Arterial stiffness in prehypertensive patients with white coat hypertension

Juraj Jug[1,2], Điđi Delalić[3], Ingrid Prkačin[2,3]

[1] Health center Zagreb - West, Zagreb, Croatia; 2 – School of medicine, University of Zagreb, Croatia; 3 – Emergency Internal Medicine Clinic, Clinical Hospital Merkur, Zagreb, Croatia

Abstract:

Introduction: White-coat hypertension (WCH) is associated with higher cardiovascular risk and increased all-cause mortality in the general population. The aim of this study was to determine whether there are differences in primary laboratory findings and pulse wave velocity (PWV) between prehypertensive patients with and without WCH.

Materials and Methods: This study included healthy 62 patients (37 women, 25 men) with prehypertension without medication based on ambulatory blood pressure monitoring [ABPM]) from one family practice in Health center Zagreb-West. Patients were divided into two groups depending on having WCH (>20 mmHg difference from in office SBP from average ABPM SBP values). Basic laboratory, anthropometric, 24h ambulatory blood pressure, and pulse wave velocity (PWV) measurements were done in all patients. Mann-Whitney U test, Kruskal-Wallis's test and descriptive statistics were used in data processing in Statistica v.12.0.

Results: WCH was found in 11 patients (17,7 %). Prehypertensive patients with WCH had significantly higher fasting glucose (median 5.7 [5.0–5.8] vs 5.3 [5.4–6.1] mmol/L; $p < 0.001$) and higher PWV (median 8.1 [7.1-8.8] vs. 9.0 [8.3–10.0] m/s; p=0.008). Patients with WCH had higher PWV in all three examined age groups (40–49 years p=0,074; 50-59 years p=0,003; 60-70 years p < 0,001). No differences were found in the concentration of potassium, LDL cholesterol, triglycerides, and body mass index (median 25.6kg/m2).

Conclusion: This pilot study indicates the possible existence of accelerated atherosclerosis in prehypertensive individuals with WCH. It is necessary to conduct research on a larger sample to confirm these findings.

KEYWORDS: Cardiometabolic risk factors, Vascular stiffness, White coat hypertension

Sažetak:

Krutost arterija u prehipertenzivnih bolesnika s hipertenzijom bijele kute

Uvod: Hipertenzija bijele kute (*engl. WCH*) povezana je s većim kardiovaskularnim rizikom i povećanom smrtnošću od svih uzroka u općoj populaciji. Cilj ovog istraživanja bio je utvrditi postoje li razlike u primarnim laboratorijskim nalazima i brzini pulsnog vala (*engl. PWV*) između prehipertenzivnih bolesnika sa i bez WCH.

Materijali i metode: Istraživanjem su obuhvaćena 62 zdrava bolesnika (37 žena, 25 muškaraca) s prehipertenzijom bez lijekova na temelju ambulantnog mjerenja krvnog tlaka (*engl. ABPM*) iz jedne obiteljske ordinacije Doma zdravlja Zagreb-Zapad. Bolesnici su podijeljeni u dvije skupine ovisno o tome imaju li WCH (>20 mmHg razlika između SBP u ordinaciji i prosječnih vrijednosti ABPM SBP). U svih bolesnika učinjena su osnovna laboratorijska, antropometrijska, 24-satna ambulantna mjerenja krvnog tlaka i brzine pulsnog vala. U obradi podataka u Statistici v.12.0 korišteni su Mann-Whitney U test, Kruskal-Wallisov test i deskriptivna statistika.

Rezultati: WCH je nađen u 11 bolesnika (17,7 %). Prehipertenzivni bolesnici s WCH imali su značajno višu glukozu natašte (medijan 5,7 [5,0–5,8] naspram 5,3 [5,4–6,1] mmol/L; p < 0,001) i viši

PWV (medijan 8,1 [7,1-8,8] naspram 9,0 [8,3] –10,0] m/s; p=0,008). Bolesnici s WCH imali su viši
PWV u sve tri ispitivane dobne skupine (40-49 godina p=0,074; 50-59 godina p=0,003; 60-70 godina
p < 0,001). Nisu pronađene razlike u koncentraciji kalija,
LDL kolesterol, trigliceridi i indeks tjelesne mase (medijan 25,6 kg/m2).
Zaključak: Ova pilot studija ukazuje na moguće postojanje ubrzane ateroskleroze u prehipertenzivnih
osoba s WCH. Za potvrdu ovih nalaza potrebno je provesti istraživanje na većem uzorku.

KLJUČNE RIJEČI: kardiometabolički čimbenici rizika, vaskularna krutost, hipertenzija bijele kute

INTRODUCTION

White coat hypertension (WCH) is defined as a condition in which the patient's arterial pressure is elevated only when measured in the physician's office; home and 24-hour ambulatory arterial pressure measurements give results that are inside the reference range for normotension (1). The prevalence of WCH is estimated to be around 30% among patients treated in hypertension clinics (2). However, the prevalence is notably lower when the physician or nursing staff are not involved in the process of arterial pressure measurement in the physician's office (3). One of the most important studies that illuminated the nature and risks of WCH was the PAMELA (Pressione Arteriose Monitorate E Loro Associazioni) Study (4). The PAMELA study was conducted on a random sample of 1651 subjects that represented the 25-64-year-old population of Monza, Italy. The subjects had their arterial pressures measured in the physician's office, at home by a semi automatic device and by a 24-hour ambulatory blood pressure monitoring (ABPM) device. The measurements obtained were used to determine the "normal" range of arterial pressure values in the general population, as well as classify and phenotype the elevated arterial pressure values into groups based on patterns and patient outcomes. The results of the study demonstrated that not only does WCH (referred to as "isolated office hypertension" in some of the articles cited) exist, it also carries an increased risk of hypertension-mediated organ remodelling. An analysis of the data from the PAMELA study by Sega et al shows that subjects with WCH had a significantly higher prevalence of left ventricular hypertrophy when compared to true normotensive subjects (5). Furthermore, an analysis of the data on plasma glucose concentrations of the PAMELA study participants over time, conducted by Mancia et al, demonstrated that participants with WCH or masked hypertension had an approximately three-fold greater risk of new-onset diabetes mellitus, compared to participants with true normotension. This increase in relative risk was the same as the one seen in patients with sustained hypertension (elevated arterial pressure values measured both at home and in the physician's office) (6). Additionally, Mancia et al measured the arterial pressure values of the PAMELA study participants 10 years following the first measurement in the study and found that participants who had white coat hypertension at the index

measurement had a significantly greater risk (odds ratio 2.5) of progressing to sustained hypertension during the 10-year period between measurements when compared to participants with true normotension (7). A 29-year follow-up of the PAMELA study population examining fatal cardiovascular (CV) event rates and all-cause mortality found that participants with WCH, but without evidence of end-organ damage had a two-fold greater adjusted risk of fatal CV events compared to normotensive participants without end-organ damage. Participants with white coat hypertension without organ damage also had a significantly higher adjusted risk (odds ratio 1.7) of developing organ damage during the follow-up period when compared to true normotensive participants, while participants with WCH and verified end-organ damage had a significantly higher adjusted risk of both CV (odds ratio 4.1) and all-cause mortality (odds ratio 2.1) when compared to true normotensive participants with verified end-organ damage (8). These results might stem from the fact that PAMELA participants with white coat hypertension also have a more unfavourable metabolic profile than normotensive participants, with higher blood concentrations of total cholesterol, triglycerides and glucose and lower blood concentrations of high-density lipoprotein cholesterol, resulting in higher rates of diabetes mellitus and metabolic syndrome (9). Taking all the aforementioned facts into account, precise phenotyping of elevated arterial pressure is of utmost importance, and offering 24-hour ABPM to patients with elevated values of arterial pressure on office measurements is both a thing of common sense, as well as endorsed by the currently available evidence and the latest European Society of Hypertension (ESH) guidelines, which state that: "Out of office blood pressure measurement by ABPM and/or home blood pressure management should be done when white coat hypertension is suspected, particularly in people with grade 1 hypertension" (1).

Given the available facts from the literature, the authors of this article were interested in whether further phenotyping of patients with white coat hypertension according to pulse wave velocity (PWV) values (an indirect measure of arterial stiffness), using oscillometric measurements of PWV immediately following the removal of the 24-hour ABPM device, would be useful in identi-

fying those patients with WCH that are at higher risk of adverse CV outcomes than others.

The aim of this study, therefore, is to determine whether there are significant differences in PWV between patients with WCH and those with true normotension.

METHODS

This cross-sectional study was conducted in four family medicine practices (FMP) in the Health Center Zagreb - West from October 2021 to April 2023 (19 months). A total of 62 subjects (37 women and 25 men) with prehypertension were included in the study, divided into two groups depending on the presence of white coat syndrome. Prehypertension is defined as a systolic arterial pressure between 120 and 139 mmHg and/or a diastolic arterial pressure between 80 and 89 mmHg measured in two or more sitting measurements at two or more physician visits (according to the eighth Joint National Committee (JNC 8) criteria). White coat syndrome (WCH) is defined by systolic blood pressure measured in the office higher than 20 mmHg in relation to the average daily arterial pressure measured by ambulatory blood pressure monitoring (ABPM). Additionally, the respondents were divided into three groups depending on their age group (40-49, 50-59, 60-69). Only those subjects who did not have any acute illness at the time of the examination and who did not have any chronic or mental illness recorded in the medical documentation were included in the research.

The device used for ABPM was the BTL Cardiopoint®. All measurements were made by one researcher. The ABPM was performed with an adequate cuff placed on the lower half of the subject's upper arm determined by the circumference of the middle part of the distal half of the upper arm. All subjects were divided into two groups (dipper ≥ 10 %, non-dipper < 10 %) according to the percentage change in the average value of night AT compared to the average daily AT values. In case of threshold values (eg more than 5 measured values of systolic AT above 170 mmHg, etc.), duration of ABPM shorter than 20 hours or less than 70% of correct measurements, ABPM was repeated two weeks after the first measurement. ABPM was performed in FMP during working hours according to a special schedule. During the morning shift, the ABPM was set every working day at 12:30 p.m. and read the next day at the beginning of the shift at 1:30 p.m. Then it was set to the next respondent according to the schedule that the device returned for reading the next day at 12:30 p.m. Each respondent was asked for information about the usual time of going to sleep and waking up. The device is set so that it measures BP every 15 minutes during the day (subject's wakefulness), and every 30 minutes during the night (subject's sleep). Subjects were warned not to bathe or shower or work with water, and to improve measurement precision, they were asked to keep a diary of their activities while wearing the device.

PULSE WAVE VELOCITY

PWV was measured with an oscillometric device Agedio® B900 (Industrielle Entwicklung Medizintechnik und Vertriebsgesellschaft GmbH (IEM), Stolberg, Germany) in a sitting position at a room temperature of 20-22 °C with the application of a wristband in the same previously described manner as in the execution of ABPM. The measurement itself lasts an average of three minutes and consists of two parts with a break of 30 seconds between them. The first measurement is a calibration (measurement of arterial pressure), while in the second measurement, the cuff is inflated to a pressure 35 mmHg higher than the measured pressure, and using the sensor in the cuff, pulse waves are detected and analysed for eight seconds, determining the central arterial pressure, the augmentation index (AIx) and evaluating the aortic PWV (PWVao). Measurements are programmed using a special application connected via Bluetooth to the specified device.

BIOCHEMICAL PARAMETERS

Biochemical parameters in the serum of the subjects were determined by sampling two tubes of 8-10 mL of venous blood. The values of hematocrit, concentration of creatinine, sodium ions, potassium ions and glucose in the serum, triglycerides, HDL, LDL and total cholesterol and urate were determined. The devices used to analyse the analysed parameters were Sysmex XN 1000 and B-C AU500. The glomerular filtration rate (GFR) was estimated by the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula.

OTHER

SCORE and SCORE 2 CV risks were determined for all subjects according to the ESC tables for regions with a high-risk person profile.

All anamnestic data and findings of the subjects were collected from the Medicus.Net system. The research was approved by the ethics committee of the institution (number 251-12-02-21-19). All respondents signed an informed consent to participate in the research.

STATISTICAL ANALYSIS

The normality of the data distribution was checked with the Kolmogorov-Smirnov test, and appropriate statistical tests were applied according to the obtained results. Numerical variables are presented as arithmetic mean and standard deviation (± SD), or median [interquartile range]. Nominal and ordinal (categorical) variables are presented by frequency distribution by group and share (%) for each analyzed group. Kruskal-Wallis test was used in order to determine the differences between the three age groups of respondents. The correlation between variables was checked by Spearman's rank correlation test. Statistical analysis of the data was performed in Statistica, StatSoft Inc., version 12.0.

RESULTS

A total of 11 subjects (18%) in this sample met the conditions for WCH. By comparing the analysed parameters between the group with and without WCH, a significant difference was found only in fasting glucose concentration and AIx. Subjects with WCH tended to have higher values of PWV, LDL and lower GFR (Table 1). In the group without WCH, there were 6 (11.7%) smokers, while in the group with WCH, not a single respondent was a smoker.

Table 1. Characteristics of patients with and without white coat hypertension (WCH).

	Without WCH **(N = 51, 82%)** Median [IQR]	**Have WCH** **(N = 11, 18%)** Median [IQR]	**P**
Age (years)	55 [47 – 58]	55 [45 – 65]	0.733
ABPM SBP (mmHg)	122 [120 – 127]	119 [117 – 126]	0.171
ABPM DBP (mmHg)	75 [71 – 78]	73 [71 – 85]	0.846
Nocturnal indices (%)	10.8 [7.3 – 15.7]	10.6 [8.2 – 13.3]	0.803
HR (/min)	72 [67 – 77]	71 [63 – 81]	1.000
GFR (mL/min/ 1,73m2)	91.0 [85.0 – 95.6]	83.6 [72.1 – 91.7]	0.093
LDLc (mmol/L)	3.6 [3.0 – 4.3]	3.8 [3.7 – 4.5]	0.133
HDLc (mmol/L)	1.4 [1.3 – 1.6]	1.4 [1.2 – 1.7]	0.561
Triglycerides (mmol/L)	1.1 [0.8 – 1.7]	1.1 [0.9 – 1.6]	0.926
Uric acid (umol/L)	294 [247 – 339]	250 [240 – 385]	0.946
PWV (m/s)	8.1 [5.9 – 10.5]	10.7 [7.3 – 15.4]	0.101
AIx (%)	22 [15 – 32]	36 [26 – 42]	0.007
BMI (kg/m2)	25 [22 – 27]	26 [24 – 30]	0.178
Fasting glucose (mmol/L)	5.3 [5.0 – 5.8]	5.6 [5.4 – 6.1]	0.046

ABPM = ambulatory blood pressure monitoring; SBP = systolic blood pressure; DBP = diastolic blood pressure; GFR = glomerular filtration rate; PWV = pulse wave velocity; BMI = body mass index; HR = heart rate; AIx = augmentation index.

By age group, WCH had 4 (36%) respondents aged 40-49, 4 (36%) aged 50-59 and 3 (27%) aged 60-69. By comparing the observed parameters according to age groups, existence of WCH and groups of respondents, a significant difference between the values of the measured PWV was determined. Accordingly, PWV values increased with age and were significantly higher in the group with WCH in all three age groups (Figure 1). The measured value of PWV correlated significantly with the difference between the systolic pressure measured in the office and the average systolic pressure measured by KMAT ($r = 0.443$; $p < 0.001$).
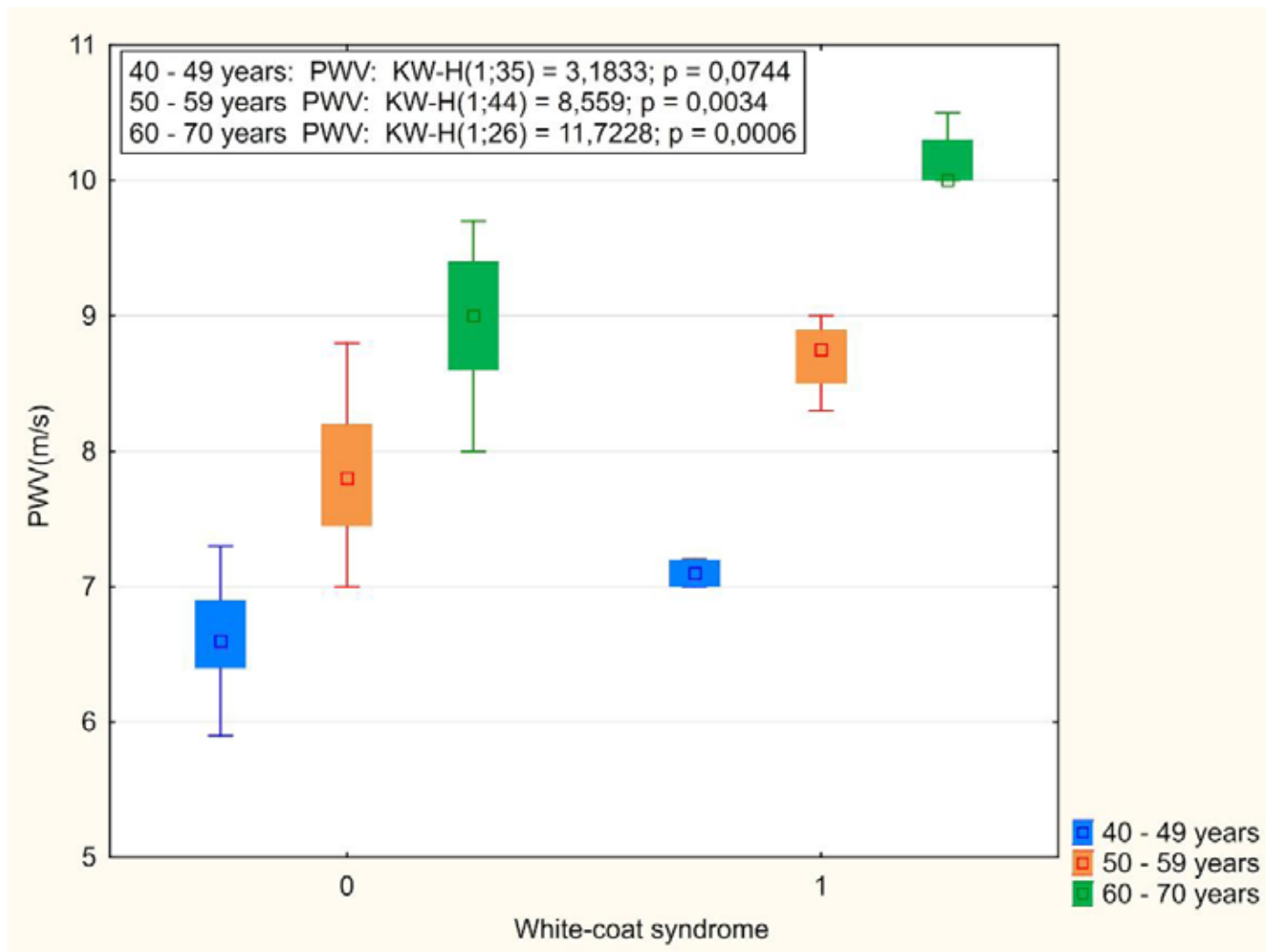
Figure 1. Pulse wave velocity (PWV) values in prehypertensive individuals with and without white coat hypertension (WCH) divided to age groups. PWV values depend on age.

Calculating CV risk according to SCORE (median 1.6 vs. 1.4 in subjects with WCH; p = 0.562) and SCORE 2 (median 3.8 vs. 2.6 in subjects with WCH; p = 0.846) tables revealed a lower median value of CV risk in the group with WCH. However, dividing by age groups, no significant difference was found between subjects with and without WCH according to the results of CV risk tables (Figure 2). Overall, according to SCORE risk, 56 respondents (90.32%) were in the low and moderate risk group, and according to SCORE 2, 39 respondents (62.90%)

had such a risk. High risk was recorded in 6 (9.68%) and 18 (29.03%) subjects according to SCORE and SCORE 2 risk, respectively. According to the SCORE 2 tables, 5 respondents had a very high risk, while according to SCORE, no one had such a risk. The measured value of PWV was shown to be significantly correlated with the results of both CV risk tables (r = 0.673; p < 0.001 for SCORE; r = 0.801; p < 0.001 for SCORE 2), while no significant correlation was found for AIx with the result of the CV risk tables.
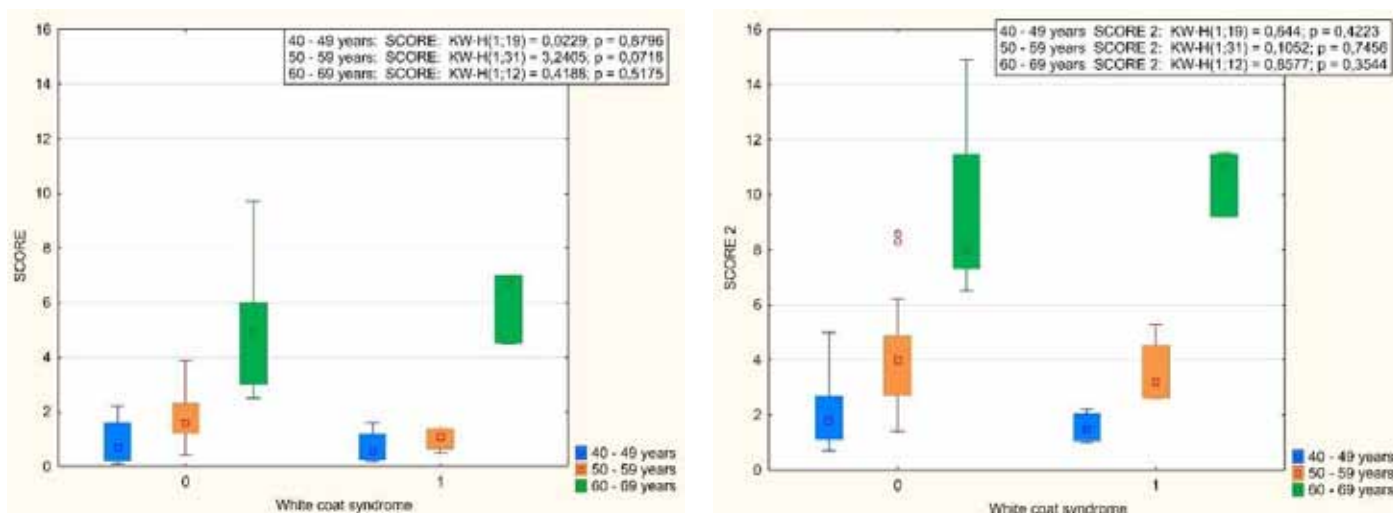
Figure 2. SCORE (left) and SCORE 2 (right) risks values in prehypertensive individuals with and without white coat hypertension depending on age group.

DISCUSSION

Besides ours, several other studies examining pulse wave velocities and arterial stiffness in patients with white coat hypertension have been conducted. A study by Rong Cao et al measured brachial-ankle pulse-wave velocity (ba-PWV) in 444 patients deemed to have white coat hypertension based on data from a single 24-hour ambulatory blood pressure monitoring (ABPM) and at least 2 arterial pressure measurements in the physician's office at separate times (10). They further split the patients according to a quantitative increase in systolic blood pressure (SBP) on office measurements when compared to 24-hour ABPM - patients with an increase lower than 9.5mmHg were deemed "low white coat effect" and those with an increase of 9.5mmHg or greater were deemed "high white coat effect". Their results demonstrated that the absolute value of b-aPVW linearly correlated with the increase in SBP attributable to white coat effect and the correlation persisted and remained statistically significant ($p = 0.004$) when the model was adjusted for age, sex, diabetes mellitus, hyperlipidemia, smoking status, family history of hypertension, BMI, serum creatinine and uric acid.

A study on 120 patients with inflammatory bowel disease (IBD) by Premužić et al found that a significantly higher proportion of IBD patients with white coat hypertension had PWV values above the 8 m/s cutoff when compared to true normotensive IBD patients (84.8 vs 30.6, $p < 0.001$). Furthermore, IBD patients with white coat hypertension had significantly higher values of central SBP and central puls pressure when compared to true normotensive IBD patients, while having similar (non-significantly different) age, gender distribution, smoking status, duration of IBD, biochemical data, proportion of patients receiving biological or immunosuppressive treatment (11). Research by

Stolarz et al compared PWV in a random sample of participants with either normotension, masked hypertension or white coat hypertension and found significantly higher values of PWV in patients with white coat hypertension when compared to those with true normotension (9.39+/-1.23 m/s vs 8.56+/-1.45 m/s; $p < 0.05$). However, the difference lost statistical significance when corrected for age, gender, BMI and smoking status (12). Saunders et al conducted a sub-group analysis of the Arterial Stiffness In lacunar Stroke and Transient ischemic attack (ASIST) study which included 32 patients with true normotension and 30 patients with white coat hypertension 14 days following an adverse cerebrovascular event (either a transient ischemic attack or a lacunar stroke) and found that patients with white coat hypertension had significantly higher carotid-femoral PWV (cfPWV) values (11.9 ± 3.0 m/s vs. 9.6 ± 2.3 m/s, $p = 0.002$) (13). Lithovius et al conducted ABPM and PWV measurements in 140 patients with type 1 diabetes mellitus and found that patients with white coat hypertension had significantly higher PWV values when compared to true normotensive patients (6.7 m/s vs 5.8 m/s, $p < 0.001$)(14). Paiva et al compared PWV values in 692 individuals divided into groups by hypertension phenotype according to data obtained by ABPM. They found that patients with controlled white coat hypertension had significantly higher office PWV values when compared to true normotensive patients (7.53 +/- 0.09 m/s vs 6.89 +/- 0.05 m/s, $p < 0.05$), while patients with uncontrolled white coat hypertension had significantly higher office (8.28 +/- 0.11 m/s vs 7.43 +/- 0.08 m/s, $p < 0.05$) and 24-hour (7.54 +/- 0.09 m/s vs 7.21 +/- 0.07 m/s, $p < 0.05$) PVW values when compared to patients with controlled hypertension (15).

Besides the individual studies cited, two meta-analyses related to the topic of arterial stiffness in white coat hypertension were published. A meta-analysis by Cai et al included 20 studies examining 1538 patients with white coat hypertension and 3582 patients with true normotension and concluded that, in the adult population, patients with white coat hypertension had significantly higher cfPWV values when compared to true normotensives [95% confidence interval (CI): 0.46-0.87, p < 0.001] (16). Another meta-analysis, conducted by Antza et al, included 7 studies and 2352 patients, and found that patients with white coat hypertension had significantly higher cfPWV values when compared to true normotensives (difference = 0.85 m/s, 95% CI: 0.48-1.22; p < 0.01). Furthermore, patients with white coat hypertension had similar (non-significantly different) values of PWV when compared to patients with sustained hypertension (difference = –0.75 m/s, 95% CI: –1.52-0.02) (17).

The results of this study are in line with the currently available literature, demonstrating significantly higher PWV values in patients with white coat hypertension compared to true normotensives. However, this association was only found in patients older than 50 years of age. This finding could be explained by the fact that arterial stiffness by itself increases with age (18), making the effects of other important factors, such as white-coat hypertension, more pronounced in patients whose arteries are stiffer at baseline (due to age-related changes in arterial tissue composition) and more prone to increases in "functional" arterial stiffness, defined by an increase in arterial tone, mediated by increased blood pressure (19).

Another important finding of our study is the fact that patients with white coat hypertension had a significantly higher fasting plasma glucose concentration when compared to true normotensive patients, which is in line with established facts from larger studies, such as the PAMELA study (9).

While our study did not establish an increase in CV risk in patients with white coat hypertension compared to true normotensive patients, the diagnostic accuracy of the instruments that we used (SCORE and SCORE2 tools) might be lower than desirable in general. A retrospective study by Karakayali et al calculated the SCORE and SCORE2 risk scores of 788 patients diagnosed with arterial hypertension and gathered data on adverse CV events from a 6-year follow-up period. They found that the diagnostic accuracy [expressed as area under the curve (AUC)] of SCORE and SCORE2 for major adverse CV and cerebrovascular events (MACCE) during a 6-year follow-up period was 0.689 and 0.724 respectively, indicating borderline acceptable diagnostic accuracy (20).

Therefore, the lack of significant differences in SCORE and SCORE2 scores in our patient cohort should not be interpreted as the lack of difference in CV risk overall between white coat hypertensive and true normotensive patients.

There are several important limitations to our study. The first one is the relatively small sample size. The second is the fact that this was a single-center study, making generalisability of our findings to the general population difficult. Furthermore, while a biochemistry panel was conducted on all participants, thyroid stimulating hormone (TSH) concentrations were not measured. According to epidemiological studies, 5-15% of the general population is affected by subclinical hypothyroidism. Patients with subclinical hypothyroidism are known to have increased PWV values, making TSH measurement an important step in removing potential confounding from studies involving PWV measurement.

Other factors that might influence PWV values, such as physical activity, alcoholic beverage consumption and nutrition were not evaluated in this study.

Finally, we have no validated method of determining both the exact duration of arterial hypertension and adherence to antihypertensive/antilipemic therapy in individual patients, both of which are factors that significantly affect PWV values.

CONCLUSION

In this single-centre cross-sectional study, patients with white coat hypertension older than 50 were found to have significantly higher values of PWV and significantly higher concentrations of fasting plasma glucose when compared to true normotensive patients. These findings add to the existing knowledge on white coat hypertension, indicating that phenotyping of elevated blood pressure using ambulatory blood pressure monitoring is of utmost importance for predicting adverse outcomes. However, more prospective multi-center studies should be conducted in order to corroborate these findings.

REFERENCES

1. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A et al. 2023 ESH Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension: Endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). J Hypertens. 2023;41(12):1874-2071.

2. Stergiou GS, Palatini P, Parati G, O'Brien E, Januszewicz A, Lurbe E et al. 2021 European Society of Hypertension practice guidelines for office and out-of-office blood pressure measurement. J Hypertens. 2021;39(7):1293-1302.

3. Grassi G, Quarti-Trevano F, Seravalle G, Dell'Oro R, Vanoli J, Perseghin G et al. Sympathetic Neural Mechanisms Underlying Attended and Unattended Blood Pressure Measurement. Hypertension. 2021;78(4):1126-1133.

4. Mancia G, Sega R, Bravi C, De Vito G, Valagussa F, Cesana G et al. Ambulatory blood pressure normality: results from the PAMELA study. J Hypertens. 1995;13(12 Pt 1):1377-90.

5. Sega R, Trocino G, Lanzarotti A, Carugo S, Cesana G, Schiavina R et al. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: Data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). Circulation. 2001;104(12):1385-92.

6. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, Grassi G et al. Increased long-term risk of new-onset diabetes mellitus in white-coat and masked hypertension. J Hypertens. 2009;27(8):1672-8.

7. Mancia G, Bombelli M, Facchetti R, Madotto F, Quarti-Trevano F, Polo Friz H et al. Long-term risk of sustained hypertension in white-coat or masked hypertension. Hypertension. 2009;54(2):226-32.

8. Mancia G, Facchetti R, Vanoli J, Dell'Oro R, Seravalle G, Grassi G. White-Coat Hypertension Without Organ Damage: Impact on Long-Term Mortality, New Hypertension, and New Organ Damage. Hypertension. 2022;79(5):1057-1066.

9. Mancia G, Bombelli M, Cuspidi C, Facchetti R, Grassi G. Cardiovascular Risk Associated With White-Coat Hypertension: Pro Side of the Argument. Hypertension. 2017;70(4):668-675.

10. Cao R, Yue J, Gao T, Sun G, Yang X. Relations between white coat effect of blood pressure and arterial stiffness. J Clin Hypertens (Greenwich). 2022;24(11):1427-1435.

11. Premužić V, Prijić R, Jelaković M, Krznarić Ž, Čuković-Čavka S, Jelaković B. White coat hypertension is another clinical characteristic of patients with inflammatory bowel disease: A cross-sectional study. Medicine (Baltimore). 2022;101(44):e29722.

12. Stolarz K, Wojciechowska W, Olszanecka A, Lubaszewski W, Cwynar M, Grozdicki T et al. Pulse wave velocity in subjects with masked hypertension and white coat hypertension. Artery Research. 2006;1:46.

13. Saunders A, Nuredini GN, Kirkham FA, Drazich E, Bunting E, Rankin P. White-coat hypertension/effect is associated with higher arterial stiffness and stroke events. J Hypertens. 2022;40(4):758-764.

14. Lithovius R, Gordin D, Forsblom C, Saraheimo M, Harjutsalo V, Groop PH. Ambulatory blood pressure and arterial stiffness in individuals with type 1 diabetes. Diabetologia. 2018;61(9):1935-1945.

15. Paiva AMG, Gomes MICM, Campana ÉMG, Feitosa ADM, Sposito AC, Mota-Gomes MA et al. Impact of hypertension phenotypes on the office and 24-h pulse wave velocity and augmentation index in individuals with or without antihypertensive medication use. Hypertens Res. 2019;42(12):1989-1995.

16. Cai P, Peng Y, Wang Y, Wang X. Effect of white-coat hypertension on arterial stiffness: A meta-analysis. Medicine (Baltimore). 2018;97(42):e12888.

17. Antza C, Vazakidis P, Doundoulakis I, Bouras E, Haidich AB, Stabouli S et al. Masked and white coat hypertension, the double trouble of large arteries: A systematic review and meta-analysis. J Clin Hypertens (Greenwich). 2020;22(5):802-811.

18. Townsend RR, Wilkinson IB, Schiffrin EL, Avolio AP, Chirinos JA, Cockcroft JR et al. American Heart Association Council on Hypertension. Recommendations for Improving and Standardizing Vascular Research on Arterial Stiffness: A Scientific Statement From the American Heart Association. Hypertension. 2015;66(3):698-722.

19. Pierdomenico SD, Coccina F, Madonna R. Pulse wave velocity in white coat and masked hypertension. J Clin Hypertens (Greenwich). 2020;22(5):812-813.

20. Karakayalı M, Püşüroğlu H, Altunova M, Yılmaz E, Güllü A. Predictive value of the SCORE, SCORE2, and pooled cohort risk equation systems in patients with hypertension. Turk Kardiyol Dern Ars. 2023;51(6):407-414.