

Management of arterial hypertension in primary care : is it enough to treat the patient based on conventional office blood pressure measurements or do we need to collect data through ABPM over 24 hours?

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**UNIVERSITY OF SPLIT
SCHOOL OF MEDICINE**

LEA PATRICIA SCHWEINICH

**MANAGEMENT OF ARTERIAL HYPERTENSION IN PRIMARY
CARE: IS IT ENOUGH TO TREAT THE PATIENT BASED ON
CONVENTIONAL OFFICE BLOOD PRESSURE MEASUREMENTS
OR DO WE NEED TO COLLECT DATA THROUGH
ABPM OVER 24 HOURS?**

Diploma Thesis

Academic Year:

2018/2019

Mentor:

Marion Tomičić, MD, GP, PhD

Split, July 2019

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Lastly, I wish to thank my closest friends and Brendan for this incredible journey together.

LIST OF ABBREVIATIONS

ABPM – ambulatory blood pressure monitoring

AOBP – automated office BP

BP – blood pressure

CKD – Chronic kidney disease

CVD – Cardiovascular disease

DBP – diastolic blood pressure

ESC – European Society of Cardiology

ESH – European Society of Hypertension

ESRD – end stage renal disease

HPBM – home blood pressure monitoring

HMOD – hypertension- mediated organ damage

HT – hypertension

ISH – Isolated systolic hypertension

MH – Masked hypertension

NICE – National Institute for Excellence

SBP – systolic blood pressure

TIA – Transient ischemic attack

WCE – white coat effect

WCHT – white coat hypertension

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1. INTRODUCTION

1.1 Arterial Hypertension

Hypertension (HT) is defined as an office systolic blood pressure (SBP) ≥ 140 and/or diastolic blood pressure (DBP) ≥ 90 mmHg, which is equivalent to a 24-h Ambulatory blood pressure measurement (ABPM) average of $\geq 130/80$ mmHg, or a home blood pressure measurement (HBPM) average $\geq 135/85$ mmHg (1).

It was estimated that hypertension affects 1.13 billion people globally in 2015 with an overall prevalence in adults of 30-45% (2). In central and eastern Europe, the prevalence is over 150 million and in Croatia the prevalence of HT is 37,5% according to the EH-UH study by Bojan Jelakovic and 44,2% and rising, according to the ERCEG study, in which even a prevalence of 78,9% and above in patients of the $\geq 7^{\text{th}}$ decade of life has been described (2,3,4).

This high prevalence of hypertension is consistent across the world, independent of income status but becomes progressively more common with advancing age, with a prevalence of $>60\%$ in people older than 60 years (5).

Hypertension is widely encountered in primary care, it is one of the most common conditions managed at primary care level and on top of that it is one of the most common reasons for a medical appointment and drugs prescription (6).

From this prevalence, it is evident that hypertension is a very important public health challenge because of its complications; elevated BP was the primary global contributor to premature death in 2015. Arterial hypertension is the most important risk factor for cardiovascular disease, not only because of its high prevalence but also because of the aging population. Since it is the most common contributor to chronic disease and can lead to complications, including cardiovascular, cerebrovascular, and renal diseases, that are major causes of morbidity and mortality, it is important find and identify the hypertensive patient, to support him in the management of the disease and to have good guidelines to adhere to in the management (7).

To do so, the European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines for the management of arterial hypertension summarize and evaluate available evidence with the aim of assisting health professionals in selecting the best management strategies for an individual with HT. They were first published in 2003 and their last edition was available online since August 2018, these include new evidence on the

necessity to treat 2nd and 3rd grade quicker and to achieve the goal BP value much faster (within 3 month) (8).

1.2 Types and Etiology of Hypertension

In most patients hypertension is classified as primary or idiopathic, however in around 5-10% of patients the cause of the hypertension is known or identifiable and it can be classified as secondary hypertension (9). The most common cause of secondary HT is chronic renal disease, but other causes include: sleep apnea, coarctation of the aorta, glucocorticoid excess like in Cushing syndrome and chronic steroid therapy, mineralocorticoid excess as seen in primary aldosteronism, drug-induced hypertension, pheochromocytoma, renovascular hypertension and thyroid or parathyroid disease (10).

Early diagnosis and treatment of secondary causes of hypertension lead to good clinical outcomes and even possible reversal of end-organ damage, but if not recognized it can lead to resistant HT (11).

Regarding the etiology, there are several factors that can increase your risk for developing hypertension; some of them are a result of genetics and unchangeable, these include a family history of HT, age, gender (< 65: ↑ men, >65: ↑ women), race (more common in African-Americans) and chronic kidney disease (CKD), some are the result of lifestyle choices and modifiable, these include lack of physical activity, unhealthy diet, especially one high in sodium, obesity, smoking, alcohol consumption, high cholesterol and stress (12).

1.3 Signs and Symptoms of Hypertension

Arterial hypertension is a so-called silent killer as very rarely any symptom can be seen in its early stages until a severe medical crisis takes place like heart attack, stroke, or chronic kidney disease. Since people are unaware of excessive blood pressure, it is only through measurements that detection can be done. Although majority of patients with hypertension remain asymptomatic, some people with HT report headaches, light-headedness, vertigo, altered vision, or fainting episode (13).

After chronic exposure of an increased arterial blood pressure hypertension mediated organ damage can result and cause damage to the vasculature, heart, brain, eyes and kidneys (14).

The pathophysiology of this process is not fully understood (15).

Hypertension is not only a known conventional risk factor for the development of atherosclerosis, which means it has a direct causal role in atherogenesis, but also it is an independent predisposing factor for heart failure, coronary artery disease, stroke, renal disease and peripheral artery disease and presents to be the most important risk factor for cardiovascular morbidity and mortality in industrialized countries (16).

Complications affecting the heart is called hypertensive heart disease, in which chronic exposure to increased BP leads to adaption, leading to left ventricular hypertrophy, diastolic dysfunction, CHF, atherosclerotic coronary artery disease, myocardial infarction and cardiac arrhythmias and can ultimately lead to heart failure (17).

The complications affecting the brain are mainly brain infarction and hemorrhage, Transient ischemic attacks (TIAs), hypertensive encephalopathy (symptoms: confusion, headache, convulsion) and dementia. Hypertension affects the kidney in that way, that it can cause renal injury and end stage renal disease (ESRD), and the eyes in that it can lead to hypertensive retinopathy (17,18).

1.4 Diagnosis and diagnostic criteria of hypertension

The definition of hypertension is clearly described in the 2018 ESC&ESH Guidelines for the management of arterial hypertension, and are dependent on the method used for measuring (Figure 1) (8).

Category	SBP (mmHg)		DBP (mmHg)
Office BP ^a	≥140	and/or	≥90
Ambulatory BP			
Daytime (or awake) mean	≥135	and/or	≥85
Night-time (or asleep) mean	≥120	and/or	≥70
24 h mean	≥130	and/or	≥80
Home BP mean	≥135	and/or	≥85

BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.
^aRefers to conventional office BP rather than unattended office BP.

©ESC/ESH 2018

Figure 1. Definitions of hypertension according to office, ambulatory, and home blood pressure levels

Source from Williams B, Mancia G, Spiering W, Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial Hypertension. European Heart Journal. 2018;3021:3104.

On top of that the office BP values are also subdivided into three different grades of hypertension Grade 1 being 140–159 systolic and/or 90–99 diastolic, Grade 2 160–179 systolic and/or 100–109, ≥ 180 and/or ≥ 110 for Grade 3 (8).

1.5 Different Methods of Measurement

In the last decades combined office and out-of-office (i.e. ambulatory or home) blood pressure measurements has increasingly been applied in clinical practice and research as they provide a comprehensive assessment of cardiovascular risk related to hypertension in a variety of clinical settings. Accurate blood pressure measurement is essential to the diagnosis and management of hypertension.

There are different methods of measuring blood pressure but the three most commonly used ways to attain BP values, being conventional office blood pressure measurement, home blood pressure monitoring and Ambulatory blood pressure monitoring.

The basic principle to measure blood pressure is based on a technique that was invented in 1896 and since then this has essentially remained the same*; Auscultatory or oscillometric semiautomatic or automatic sphygmomanometers are the basis for all three presented methods for measuring BP in and out of the doctor's office (19).

This review summarizes various methods of measuring blood pressure and evaluates advantages and disadvantages of them respectively.

1.5.1 Office Measurement of Blood Pressure and accurate BP Measurement in the Medical Office

Current clinical guidelines recommend office blood pressure measurement as the golden standard to attain BP values for the diagnosis of HT. Traditionally manual measurement techniques are used but nowadays automated office BP (AOBP) presents a common alternative to conventional manual BP measurement, hereby a fully automated sphygmomanometer is used (20).

The measurement of blood pressure is arguably the most important commonly performed office test yet it is often rushed and improper, therefore it is important to follow specific rules and conditions and to adhere to or create global guidelines for it since even small inaccuracies in measured BP can have considerable consequences on a personal patient-based but also on a national economic level (20).

There are different national and international guidelines available that give a set of instructions to ensure the most accurate blood pressure measurement to base further decisions on management and treatment of hypertension on.

To assure a correct reading of BP values these instructions should be followed:

The patient should not drink caffeinated or alcoholic beverages, smoke or exercise less than 30 minutes before the measurement. Also he should sit quietly and comfortably in a calm environment for five minutes before testing without talking. The non- dominant hand should be resting comfortably on a flat surface at the level of the heart. Furthermore, it is important for the patient to sit still with the legs uncrossed and the feet flat on the floor, the back being straight and supported (21).

The physician should record three BP measurements, with 1-2 minutes of rest in between and only do further measurements if the discrepancy between the first to readings is more than 10 mmHg or if the patient has varying BP values due to arrhythmias such as atrial fibrillation. The BP value documented should be the average of the last two BP measurements.

The cuff should be placed correctly on bare skin with the bottom of the cuff above the bend of the elbow and the appropriate, well-fitting cuff size should be chosen so that the inflatable part will cover at least 80% of the upper arm. **In most patients a standard bladder cuff, being 12-13 cm wide and 35cm long are suitable but larger or smaller cuffs should be available (21,22).

If the auscultatory method is used, the practitioner should listen with the stethoscope while simultaneously observing the sphygmomanometer the Korotkoff phase one, the appearance of a sharp “thud” is taken as the systolic BP value and Korotkoff phase five, the disappearance of the thud as the diastolic BP value (22).

It is important to conduct BP recording on both arms at the first visit and to note any between-arm difference, hereby the higher value is always used as the reference.

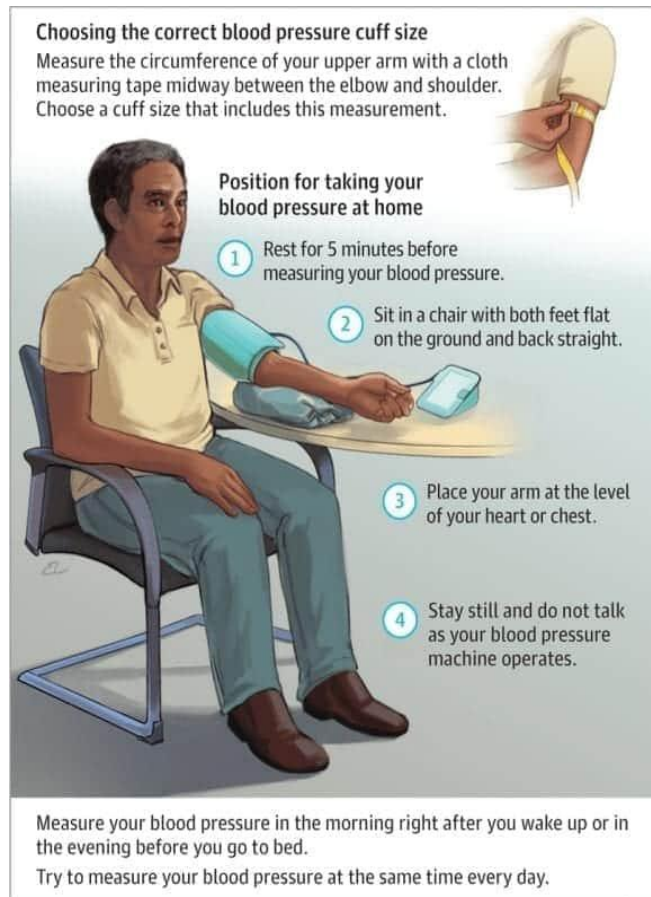


Figure 2. Measuring BP correctly

Source from Sigurdsson A. 12 Steps to Diagnose High Blood Pressure- Understanding Hypertension. JAMA. 2017;318(3):310.

Several factors have been identified that can influence the accuracy of blood pressure measure. (Table 1)

Factor	Magnitude of systolic/diastolic blood pressure discrepancy (mm Hg)
Talking or active listening	10/10
Distended bladder	15/10
Cuff over clothing	5–50/
Cuff too small	10/2–8
Smoking within 30 minutes of measurement	6–20/
Paralyzed arm	2–5/
Back unsupported	6–10/
Arm unsupported, sitting	1–7/5–11
Arm unsupported, standing	6–8/

Table 1. Factors influencing the accuracy of blood pressure measurement

Adapted from Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360(9349):1903–13.

These factors should be considered for accurate measurement because the overestimation of the patients' blood pressure can erroneously label people as hypertensive and potentially result in unnecessary dietary restrictions, exposure to potential side effects. Control of blood pressure begins with accurate measurement leading to appropriate diagnosis and treatment decisions (23).

1.5.2 At Home Measurement of Blood Pressure and its Advantages and Disadvantages

Home blood pressure monitoring (HBPM) is a way of self-monitoring it is most commonly done with an automatic, cuff-style, bicep (upper-arm) monitor with. Hereby it is important to make sure that the device is properly calibrated and validated and that the correct cuff size is chosen.

The National Institute for Excellence (NICE) guidelines for HBPM

- for each BP recording, two consecutive measurements are taken, at least 1 minute apart with the person seated;
- BP is recorded twice daily, ideally in the morning and evening; and
- BP recording continues for at least 4 days, ideally for 7 days.

Whereas the measurements of the first day should be discarded (24)

The threshold for diagnosis of hypertension is set at $\geq 135/85$ mmHg, which equals an office-based value of $\geq 140/90$ mmHg (Figure 1).

Similar to office based hypertension monitoring there are certain rules that should be followed to ascertain a more precise and accurate measurement, in short those include: no smoking, exercising and drinking of caffeinated beverages or alcohol within 30 min of measurement; resting chair more than 5 minutes with the arm resting on heart level, avoiding to talk, feet flat on the floor with back straight and supported... (see above: office based BP monitoring).

Advantages	Disadvantages
Can take Multiple readings over an extended period of time	devices can be inaccurate (e.g. not calibrated correctly)
Avoid white- coat effect when measuring BP	Accuracy dependent on cuff placement
Reproducible	May lead to anxiety and excessive monitoring
Better predictor of CV morbidity and mortality than office BP	Risks changes of treatment when using casual measurements without guidance of a doctor
Can diagnose white-coat and masked hypertension	No nocturnal readings
Leads to better understanding of hypertension management for the patient	In many countries not yet reimbursed by insurance companies
Remote monitoring by health care professionals possible due to telemonitoring	
Detects increased BP variability	

Table 2. Advantages and Disadvantages of Home Blood Pressure Monitoring

Adapted from George J, MacDonald T. Home Blood Pressure Monitoring. ECR. 2015;10(2):95–101

1.5.3 24h Ambulatory Blood Pressure Measurement

In ABPM blood pressure is measured over a time span of 24 consecutive hours and therefore during normal daily activities, and provides an analysis and average of BP readings over that defined period. Measurements are obtained every 20 minutes during the day and every 30 min during the night.

The analysis commonly includes true mean BP values for daytime, night- time and 24hrs measurements, furthermore it can reveal the so called “night-time dip” and be divided into dipping patterns whereas non-dippers have a BP drop of less than 10% and dippers of more than 10% of the daytime average BP values. Additionally, ABPM may reveal an excessive morning blood pressure surge; which is associated with increased risk of stroke in elderly people with high blood pressure (25).

The diagnostic threshold value for the diagnosis of hypertension is set as $\geq 130/80$ mmHg over 24hrs, $\geq 130/80$ mmHg for daytime, $\geq 120/70$ mmHg for night time average. These thresholds are set lower than the value for office BP measurements ($\geq 140/90$) since ABPM measured values are on average lower than those measured in office (Figure 1).

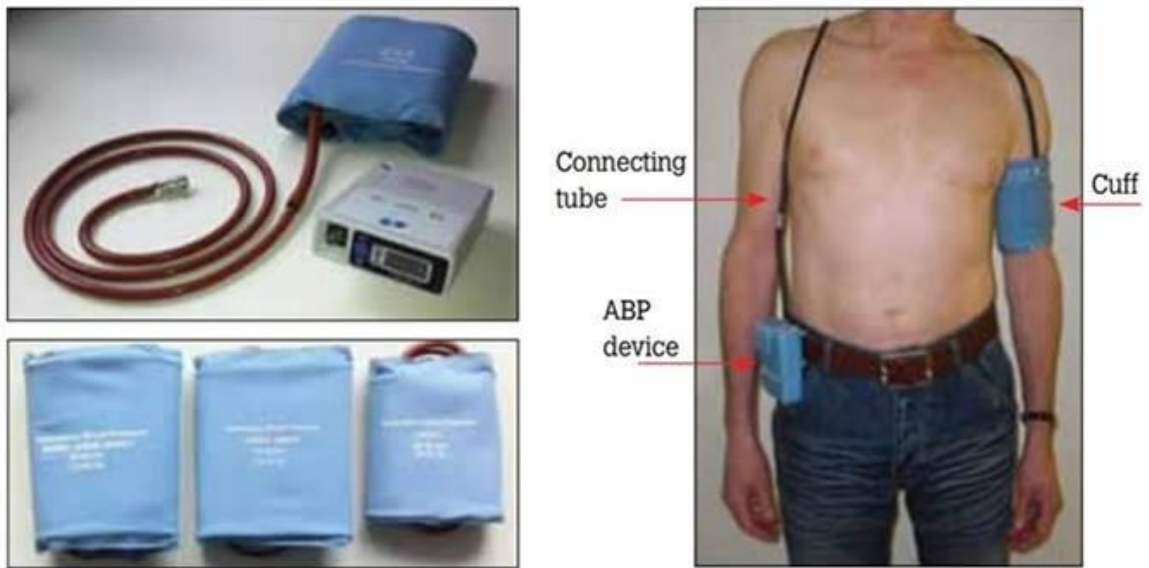


Figure 1. Example of ambulatory monitors (upper left), multiple cuff sizes (lower left) and when fitted to a patient (right)

Use of these images does not constitute endorsement by the National Heart Foundation of Australia, nor the High Blood Pressure Council of Australia

Figure 3. Example of ambulatory monitors

Available from Image Credit: National Heart Foundation and High Blood Pressure Research Council of Australia Ambulatory Blood

The clinical indications for 24 hours ambulatory blood pressure measurement include the following; it helps in the exclusion of white of coat hypertension, with the diagnosis borderline hypertension, with the decision-making on treatment for elderly patients, with the identification nocturnal hypertension, assessment of patients with resistant hypertension, determination of efficacy of drug treatment, diagnosis and treatment hypertension in pregnancy, diagnosis hypotension (26).

1.5.3.1 Advantages and Disadvantages of ABPM an Office Measurement

24-hour ambulatory blood pressure monitoring is the most accurate method for the confirmation and diagnosis of hypertension, henceforth the NICE Guideline UK recommend that every patient who had a clinical blood pressure measurement of 140/90 mmHg or higher should be offered a ABPM to confirm the diagnosis and to identify the patients who do not have true hypertension, thereby reducing unnecessary treatment in people who don't.

ABPM has also been shown to be superior to other methods of multiple blood pressure measurement for predicting blood pressure-related clinical events.

ABPM	Office
+ diagnosis white-coat and masked hypertension	+ cheap
+ stronger prognostic evidence	+ widely available
+ night-time readings	+ automated: programmed to start measuring blood pressure after set time following(minimize WCE), take several readings and provide the average value (29)
+ measurement in real life setting	
+ additional prognostic BP phenotypes	
+ abundant information from a single measurement session, including short term BP variability	– white-coat effect
+ best predict all-cause and cardiovascular mortality (27)	– observers digit preference, observer bias (29)
– expensive, sometimes limited availability (> not spend money on unnecessary treatment)	– only static BP available
– can be uncomfortable	– potential for measurement error
– „ABPM effect“: pressor effect (increased BP) during first 10h of measurement (28)	– no nocturnal readings

Table 3. Comparison ABPM and Office measurement

Adapted from Williams B, Mancia G, Spiering W, Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial Hypertension. European Heart Journal. 2018;00:1-98.

A major advantage of ABPM is that it facilitates the diagnosis/identification of white-coat and masked hypertension.

1) White coat hypertension

White coat hypertension is a phenomenon in which the patient who is not on previous treatment for hypertension displays elevated blood pressure when they are around doctors, hence when measured in office but with normal BP values when measured by ABPM or HBPM. The prevalence of white coat hypertension is 15 to 30% of the subjects with an elevated office BP (30).

Risk factors for this phenomenon include female sex, age, non-smoking, recent diagnosis with hypertension, pregnancy (31).

WCHT can be seen in all grades of hypertension but is most commonly seen in grade 1 hypertension, furthermore it is more commonly seen in patients without signs of HMOD and as recent studies showed, the cardiovascular risk is lower compared to patients with sustained HT (32).

On the other hand, patients with WCE have a greater sympathetic activity, higher prevalence of metabolic risk factors, more common asymptomatic cardiac and vascular damage, a higher long- term risk of new- onset diabetes and higher rates of developing sustained hypertension and LVH (33).

2) Masked hypertension

Masked hypertension (MH) refers to having a normal blood pressure in the medical office or clinic but an increased BP out of the office with an ambulatory daytime BP or home BP > 135/85 mmHg. The prevalence of masked hypertension is reported to be between 15% to 30% among patients with a normal office BP and varies depending on the presence of certain risk factors in the population: relatively young age, male sex, contraceptive use in women, stress or increased physical activity and smoking or drinking habits (34,35).

It increases the risk for target organ damage especially in the presence of metabolic risk factors, high left ventricular mass index and carotid intima-media thickness and cardiovascular events and should be searched for in patients with an increased risk for cardiovascular complications like patients with kidney disease or diabetes (35,36). The high prevalence of MH would suggest the necessity for measuring out-of-office BP in persons with apparently normal or well-controlled office BP.

3) Resistant hypertension

Resistant hypertension is defined as blood pressure that remains above the treatment aim despite of the concurrent use of three antihypertensive agents of different classes. Ideally, one of the 3 agents should be a diuretic and all agents should be prescribed at optimal dose amounts. In westernized countries the prevalence of resistant hypertension is estimated to be approximately 10% of hypertensive patients (37).

When diagnosing resistant hypertension, it is of utmost important to eliminate secondary causes of resistant hypertension like obstructive sleep apnoea, renal disease e.g. renal parenchymal disease, renal artery stenosis or endocrinological diseases e.g. primary aldosteronism, Cushing's disease, hyperparathyroidism, coarctation of aorta, pheochromocytoma or intracranial tumors (38).

But the major reason for the failure to treat hypertension remains the non-adherence in taking prescribed antihypertensive medications and must be ruled out underlining the importance of primary care to help in the individual supervision of the hypertensive patient (39).

1.6 Management of Hypertension

The treatment for arterial HT varies depending on the patients grade of hypertension and his comorbidities. Therefore the clinical evaluation of the patient is important to establish the diagnosis and grade of hypertension, to identify concomitant diseases and to check for evidence of HMOD.

Essentially the workup for this consists of the following parts: taking medical history, physical exam, clinical investigations and obtaining routine laboratory studies. This approach will help to detect and assess the presence of HMOD, find potential secondary causes of HT, assess cardiovascular risk factors and to gather baseline values for determination of the effectiveness of treatment (40).

The first step in the evaluation of HT is taking a detailed medical history which should include family and personal history of HT, CVD, stroke, or renal disease, family and personal risk factors (e.g. Familial hypercholesterinemia), smoking and alcohol consumption history, dietary history, lifestyle choices, sleep history, history of erectile dysfunction, hypertension in pregnancy, furthermore the history should include asking for symptoms of HMOD, CVD, stroke, renal and retinal disease and asking targeted questions that could point towards a secondary cause of hypertension, like an early onset or sudden development with sudden worsening of the BP (41).

The physical examination and laboratory testing are an important part of the evaluation of HT as it can help in the assessment of suspected secondary causes or to detect signs of existing comorbidities or HMOD (41).

For the physical examination special attention should be paid on calculating the BMI, waist circumference and hip to waist ratio. The initial workup should include the following routine laboratory tests including urinalysis, hemoglobin and hematocrit, fasting blood glucose and HbA1c, serum sodium, potassium, creatinine (or GFR), calcium and a lipid profile including total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides. Blood uric acid, and blood liver function test and 12 lead ECG (41).

The clinical evaluation of hypertension mediated organ damage in patients with hypertension has to include the examination of the most commonly affected organ systems, namely the heart, blood vessels, kidney, eyes and brain.

In all hypertensive patients 12 lead ECG has to be done to rule out HMOD of the heart and to investigate for evidence of the heart muscle thickening up (may also be seen on chest x ray)

suggesting left ventricular hypertrophy. Moreover, echocardiography should be done if less efficient function of left ventricular failure is suspected or if abnormalities were seen on ECG. Pathology of the blood vessels ought to be examined with as US of the carotid arteries especially in patients with stroke or TIA (42).

HMOD affecting the kidney should be tested by measuring serum creatinine and eGFR, this is recommended in all hypertensive patients just like measuring the presence of leakage of protein into urine in form of the albumin: creatinine ratio. In addition to that renal US and Doppler examination are indicated in patients with reduced renal function, albuminuria or if there is a suspicion of secondary hypertension (42).

Pathology of the eyes is detected by fundoscopy, which is recommended in all grade 2 or 3 hypertensive patients. A brain MRI or CT should be done in the hypertensive patient with neurological symptoms to recognize brain infarctions, microbleeds or white matter lesions (42).

Certain tests should be done if there are suspicions of HT with an identifiable causes also known as secondary HT, these include measuring eGFR if there is suspicion of Chronic kidney disease, dexamethasone suppression test to rule out Cushings disease, CTA if coarctation of aorta is suspected, drug screening if drug induced HT suspected, plasma aldosterone to renin activity ratio (ARR) and 24-hour urinary aldosterone level to rule out primary aldosteronism, 24-hour urinary metanephrine and normetanephrine for pheochromocytoma, Sleep study with oxygen saturation to eliminate the diagnosis of sleep apnea, Doppler flow US, MRA or CTA for Renovascular hypertension and Thyroid stimulating hormone level and serum parathyroid hormone level for thyroid or parathyroid disease (43).

When to initiate antihypertensive treatment

Hypertension must be adequately controlled to reduce cardiovascular events and mortality, when to initiate treatment is displayed in the table below (Figure 3).

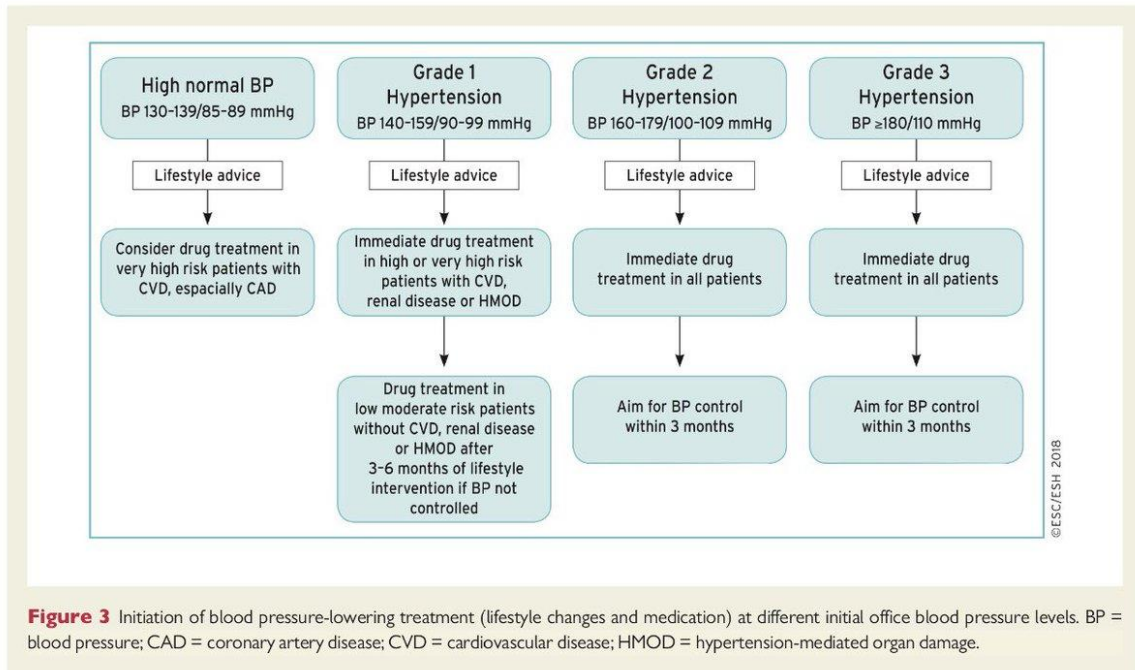


Figure 4. Initiation of blood pressure-lowering treatment (lifestyle changes and medication) at different initial office blood pressure levels.

Available from Williams B, Mancia G, Spiering W, Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial Hypertension. European Heart Journal. 2018;00:1-98.

A variety of different treatment strategies exist in different guidelines but overall diuretics (thiazides etc.) are often recommended as the first line of therapy for most people who have high blood pressure but there are various classes of drugs commonly used such as ACE inhibitors, ARBs, Calcium channel blockers (Figure 4) (44)

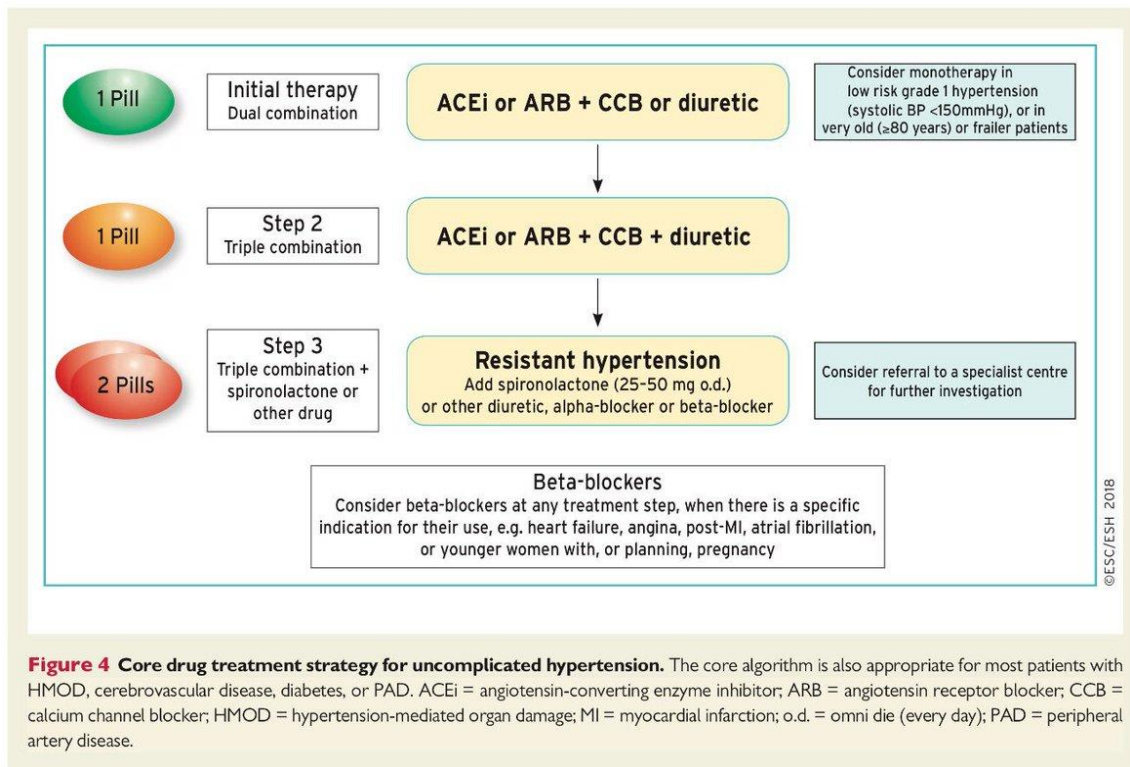


Figure 5. Pharmacological treatment Core drug treatment strategy for uncomplicated hypertension.

Available from Williams B, Mancia G, Spiering W, Rosei E, Azizi M, Burnier M et al. 2018 ESC/ESH Guidelines for the management of arterial Hypertension. European Heart Journal. 2018;00:1-98.

2. OBJECTIVES

The purpose of our study was to

- Compare results of different methods of measuring blood pressure and to compare their accuracy.
- Compare Office systolic BP with ABPM average systolic BP, Office diastolic BP with ABPM average diastolic BP, Office systolic BP with ABPM day-time systolic BP, Office diastolic BP with ABPM day-time diastolic BP.
- Elaborate whether it is enough to treat the patient based on conventional office blood pressure measurement or whether we need to collect data through ABPM over 24hrs?
- elaborate how BP is measured in offices of the Community Health Center Split and whether BP is measured according to recent Guidelines.
- Main Hypotheses: It is not enough to make a decision about the management of the hypertensive patient based on office BP measurements but ABPM is needed for correct decision-making to avoid over- and undertreatment of the patient.

3. MATERIAL AND METHODS

3.1. Study design

The study was conducted as a retrospective cross-sectional study.

3.2. Study sample

In this study 168 patients were included, they were treated in eight offices of specialists of family medicine in Spil, which are part of the Community health center Split, during the period of 1st September 2018 and 1st of April 2019.

3.3. Method of collecting and analyzing data

The study material was collected from eight offices of specialists of family medicine in Split, which are part of the Community health center Split. Gathering the materials from the specialists databases and archives the patients and the medical histories were reviewed and inserted in Microsoft Excel program.

We created questionnaire which consisted of several parts, in the first part we collect data on gender, age, personal and family medical history, which included asking about the occurrence of CV disease and CV incidents, kidney disease, diabetes and arterial fibrillation, and also whether other chronic diseases are known. In another part we included smoking history, Height, weight, waist- hip ratio and BMI. The next part we collected data on the last biochemical lab attained, including: lipid analysis, uric acid, glucose, liver panel, sodium and potassium. In the last section data from the results of the patients 24 hour ABPM and results from last BP measurements in office were collected. The questionnaire was filled in from data from the physicians databases.

Furthermore, we asked the eight specialists of family medicine who took part in the data collection about how they themselves measure BP in everyday practice, so that we can later compare that to the current guidelines of measuring BP

The criteria of inclusion were: all patients in the period of 1st September 2018 and 1st of April 2019 who did ABPM measurements and are patients of the eight family medicine specialists that participated.

3.4. Statistical analysis

By using the medical history and discharge papers of the patients, the parameters needed were analyzed and shown in figures and tables. Microsoft Excel and Microsoft Word were used to make the tables and figures.

Our data was analyzed for statistical purposes with STATISTICA 12 software. Data distribution was assessed by the Kolmogorov-Smirnov test. To test for correlation the Pearson's correlation coefficient was used. In our statistical analysis we displayed the average and standard deviation for normal distributed variables, and for non - normal distributed variables the median and interquartile range (IQR) was calculated. The difference between the blood pressures was analyzed using the T-test and additionally, with the Chi-Square test we tested homogeneity by categorical variables. Statistical significance was set at $P < 0.05$.

4. RESULT

PART 1

Out of 168 examinees arterial hypertension occurred in 68 male (40.48%) and in 100 female (59.52%). The difference by gender was significant ($\chi^2=6.10$; $p=0.014$).

The median of age of the examinees was 64 years (IQR=55-70). The distribution in different age groups can be seen in Table 1. The majority of patients are in age group 61-80 years ($\chi^2=102.29$; $p<0.001$).

Table 1. Patients by age group

Age group	n	%	X	p*
20-40	12	7.14		
41-60	58	34.52		
61-80	88	52.38		
81-100	10	5.95	102.29	<0.001

* χ^2 test

The average BMI was 27.19 kg/m² (SD=3.6). In our sample the female examinees have significant higher BMI ($t=3.03$; $p=0.003$). There was no correlation found between age and BMI index ($r=-0.01$; $p=0.941$).

PART 2

The average value of the office BP was 138.93 mmHg (SD=22.37) for the systolic and 82.14 mmHg (SD=13.07) for the diastolic BP. Average systolic ($t=-0.62$, $p=0.53$) and diastolic ($t=-7.79$, $p=0.00$) office BP are lower than the cut off value from the last European guidelines for arterial hypertension (SBP ≥ 140 , DBP ≥ 90).

The average ABMP was 134.93 mmHg (SD= 13.35) for systolic and 76.92 mmHg (SD= 9.04) for the diastolic BP. The average ABMP systolic ($t=4.77$, $p=0.000004$) BP are higher than the cut off value from the last European guidelines (≥ 130) and diastolic ($t=-4.41$, $p=0.000018$) BP are lower than the cut off value from the last European guidelines (≥ 80). The average value of the office BP, ABPM and daily ABPM can be seen in Table 2.

Table 2. BP values attained from different methods of BP measurement

	n	Average	SD
Office syst	168	138.93	22.37
Office diast	168	82.14	13.07
Average ABPM syst	168	134.92*	13.36**
Average ABPM diast	168	76.92*	9.042**
Day ABPM sys	168	139.49*	13.35
Day ABPM diast	168	80.86*	9.52**

Average daytime systolic are significantly higher ($t = 4.36$, $p = 0.000023$) than the cut off value from the last European guidelines (≥ 135).

PART 3

In Table 3 the correlation between age and BP is shown. Older examines have lower average 24 h diastolic BP ($r = -0.41$; $p < 0.001$) and lower daily diastolic BP ($r = -0.44$; $p < 0.001$). Correlations between office BP (systolic and diastolic), average 24 h systolic and average daytime systolic with age are not founded (p values > 0.050).

Table 3. Correlation between age and BP

		Office syst	Office diast	Average ABPM syst	Average ABPM diast	Daily ABPM syst	Daily ABPM diast
Age	r	0.14	-0.09	0.03	-0.41	0.00	-0.44
	P*	0.078	0.273	0.671	<0.001	0.958	<0.001

*Pearson correlation

Table 4 shows the correlation between gender and BP. Average 24h diastolic BP is significantly lower in female examinees ($t=2.81$; $p=0.006$) and average daytime diastolic BP was significant higher in male examinees ($t=2.18$; $p=0.031$). We didn't find significant difference in office systolic and diastolic BP or between average daytime systolic and diastolic BP by gender ($p>0.050$).

Table 4. Correlation between gender and BP

	Female		Male		t	df	p*
	Mean	SD	Mean	SD			
Office syst	138.31	21.71	139.84	23.43	0.43	166	0.665
Office diast	81.88	12.35	82.51	14.16	0.31	166	0.758
Average ABPM syst	134.12	13.74	136.10	12.79	0.94	166	0.347
Average ABPM diast	75.34	8.49	79.25	9.39	2.81	166	0.006
Day ABPM sys	139.01	13.56	140.19	13.10	0.56	166	0.575
Day ABPM diast	79.56	9.15	82.78	9.79	2.18	166	0.031

*t-test

PART 4

We compared the average value of office systolic and diastolic BP with the average systolic and diastolic ABPM BP values. Office systolic BP was significant higher ($t= 3.47$; $p<0.001$) as well as office diastolic BP ($t=6.11$; $p<0.001$) (Figure 1 and 2).

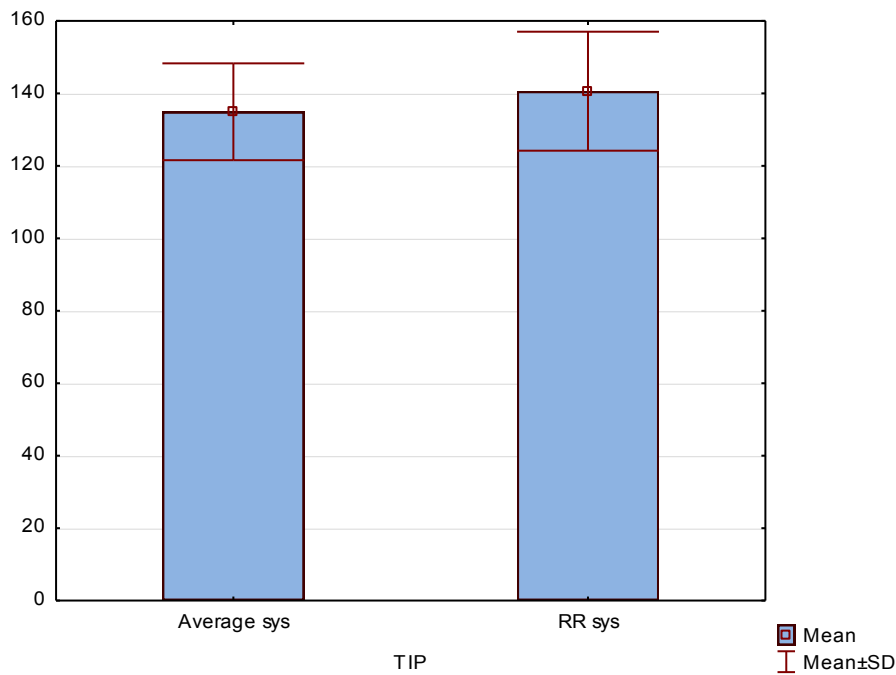


Figure 1. Comparison Average ABPM systolic and office systolic measurements

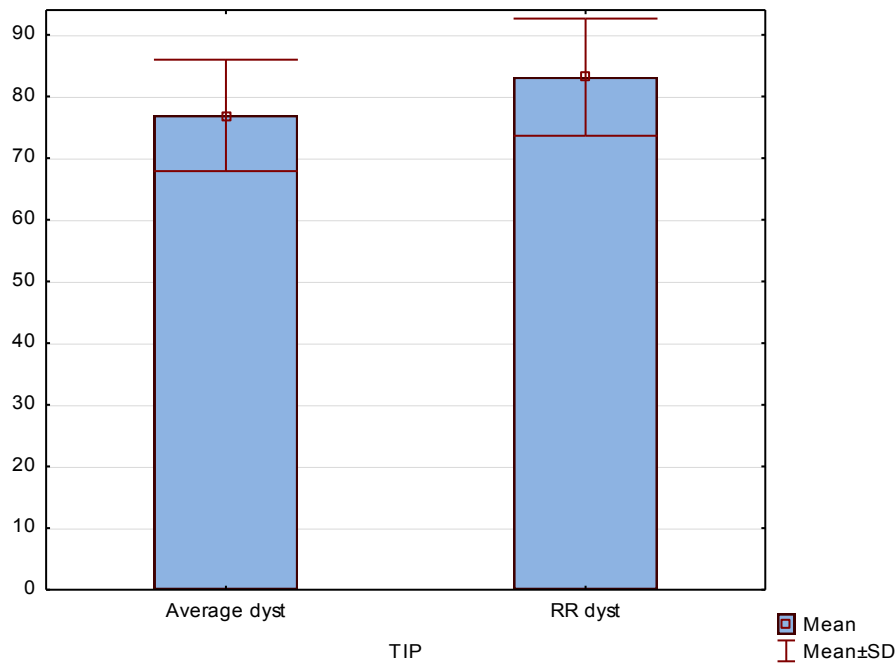


Figure 2. Comparison Average ABPM diastolic and office systolic measurements

Also, there was a positive and significant correlation between the office systolic and diastolic BP and the average 24 h systolic and diastolic BP values attained by ABMP. Examinees with a higher average systolic and diastolic BP also have increased values of office systolic and diastolic BP. That correlation is significant for systolic ($r=0.32$; $p<0.001$) and diastolic BP ($r=0.25$; $p=0.001$). We didn't find significant difference between office systolic and average daytime systolic BP ($t=6.11$; $p=0.496$) but office diastolic BP was significantly higher than average daytime diastolic BP ($t=2.17$; $p=0.030$).

Examinees with a higher average daytime systolic and diastolic BP also have increased values of office systolic and diastolic BP. That correlation is significant for systolic ($r=0.30$; $p<0.001$) and diastolic BP ($r=0.28$; $p<0.001$).

5. DISCUSSION

In this study we tried to elaborate whether it is enough to treat the patient based on conventional office blood pressure measurement or if we need to collect data through ABPM over 24hrs for the decision making on the management of arterial hypertension in primary care.

We included 168 examinees with arterial hypertension in the Community health center Split, which included eight medical offices of specialists of family medicine in Split.

In my thesis we investigated the different types of measurement in primary care and how the different sort of measuring can affect the management of hypertension.

After doing our statistical analysis we found that the office systolic and diastolic BP values were normotensive as such, but borderline to the hypertensive values established by the ESC guidelines.

On the other hand, the measurements attained by ABPM revealed grade 1 hypertensive systolic values in both the average ABPM and the day- time ABPM the measurement among the examinees of the Community health center Split. Hereby with ABPM measurement isolated systolic hypertension (ISH) was revealed, since the diastolic values were normotensive in both average and day- time ABPM measurements.

These results are different from what we initially predicted as an outcome of this study, we expected that the BP measurements would be increased BP due to white coat effect and nervousness but that the ABMP would then reveal normotensive values.

There are several factors that can explain why we did we not get the results we anticipated. Firstly, it is important elaborate how the BP was measured in offices of community health center, whether measured according to Guidelines, applied guidelines? Because if not and done in a rush this can lead to imprecise measurements (see below). the ways the eight different doctors attain their BP measurements are not going to be identical and even one single physician probably measures BP differently with different patients and since our study was conducted as a retrospective study we have to trust the physicians with their provided information on how they measure BP.

As discussed the measurement of office blood pressure must follow specific rules and conditions to be reliable. In spite of that, these requirements are often not followed in clinical practice, leading to inaccurate BP readings.

We've asked the eight specialists of family medicine in Split whose offices are part of the Community health center Split, how they measure their patients BP in everyday practice. All of them stated to adhere to certain rules, like measuring on the right arm, using appropriate cuff size, positioning the patient correctly, BUT in one aspect did all of them, that is that they routinely only measure once instead of the recommended three times.

This might be since in everyday practice with a hectic schedule it might not be possible and inconvenient to apply measurement guidelines. So the accuracy of the measured values in office is questionable.

Another factor that contributes to the fact that we didn't get the expected result of the BP values measured in office being increased and hypertensive, because 164 out of 168 of the examines in our sample were receiving hypertensive treatment during the gathering of the data, which would decrease the incidence of e.g. white coat HT. Furthermore, the examinees included in this study for the most part know their family doctor very well and have developed a tight and trusting relationship, since often they have been their patient for a long period and therefore they are not feeling anxious when their BP gets measured. Often it might also be the nurse that does the BP evaluation before the patient sees the doctor, and that is in general also a good strategy to avoid a falsely increased BP.

Another limitation is that we do not know what the individual examinees indications were to get an ABPM in the first place, the physician must have ordered the ABPM for a reason, for example because the examinees had higher blood values with home BP measurement, to exclude masked hypertension; this would explain why the ABPM values would be higher than office values.

If you compare our results with other studies done on this topic, you frequently find similar results; In a big systematic review and meta-analysis study published in 2017, it is stated that isolated office BP measurements is not sufficient to confirm the presence of poor BP control and that there is a big probability of underestimating or overestimating BP control, when only using office BP measurements. It states that the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure has already approved ABPM for the diagnosis of HT for a long time, and that many physicians in primary care ABPM the golden standard for diagnosing HT and accurately assessing cardiovascular risk, no matter how the office measurements. Whereas until now the office BP is mostly accepted as the reference standard of diagnosis of HT. The study further concludes that the

US Preventive Services Task Force (USPSTF) recommends to always confirm the diagnosis by out of office techniques before starting hypertensive treatment. All in all, it comes to the conclusion that even though there is substantial research that supports ABPM it is not yet integrated enough into the routine management of arterial hypertension in primary care, it claims guideline like those of the European Society of Hypertension would continuously restrain APMPs use in diagnosis and treatment management of HT (45).

Another study has also concluded that also the patients themselves do not put a lot of confidence in office BP measurement compared to ABPM measurements, which is also an important fact to take into consideration when making decisions in making strategies to diagnose HT and better the medication adherence (46).

In our study, if we would only consider the BP results that we got through office measurement we would think everything is ok and the 168 patients are on average well regulated, but if we look at the results that we got from ABPM, only then did we realize that they might not be so well regulated after all and that in reality ISH or masked hypertension is present (47).

These results just come to show that it is definitely useful to utilize ABPM, so that you can assess the patients BP “under the surface”, more detailed and to look for variability of HT to check if the patient is well regulated, so that based on this, you can make accurate decisions on the further management of the patient. This explains why it is so important that the NICE guideline recommend to get ABPM at least ones in a lifetime.

His need for accuracy of BP measurement through ABPM is so important because it is important to avoid overtreatment in patients with white coat hypertension or the white coat effect and undertreatment of patients with masked hypertension.

The result of our thesis was that we revealed an average isolated systolic hypertension in our sample. Isolated systolic hypertension is the most common form of hypertension in the older population, 30% of women and 20% of men of people older than 65 have this phenomenon. In young patients the diastolic BP is more likely to increase and in the older patients systolic pressure usually goes up when you age. The pathological changes that lead to this condition include endothelial dysfunction, vascular stiffness, increased release of pro-inflammatory mediators and elastin calcification (47).

Risk factors of ISH are increasing age, female sex, a family history of HT, and African- American heritage. The result that an average ISH was revealed in our sample coincides with the risk factors within our sample, since more women were part of the sample (59.52%), and mostly older people whereas the majority of patients (52.23%) are in the age group of 61-80 years with an age median of 64 (47).

It is important to identify since it is associated with a significantly higher risk of cardiovascular and cerebrovascular morbidity and mortality - and this is exactly what the ABPM in our study did, making it more precise and important for decision-making in management of HT.

As a conclusion we can say that even though traditionally office BP measurement was recommended as the golden standard method for diagnosing HT, in reality in routine clinical practice it is relatively inaccurate and dependent on many internal and external influencing factors.

Often these guidelines do not take into account that there are widely recognized problems associated with the quality of manual BP measurement in routine clinical practice and a white coat response is a common response.

Therefore, the most recent guidelines recommend 24-h ABPM for diagnosing hypertension. Since as it did in our study, ABPM provides more accurate readings it also has stronger prognostic value and best predicts all-cause and cardiovascular mortality. The advantages of ABMP over office BP measurement support its use in routine clinical practice (20).

Since manual BP devices are cheap and easily accessible it does make sense that they are more commonly used around the globe but with my thesis I want to emphasize that the measurement of BP using the auscultatory method must follow specific rules and conditions to be reliable. Nonetheless, these requirements are often not followed in clinical practice, resulting in inaccurate BP readings leading to an inaccurate management of the patients BP status (48).

6. CONCLUSION

1. In our study we were able to display the importance of measuring the patients BP at least once ABPM besides Office measurement to make the correct choice for the management of HT and to prevent overtreatment in case of WCHT or WCE or undertreatment in the case of MH.
2. The results of our study are in coherence with previous studies that state that isolated office BP measurements is not sufficient to confirm the presence of poor BP control and that there is a big probability of underestimating or overestimating BP control, when only using office BP measurements. recommends to always confirm the diagnosis by out of office techniques before starting hypertensive treatment.
3. In our study we have also established the importance of adhering to certain guidelines when measuring BP in office to make sure the BP values are as accurate as possible for future management of HT in primary care.
4. After questioning eight specialists of family medicine in Split whose offices are part of the Community health center Split, how they measure their patients BP in everyday practice, all of them stated to adhere to most of the rules of measurement, BUT in one aspect did all of them not adhere and that is that they routinely only measure once instead of the recommended three times. This might be since in everyday practice with a hectic schedule it might not be possible and inconvenient to apply measurement guidelines. So the accuracy of the measured values in office is questionable.

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8. SUMMARY

Objectives: In this study we tried to elaborate whether it is enough to treat the patient based on conventional office blood pressure measurement or if we need to collect data through ABPM over 24hrs for the decision making on the management of arterial hypertension in primary care.

Subject and method: In this study 168 patients were included, they were treated in eight offices of specialists of family medicine in Split, which are part of the Community health center Split, during the period of 1st September 2018 and 1st of April 2019. We compared office systolic BP with ABPM average systolic BP, office diastolic BP with ABPM average diastolic BP, office systolic BP with ABPM day-time systolic BP, office diastolic BP with ABPM day-time diastolic BP and compared these with the reference values from the European Guidelines.

Results: The average value of the office BP was 138.93 mmHg (SD= 22.37) for the systolic and 82.14 mmHg (SD=13.07) for the diastolic BP. The average ABPM was 134.93 mmHg (SD= 13.35) for systolic and 76.92 mmHg (SD= 9.04) for the diastolic BP. The office BP measurements were normotensive but the ABPM revealed systolic values that are hypertensive in both average and daytime measurement with normotensive diastolic values.

Conclusion: As a conclusion we can say that even though traditionally office BP measurement was recommended as the golden standard method for diagnosing HT, in reality in routine clinical practice it is relatively inaccurate and dependent on many internal and external influencing factors.

Therefore the most recent guidelines recommend 24-h ABPM for diagnosing hypertension. Since as it did in our study, ABPM provides more accurate readings it also has stronger prognostic value and best predicts all-cause and cardiovascular mortality. The advantages of ABPM over office BP measurement support its use in routine clinical practice.

9. CROATIAN SUMMARY

Cilj istraživanja: Istražiti i pokazati da li je mjerenje arterijskog tlaka u ordinaciji obiteljskog liječnika dostatno za procjenu reguliranosti bolesnika koji boluju od arterijske hipertenzije ili trebamo koristiti podatke dobivene 24 satnim kontinuiranim mjerenjem arterijskog tlaka (KMAT) pri donošenju odluke o mijenjanju antihipertenzivne terapije.

Materijali i metode: Provedeno je retrospektivno presječno istraživanje u osam ordinacija obiteljske medicine Doma zdravlja Splitsko-dalmatinske županije. U istraživanje je uključeno 168 ispitanika kojima je u periodu od 01. rujna 2018. do 01. travnja 2019. urađeno 24 satno KMAT-a. Usporedili smo prosječne vrijednosti ordinacijskog arterijskog tlaka (sistoličkog i dijastoličkog) sa vrijednostima dobivenim KMAT-om (prosječni 24 satni te prosječni dnevni arterijski tlak). Navedene vrijednosti arterijskog tlaka usporedili smo sa recentnim europskim smjernicama za dijagnosticiranje i liječenje arterijske hipertenzije.

Rezultati: Prosječna vrijednost ordinacijskog arterijskog tlaka bila je $138,93 \pm 22,37$ za sistolički i $82,14 \pm 13,07$ mmHg za dijastolički tlak. Prosječna vrijednost 24 satnog tlaka dobivena KMAT-om bila je $134,93 \pm 13,35$ mmHg za sistolički i $76,92 \pm 9,04$ mmHg za dijastolički tlak. Na temelju prosječne vrijednosti ordinacijskog tlaka ispitanici dobro regulirani hipertoničari, ali rezultati KMAT-a ukazuju na nereguliranu, izoliranu sistoličku hipertenziju.

Zaključak: Premda je ambulanto izmjeren tlak zlatni standard za postavljanje dijagnoze arterijske hipertenzije u svakodnevnom radu može biti relativno nepouzdan, jer je podložan nizu čimbenika od strane liječnika i bolesnika. Zbog toga niz istraživanja podupire i preporuča da se bolesniku uradi KMAT. Osim točnijeg uvida u reguliranost arterijske hipertenzije, rezultati dobiveni KMAT-om bolji su prognostički pokazatelj razvoja kardiovaskularnih bolesti i mortaliteta. Prednosti ove metode mjerenja tlaka u odnosu na tlak izmjeren u ordinaciji govore u prilog rutinskom korištenju KMAT-a u svakodnevnom radu obiteljskog liječnika.

10. CURRICULUM VITAE

Personal Data

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<i>02.01 – 02.03.2019</i>	Erasmus at the Internal Medicine department at the "Gemeinschaftskrankenhaus Havelhöhe" hospital in Berlin, Germany
<i>04.07 – 30.09.2017</i>	Internship at the Infectology Department of the KBC Split, Croatia
<i>01.06 – 30.08.2013</i>	Clinical trainee-ship on the geriatric ward at the Protestant Hospital in Münster, Germany
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