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Pulse Wave Analysis in Obese Children with and without Metabolic Syndrome

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What is already known on this topic?

In the latest arterial hypertension guidelines published for adult patients, pulse wave analysis (PWA) is recommended because of its high predictability, easy applicability, and reproducibility when determining cardiovascular risk. Evidence about PWA in children and adolescents with metabolic syndrome (MS) is limited.

What this study adds?

This study showed that additional risk factors other than obesity, which are required for the diagnosis of MS, appear to contribute to an increase in 24-hour and daytime central systolic and diastolic blood pressure. This suggests that PWA may be helpful when determining cardiovascular risk and target organ damage in obese children with MS.

Abstract

Objective: To compare pulse wave analysis (PWA) of obese children with and without metabolic syndrome (MS) with healthy, non-obese children and to evaluate the association between PWA findings and additional risk factors present in children with MS and obesity.

Methods: From the obese patients examined between June 2019 and June 2021, 41 patients with MS, 36 obese patients without MS, and 34 healthy non-obese children of similar age and gender were evaluated retrospectively. Anthropometric measurements, biochemical evaluation, 24-hour ambulatory blood pressure (BP) measurement (ABPM), left ventricular mass index (LVMI) and PWA measurements were compared.

Results: When the three groups were compared, weight standard deviation score (SDS), height SDS and body mass index SDS were all significantly higher in the MS group ($p < 0.05$). The following measurements were significantly higher in both MS and non-MS obese patients compared to the control group: from ABPM measures, the systolic and mean arterial pressure BP SDSs load; from PWA, the night central systolic BP, 24-hour, day and night pulse pressure values and 24-hour, day and night pulse wave velocity (PWV) rates; and from cardiac evaluations, the LVMI and relative wall thickness measurements (all $p < 0.05$). Furthermore, the 24-hour and daytime central systolic (cSBP) and diastolic BP (cDBP) values were significantly different between the three groups, being the highest in the MS group ($p < 0.05$).

Conclusion: Obesity causes higher office, ambulatory and central BP, PWV and LVMI. However our results suggest that additional risk factors associated with MS do not contribute to these parameters, except for 24-hour and daytime cSBP and cDBP values.

Keywords: Children, pulse wave analysis, metabolic syndrome, obesity

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Introduction

Metabolic syndrome (MS) is a cluster of medical problems that put patients at risk for cardiovascular diseases. There are different definitions proposed by different research groups for the definition of MS in children (1). All of these definitions include high body mass index (BMI) and waist circumference measurement, high triglyceride and low high density lipoprotein (HDL) cholesterol levels, high blood pressure (BP) and high fasting blood glucose or high fasting insulin level. The International Diabetes Federation (IDF) recommends that definitions be evaluated separately according to age groups due to age-related variability in children (2). The most important reason for the increase in the frequency of MS in children is the increase in the prevalence of obesity (3). It is known that obesity carries a risk for cardiovascular diseases, and the risk is greater in the presence of MS due to additional components.

The most common target organ damage seen in both adults and children with hypertension (HT) is an increase in left ventricular mass and increased carotid intima-media thickness (4,5). The concept of arterial stiffness (AS) has also emerged in recent years as a strong independent predictor of cardiovascular events. AS is a measure of the viscoelasticity of the vessel wall and is also a strong independent indicator of cardiovascular events (6). Pulse wave analysis (PWA), which evaluates the response and wave reflections created by the pressure on the vessel wall created during the progression of the pulse wave originating from the aortic arch to the periphery, is the most commonly used method to evaluate AS (7,8). In case of increased AS, the central systolic BP (cSBP) increases, central diastolic BP (cDBP) decreases, central pulse pressure (cPP) rises, and left ventricular mass and load increase (9).

PWA can be used to investigate vascular structures by looking at parameters such as pulse wave velocity (PWV) and augmentation index (AIx) (10). PWV is the rate of passage of the pulse wave between two points in the arterial system (11). The most important factors affecting PWV are age and BP. PWV has been shown to be high in chronic diseases, such as kidney failure, obesity and diabetes mellitus (12,13). In cases with increased AS, the back reflection wave reaches the aortic root earlier than diastole since the PWV is high. Adding to the forward wave causes an increase in the amplitude of the wave and the systolic pressure. This percentage of increase is expressed as the AIx (14). High AIx values are associated with increased PWV, in other words with AS. AIx is a normalized index based on 75 beats per minute due to heart rate differences (AIx@75). In the latest arterial HT guidelines published for adult patients, PWA is recommended because of its high predictivity, easy applicability and reproducibility in determining cardiovascular risk (15).

The aim of this study was to compare the PWA of obese children with and without MS with healthy non-obese children and to evaluate the effects of additional MS-associated risk factors in addition to obesity.

Methods

Study Population

The protocol of this single-center, cross-sectional study was approved by the Ethics Committee of University Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (decision no: 2021/10-09, date: 15.10.2021). The results of ambulatory BP monitoring (ABPM) and PWA performed in obese (BMI ≥95th percentile) children with or without MS and non-obese (BMI <85th percentile) children who attended the pediatric outpatient clinic between June 2019 and June 2021 were analyzed retrospectively. Patients aged between 10 and 18 years (because it is difficult to diagnose MS at <10 years of age) and taller than 120 cm (as ABPM reference data was compiled in children with a height of 120 cm and above) were included. Patients with missing data, or had an additional chronic disease, such as cardiac disease, chronic kidney disease, hyperthyroidism or hypothyroidism, were not included in the study. The data of children whose BP was measured to be high for any reason and who were referred to us for further examination, whose office BP and ABPM were evaluated as normal, who were not hypertensive, healthy, and not obese during follow-up, were evaluated as the control group.

Anthropometric Measurement

Weight measurement was carried out by removing all outer clothing and shoes using a digital scales suitable for adults, sensitive to 100 g. Height measurements accurate to the nearest centimeter were performed using a rigid stadiometer. Height was measured while the child was standing. The measurement was performed on a hard surface, barefoot and without a hat on, with the child's back facing the measuring instrument, with the most protruding part of the head, shoulders, hips and heels in full contact with the measuring instrument, with the arms hanging down, the heels together, and the head straight. The hard and flat and moving head of the measuring instrument was partially touched to the upper part of the head, and this point was read from the scale and the height was determined. Weight and height percentiles were calculated using Turkish national reference data (16). BMI was calculated as the ratio

of body weight (kg) to height in metres squared (m^2). The standard deviation (SD) score (SDS) of BMI was calculated using the Child Metrics program (17). On the BMI reference curve, which was prepared for Turkish children and adjusted for age and gender, those with BMI values between the 85th percentile and the 95th percentile were defined as "overweight", and those above the 95th percentile were defined as "obese" (16).

Waist circumference was measured at the end of expiration from the midpoint between the lower edge of the last rib and the apex of the iliac crest while standing comfortably with the feet approximately 25-30 cm apart. Waist circumference percentiles were evaluated according to percentiles calculated for Turkish children (18). The presence of puberty was evaluated as having physical examination findings compatible with at least Tanner 2 (19,20).

The criteria recommended by the IDF were used for the diagnosis of MS (2).

Biochemical Tests

Fasting glucose, creatinine, uric acid, sodium, potassium, alanine aminotransferase (ALT), free T4, thyroid stimulating hormone (TSH), insulin levels and lipid profiles (total cholesterol, HDL cholesterol and triglycerides) were measured in blood samples taken in the morning after overnight fasting. Blood glucose levels were measured by the glucose oxidase method and serum lipid profiles were measured using routine enzymatic methods. Insulin measurements were made by the immunofluorometric method. An oral glucose tolerance test (OGTT) was performed to detect insulin resistance (IR). The OGTT used 1.75 g/kg (maximum 75 g) glucose administered orally, and blood samples were taken for glucose and insulin measurements at 0, 30, 60, 90 and 120 minutes (21). Homeostasis model assessment (HOMA) of IR was calculated using the Child Metrics program with the formula: fasting plasma glucose (mg/dL) x fasting plasma insulin (μU/mL) / 405 (17). HOMA-IR levels > 2.5 for prepubertal and > 4 for pubertal (Tanner ≥2) participants were defined as IR (22).

Office BP Measurements

Office BP was measured three times at 2-minute intervals on the right arm, after 5 minutes of rest, with aneroid devices calibrated by an experienced nurse, with cuffs appropriate for the child's age, and the last two BPs were averaged for analysis. Office systolic BP (SBP) and diastolic BP (DBP) measurements of all patients were evaluated according to the American Academy of Pediatrics 2017 (AAP-2017) HT guideline (23).

ABPM Measurements and PWA

Office and ABPM and central BP measurement of the patients were evaluated with an oscillometric PWA-ABPM device (Mobil-O-Graph; IEM, Stolberg, Germany) (24).

Daytime measurements were made at 15-minute intervals, and nighttime measurements were performed at 30-minute intervals. The results of the measurement yielded skewness (L), median (M) and coefficient of variation (S), which were converted to SDSs by the LMS method. SDSs were calculated using the Child Metrics program according to the published reference LMS tables for healthy children (17,25). The ratio of BP values above the ambulatory 95th percentile was defined as "BP load". Patients with < 10 % reduction in BP at night compared to the daytime period were defined as "dipper". In ABPM measurements, measurements above the 95th percentile were accepted as HT (23).

The variables measured during PWA included: 24-hour daytime and nighttime SBP (mmHg); 24-hour daytime and nighttime DBP (mmHg); 24-hour daytime and nighttime mean arterial pressure (mmHg) (MAP) [(MAP) = (SBP + 2 DBP) / 3]; daytime and nighttime systolic load (%); daytime and nighttime diastolic load (%); systolic and diastolic dip; 24-hour daytime and nighttime cSBP (mmHg); 24-hour daytime and nighttime cDBP (mmHg); 24-hour daytime and nighttime cPP (mmHg); [cPP = cSBP-cDBP]; 24-hour daytime and nighttime PWV (m/s); and 24-hour daytime and nighttime AIx standardized across 75 heart beats (AIx@75) (10). Central BP indicates BP at the aortic root and is usually lower than the brachial artery measurement (26).

Echocardiographic Assessment

All children included in the study were evaluated by the same pediatric cardiologist with the same echocardiography device. Left ventricular mass index (LVMI) was calculated according to the Devereux formula and indexed to height $(m)^{2.7}$. LVM (grams): 0.8 × 1.04 [(LVEDD + IVST + PWT)-(LVEDD)] + 0.6 where LVEDD is the left ventricular end-diastolic diameter, IVST is the interventricular septum thickness and PWT is the posterior wall thickness (27,28). Left ventricular hypertrophy (LVH) is defined as an LVMI that exceeds the 95th percentile for sex and age in normal children and adolescents (28). The LVH index was obtained by dividing the LVMI by the 95th percentile for that age and gender. The relative wall thickness (RWT) was calculated by the formula: RWT = 2 × PWTd/LVIDed (PWTd: posterior wall thickness diastole, LVIDd: left ventricle internal diameter diastole) (29).

Statistical Analysis

All statistical evaluations were performed using Statistical Package for the Social Sciences for Windows, version

24.0 (IBM Inc., Armonk, NY, USA). Discrete variables are expressed as counts (percentage), continuous variables with normal distribution were calculated as mean ± SD, and continuous variables with non-normal distribution as median (interquartile ranges; 25-75%). The Kolmogorov-Smirnov test was used to evaluate the distribution of continuous variables. Normally distributed variables were evaluated with the ANOVA test and *post-hoc* analyses were performed with the Tukey test in homogeneous groups and with Tamhane's T2 test in heterogeneous groups. For non-parametric distribution, variables were evaluated first with the Kruskal-Wallis test for the three groups and then with the Mann-Whitney U test to determine the group that caused the difference. Depending on the distribution type of the variable, Pearson or Spearman's analysis was performed. A $p < 0.05$ was considered statistically significant for all statistical evaluations.

Results

Of the 111 patients included in the study, 36 (32.4%) were non-MS obese and 41 (36.9%) patients had MS. There were 34 (30.6%) healthy non-obese children in the control group (Figure 1). The mean age and gender were similar between the three groups. The characteristics of the demographic and laboratory findings of the study population are given in Table 1. Height SDS was significantly higher in the MS group compared to the other two groups. Weight SDS and BMI SDS were significantly different between the three groups. Uric acid, total cholesterol, ALT, and TSH levels were similar in the MS and non-MS obese groups, but significantly lower in the control group. Triglyceride levels were significantly higher in the MS group compared to the other two groups. HOMA-IR was significantly higher in the MS group than in the non-MS obese group. All children were euthyroid.

The office BP measurement and 24-hour ABPM results were compared and are shown in Table 2. Office SBP SDS values, 24-hour daytime and nighttime SBP SDS values, 24-hour daytime and nighttime MAP SDS values, daytime and nighttime systolic load, and nighttime diastolic load were similar in the MS and the non-MS obese groups, which were higher than the control group. Office DBP SDS values and daytime DBP load were significantly higher in the MS group than the other two groups. The 24-hour daytime and nighttime DBP SDS and systolic and diastolic dip rates were similar in all groups.

When PWA data were evaluated, 24-hour and daytime cSBP values were higher in the MS group compared to the other two groups. Moreover, 24-hour and daytime cDBP values were higher in the MS group than the control group, but similar between the MS and non-MS obese patients. Nighttime cSBP values, 24-hour daytime and nighttime PP values, and 24-hour daytime and nighttime PWV values were similar in the group with MS and in the non-MS obese group and were higher than the control group (Figure 2). Both 24-hour daytime and nighttime PWV were significantly correlated with BMI SDS, for each group ($r = 0.356$, $p = 0.001$; $r = 0.37$, $p = 0.001$; and $r = 0.315$, $p = 0.005$, respectively).

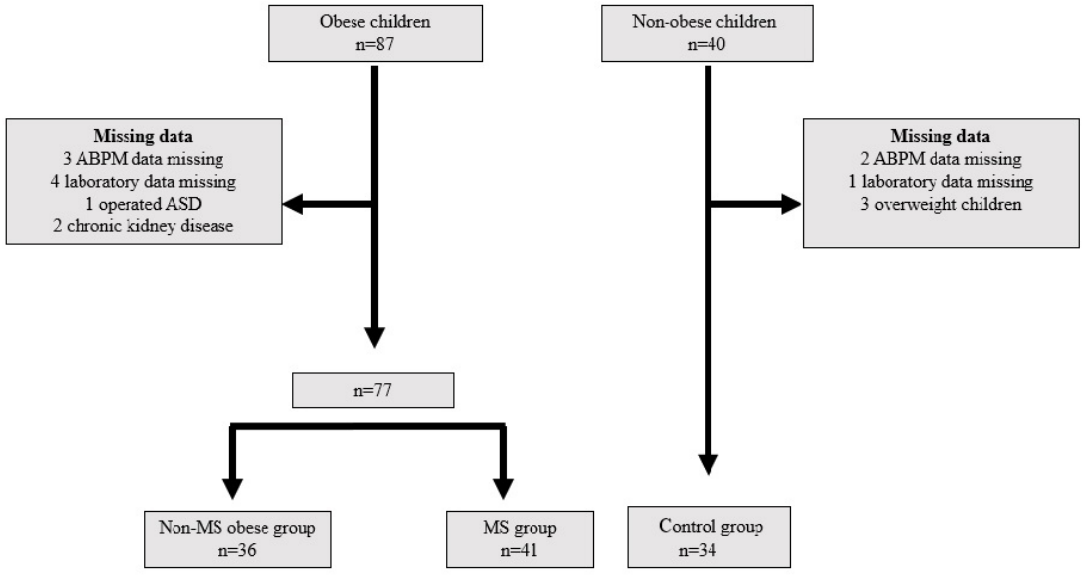

Figure 1. Study sample selection

ABPM: ambulatory blood pressure measurement, MS: metabolic syndrome

LVMI, LVMI/95P and RWT measurements were significantly higher in the MS and non-MS obese groups than the control group (Table 3). LVMI, LVMI/95P and RWT measurements tended to be higher in the MS group compared to the non-MS obese group, but the difference was not significant.

Discussion

The results of this study showed that both 24-hour and daytime cSBP and cDBP were higher in the MS group than the other two groups. In addition, LVH, as an indicator of end organ damage, was more frequent in the non-MS obese

Table 1. Comparison of demographic and laboratory findings

	Non-MS obese group	MS group	Control group	p
Age (years)	12.50 (11.00-15.00)	14.00 (12.00-15.00)	13.00 (11.00-15.25)	0.734
Male, n (%)	14 (38.9)	10 (24.4)	13 (38.2)	0.301
Weight SDS	2.76 ± 1.08	3.60 ± 1.06	-0.13 ± 1.15	**< 0.01***
Height SDS	0.31 (-0.77-1.06)	0.94 (-0.07-2.00)**	-0.13 (-0.88-0.87)	0.002
BMI SDS	2.61 (2.10-3.10)	2.88 (2.64-3.41)	-0.15 (-1.29-0.80)	**< 0.01***
Glucose (mg/dL)	88.20 ± 7.73	88.19 ± 7.90	89.46 ± 9.55	0.770
Creatinine (mg/dL)	0.60 (0.60-0.70)	0.70 (0.60-0.70)	0.60 (0.59-0.70)	0.179
Uric acid (mg/dL)	5.30 (4.50-5.80)	5.60 (5.07-6.82)	4.00 (3.50-4.67)**	< 0.01
Triglyceride (mg/dL)	103.17 ± 27.79	132.86 ± 61.00**	90.77 ± 39.93	0.005
Total cholesterol (mg/dL)	175.30 ± 31.60	171.00 ± 33.80	150.25 ± 38.20**	**0.019**
ALT (IU/L)	23.00 (17.00-34.00)	22.00 (14.50-40.50)	12.00 (10.00-15.00)**	< 0.01
Free T4 (mIU/L)	0.78 (0.71-0.89)	0.81 (0.72-0.94)	0.86 (0.78-0.91)	0.087
TSH (ng/dL)	2.40 (1.95-2.95)	2.32 (1.73-3.40)	1.80 (1.14-2.26)**	0.044
HOMA-IR	3.10 (2.40-4.40)	4.43 (3.07-6.18		**0.008***
Microalbumin/creatinine (mg/g)	5.57 (3.02-21.52)	7.00 (5.00-16.80)	8.49 (4.62-21.95)	0.423

*The results of all groups were statistically different from each other.
**The results were significantly different from the other two groups.
SDS: standard deviation score, BMI: body mass index, ALT: alanine aminotransferase, TSH: thyroid stimulating hormone, HOMA-IR: homeostasis model assessment of insulin resistance, MS: metabolic syndrome

Table 2. Comparison of office and 24-hour blood pressure data

	Non-MS obese group	MS group	Control group	p
Office systolic BP SDS	1.13 [(0.77)-(2.00)]	1.88 [(0.46)-(2.33)]	0.20 [(-0.64)-(1.08)]*	< 0.01
Office diastolic BP SDS	0.95 ± 0.86	1.15 ± 0.91*	0.57 ± 0.68	0.01
24-h systolic BP SDS	-0.02 ± 0.99	0.28 ± 1.17	-1.14 ± 0.74*	< 0.01
Daytime systolic BP SDS	-0.35 ± 1.00	-0.08 ± 1.08	-1.36 ± 0.83*	< 0.01
Nighttime systolic BP SDS	0.69 [(0.20)-(1.53)]	0.76 [(0.11)-(1.79)]	-0.34 [(-0.59)-(0.35)]*	< 0.01
24-h diastolic BP SDS	-0.51 ± 1.02	-0.32 ± 1.10	-0.82 ± 0.82	0.11
Daytime diastolic BP SDS	-0.83 ± 1.00	-0.75 ± 0.96	-1.16 ± 0.82	0.18
Nighttime diastolic BP SDS	-0.67 ± 1.08	0.65 ± 1.10	0.33 ± 1.02	0.34
24-h MAP SDS	0.78 [(0.20)-(1.34)]	1.02 [(0.43)-(1.74)]	-0.05 [(-0.45)-(0.60)]*	< 0.01
Daytime MAP SDS	0.38 ± 1.05	0.71 ± 1.19	-0.30 ± 0.71*	< 0.01
Nighttime MAP SDS	1.55 [(1.07)-(2.49)]	1.66 [(1.06)-(2.83)]	0.84 [(0.32)-(1.43)]*	< 0.01
Daytime systolic load (%)	13.00 [(6.00)-(21.25)]	19.00 [(9.50)-(34.50)]	3.50 [(0.00)-(7.25)]*	< 0.01
Nighttime systolic load (%)	23.00 [(9.75)-(44.25)]	33.00 [(8.00)-(56.50)]	1.00 [(0.00)-(12.75)]*	< 0.01
Daytime diastolic load (%)	8.50 [(4.00)-(16.50)]	14.00 [(6.50)-(22.00)]*	7.00 [(3.50)-(10.50)]	0.01
Nighttime diastolic load (%)	19.50 [(8.25)-(38.00)]	15.00 [(3.00)-(38.00)]	5.50 [(0.00)-(15.50)]*	< 0.01
Systolic dip	7.35 [(0.02)-(10.42)]	6.40 [(3.17)-(10.90)]	5.55 [(3.07)-(10.32)]	0.81
Diastolic dip	12.30 [(6.57)-(14.37)]	11.70 [(5.95)-(18.85)]	13.95 [(6.70)-(20.30)]	0.53

*The results were significantly different from the other two groups.
SDS: standard deviation score, BP: blood pressure, MAP: mean arterial pressure

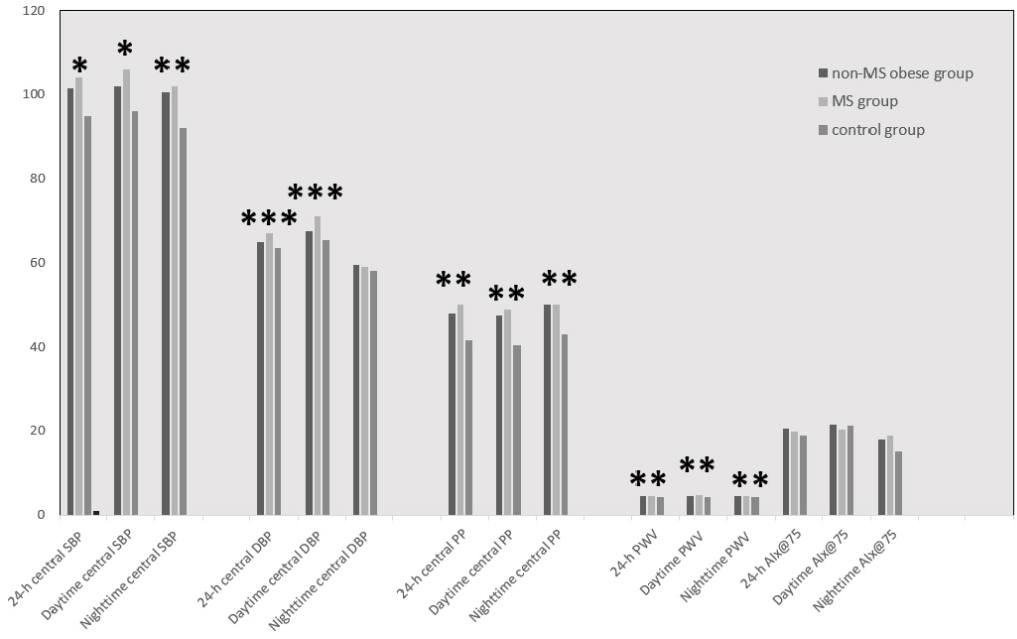

Figure 2. Comparison of PWA data

*The results of all three groups were statistically different from each other.

**Control group was significantly lower than the MS and non-obese MS groups.

***MS group was higher than the control group.

MS: metabolic syndrome, SBP: systolic blood pressure, DBP: diastolic blood pressure, PWA: pulse wave analysis, PP: pulse pressure

Table 3. Comparison of echocardiographic findings between the groups

	Non-MS obese group	MS group	Control group	p
LVMI (g/m$^{2.7}$)	35.85 (33.17-39.62)	37.85 (30.85-44.95)	31.55 (26.30-36.80)*	< 0.01
LVMI/95th percentile	0.95 (0.83-1.05)	0.97 (0.84-1.19)	0.82 (0.70-0.95)*	< 0.01
RWT	0.40 ± 0.70	0.41 ± 0.68	0.34 ± 0.11*	< 0.01

*The results were significantly different from the other two groups.
LVMI: left ventricular mass index, RWT: relative wall thickness, MS: metabolic syndrome

and MS groups compared to the control group, whereas it was similar between the two obese groups. Considering that 17% of the non-MS obese group was hypertensive and 61% of the MS group was hypertensive, we hypothesize that LVH in these patients was not affected by high BP, but by existing obesity status.

High HOMA-IR and triglyceride levels are expected in MS. However, obesity was associated with the difference identified in uric acid, total cholesterol, ALT and TSH values. Free T4 and TSH values were within normal ranges in all participants, and none of our patients had hypothyroidism or hyperthyroidism.

The Mobil-O-Graph device used to assess cSBP in children and adolescents has been shown to perform well compared to simultaneous invasive recordings (30). In recent years, it has been found that central BP measurement is superior in determining cardiovascular risk, especially in young adults (31). Studies in hypertensive adults have shown that cardiovascular mortality and hypertensive target organ damage are better correlated with cSBP and cPP than with brachial arterial BP (32,33). In children, because the brachial artery is more elastic, accumulation of pulse waves results in higher brachial BP measurements, but central BPs are within normal ranges. Therefore, central BP measurement in children and young adults may prevent the detection of more HT with peripheral ABPM measurements. A study by Totaro et al. (34) showed that adults with higher cSBP had higher cIMT, LVMI, PWV, and lower brachial artery dilatation. However, patients with higher cSBP had a significantly higher BMI (mean BMI 38.7), and 42.9% of them had type 2 diabetes mellitus. Few studies have been conducted in childhood. Litwin et al. (35) found significantly higher cIMT, LVMI, and PWV values in adolescents with both younger age and lower BMI and higher cSBP. They also showed that children with primary HT with severe ambulatory HT had

normal central BP values and determined that central BP measurements had the same or higher power as ABPM in predicting end-organ damage. In the present study, 24-hour and daytime cSBP and cDBP measurements were higher in the MS group. LVMI, a marker of target organ damage, was similar in the obese groups with and without MS. However, in both it was higher than the control group.

Since the rate of obesity, IR and cardiac disease is gradually increasing in children and adolescents, it is necessary to screen children in the risk group to identify those at risk of later and atherosclerosis and enable early intervention (36). The literature contains many conflicting reports regarding the change in PWV in children with obesity. In some studies, it has been shown that there is an increase in PWV with obesity (37,38). In contrast, some studies have shown a "paradoxical" decrease in PWV with obesity (39). The paradoxical reduction has been attributed to precocious puberty and increased body size in obese children (40). Another hypothesis is that the decrease in PWV is a short-term adaptation, does not continue in the long term, and increases in time in longitudinal studies (41). In the present study the PWV was similar in the MS and the non-MS obese groups, but in both it was higher than the control group. PWV increase was correlated with BMI SDS increase. Although HOMA-IR was significantly higher in the MS group compared to the non-MS obese group, PWV was similar between these groups. The effects of IR may not be reflected in the PWV yet because of the cross-sectional design of the study.

In a recently published study, it was shown that 24-hour cSBP and 24-hour PWV values in obese children and adolescents were higher in obese subjects, but 24-hour AIx@75 values were not different from non-obese subjects. These results of our study were similar. In obese cases, the total blood volume and thus the stroke volume increases, whereas the total peripheral resistance decreases, the heart rate remains within the normal range or slightly increases to keep the BP at normal levels. As a result of this, augmentation pressure and AIx@75 values remain low in obese cases (42). In the present study, although central and peripheral values were higher in obese subjects than in non-obese subjects, AIx@75 values were similar between the groups.

Study Limitations

We believe that our study was the first in which the PWA of children with and without MS was evaluated using the oscillometric technique. However, it has limitations such as cross-sectional and retrospective design. Considering that PWV increases with age, performing longitudinal studies allows a better evaluation. The relatively small number of patients may also have introduced some degree of error during the analysis of the study results.

Conclusion

ABPM data were similar to the non-MS obese group, with slightly higher values in the MS group. Both 24-hour and daytime central SBP and DBP measurements were higher in the MS group. Obesity was associated with higher office, ambulatory, and central BP, PWV, and LVMI, but the additional MS-associated risk factors beyond obesity did not appear to contribute, with the exception of 24-hour and daytime cSBP and cDBP, which were significantly higher in the MS obese group.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of University Health Sciences Turkey, İzmir Tepecik Training and Research Hospital (decision no: 2021/10-09, date: 15.10.2021).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Cemaliye Başaran, Gökçen Erfidan, Özgür Özdemir-Şimşek, Cem Karadeniz, Bumin Nuri Dündar, Belde Kasap-Demir, Design: Cemaliye Başaran, Gökçen Erfidan, Özgür Özdemir-Şimşek, Data Collection or Processing: Cemaliye Başaran, Seçil Arslansoyu-Çamlar, Demet Alaygut, Fatma Mutlubaş, Analysis or Interpretation: Cemaliye Başaran, Seçil Arslansoyu-Çamlar, Demet Alaygut, Fatma Mutlubaş, Cem Karadeniz, Bumin Nuri Dündar, Belde Kasap-Demir, Literature Search: Cemaliye Başaran, Belde Kasap-Demir, Writing: Cemaliye Başaran.

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