Effect of changes in BMI and waist circumference on ambulatory blood pressure in obese children and adolescents

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Background: Weight reduction has been accompanied with a reduction in clinic blood pressure (BP) in children and adolescents; however, the effect on ambulatory BP (ABP) is uncertain. The objective was to investigate the impact of weight changes on ABP in obese children and adolescents.

Methods: Sixty-one severely obese patients aged 10–18 years underwent lifestyle intervention at the Children's Obesity Clinic. Patients were examined with ABP monitoring at baseline and after 1 year of treatment (follow-up). To account for growth, BP and BMI were standardized into z scores, whereas waist circumference was indexed by height [waist/height ratio (WHR)].

Results: Patients experienced a reduction at follow-up in the degree of obesity [ΔBMI z score: −0.21, 95% confidence interval (CI) −0.32 to −0.10, $P = 0.0003$; and ΔWHR: −0.02, 95% CI −0.03 to −0.004, $P = 0.009$]. Δ24-h, Δdaytime and Δnight-time SBP and DBP in mmHg and changes in equivalent z scores were related to ΔBMI z scores and ΔWHR. These relationships were reproduced in multiple regression analyses adjusted for relevant confounders, for example, a reduction in one BMI z score corresponds to a reduction in 24-h SBP by 6.5 mmHg ($P < 0.05$). No relationship was found between changes in these anthropometric obesity measures and changes in clinic BP.

Conclusion: Changes in obesity measures were closely related to changes in ABP, but not to changes in clinic BP, in severe obese children and adolescents after 1 year of lifestyle intervention. The findings emphasize the use of 24-h ABP measurements in children and adolescents.

Keywords: adolescence, ambulatory blood pressure monitoring, arm circumference, blood pressure, BMI z score, children, night-time, non-dipping, obesity, weight reduction

Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; DXA, dual-energy x-ray absorptiometry; HR, heart rate; MAP, mean arterial blood pressure; PP, pulse pressure; WHR, waist/height ratio

INTRODUCTION

Obesity is associated with elevated blood pressure (BP) in children and adolescents [1,2], and weight reduction has been accompanied with a reduction in clinic BP [3–5]. Ambulatory BP (ABP) is the most precise measure to evaluate the BP burden [6–8], and weight-associated reduction in ABP has been related to a reduction in risk factors of cardiovascular disease in adults [9]. Knowledge is lacking on the effect of weight reduction on ABP in children and adolescents, and it is unknown whether changes in ABP are more closely related to changes in the degree of obesity when compared to changes in clinic BP.

Anthropometric and BP measurements over time during childhood are complicated by the influence of growth. However, actual measured values of BMI and BP can be standardized into z scores in respect to normative reference populations [10,11]. An ABP z score value of zero is the expected mean in respect to sex and height of the reference population [8,12]. Waist circumference – a surrogate for abdominal fat – can be indexed by height representing growth when comparing measurements over time [13–15].

The objective of the present study is to investigate whether weight changes are more closely related to changes in ABP than changes in clinic BP in severe obese children and adolescents after 1 year of lifestyle intervention.

METHODS

Design and patients

Recruitment period was from January 2011 to January 2012, and continued until 100 obese Caucasian patients were

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enrolled. Inclusion criteria were an age of 10–18 years in newly referred children and adolescents to the Children's Obesity Clinic [16]. The tertiary obesity clinic receives paediatric patients with a BMI above the 90th percentile (equal to a z score of 1.28) for sex and age according to the Danish BMI charts [11]. Patients underwent a structured lifestyle intervention based on a family-centred approach involving behaviour-changing techniques as given in The Children's Obesity Clinic's Treatment (TCOCT) protocol [16]. In this protocol, 90 advice and advice strategies on low-calorie diet and activity are defined, although none specific on salt restriction. A typical treatment plan includes 10–20 items given at the first visit to implement lifestyle changes aimed to achieve reduction in obesity.

Baseline examination was no more than 60 days before or after the first visit in the clinic. The primary treatment endpoint was a change (Δ) in BMI z score – responders having a ΔBMI z score below zero, and non-responders a ΔBMI z score above zero. Social status was evaluated on a scale 1–5 with those with the lowest social class scored 5 [16].

The study was declared to ClinicalTrials.gov (NCT01310088), The Danish Data Agency and approved by The Scientific Ethical Committee of Region Zealand. Written informed consent was obtained from parents and patients aged 18 according to the Helsinki Declaration.

Anthropometry and obesity measures

Height was measured to the nearest 0.1 cm and weight to the nearest 0.1 kg wearing light indoor clothes without shoes using an integrated calibrated weight and stadiometer (ADE, Modell MZ10023, Germany). BMI (kg/m^2) was calculated into BMI z scores according to a Danish standard population in respect to age and sex [11]. Waist circumference was measured to the nearest 0.1 cm with participants standing using a stretch-resistant tape at the level of the midpoint between lower margin of the last palpable rib and top of the iliac crest. Waist/height ratio (WHR) was calculated as waist (cm) divided by height (cm).

Total body fat percentage was measured by dual-energy X-ray absorptiometry (DXA) scanning (Lunar iDXA; GE Healthcare, enCore version 13.20.033, Madison, Wisconsin, USA). The DXA scan is included in the treatment protocol at The Children's Obesity Clinic, and patients had these performed close to inclusion in the clinic. Only DXA scans performed less than 60 days before or after baseline were included in the analyses. Fifty-one (83.6%) patients had a DXA scan at baseline and at follow-up.

Blood pressure measures

Brachial clinic BP was measured after a rest of minimum 10 min in supine position with the oscillometric device Omron 705IT validated in children and adolescents [17]. Upper brachial arm circumference was measured to the nearest 0.1 cm. An appropriate cuff size – small (arm circumference <22 cm), medium (arm circumference 22–32 cm), and large (arm circumference ≥32 cm) – was used as recommended by the manufacturer. Mean of the last two out of three BP measurements was reported and calculated into z scores according to an American standard population based on individuals' sex, age and height [10]. Clinic heart rate (HR) was measured during 20 s with the SphygmorCor 9.0 device (AtCor Medical, Sydney, Australia).

Ambulatory BP was measured with the oscillometric device Boso/A&D TM-2430 validated in children and adolescents [18]. The device was mounted on the upper brachial arm using an appropriate cuff size, small (arm circumference <22 cm), medium (arm circumference 22–32 cm), and large (arm circumference ≥32 cm). The device was programmed to measure with 15-min intervals during day (0700–2200 h) and 30-min intervals during the night (2200–0700 h). Patients were asked to keep a diary of their sleep time interval to differentiate awake (daytime) from sleep (night-time) in the BP analyses. Mean values of ambulatory SBP and DBP and HR were calculated into z scores according to a German standard population based on sex and height [8,12]. Only patients having a valid ABP monitoring (ABPM) with at least 20 valid BP measurements during daytime, and at least seven during night-time were included in the analysis [6].

Dipping status [19] was determined as being the percentage of night-time reduction in BP calculated as (mean daytime SBP − mean night-time SBP) × 100/mean daytime SBP, and repeated for DBP. Non-dipping was defined as a nocturnal BP reduction of less than 10%.

Blood pressure classification was based on cut-off levels of either SBP or DBP, clinic and 24-h BP [8]; normotension (clinic and ABP <95th percentile), white-coat hypertension (clinic BP ≥95th percentile and ABP <95th percentile), masked hypertension (clinic BP <95th percentile and ABP ≥95th percentile), and hypertension (clinic and ABP ≥95th percentile).

Statistics

Statistical analyses were performed using SAS software (version 9.2; SAS Institute, Cary, North Carolina, USA). Statistical significance was defined as a P level below 0.05 on two-sided tests. Results were reported as mean ± SD, mean, 95% confidence interval (CI), or median [interquartile range (IQR)] dependent on whether data were normally distributed.

Potential differences in measures between sexes at baseline were investigated with unpaired Student's t-tests and Wilcoxon signed-rank sum test. Chi-square tests were used for sex distributions at baseline since expected values were above 5.

Differences in measurements between baseline and follow-up were investigated with paired Student's t-tests or Wilcoxon signed-rank test dependent on whether differences were normally distributed or not.

In linear regression analyses, we investigated how changes in anthropometric measures were inter-related. Likewise, changes in BP (outcome) were investigated in relation to changes in obesity measures (explanatory variable), that is ΔBMI z score, ΔWHR, and ΔDXA total body fat percentage.

In multiple regression analyses, relations between changes in BP and changes in obesity measures were adjusted for sex and for baseline confounders consisting of age, height, arm circumference, cuff size, the specific BP variable, as well as the corresponding obesity measure, that

is the baseline measure of either BMI z score, WHR, or ΔDXA total body fat percentage. The rationale of the multiple regression models was that patients in this respect were homogeneous at baseline when evaluating whether the change in the obesity measures was related to changes in the BP. In order to pool data from the two sexes, we tested for a possible interaction of sex with the explanatory variable of interest, that is change in the obesity measure.

Analyses were repeated for BP z scores instead of BP in mmHg. The standardization of clinic BP in mmHg into clinic BP z scores accounts for the influence of sex, age, and height, whereas the standardization of ABP in mmHg into ABP z scores accounts for sex and height. To avoid over adjustment, sex, age, and height were not added in the clinic BP z score regression models, and sex and height were not added in the ABP z score regression models.

In multiple regression sub-analyses using the same general linear models, we investigated the potential impact of changes in arm circumference on changes in systolic ABP in mmHg and z scores. Here, the ΔBMI z score variable was replaced by the Δarm circumference variable when adjusting for the above-stated confounders.

RESULTS

Characteristics of the study population

Data are based on 61 severe obese patients [33 (54.1%) girls] having a valid ABPM at both baseline and at follow-up. Median age was 12.5 years at baseline (Table 1), and the median follow-up time was 364 (IQR 363–371) days.

Initially, 104 patients (71% of invited patients) were examined at baseline, whereas 74 patients were evaluated at follow-up. Eleven patients did not have valid ABPMs, whereas two patients were excluded from the analyses, one due to onset of influenza symptoms at follow-up and the other due to a chronic kidney disease (nephrectomized). None of the remaining patients were diagnosed as having secondary hypertension.

The included 61 patients were representative in respect to sex, age, BMI z score, and social status when compared to the 11 followed up patients without ABPM (online Table 1, http://links.lww.com/HJH/A350), and the 30 patients lost to follow-up (online Table 2, http://links.lww.com/HJH/A351).

Eleven patients used medication: three had a history of asthma or allergy symptoms, three due to gastro-intestinal symptoms, three used birth control medication, and two used a synthetic hormonal supplementation (one patient a thyroid-hormone analogue for hypothyroidism, and one patient an antidiuretic-hormone analogue for nocturnal enuresis). Use of medication had not changed at follow-up. One patient was a smoker throughout the study.

Sex characteristics at baseline

No differences were found between sexes in age, height, weight, BMI z score, WHR or arm circumference at baseline (data not shown). Girls had a higher DXA total body fat percentage [girls $45.5 \pm 3.9\%$ ($N = 30$) vs. boys $42.5 \pm 5.7\%$ ($N = 21$), $P = 0.03$].

No differences were found between sexes in ABP in mmHg and HR, as well as in the equivalent z scores at baseline (data not shown). Furthermore, clinic SBP in mmHg and z scores, and clinic HR did not differ between sexes at baseline (data not shown). However, girls had a higher clinic DBP in mmHg (girls 63.5 ± 6.0 vs. boys 60.4 ± 5.3 mmHg; $P = 0.04$) and z score (girls 0.67 ± 0.65 vs. boys 0.17 ± 0.51; $P = 0.002$) when compared to boys at baseline.

Changes in obesity measures

Forty-four (72.1%) patients experienced a reduction in their BMI z score (responders) and a higher number of boys were responders when compared to girls [$N_{boys} = 24$ (85.7%) vs. $N_{girls} = 20$ (60.6%); $P = 0.03$]. BMI z score, WHR, and DXA total body fat percentage were significantly lower at follow-up despite an increased height and weight, though with no change in BMI, waist circumference, or arm circumference (Table 1).

In linear regression analyses, changes in anthropometric measures were strongly inter-related; Δarm circumference was related to ΔBMI z score ($\beta = 2.6$, 95% CI 1.7–3.5, $R^2 = 0.369$, $P < 0.0001$) and ΔWHR ($\beta = 24.6$, 95% CI 15.8–33.5, $R^2 = 0.343$, $P < 0.0001$), and ΔWHR related to ΔBMI z score ($\beta = 0.07$, 95% CI 0.05–0.09, $R^2 = 0.446$, $P < 0.0001$).

Changes in blood pressures

The number of daytime BP readings ($\Delta\ -0.6 \pm 8.3$, $N_{baseline}$ 59.3 ± 7.1 vs. $N_{follow\text{-}up}$ 58.7 ± 6.2, $P = 0.58$) and night-time BP readings ($\Delta\ 0.1 \pm 4.6$, $N_{baseline}$ 16.8 ± 3.6 vs. $N_{follow\text{-}up}$ 16.9 ± 4.4, $P = 0.87$) did not differ between baseline and follow-up.

TABLE 1. Anthropometrics and obesity measures at baseline and follow-up

	Baseline ($N = 61$) Mean ± SD or median (IQR)	Follow up ($N = 61$) Mean ± SD or median (IQR)	Difference (Δ) Mean (95% CI)	*P* value
Age (years)	12.5 (11.3–14.3)	13.6 (12.3–15.2)	1.0 (0.997 to 1.02)	<0.0001
Height (cm)	159.9 ± 10.8	164.9 ± 9.3	5.0 (4.1 to 6.0)	<0.0001
Weight (kg)	66.9 (58.3–86.6)	72.2 (63.0–88.4)	4.2 (2.7 to 5.7)	<0.0001
BMI (kg/m^2)	27.2 (24.2–30.9)	26.6 (23.7–31.7)	−0.01 (−0.5 to 0.5)	0.97
BMI z score	2.73 ± 0.60	2.52 ± 0.84	−0.21 (−0.32 to −0.10)	0.0003
Waist (cm)	96.7 ± 14.4	97.1 ± 16.3	0.4 (−1.3 to 2.1)	0.63
Waist/height ratio	0.60 ± 0.07	0.58 ± 0.09	−0.02 (−0.03 to −0.004)	0.009
Arm circumference (cm)	30.0 ± 4.1	30.1 ± 4.4	0.1 (−0.3 to 0.6)	0.56
DXA total body fat (%) ($N = 51$)	44.2 ± 4.9	40.8 ± 7.2	−3.4 (−4.5 to −2.3)	<0.0001

CI, confidence interval; IQR, interquartile range.
Ten (16.4%) patients lacked a dual-energy x-ray absorptiometry (DXA) scan at baseline why comparison of DXA total body fat percentage is based on $N = 51$ DXA scans.

No significant differences were found between ABP in mmHg at baseline and follow-up (Table 2). When calculating ABP z scores, a reduction was found in daytime SBP, DBP, and mean arterial blood pressure (MAP) z scores and a trend in 24-h DBP z score reduction at follow-up, but no difference was found in night-time BP z scores (Table 3).

No differences were found in dipping status between baseline and follow-up: systolic non-dipping: N_{baseline} 18 (29.5%) vs. $N_{\text{follow-up}}$ 18 (29.5%) ($P=1.00$), where 36 (59.0%) patients were consistent systolic dippers, 11 (18.0%) non-dippers and 14 (23.0%) had a mismatch in their systolic dipping status. Diastolic non-dipping: N_{baseline} 10 (16.4%) vs. $N_{\text{follow-up}}$ 12 (17.7%) ($P=0.64$), where 43 (70.5%) were consistent dippers, 4 (6.6%) were non-dippers and 14 (23.0%) had a mismatch in their diastolic dipping status.

Clinic SBP and DBP in mmHg as well as clinic HR did not differ between baseline and follow-up (Table 2). Surprisingly, clinic SBP z score was higher at follow-up, whereas no difference was found in clinic DBP z score (Table 3).

Blood pressure classification status at baseline was as follows: 33 (54%) patients were normotensive, 12 (20%) were white-coat hypertensive, 6 (10%) masked hypertensive and 10 (16%) were hypertensive. At follow-up, 19 (31%) patients were normotensive, 23 (38%) were white-coat hypertensive, 5 (8%) masked hypertensive and 14 (23%) were hypertensive. Thirty-six (59%) patients had a normal ABP (<95th percentile) and five (8%) patients an elevated ABP (≥95th percentile) at both baseline and follow-up. Twenty-five (41%) had a normal clinic BP (<95th percentile) and 11 (18%) an elevated clinic BP (≥95th percentile) at both baseline and follow-up.

Relationship between changes in obesity measures and changes in blood pressures

Changes in ambulatory SBP and DBP's in mmHg and z scores (24-h, daytime and night-time) were related to changes in BMI z scores in both unadjusted and adjusted analyses (Tables 4 and 5). There was only a trend for the unadjusted relation of changes in night-time DBP z score and the adjusted relation of changes in night-time DBP in mmHg. Figure 1 displays the unadjusted relations of changes in daytime and night-time SBP z scores with changes in BMI z scores. Furthermore, unadjusted and adjusted relations were found for changes in ABP in mmHg and z scores with changes in WHR.

On the contrary, no significant relationship was found between changes in clinic SBP or DBP in mmHg or z scores, and changes in BMI z score or WHR in linear or multiple regression analyses (Tables 4 and 5). Also, no relationship was found between changes in either clinic or ABP in mmHg or z scores and changes in DXA total body fat percentage for the 51 patients having a DXA scan.

In multiple regression sub-analyses, changes in ambulatory SBP in mmHg were related to changes in arm circumference: Δ24-h BP ($\beta_{\Delta\text{arm circumference}}=1.2$, 95% CI 0.1 to 2.3, $P=0.03$/model: $P=0.005$, $R^2=0.331$), Δdaytime BP ($\beta_{\Delta\text{arm circumference}}=1.1$, 95% CI −0.04 to 2.2, $P=0.059$/model: $P=0.003$, $R^2=0.349$), and Δnight-time BP ($\beta_{\Delta\text{arm circumference}}=1.6$, 95% CI 0.07 to 3.03, $P=0.04$/model: $P=0.009$, $R^2=0.309$). Likewise, significant adjusted relations were found between changes in ambulatory SBP z scores and changes in arm circumference (models $P<0.05$ with a minimum R^2 of 220).

DISCUSSION

The main finding of the present study was that changes in anthropometric obesity measures were associated with changes in 24-h, daytime and night-time BP, whereas no association was found with changes in clinic BP.

Previous studies have investigated the effect of weight reduction on clinic BP in children and adolescents [3–5,20,21]; however, knowledge is lacking on the effect of ABP.

Ambulatory and clinic BPs in mmHg were not reduced at follow-up, although the obese patients experienced a

TABLE 2. Blood pressure in mmHg at baseline and follow-up

Variable	Baseline ($N=61$) Mean ± SD	Follow-up ($N=61$) Mean ± SD	Difference (Δ) Mean ± SD	*P* value
Clinic SBP (mmHg)	110.8 ± 9.2	112.8 ± 7.6	2.0 ± 8.2	0.06
Clinic DBP (mmHg)	62.1 ± 5.9	61.5 ± 6.2	−0.6 ± 5.1	0.36
Clinic HR (b.p.m.)	67.0 ± 10.1	65.9 ± 10.1	−1.1 ± 8.5	0.31
24-h SBP (mmHg)	121.2 ± 7.2	120.3 ± 9.1	−0.9 ± 8.1	0.41
24-h DBP (mmHg)	70.7 ± 4.8	69.4 ± 6.4	−1.3 ± 6.2	0.10
24-h MAP (mmHg)	87.5 ± 5.2	86.3 ± 6.9	−1.2 ± 6.6	0.17
24-h PP (mmHg)	50.5 ± 5.0	50.9 ± 5.7	0.5 ± 4.2	0.39
24-h HR (bpm)	79.6 ± 7.7	79.3 ± 8.1	−0.3 ± 6.7	0.74
Daytime SBP (mmHg)	124.9 ± 7.8	123.9 ± 9.6	−1.0 ± 8.5	0.36
Daytime DBP (mmHg)	73.7 ± 5.8	72.1 ± 6.8	−1.6 ± 6.3	0.053
Daytime MAP (mmHg)	90.7 ± 6.1	89.3 ± 7.4	−1.4 ± 6.8	0.11
Daytime PP (mmHg)	51.2 ± 5.3	51.8 ± 6.0	0.6 ± 4.6	0.33
Daytime HR (bpm)	82.1 ± 8.0	82.2 ± 8.2	0.1 ± 7.3	0.93
Night-time SBP (mmHg)	108.0 ± 9.4	108.3 ± 11.1	0.3 ± 11.1	0.84
Night-time DBP (mmHg)	60.0 ± 6.5	60.4 ± 8.5	0.4 ± 9.4	0.75
Night-time MAP (mmHg)	76.0 ± 7.0	76.5 ± 9.1	0.5 ± 9.7	0.68
Night-time PP (mmHg)	48.0 ± 6.2	47.9 ± 6.4	−0.1 ± 6.3	0.91
Night-time HR (bpm)	70.6 ± 9.4	68.7 ± 10.0	−1.9 ± 7.4	0.048

BP, blood pressure; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure.

TABLE 3. Blood pressure z scores at baseline and follow-up

	Baseline ($N = 61$) Mean ± SD	Follow-up ($N = 61$) Mean ± SD	Difference (Δ) Mean ± SD	*P* value
Clinic SBP z score	1.52 ± 1.13	1.86 ± 0.89	0.35 ± 0.81	0.002
Clinic DBP z score	0.44 ± 0.63	0.45 ± 0.62	0.01 ± 0.46	0.83
24-h SBP z score	1.14 ± 0.97	0.82 ± 1.25	−0.33 ± 1.22	0.04
24-h DBP z score	0.60 ± 0.88	0.32 ± 1.18	−0.28 ± 1.11	0.051
24-h MAP z score	1.01 ± 1.00	0.73 ± 1.30	−0.29 ± 1.27	0.08
24-h HR z score	−0.22 ± 0.95	−0.08 ± 1.02	0.13 ± 0.870	0.23
Daytime SBP z score	0.95 ± 0.97	0.59 ± 1.15	−0.36 ± 1.12	0.01
Daytime DBP z score	0.22 ± 1.09	-0.11 ± 1.18	−0.32 ± 1.13	0.03
Daytime MAP z score	0.77 ± 1.23	0.43 ± 1.19	−0.34 ± 1.23	0.04
Daytime HR z score	−0.78 ± 0.97	−0.63 ± 0.95	0.15 ± 0.91	0.19
Night-time SBP z score	0.72 ± 1.11	0.64 ± 1.44	−0.08 ± 1.41	0.65
Night-time DBP z score	0.70 ± 1.01	0.69 ± 1.28	−0.01 ± 1.46	0.95
Night-time MAP z score	0.78 ± 1.16	0.81 ± 1.64	0.04 ± 1.73	0.87
Night-time HR z score	0.15 ± 0.98	0.05 ± 1.01	−0.10 ± 0.82	0.35

BP, blood pressure; HR, heart rate; MAP, mean arterial pressure.
Mean clinic BP values were calculated into BP z scores in respect to sex, age and height [10]. Mean ambulatory BP values were calculated into BP z scores in respect to sex and height [12].

weight reduction when evaluated on a group level. However, not all patients were responders, and the mixture of patients reducing and gaining weight possibly influenced the BP differently. When changes in ABP in mmHg were related to changes in obesity measures, that is evaluated as a continuum, patients losing or gaining weight by one BMI z score had a corresponding decrease or increase in, for example, systolic 24-h BP of 6.5 mmHg, respectively. BPs in mmHg are clinically interpretative; however, z scores account for growth, and the relationship was also found for changes in ABP z scores (Fig. 1).

Daytime SBP and DBP z scores were reduced at follow-up despite that no difference was found in corresponding daytime BPs in mmHg at follow-up. The discrepancies between ABP z scores and in mmHg might be explained by the natural age-related increase in BP in mmHg [12], whereas the lack of a relationship between changes in DXA total body fat percentage and changes in ABP might be explained by a lower statistical power.

No relationship was found between changes in obesity measures and changes in clinic BP in mmHg or z scores. This negative finding may be due to the limited number of clinical BP readings compared to the 24-h BP measurement. Contrary to anticipated [5,21], clinic SBP z scores were higher at follow-up despite that no significant difference was found in clinic SBP in mmHg between baseline and follow-up. Hence, the worse distribution of the BP categories at follow-up is likely attributed to the higher clinic SBP z scores, as the 24-h BP z score level did not rise at follow-up.

High sympathetic activity in the severe obese patients might explain the high frequency of white-coat hypertension, which might impact on the discrepancy between clinic and ABP responses to weight changes [22]. Alternatively, the higher clinic SBP z scores at follow-up might merely be due to differences in methodology of the clinic BP measurements in respect to the normative reference material [10] from where the clinic BP z scores are calculated. In the present study, clinic BP was measured in supine position with an oscillometric device [17] and calculated into z scores. In the Fourth Report on diagnosis and treatment of high BP in children and adolescents by an American working group [10], clinic BP was measured sitting with an auscultatory mercury sphygmomanometer.

Difficulties when dealing with growth when evaluating BP over time in obese children and adolescents are acknowledged in a meta-analysis investigating the impact of weight reduction on cardiovascular risk factors in obese

TABLE 4. Relationship between changes in obesity measures and changes in blood pressures in mmHg

	Δ BMI z score		Δ Waist/height ratio	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Δ clinic SBP (mmHg)	0.6 (0.82)	−1.3 (0.59)	−3.2 (0.90)	1.35 (0.95)
Δ clinic DBP (mmHg)	2.6 (0.09)	1.6 (0.35)	21.7 (0.15)	16.20 (0.29)
Δ 24-h SBP (mmHg)	6.1 (0.01)	6.5 (0.01)	48.2 (0.04)	53.6 (0.02)
Δ 24-h DBP (mmHg)	4.6 (0.01)	4.2 (0.03)	36.3 (0.045)	35.1 (0.06)
Δ Daytime SBP (mmHg)	6.0 (0.02)	6.4 (0.01)	45.3 (0.07)	51.5 (0.03)
Δ Daytime DBP (mmHg)	4.3 (0.02)	3.8 (0.050)	26.0 (0.16)	26.0 (0.15)
Δ Night-time SBP (mmHg)	6.8 (0.04)	7.2 (0.04)	61.2 (0.06)	63.0 (0.054)
Δ Night-time DBP (mmHg)	6.0 (0.03)	5.3 (0.07)	72.4 (0.008)	60.7 (0.03)

Results are β coefficients (*P* values) of regression analyses of ΔBP (outcome) in relation to Δobesity measure (explanatory variable), that is ΔBMI z score or Δwaist/height ratio. Unadjusted analyses are simple linear regression. Adjusted analyses are multiple regression analyses adjusted for sex and for baseline measures of age, height, arm circumference, cuff size, the specific BP variable, as well as the corresponding obesity measure, that is the baseline measure of either BMI z score or WHR. All multiple regression models had a *P* less than 0.05, a minimum R^2 of 0.255 and no interaction of sex with the Δobesity measure.

TABLE 5. Relationship between changes in obesity measures and changes in blood pressure z scores

	Δ BMI z score		Δ Waist/height ratio	
	Unadjusted	Adjusted	Unadjusted	Adjusted
Δ Clinic SBP z score	−0.16 (0.50)	−0.12 (0.58)	−1.16 (0.63)	0.82 (0.68)
Δ Clinic DBP z score	0.16 (0.23)	0.21 (0.15)	1.72 (0.20)	2.41 (0.07)
Δ 24-h SBP z score	1.09 (0.002)	1.12 (0.002)	8.79 (0.01)	9.63 (0.004)
Δ 24-h DBP z score	0.85 (0.009)	0.90 (0.01)	6.65 (0.04)	7.47 (0.02)
Δ Daytime SBP z score	0.97 (0.003)	0.98 (0.003)	7.57 (0.02)	8.35 (0.007)
Δ Daytime DBP z score	0.77 (0.02)	0.81 (0.01)	4.65 (0.16)	5.80 (0.06)
Δ Night-time SBP z score	1.08 (0.01)	1.22 (0.006)	9.41 (0.02)	9.94 (0.01)
Δ Night-time DBP z score	0.84 (0.054)	0.85 (0.047)	10.71 (0.01)	9.44 (0.02)

Results are β coefficients (*P* values) of regression analyses of Δ BP z score (outcome) in relation to Δobesity measure (explanatory variable), that is ΔBMI z score or Δwaist-height ratio. Unadjusted analyses are simple linear regression. Adjusted analyses are multiple regression analyses adjusted for baseline measures of arm circumference, cuff size, the specific BP variable as well as the corresponding obesity measure, that is the baseline measure of either BMI z score or WHR. Additionally, changes in ambulatory BP z scores were adjusted for baseline age. All multiple regression models had a *P* value less than 0.05 and a minimum R^2 of 0.196.

children and adolescents [20]. However, clinical oscillometric BP devices are observer-independent. Karatzi *et al.* [23] have found that out-of-office BP, measured as home BP, was more closely related to the degree of obesity than clinic BP. They used the same clinical oscillometric BP device as in the present study [23]. In agreement, the findings in our study suggest that out-of-office BP seems superior to clinic BP when detecting changes in obesity.

Cuff size and arm circumference have an impact on BP measurements [24,25] – and the recognition is probably underestimated [26] – why we adjusted for baseline measures of these. We also found that changes in anthropometric and obesity measures were very strongly interrelated – being collinear in statistical terms. The multiple regression sub-analyses of changes in ambulatory SBP were related to changes in arm circumference, as for changes in BMI z score. However, being collinear, Δarm circumference and ΔBMI z score could not be included as explanatory variables in the same regression model. Hence, it is difficult to evaluate how changes in obesity measures affect ABPs

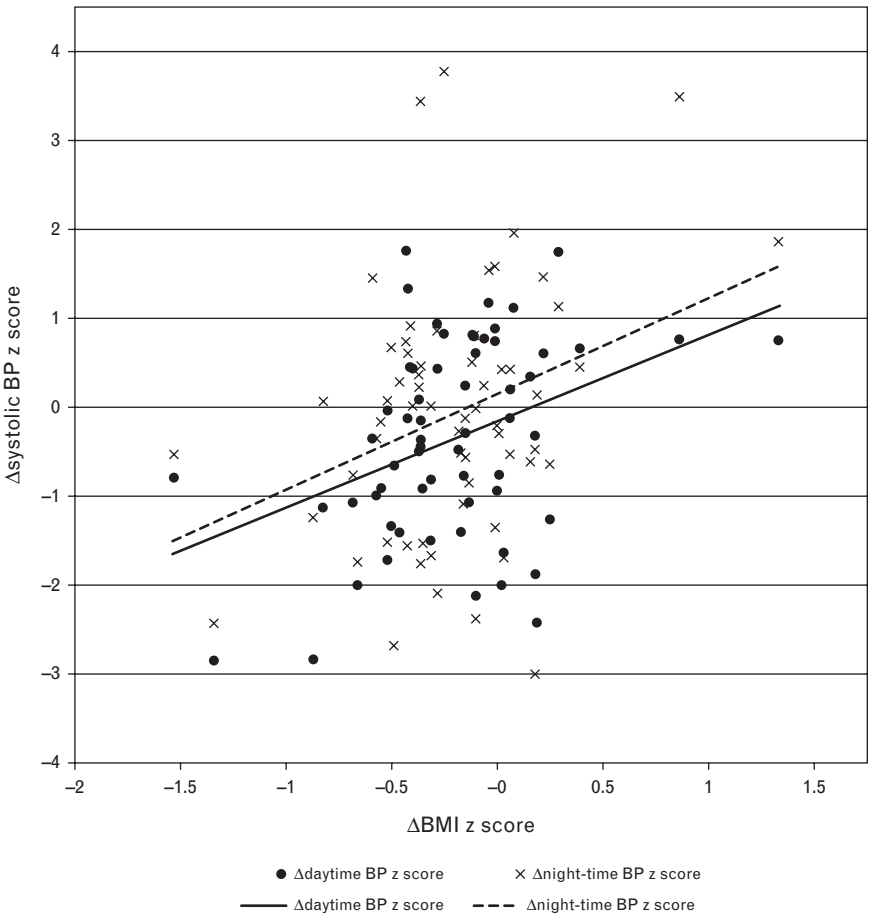

FIGURE 1 Changes in systolic daytime and night-time BP z scores in relation to changes in BMI z score. B coefficients of plotted linear regressions are listed in Table 5. BP, blood pressure.

independent of changes in arm circumference. Our primary treatment endpoint was difference in BMI z score, and not difference in arm circumference. Recommended cuff sizes and methodologies were used and we adjusted for arm circumference and cuff size. This implies that changes in anthropometric obesity measures are biologically associated with changes in ABP.

Patients were still severely obese at follow-up [27], with a WHR above a suggested cut-off point of 0.50 [15]. However, long-term treatment of obesity in children and adolescents is complicated [20,28], and the net weight reduction in our study population was close to the expected 12 months treatment results of the clinic [16]. Despite this, changes in BMI z score and WHR were associated with changes in ABP.

There are limitations to the present study. First, we did not include puberty measures, and these can potentially influence the BP [29]. Second, we did not have data on physical activity, and intervention programmes incorporating exercise may also have a better effect on the BP [3]. Third, the quality of sleep at baseline and follow-up might have been different. In this respect, only valid ABPM using individual sleep time intervals were included. Fourth, regression towards the mean can have influenced our results, why we adjusted for both the BP and the obesity measure at baseline. Fifth, use of medication and smoking can affect the BP. However, the single smoker and patients using medication did not change status throughout the study, and as patients were their own controls, a potential bias herein will most probably have the same impact at both baseline and follow-up. Hence, these patients were included in the analyses in order to limit loss of statistical power.

In conclusion, changes in BMI z score and WHR were closely related to changes in ABP in severe obese children and adolescents after 1 year of lifestyle intervention. Associations were consistent when ABP was evaluated in standardized values that accounted for growth. No relationship was found between changes obesity measures and changes in clinic BP.

In perspective, the study suggests that changes in ABP are more closely related to changes in the degree of obesity as compared to changes in clinic BP. The findings emphasize the use of 24-h ABP measurements in children and adolescents. Furthermore, it is reassuring that weight change is accompanied with a change in 24-h BP as ABP is the most precise measure to evaluate the BP burden [6–8].

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Conflicts of interest

All authors declare that there are no conflicts of interest in respect to executing, analysing or reporting the present research project.

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Reviewer's Summary Evaluation

Reviewer 2

This is a carefully conducted study on the effects of lifestyle modification on blood pressure levels in obese children. Such evidence is very limited, yet very important due to the growing pediatric obesity epidemic worldwide. The main advantage is the one year follow-up, which allowed the investigation of the effects of changes in the degree of obesity induced by lifestyle intervention on the blood pressure levels. The main problem is the small sample size, yet the use of 24 h ambulatory blood pressure monitoring demonstrated a significant association, which was missed when using clinic blood pressure measurements.