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Review

Cardiovascular Consequences of Childhood Obesity

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ABSTRACT

Childhood and adolescent overweight and obesity is an important and increasingly prevalent public health problem in Canada and worldwide. High adiposity in youth is indicated in clinical practice by plotting body mass index on appropriate percentile charts normed for age and sex, although waist measures might be a further tool. High adiposity can lead to adiposopathy in youth, with associated increases in inflammation and oxidative stress, changes in adipokines, and endocrinopathy. This is manifest as cardiometabolic risk factors in similar patterns to those in noted in obese adults. Obesity and cardiometabolic risk factors have been shown to be associated with vascular changes indicative of early atherosclerosis, and ventricular hypertrophy, dilation, and dysfunction. These cardiovascular consequences are evident in youth, but childhood obesity is also predictive of similar consequences in adulthood. Childhood obesity and risk factors have been shown to track into adulthood and worsen in most individuals. The result is an exponential acceleration of atherosclerosis, which can be predicted to translate into an epidemic of premature cardiovascular disease and events. A change in paradigm is needed toward preventing and curing atherosclerosis and not just preventing cardiovascular disease. This would necessarily create an imperative for preventing and treating childhood obesity. Urgent attention, policy, and action are needed to avoid the enormous future social and health care costs associated with the cardiovascular consequences of obesity in youth.

RÉSUMÉ

La surcharge pondérale et l'obésité chez l'enfant et chez l'adolescent constituent un problème de santé publique de plus en plus répandu au Canada et dans le monde entier. Dans la pratique clinique, l'adiposité élevée chez les jeunes est déterminée par le graphique de l'indice de masse corporelle sur les tableaux appropriés des percentiles normalisés selon l'âge et le sexe, bien que la mesure du tour de taille puisse s'avérer un outil complémentaire. L'adiposité élevée peut entraîner une adiposopathie chez les jeunes, ainsi que des augmentations de l'inflammation et du stress oxydatif, des changements engendrés sur les adipokines et une endocrinopathie. Cela se manifeste par des facteurs de risque cardiométabolique dans des modèles similaires à ceux des adultes obèses. Il a été démontré que l'obésité et les facteurs de risque cardiométabolique sont associés à des changements vasculaires évoquant l'apparition précoce de l'athérosclérose et de l'hypertrophie, de la dilatation et du dysfonction ventriculaire. Ces conséquences cardiovasculaires sont évidentes chez les jeunes, mais l'obésité infantile permet également de prédire des conséquences similaires à l'âge adulte. Il a été démontré que l'obésité et les facteurs de risque présents durant l'enfance se poursuivent jusqu'à l'âge adulte et s'aggravent chez la plupart des individus. Il en résulte une croissance exponentielle de l'athérosclérose, qui peut se traduire par une épidémie de maladies et d'événements cardiovasculaires de survenue précoce. Un changement de paradigme s'impose pour prévenir et traiter l'athérosclérose, et non seulement prévenir la maladie cardiovasculaire, d'où l'obligation de prévention et de traitement de l'obésité infantile. Il est nécessaire d'y accorder une attention immédiate, de créer de toute urgence des politiques et d'intervenir rapidement pour éviter que les conséquences cardiovasculaires de l'obésité chez les jeunes imposent dans le futur des coûts importants à la société et aux soins de santé.

Obesity is an important public health problem in Canada, escalating morbidity and mortality, and societal and health care costs.[1] In 2006, direct health care costs related to overweight and obesity were estimated at $6 billion, accounting for 4.1% of total health care expenditures in Canada.[2] Secular trends from national health surveys indicate that the prevalence of pediatric obesity is either increasing or has plateaued. The trend has also been for a greater proportion of the increases in body mass index (BMI) to be attributable to increases in abdominal adiposity.[3] From 3 Canadian national health surveys, the prevalence of increased waist circumference in 12- to 19-year-olds increased from 1.8% in 1981 to 2.4% in 1988 and to 12.8% in 2007-2009.[4] Recent data from the Canadian Health Measures Survey suggests that although approximately a third of 5- to 17-year-olds would be classified as overweight or obese, there has not been an increase during

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the past decade.[5] This has not been the case globally, where the prevalence of overweight and obesity in children and adolescents increased from 1980 to 2013 to 23.8% of boys and 22.6% of girls in developed countries.[6] Longitudinal studies have shown that overweight children become obese adults.[7] Further, more than a third of normal weight children will become overweight as young adults. The implications of these data are staggering for the future health of the population and the health care system. This has been particularly evident in the United States, where it might be projected based on current trends that by 2030, 86.3% of adults will be overweight or obese, with a further projection (albeit unlikely) that all adults would be overweight or obese by 2048.[8] Unfortunately, evidence has yet to suggest a substantial effect of current interventions for either the prevention or management of childhood obesity.[9]

Are We Programming Children to Be Obese?

There is increasing evidence that early life is a critical time for influencing later cardiovascular risk and vascular health. The in utero environment is influenced by maternal obesity, possibly mediated by low-grade inflammation or cardiovascular risk factors, particularly gestational diabetes, and might have adverse developmental programming influences on the offspring, predisposing them to obesity and accelerated atherosclerosis.[10,11] Excessive weight gain from birth to 18 months of age has been shown to be associated with later overweight and obesity, greater central adiposity, and higher blood pressure and C-reactive protein, leading to greater carotid extra-medial thickness measured at age 8 years.[12,13] A similar association, including greater arterial stiffness, was noted in children assessed at age 5 years.[14] A protective effect of breastfeeding on the risk of obesity in later life has been observed in multiple studies.[15] Early life conditioning and lifestyle factors have been shown to be effective predictors of adult obesity.[16] The strongest of these factors is the presence of overweight in childhood, more so with an earlier age of onset. When it comes to obesity, children do not grow out of it, but grow more entrenched into it.

Measurement and Patterns of Adiposity in Children

Anthropometry is used as a surrogate measure to reflect the magnitude of adiposity. In clinical practice, BMI expressed as an age and sex-specific population-based percentile is used to define overweight ($\geq$ 85th percentile) and obesity ($\geq$ 95th percentile), with some defining severe obesity as $\geq$ 99th percentile. The reference standard and the cut points used can influence prevalence estimates. For example, from 2004 Canadian data, the prevalence of overweight and obesity combined was 35% using growth curves from the World Health Organization, 26% using International Obesity Task Force charts, and 28% using US Centers for Disease Control charts.[17] Percentile charts with cut points based on national/population-specific reference data are superior.[18] Use of BMI alone has been believed to have high specificity but low sensitivity to detect high adiposity.[19] Assessment of waist circumference and normalization as either an age and sex-specific percentile, waist to height ratio, or waist to hip ratio have similar associations with level of adiposity as BMI when used alone.[20] They might have stronger associations with related cardiometabolic risk when used together with BMI.[21,22] It should be recognized that the relationship of measures of adiposity with cardiometabolic risk and cardiovascular consequences are continuous and nonlinear, and that cut points loosely reflect inflection points where risk intensifies and accelerates. In addition, particularly in children, cross-sectional assessments are less meaningful than longitudinal trends, reflective of duration and intensification of exposure.

Other measures that are used less frequently in clinical settings might include skin fold thicknesses, bioelectrical impedance, plethysmography, dual energy X-ray absorptiometry scans, and magnetic resonance imaging. The site of fat deposition, particularly ectopic fat, might have an important effect on cardiometabolic risk and vascular health.[23] In children and adolescents, magnetic resonance imaging has been useful to define increased cardiometabolic derangements associated with ectopic fat accumulation in the pancreas and liver,[24] muscles,[25] and epicardium.[26]

Cardiometabolic Effects

Although high adiposity itself can drive cardiovascular disease risk, much of the risk is mediated by associated cardiometabolic risk factors. In addition to quantitative and qualitative aspects of adiposity, adipocyte and adipose tissue anatomic and functional abnormalities contribute to a pathophysiologic process termed adiposopathy.[27] The presence of cardiometabolic derangements vary between individuals with the same degree of adiposity, and environmental, behavioural, and genetic factors might be key influencers. Adiposopathy might be indicated by the presence of inflammatory markers, markers of oxidative stress, altered levels of adipokines, and endocrine abnormalities, particularly insulin resistance, all of which have been noted in obese youth.[28] These derangements might drive combined dyslipidemia (high triglycerides, low high-density lipoprotein [HDL] cholesterol, high non-HDL cholesterol, and increased low-density lipoprotein [LDL] particle numbers and reduced particle size), hypertension, and type 2 diabetes, which are evident in overweight and obese youth, as noted in a systematic review and meta-analysis of 63 studies including 49,200 children.[29] This has been confirmed in Canada from the Canadian Health Measures Survey, which additionally noted higher C-reactive protein in overweight and obese children and adolescents.[30] These risk factors, and inflammation and oxidative stress associated with adiposopathy, contribute to endothelial dysfunction and initiation and acceleration of atherosclerosis.[31]

The concept of the metabolic syndrome as defined in adults translates less well to children.[32] Nonetheless, in a study that combined longitudinal cohorts from the Bogalusa Heart Study and Cardiovascular Risk in Young Finns Study explored the utility of 4 definitions of pediatric metabolic syndrome and their components for predicting type 2 diabetes and high carotid intima-media thickness (CIMT) in adulthood (age 24-41 years).[33] Youth with metabolic syndrome had a 2- to 3-fold greater likelihood of having type 2 diabetes and high CIMT as adults, although prediction using childhood BMI alone was equivalent or superior to youth metabolic syndrome classifications.