Editorial Commentary

What Is the Significance of Increased Carotid Intima Media Thickness in Hypertensive Adolescents?

Joseph T. Flynn

Fortunately, common cardiovascular sequelae of long-standing hypertension in adults, such as myocardial infarction and stroke, are not seen in hypertensive children and adolescents. However, it is well established that persistent blood pressure elevation in the young can produce other target-organ effects. Chief among these are left ventricular hypertrophy (LVH), which may be present in ≤30% of children at the time of diagnosis of hypertension, and abnormal left ventricular geometry, which is typically seen in those with more severe blood pressure elevation. LVH can be seen even in adolescents with even mild blood pressure elevation and is probably the most readily assessed target-organ effect of hypertension in the young because of the wide availability of echocardiography. Its importance as a cardiovascular risk factor was recently highlighted by the National High Blood Pressure Education Program (NHBPEP) Working Group on High Blood Pressure in Children and Adolescents, which recommended that echocardiograms be obtained as part of the initial evaluation of children and adolescents with confirmed hypertension. It was further recommended that if LVH is found, the antihypertensive therapy should be intensified.

Other consequences of hypertension almost certainly develop in young hypertensive subjects but are more difficult to demonstrate. These include renal damage, hypertensive retinopathy, and cognitive impairment. Hypertensive renal damage probably first manifests as microalbuminuria and later progresses to end-stage renal disease; indeed, hypertension is one of the leading causes of chronic kidney disease in adults. In children, however, the incidence of renal damage from isolated hypertension has not been established, and although a small number of children with end-stage renal disease allegedly attributable to hypertension are seen in the United States each year, screening for hypertensive renal damage was not recommended by the NHBPEP Working Group because of the lack of data on which to base a recommendation.

Retinal changes, when systematically looked for, occur in a large number of hypertensive children and adolescents, especially those with diastolic hypertension, but are typically mild, requiring referral to an experienced ophthalmologist to detect. Although retinal exams have been recommended for hypertensive children, in practice this is a difficult marker to routinely follow as part of patient management. Cognitive impairment has been reported recently in children with elevated blood pressure, but to date, the clinical manifestations of this have not been systematically assessed in a representative population of hypertensive children. Therefore, although this is potentially another important adverse effect of hypertension in the young, more data are needed to fully determine its significance.

The other recently described vascular abnormality in hypertensive children and adolescents is increased carotid intima medial thickness (cIMT). Increased cIMT is well established as a correlate of atherosclerosis in adults, typically occurring in conjunction with other cardiovascular risk factors. In prospective studies, increased cIMT has been associated with increased rates of coronary heart disease events, especially in individuals with higher blood pressure, dyslipidemia, and cigarette smoking. In young adults, cIMT has been demonstrated to be greater in those with features of the metabolic syndrome, such as obesity and impaired glucose tolerance, and to increase as the number of components of the metabolic syndrome increase. Given these strong associations, assessment of cIMT has been proposed as a noninvasive measure of cardiovascular disease burden in adults.

cIMT in hypertensive children and adolescents has become a focus of interest relatively recently. Sorof et al studied a small group of hypertensive adolescents with carotid ultrasonography and echocardiography and found that subjects in the highest cIMT quartile had significantly greater left ventricular mass index than those in the lower cIMT quartiles. Of note, there was also a significant correlation between cIMT and markers of obesity, including weight and body mass index (BMI). The authors speculated that given the strong association between greater cIMT and LVH in their study population, increased cIMT perhaps represented a similar adaptive process to that responsible for the development of LVH and could, therefore, serve as an additional marker of increased cardiovascular risk in these young individuals.

Similarly, Litwin et al in a study that included ambulatory blood pressure monitoring (ABPM), femoral and carotid IMT measurement, and assessments of biochemical parameters and vascular function in both normotensive and hypertensive subjects, found that vascular thickness was increased in hypertensive adolescents compared with controls and was associated with decreased vascular distensibility and elasticity. Vascular thickness correlated with systolic blood pressure and pulse pressure, as well as with some biochemical measures of cardiovascular risk, including homocysteine, high-density lipoprotein, and apolipoprotein A1. As in the study by Sorof et al, BMI was a significant predictor of IMT.
Other studies of cIMT in hypertensive children and adolescents have demonstrated similar associations, most notably the association between increased IMT and anthropometric parameters, such as weight, height, and BMI. Given the ongoing obesity epidemic among children and adolescents in the United States and other nations, this makes it difficult to separate out the effect of blood pressure from body growth as the explanation for increased vascular thickness in this age group. It is understandable, therefore, that the NHBPEP Working Group did not consider cIMT to be “ready” as a marker of increased cardiovascular risk in the young.2

In this issue of Hypertension, Lande et al10 report the first study of cIMT in hypertensive adolescents that corrects for the effects of body mass. They found that cIMT was greater in hypertensive subjects than in controls matched for age, gender, and BMI and that it was correlated with several ABPM parameters. Although LVH was common in their hypertensive subjects, left ventricular mass was not correlated with ABPM, a finding that is inconsistent with many recently published pediatric studies and perhaps reflects the relatively small population studied. A further weakness is the lack of assessment of metabolic comorbidities of hypertension, such as hyperlipidemia or impaired glucose tolerance, factors that would have likely been present given the elevated BMI in both the hypertensive and control groups. Despite these limitations, the present study does resolve the crucial issue of whether the increased vascular thickness is a consequence of growth or of elevated blood pressure: It is the blood pressure.

But does this mean that these adolescents have early atherosclerosis? At present, available data cannot answer this question. However, the implications of present data are frightening: elevated blood pressure in children and adolescents leads to increased vascular thickness6,7,10 and abnormal vascular function,7 as well as abnormal cardiac structure and function,1,6,10 all of which are occurring in a metabolic milieu6 that leads to increased rates of coronary heart disease events.8 What is needed is further research to tie together the seemingly loose ends in the available pediatric cIMT data. Only then will cIMT join left ventricular hypertrophy as an accepted measure of hypertensive target-organ damage in children and adolescents.

Disclosures

None.

References

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