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Laboratório de Imunopatologia Keizo Asami
Programa de Pós-graduação em Biologia Aplicada à Saúde

Novos métodos de triagem para distúrbios pressóricos na infância e adolescência

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Recife - PE
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Orientador: Dr. Wilson Nadruz Júnior
Coorientadora: Dra. Sandra da Silva Mattos

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Para meu pai, minha mãe e irmã, que mesmo distantes torcem constantemente por mim. E minha amada Marianna, cuja proximidade torna minha vida mais feliz.

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“A person who never made a mistake never tried anything new”

Albert Einstein

RESUMO

A hipertensão arterial sistêmica (HAS) é o principal fator de risco para doenças cardiovasculares de alta morbimortalidade. Sua prevalência vem aumentando na faixa etária pediátrica, principalmente devido à epidemia de obesidade. Entretanto, o subdiagnóstico de distúrbios pressóricos na infância é uma constante. Um dos principais fatores para isto é o complexo processo diagnóstico da HAS na faixa etária pediátrica, que é dependente da análise de múltiplos gráficos de percentis separados por gênero, altura e idade. Algumas ferramentas foram descritas para facilitar o diagnóstico de HAS na infância, entretanto mudanças recentes nos valores diagnósticos da pressão arterial (PA) em crianças e adolescentes praticamente anularam sua eficácia. Portanto, o objetivo desta tese é descrever pontos de corte de acordo com o guideline mais recente para a razão entre pressão arterial e altura e suas variáveis na população brasileira e americana, além de descrever novas equações baseadas na altura para triagem de distúrbios pressóricos na infância. Para isto foi realizado um estudo retrospectivo, baseado na análise de prontuários de pacientes de uma clínica de cardiologia pediátrica localizada no nordeste brasileiro e do estudo NHANES realizado na população americana. Os pacientes foram classificados com e sem distúrbios pressóricos de acordo com o novo e antigo guideline. Pontos de corte foram obtidos a partir de curvas ROC para a razão entre PA e altura, entre PA e altura modificada e entre a nova razão entre PA e altura modificada. Valores pré-teste e pós-teste foram utilizados para comparar tais métodos em ambas as populações. Além disso, novas equações baseadas apenas na altura foram criadas a partir da regressão linear dos valores diagnósticos para PA elevada publicados no novo guideline. Estas equações foram comparadas com outros métodos de triagem de distúrbios pressóricos na infância por meio dos valores pré-teste e pós-teste, além do índice kappa (método estatístico para avaliar o nível de concordância ou reprodutibilidade entre dois conjuntos de dados). Após tais análises, verificou-se que a nova razão entre PA e altura modificada demonstrou maior valor preditivo positivo e especificidade quando comparada a razão entre PA e altura e a razão entre PA e altura modificada. Além disso, os pontos de corte obtidos foram semelhantes em ambas as populações. As equações baseadas na altura apresentaram maior valor preditivo positivo e especificidade do que todos os outros métodos, tendo sensibilidade e valor preditivo negativo semelhantes. Adicionalmente, foi o único método a apresentar uma correlação muito boa com o padrão ouro de acordo com o índice kappa. Desta forma, novos pontos de corte da razão entre PA e altura e suas variáveis foram descritos para o diagnóstico de distúrbios pressóricos na infância de acordo com o novo guideline. A nova razão entre PA e altura modificada apresentou melhores resultados. Também foram descritas novas equações baseadas na altura para a identificação de distúrbios pressóricos na infância. Estas equações apresentaram resultados superiores aos outros métodos de triagem.

Palavras chaves: Hipertensão. Triagem. Altura. Pediatria.

ABSTRACT

Systemic arterial hypertension (SAH) is the main risk factor for cardiovascular diseases. Its prevalence has been increasing in the pediatric age group, mainly due to the epidemic of obesity. However, the underdiagnosis of blood pressure disorders in childhood is a constant. One of the main factors is the complex diagnosis of hypertension in the pediatric age group, which is dependent on the analysis of multiple percentiles tables separated by gender, height and age. Some tools have been described to reduce this problem; however, recent changes in the diagnostic values of blood pressure (BP) in children and adolescents practically nullified its effectiveness. Therefore, the objective of this thesis is to describe cutoff points according to the new guideline for blood pressure to height ratio and its variants in the Brazilian and American children and describe new height-based equations for screening for blood pressure disorders in childhood. To do so, a retrospective study was carried out based on the analysis of patient charts of a pediatric cardiology clinic located in northeastern Brazil and the NHANES study performed in the American population. Patients from both populations were classified with and without blood pressure disorders according to the previous and the new guideline, published in September 2017. Cut-off points were obtained from ROC curves for blood pressure to height ratio, for modified blood pressure to height ratio and new modified blood pressure to height ratio. Pre-test and post-test values were used to compare such methods with each other in both populations. In addition, new height-based equations were created from linear regression of the diagnostic values for high BP published in the last guideline. These equations were compared with other methods of screening for blood pressure disorders in childhood through pre-test, post-test and kappa index values (statistical method to evaluate the level of agreement or reproducibility between two data sets). Overall, the new modified blood pressure to height ratio showed a higher positive predictive value and specificity when compared to the blood pressure to height ratio and the modified blood pressure to height ratio. In addition, the cutoff points obtained were similar in both populations. The height-based equations presented higher positive predictive value and specificity than all other methods, maintaining similar sensitivity and negative predictive value. Additionally, it was the only method to present a very good correlation with the gold standard according to the kappa index. In conclusion, new cutoff points for methods that use the ratio between BP and height were demonstrated according to the new guideline. Among these methods, the new blood pressure to height ratio presented better results. New equations based on height were described to identify blood pressure disorders in childhood. These equations presented better results than other screening methods.

Keywords: hypertension. Screening. Height. Pediatrics.

LISTA DE ABREVIATURAS E SIGLAS

Acc.	*Accuracy*
AUC	*Area Under Curve*
AVC	Acidente Vascular Cerebral
BMI	*Body Mass Index*
BP	*Blood Pressure*
BPHT	*Blood Pressure to Height Ratio*
CDC	*Centers for Disease Control and Prevention*
CI	*Confidence Interval*
DBP	*Diastolic Blood Pressure*
HAS	Hipertensão Arterial Sistêmica
IAM	Infarto Agudo do Miocárdio
MBPHR3	*New modified Blood Pressure to height ratio*
MBPHR7	*Modified Blood Pressure to height ratio*
MBPHT	*Modified Blood Pressure to height ratio*
NHANES	*National Health and Nutrition Examination Survey*
NLR	*Negative Likelihood Ratio*
NMBPHT	*New modified Blood Pressure to height ratio*
NPV	*Negative Predictive Value*
PA	Pressão Arterial
PAD	Pressão Arterial Diastólica
PAS	Pressão Arterial Sistólica
PLR	*Positive Likelihood Ratio*
PPV	*Positive Predictive Value*
ROC	*Receiver Operating Characteristic*
SBP	*Systolic Blood Pressure*
Sens.	*Sensitivity*
Sp.	*Specificity*
The Fourth Report	*The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents*

SUMÁRIO

1 INTRODUÇÃO

A hipertensão arterial sistêmica (HAS) é o principal fator de risco para algumas condições de alta morbimortalidade, como o acidente vascular encefálico (AVC) e infarto agudo do miocárdio (IAM). A prevalência da HAS vem aumentando ao redor do mundo, inclusive na faixa etária pediátrica, devido principalmente à atual epidemia de obesidade.

Entretanto, apesar da prevalência da HAS estar aumentando na faixa etária pediátrica, esta condição é frequentemente subdiagnosticada em crianças e adolescentes. Apesar de não ser o único fator, o complexo processo diagnóstico da HAS em crianças e adolescentes tem papel de destaque para tal. Diferentemente dos adultos, em que o diagnóstico de HAS possui pontos de corte pré-estabelecidos, os valores normais da pressão arterial (PA) na faixa etária pediátrica variam de acordo com a altura, gênero e idade. Isto leva a necessidade de análise concomitante de diversas tabelas de percentis, o que aumenta as chances de erro diagnóstico.

Algumas ferramentas foram criadas para facilitar o diagnóstico de HAS na infância. Elas podem ser divididas simplificadamente em:

1. Equações para definir o maior valor da PA normal;
2. Tabelas simplificadas;
3. Pontos de corte definidos pela razão entre PA e altura e
4. Pontos de corte simplificados.

Apesar das equações serem de mais fácil utilização, os métodos que possuem melhor acurácia na identificação de pressão arterial elevada são as tabelas simplificadas para crianças e a razão entre PA e altura para adolescentes.

O fato de a razão entre PA e altura não ser tão eficaz em crianças levou a elaboração da razão entre PA e altura modificada. Nela tenta-se corrigir a grande variação dos pontos de corte determinados pelo método utilizando-se a altura estimada das crianças aos 13 anos em vez da altura atual. Isto levou a um aumento da sensibilidade e especificidade do método na faixa etária pediátrica. Em 2016, entretanto, foi elaborada uma nova razão entre PA e altura modificada a partir da análise estatística de fatores de correção da altura estimada aos 13. Apesar da maior sensibilidade e especificidade deste novo método, não foi apontada nenhuma hipótese fisiológica para este achado. Além disto, este método só foi testado na população chinesa.

Outro fato que merece especial atenção é que as equações criadas para definir o maior valor da PA normal utilizam apenas a idade como variável determinante. Entretanto, alguns trabalhos demonstram que a variação da PA está mais atrelada à altura do que a idade. Portanto, equações baseadas na altura, em vez da idade, poderiam aumentar a sensibilidade e especificidade do método.

Logo, o objetivo desta tese é descrever os pontos de corte ideais para a nova razão entre PA e altura modificada na população brasileira e americana. Além disso, também serão descritas novas equações baseadas na altura e sua correlação com os padrões definidos no mais recente *guideline* para triagem de distúrbios pressóricos na infância.

1.1 PROBLEMATIZAÇÃO

1.1.1 Hipertensão arterial sistêmica (HAS) nos adultos, uma visão geral

A HAS é definida como níveis pressóricos aumentados de forma sustentada com base na média de duas ou mais aferições realizadas por profissionais de saúde em momentos distintos (SOCIEDADE BRASILEIRA DE CARDIOLOGIA, 2016). Em adultos, tal condição ocorre quando a pressão arterial (PA) se encontra acima de 140mmHg para pressão arterial sistólica (PAS) e 90 mmHg para diastólica (PAD). Estes níveis pressóricos acabam por causar danos a órgãos-alvo, principalmente quando associados a outros fatores de risco, como a dislipidemia e a obesidade (WEBER et al., 2014). Além disso, a HAS é um dos principais fatores de risco para condições de alta morbimortalidade e prevalência populacional, estando associada a 45% das mortes cardíacas e 51% das mortes decorrentes de acidente vascular encefálico (AVC) (LIM et al., 2012).

1.1.2 Fatores de risco

A HAS é bastante prevalente na população adulta, podendo atingir até 41% da população brasileira a depender do estudo analisado (OLMOS; LOTUFO, 2002). Entretanto, não é uma condição de distribuição uniforme. Alguns fatores de risco para presença de HAS são exaustivamente relatados na literatura médica. São eles:

- Idade: há um aumento da prevalência de HAS de forma linear a idade (PICON et al., 2013). Desta forma, espera-se um aumento desta condição de acordo com a tendência de envelhecimento populacional;
- Etnia: a HAS é mais observada em pacientes negros do que em outras etnias (FUCHS, 2011);
- Peso: a presença de sobrepeso e obesidade aumenta consideravelmente as chances de desenvolvimento de HAS (JIANG et al., 2016);
- Sedentarismo: também correlacionada com o aumento da PA e a presença de obesidade (BEUNZA et al., 2007). Algumas pesquisas demonstram que até 51% da população adulta é insuficientemente ativa (MALTA, DEBORAH CARVALHO; ANDRADE, S; STOPA, S; PEREIRA, C; SZWARCWALD, 2015);
- Ingesta de sal: um dos principais fatores de risco para HAS (HE; MACGREGOR, 2010; ZHAO et al., 2011). Um estudo nacional demonstrou que a média de consumo de sal é aproximadamente duas vezes maior do que o recomendado na população brasileira (DATASUS, [s.d.]). Apesar disto, apenas 15,5% das pessoas entrevistadas reconhecem o excesso de consumo de sal;
- Fatores socioeconômicos: alguns trabalhos demonstram que quanto menor o nível de escolaridade, maior a prevalência de HAS numa determinada população (CONEN et al., 2009; GROTTO; HUERTA; SHARABI, 2008).
- Ingestão de álcool: meta-análise de 2012 demonstrou que baixo consumo de álcool (menos que 10 g ao dia) teria efeito protetor em relação a HAS, enquanto que o consumo maior que 30g ao dia estaria associado com a presença de HAS (BRIASOULIS; AGARWAL; MESSERLI, 2012).

1.1.3 Pré-hipertensão

Apesar de HAS ocorrer somente quando a PA está acima de 140/90 mmHg, indivíduos com PAS maior que 120 e menor que 140 mmHg ou PAD maior que 80 mmHg e menor que 90 mmHg apresentam maior risco de desenvolver HAS e de apresentar alterações cardiovasculares do que indivíduos com PA abaixo de 120/80mmHg (BOOTH et al., 2017). Esta condição é chamada, em adultos, de pré-hipertensão e indivíduos que a possua também necessitam de acompanhamento adequado.

1.1.4 HAS na infância e adolescência

Três fatores são particularmente diferentes na HAS da infância: sua prevalência é bem menor, há proporcionalmente mais casos de hipertensão secundária e não há pontos de corte fixos para definição diagnóstica (VILLAGE, 2004).

1.1.5 Prevalência e etiologia de HAS na infância

A prevalência de HAS na população pediátrica varia entre 0,8% a 8,2% a depender dos critérios utilizados e o número de aferições realizadas (FIGUEIRINHA; HERDY, 2017). Em relação à etiologia, a HAS é dividida em dois grandes grupos: primária e secundária (VILLAGE, 2004). A HAS primária não possui uma causa identificável, sendo atribuída a fatores genéticos e ambientais. Na HAS secundária há uma causa orgânica para elevação patológica da PA. Caso esta causa seja solucionada, a PA também voltará aos valores normais. Exemplos são o feocromocitoma e coarctação da aorta.

Como relatado anteriormente, as causas secundárias são bem mais comuns em crianças do que em adultos (VILLAGE, 2004). Logo, a probabilidade de HAS secundária é proporcional a PA e inversamente proporcional a idade. Além disso, a HAS primária geralmente é assintomática, enquanto que a forma secundária possui sintomatologia peculiar a cada patologia.

Usualmente, a HAS causa danos a órgãos-alvo a depender do tempo em que está instalada e o nível pressórico atingido (VILLAGE, 2004). Este fato torna importante o diagnóstico de distúrbios pressóricos na infância, pois crianças hipertensas têm uma chance bastante elevada de se tornarem adultos hipertensos (JOSHI et al., 2014). Denomina-se tal fenômeno de *tracking*.

Entretanto, alguns estudos evidenciam presença de lesão em órgãos alvo típicas da HAS em crianças e adolescentes recém-diagnosticados com HAS moderada (BRADY et al., 2008). Além disso, a presença de obesidade e de consumo de alimentos com alto teor de sódio estão cada vez mais prevalentes na faixa etária pediátrica, aumentando a prevalência de HAS nesta população (FALKNER, 2008; FLYNN, 2013).

1.1.6 Processo diagnóstico de HAS na infância

Vários *guidelines* para diagnóstico de HAS na infância orientam a aferição da PA em crianças a partir dos três anos de idade (FLYNN; FALKNER, 2017; SOCIEDADE BRASILEIRA DE CARDIOLOGIA, 2016; VILLAGE, 2004). Desta forma, objetiva-se diagnosticar precocemente os casos de HAS secundária e primária, a primeira para resolução rápida da causa base e a última para controle pleno dos níveis pressóricos antes da lesão em órgãos-alvo ou da evolução para doença aterosclerótica na vida adulta.

Logo, a aferição da PA é a condição base para o diagnóstico da HAS. O método mais utilizado é o indireto, com técnica auscultatória e esfigmomanômetro aneroide calibrado (VILLAGE, 2004). Porém, a aferição da PA em crianças e adolescentes possui algumas nuances.

O tamanho do manguito é um dos principais fatores na correta aferição da PA em crianças e adolescentes. Manguitos de tamanhos inadequados podem superestimar ou subestimar o valor real da PA. A largura da bolsa de borracha deve ter aproximadamente 40% da circunferência do braço, enquanto seu comprimento deve alcançar aproximadamente 80%. Outro fator importante é o repouso da criança antes da aferição da PA. Recomenda-se que o paciente esteja sentado por cinco minutos, com costas apoiadas e pés no chão. O braço utilizado deve ser o direito, devido à possibilidade de coarctação da aorta nestes pacientes (que levaria a PA falsamente diminuídas no membro esquerdo) (VILLAGE, 2004).

Diferentemente dos adultos, o diagnóstico de HAS na faixa etária pediátrica não possui pontos de cortes fixos para PAS e PAD. Existem duas razões principais para isto: a quase inexistência de estudos longitudinais correlacionando a PA aferida na infância com o advento de complicações cardiovasculares na vida adulta (XI et al., 2017) e a variação fisiológica da PA durante o crescimento (VILLAGE, 2004).

A variação fisiológica da PA durante o crescimento está atrelada a três variáveis: gênero, idade e altura (VILLAGE, 2004). Usualmente a maior variação ocorre até o período do estirão na adolescência (KUCZMARSKI et al., 2002). Após este, a PA está muito próxima da apresentada na idade adulta.

Desta forma, de acordo com o *The Fourth Report* (VILLAGE, 2004), para classificar uma criança como normotensa ou hipertensa os seguintes passos devem ser dados:

- identificar o percentil de altura segundo idade e sexo pelas tabelas de crescimentos do CDC (figura 1 e 2);
- identificar o percentil da PA segundo a idade, o sexo e a altura nas tabelas de pressão arterial (tabela 1 e 2);
- classificar a criança de acordo com os pontos de corte:
    - PAS ou PAD< percentil 90 = normotenso;
    - PAS ou PAD ≤ percentil 95 e maior que percentil 90 = pré-hipertenso;
    - PAS ou PAD>percentil 95 e menor que percentil 99 + 5mmHg = hipertenso grau I;
    - PAS ou PAD>percentil 99 + 5mmHg = hipertenso grau II.

Uma metodologia semelhante é utilizada no novo *guideline* (FLYNN et al., 2017), com algumas diferenças:

- PAS ou PAD ≤ percentil 95 e maior que percentil 90 = pressão arterial elevada em vez de pré-hipertensão;
- PAS ou PAD>percentil 95 e menor que percentil 95 + 12 mmHg = hipertenso grau I;
- PAS ou PAD>percentil 95 + 12 mmHg = hipertenso grau II;
- Foram estabelecidos pontos de cortes fixos (semelhante aos adultos) em crianças acima de 13 anos.

1.1.7 Subdiagnóstico de HAS na infância e adolescência

Apesar da importância da HAS no contexto da saúde pública, tal condição é frequentemente subdiagnosticada em crianças e adolescentes (CUNNINGHAM, 2008; HANSEN; GUNN; KAELBER, 2007). Um estudo realizado com dados derivados de prontuários com mais de 14000 crianças e adolescentes demonstrou que 507 (3,6%) tinham HAS. Entretanto, apenas 131 destes tinham o diagnóstico descrito no prontuário ou estavam sendo tratados (HANSEN; GUNN; KAELBER, 2007). Os autores afirmam que vários fatores podem contribuir para isto, como: a ideia errônea de que HAS é muito infrequente na faixa etária pediátrica, a falta de manguitos apropriados para realizar o diagnóstico e as várias etapas para realizar o diagnóstico de HAS na faixa etária pediátrica (HANSEN; GUNN; KAELBER, 2007).

1.1.8 Métodos de triagem para HAS na infância e adolescência

Numa tentativa de auxiliar os profissionais de saúde na correta identificação de HAS, vários autores descreveram ferramentas para o diagnóstico de pré-hipertensão e HAS na infância e adolescência (CHIOLERO; PARADIS, 2013; MA C, WANG R, LIU Y, LU Q, LU N, TIAN Y, ET AL, 2017). Tais ferramentas podem ser divididas, basicamente, em:

- Tabelas simplificadas (ARDISSINO et al., 2004; KAELBER; PICKETT, 2009; MITCHELL et al., 2011);
- A razão entre PA e altura (LU et al., 2011);
- Equações para determinar o valor normal máximo da PA (BADELI; SAJEDI; SHAKIBA, 2010; SOMU; SUNDARAM; KAMALANATHAN, 2003);
- Pontos de corte simplificados (XI et al., 2017).

1.1.9 Tabelas simplificadas

Neste grupo encontram-se as tabelas descritas por Kaelber e colaboradores (KAELBER; PICKETT, 2009) (supplementary table 6 do capítulo III), por Mitchell e colaboradores (MITCHELL et al., 2011) (supplementary table 5 do capítulo III) e Ardissino e colaboradores (ARDISSINO et al., 2004) (tabela 3).

A tabela de Kaelber foi inicialmente descrita em 2009. Resumidamente, os criadores desta tabela utilizaram dados derivados do *The Fourth Report* e criaram uma tabela em que apenas a idade e o gênero eram utilizados para

classificar o paciente entre normotenso ou com distúrbio pressórico (KAELBER; PICKETT, 2009). Os descritos com distúrbio pressórico deveriam ser submetidos as orientações do *The Fourth Report*. Para tal, eles utilizaram o limite inferior da altura (percentil 5) para descrever os pontos de corte para PA máxima normal (percentil 90). Desta forma, se reduziria o número de pacientes em que a análise completa da PA seria necessária, pois o método possui uma alta sensibilidade. A tabela criada por Mitchell e colaboradores (MITCHELL et al., 2011) utilizou metodologia semelhante, porém dividida em grupos de idade de três anos.
Por outro lado, a tabela proposta de Ardissino e colaboradores consideraram a altura da criança, em vez da idade, para produzir pontos de corte específicos (ARDISSINO et al., 2004). Entretanto, a mesma foi descrita para identificar apenas HAS.

1.1.10 A razão entre PA e altura

A razão entre PA e altura foi inicialmente descrita em 2011 por Lu e colaboradores (LU et al., 2011). Este método funciona dividindo a PAS e a PAD pela altura da criança. O resultado desta divisão seria, então, comparado com um ponto de corte específico derivado da análise de uma população da qual a criança pertenceria. Caso o resultado fosse maior, tal adolescente seria classificada como hipertensa e o diagnóstico teria que ser confirmado posteriormente de acordo com o *The Fourth Report* (VILLAGE, 2004). Caso o resultado fosse inferior, então o adolescente seria classificado como normotenso.
Apesar da facilidade do método, o mesmo demonstrou ter dois problemas: a variação dos pontos de corte obtidos em diferentes populações (EJIKE; YIN, 2013; GALESCU et al., 2012; KELISHADI et al., 2014; LU et al., 2013) e não ter resultados muito satisfatórios em indivíduos com idade inferior a 13 anos (GUO et al., 2013).
Numa tentativa de resolver o problema da baixa performance do método em crianças, descrevemos uma modificação desta fórmula substituindo a altura pela altura estimada aos treze anos (MOURATO et al., 2015). Com isto, foram encontrados melhores resultados pré-teste e pós-teste do método em crianças brasileiras (MOURATO et al., 2015) e chinesas (DONG et al., 2016). A razão’

desta mudança é que a alta variação da altura nesta faixa etária (principalmente dos seis anos até os treze anos) levaria a uma grande variância da razão entre PA e altura. Utilizando a altura estimada aos treze anos, tal variância seria reduzida e o método mais confiável. A fórmula utilizada para altura estimada aos treze anos foi Altura estimada aos treze anos = Altura +7 x (13-idade), considerando que a criança cresce, em média, sete centímetros ao ano.

Em 2016, autores chineses demonstraram que a utilização da fórmula Altura + 3 x (13-idade) em vez da altura estimada aos treze anos melhorava os resultados pré-teste e pós-teste do método (MA et al., 2016). Entretanto, nenhuma razão foi salientada pelos autores para tal. Além disso, a superioridade deste método não foi comprovada em outras populações.

1.1.11 Equações para determinar o valor máximo normal da PA

Nesta categoria existem duas equações para determinar a PA máxima normal: as fórmulas de Somu e colaboradores (SOMU; SUNDARAM; KAMALANATHAN, 2003) e as fórmulas de Badeli e colaboradores (BADELI; SAJEDI; SHAKIBA, 2010).

As fórmulas de Somu foram inicialmente descritas em 2003 (SOMU; SUNDARAM; KAMALANATHAN, 2003). Elas foram obtidas a partir da regressão linear da idade em relação ao percentil 95 da PAS e PAD, considerado apenas o percentil 50 da altura para ambos os gêneros. Vale salientar que o método foi descrito antes da definição de pré-hipertensão na faixa etária pediátrica estabelecida em 2004 com o The Fourth Report(VILLAGE, 2004). Logo, tal método considerou apenas a identificação de crianças hipertensas.

Numa tentativa de resolver tal problema, Badeli e colaboradores descreveram fórmulas semelhantes à de Somu com metodologia quase idêntica (BADELI; SAJEDI; SHAKIBA, 2010). A diferença foi a utilização do percentil 90 (em vez de 95) da PAS e PAD na elaboração da fórmula. Logo, as equações de Badeli podem ser utilizadas para identificar presença de pré-hipertensão ou hipertensão. As formulas de Badeli podem ser vistas na *supplementary table 7* no capítulo III, enquanto as fórmulas de Somu podem ser vistas na tabela 4.

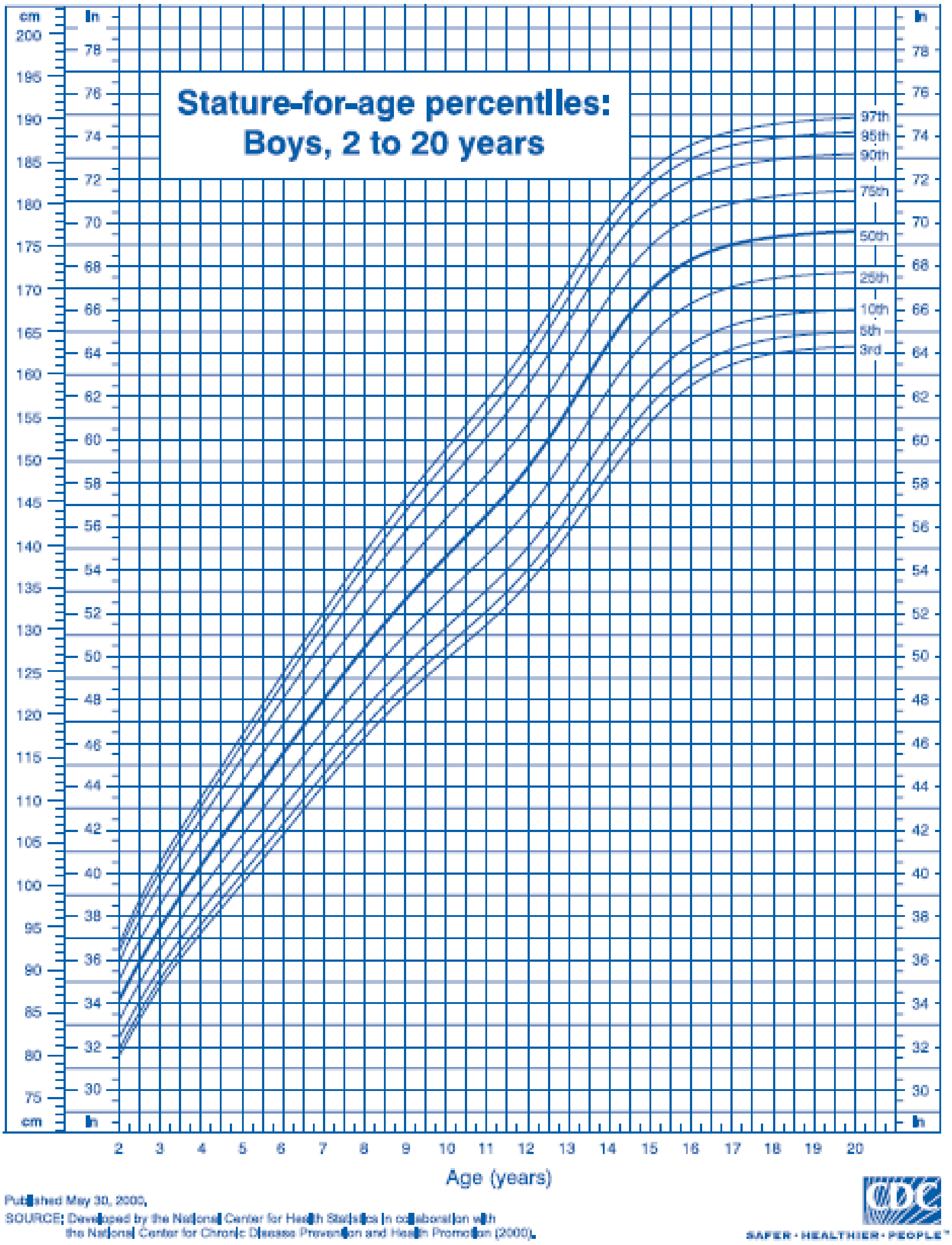
1.1.12 Comparação entre os métodos

Em um artigo anterior, foram avaliados os resultados pré-teste e pós-teste de cada um destes métodos (tabelas 5 e 6), com exceção das fórmulas descritas por Badeli (MOURATO; FILHO; MATTOS, 2014). De forma simplificada, as tabelas propostas por Mitchell e Charlene apresentaram melhor sensibilidade em crianças e adolescentes, enquanto que a razão entre PA e altura apresentou melhores resultados em adolescentes. Entretanto, nota-se que a tabela proposta por Ardissino apresenta ótima acurácia para hipertensão, levantando a hipótese que fórmulas baseadas em altura, em vez da idade, pode ser um bom método para triagem de distúrbios pressóricos na infância.

1.1.13 Novo *guideline* para diagnóstico de distúrbios pressóricos na infância

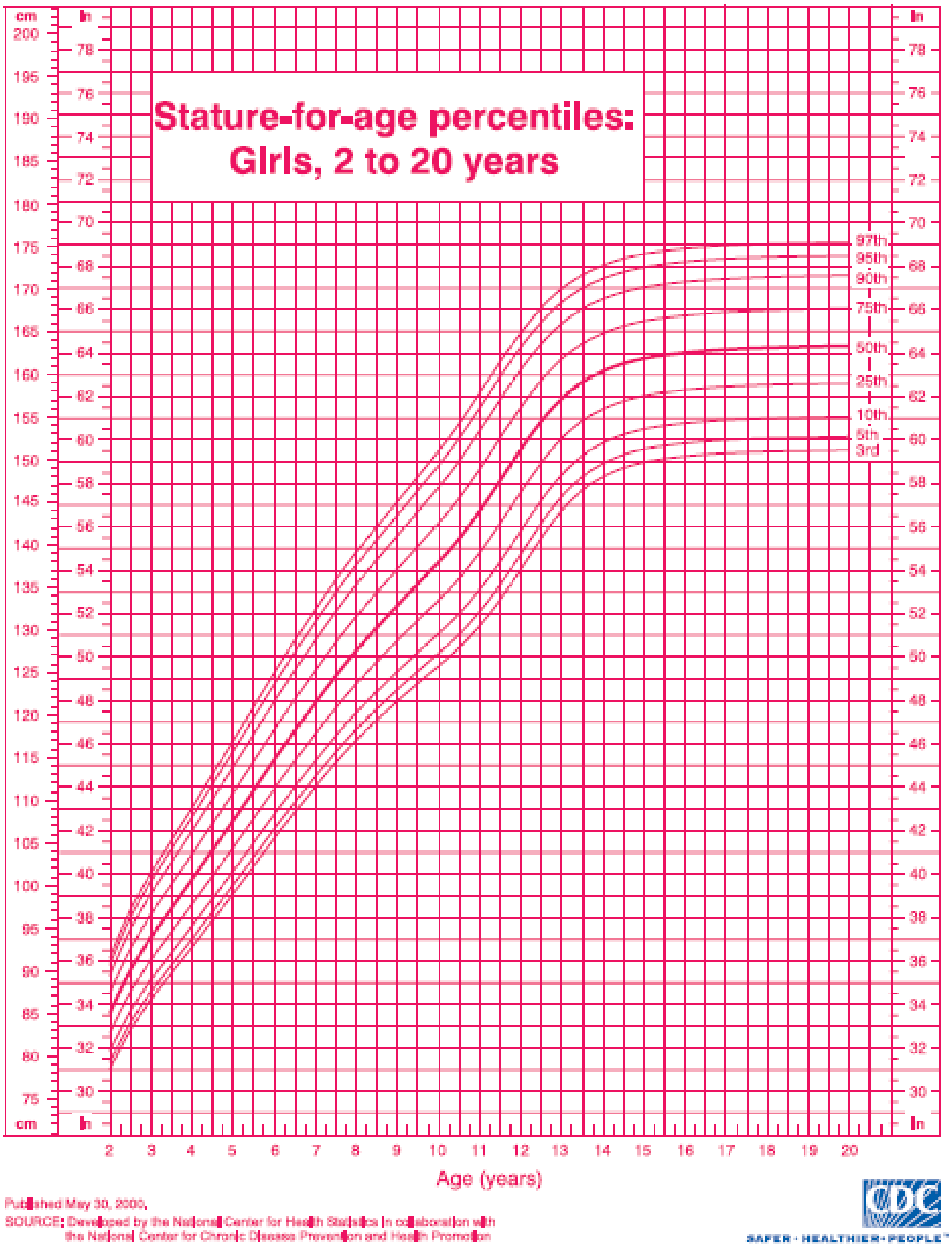
Recentemente, um novo *guideline* para diagnóstico de distúrbios pressóricos na infância foi publicado (FLYNN et al., 2017). Nele, modificou-se a metodologia para obtenção dos valores de percentis para PAS e PAD para excluir pacientes obesos da amostra. Desta forma, os valores para diagnóstico de distúrbios pressóricos em crianças e adolescentes caíram (FLYNN et al., 2017). Logo, os métodos descritos anteriormente, que eram baseados no *guideline* antigo (VILLAGE, 2004), necessitam ser revalidados de acordo com esta nova definição.

Figura 1: percentil de altura pela CDC-meninos



Fonte: *Centers for Disease Control and Prevention* (CDC)

Figura 2: Percentil da altura pela CDC - meninas



Fonte: *Centers for Disease Control and Prevention* (CDC)

Tabela 1: Percentil da PA – meninos

Blood Pressure Levels for Boys by Age and Height Percentile

Age (Year)	BP Percentile ↓	Systolic BP (mmHg)							Diastolic BP (mmHg)						
		← Percentile of Height →							← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

Fonte: Village, 2014

Tabela 2: Percentil da PA-meninas

Blood Pressure Levels for Girls by Age and Height Percentile

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

Fonte: Village, 2014

Tabela 3: tabela de Ardissino modificada

Height in cm	Blood Pressure (mmHg)			
	Male gender		Female gender	
	Systolic	Diastolic	Systolic	Diastolic
55	97	70	99	70
60	106	68	108	68
70	110	69	111	70
80	104	59	105	60
90	108	63	107	64
100	110	67	108	68
110	113	73	110	72
120	115	79	113	76
130	117	82	117	79
140	120	83	119	81
150	124	85	123	83
160	127	85	127	85
170	127	85	127	85
180	127	85	127	85
190	127	85	-	-

Fonte: ARDISSINO et al., 2004

Tabela 4: fórmulas de Somu

Somu's formulae[6]

Blood Pressure	Age	Formula
Systolic (mmHg)	Between 1 and 17 years	100 + (age in years x 2)
Diastolic (mmHg)	Between 1 and 11 years	60 + (age in years x 2)
	Between 11 and 17 years	70 + (age in years)

Fonte: SOMU; SUNDARAM; KAMALANATHAN, 2003

Tabela 5: Sensibilidade, especificidade e acurácia dos diferentes métodos (MOURATO; FILHO; MATTOS, 2014)

	5-13 years			**13-18 years**		
	Sens.	**Sp.**	**Acc.**	**Sens.**	**Sp.**	**Acc.**
BP ≥ 90th Percentile for gender, age, and height						
Ardissino et al.	63.65%	99.82%	96.09%	60.68%	99.68%	93.65%
Mitchell et al.	97.20%	77.48%	79.52%	97.43%	84.68%	86.65%
Kaelber et al.	97.20%	88.30%	89.22%	97.43%	91.25%	92.20%
Lu et al.	93.76%	64.25%	67.30%	99.14%	85.46%	87.58%
Somu et al.	58.49%	99.77%	95.51%	51.28%	100%	92.47%
BP ≥ 95th Percentile for gender, age, and height						
Ardissino et al.	89.92%	98.53%	98.02%	91.80%	97.55%	97.09%
Mitchell et al.	96.26%	73.94%	75.27%	96.72%	78.01%	79.52%
Kaelber et al.	95.52%	84.22%	84.89%	96.72%	84.05%	85.07%
Lu et al.	91.79%	77.61%	78.45%	95.08%	91.66%	91.94%
Somu et al.	84.32%	98.70%	97.84%	85.24%	98.85%	97.75%

Fonte: MOURATO; FILHO; MATTOS, 2014

Tabela 6: Valor preditivo positivo, negativo, razão de verossimilhança positiva e negativa entre os métodos

	5-13 years				13-18 years			
	PLR	NLR	PPV	NPV	PLR	NLR	PPV	NPV
	BP ≥ 90th Percentile							
Ardissino et al.	367.11	0.36	97.69%	95.98%	194.19	0.39	97.26%	93.27%
Mitchell et al.	4.32	0.04	33.21%	99.59%	6.36	0.03	53.77%	99.45%
Kaelber et al.	8.31	0.03	48.92%	99.64%	11.14	0.03	67.06%	99.49%
Lu et al.	3.93	0.25	31.16%	97.19%	23.27	0.20	81.03%	96.41%
Somu et al.	262.38	0.42	96.80%	95.43%	[a]	0.49	100%	91.82%
	BP ≥ 95th Percentile							
Ardissino et al.	61.41	0.10	79.54%	99.36%	37.59	0.08	76.71%	99.27%
Mitchell et al.	3.70	0.05	18.96%	99.68%	4.40	0.04	27.83%	99.63%
Kaelber et al.	6.05	0.05	27.71%	99.66%	6.06	0.04	34.71%	99.66%
Lu et al.	4.10	0.11	20.60%	99.33%	11.41	0.05	50.00%	99.53%
Somu et al.	64.92	0.16	80.43%	99.00%	74.16	0.15	86.67%	98.71%

Fonte: MOURATO; FILHO; MATTOS, 2014

1.2 OBJETIVOS

1.2.1 Geral

Demonstrar novas equações baseadas em altura para triagem de distúrbios pressóricos na infância.

1.2.2 Específicos

- Comparar valores pré-teste e pós-teste das novas equações baseadas em altura com outros métodos de triagem de distúrbios pressóricos na infância e adolescência;
- Verificar se a nova razão entre pressão arterial e altura modificada é um bom método para o diagnóstico de distúrbios pressóricos na infância;
- Determinar novos pontos de corte para a razão entre pressão arterial e altura e suas variantes para diagnóstico de distúrbios pressóricos na infância na população brasileira e americana.

2 MÉTODOS

2.1 POPULAÇÕES

- População brasileira: esta população foi obtida retrospectivamente de dados de prontuários de pacientes acompanhados numa clínica de cardiologia pediátrica localizada em Recife, Brasil. A análise incluiu pacientes com idade entre 8 e 13 anos e com os seguintes dados devidamente preenchidos: altura, peso, pressõ arterial sistólica e pressão arterial diastólica, Apenas a primeira aferição da pressão arterial foi consiedarada. Um total de 2936 pacientes foram incluídos na análise desta população;
- População Americana: esta população foi derivada de dados do NHANES 1999-2014. O CDC conduz está pesquisa desde o ano de 1999 na população Americana não institucionalizada. Apenas indivíduos entre 8 e 13 anos de idade e com informações completas sobre o peso, idade, gênero, PAS e PAD foram incluídos, totalizando 6541 casos.

2.2 DEFINIÇÃO DE DISTÚRBIO PRESSÓRICO

Distúrbio pressórico foi definido como PAS ou PAD maior ou igual ao percentil 90 e hipertensão como PAS ou PAD maior que o percentil 95 de acordo com o *The Fourth Report* ou com o ultimo *guideline* a depender da análise realizada.

2.3 CLASSIFICAÇÃO DO PACIENTE EM RELAÇÃO AO ÍNDICE DE MASSA CORPORAL (IMC)

Excesso de peso foi definido como um IMC entre os percentis 85 e 95 e obesidade como um IMC maior ou igual ao percentil 95 de acordo com as diretrizes do CDC.

2.4 AFERIÇÃO DA PA,DO PESO E DA ALTURA

A PA da população brasileira foi medida em ambulatórios clínicos de acordo com a rotina do serviço. Isso incluiu a medida da PA pelo método auscultatório com tensiômetro aneróide e com tamanho dos manguitos apropriados para a idade. A altura foi medida com um estadiômetro e o peso com balança eletrônica. Os métodos de aferição na população americana foram descritos previamente. Resumidamente, a PA foi medida com esfigmomanômetro de mercúrio seguindo as recomendações da *American Heart Association*, enquanto a altura e o peso foram medidos de acordo com o manual de antropometria do NHANES.

2.5 OBTENDO OS PONTOS DE CORTE PARA A RAZÃO ENTRE PA E ALTURA E SUAS VARIANTES

- A razão entre PA e altura foi calculada dividindo-se a PAS ou PAD (mmHg) pela altura (cm);
- A razão entre PA e alturma modificada foi calculada dividindo-se a PAS ou PAD por 7 x (13-idade (em anos));
- A nova razão entre PA e altura foi calculada dividindo-se a PAS ou PAD por 3 x (13-idade (em anos));
- Curvas ROC (*Characteristic Operator Characteristics*) foram plotadas para identificar os pontos de corte ideais para cada método de acordo com o índice de Younden (sensibilidade + especificidade-1) para PAS e PAD. Duas análises foram feitas: uma considerando o *The Fourth Report* como o padrão ouro e outra considerando o mais recente *guideline* como padrão ouro.

2.6 COMPARAÇÃO ENTRE OS MÉTODOS BASEADOS NA RAZÃO ENTRE PA E ALTURA COM O PADRÃO-OURO

Todos os pacientes foram classificados com ou sem distúrbio pressórico ou hipertensão de acordo com cada método. A sensibilidade, especificidade, valor preditivo positivo (VPP) e valor preditivo negativo (VPN) foram calculados com seus respectivos intervalos de confiança. O teste do qui-quadrado foi usado para comparar variáveis categóricas com um valor de p <0,05 considerado estatisticamente significante.

2.7 CONSTRUÇÃO DE EQUAÇÕES DE PA E ANÁLISE DA SUA EFICÁCIA

Foram construídas equações baseadas em altura utilizando os valores dos percentis 90 para PAS e PAD e respectivos valores de altura da atual diretriz de manejo da PA elevada em crianças e adolescentes. Equações baseadas em altura foram construídas a partir de modelos de regressão linear relacionando PAS e PAD com altura e utilizando dados combinados de meninos e meninas.

Para análise secundária, utilizamos a mesma abordagem para construir as equações da PA utilizando os valores dos percentis 90 para PAS e PAD e os valores de altura da diretriz anterior (The Fourth Report). A construção das equações da PA utilizando dados da diretriz anterior foi realizada para permitir a comparação de equações da PA baseadas na altura com métodos adicionais de triagem da desordem da PA descritos antes da liberação da diretriz atual.

Dados descritivos foram apresentados como média ± desvio padrão. O teste do qui-quadrado foi utilizado para comparar variáveis categóricas. As curvas ROC foram construídas para cada método de triagem e comparadas com o método padrão-ouro para identificação de distúrbios da PA, baseado nas definições da atual diretriz ou nas definições da diretriz anterior para análise secundária. A sensibilidade, especificidade, área sob a curva, valor preditivo positivo e valor preditivo negativo para cada método foram calculados em cada população estudada. A concordância entre cada método e o respectivo método padrão-ouro foi calculada pelo coeficiente kappa e força de concordância categorizada como ruim (kappa <0,20), regular (kappa entre 0,21 e 0,40), moderada (kappa entre 0,41 e 0,60), boa (kappa entre 0,61 e 0,80) e muito bom (kappa entre 0,81 e 1,00) 21.

Na análise principal, comparamos o desempenho das equações da PA (construídas utilizando dados da diretriz atual) e outros métodos de rastreamento para detectar distúrbios da PA definidos de acordo com ambas as diretrizes.

Valores de p <0,05 foram considerados estatisticamente significativos. Todas as análises foram realizadas usando MedCalc 17.4..

Maiores detalhes sobre as metodologias aqui apresentadas podem ser vistas nos capítulos 1, 2 e 3.

3 ARTIGO 1: A NEW MODIFIED BLOOD PRESSURE-TO-HEIGHT RATIO ALSO SIMPLIFIES THE IDENTIFICATION OF HIGH BLOOD PRESSURE IN AMERICAN CHILDREN.

Dear Dr. Mourato:

It is a pleasure to accept your manuscript entitled "A new modified blood pressure-to-height ratio also simplifies the identification of high blood pressure in American children." in its current form for publication in the Hypertension Research. The comments of the reviewer(s) who reviewed your manuscript are included at the foot of this letter.

Please note that current referencing format of Hypertension Research requests ALL authors of manuscripts cited in the body of the text to be listed in the References section. If you have truncated the number of authors in the References section, we ask you kindly to update your manuscript to reflect this change and send to the Editorial Office as attachment to an email. Full details are available at in the Instruction to Authors.

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Thank you for your fine contribution. On behalf of the Editors of the Hypertension Research, we look forward to your continued contributions to the Journal.

Sincerely,

Toshihiko Ishimitsu, MD, PhD.
Editor-in-Chief, Hypertension Research
eic-htr@jpnsh.jp

This is a pre-copyedited, author-produced version of an article accepted for publication in Hypertension Research following peer review. The version of record "Mourato FA, Nadruz Junior W, Mattos S da S. A new modified blood pressure-to-height ratio also simplifies the identification of high blood pressure in American children. Hypertens Res.. 2017 Aug 9;40(8):792–3." is available online at https://doi.org/10.1038/hr.2017.34.

Title: A new modified blood pressure-to-height ratio also simplifies the identification of high blood pressure in American children.

Running head: New modified blood pressure to height ratio in American children.

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Conflict of interest: nothing to declare.

We read with great interest the paper by Ma et al.[1] that was published in Hypertension Research in December 2016. The authors reported that a new modified blood pressure (BP)-to-height ratio formula (MBPHR3 = BP/(height (cm)+3 * (13 − age in years))) was an accurate index for the screening of hypertension in Han children aged 7–12 years.

Systemic arterial hypertension is often underdiagnosed among children and adolescents[2]. Many factors contribute to that, but the intricate diagnostic process is the major one[2]. Unlike adults, healthy BP levels in children and adolescents vary with gender, age and height[3]. This generates the need to analyze multiple percentile tables to establish a correct diagnosis, a process that hardly applies to busy pediatric clinical scenarios.

In 2011, Lu et al described the BP-to-height ratio (BPHT) as a good screening method to identify hypertension in Chinese adolescents[4]. Subsequently, such findings were confirmed in other populations[5]. However, despite the method's great efficacy in adolescents, it showed less encouraging results in children[6]. To overcome this problem, we proposed a modified BP-to-height ratio formula (MBPHR7 = BP/(height (cm)+7 * (13 − age in years)[7]. The rationale for this formula was that the great difference in height and BP among children under thirteen years negatively influence the accuracy of the BPHT screening method, and that the use of MBPHR7 could partially nullify such influence. This hypothesis was tested in Brazilian children, and MBPHR7 showed better results than BPHT. Interestingly, the new formula reported by Ma et al (MBPHR3), which was based on our previously published MBPHR7[7], but used the factor 3 instead of 7, was associated with a greater accuracy in identifying hypertension in Chinese children as compared with the BPHT and MBPHR7 formulae [1]. However, as also stated by the authors, confirmation of this finding in other populations is required.

To verify the MBPHR3 efficacy among American children, we used data from the National Health and Nutrition Examination Survey (NHANES) 1999-2014. The details of this survey have been described elsewhere[8]. Briefly, the National of Health Statistics of the Centers for Disease Control and Prevention (CDC) conducts this survey since 1999 in a non-institutionalized American population. Written confirmed consent and assent were obtained from parents and their children. Only patients with systolic BP (SBP) and diastolic BP (DBP) measurements and complete data for height, weight, gender and age between 8-12 years were included in the present analysis (only children older than 8 years had measured BP values). A total of 6587 cases were analyzed.

The MBPHR7 formula was: SBP or DBP (mmHg)/ (Height(cm)+7x(13-age(in years)). The MBPHR3 formula was: SBP or DBP (mmHg)/ (Height(cm)+3x(13-age(in years)). BPHT was estimated as SBP or DBP (mmHg)/Height (cm). Receiver Operator Characteristics curves (ROC) were plotted to identify optimal thresholds for each method with the Younden's index (sensitivity+specificity-1). Body mass index (BMI) was calculated as weight (Kg)/height^2(m^2) and classified as underweight, normal, overweight or obese in accordance with the tables presented by the CDC. The gold standard for the diagnosis of hypertension and pre-hypertension was based on the definitions of The Fourth Report on diagnosis, evaluation, and treatment of high BP in children and adolescents[2]. Such guideline uses gender, age and height to determinate the normal values of BP in children and adolescents. Therefore, hypertension was defined as SBP or DBP ≥95th percentile and pre-hypertension as SBP or DBP ≥ 90th percentile and <95th percentile. Afterwards, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of each method were calculated with the respective confidence intervals. The software used was MedCalc 16.8.4 (Software bvba, Ostend, Belgium).

A total of 3269 boys with mean±SD SBP of 103.5±9.7 mmHg; DBP of 54.5±12.0 mmHg; height 144.2±11.3 cm; BMI of 19.9±4.7 kg/m^2 and 3318 girls with SBP of 102.7±10.0 mmHg; DBP 55.6±11.1; height of 145.0±11.5 cm; BMI 20.4±5.0 kg/m^2 were included in the present study. Additionally, 3.92% of the participants were pre-hypertensive and 2.84% hypertensive. Regarding BMI, 18.02% were on overweight and 24.96% were obese.

The supplementary file demonstrates the ROC curves used to identify pre-hypertension and hypertension based on SBP and DBP values according to the studied methods (MBPHR3, MBPHR7 and BPHT). Table 1 shows the yielded cutoff points for each method and their respective values of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with confidence intervals. MBPHR3 showed higher specificity and PPV than MBPHR7 and BPHT, with similar sensitivity in most cases. Thus, the current analysis reinforces the possibility of using MBPHR3 as a screening method for high BP in children.

Regarding the equation elaboration, the MBPHR7 uses factor 7 to describe the mean height variation per year between 5 and 13 years (approximately 7 cm per year). Ma et al identified that factor 3 is superior for diagnostic purposes, but only a minority of children grow only 3 cm per year. At a first glance, this may seem as a counterpoint to the logic of MBPHR3. However, it has been demonstrated that the progressive increase of BP in children and adolescents is more correlated with the growth of the trunk instead of the whole body[9]. Coincidentally, the trunk grows approximately 3 to 4 cm per year in this age group[10]. Therefore, we believe that this new formula is more efficient because it probably considers the variation in the size of the trunk, instead of the whole body.

In conclusion, MBPHR3 showed better results than MBPHR7 and BPHT in identifying hypertension and pre-hypertension in American children aged 8-12 years with a low number of cut-off points. This fact may be related to the higher correlation between the variation of trunk size and BP. The use of this method may improve the diagnosis of high BP in children and thus prevent the progression of this condition.

Conflict of interest: The authors declare no conflict of interest.

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Table 1: Cut-off points, pre-tests and post-tests of BPHT, MPBHR3 and MPBHR7.

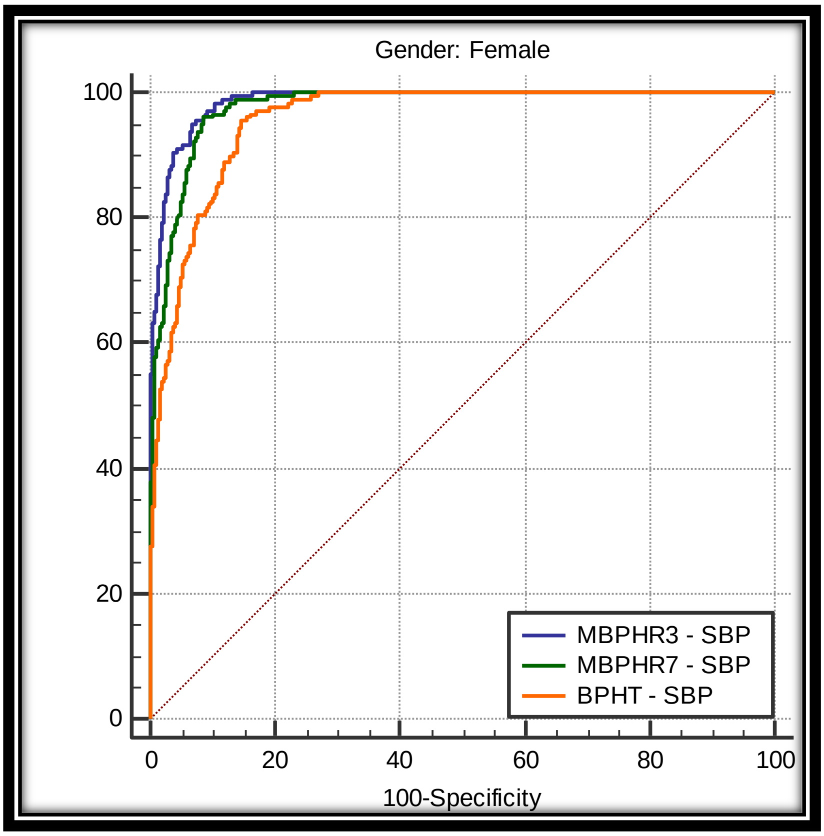
			Cut-off points (SBP/DBP)	Sensitivity (CI), %	Specificity (CI), %	PPV (CI), %	NPV (CI), %
BPHT	BP≥90th	Male	0.79/0.50	92.7 (88.4-95.8)	84.8 (83.5-86.1)	30.3 (26.9-34.0)	99.4 (99.0-99.6)
		Female	0.77/0.50	96.0 (92.6-98.2)	82.3 (80.9-83.6)	28.5 (25.3-31.8)	99.6 (99.3-99.8)
	BP≥95th	Male	0.81/0.51	98.8 (93.2-100)	87.4 (86.2-88.6)	16.5 (13.3-20.1)	100 (99.8-100)
		Female	0.80/0.52	95.3 (89.4-98.5)	88.8 (87.7-89.9)	22.1 (18.4-26.2)	99.8 (99.6-99.9)
MPBHR3	BP≥90th	Male	0.76/0.48	93.1 (88.9-96.1)	92.7 (91.7-93.6)	47.5 (42.7-52.4)	99.5 (99.1-99.7)
		Female	0.74/0.48	96.0 (92.6-98.2)	89.8 (88.7-90.9)	40.9 (36.8-45.3)	99.7 (99.4-99.8)
	BP≥95th	Male	0.78/0.49	97.5 (91.3-99.7)	94.0 (93.1-94.8)	29.0 (23.6-34.8)	99.9 (99.8-100)
		Female	0.77/0.50	97.2 (92.0-99.4)	95.4 (94.6-96.1)	41.3 (35.1-47.6)	99.9 (99.7-100)

MPBHR7	BP≥90th	Male	0.69/0.44	96.8 (93.5-98.7)	86.2 (85.0-87.4)	33.4 (29.8-37.3)	99.7 (99.4-99.9)
		Female	0.69/0.45	95.1 (91.5-97.6)	90.3 (89.2-91.3)	41.9 (37.6-46.3)	99.6 (99.3-99.8)
	BP≥95th	Male	0.71/0.47	97.5 (91.3-99.7)	90.8 (89.8-91.8)	21.1 (17.0-25.6)	99.9 (99.7-100)
		Female	0.70/0.45	96.3 (90.7-99.0)	89.9 (88.9-91.0)	24.2 (20.2-28.5)	99.9 (99.6-100)

Legend: BP-blood pressure; BPHT-BP to height ratio; CI-confidence interval; DBP-diastolic BP; MBPHR3-modified BP to height ratio (with factor 3); MBPHR7-modified BP to height ratio (with factor 7); NPV- negative predictive value; PPV- positive predictive value; SBP – systolic BP

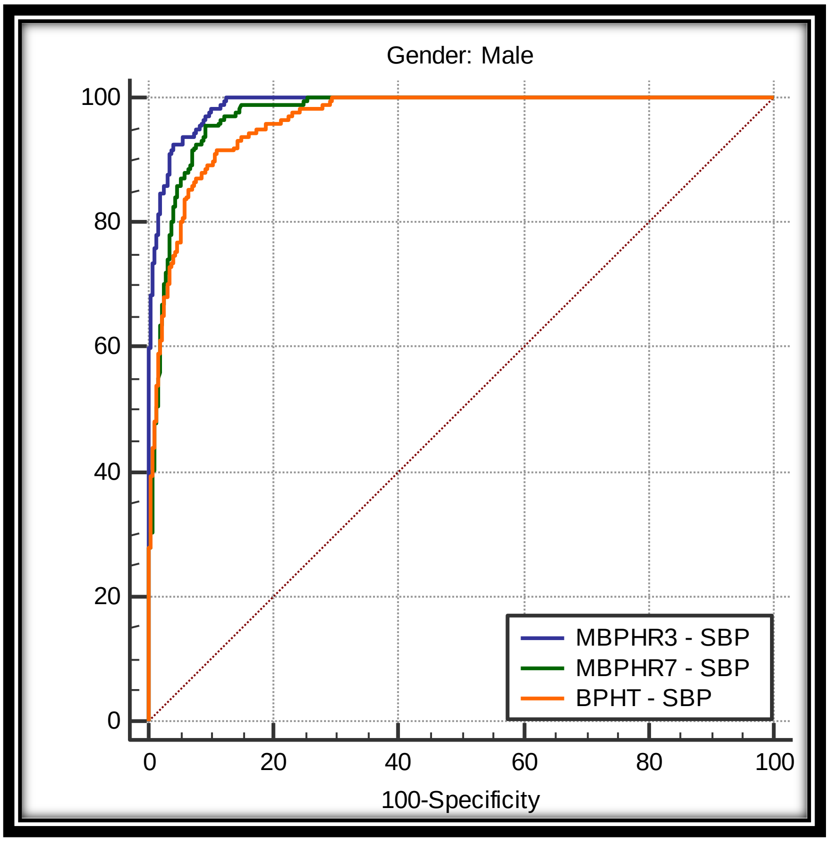
Supplementary File

Figure 1: ROC curves comparison for systolic arterial blood pressure equal or higher than the 90th percentile per formula for female gender by equation.



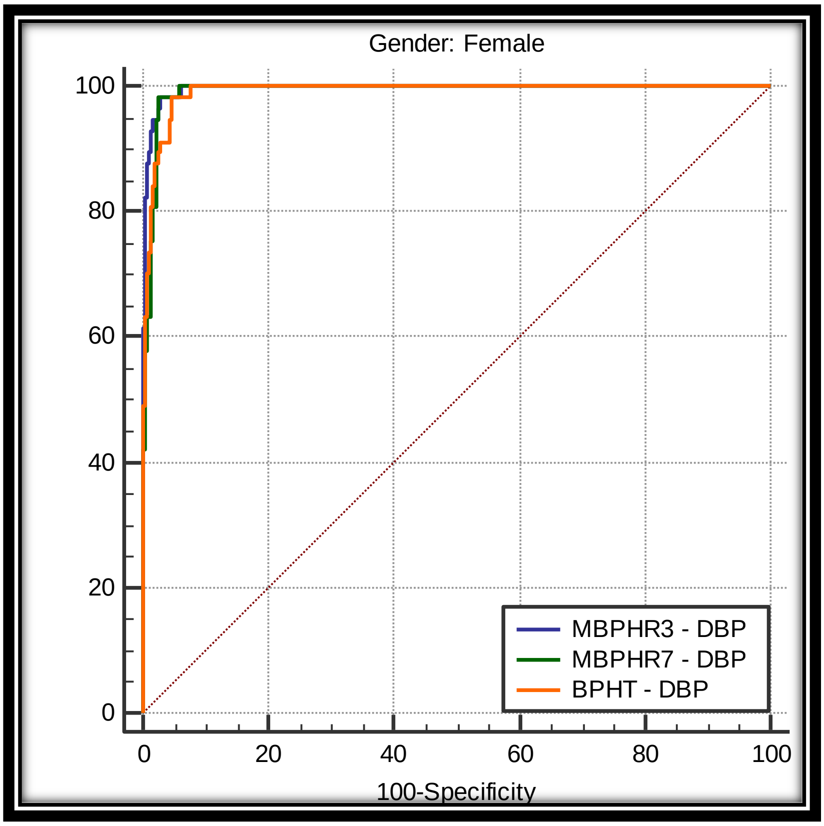
Legend: BPHT – blood pressure to height ratio. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7. SBP – systolic blood pressure.

Figure 2: ROC curves comparison for systolic arterial blood pressure equal or higher than the 90th percentile per formula for male gender by equation.



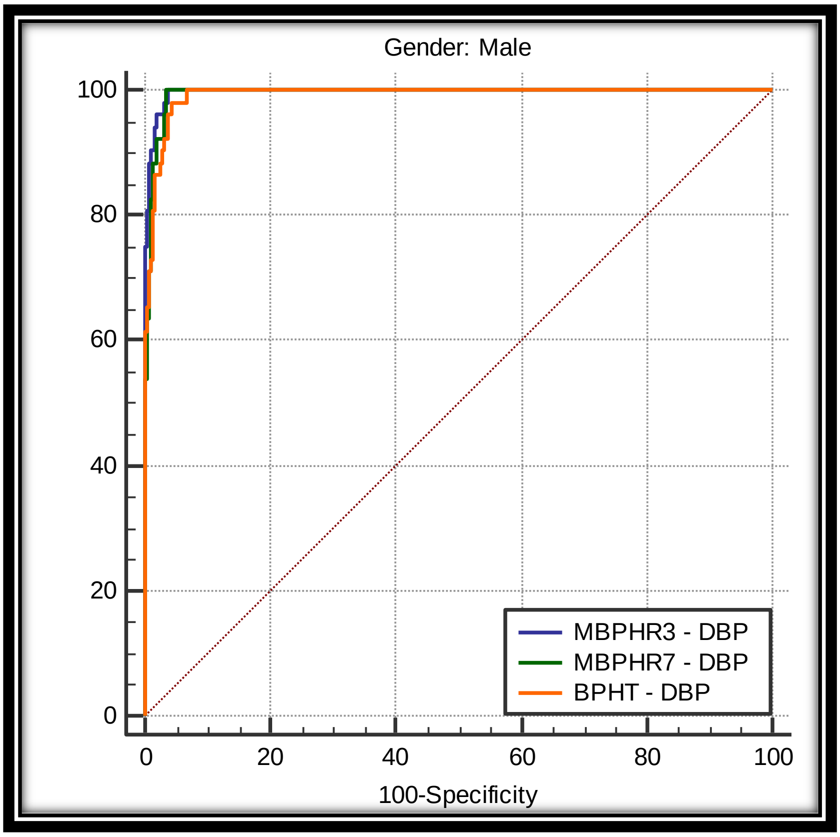
Legend: BPHT – blood pressure to height ratio. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7. SBP – systolic blood pressure.

Figure 3: ROC curves comparison for diastolic arterial blood pressure equal or higher than the 90th percentile per formula for female gender by equation.



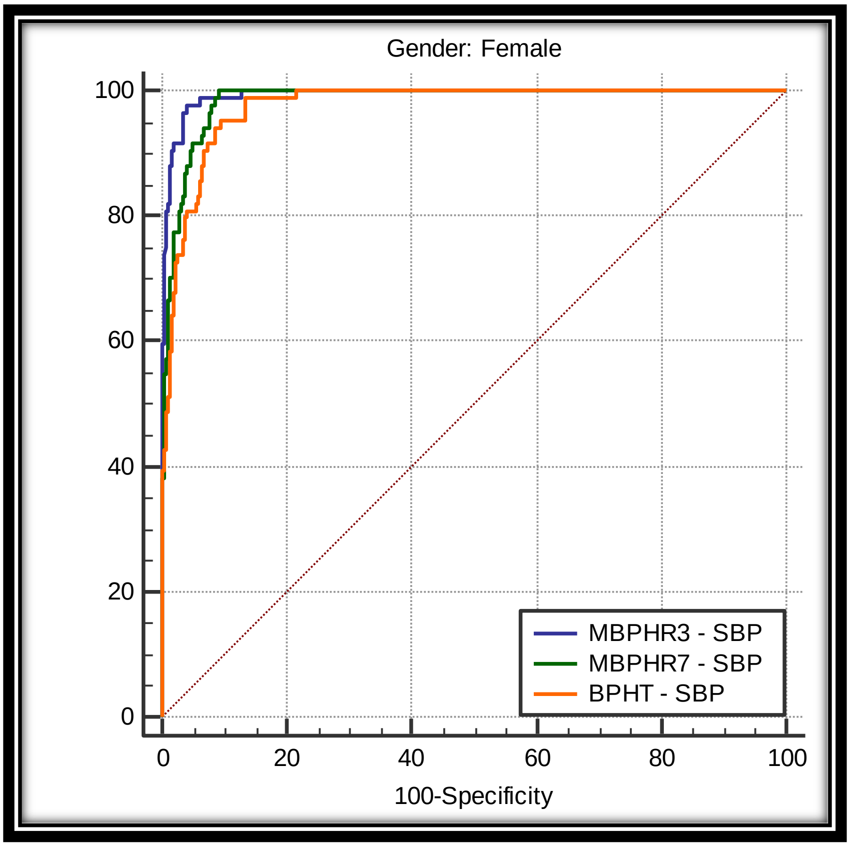
Legend: BPHT – blood pressure to height ratio. DBP – diastolic blood pressure. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7.

Figure 4: ROC curves comparison for diastolic arterial blood pressure equal or higher than the 90th percentile per formula for male gender by equation.



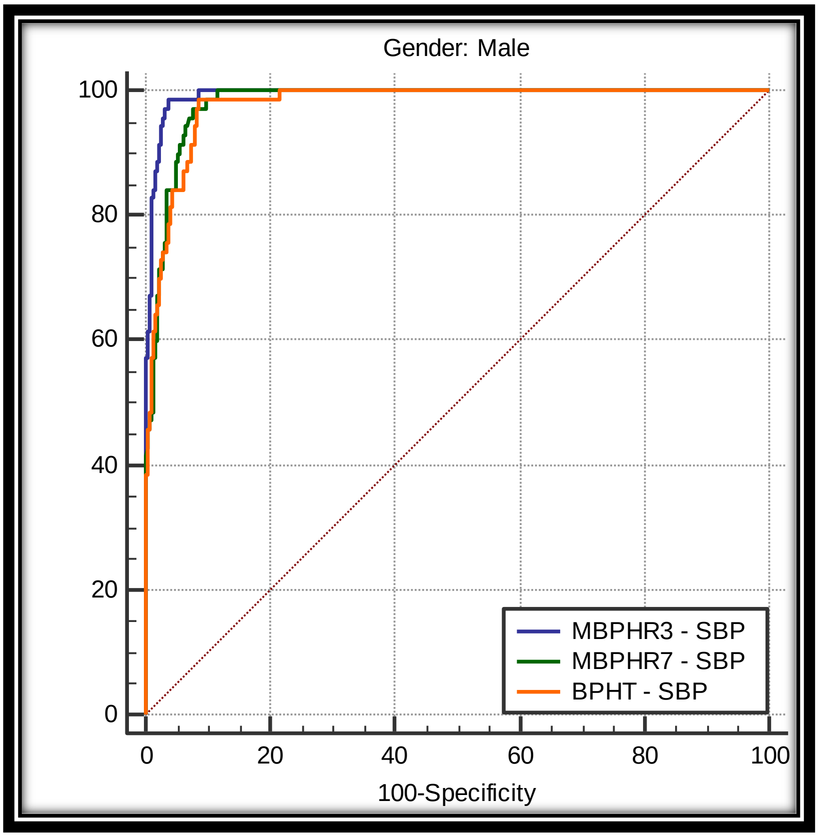
Legend: BPHT – blood pressure to height ratio. DBP – diastolic blood pressure. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7.

Figure 5: ROC curves comparison for systolic arterial pressure equal or higher than the 95th percentile per formula for female gender by equation.



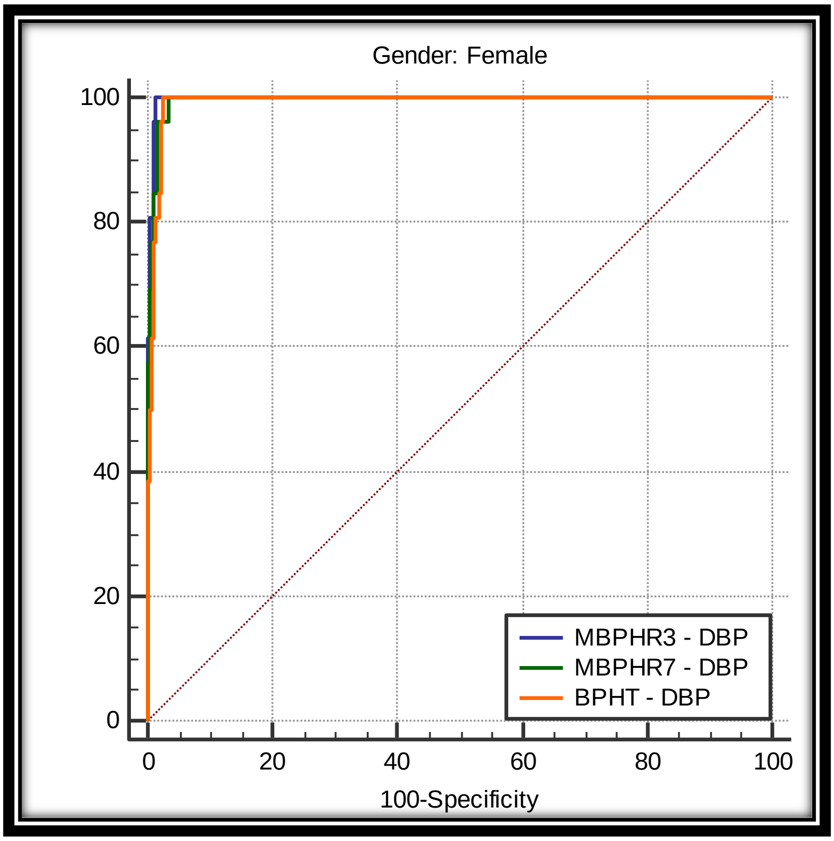
Legend: BPHT – blood pressure to height ratio. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7. SBP – systolic blood pressure.

Figure 6: ROC curves comparison for systolic arterial pressure equal or higher than the 95th percentile per formula for male gender by equation.



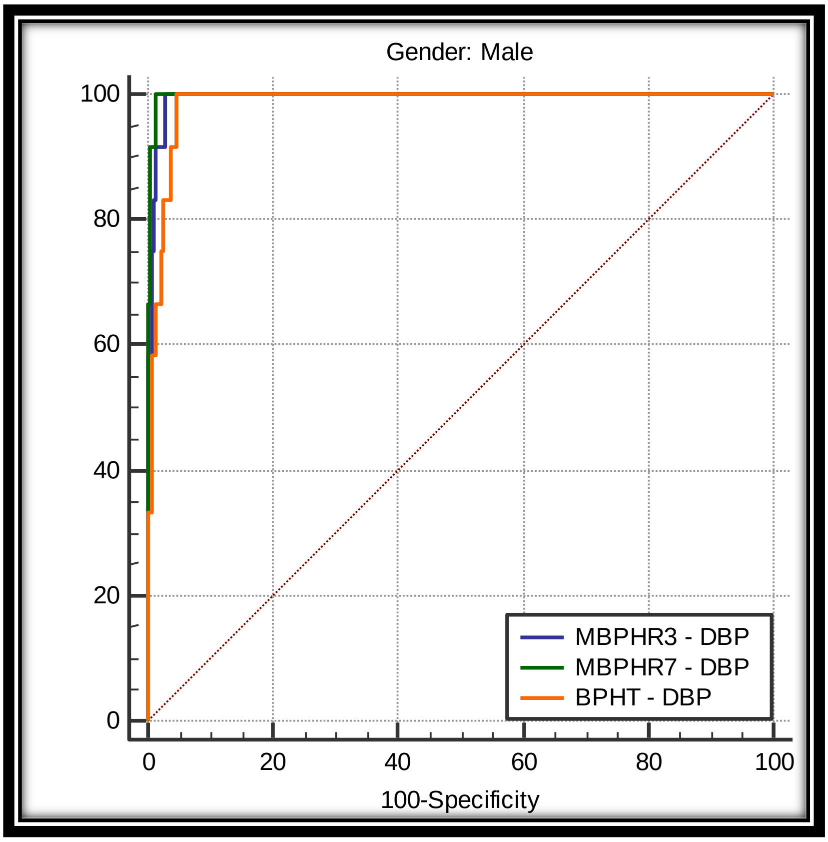
Legend: BPHT – blood pressure to height ratio. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7. SBP – systolic blood pressure.

Figure 7: ROC curves comparison for diastolic arterial pressure equal or higher than the 95th percentile per formula for female gender by equation.



Legend: BPHT – blood pressure to height ratio. DBP – diastolic blood pressure. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7.

Figure 8: ROC curves comparison for diastolic arterial pressure equal or higher than the 95th percentile per formula for male gender by equation.



Legend: BPHT – blood pressure to height ratio. DBP – diastolic blood pressure. MBPHR3 – modified blood pressure to height ratio with factor 3. MBPHR7 - modified blood pressure to height ratio with factor 7.

4 ARTIGO 2: PERFORMANCE OF BLOOD PRESSURE-TO-HEIGHT RATIO AND DERIVED VARIANTS AS SCREENING TOOLS FOR THE DIAGNOSIS OF HIGH BLOOD PRESSURE IN CHILDREN

Publicado na revista "*Journal of Clinical Hypertension*".
Fator de impacto: 3,242 (2016)

07-Nov-2017

Dear Dr. Mourato:

It is a pleasure to accept your letter to the editor entitled "Performance of blood pressure-to-height ratio and derived variants as screening tools for the diagnosis of high blood pressure in children" in its current form for publication in The Journal of Clinical Hypertension.

Felipe: I wonder whether the title could be simplified and shortened. For instance:
"New Modifications of the Blood Pressure to Height Ratio for the Diagnosis of High Blood Pressure in Children" We find that shorter and simpler titles increase the readership of items in the Journal. Your choice. If you decide to make this change please do so when you receive your proofs from the publisher -- that way we will not delay publication of your interesting work. With kind regards. Michael

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Thank you for your fine contribution. On behalf of the Editors of The Journal of Clinical Hypertension, we look forward to your continued contributions to the Journal.

Sincerely,
Dr. Michael Weber
Editor in Chief

DOI: 10.1111/jch.13178

LETTER TO THE EDITOR

WILEY

New modifications of the blood pressure-to-height ratio for the diagnosis of high blood pressure in children

To the Editor

High blood pressure (BP) is frequently underdiagnosed in the pediatric population mainly due to the complex diagnosis process,[1] which involves the analysis of multiple tables and charts. The BP-to-height ratio (BPHT) is a simple screening tool that has shown good ability to identify high BP in children.[2] Conversely, variations in this formula, including the modified BP-to-height ratio (MBPHT)[3] and the new modified BP-to-height ratio (NMBPHT),[4,5] have been reported to provide better screening performance than the original BP-to-height ratio. However, a recent guideline changed the BP percentiles values in children and adolescents,[6] virtually nullifying these findings. Therefore, we calculated new cut-off points for BPHT, MBPHT, and NMBPHT using data from the new guideline and compared the performance of these methods to diagnose high BP in large Brazilian and American populations.

This study included subjects that ranged in age from 8 to 13 years and with complete information on height, weight, sex, systolic BP (SBP), and diastolic BP (DBP) from 2 distinct populations. The first population (n = 2936; 1241 girls) was obtained from a database built from medical charts in a pediatric cardiology center in Brazil.[3] The second population (n = 6541; 3298 girls) was obtained from data derived from the National Health and Nutrition Examination Survey (NHANES) 1999-2014.[7-9] Only the first BP measurement was used in the analyses and details regarding the acquisition of data are reported elsewhere.[3,7-9] BP disorders were defined as SBP or DBP ≥90th percentile and hypertension was defined as SBP or DBP ≥95th percentile according to the most recent guideline.[6] The BPHT formulas were: SBP or DBP (mm Hg)/Height (cm). The MBPHT formulas were: SBP or DBP (mm Hg)/7 × (13 − age [in years]). The NMBPHT were: SBP or DBP (mm Hg)/3 × (13 − age [in years]). Receiver Operator Characteristics (ROC) curves were plotted to identify optimal SBP and DBP cut-off points to identify BP disorders or hypertension. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were

TABLE 1 Performance of BPHT, MBPHT, and NMBPHT to detect BP disorders (BP ≥ 90th percentile) and hypertension (BP ≥ 95th percentile) in Brazilian children

	Cut-off points (SBP/DBP)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
BPHT-BP ≥ 90th percentile					
Male	0.77/0.49	96.3 (93.3-98.2)	77.6 (75.4-79.8)	44.9 (42.5-47.4)	99.1 (98.4-99.5)
Female	0.76/0.49	98.3 (95.1-99.7)	74.3 (71.5-76.9)	38.8 (36.4-41.3)	99.6 (98.9-99.9)
MBPHT-BP ≥ 90th percentile					
Male	0.67/0.42	100 (98.6-100)	77.5 (75.3-79.7)	45.8 (43.4-48.2)	100
Female	0.66/0.43	100 (97.9-100)	78.5 (75.9-80.9)	43.6 (40.8-46.4)	100
NMBPHT-BP ≥ 90th percentile					
Male	0.73/0.48	98.9 (96.8-99.8)	88.1 (86.3-89.8)	61.2 (57.8-64.6)	99.8 (99.3-99.9)
Female	0.74/0.47	98.9 (96.0-99.9)	89.7 (87.7-91.4)	61.4 (57.1-65.5)	99.8 (99.2-99.9)
BPHT-BP ≥ 95th percentile					
Male	0.79/0.49	98.9 (95.9-99.9)	78.0 (75.9-80.1)	34.1 (32.0-36.3)	99.8 (99.3-100)
Female	0.79/0.49	97.6 (93.1-99.5)	80.9 (78.5-83.2)	36.4 (33.6-39.3)	99. 7 (99.0-99.9)
MBPHT-BP ≥ 95th percentile					
Male	0.69/0.45	98.3 (95.1-99.6)	89.0 (87.3-90.5)	50.7 (47.1-54.3)	99.8 (99.3-99.9)
Female	0.69/0.44	98.4 (94.3-99.8)	88.4 (86.3-90.2)	48.6 (44.6-52.7)	99.8 (99.2-100)
NMBPHT-BP ≥ 95th percentile					
Male	0.75/0.48	98.3 (95.1-99.6)	88.4 (86.6-89.9)	49.3 (45.8-52.8)	99.8 (99.3-99.9)
Female	0.75/0.47	99.2 (95.6-100)	84.0 (81.7-86.1)	40.2 (37.7-44.2)	99.9 (99.3-100)

BP, blood pressure; BPHT, BP-to-height ratio; CI, confidence interval; DBP, diastolic BP; MBPHT, modified BP-to-height ratio; NMBPHT, new modified BP-to-height ratio; NPV, negative predictive value; PPV, positive predictive value; SBP, systolic BP.

TABLE 2 Performance of BPHT, MBPHT, and NMBPHT to detect BP disorders (BP ≥ 90th percentile) and hypertension (BP ≥ 95th percentile) in American children

	Cut-off points (SBP/DBP)	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
BPHT-BP ≥ 90th percentile					
Male	0.77/0.48	93.3 (90.7-95.4)	81.9 (80.4-83.3)	48.0 (45.9-50.0)	98.6 (98.0-99.0)
Female	0.76/0.47	95.8 (93.6-97.4)	80.7 (79.2-82.2)	45.8 (43.8-47.7)	99.1 (98.7-99.4)
MBPHT-BP ≥ 90th percentile					
Male	0.66/0.42	98.0 (96.3-99.0)	75.7 (74.1-77.3)	42.0 (40.3-43.6)	99.5 (99.1-99.7)
Female	0.66/0.43	95.0 (92.6-96.8)	81.5 (80.0-82.9)	46.5 (44.5-48.5)	99.0 (98.5-99.3)
NMBPHT-BP ≥ 90th percentile					
Male	0.73/0.45	97.6 (95.8-98.7)	86.0 (84.6-87.3)	55.5 (53.2-57.8)	99.5 (99.1-99.7)
Female	0.72/0.44	99.2 (97.9-99.8)	82.0 (80.5-83.4)	48.2 (46.3-50.2)	99.8 (99.5-99.9)
BPHT-BP ≥ 95th percentile					
Male	0.79/0.49	97.6 (94.9-99.1)	84.4 (83.1-85.7)	34.4 (32.5-36.3)	99.8 (99.5-99.9)
Female	0.78/0.49	97.5 (94.6-99.1)	84.2 (82.9-85.5)	32.6 (30.8-34.5)	99.76 (99.5-99.9)
MBPHT-BP ≥ 95th percentile					
Male	0.68/0.44	95.6 (92.3-97.8)	83.4 (82.0-84.7)	32.5 (30.7-34.4)	99.6 (99.2-99.8)
Female	0.68/0.43	97.5 (94.1-99.1)	84.3 (83.0-85.6)	32.7 (30.9-34.6)	99.8 (99.5-99.9)
NMBPHT-BP ≥ 95th percentile					
Male	0.75/0.46	100 (98.5-100)	79.4 (77.9-80.9)	28.9 (27.4-30.3)	100
Female	0.74/0.46	99.2 (97.0-99.9)	87.6 (86.4-88.8)	38.5 (36.3-40.7)	99.9 (99.7-100)

BP, blood pressure; BPHT, BP-to-height ratio; CI, confidence interval; DBP, diastolic BP; MBPHT, modified BP-to-height ratio; NMBPHT, new modified BP-to-height ratio; NPV, negative predictive value; PPV, positive predictive value; SBP, systolic BP.

calculated with their respective 95% confidence intervals for each method. The classification of BP disorders and hypertension according to the most recent guideline[6] was considered the gold standard.

Brazilian boys and girls with mean ± SD age = 10.0 ± 1.4 and 9.9 ± 1.4 years, SBP = 102.6 ± 10.0 and 102.1 ± 9.7 mm Hg, DBP = 63.1 ± 8.3 and 62.9 ± 7.9 mm Hg, height = 139.6 ± 10.3 and 139.2 ± 11.9 cm, weight = 35.5 ± 11.8 and 36.8 ± 11.5 kg, respectively, and American boys and girls with age = 10.1 ± 1.4 and 10.1 ± 1.4 years, SBP = 103.5 ± 9.7 and 102.7 ± 10.0 mm Hg, DBP = 54.5 ± 12.0 and 55.6 ± 11.1 mm Hg, height = 144.2 ± 11.3 and 145.1 ± 11.5 cm, weight = 42.3 ± 14.5 and 43.9 ± 15.2 kg, respectively, were included in the analyses. BP disorders were present in 14.8% and 15.2%, while hypertension was found in 10.2% and 7.5% of Brazilian and American children, respectively.

The cut-off points and performance of BPHT, MBPHT, and NMBPHT in Brazilian and American children are presented in Tables 1 and 2, respectively. All methods had high sensitivity and NPV in all studied scenarios. However, NMBPHT showed superior specificity and PPV for the diagnosis of BP disorders in American and Brazilian children. Regarding the identification of hypertension, BPHT, MBPHT, and NMBPHT tended to show similar specificity and PPV in American children, while MBPHT appeared to show better performance in Brazilian children.

The present study described novel cut-off points for BPHT, MBPHT, and NMBPHT, which were built using new guideline data.[6] Consistent with studies based on the former guideline[10] for BP management in children,[4,5] we also showed that NMBPHT had greater performance to detect BP disorders. This superiority can be explained by the better ability of this formula to capture trunk's growth,[5] which is more correlated with BP than whole body's growth.[11] These findings suggest that NMBPHT is a useful tool for the screening of BP disorders in children.

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CONFLICT OF INTEREST

None.

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5 ARTIGO 3: HEIGHT-BASED EQUATIONS CAN IMPROVE THE DIAGNOSIS OF ELEVATED BLOOD PRESSURE IN CHILDREN

Aceito pela revista "*American Journal of Hypertension*".
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Dear Dr. Mourato,

I am pleased to inform you that your submission titled "HEIGHT-BASED EQUATIONS CAN IMPROVE THE DIAGNOSIS OF ELEVATED BLOOD PRESSURE IN CHILDREN" has been accepted for publication. Your contribution will help the American Journal of Hypertension maintain its status as a forum for scientific inquiry of the highest standard.

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HEIGHT-BASED EQUATIONS CAN IMPROVE THE DIAGNOSIS OF ELEVATED BLOOD PRESSURE IN CHILDREN

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Running head: BP screening equations in children

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Keywords: blood pressure; diagnosis; hypertension; screening; pediatrics; height.

Abstract

Background: High blood pressure is usually underdiagnosed in children and adolescents, particularly due to its complex diagnosis process. This study describes novel height-based equations for the detection of blood pressure (BP) disorders (BP>90th percentile) and compares the accuracy of this approach with previously described screening methods to identify BP disorders.

Methods: Height-based equations were built using the 90th percentile values for systolic and diastolic BP and respective height values from the current guideline of high BP management in children. This guideline was also used as the gold standard method for identification of BP disorders. The equations were tested in Brazilian (n=2,936) and American (n=6,541) populations of children with 8–13 years-old.

Results: the obtained equations were 70+0.3*height (in cm) for systolic BP and 35+0.25*height (in cm) for diastolic BP. The new equations were tested in Height-based equations presented sensitivity and negative predictive value of near 100% and specificity >91%, and showed higher specificity and positive predictive value when compared to other screening tools. Importantly, height-based equations had greater agreement (kappa coefficient=0.75–0.81) with the gold standard method than the other methods (kappa coefficient=0.53–0.73). Further analysis showed that alternative height-based equations designed to identify hypertension (BP≥95th percentile) also showed superior performance (kappa coefficient=0.89–0.92) compared to other screening methods (kappa coefficient=0.43–0.85).

Conclusions: These findings suggest that the use of height-based equations may be a simple and feasible approach to improve the detection of high BP in the pediatric population.

Introduction

Hypertension is progressively affecting the pediatric age group, raising the need for additional efforts to prevent such risk factor in this population[1,2]. A recent guideline[3] established that adolescents ≥13 years of age with systolic blood pressure (SBP) above 120 mmHg or diastolic blood pressure (DBP) above 80 mmHg are considered to have blood pressure (BP) disorders, which include elevated BP (formerly termed "pre-hypertension") and hypertension. However, in children <13 years of age, those thresholds vary according to individuals' age, sex and height[3]. This nuance makes the diagnosis of BP disorders more challenging in the pediatric age group, requiring the constant analysis of charts and tables of percentiles for the correct diagnosis. Moreover, this diagnostic approach is pointed out as a major reason for the underdiagnosis of BP disorders in this population[4].

Some methods have been described to simplify the diagnosis of BP disorders in the pediatric population[5]. They include the use of simplified tables[6,7], cutoffs determined by the ratio between BP and height[8,9], equations to determinate the maximum normal BP value per patient[10,11] and simplified BP cutoffs[12]. However, each method has specific disadvantages. Simplified tables require the use of the table itself, while cutoffs determined by BP-to-height ratio may vary among different populations and genders. BP equations, in turn, have shown lower sensitivity and specificity when compared with other screening methods[13].

One potential explanation for the lower accuracy of BP equations to detect BP disorders may be the choice of the adjusting variable included in the formulae. BP equations built to date are based on regression analyses using age as the main adjusting variable[10,11]. Interestingly, alternative methods that use height as the main adjusting variable have consistently shown good accuracy[13], raising the hypothesis that including height into BP equations might improve the detection of BP disorders. Additionally, recent guideline[3] recommendations changed the values of BP percentiles for children, thus invalidating the cutoffs obtained from the aforementioned methods[8–11] and supporting the need of novel analysis using data from current guidelines aiming to facilitate the diagnosis of BP disorders. The objective of this study is to describe simple height-based equations built from current guideline data[3] for the detection of BP disorders and compare the accuracy of this new methodology with previously described methods in two different populations.

Methods

Study populations

Study Population 1 was retrospectively obtained from a medical database including 17,083 children and adolescents evaluated in a pediatric cardiology center from northeast Brazil[14]. Only individuals with age between 8 and 13 years old who had complete information on height, weight, sex, SBP and DBP were included, leaving 2,936 subjects for the current analysis.

Study Population 2 included subjects from the National Health and Nutrition Examination Survey (NHANES) 1999–2014 database. The details of this survey have been described elsewhere[15]. Only subjects with age between 8 (only patients with 8 years or more had their blood pressure measured) and 13 years old, and with complete information on height, weight, sex, SBP and DBP were included, leaving 6,541 subjects for the current analysis.

Clinical variables

BP, height and weight measurements from study population 1 were performed as previously described[14]. Briefly, BP was measured by the auscultatory method using aneroid sphygmomanometers (BIC, Itupeva, Brazil), and appropriate cuffs' size for the age. Height was measured using a stadiometer (Caumaq 101PL, Cachoeira do Sul, Brazil) and weight was measured using an electronic scale (Black&Decker BK30, Shandong, China). The methods of BP measurement in study population 2 were described elsewhere[16]. Briefly, BP was measured using mercury sphygmomanometers following recommendations from the American Heart Association, while height and weight were measured according to NHANES Anthropometry Procedures Manual[17]. This study only considered the first BP measurement in the analysis.

BP disorder was defined as a value of SBP or DBP >90th percentile, thus including BP levels >90th percentile and <95th percentile (elevated BP) and BP levels ≥95th percentile (hypertension).

Body mass index (BMI) was calculated as weight (kg) divided by height (m) squared. Overweight was defined as a BMI between the 85th and 95th percentiles and obesity was defined as a BMI greater than or equal to the 95th percentile according to CDC[18].

Construction of BP equations

For the main analysis, we built height-based equations using the 90th percentiles values for SBP and DBP and respective height values from the current guideline of management of high BP in children and adolescents[3]. Height-based equations were constructed from linear regression relating SBP and DBP with height and used combined data from both boys and girls. Later, a mountain plot was created by computing a percentile for each ranked difference between the results of the new formulae and the 90th percentile of SBP and DBP by height, gender and age reported in the current guideline[3]. For sensitivity analysis, we used the same approach to construct alternative BP equations using the 95th percentiles values for SBP and DBP from the current guideline[3].

For secondary analysis, we used the same approach to construct BP equations using the 90th percentiles values for SBP and DBP and height values from the previous guideline (The Fourth Report)[19], instead of the current guideline[3]. The construction of BP equations using data from the previous guideline was performed to allow the comparison of height-based BP equations with additional BP disorder screening methods[6,7,10,20] described before the release of current guideline.

Statistical analysis

Descriptive data are presented as mean ± standard deviation. Chi-square method was used to compare categorical variables. Each screening method were compared with the gold standard method for identification of BP disorders, which was based on the definitions of the current guideline[3] for the main analysis or on the definitions of the previous guideline (The Fourth Report)[19] for secondary analysis. The sensitivity, specificity, area under curve (AUC), positive predictive value (PPV) and negative predictive value (NPV) for each method were calculated in both populations. The agreement between each method and the respective gold standard method was calculated using the kappa coefficient and the strength of agreement categorized as poor (kappa<0.20), fair (kappa between 0.21 and 0.40), moderate (kappa between 0.41 to 0.60), good (kappa between 0.61 and 0.80) and very good (kappa between 0.81 and 1.00)[21].

In the main analysis, we compared the performance of BP equations and other screening methods to detect BP disorders defined according to the current guideline[3]. The other screening methods included: 1) the new screening table described in the current clinical practice guideline (CPG table)[3], 2) the simplified cutoffs described by Xi et al[12] (SBP ≥110 mmHg and/or DBP ≥70 mmHg for children between 6 to 11 years, and SBP ≥120 mmHg and/or DBP≥80 mmHg for adolescents aged 12 to 17 years) and 3) the BP-to-height ratio cutoffs[20]. Regarding the latter method, we calculated new cutoffs for BP disorders with ROC curves, using the current guideline as the gold standard (**Supplementary table 1**). As a sensitivity analysis, we built alternative height-based equations aiming to identify hypertension (SBP or DBP ≥95th percentile) and compared their performance with two other screening methods: 1) BP-to-height ratio, with new calculated cutoffs for hypertension for both populations utilizing ROC curves (**Supplementary table 2**) and 2) the simplified cutoffs[12] for hypertension (SBP ≥120 mmHg and/or DBP ≥80 mmHg for children between 6 to 11 years, and SBP ≥130 mmHg and/or DBP≥85 mmHg for adolescents aged 12 to 17 years).

In secondary analysis, we compared the performance of BP equations (built using data from the previous guideline–Fourth report)[19], with the table proposed by Kaelber et al[6], the simplified cutoffs[12] and the BP-to-height ratio cutoffs to detect BP disorders defined according to the previous guideline[19]. In addition, we evaluated the performance of the table proposed by Mitchell et al[7] and the equations described by Badeli et al[10], which were built solely using data from the previous guideline. Regarding the BP-to-height method, we used cutoffs that were previously reported for population 1[14] (**Supplementary table 3**). Although cutoffs were previously described for population 2[22], there were differences in patients' selection in that aforementioned study in comparison with the present report. Therefore, we calculated new cutoffs for BP disorders for population 2 using ROC curves (**Supplementary table 4**). The other studied methods are detailed in **Supplementary tables 5 to 7**.

P-values <0.05 were considered statistically significant. All analyses were performed using MedCalc 17.4 (Ostend, Belgium).

Results

Table 1 describes the characteristics of the studied populations. BP disorders, determined according to the current guideline definitions[3], were present in 13% of the American population and 14% of the Brazilian population. Overweight and obesity were present in 42.7% and 37.5% of American and Brazilian individuals, respectively.

Height-based equations obtained from the current guideline to detect BP disorders (BP >90th percentile):

The results of linear regression models relating the 90th percentiles values for SBP or DBP and respective height values from the current guideline[3] are shown in **Figure 1**. The constant and the coefficient obtained for height were rounded to values that are easier to remember and within the confidence intervals. Therefore, the following equations for the lowest values of elevated BP (90^{th} percentile) were obtained:

- SBP 90th = 70 + 0.3 x height (in cm);
- DBP 90th = 35 + 0.25 x height (in cm);

Figure 2 shows the Mountain Plots for the difference between the 90^{th} percentile for SBP or DBP values derived from the current guideline[3] and obtained SBP or DBP values from the formulae in children between 8 and 13 years. The maximum difference between the formulae and the gold standard method BP values was approximately 3 mmHg for SBP and 6 mmHg for DBP.

Table 2 shows the results of sensitivity, specificity, AUC, PPV and NPV, as well as kappa coefficients for the studied methods to detect BP disorders according to the gold standard method (current guideline definition)[3]. All studied methods had great sensitivity and NPV in both populations. In particular, the sensitivity and NPV of height-based equations was 100%. In both populations, height-based equations had greater specificity, AUC and PPV than the CPG table, simplified cutoffs and BP-to-height cutoffs. In American, height-based equations showed a very good agreement with the gold standard method to detect BP disorders (kappa coefficient = 0.80), while the kappa coefficients for the other studied methods were remarkably lower (from 0.53 to 0.61). In Brazilian individuals, height-based equations showed good agreement for height-based equations (kappa coefficient = 0.75), slightly better than the CPG table (kappa coefficient = 0.73).

Height-based equations obtained from the current guideline to detect hypertension (BP ≥95th percentile):

As a sensitivity analysis, we built the following height-based equations **(detailed in Supplementary Figures 1 and 2)** to identify hypertension using the 95^{th} percentiles values for SBP or DBP and respective height values from the current guideline[3]:

- SBP 90th = 75 + 0.3 x height (in cm);
- DBP 90th = 40 + 0.25 x height (in cm);

The results of sensitivity, specificity, AUC, PPV, NPV and kappa coefficient for height-based equations, simplified cutoffs, and BP-to-height cutoffs to detect hypertension (BP ≥ 95th percentile) using the current guideline[3] as the gold standard are shown in **Table 3**. The κappa coefficient of height-based equations with the gold standard method was 0.92 and 0.89 in the Brazilian and American populations, respectively, while the other methods had inferior agreement with the gold standard.

Height-based equations obtained from the previous guideline to detect BP disorders (BP >90th percentile):

As a secondary analysis, we built height-based equations to detect BP disorders (BP >90th percentile) using data from the previous guideline (Fourth report)[19]:

- SBP 90th = 70 + 0.33 x (height in cm);
- DBP 90th = 40 + 0.25 x (height in cm);

Table 4 shows the results of sensitivity, specificity, AUC, PPV, NPV and kappa coefficient for several methods to detect BP disorders using the previous guideline[19] as the gold standard. All studied methods showed great sensitivity and NPV, but height-based equations showed greater specificity, PPV and AUC in both populations. The agreement of height-based equations with the previous guideline (κappa coefficient) was very good while the other methods had remarkably lesser agreement with the gold standard method in both populations.

Discussion

In this study, we described simple height-based equations as screening methods to identify BP disorders (BP >90th percentile) and compared the ability of this novel approach and previously reported screening methods to detect BP disorders in large samples of American and Brazilian children. Our analysis highlights that height-based equations consistently showed superior ability to detect high blood pressure and hypertension, as reflected by higher specificity, PPV and AUC, and greater agreement with the gold standard method when compared to several other screening methods. These findings suggest that height-based equations may be a simple and feasible approach to improve the detection of high BP in children.

The detection of BP disorders in children have classically required the joint analysis of various tables and charts, which is considered a major reason for the underdiagnosis of these conditions in the pediatric population[4,23]. Although the current guideline[3] establishes that adolescents (13 years or more) with SBP above 120 mmHg or DBP above 80 mmHg are considered to have elevated BP, the use of tables and charts are still necessary to detect elevated BP levels in children below 13 years. In this report, we described simple height-based equations to determine the 90th percentile of SBP and DBP according to the most recent guideline[3]. Then, we compared the performance of these new formulae with other methods (CPG table[3], simplified cutoffs[12] and BP-to-height cutoffs[20]) to detect BP disorders in American and Brazilian children ranging from

8 to 13 years. Our analysis showed that all studied methods had high sensitivity and NPV. However, height-based equations showed higher PPV as well as higher specificity and AUC. These findings are significant because a higher PPV leads to a better identification of children with high blood pressure. More importantly, novel height-based equations had high agreement with the gold standard method (kappa coefficients ranging from 0.75 to 0.81), which was greater than those observed from other methods. Likewise, results of sensitivity analysis demonstrated that alternative height-based equations aiming to detect hypertension (BP ≥95th percentile), instead of BP disorders, showed remarkably better performance as compared to other screening methods designed to detect hypertension. However, the novel height-based equations showed a lower sensitivity to identify hypertension than BP-to-height ratio, despite the better agreement with the gold standard. Therefore, in a scenario where the purpose is not missing patients with hypertension, the 95th percentile height-based equations are not necessarily the best method. On the other hand, the difference between the novel height-based equations to identify hypertension (≥95th percentile) from those to identify high blood pressure (≥90th percentile) is only 5 mmHg for both SBP and DBP. Therefore, when the equations are used in a clinical scenario, a difference greater or equal to 5 mmHg between the measured BP and the 90th percentile new equations indicates a high probability of hypertension, practically identifying the child's blood pressure category.

Height-based equations may offer some practical advantages when compared to previously reported BP screening tools. First, they do not require the use of additional tables, as proposed by other methods[5]. Second, they can be uniformly used across different populations, which is not applicable to the BP-to-height ratio method, due to the variety of the cutoffs obtained in different studies[8,9,14,20,24,25]. Third, our height-based equations were built using data from current guidelines[3], while most of available screening methods were built using data from the previous guideline[19]. Given that the current guideline excluded overweight and obese patients from normative BP tables[3,26], several screening methods reported hitherto[7,11,20] may have become inappropriate to detect BP disorders. Fourth, height-based equations are simple, easy to memorize and do not vary according to age and gender, thus differing from other methods[4,7]. These facts allied with a higher PPV and a better agreement with the gold standard turn such method an easy to use and reliable tool to identify children with high blood pressure.

At a first glance, the new equations described herein may appear as variants of Badeli *et al* equations[10], which were built from regression analysis of 90th BP percentile values according to age. However, our equations were based on height, instead of age. This is an important difference, because BP values have been demonstrated to vary more with height than with age [27]. This is an important fact in the construction of screening methods for blood pressure disorders. For example, in a comparison between eleven methods for hypertension screening in childhood[13], it was showed that a method based on height only[28] showed better PPV and clinical utility (other methods with high PPV worked better only in taller children) with similar sensitivity, specificity and NPV. Furthermore, the Badeli *et al* equations were built according to the 50th percentile for height[10], with consequent lower performance at the extremes of height[10,11]. In order to compare the ability of our height-based equations and age-based equations reported by Badeli *et al* to detect BP disorders, we performed secondary analysis considering data from the previous guideline[19] as the gold standard method as well as the template to build the formulae. The previous guideline was used in such analysis because the equations reported by Badeli *et al* have not been updated to the current guideline[3]. Our results demonstrated that the accuracy of height-based equations to detect BP disorders was greater than that of age-based equations, strengthening the notion that screening methods based on height instead of age may have greater ability to detect BP disorders in children. Notably, height-based equations showed remarkably higher agreement with the gold standard method (kappa coefficient = 0.90 and 0.92 in the Brazilian and American population, respectively), than age-based equations (kappa coefficient = 0.64 and 0.40 in the Brazilian and American population, respectively). Furthermore, the accuracy of height-based equations was greater than several other studied screening methods that used the previous guideline as the gold standard method, demonstrating the superior ability of height-based equations to detect BP disorders regardless of the guideline used to define BP alterations.

This study has some limitations. First, data from population 1 were based on retrospective analysis of patients' charts, while a prospective design would have been more appropriate to obtain the data. Second, we used only one BP measurement from each studied subject, which might have overestimated the prevalence of BP disorders in the studied populations, given that an increasing number of measurements tends to reduce the obtained BP of children[29]. We believe, however, that this fact is not a significant limitation to our study, because our aim was to evaluate the performance of height-based equations for the identification of BP disorders, and not to establish a precise prevalence of BP disorders in the studied populations. Third, we only used information from Brazilian and American children. Thus, it is necessary to confirm the current findings in other populations.

In conclusion**,** our analysis showed that height-based equations have high sensitivity and NPV as well as great agreement with the gold standard method to detect BP disorders in American and Brazilian children. In addition, height-based equations showed superior ability to detect BP disorders and greater agreement with the gold standard method. These findings suggest that the use of height-based equations may be a simple and feasible approach to improve the detection of BP disorders in children.

Disclosure:

The authors declare no conflict of interest.

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Table 1: general characteristics of the studied populations

Variables	Brazilian Population		American Population	
Sex	Male	Female	Male	Female
Number of patients	1695	1241	3243	3298
Age, years	10.0 ± 1.4	9.9 ± 1.4	10.1 ± 1.4	10.11 ± 1.4
SBP, mmHg	102.6 ± 10.0	102.1 ± 9.7	103.5 ± 9.7	102.7 ± 10.0
DBP, mmHg	63.1 ± 8.3	62.9 ± 7.9	54.5 ± 12.0	55.6 ± 11.1
Height, cm	139.6 ± 10.3	139.2 ± 11.9	144.2 ± 11.3	145.1 ± 11.5
Weight, kg	35.5 ± 11.8	36.8 ± 11.5	42.3 ± 14.5	43.9 ± 15.2

Legend: Continuous variables are presented as mean ± standard deviation. SBP – systolic blood pressure; DBP – diastolic blood pressure.

Table 2: Performance of height-based equations and other methods to detect blood pressure disorders (blood pressure >90th percentile) according to the current guideline[3]

Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Kappa coefficient (95% CI)
Brazilian population						
CPG table	99.5 (98.2–99.9)	90.6 (89.4–91.8)	0.95 (0.94–0.96)	63.4 (60.5–66.2)	99.9 (99.6–99.9)	0.73 (0.70–0.76)
Simplified cutoffs	100 (99.1–100)	81.3 (79.7–82.8)	0.91 (0.89–0.92)	46.5 (44.5–48.5)	100	0.55 (0.51–0.58)
BP-to-height ratio	97.2 (95.2–98.4)	76.3 (74.4–77.8)	0.86 (0.85–0.88)	42.3 (40.5–44.0)	99.3 (98.8–99.6)	0.48 (0.45–0.51)
Height-based equations	100 (99.1–100)	91.6 (90.5–92.7)	0.96 (0.95–0.97)	66.1 (63.1–68.9)	100	0.75 (0.72–0.78)
American population						
CPG table	99.9 (99.3–100)	85.8 (84.9–86.7)	0.93 (0.92–0.94)	51.4 (49.8 – 53.0)	99.9 (99.8-100)	0.61 (0.59–0.63)
Simplified cutoffs	94.7 (93.0–96.1)	86.2 (85.3–87.1)	0.90 (0.89–0.91)	50.7 (49.0–52.4)	99.1 (98.8–99.3)	0.59 (0.57–0.61)
BP-to-height ratio	94.5 (92.9–95.9)	81.3 (80.2–82.3)	0.88 (0.87–0.89)	46.8 (45.4–48.2)	98.8 (98.5–99.1)	0.53 (0.51–0.56)

Height-based equations	100 (99.5–100)	94.1 (93.5–94.7)	0.97 (0.96–0.98)	71.9 (69.8 – 74.0)	100	0.80 (0.79–0.83)

Legend: AUC–area under curve; BP–blood pressure; CI–confidence interval; NPV–negative predictive value; PPV–positive predictive value.

Table 3: Performance of height-based equations to detect hypertension (blood pressure ≥95th percentile) according to the current guideline[3]

Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Kappa coefficient (95% CI)
			Brazilian population			
Simplified cutoffs	81.6 (76.8-85.8)	99.3 (99-99.6)	0.90 (0.89-0.91)	93.5 (89.9-95.9%)	97.9 (97.4-98.4)	0.85 (0.82-0.89)
BP-to-height ratio	98.3 (96.1-99.4)	79.2 (77.6-80.8)	0.89 (0.88-0.90)	35.0 (33.3-36.8)	99.7 (99.4-99.9)	0.43 (0.39-0.46)
Height-based equations	95.0 (91.8–97.2)	98.9 (98.4–99.2)	0.97 (0.96–0.98)	90.7 (87.2–93.4)	99.4 (99.0-99.7)	0.92 (0.89–0.94)
			American population			
Simplified cutoffs	52.9 (48.4-57.4)	99.4 (99.2-99.6)	0.76 (0.75-0.77)	88.0 (84.0-91.2)	96.3 (96.0-96.6)	0.64 (0.60-0.68)
BP-to-height ratio	97.5 (95.8-98.7)	84.3 (83.4-85.2)	0.91 (0.90-0.92)	33.5 (32.2-34.8)	99.8 (99.6-99.9)	0.43 (0.41-0.46)

Height-based equations	87.1 (83.8–90.0)	99.1 (98.8–99.3)	0.93 (0.92–0.94)	88.7 (85.8 – 91.1)	98.9 (98.7 – 99.2)	0.89 (0.87–0.91)

Legend: AUC–area under curve; BP–blood pressure; CI–confidence interval; NPV–negative predictive value; PPV–positive predictive value.

Table 4: Performance of height-based equations and other methods to detect blood pressure disorders (blood pressure >90th percentile) according to the previous guideline[19]

Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	AUC (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)	Kappa coefficient (95% CI)
Brazilian population						
Mitchell table	97.6 (95.0–99.0)	83.7 (82.3–85.1)	0.91 (0.90–0.92)	39.0 (36.9–41.1)	99.7 (99.4–99.8)	0.49 (0.45–0.52)
Kaelber Table	97.6 (95.0–99.0)	90.6 (89.5–91.7)	0.94 (0.93–0.95)	52.6 (49.7–55.6)	99.7 (99.4–99.9)	0.64 (0.60–0.68)

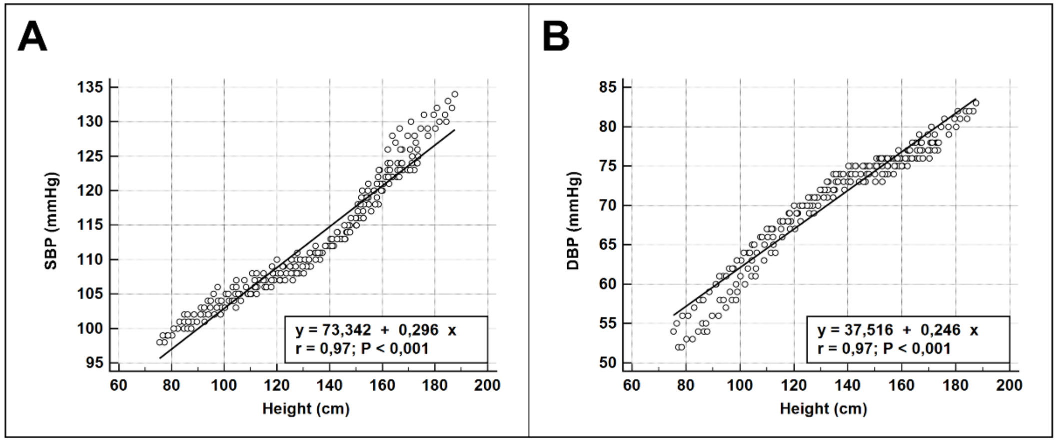
BP-to-height ratio	91.6 (87.8–94.6)	87.1 (85.7–88.3)	0.89 (0.88–0.90)	43.0 (40.5–45.6)	99.00 (98.5–99.3)	0.52 (0.48–0.56)
Badeli Equation	99.0 (98.5–99.3)	90.5 (89.4–91.6)	0.94 (0.93–0.95)	52.4 (49.5–55.4)	99.7 (99.4–99.9)	0.64 (0.60–0.68)
Simplified cutoffs	98.9 (97.0–99.8)	77.2 (75.6–78.8)	0.88 (0.87–0.89)	31.7 (30.2–33.2)	99.9 (99.6–99.9)	0.39 (0.36–0.42)
Height-based equations	96.2 (93.2–98.1)	98.4 (97.9–98.9)	0.97 (0.97–0.98)	86.8 (82.9–89.9)	99.6 (99.3–99.8)	0.90 (0.88–0.93)
American population						
Mitchell table	100 (99.2–100)	79.7 (78.7–80.7)	0.90 (0.89–0.91)	26.5 (25.5–27.5)	100	0.35 (0.32–0.37)
Kaelber Table	100 (99.2–100)	83.0 (82.0–83.9)	0.91 (0.91–0.92)	29.9 (28.7–31.1)	100	0.40 (0.37–0.42)
BP-to-height ratio	97.1 (95.1–98.4)	81.8 (80.8–82.7)	0.89 (0.89–0.90)	27.8 (26.7–29.0)	99.7 (99.6–99.8)	0.37 (0.34–0.39)
Badeli Equation	100 (99.2–100)	83.2 (82.2–84.1)	0.92 (0.91–0.92)	30.1 (28.9–31.3)	100	0.40 (0.37–0.43)

Simplified cutoffs	99.5 (98.4–99.9)	80.9 (79.9–81.9)	0.90 (0.90–0.91)	27.5 (26.4–28.5)	99.9 (99.8–100)	0.36 (0.34–0.39)
Height-based equations	97.7 (95.9–98.9)	99.1 (98.8–99.3)	0.98 (0.98–0.99)	88.4 (85.5–90.8)	99.8 (99.7–99.9)	0.92 (0.90–0.94)

Legend: AUC–area under curve; BP–blood pressure; CI–confidence interval; NPV–negative predictive value; PPV–positive predictive value.

Figure captions:

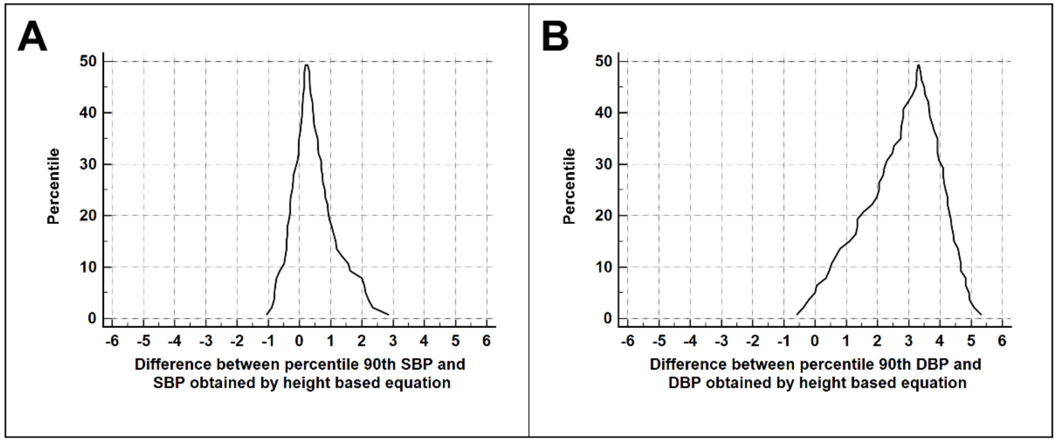
Figure 1.



Linear regression analysis between the 90th percentile values for systolic (A) and diastolic (B) blood pressure and height values obtained from the current guideline.

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Figure 2.



Mountain plots for the difference in systolic (A) and diastolic (B) blood pressure between the 90th percentile values from the current guideline and the values obtained with height-based equations in children between 8 and 13 years.

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

ONLINE SUPPLEMENT

HEIGHT-BASED EQUATIONS CAN IMPROVE THE DIAGNOSIS OF ELEVATED BLOOD PRESSURE IN CHILDREN

FA Mourato; SS Mattos; JL. Lima-Filho; MF Mourato; W Nadruz Jr.

Supplementary table 1: Cutoffs for blood pressure-to-height ratio obtained in Brazilian and American children to identify blood pressure disorder (BP>90th percentile) considering the current guideline[1] as the gold standard method

	Brazilian Children		American Children	
	SBP	DBP	SBP	DBP
Male	0.77	0.49	0.77	0.48
Female	0.76	0.49	0.76	0.47

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Supplementary table 2: Cutoffs for blood pressure-to-height ratio obtained in Brazilian and American children to identify blood pressure disorder (BP≥95th percentile) considering the current guideline[1] as the gold standard method

	Brazilian Children		American Children	
	SBP	DBP	SBP	DBP
Male	0.79	0.49	0.79	0.49
Female	0.79	0.49	0.78	0.49

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Supplementary table 3: Cutoffs for blood pressure-to-height ratio obtained in Brazilian children (from Mourato et al[2]) to identify blood pressure disorder (BP>90th percentile) considering the previous guideline[3] as the gold standard method.

	Brazilian Children	
	SBP	DBP
Male	0.82	0.52
Female	0.80	0.50

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Supplementary table 4: Cutoffs for blood pressure-to-height ratio obtained in American children to identify blood pressure disorder (BP>90th percentile) considering the previous guideline[3] as the gold standard method.

	American Children	
	SBP	DBP
Male	0.79	0.50
Female	0.77	0.50

DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Supplementary table 5: Mitchell table

Systolic Blood Pressure (mmHg)		Diastolic Blood Pressure (mmHg)
	Between 3 and 6 years	
≥100		>60
	Between 6 and 9 years	
≥105		>70
	Between 9 and 12 years	
≥110		>75
	Between 12 and 15 years	
≥115		>75
	≥15 years	
≥120		≥80

Supplementary table 6: Kaelber table

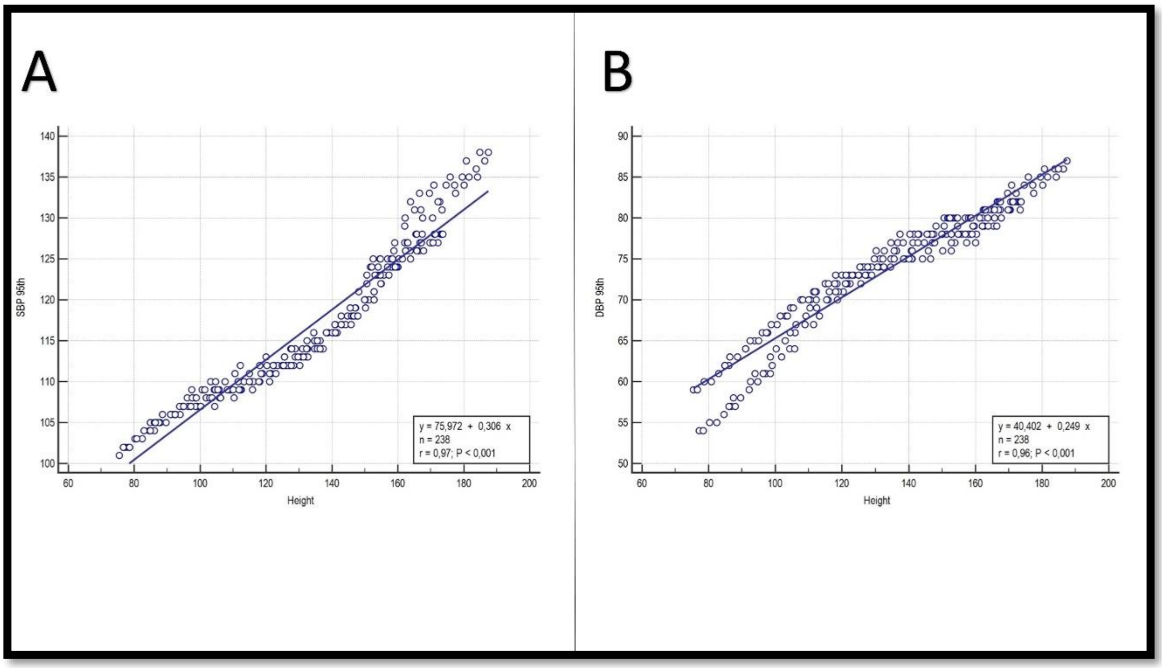
Age in years	Blood pressure	
	Male	Female
	SBP/DBP	SBP/DBP
3	100/59	100/61
4	102/62	101/64
5	104/65	103/66
6	105/68	104/68
7	106/70	106/69
8	107/71	108/71
9	109/72	110/72
10	111/73	112/73
11	113/74	114/74
12	115/74	116/75
13	117/75	117/76
14	120/75	119/77
15	120/76	120/78
16	120/78	120/78
17	120/80	120/78
≥18	120/80	120/80

Legend: SBP-Systolic Blood Pressure; DBP-Diastolic Blood Pressure

Supplementary table 7: Badeli equations

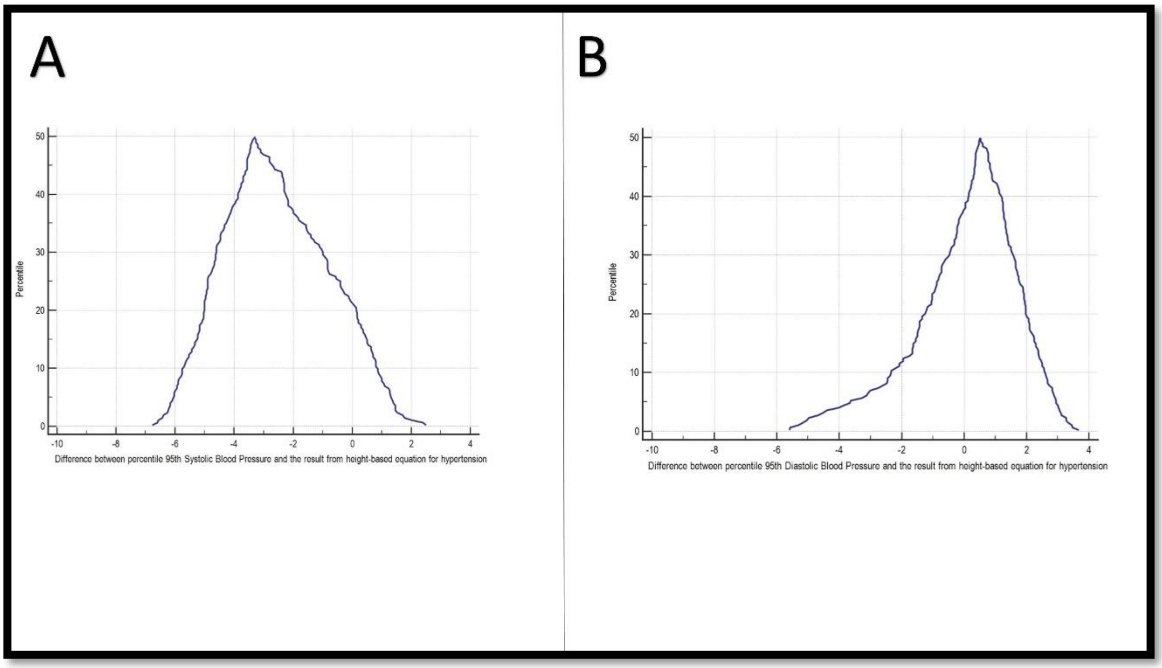
Age in years	Systolic Blood Pressure	Diastolic Blood Pressure
3 to 7 years old	≥ age + 96	≥ 2 × age + 55
8 to 13 years old	≥ 2 × age + 91	≥ age + 63
Above 14 years old	≥ 120	≥ 75

Supplementary figure 1. Linear regression analysis between the 95th percentile values for systolic (A) and diastolic (B) blood pressure and height values obtained from the current guideline[1]



DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

Supplementary figure 2. Mountain plots for the difference in systolic (A) and diastolic (B) blood pressure between the 90th percentile values from the current guideline[1] and the values obtained with height-based equations.



DBP – Diastolic blood pressure; SBP – Systolic blood pressure.

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6 CONSIDERAÇÕES FINAIS

A HAS é um problema de saúde pública que cada vez mais atinge a faixa etária pediátrica, principalmente devido à epidemia de obesidade. Crianças que apresentam HAS têm maiores chances de se tornarem adultos hipertensos, com maior probabilidade de desenvolver problemas cardiovasculares. Além disso, há um subdiagnóstico de HAS nesta faixa etária, o qual pode levar a falta de tratamento precoce e piora do quadro na idade adulta.

Alguns pontos foram destacados como responsáveis para tal subdiagnóstico, sendo o complicado processo diagnóstico de HAS na infância um dos principais. O fato de utilizar as tabelas de percentil separadas por gênero, idade e altura consome bastante tempo nas consultas pediátricas, o que torna sua aplicabilidade inviável em ambulatórios lotados. Várias ferramentas foram descritas para lidar com tal problema, entretanto poucas delas estão adaptadas ao mais recente *guideline* de diagnóstico de HAS na infância.

O foco desta tese foi trabalhar em torno de tais problemas. Inicialmente descrevemos novos pontos de corte para a nova razão entre PA e altura modificada na população americana e a comparamos com a razão entre PA e altura e a razão entre PA e altura modificada. Além disso, descrevemos uma possível razão para superioridade de tal método, baseada na maior relação da PA normal com o crescimento do tronco em vez do corpo inteiro. Com o lançamento do novo *guideline*, realizamos o mesmo trabalho incluindo a população brasileira e considerando os novos padrões diagnósticos como padrão-ouro. Foi então demonstrada a superioridade da nova razão entre PA e altura modificada em relação aos outros métodos, além do estabelecimento de novos pontos de corte para a razão entre PA e altura modificada e suas variações.

Entretanto, consideramos que a nova razão entre PA e altura modificada não é o método perfeito para triagem de hipertensão na infância por exigir o estabelecimento de pontos de corte específicos para cada população e exigir do profissional de saúde a memorização dos mesmos.

Diante disto, descrevemos uma nova fórmula para determinação da maior PA normal de acordo com a altura da criança. Esta fórmula demonstrou um índice de correlação superior aos outros métodos descritos tanto no *guideline* antigo como no atual, com ótima sensibilidade, especificidade e valor preditivo negativo. Além disso, é de mais fácil memorização e não exige o estabelecimento de pontos de corte específicos por população, sendo possível seu uso universal.

Esta tese descreve novas ferramentas para a triagem adequada de distúrbios pressóricos na infância e adolescência, as quais podem ter um impacto positivo no manejo da HAS nesta população.

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