Challenges of Existing Pediatric Dyslipidemia Guidelines
Call for Reappraisal

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Existing guidelines for screening and managing lipoprotein abnormalities in children and adolescents are based on a consensus document published over 15 years ago by the National Cholesterol Education Program (NCEP) Expert Panel on Blood Cholesterol Levels in Children and Adolescents.1 This document was based on evidence that elevated levels of low-density lipoprotein (LDL) cholesterol are highly correlated with development of atherosclerotic cardiovascular disease (ASCVD) in adults and on pathological data suggesting that dyslipidemia in children and adolescents was associated with early arterial plaque development. The panel recommended 2 strategies to address abnormal lipoprotein levels in children: a population-based approach (dietary recommendations) and a targeted screening approach (selective screening based on family history of ASCVD and/or parental hypercholesterolemia). The guidelines recommended dietary and lifestyle interventions for children with elevated LDL cholesterol levels. They proposed that drug therapy only be considered when LDL cholesterol levels are ≥190 mg/dL or ≥160 mg/dL, with concomitant ASCVD risk factors (≥2) or with a family history of ASCVD.

Since the initial publication of the existing guidelines, many significant challenges have emerged that deserve attention. First, accumulating data suggest that the guidelines significantly underestimated the number of children who would be targeted for lipoprotein screening. Second, the guidelines do not account for variations in lipids due to race, gender, and pubertal status, all of which are known to have a clinically relevant impact on lipoprotein values. Third, there is a singular focus on LDL cholesterol with no emphasis on high-density lipoprotein (HDL) cholesterol and triglycerides and their role in mediating cardiovascular risk. Fourth, insufficient consideration was given to the role of obesity and other related metabolic risk factors (insulin resistance, glucose intolerance, etc) in relation to lipoprotein abnormalities. Fifth, the treatment recommendations are likely outdated, as they recommend using bile acid–binding resins as first-line therapy. Since the initial publication of the guidelines, statins have been shown to be the preferred pharmacological treatment in children and adolescents.2 Lastly, probably because of the many factors mentioned above, acceptance and implementation of the recommendations in a general sense has been suboptimal.

In an attempt to address some the challenges associated with the existing pediatric lipid guidelines, Magnussen et al3 present a study in this issue of Circulation comparing the value of the National Health and Nutrition Examination Survey (NHANES) lipoprotein classifications for children and adolescents with those of the NCEP in predicting abnormal adult lipoprotein levels. Their study used combined data from 3 separate longitudinal cohort studies (Childhood Determinants of Adult Health Study, Cardiovascular Risk in Young Finns Study, and Bogalusa Heart Study) that had patients’ lipoprotein data available from childhood to adulthood. Lipoprotein variables in childhood were classified according to NCEP and NHANES cut points and were compared for their ability to predict abnormal lipoprotein levels in adulthood. The results showed that the NHANES cut points were more strongly predictive of low HDL cholesterol levels than were the NCEP criteria. However, the NCEP cut-points fared better in terms of predicting elevated total cholesterol, LDL cholesterol, and triglycerides in adulthood. These data are an important addition to the literature and will certainly prove valuable when the existing pediatric lipoprotein guidelines are reevaluated and updated.

The role of obesity and insulin resistance in relation to pediatric dyslipidemia deserves considerable attention. Obesity-associated dyslipidemia is distinctly different from the more clear-cut LDL cholesterol elevations in children with familial hypercholesterolemia. Obese children, especially those with insulin resistance, tend to have decreased HDL cholesterol levels and increased triglycerides (markers of the adult metabolic syndrome) but often do not have elevated levels of LDL cholesterol. A recent study in over 3000 adolescents using the modified Adult Treatment Panel III cut points for serum triglycerides (≥110 mg/dL) and waist circumference (≥90th percentile for age and sex) has shown that the concomitant presence of these criteria was significantly associated with a clustering of metabolic abnormalities characteristic for the metabolic syndrome.4 The complexity of obesity-associated dyslipidemia is underscored by the findings of Magnussen et al3 that childhood overweight/obesity status is a better predictor of adult HDL cholesterol levels than actual lipid screening. This is not particularly surprising, as adiposity and insulin resistance are linked with low HDL cholesterol levels via hyperinsulinemia and increased cholesterol ester transfer protein levels.5 6 Furthermore, because childhood obesity tracks strongly into adulthood,5 it is
reasonable to expect a strong association between obesity in childhood and low HDL cholesterol in later in life. Therefore, reducing body fat and increasing levels of physical activity should be primary targets of therapy to correct dyslipidemia in obese children. This approach is supported by multiple studies that have shown the efficacy of weight reduction in improving lipoprotein levels in pediatric obesity.5–11

The fundamental goal of defining abnormal lipoprotein levels in children and adolescents is to identify those children at the highest risk of developing ASCVD. Although there have been no randomized trials conducted that assessed the impact of risk modification during childhood on later cardiac event rates (and it is unlikely that any will be performed because of cost and time limitations), the aggressive treatment approach is supported by a wealth of data suggesting that ASCVD occurs over a lifetime, with beginnings traced to early childhood.12 The lipoprotein profile is only one of many factors related to ASCVD, and one must account for the totality of the risk burden. For example, high-risk pediatric patients with disease states associated with accelerated atherosclerosis (Kawasaki disease, diabetes mellitus types 1 and 2, previous cardiac transplants, chronic kidney disease, congenital heart disease, chronic inflammatory disease, childhood cancer)13 should be given special consideration when establishing cut points for dyslipidemia. In these children, intensive cardiovascular risk reduction is of great importance.

In summary, in light of the current findings by Magnussen et al1 and accumulating data in the field of pediatric dyslipidemia since the publication of the original guidelines, it is clear that the time has now come to develop revised and updated consensus recommendations. These recommendations should (1) address the roles of race, gender, and pubertal status in relation to lipoprotein levels; (2) provide updated treatment recommendations for elevated LDL cholesterol based on the available evidence supporting the use of statins in children and adolescents; (3) address elevated triglycerides and low HDL cholesterol; and (4) provide lipoprotein screening guidelines and cut points for high-risk pediatric patients in whom more aggressive risk factor management is warranted. The current childhood obesity epidemic, the substantial new knowledge about dyslipidemia in children, and the associated cardiometabolic risk highlight the need for reevaluation of our approach to lipid abnormalities in the young.

Disclosures

None.

References


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