

Elevated blood pressure, cardiometabolic risk and target organ damage in youth with overweight and obesity

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Abstract *Background and aim:* To compare cardiometabolic risk profile and preclinical signs of target organ damage in youth with normal and elevated blood pressure (BP), according to the American Academy of Pediatrics (AAP) guidelines.

Methods and results: This cross-sectional multicenter study included 2739 youth (5-17 year-old; 170 normal-weight, 610 overweight and 1959 with obesity) defined non hypertensive by the AAP guidelines. Anthropometric, biochemical and liver ultrasound data were available in the whole population; carotid artery ultrasound and echocardiographic assessments were available respectively in 427 and 264 youth. Elevated BP was defined as BP \geq 90th to $<$ 95th percentile for age, gender and height in children or BP \geq 120/80 to $<$ 130/80 in adolescents. The overall prevalence of elevated BP was 18.3%, and significantly increased from normal-weight to obese youth. Young people with elevated BP showed higher levels of body mass index (BMI), insulin resistance and a higher prevalence of liver steatosis (45% vs 36%, $p < 0.0001$) than normotensive youth, whilst they did not differ for the other cardiometabolic risk factors, neither for carotid intima media thickness or left ventricular mass. Compared with normotensive youth, individuals with elevated BP had an odds ratio (95%CI) of 3.60 (2.00–6.46) for overweight/obesity, 1.46 (1.19–1.78) for

Acronyms: AAP, American Academy of Pediatrics; BP, blood pressure; ALT, alanine amino transferase; BMI, body mass index; cIMT, carotid intima media thickness; HDL-C, high-density lipoprotein-cholesterol; HOMA-IR, Homeostasis Model Assessment for Insulin Resistance; HTN, hypertension; IVST, interventricular septum thickness; LVDD, left ventricular diastolic diameter; LVMi, left ventricular mass index; NW, normal weight; OB, obesity; OW, overweight; PWT, posterior wall thickness; RWTa, relative wall thickness; SDS, standard deviation score; TC, total cholesterol; Tg, triglycerides; WhtR, waist to height ratio.

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insulin-resistance and 1.45 (1.19–1.77) for liver steatosis, controlling for centers, age and prepubertal stage. The odds for insulin resistance and liver steatosis persisted elevated after correction for BMI-SDS.

Conclusion: Compared to normotensive youth, elevated BP is associated with increased BMI, insulin resistance and liver steatosis, without significant target organ damage.

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Introduction

The epidemic expansion of pediatric obesity has raised a growing interest on the assessment and stratification of cardiometabolic risk for both preventive and therapeutic purposes [1]. Recently, the American Academy of Pediatrics (AAP₂₀₁₇) [2] released new guidelines for the screening and diagnosis of high blood pressure (BP) in children and adolescents, that are expected to significantly modify the epidemiological and clinical approach. The new reference standards are based on lowered BP values calculated in the general population of children and adolescents, since youth with overweight/obesity (OW/OB) were excluded from the database used to build the BP percentiles [3]. In addition, the term “prehypertension” was replaced by “elevated blood pressure”, in order to be consistent with the American Heart Association/American College of Cardiology guidelines. The cut-offs of BP \geq 90th to $<$ 95th percentile for age, gender and height were used to define elevated BP in children, while fixed cut-offs (\geq 120/80 to $<$ 130/80 mmHg) were proposed in adolescents.

A very recent systematic review and meta-analysis based on studies published before 2018, reported a pooled prevalence of 9.7% for prehypertension and 4% for hypertension (HTN) in youth $<$ 19 years [4]. Of course, the prevalence of both conditions is bound to increase with the systematic use of the new BP classification [5].

With few exceptions [6], most studies have shown that the old and new BP cut-points are effective in identifying subjects with HTN and altered cardiovascular risk profile [7–9], but they are conflicting on target organ damage [6,7,10,11]. In addition, whether individuals assigned to the subgroup with elevated BP according to the AAP₂₀₁₇ guidelines have worse cardiometabolic risk profile compared with normotensive youth is still unknown.

Therefore, this study was designed to investigate if young people classified as elevated BP show worse cardiometabolic risk profile than normotensive youth, in a large sample of outpatient children and adolescents with high prevalence of overweight or obesity. As an ancillary project, we also compared preclinical signs of organ damage, by measuring carotid intima media thickness (cIMT) and left ventricular mass (LVM).

Methods

Study population

The individuals included in this study were recruited within the CARITALY Study, a cross sectional study

undertaken by the Childhood Obesity study Group of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED). This study aimed to analyze cardiometabolic risk factors in Italian children and adolescents with OW/OB referred to secondary or tertiary centers for the diagnosis and care of obesity [12]. Data analyzed in the present study were relative to children aged 5–17 years, observed in the period 2003–2016 in nine centers homogeneously distributed throughout Italy (three in the north, three in the center and three in the south), in whom complete anthropometric, biochemical and liver ultrasound data were available. An additional group of normal weight youth (NW) was also recruited in two centers (Pozzuoli and Rome) as previously described [13,14]. The initial sample was constituted by 4031 young people, of whom 188 were NW, 842 were OW and 3001 were OB. Youth classified as HTN according to the AAP₂₀₁₇ guidelines ($n = 1292$, of whom 742 boys, 18 NW, 232 OW, and 1042 OB), were excluded.

Therefore, the present analysis regarded 2739 youth (1420 boys) of whom 170 were NW, 610 OW and 1959 OB. This retrospective study was approved by the Ethics Committee of the University of Campania “Luigi Vanvitelli” (reference number 834/2016) and conformed to the guidelines of the European Convention of Human Rights and Biomedicine for Research in Children as elsewhere described [15]. The study was in accordance with the 1975 Declaration of Helsinki, revised in 1983, and informed consent was obtained from the parents or tutors of all participants.

Anthropometric and biochemical variables

Height, weight, and waist circumference were measured in each center by a single trained operator as previously described [12]. Body mass index (BMI) was transformed into standard deviation score (SDS), based upon the Italian BMI percentiles [16]. The waist-to-height ratio (WHtR) was calculated as an index of abdominal adiposity.

Fasting plasma glucose and insulin, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (Tg) and alanine aminotransferase levels were analyzed in the centralized laboratory of each center. All centers belong to the Italian National Health System and are certified according to International Standards ISO 9000 (www.iso9000.it/), undergoing semi-annual quality controls and inter-lab comparisons. The Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) was calculated according to the following formula: [fasting plasma

glucose (mg/dl) x fasting plasma insulin (μ U/ml)/405]. The Tg to HDL-C (Tg/HDL-C) ratio and TC to HDL-C (TC/HDL-C) ratio were calculated as indices of atherogenic dyslipidemia.

Blood pressure measurement

BP was measured following the recommendations by the European Society of Hypertension [17]. Briefly, measurements were performed after 5 min of resting in a quiet room, by using an aneroid sphygmomanometer and appropriate sized arm cuff on the right arm. Three measurements were obtained every 2 min and the mean of the last two values was used in the analyses. K1 was used for Systolic BP (SBP) and K5 for diastolic BP (DBP) as previously described [18].

Liver ultrasound scan

Abdominal ultrasound scan was available in all participants. Abdominal ultrasound was performed in a clinical setting, and a single expert operator in each center was blinded to clinical and biological data [15]. Abdominal ultrasound scan was included in the diagnostic work up, therefore the operator was blinded regarding the presence of steatosis. A skilled operator identified the presence of liver steatosis with a qualitative standard method based on the presence of increased echogenicity (brightness) of the liver as compared with the renal cortex. Liver steatosis was assessed as present or absent.

Carotid artery ultrasound

The evaluation of common cIMT was available in 427 children of whom 219 were boys, 124 NW, 163 OW and 140 OB. Participants were recruited in Rome (Sapienza University) as previously reported [13]. The evaluation of cIMT was performed since 2003 as an internal protocol. B-mode ultrasound examinations were performed with a commercially available system equipped with a 7–13 MHz linear array probe. Quantitative B-mode ultrasound measurements of cIMT were done following a standardized protocol. The reported cIMT was computed as the mean of cIMT of far walls of both common carotid arteries of both carotid bulbs as previously described [13].

Echocardiographic evaluation

Echocardiographic measurements were available in 264 young people of whom 141 were boys, 22 NW, 83 OW and 159 OB, recruited in the centers of Pozzuoli and Rome, as previously reported [14,19]. The echocardiographic assessment was performed using a commercial instrument by a single skilled operator in each center. LVM, expressed in grams (g), was calculated with standard procedures [20] and normalized for height in $m^{2.7}$ (LVM index). Relative wall thickness (RWT) was calculated from posterior wall thickness (PWT), interventricular septum thickness (IVST) and left ventricular diastolic diameter (LVDD) according to

the following formula: $(PWT + IVST)/LVDD$; RWT was normalized for age using the formula $RWT - 0.05 \times \text{age (years)} - 10$ (RWTa), as previously suggested [21].

Definitions

Non-hypertensive status was defined as BP < 90th percentile for gender, age and height in children (aged <13 years) and <120/80 in adolescents (aged ≥ 13 years). Elevated BP was defined as BP ≥ 90 th to <95th percentile for age, gender and height in children or $\geq 120/80$ to <130/80 in adolescents.

Prepubertal stage was defined by the Tanner Stage I (no breast development in girls and testicular volume below 4 ml in boys). NW, OW and OB were defined according to the Italian growth charts for BMI [16]. Insulin resistance was defined as Homeostasis Model Assessment for Insulin Resistance (HOMA-IR) ≥ 97 th percentile for age and sex in normal weight children, as previously described [22].

Statistical methods

Values were expressed as mean \pm standard deviation or absolute and relative frequencies. The variables with skewed distribution were log-transformed for the statistical analyses and expressed as median and interquartile range in the tables. The Student's *t* test or ANOVA were used to analyze differences between two or more groups. ANCOVA was employed to assess the differences between groups after correction for age, prepubertal stage, centers and BMI-SDS. Chi-square or Fisher's exact test, as appropriate, were used to compare proportions. The Odds ratios (ORs) for OW/OB, insulin resistance and liver steatosis in individuals with elevated BP were tested by logistic regression analysis using the backward procedure adjusted for centers, age, prepubertal stage. The ORs for insulin resistance and liver steatosis were also adjusted for BMI-SDS. A *P* value < 0.05 was considered statistically significant. The statistical analysis was performed using the IBM SPSS Statistics, version 20.0.

Results

Two thousand seven hundred thirty-nine Italian children and adolescents (1420 males, 51.8%) defined non hypertensive by the AAP₂₀₁₇ guidelines were included in the study. The descriptive characteristics of the study population divided by BMI categories are shown in Table 1. The overall prevalence of elevated BP according to AAP₂₀₁₇ reference values was 18.3% and a significant increase was found across BMI categories.

The mean levels of the traditional cardiometabolic risk factors and preclinical signs of cardiovascular damage in youth with normal and elevated BP are shown in Table 2. Youth with elevated BP were older and less frequently prepubertal, and exhibited higher levels of BMI/BMI-SDS than normotensive youth. Among the cardiometabolic risk factors, only the HOMA-IR index was higher in the group with elevated BP, independently of confounding

factors such as centers, age, prepubertal stage and BMI-SDS. The characteristics of the subsamples who underwent carotid artery ultrasound or echocardiographic evaluation distinguished in youth with normal and elevated blood pressure are shown in Table 3. No significant difference was found in cIMT, LVMI and RWTA between youth with normal and elevated BP. The frequency of insulin resistance and liver steatosis in youth with normal and elevated BP is shown in Fig. 1. Compared with normotensive youth, individuals with elevated BP showed significant ORs for overweight/obesity status, insulin resistance and liver steatosis, as shown in Table 4.

Discussion

In the present study we demonstrated that children and adolescents with elevated BP showed an altered metabolic risk profile characterized by obesity, insulin resistance, and liver steatosis. They did not exhibit significantly altered lipid profile and preclinical signs of cardiovascular damage, compared with normotensive youth.

The AAP₂₀₁₇ guidelines for the screening, diagnosis and management of high BP in the pediatric population [2] have substituted the previous guidelines that have been used for many years, that included also OW or OB to classify normotension and hypertension stages [3]. The consequence is the increased prevalence of individuals classified as hypertensive, especially in OW/OB individuals [5].

Long-term prospective studies linking childhood BP to cardiovascular disease in adulthood, or trials demonstrating the effect of BP reduction in children on the

reduction of cardiovascular disease in adulthood are lacking [23]. Therefore, unlike adults in whom the definition of HTN is based on a true risk of cardiovascular events and death, HTN in childhood can be only defined on the ranking of BP within a reference population. Consequently, any study approaching the association between BP and cardiovascular risk is inevitably limited by the use of a statistical rather than epidemiological criterion.

The features of the borderline category with elevated BP, classified according to the new AAP₂₀₁₇ guidelines, have been scarcely investigated until now. Prevalence of 14.3% and 16% were respectively reported in a large sample of Italian children and adolescents referred to a Pediatric Center for Cardiovascular Risk Prevention [6] and in a multiethnic population of adolescents of whom 59% had OB and 30% diabetes [7]. In our sample the prevalence of elevated BP was 7.6% in NW, 14.9% in OW and 20.3% in OB youth. These data confirm the linear relationship between BP and increasing adiposity [24].

We found that children and adolescents with elevated BP were more insulin resistant and exhibited higher odds for liver steatosis, compared with normotensive youth, independently of BMI. The link between insulin resistance and high BP is supported by numerous clinical and epidemiologic evidences in adults [25] as well as in children [9,10,26,27]. Our findings also confirm previous data reported by our group in a smaller sample of obese youth classified as pre-hypertensive according to the Fourth Report [10]. The mechanisms underlying insulin resistance and high BP are multiple and not definitively clarified yet. Even though both conditions are associated with an unhealthy lifestyle and a systemic low-grade

Table 1 Descriptive characteristics of the groups separated by categories of BMI.

<i>n</i> = 2739	Normal weight	Overweight	Obese	<i>P</i> value
	170	610	1959	
Age, years	11.1 ± 2.7	10.7 ± 2.3	10.5 ± 2.8	0.011
Males, number (%)	80 (47)	317 (52)	1023 (52)	0.433
Prepubertal stage, number (%)	17 (10)	140 (23)	704 (36)	<0.0001
BMI, kg/m ²	18.7 ± 2.2	23.4 ± 2.0	29.4 ± 4.53	<0.0001
BMI-SDS	-0.10 ± 0.65	1.32 ± 0.24	2.27 ± 0.41	<0.0001
WHR	0.45 ± 0.06	0.54 ± 0.05	0.63 ± 0.07	<0.0001
FPG (mg/dl)	83.2 ± 7.1	84.8 ± 8.4	84.5 ± 9.0	0.010
FPI (mU/mL)	7.0 (4.1–10.3)	11.4 (7.4–15.6)	14.0 (9.4–20.0)	<0.0001
HOMA-IR	1.5 (0.8–2.2)	2.3 (1.5–3.3)	2.9 (1.9–4.2)	<0.0001
Cholesterol (mg/dl)	164.9 ± 33.2	158.8 ± 31.3	156.1 ± 30.7	<0.0001
HDL-C (mg/dL)	58.7 ± 14.1	51.8 ± 13.9	47.8 ± 12.0	<0.0001
Triglycerides (mg/dL)	60.1 (50.0–80.0)	68.0 (50.0–95.8)	78.0 (57.0–108.0)	<0.0001
Tg/HDL-C ratio (mg/dL)	1.1 (0.8–1.6)	1.3 (0.9–2.0)	1.7 (1.1–2.5)	<0.0001
TC/HDL-C ratio	2.9 ± 0.8	3.2 ± 0.9	3.4 ± 1.0	<0.0001
ALT (IU/L)	16.0 (12.8–19.3)	19.0 (15.0–26.0)	21.0 (16.0–30.0)	<0.0001
Systolic BP (mmHg)	100.8 ± 9.1	104.1 ± 10.1	104.4 ± 10.9	<0.0001
Diastolic BP (mmHg)	61.7 ± 6.7	64.6 ± 7.6	64.1 ± 7.6	<0.0001
Elevated BP (%)	13 (7.6)	91 (14.9)	397 (20.3)	<0.0001

Data are expressed as mean ± standard deviation, median (25th–75th percentile) or *n* (%), when appropriate.

Abbreviations: ALT: alanine amino transferase; BMI: body mass index; SDS: standard deviation score; BP: blood pressure; FPG: fasting plasma glucose; FPI: fasting plasma insulin; HDL: high-density lipoprotein cholesterol; HOMA-IR: Homeostasis Model Assessment for Insulin Resistance; Tg/HDL-C: triglycerides/HDL-Cholesterol; TC/HDL-C: Total Cholesterol/HDL-Cholesterol; WHtR: waist to height ratio.

inflammation, increased renal sodium retention and increased activation of the sympathetic nervous system may also play a role [28].

Emerging studies documented that liver steatosis and high BP are also strictly associated, independent of other traditional cardiovascular risk factors [29–31]. With specific regard to children, two studies found a nearly doubled prevalence of elevated BP in obese children with nonalcoholic fatty liver disease compared to those without nonalcoholic fatty liver disease, respectively 32% versus 16% [31] and 61% versus 36.6% [32]. Also in this case insulin resistance appears to be the main mechanism linking these two apparently different conditions, creating a vicious circle. Indeed, insulin resistance causes fatty liver disease by enhancing ectopic fat deposition and, in turn, nonalcoholic fatty liver disease promotes insulin resistance through increased fatty acids, inflammation, and endoplasmic reticulum stress in the liver. Hepatokines released by fatty liver may mediate the

action of insulin on the vascular wall, causing the proinflammatory effects of perivascular fat and potentially contributing to the development of cardiovascular disease [33]. Also, *in vitro* studies demonstrated that activation of sympathetic nervous system is implicated in increased hepatic fibrogenesis in patients with nonalcoholic fatty liver disease through the effects of sympathetic neurotransmitters on hepatic stellate cells [34], and modulation of the fibrogenic function of hepatic stellate cells. Interestingly, Hurr et al. demonstrated that male mice fed with a high fat diet developed liver steatosis, that was significantly reduced by sympathetic denervation [35].

With regard to the early cardiovascular damage, we found that elevated BP was not significantly associated with increased cIMT or left ventricular mass and RWTa. Our findings are in agreement with Antolini et al. [6], who also reported no association with left ventricular mass. In contrast, Khoury et al. [7] found increased odds of abnormal measures of both left ventricular mass and cIMT with worsening BP categories, as defined by the AAP₂₀₁₇. Specifically, the group with elevated BP showed a two-to threefold higher risk of LV hypertrophy and high cIMT compared with normotensive youth. We cannot exclude that the dissimilarities found with our findings might be explained by the different study cohorts, since Khoury

Table 2 Cardiometabolic risk factors and preclinical signs of cardiovascular damage in youth with normal and elevated blood pressure.

	Normal BP 2238	Elevated BP 501	P value
Age, years	10.4 ± 2.6	11.6 ± 2.6	<0.0001
Male gender, number (%)	1150 (51)	270 (54)	0.310
Prepubertal, number (%)	761 (34)	100 (20)	<0.0001
BMI, kg/m ²	27.0 ± 5.0	28.9 ± 5.0	<0.0001
BMI-SDS	1.9 ± 0.78	2.1 ± 0.68	<0.0001
WHTR	0.60 ± 0.08	0.60 ± 0.08	0.313
FPG (mg/dl)	84.5 ± 8.7	84.7 ± 8.9	0.450*
FPI (mU/mL)	12.3 (8.1–17.8)	14.4 (9.9–21.9)	0.028*
HOMA-IR	2.6 (1.7–3.8)	3.0 (2.0–4.6)	0.026*
Cholesterol (mg/dl)	157.3 ± 31.1	157.5 ± 31.6	0.740*
HDL-C (mg/dL)	49.6 ± 13.6	48.4 ± 13.8	0.647*
Triglycerides (mg/dL)	74.0 (55.0–103.0)	77.0 (56.0–106.5)	0.654*
Tg/HDL-C ratio (mg/dL)	1.5 (1.0–2.3)	1.7 (1.1–2.6)	0.679*
TC/HDL-C ratio	3.3 ± 0.9	3.4 ± 1.0	0.362*
ALT (IU/L)	20.0 (16.0–28.0)	20.0 (16.0–29.0)	0.162*
Systolic BP (mmHg)	101.3 ± 9.3	116.9 ± 6.1	<0.0001*
Diastolic BP (mmHg)	63.2 ± 7.4	68.3 ± 6.8	<0.0001*

Data are expressed as mean ± standard deviation, median (25th–75th percentile) or n (%), when appropriate. *P value adjusted for centers, age, prepubertal stage and BMI-SDS.

Abbreviations: ALT: alanine amino transferase; BMI: body mass index; SDS: standard deviation score; BP: blood pressure; FPG: fasting plasma glucose; FPI: fasting plasma insulin; HDL: high-density lipoprotein cholesterol; HOMA-IR: Homeostasis Model Assessment for Insulin Resistance; Tg/HDL-C: triglycerides/HDL-Cholesterol; TC/HDL-C: Total Cholesterol/HDL-Cholesterol; WHTR: waist to height ratio.

Table 3 Characteristics of subsample with carotid artery ultrasound and echocardiographic evaluation in youth with normal and elevated blood pressure.

cIMT group	Normal BP 359	Elevated BP 68	P value
Age, years	10.4 ± 2.8	11.7 ± 3.0	<0.0001
Male gender, number (%)	178 (50)	41 (60)	0.105
Prepubertal, number (%)	47 (13)	5 (7)	0.185
BMI, kg/m ²	22.4 ± 4.2	25.6 ± 4.3	<0.0001
BMI-SDS	1.0 ± 1.0	1.5 ± 0.8	<0.0001
Systolic BP (mmHg)	101.8 ± 7.7	117.3 ± 5.7	<0.0001*
Diastolic BP (mmHg)	62.7 ± 6.3	66.0 ± 5.9	<0.0001*
cIMT (mm)	0.51 ± 0.08	0.53 ± 0.08	0.418*
Echocardiographic group	211	53	
Age, years	10.0 ± 2.5	11.3 ± 3.0	<0.0001
Male gender, number (%)	110 (52)	31 (59)	0.407
Prepubertal, number (%)	52 (25)	9 (17)	0.237
BMI, kg/m ²	25.4 ± 5.1	27.0 ± 4.5	0.032
BMI-SDS	1.7 ± 0.8	1.9 ± 0.6	0.083
Systolic BP (mmHg)	102.2 ± 7.9	117.1 ± 5.1	<0.0001**
Diastolic BP (mmHg)	61.3 ± 6.8	67.4 ± 6.4	<0.0001**
LVMi (g/h ^{2.7})	40.9 ± 13.1	41.1 ± 12.0	0.401**
RWTa	0.36 ± 0.07	0.34 ± 0.06	0.058**

*P value adjusted for age and BMI-SDS. **P value adjusted for centers, age and BMI-SDS

Abbreviations: cIMT: carotid intima media thickness; LVMi: left ventricular mass index; RWTa: relative wall thickness adjusted for age.

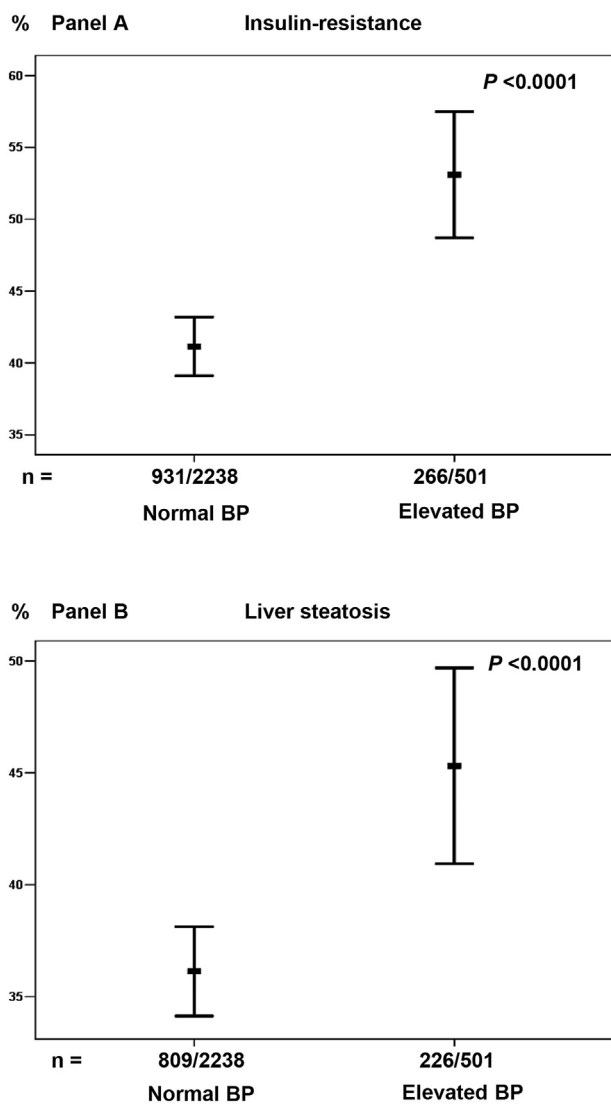


Figure 1 Proportions (mean and 95% CI) of youth with insulin resistance (Panel A) or liver steatosis (Panel B) among groups with normal (n = 2238) or elevated (n = 501) blood pressure (BP).

et al. [7] analyzed individuals who were older than our population and exhibited high cardiovascular risk (30% showed type 2 diabetes), while our population was not affected by diabetes.

Table 4 Odds ratio (CI 95%) for obesity, insulin resistance and liver steatosis in youth with elevated blood pressure compared to normotensive individuals.

	Normal BP	Elevated BP	P value
Overweight/Obesity	1.00	3.60 (2.00–6.46)	<0.0001 ^a
Insulin resistance	1.00	1.46 (1.19–1.78)	<0.0001 ^a
	1.00	1.26 (1.03–1.53)	0.033 ^b
Liver steatosis	1.00	1.45 (1.19–1.77)	<0.0001 ^a
	1.00	1.25 (1.02–1.54)	0.036 ^b

^a Adjusted for centers, age, prepubertal stage.

^b Adjusted for centers, age, prepubertal stage and BMI-SDS.

Moreover, while none of these studies provided data about the metabolic features of children and adolescents with elevated BP, we found that the sole abnormality was the increased glucose disposal as represented by the HOMA-IR, which well couples with the evidence of increased probability of liver steatosis [36].

This study presents some limitations, such as the cross-sectional design and the lack of information about the body composition. In addition, the sample presented a very high prevalence of overweight and obese youth, especially in the subsample who underwent echocardiographic evaluation. Thus, our results may not be generalizable to the whole pediatric population. Moreover, the association between elevated BP and altered metabolic risk profile was demonstrated on the basis of a single BP measurement, therefore we cannot exclude that this methodological approach might have influenced the results. The strength of our study is based on the comprehensive analysis of the biochemical cardiometabolic risk factors, and liver, carotid and echocardiographic profiles. Furthermore, we performed adjusted analyses, that included also BMI, to confirm the independent risk of elevated BP for both insulin resistance and liver steatosis.

In conclusion, this study demonstrates that youth with elevated BP exhibit an altered metabolic risk profile, but no preclinical signs of cardiovascular damage. Therefore, early diagnosis of elevated BP levels might be critically important, in order to pursue lifestyle changes, such as lose weight, eat a healthy diet lower in fat, saturated fat, cholesterol, and sodium, and higher in potassium, get regular physical activity and, with special consideration for adolescents, avoid smoking and alcohol. In this way the trajectories toward HTN and worsening of the cardiometabolic risk profile can be prevented in these subjects.

Author contributions

P. Di Bonito conceived and designed the study, and performed the statistical analyses. L. Pacifico, M. R. Licenziati, C. Maffei, A. Morandi, M. Manco, E. Miraglia del Giudice, A. Di Sessa, G. Campana, N. Moio, M.G. Baroni, C. Chiesa were responsible for the acquisition of patients and data. P. Di Bonito, G. Valerio contributed to the analysis. P. Di Bonito, G. Valerio and G. de Simone contributed to the interpretation of the data. P. Di Bonito and G. Valerio drafted the manuscript. All authors critically read and revised the manuscript and approved the final version.

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Declaration of Competing Interest

Nothing to disclose.

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