP Dipping, %	4.05±3.99	3.99±5.09	5.76±2.78	7.62±2.66	5.26±3.96

*Note.*CH-Controlled hypertension, WCEUH-White-Coat effect in uncontrolled hypertension, MEUH-Masked effect in uncontrolled hypertension, SUH-Sustained uncontrolled hypertension, SBP-Systolic blood pressure, DBP-Diastolic blood pressure, PP-Pulse pressure, ABP-Ambulatory blood pressure.

Comparing means between BP pattern groups, results specified in table 3, we observed mean clinic SBP and DBP normal in CH and MEUH, and raised in SUH and WCEUH groups, and mean twenty-four hour SBP and DBP normal in CH and WCEUH and raised in SUH and MEUH, in agreement with the definitions mentioned above. We can say though clinic BP means are closed as values for CH and MEUH groups(127.27±6.22 mmHg vs. 127.43±5.36 mmHg) and for WCEUH and SUH groups(161.86±10.73 mmHg vs. 163.95±13.36 mmHg). Twentyfour hour ambulatory blood pressure means are raised in WCEUH group versus CH group(122.86±1.18/75.16±0.88 mmHg vs. 119.64±1.53/72.33±1.26 mmHg) and in SUH group versus MEUH group(149.31±4.46/89.93±0.87 mmHg vs. 140.37±2.25/87.31±0.88mmHg), these reports remain preserved also for daytime and night-time blood pressure within these groups.

Olesen et al[21]manage to show that 24hPP is a good predictor for LVH (1.24 (1.09–1.42) $p<0.01$ for target organ damage). The results in our study for 24hPP(table 3)show that: mean PP is greater in SUH and MEUH than in CH and WCEUH; daytime PP is more than 60mmHg only in SUH group, in MEUH, WCEUH and CH is still raised but it doesn't reach these value; night-time PP does not reach 60 mmHg, but it is still raised in all BP pattern groups. Considering what Olesen et al.[21] found out,and the results of our study we could foresee that PP is important for cardiac damage management, but we wanted instead to show thatnocturnal SBP and DBP dipping factor correlates with LVH as others managed to show in their studies[22,23]. We divided the cohort into two groupsone with LVH with a total of 135 patients and one without LVH with a total of 108 patients. Nocturnal dipping divided the samplebetween systolic blood pressure dippers and diastolic blood pressure dippers(fig. 2).

Results from table 4 and table 5 show an important association between BP category pattern, left ventricular hypertrophy and the number of patients with elevated nighttime BP(non-dippers in our case)especially in WCEUH followed by MEUH and SUH ($p<0.01$)which regards nocturnal SBP dipping and more in SUH, MEUH followed by WCEUH which regards nocturnal DBP dipping ($p<0.05$). Also in the CH group more than half of the patients were non-dippers with LVH, $p<0.01$ for nocturnal SBP dipping factor and less than half for nocturnal DBP dipping factor($p<0.05$). Meta-analysis[19], and many research articles[15, 23-25] established important proves that masked effect and sustained hypertension are risk factors for target organ damage such as LVH. In our study, we found an important number of patients with LVH even after a year of treatment and elevated nocturnal non-dipping factor which could mean their cardiovascular risk is even bigger.

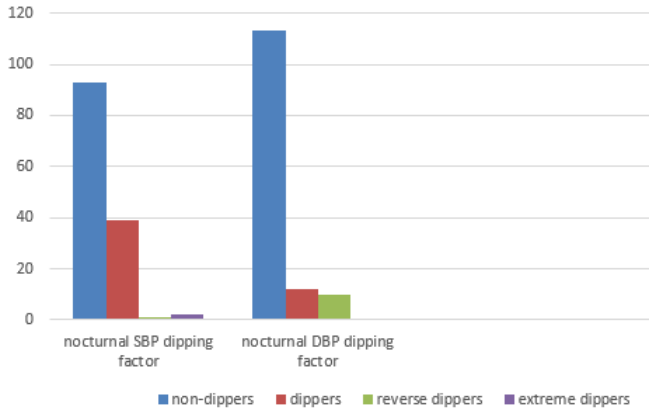

Fig. 2. Dipping category in the study cohort

Table 4

NOCTURNAL SBP DIPPING*BP PATTERN GROUPS*LEFT VENTRICULAR HYPERTROPHY

Left Ventricular Hypertrophy			Hypertension Patterns CH n=102	WCEUH n=34	MEUH n=46	SUH n=61	Total n=243	p-value
Yes	Nocturnal SBP Dipping	non-dippers	53	19	13	8	93	<0.01
No	Nocturnal SBP Dipping	non-dippers	44	15	10	9	78	<0.01
Total	Nocturnal SBP Dipping	non-dippers	97	34	23	17	171	<0.01

Note. CH-Controlled hypertension, WCEUH-White-Coat effect uncontrolled hypertension, MEUH-Masked effect uncontrolled hypertension, SUH-Sustained uncontrolled hypertension, SBP-Systolic Blood Pressure, p value-level of significance <0.05

Table 5

NOCTURNAL DBP DIPPING*BP PATTERN*LEFT VENTRICULAR HYPERTROPHY

Left Ventricular Hypertrophy			Hypertension Patterns CH n=102	WCEUH n=34	MEUH n=46	SUH n=61	Total n=243	p-value
Yes	Nocturnal DBP Dipping	non-dippers	46	14	26	27	113	<0.05
No	Nocturnal DBP Dipping	non-dippers	35	11	18	20	84	<0.01
Total	Nocturnal DBP Dipping	non-dippers	81	25	44	47	197	<0.01

Note. CH-Controlled hypertension, WCEUH-White-Coat effect untreated hypertension, MEUH-Masked Effect Uncontrolled Hypertension, SUH-Sustained Uncontrolled Hypertension, DBP-Diastolic Blood Pressure, p value-level of significance <0.05

Study limitation

This cross-sectional study has potential limitations. First of all, we used electrocardiography for establishing the presence of LVH instead of echocardiography which is more accurate. Secondly can occur biases because we have small groups of reverse dippers, dippers and extreme dippers, and a large group of non-dippers.

Conclusions

In conclusion at the subjectswhich are known like hypertensives and have had LVH determined electrocardiographic, ABPM pattern like masked or uncontrolled BP have a raising cardiovascular risk that could be reduced if the patients are well investigated by general practitioners in primary health care.

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