References

1. Lonhart JA, Edwards AR, Agarwal S, Lucas BP, Schroeder AR. Consent rates reported in published pediatric randomized controlled trials. J Pediatr 2020;227:281-7.
2. Lombardi D, Squirs L, Shjostedt P, Eichler I, Turner MA, Thompson C. Industry and patient perspectives on child participation in clinical trials: the Pediatric Assent Initiative Survey Report. Ther Innov Regul Sci 2018;52:29-37.
3. European Network of Pediatric Research at the European Medicines Agency. Informed consent for paediatric clinical trials in Europe. https://www.ema.europa.eu/en/documents/other/informed-consent-paediatric-clinical-trials-europe-2015_en.pdf. Accessed July 15, 2020.
4. Gates A, Caldwell P, Curtis S, Dans L, Fernandes RM, Hartling L, et al. Consent and recruitment: the reporting of paediatric trials published in 2012. BMJ Paediatr Open 2018;2:e000369.
5. Treweek S, Mitchell E, Pitkethly M, Cook J, Kjeldstrøm M, Taskila T, et al. Strategies to improve recruitment to randomised controlled trials. Cochrane Database Syst Rev 2010MR000013.
6. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux P, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.
7. Saint-Raymond A, Hill S, Martines J, Bahl R, Fontaine O, Bero L. CONSORT 2010. Lancet 2010;376:229-30.
8. Plint AC, Moher D, Morrison A, Schulz K, Altman DG, Hill C, et al. Does the CONSORT checklist improve the quality of reports of randomised controlled trials? A systematic review. Med J Aust 2006;185:263-7.

Automated Office Blood Pressure Measurement for the Diagnosis of Hypertension

Accurate blood pressure (BP) measurements are important for the diagnosis and treatment of hypertension in children and adolescents. Hypertension is a significant risk factor for a number of chronic conditions in children and adults, including cerebrovascular disease, coronary artery disease, congestive heart failure, renal failure, and stroke. Unfortunately, the prevalence of pediatric hypertension has significantly increased as a result of childhood obesity.[1] Hypertension is routinely diagnosed using office BP measurements, which should be interpreted using the Task Force Office Blood Pressure reference thresholds guidelines.[2-4] This process requires knowledge of the patient's height percentile.

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There are a number of methods for BP measurements, and we are about to learn that there now is another one which may serve as an attractive alternative. The 4 most widely used methods are conventional manual BP measurement through the use of a sphygmomanometer (now rarely used due to mercury concerns); an aneroid or oscillometric device (often also named a digital device) in the clinic setting and herein referred to as office BP; conventional BP measurement, through the use of an aneroid or oscillometric device outside of the clinic setting; arterial BP measurement, an invasive method usually done in a hospital setting; and ambulatory 24-hour BP monitoring (ABPM) using an oscillometric device.

Office BP is used most often in the clinical setting. However, one-third of children with office BP-based hypertension also have white-coat hypertension, which does not require treatment.[5,6] Furthermore, office BP measurements are insensitive to masked and nighttime hypertension, which can independently influence end-organ damage.[6,7]

ABPM is used in clinical practice to better characterize hypertension and to guide therapeutic decisions.[5-7] This method can diagnose white-coat, masked, and nighttime hypertension. The American Academic of Pediatrics and the European Society of Hypertension published guidelines for the use of ABPM.[2-4] There is also a version for Canada.[8] Abnormal ABPM readings and confirmation of end-organ damage serve as the gold standard for the diagnosis of hypertension. Although there are some differences when applying either the American or European guidelines,[9] all of them call for the use of ABPM for the confirmation of hypertension. Furthermore, routine ABPM is strongly recommended to regularly assess severity and determine circadian BP patterns. However, ABPM is not widely available because it involves specialized instrumentation, trained staff, and other costs that are nonreimbursable in many regions of the world. In fact, reimbursement for ABPM varies widely among the different states in the US and in Canada. Another limitation is the frequent need for shipment of the ABPM monitor at cost for the hospitals, which is not reimbursed. Moreover, wearing the ABPM monitor for 24 hours is not convenient for small patients and may explain the significant intrapatient variability of ABPM in the pediatric setting.[10] As such, an abbreviated version of automated BP monitoring would be desirable.

In this volume of *The Journal*, Coral Hanevold et al describes a novel study that determined the level of agreement between automated office BP (AOBP), auscultated (manual) office BP, and ABPM to correctly identify hypertension in patients less than 18 years of age.[11] Hanevold et al introduced us to a fifth method, and it is essentially the measurement of BP

ABPM	Ambulatory 24-hour blood pressure monitoring
AOBP	Automated office blood pressure
BP	Blood pressure

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by an automated device, without staff assistance, in an effort to address the limitations of the standard office BP, decrease the white coat effect, and approximate the ABPM readings. Hanevold's group analyzed automated office AOBP measurements from 2016 to 2018 using the BpTRU device (BpTRU Medical Devices Ltd, Coguitlam, British Colombia, Canada); which has been validated for children. This device has 6 automated office AOBP measurements programmed by factory settings and Hanevold's group discarded the first one, to average the remaining five readings. In children <13 years of age, daytime ambulatory hypertension was diagnosed if mean BPs were ≥95th percentile and BP loads were ≥25%. In children ≥13 years of age, ABPM thresholds for daytime hypertension of 130/80 mm Hg were used.[11] To ensure adequacy of the ABPMs, the authors used the number of measurements specified in the 2014 American Heart Association criteria.

Hanevold's group described 187 patients with or without hypertension, regardless of BP treatment. Of these, 120 patients had a rest period and 67 had no rest period. The majority of patients were adolescents, but 52 were <13 years of age. Patients were predominantly male. In the majority of cases, ABPM, manual office BP, and automated office BP were done on the same day. On ABPM, 32% of patients had hypertension. Indeed, the authors found that automated office BP was slightly more accurate in correctly identifying hypertension (65% agreement) than manual office BP (58% agreement). The best overall agreement was seen if both manual office BP and automated office BP showed hypertension (70%); however, sensitivity was low. Specificity was better if both AOBP and manual office BP showed hypertension and in children under 13 years of age, it was 86%. The authors also performed a detailed analysis using adult thresholds for the older children. Finally, they assessed the percentage of correct classification and concluded that 49% of patients with hypertension would be misclassified. Their final conclusion was that ABPM has an ongoing role in the evaluation of hypertension in children and for now, it cannot be replaced by AOBP.

This study adds important new evidence about the use of automated office BP in the pediatric setting.[11] Although these preliminary findings may be discouraging, they compel us to consider evaluating this method further. Automated office BP is recommended for adults by Hypertension Canada and supported for adults by the American Heart Association and the European Society of Hypertension.[12-14] The study by Hanevold et al suggests a limited role for automated office BP in children, but this method may have an important role in identifying patients better suited for the scarcely available ABPM, especially because the combination of office BP and automated office BP seems to identify patients with hypertension more correctly than office BP alone, which may substantially decrease the need for ABPM to confirm hypertension.

Although the retrospective study by Hanevold et al represents a description of a real-world clinical experience, it also provides empirical evidence that calls for the need to do a multicenter, prospective study of children suspected to have hypertension. This retrospective study included patients with hypertension and one consideration would be to start with treatment-naïve patients, who have all measurements done on the same day. Data could be stratified by age, sex, and validated standardized body mass index z-scores (particularly in morbidly obese children, where the World Health Organization criteria could be applied.) The standard definitions for elevated office BP readings could be those described by the 2017 pediatric criteria by Flynn et al and the 2014 ABPM guidelines led by the same author with consideration for the number and kind of devices.[2] The setup also has to be given some consideration, because a number of children need a caregiver in the room, so standardizing this methodology would decrease the introduction of bias. Comparisons by the number of BP readings as well as systolic and diastolic differences would need to be included. For the routine workflow in the clinics, a determination of the minimum number of measurements that yields the best predictive classification of hypertension would be ideal. Alternating the first reading method (manual readings vs automated device) also would need to be considered.

Unfortunately, manufacturers of ABPM machines have not agreed on any standardization, compared with what we have for creatinine (isotope-dilution mass spectrometry traceability) and for cystatin C (international certified reference materials).[15,16] ABMP machine manufacturers do not even share the algorithms for the calculation of the systolic and diastolic BP. We need consistent certification of ABPM machines for children and standardized programs with appropriate reference intervals. The undersigned believe that there may be value to include a feature for automated office BP for all ABPM machines that are certified for children, because the ideal program (ie, number of measurements, discarding of the first measurement, interval of repeat measurements) has yet to be determined. It is also necessary to advocate for reimbursement of the testing, especially because guidelines call for the routine use of ABPM in patients with chronic kidney disease.

We would like to mention a cross-sectional survey among the Canadian Pediatric Nephrology centers in terms of the adherence to guideline recommendations (unpublished results, Filler G, Fall 2019).[8] We noted that 72.7% of centers cannot provide the test to all patients with chronic kidney disease for various reasons that include the number of machines available and reimbursement of all associated costs. Only 27.3% of centers stated that they can accommodate the recommendation of the new American Academy of Pediatrics guidelines.[2] In Canada, most centers use the aging Spacelab 90207 model, presumably because it has published reference intervals.[17,18] However, all the centers have the ability and trained personnel to perform ABPM. Mostly, the machines are privately funded through foundations, and in all but 2 provinces there is no reimbursement. In the Canadian provinces where there is reimbursement, the amounts fall short of that for similar tests such as a Holter monitor. It seems that most of the provinces made no contribution to funding and maintaining the emerging

standard of ABPM for the diagnosis and monitoring of hypertension. The majority of centers seem to have insufficient resources to confirm the diagnosis of hypertension, which raises the concern that patients with white coat hypertension may have received unnecessary treatment.[19] Automated office BP in combination with office BP may aid with a more judicious selection of ideal patients for ABPM.

Automated office BP (especially when combined with office BP) may be a feasible tool to strategically and sparingly use the scarce resource of ABPM for the diagnosis of hypertension. Although Hanevold et al feel that neither office BP nor AOBP accurately diagnose daytime hypertension, the combination of both methods may improve the identification of patients who need ABPM.[11] We encourage continuing research into automated office BP for the identification and treatment of hypertension. Hanevold et al should be congratulated for their contribution and the ongoing efforts to improve the diagnosis and management of hypertension in children. ■

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References

1. Sorof JM, Lai D, Turner J, Poffenbarger T, Portman RJ. Overweight, ethnicity, and the prevalence of hypertension in school-aged children. Pediatrics 2004;113:475-82.
2. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics 2017;140:e20171904.
3. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555-76.
4. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens 2016;34:1887-920.
5. Sorof JM, Portman RJ. White coat hypertension in children with elevated casual blood pressure. J Pediatr 2000;137:493-7.
6. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. J Am Coll Cardiol 2005;46:508-15.
7. Sharma AP, Mohammed J, Thomas B, Lansdell N, Norozi K, Filler G. Nighttime blood pressure, systolic blood pressure variability, and left ventricular mass index in children with hypertension. Pediatr Nephrol 2013;28:1275-82.
8. Dionne JM. Updated guideline may improve the recognition and diagnosis of hypertension in children and adolescents; review of the 2017 AAP Blood Pressure Clinical Practice Guideline. Curr Hypertens Rep 2017;19:84.
9. Sharma A, Altamirano-Diaz L, Grattan M, Filler G, Sharma AP. Comparative analysis of American Heart Association and European Society of hypertension ambulatory blood pressure thresholds for diagnosing hypertension in children. Kidney Int Rep 2020;5:611-7.
10. Hanevold CD, Miyashita Y, Faino AV, Flynn JT. Changes in ambulatory blood pressure phenotype over time in children and adolescents with elevated blood pressures. J Pediatr 2020;216:37-43.e2.
11. Hanevold CD, Faino AV, Flynn JT. Use of automated office blood pressure measurement in the evaluation of elevated blood pressures in children and adolescents. J Pediatr 2020;227:204-11.e6.
12. Leung AA, Daskalopoulou SS, Dasgupta K, McBrien K, Butalia S, Zarnke KB, et al. Hypertension Canada\s 2017 Guidelines for Diagnosis, Risk Assessment, Prevention, and Treatment of Hypertension in Adults. Can J Cardiol 2017;33:557-76.
13. Muntner P, Shimbo D, Carey RM, Charleston JB, Gaillard T, Misra S, et al. Measurement of blood pressure in humans: a scientific statement from the American Heart Association. Hypertension 2019;73:e35-66.
14. Stergiou GS, Parati G, Vlachopoulos C, Achimastos A, Andreadis E, Asmar R, et al. Methodology and technology for peripheral and central blood pressure and blood pressure variability measurement: current status and future directions - position statement of the European Society of Hypertension Working Group on blood pressure monitoring and cardiovascular variability. J Hypertens 2016;34:1665-77.
15. Hetu PO, Gingras ME, Vinet B. Development and validation of a rapid liquid chromatography isotope dilution tandem mass spectrometry (LC-IDMS/MS) method for serum creatinine. Clin Biochem 2010;43:1158-62.
16. Grubb A, Blirup-Jensen S, Lindstrom V, Schmidt C, Althaus H, Zegers I, et al. First certified reference material for cystatin C in human serum ERM-DA471/IFCC. Clin Chem Lab Med 2010;48:1619-21.
17. Soergel M, Kirschstein M, Busch C, Danne T, Gellermann J, Holl R, et al. Oscillometric twenty-four-hour ambulatory blood pressure values in healthy children and adolescents: a multicenter trial including 1141 subjects. J Pediatr 1997;130:178-84.
18. Wuhl E, Witte K, Soergel M, Mehls O, Schaefer F. German Working Group on Pediatric H. Distribution of 24-h ambulatory blood pressure in children: normalized reference values and role of body dimensions. J Hypertens 2002;20:1995-2007.
19. Briasoulis A, Androulakis E, Palla M, Papageorgiou N, Tousoulis D. White-coat hypertension and cardiovascular events: a meta-analysis. J Hypertens 2016;34:593-9.