Dyslipidemia in Kids Predicts Carotid Thickening

BY SHERRY BOSCHERT

Adolescents with dyslipidemia—especially those who were overweight or obese—were more likely than were adolescents with normal lipid levels to have increased carotid artery intima-media thickness by young adulthood, a study of 1,711 people found.

The study also found the single set of cut points used to identify adolescent dyslipidemia in the National Cholesterol Education Program (NCEP) guidelines worked as well as age- and sex-specific cut points derived from growth curve data in three National Health and Nutrition Examination Surveys (NHANES) to predict increased carotid intima-media thickness in young adulthood (J. Am. Coll. Cardiol. 2009;53:860-9 [doi:10.1016/j.jacc.2008.09.061]). This argues in favor of using the simpler, fixed NCEP approach rather than the percentile-based NHANES approach, reported Costan G. Magnussen of the University of Tasmania (Australia).

Mr. Magnussen and his associates analyzed data from three large population-based, prospective cohort studies: the Finnish Cardiovascular Risk in Young Finns Study, the U.S.-based Bogalusa Heart Study, and the Australian Childhood Determination of Adult Health Study. Lipid and lipoprotein levels were measured in adolescents between the ages of 12 and 18 years and again when they were between the ages of 29 and 30 years, at which time they also had an ultrasound to measure carotid intima-media thickness, a surrogate for the risk of developing atherosclerotic cardiovascular disease.

In a previous analysis of this same data set, Mr. Magnussen and his associates found that adolescents with borderline or high-risk dyslipidemia were significantly more likely than were those with normal lipid levels to have dyslipidemia as adults after a mean follow-up of 20 years (Circulation 2008;117:32-42).

In the current study, adolescent dyslipidemia increased the relative risk for high intima-media thickness in adulthood by 60%-250%, and the higher risk was seen regardless of adult lipid and lipoprotein levels.

Adult carotid intima-media thickness was substantially higher in those who had been overweight or obese adolescents with dyslipidemia. The investigators estimated that overweight or obese 15-year-olds with dyslipidemia would show a difference in intima-media thickness of 0.11 mm in males or 0.08 mm in females by age 35 years, compared with normal-weight 15-year-olds with normal cholesterol levels.

The end point of increased intima-media thickness in young adulthood provides "a more solid end point than we've had before," said Dr. Roberta Williams, who was not involved in the study.

"Something structurally will happen. If you are both overweight/obese *and* have abnormal lipid levels, it is highly likely that you are headed for having real changesin your vascular bed as an adult," said Dr. Williams, chair of pediatrics at the University of Southern California, Los Angeles. She said she has no conflicts of interest related to this topic.

If you are obese and have dyslipidemia, it is likely that you will have changes in your vascular bed as an adult.

DR. WILLIAMS

The positive predictive value of adolescent dyslipidemia was low (ranging from 11% to 37% depending on weight and type of dyslipidemia), a fact that may be explained in part by normal fluctuations during adolescence in levels of lipoproteins, which are "building blocks"' for some hormones, she said. As a result, it's hard to tell which adolescents with dyslipidemia will go on to have increased intima-media thickness.

But the study found a high negative predictive value (ranging from 81% to 90%), meaning that adolescents without dyslipidemia are unlikely to develop cardiovascular disease as young adults. "This does not mean that they should go out and have a double cheeseburger," she said.

In an editorial commenting on the study, Dr. Stephen R. Daniels noted that the findings do not settle the question of whether all adolescents or targeted populations should be screened for dyslipidemia. Current guidelines recommend screening based on family history or the presence of other risk factors such as obesity, diabetes, or hypertension.

The study addresses neither the morbidity and mortality outcomes after adolescent dyslipidemia is identified, nor the costs or acceptability of screening, noted Dr. Daniels, professor and chairman of pediatrics at the University of Colorado at Denver (J. Am. Coll. Cardiol. 2009;53:870-1 [doi:10.1016/j.jacc.2008.11.037]).

"A substantially greater base of information is needed that will require additional investigation," he commented.

Dr. Magnussen and his associates reported having no potential conflicts of interest related to this study. Dr. Daniels has been a consultant for Abbott Laboratories and Merck/Schering-Plough Pharmaceuticals, which market anticholesterol medications. ■

Opinion-Based ACC/AHA Recommendations Raise Concern

BY MITCHEL L. ZOLER

Nearly half of the current clinical practice recommendations issued by the American College of Cardiology and the American Heart Association are based on expert opinion, case studies, or standards of care, and hence are not evidence based.

This may or may not be a problem, but it highlights the need for more studies to produce the data to fully substantiate how cardiovascular disease should be managed.

The American College of Cardiology and the American Heart Association "fully support the idea that as much as possible, we should have an evidence base, but there are many clinical situations where the studies have just not been done," said Dr. Sidney C. Smith Jr., professor of medicine and director of the center for cardiovascular science and medicine at the University of North Carolina at Chapel Hill. And in some cases it does not make sense to test standard practice in a controlled study, such as running an ECG on patients with chest pain, he noted.

Dr. Smith disagreed with the notion that practice guidelines should be produced only when study results back them up. "There are situations when providers, patients, and payers need recommendations; it's important that we get the best opinion possible and indicate that it is expert opinion and not based on the results of a randomized, controlled trial.

"Evidence-based medicine has tremendous promise for our patients, and we've made tremendous progress in the past decade to develop recommendations based on evidence, but we have much more work to do. It's a good time to invest" in better medicine, said Dr. Smith, who is also a former chief science officer for the AHA and currently chairs the ACC/AHA Task Force on Practice Guidelines.

Dr. Smith was the initiator of and coauthor of a recently reported study that quantified the level of evidence behind all 2,711 practice recommendations contained in the 16 current guidelines promoted by the ACC and AHA joint program (JAMA 2009;301:831-41). Among these recommendations 11% were backed by level A evidence, defined as evidence coming from multiple randomized trials or meta-analyses; 39% were rated as having level B evidence, defined as evidence from a single randomized trial or from nonrandomized studies; and 48% were derived from level C evidence, meaning expert opinion, case studies, or standards of care (total is less than 100% because of rounding).

But not all experts who deal with crafting clinical practice recommendations take as benign a view of basing them on level C evidence.

"I think expert opinion is quite misleading" when used as the basis for a practice recommendation, said Dr. Diana B. Petitti, professor of biomedical informatics at Arizona State University in Phoenix and vice chair of the U.S. Preventive Services Task Force (USPSTF), a panel organized by the federal Agency for Healthcare Research and Quality to formulate practice recommendations for clinical preventive services.

"Expert opinions imply that there is something that the experts know that the clinician doesn't know. I don't think it's always appreciated that it's only opinion. I prefer to say [when producing a practice recommendation] that there is no evidence of the kind we believe in that allows us to say you should do or not do this practice," she said in an interview. "There is a tendency to make guidelines and recommendations seem authoritative. I believe that physicians think that there is a great deal more behind authoritative recommendations than there might be when you lift the lid of the box and see what's underneath."

Dr. Petitti prefers the USPSTF approach, which distinguishes opinion-based recommendations from evidence-based ones, and also labels opinion statements to avoid categorizing them as recommendations.

She also noted that when study results are lacking, the USPSTF often goes through a "chain of evidence" process, an attempt to build a "plausible pathway" from the existing evidence to a recommendation. She gave the example of building an evidence chain to say that weight loss prevents cardiovascular disease. In the absence of direct evidence, the USPSTF would focus instead on documenting the evidence that weight loss improves hypertension and serum lipids, and has other proven benefits that in aggregate establish the broader premise.

Dr. Petitti also finds fault with two other aspects of ACC/AHA guidelines: the involvement of experts with conflicts of interest—a problem that the ACC and AHA attempt to resolve by full disclosure of potential conflicts, and the huge number of recommendations generated.

"I think people are naive about their ability to make unbiased judgments in the face of personal financial or intellectual interests," said Dr. Petitti, who said she prefers to completely bar people with a conflicting interest in a recommendation from voting.

The shear number of ACC/AHA recommendations is overwhelming and in fact a barrier to physicians seeking to follow them in practice, she added.

One solution is to conduct studies that focus on the issues where more data are needed. A new charge to the ACC/AHA committees that produce practice recommendations is to identify what areas need more study, Dr. Smith said. The AHA would then advocate to groups like the National Institutes of Health to get these studies funded. ■