Systematic Review and Meta-Analysis

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Performance of obesity indices for screening elevated blood pressure in pediatric population

Systematic review and meta-analysis

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Abstract

Background: Hypertension is closely related with obesity in pediatric population. Obesity indices were used for screening elevated blood pressure (BP) in children and adolescents. The present study was to perform a meta-analysis to assess the performance of obesity indices, body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR), for identifying elevated BP in children and adolescents.

Methods: Data sources were PubMed, EMBASE, Web of Science, Cochrane, and SCOPUS up to May 2016. Studies providing measures of diagnostic performance of obesity indices and using age-, sex-, and height-specific BP 95% as reference standard (the definition of United State Fourth Report) were included. We extracted available data on true-positive, false-positive, true-negative, and false-negative to construct a 2×2 contingency table and computed the pooled summary statistics for the sensitivities and specificities to estimate the diagnostic performance.

Results: Nine eligible studies that evaluated 25,424 children and adolescents aged 6 to 18 years were included in the meta-analysis. The pooled sensitivities were 42% (BMI), 42% (WC), and 43% (WHtR). The pooled specificities were 80% (BMI), 75% (WC), and 77% (WHtR). The areas under the curve (AUCs) of obesity indices were 0.7780 (BMI), 0.7181 (WC), and 0.6697 (WHtR), respectively. In this meta-analysis, the BP measurements were based on 3 visits in only 1 study. The prevalence of hypertension may be overestimated in these studies.

Conclusions: The present meta-analysis showed that the performance of obesity indices for identifying elevated BP was poor. Our findings do not support the performance of WC and WHtR is superior to BMI to help identify children with elevated BP.

Abbreviations: AUC = area under the curve, BMI = body mass index, BP = blood pressure, CI = confidence interval, DOR = diagnostic odds ratio, LR− = negative likelihood ratio, LR+ = positive likelihood ratio, QUADAS = Quality Assessment for Studies of Diagnostic Accuracy, VAT = visceral adipose tissue, WC = waist circumference, WHtR = waist-to-height ratio.

Keywords: children, hypertension, meta-analysis, obesity indices

1. Introduction

In the last decade, childhood hypertension has become an important health issue due to its rising prevalence and associated damage.[1] Childhood blood pressure (BP) is associated with BP in later life. Systematic analysis had showed the tracking of BP from childhood to adulthood.[2] Hypertension in children is associated with early vascular aging and left ventricular hypertrophy or dysfunction.[3–6]

The epidemic of childhood obesity plays an important role in the development of hypertension. Childhood overweight and obesity have increased dramatically since 1990.[7] Recent systematic analysis shows that the overall prevalence of overweight including obesity has reached approximately 23.8% for boys and 22.6% for girls in developed countries and 12.9% for boys and 13.4% for girls in developing countries.[8] Obese children and adolescents are often accompanied with increased cardiovascular risk factor. Obesity increases the occurrence of hypertension 3-fold while favoring the development of insulin resistance, hyperlipidemia, and salt sensitivity.[9,10] Obese children and adolescents also have unhealthy living habit, such as excess dietary Na intake and low physical activity.[11,12] Children with hypertension, especially with hypertension coexisting with obesity, have more serious left ventricular hypertrophy and dysfunction.[13]

In the absence of evidence-based guidelines for high BP screening in asymptomatic children and adolescents,[14] a reasonable strategy is to screen those who are at high risk. Obesity indices can be used to target a high-risk population for BP screening until current evidence gaps are filled.[15] Therefore, obesity indices were used for screening elevated BP in pediatric

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population. Body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR) are the most common indices used to determine elevated BP in children and adolescents. The aim of this systematic review was to meta-analyze the performance of obesity indices, BMI, WC, and WHtR, for identifying elevated BP in children and adolescents.

2. Methods literature review

2.1. Search strategy and eligibility criteria

We performed a systematic review of published articles in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines (http://www.prisma-statement.org/). The predefined inclusion criteria for study selection were: the study must have assessed the performance of BMI, WC, and WHtR to identify elevated BP or hypertension in children and adolescents aged 0 to 18 years; (ii) provided a 2 × 2 diagnostic table to allow for meta-analysis or information to calculate these values; and used an age-, sex-, and height-specific BP 95% as reference standard (the definition of US Fourth Report).[16] We excluded editorials, reviews, and abstracts from conference proceedings. The research was limited to studies in humans and the English language.

We conducted systematic search in the bibliographic databases PubMed, EMBASE, Web of Science, Cochrane, and SCOPUS from inception to May 4, 2016. First, 4 keyword categorical searches were conducted: hypertension or synonyms (e.g., elevated blood pressure); children or adolescents or synonyms (e.g., teenage); screening or equivalent (e.g., sensitivity and specificity); (iv) body mass index or BMI, waist or waist circumference or WC, waist-to-height ratio or WHtR or waist to stature ratio or WSR. Second, categories "i" to "iv" were combined using "and," and duplicates were removed. In addition, the related literatures and reference lists of the identified articles were searched for relevant publications. This study was approved by the ethics committee of the First Hospital of Qinhuangdao.

2.2. Study selection and quality assessment

We eliminated irrelevant articles from our primary search on the basis of information in title and abstract. Once papers had been identified on the basis of information in the title and abstract, full papers were obtained for all relevant studies. Two reviewers (C-MM and RW) independently read the full papers obtained from the search for relevance. All studies that did not meet the inclusion criteria or that met the exclusion criteria were removed. Disagreements between the 2 reviewers regarding study inclusion were resolved by a face-to-face discussion upon the full-text assessment. Eligible studies were further reviewed.

The methodological quality of each study was assessed using a checklist based on the Quality Assessment for Studies of Diagnostic Accuracy (QUADAS) tool,[17] which enables reviewers to evaluate the quality of studies. Disagreement between the reviewers on individual items was resolved by a consensus meeting with a 3rd reviewer (F-ZY).

2.3. Data extraction

Data were extracted from primary studies by the 2 reviewers (C-MM and RW) independently. Data regarding the population, screening tools used to define elevated BP and diagnostic criteria of elevated BP were extracted. We also extracted available data on true-positive, false-positive, true-negative, and false-negative to construct a 2 × 2 contingency table.

2.4. Data synthesis and statistical analysis

From the extracted data, arranged in 2 × 2 contingency tables, we computed the pooled summary statistics for the sensitivities, specificities, likelihood ratios, and diagnostic odds ratios (DORs) to estimate the diagnostic performance. All statistics are reported as point values with 95% confidence intervals (CIs). The heterogeneity of all diagnostic test parameters was evaluated with the inconsistency index (I^2). The I^2 statistic is defined as the percentage of variability due to heterogeneity beyond that from chance; values greater than 50% represent the possibility of substantial heterogeneity.

The comparison of diagnostic accuracy between BMI, WC, and WHtR were performed by constructing the summary receiver operating characteristic curves with pertinent areas under the curve (AUCs). AUC presents an overall summary of test performance. Perfect tests have AUCs close to 1, whereas poor tests have AUCs close to 0.5. The summary receiver operating characteristic plots were constructed using the Moses–Shapiro–-Littenberg model.

In addition, multivariate meta-regression analyses were conducted to compare the diagnostic performance between BMI, WC, and WHtR after the adjustment of other study-specific covariates. These variables were chosen a priori as potential causes of between-study heterogeneity and included: BP measurement method, the number of office visit, sample size, region, and quality assessment score.

Studies were also grouped based on BP measurement method: auscultatory method, oscillometric method or Finapres apparatus; and the number of office visit: 3 visits, other. Given geographic differences, studies were grouped based on region of the study population into: North America and South America, Europe, Asia, and Africa. Finally, studies were categorized into 2 subgroups based on QUADAS score (QUADAS score < 10 and QUADAS score ≥ 10).

The diagnostic threshold (cut-off) bias was also evaluated as a cause between study heterogeneity. Begg test and Egger test was conducted to examine the possible publication bias of the studies regarding the performance of obesity indices in detecting elevated BP. Analyses were performed using the Meta-Disc 1.4 statistical software (Unit of the Clinical Biostatistics team of the Ramony Cajal Hospital in Madrid, Spain) and STATA version 12.0 (STATA Corporation, College Station, TX).

3. Results

Figure 1 summarizes the selection process of studies. In total, 3607 references were obtained using PubMed, EMBASE, Web of Science, Cochrane, and SCOPUS. An additional 6 full-text articles were included after scanning the related literatures and reference lists of the studies selected for inclusion. Eventually, a total of 9 studies were included in the present review.[18–26] The quality of the included articles is summarized in Table 1.

Table 1 shows details of these 9 papers. Studies were between 2007 and 2015, in 7 different countries, United States, Brazil, South Africans, Canada, Switzerland, Indian, and Lithuania. Seven eligible studies that evaluated 25,424 children and adolescents aged 6 to 18 years were included in the meta-

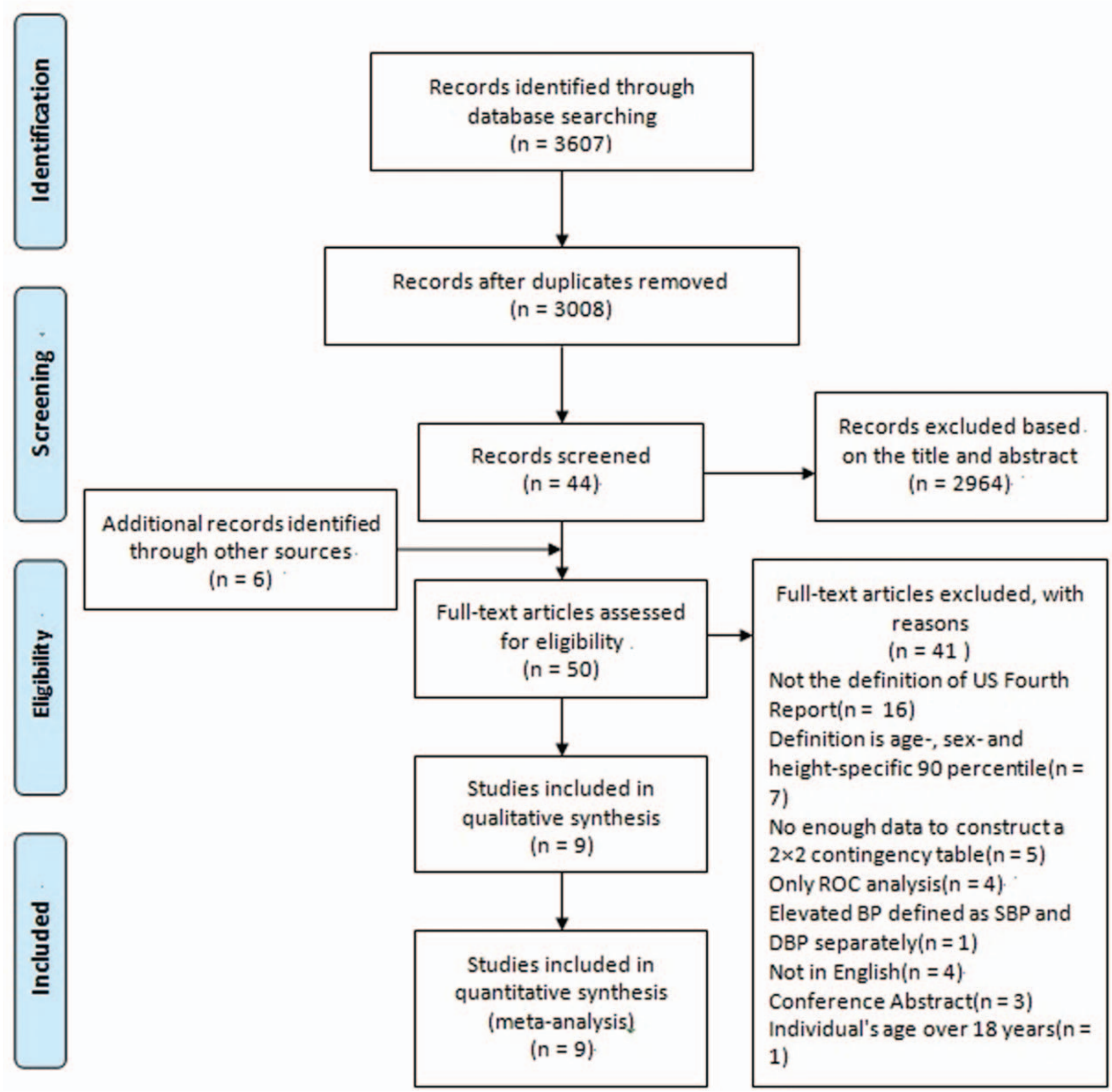

Figure 1. Flowchart of selection of studies and specific reasons for exclusion from the meta-analysis.

Table 1

Characteristics of studies included in the meta-analysis.

Study	Study year	Country	N (boys/girls)	Age, years	BP measurement method	The times of BP visit	Screening tool	QUADAS
Rosa et al 2007[18]	2003–2004	Brazil	456 (203/253)	12–17	Oscillometric method	2	BMI and WC	12
Fernandes et al 2011[19]	2008	Brazil	358 (358/0)	8–18	Oscillometric method	1	BMI and %BF	10.5
Christofaro et al 2011[20]	2007	Brazil	1021 (493/528)	10–17	Oscillometric method	1	BMI and WC	10.5
Motswagole et al 2011[21]	2000–2001	South Africans	688 (321/367)	9-15	Finapres apparatus (finger arterial pressure)	Not reported	WHtR	9.5
Khoury et al 2012[22]	2009–2010	Canada	3248 (1625/1623)	14–15	Oscillometric method	3	BMI and WHtR	9
Chiolero et al 2013[23]	2005–2006	Switzerland	5207 (2621/2586)	10.1–14.9	Oscillometric method	1	BMI and WHtR	10
Kajale et al 2014[24]	2011–2012	Indian	6402 (3523/2879)	6–18	Auscultatory method	1	BMI, WC, WHtR, TSFT, and Wrist	10
Bauer et al 2015[25]	2006	United States	6097 (2902/3195)	10–13	Oscillometric method	1	BMI, WC, and WHtR	10
Kuciene et al 2015[26]	2012–2013	Lithuania	1947 (962/985)	12–15	Oscillometric method	1	BMI, WC, and NC	11.5

%BF = percentage of body fat, BMI = body mass index, BP = blood pressure, NC = neck circumference, QUADAS = Quality Assessment for Studies of Diagnostic Accuracy, TSFT = tricep skin-fold thickness, WC = waist circumference, WHtR = waist-to-height ratio.

Table 2

The sensitivities, specificities, likelihood ratios, and diagnostic odds ratios of obesity indices for identifying elevated blood pressure.

Study	Screening tool	Cut-off values for tool	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Diagnostic odds ratio
BMI							
Rosa et al 2007	BMI	Brazilian criteria:90th percentile	0.52 (0.30–0.74)	0.81 (0.77–0.84)	2.74 (1.74–4.30)	0.59 (0.38–0.92)	4.65 (1.91–11.32)
Fernandes et al 2011	BMI	IOTF criteria: age- and sex-specific cut-off values linked to adult obesity cut-off value of 25 kg/m^2	0.39 (0.29–0.49)	0.88 (0.83–0.91)	3.11 (2.06–4.68)	0.70 (0.59–0.83)	4.44 (2.55–7.73)
Christofaro et al 2011	BMI	IOTF criteria: age- and sex- specific cut-off values linked to adult obesity cut-off value of 25 kg/m^2	0.34 (0.26–0.43)	0.83 (0.80–0.85)	2.01 (1.51–2.68)	0.79 (0.69–0.91)	2.54 (1.67–3.84)
Khoury et al 2012	BMI	WHO growth standards: age- and sex-specific 95th percentile	0.43 (0.34–0.53)	0.82 (0.81–0.84)	2.47 (1.98–3.09)	0.69 (0.58–0.81)	3.60 (2.47–5.27)
Chiolero et al 2013	BMI	CDC 2000 reference charts: age- and sex-specific 85th percentile	0.31 (0.27–0.35)	0.88 (0.87–0.89)	2.60 (2.25–3.00)	0.78 (0.74–0.83)	3.32 (2.73–4.04)
Kajale et al 2014	BMI	Boys: 6–12 years 17.5 kg/m^2; 13–15 years 21.8 kg/m^2; 16–18 years 26.1 kg/m^2; girls: 6–9 years 16.1 kg/m^2; 10–14 years 19.2 kg/m^2; 15–18 years 22.7 kg/m^2	0.75 (0.70–0.79)	0.75 (0.74–0.76)	2.97 (2.76–3.20)	0.33 (0.28–0.40)	8.92 (6.97–11.41)
Bauer et al 2015	BMI	CDC 2000 reference charts: age- and sex-specific 96th percentile	0.44 (0.40–0.48)	0.76 (0.75–0.77)	1.86 (1.68–2.06)	0.73 (0.68–0.79)	2.54 (2.13–3.02)
Kuciene et al2015	BMI	IOTF criteria: age- and sex-specific cut-off values linked to adult obesity cut-off value of 25 kg/m^2	0.30 (0.26–0.34)	0.89 (0.87–0.90)	2.67 (2.19–3.26)	0.79 (0.75–0.84)	3.37 (2.62–4.35)
Pooled results			0.42 (0.40–0.44)	0.80 (0.80–0.81)	2.49 (2.09–2.97)	0.67 (0.58–0.77)	3.80 (2.71–5.33)
I^2			96.9%	98.5%	88.6%	93.3%	90.3%
WC							
Rosa et al 2007	WC	Age- and sex-specific 75th percentile	0.45 (0.23–0.68)	0.77 (0.73–0.81)	2.00 (1.19–3.35)	0.71 (0.48–1.06)	2.82 (1.13–7.00)
Christofaro et al 2011	WC	Age- and sex-specific 80th percentile	0.29 (0.21–0.38)	0.91 (0.88–0.92)	3.09 (2.19–4.36)	0.78 (0.70–0.88)	3.95 (2.51–6.22)
Kajale et al 2014	WC	Boys: 6–12 years 68 cm; 13–15 years 81 cm; 16–18 years 90 cm; girls: 6–9 years 62 cm; 10–14 years 77 cm; 15–18 years 87 cm	0.71 (0.66–0.76)	0.69 (0.68–0.70)	2.32 (2.15–2.50)	0.41 (0.35–0.49)	5.61 (4.43–7.11)
Bauer et al 2015	WC	NHANES III: age- and sex-specific 92th percentile	0.41 (0.37–0.46)	0.76 (0.74–0.77)	1.69 (1.52–1.88)	0.78 (0.72–0.83)	2.18 (1.83–2.60)
Kuciene et al 2015	WC	age- and sex-specific 75th percentile	0.25 (0.21–0.29)	0.91 (0.89–0.92)	2.71 (2.17–3.39)	0.83 (0.79–0.87)	3.28 (2.50–4.30)
Pooled results			0.42 (0.40–0.45)	0.75 (0.75–0.76)	2.28 (1.84–2.83)	0.69 (0.56–0.84)	3.43 (2.22–5.31)
I^2			98.0%	99.2%	87.5%	95.0%	90.2%
WHtR							
Motswagole et al 2011	WHtR	0.41	0.62 (0.52–0.70)	0.52 (0.48–0.56)	1.29 (1.09–1.52)	0.74 (0.58–0.94)	1.75 (1.16–2.62)
Khoury et al 2012	WHtR	0.5	0.43 (0.33–0.52)	0.82 (0.80–0.83)	2.34 (1.87–2.93)	0.70 (0.60–0.82)	3.33 (2.28–4.87)
Chiolero et al 2013	WHtR	0.5	0.24 (0.21–0.28)	0.91 (0.90–0.92)	2.68 (2.26–3.17)	0.83 (0.80–0.87)	3.21 (2.59–3.97)
Kajale et al 2014	WHtR	Boys: 6–12 years 0.50; 13–15 years 0.53; 16–18 years 0.53; girls:6–9 years 0.51; 10–14 years 0.51; 15–18 years 0.55	0.73 (0.68–0.77)	0.70 (0.68–0.71)	2.38 (2.21–2.56)	0.39 (0.33–0.47)	6.03 (4.75–7.65)
Bauer et al 2015	WHtR	0.54	0.40 (0.36–0.45)	0.72 (0.70–0.73)	1.43 (1.28–1.59)	0.83 (0.78–0.89)	1.72 (1.44–2.05)
Pooled results			0.43 (0.41–0.45)	0.77 (0.76–0.77)	1.93 (1.44–2.60)	0.68 (0.55–0.84)	2.88 (1.74–4.75)
I^2			98.3%	99.6%	96.1%	95.7%	94.8%

BMI = body mass index, CDC = Centers for Disease Control, IOTF = International Obesity Task Force, WC = waist circumference, WHO = World Health Organization, WHtR = waist-to-height ratio.

analysis. The study population size ranged from 358 to 6402 participants. BMI was used in 8 studies, WC was used in 5 studies, and WHtR was used in 5 studies.

3.1. The performance of BMI

Meta-analysis showed pooled sensitivity to detect elevated BP of 0.42 (95%CI: 0.40–0.44) and pooled specificity of 0.80 (95%CI: 0.80–0.81). Positive likelihood ratio (LR+) was 2.49 (95% CI: 2.09–2.97), negative likelihood ratio (LR−) was 0.67 (95% CI: 0.58–0.77), and DOR was 3.80 (95%CI: 2.71–5.33) (Table 2). Heterogeneity was observed across studies (I^2 = 88.6%–98.5%). Spearman correlation coefficient (Logit [sensitivity] vs Logit [1 − specificity]) was 0.952 (P = 0.000). They revealed evidence supporting the diagnostic threshold (cut-off) bias as a cause of heterogeneity. The Begg test and Egger test did not reveal significant publication bias (P = 0.266 and 0.634).

3.2. The performance of WC

Meta-analysis showed pooled sensitivity to detect the elevated BP of 0.42 (95%CI: 0.40–0.45) and pooled specificity of 0.75 (95% CI: 0.75–0.76). LR+ was 2.28 (95%CI: 1.84–2.83), LR− was 0.69 (95%CI: 0.56–0.84), and DOR was 3.43 (95%CI: 2.22–5.31) (Table 2). Heterogeneity was observed across studies (I^2 = 87.5%–99.2%). Spearman correlation coefficient (Logit [sensitivity] vs Logit [1 − specificity]) was 0.900 (P = 0.037). They revealed evidence supporting the diagnostic threshold (cut-off) bias as a cause of heterogeneity. The Begg test and Egger test did not reveal significant publication bias (P = 1.000 and 0.641).

3.3. The performance of WHtR

Meta-analysis showed pooled sensitivity to detect the elevated BP of 0.43 (95%CI: 0.41–0.45) and pooled specificity of 0.77 (95% CI: 0.76–0.77). LR+ was 1.93 (95%CI: 1.44–2.60), LR− was

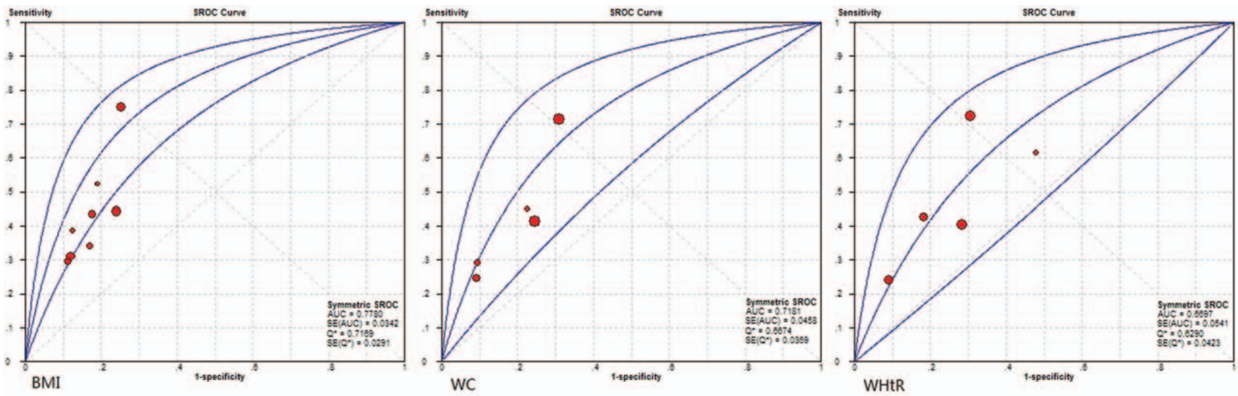

Figure 2. The summary receiver operating characteristic (SROC) curves for the studies examining obesity indices for the assessment of elevated blood pressure in children and adolescents.

0.68 (95%CI: 0.55–0.84), and DOR was 2.88 (95%CI: 1.74–4.75) (Table 2). Heterogeneity was observed across studies (I^2=94.8%–99.6%). Spearman correlation coefficient (Logit [sensitivity] vs Logit [1 − specificity]) was 0.800 (P=0.104). The diagnostic threshold (cut-off) bias was not a cause of heterogeneity. The Begg test and Egger test did not reveal significant publication bias (P=1.000 and 0.739).

3.4. Comparison between BMI, WC, and WHtR

The AUCs of obesity indices were 0.7780 (BMI), 0.7181 (WC), and 0.6697 (WHtR), respectively (Fig. 2). Multivariate meta-regression analysis showed that the diagnostic accuracy of BMI and WC was similar even after adjusting covariates (RDOR= 0.83, 95%CI: 0.65–1.05, P=0.112) (Table 3). Multivariate meta-regression analysis showed that the diagnostic accuracy of BMI and WHtR was similar even after adjusting covariates (RDOR=0.79, 95%CI: 0.59–1.05, P=0.098) (Table 3).

4. Discussion

The present meta-analysis showed that the obesity indices have low pooled sensitivity and moderate pooled specificity in identifying elevated BP. Pooled results from the obesity indices showed that sensitivities were only 42% and 43%, suggesting over half of children with undiagnosis. Although the prevalence of hypertension in normal weight is low, the number of children living with hypertension in normal weight is not low. Obesity indices are not appropriate screening methods for elevated BP in children. However, this does not mean that obesity indices cannot be used in clinical practice.

Obesity is an important driver of the increased prevalence in childhood hypertension.[27] A lot of epidemiologic research confirmed the association between obesity and increased risk for hypertension.[27–31] Successful weight loss can improve BP status in obese children.[32,33] The evaluation of obesity is very important in childhood hypertension management. However, BP also should be measured in children with normal weight.

As is well known, body fat distribution is closely related to the occurrence and development of cardiovascular disease.[34] Visceral adipose tissue (VAT) accumulation was associated with greater free fatty acids flux[35] and insulin resistance and increased risk of hypertension.[36] WC and WHtR are good markers of abdominal obesity, and BMI is a marker of increases in overall adiposity. Magnetic resonance imaging and computed tomography are considered to be the most accurate approaches

Table 3

Multivariate meta-regression analyses to compare the diagnostic performance between BMI, WC, and WHtR after the adjustment of other study-specific covariates.

Variable	Relative DOR (95%CI)	*P*
BMI vs WC		
Obesity indices (BMI vs WC)	0.83 (0.65–1.05)	0.112
Region of the study population (North America and South America vs Europe, Asia, and Africa)	1.13 (0.86–1.50)	0.307
Sample size	0.99 (0.99–1.00)	0.060
BP measurement method (Auscultatory method vs other method)	0.37 (0.26–0.55)	0.000
The number of office visit (3 BP visits vs others)	0.85 (0.49–1.47)	0.522
Quality of study (QUADAS score < 10 vs QUADAS score ≥ 10)	0.85 (0.49–1.47)	0.522
BMI vs WHtR		
Obesity indices (BMI vs WHtR)	0.79 (0.59–1.05)	0.098
Region of the study population (North America and South America vs Europe, Asia, and Africa)	1.36 (0.99–1.86)	0.052
Sample size	0.99 (0.99–1.00)	0.251
BP measurement method (Auscultatory method vs other method)	0.39 (0.26–0.59)	0.001
The number of office visit (1 BP visit vs others)	0.36 (0.16–0.83)	0.024
Quality of study (QUADAS score < 10 vs QUADAS score ≥ 10)	1.90 (0.90–4.01)	0.080

BMI = body mass index, BP = blood pressure, CI = confidence interval, DOR = diagnostic odds ratio, QUADAS = Quality Assessment for Studies of Diagnostic Accuracy, WC = waist circumference, WHtR = waist-to-height ratio.

for the quantification of VAT. WC and WHtR were also strongly correlated with VAT assessed by magnetic resonance imaging and computed tomography.[37,38] However, our study indicates that WC and WHtR were no better than BMI to identify the risk of elevated BP in children.

Unlike adults, BMI is equivalently predictive and provides sufficient information to assess visceral adiposity in children and adolescents. WC does not add additional predictive value.[39] Harrington et al[40] found that 95th Centers for Disease Control and Prevention BMI percentile is a useful threshold for the prediction of elevated levels of VAT in children and adolescents. WC and BMI are equally correlated with VAT in a pediatric population. The amount of VAT in young adult men was associated with BMI changes specifically during adolescence.[41] So, WC and WHtR are not better screening tools than BMI for childhood hypertension.

The study has 2 limitations. First, repeated BP measurements are required to confirm the diagnosis of hypertension in children and adolescents. The prevalence of hypertension tends to decrease in subsequent visits.[28] In this meta-analysis, the BP measurements were based on 3 visits in only 1 study.[22] The prevalence of hypertension may be overestimated in these studies. Second, some new obesity indices, such as neck circumference[26] and mid-upper arm circumference,[42] had been used to screen elevated BP in children. These obesity indices were not in the meta-analysis because related research is few.

In conclusion, the present meta-analysis showed that the association with BP may not be strong enough for both indices to be used as efficient tools to identify elevated BP in children. Our findings do not support the performance of WC and WHtR is superior to BMI to help identify children with elevated BP.

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