Youth With Obesity and Obesity-Related Type 2 Diabetes Mellitus Demonstrate Abnormalities in Carotid Structure and Function

Elaine M. Urbina, MD; Thomas R. Kimball, MD; Connie E. McCoy, RVT; Philip R. Khoury, MS; Stephen R. Daniels, MD, PhD; Lawrence M. Dolan, MD

Background—Adults with obesity or type 2 diabetes mellitus (T2DM) are at higher risk for stroke and myocardial infarction. Increased carotid intima-media thickness (cIMT) and stiffness are associated with these adverse outcomes. We compared carotid arteries in youth who were lean, were obese, or had T2DM.

Methods and Results—Carotid ultrasound for cIMT measurement was performed, the Young elastic modulus and beta stiffness index were calculated, and anthropometric and laboratory values and blood pressure were measured in 182 lean, 136 obese, and 128 T2DM youth (aged 10 to 24 years). Mean differences were evaluated by ANOVA. Independent determinants of cIMT, Young elastic modulus, and beta stiffness index were determined with general linear models. Cardiovascular risk factors worsened from lean to obese to T2DM groups. T2DM subjects had greater cIMT than that in lean and obese subjects for the common carotid artery and bulb. For the internal carotid artery, cIMT measurements in both obese and T2DM groups were thicker than in the lean group. The carotid arteries were stiffer in obese and T2DM groups than in the lean group. Determinants of cIMT were group, group×age interaction, sex, and systolic blood pressure for the common carotid artery ($r^2=0.17$); age, race, and systolic blood pressure for the bulb ($r^2=0.16$); and age, race, sex, systolic blood pressure, and total cholesterol for the internal carotid artery ($r^2=0.21$). Age, systolic blood pressure, and diastolic blood pressure were determinants of all measures of carotid stiffness, with sex adding to the Young elastic modulus ($r^2=0.23$), and body mass index Z score, group, and group×age interaction contributing to the beta stiffness index ($r^2=0.31$; all $P<0.0001$).

Conclusions—Youth with obesity and T2DM have abnormalities in carotid thickness and stiffness that are only partially explained by traditional cardiovascular risk factors. These vascular changes should alert healthcare practitioners to address cardiovascular risk factors early to prevent an increase in the incidence of stroke and myocardial infarction. (Circulation. 2009;119:2913-2919.)

Key Words: carotid arteries ■ elasticity ■ obesity ■ pediatrics ■ risk factors

Adults with obesity or type 2 diabetes mellitus (T2DM) are at higher risk for stroke and myocardial infarction. Evidence of target organ damage in the carotid arteries (increased thickness and stiffness) is also associated with adverse cardiovascular outcomes even after adjustment for age. Because adults with obesity and T2DM are at risk for developing increased carotid intima-media thickness (cIMT) and carotid stiffness, we sought to determine whether similar carotid structural and functional abnormalities exist in youth with obesity or T2DM compared with lean controls.

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Methods

Study Population
The study population consisted of 446 youth who were examined as part of an ongoing study of the cardiac and vascular effects of obesity and T2DM in adolescents and young adults (aged 10 to 24 years; 65% nonwhite, 39% male). Diagnosis of T2DM (for T2DM group, $n=128$) was made by the primary provider. Chart review was performed to include only diabetic subjects who were islet cell antibody negative (glutamic acid decarboxylase, islet cell antigen 512, insulin autoantibodies), who had no evidence of other specific type of diabetes, and who did not require insulin in the basal state to prevent diabetic ketoacidosis. All obese subjects underwent a 2-hour oral glucose tolerance test to rule out subclinical T2DM according to American Diabetes Association guidelines. Pregnant females were excluded from the study.

Before enrollment in the study, written informed consent was obtained from subjects aged ≥18 years or from the parent or guardian for subjects aged <18 years. Written assent was also obtained for subjects aged <18 years according to the guidelines established by the institutional review board at Cincinnati Children’s Hospital.

Data Collection
After a minimum 10-hour overnight fast, participants had questionnaire, anthropometric, blood pressure (BP), laboratory, and carotid
artery data collected. An average of 2 measures of height was obtained with a calibrated stadiometer (Veeder-Rood, Elizabeth-town, NC) by trained personnel. Weight was also measured twice and averaged with the use of a Health-O-Meter electronic scale. Body mass index (BMI) was calculated as kilograms per meter squared. Lean (lean group, n=182) was defined as BMI <85th percentile, and obesity (obese group, n=136) was defined as BMI >95th percentile according to Centers for Disease Control and Prevention growth charts. BP was measured according to the standards of the Fourth Report on BP in Children.8

Fasting plasma glucose was measured with the use of a Hitachi model 704 glucose analyzer with intra-assay and interassay coefficients of variation of 1.2% and 1.6%, respectively.9 Plasma insulin was measured by radioimmunossay with an anti-insulin serum raised in guinea pigs,101I-labeled insulin (Linco, St Louis, Mo), and a double antibody method to separate bound from free tracer. This assay has a sensitivity of 2 pmol and has intra-assay and interassay coefficients of variation of 5% and 8%.10 Assays of fasting plasma lipid profiles were performed in a laboratory that is National Heart, Lung, and Blood Institute/ Centers for Disease Control and Prevention standardized with the low-density lipoprotein cholesterol concentration calculated with the use of the Friedewald equation. C-reactive protein (CRP) was measured with the use of a high-sensitivity enzyme-linked immunosorbent assay. Glycosylated hemoglobin A1c (HbA1c) was measured in red blood cells by high-performance liquid chromatography methods. Duration of disease was measured from the date of diagnosis to the date of study.

Carotid Ultrasonography

Carotid ultrasound studies were performed by a single registered vascular technologist who was blinded to subject group assignment. The carotid arteries were evaluated with a high-resolution B-mode ultrasonography with the use of a GE Vivid 7 ultrasound imaging system with a high-resolution linear array vascular ultrasound variable-frequency transducer centered at 7.5 MHz. For each subject, each carotid wall and segment was examined independently from continuous angles to identify the thickest cIMT. Multiple digital image loops were digitally transmitted with the Camtronic Medical System for offline reading and analyses. A trace technique was employed to measure the maximum carotid thickness from leading edge (lumen-intima) to leading edge (media- adventitia). This technique was found to be more reproducible than point-to-point measurements (coefficients of variation for repeat readings 5.3% to 8.0% for trace versus 8.4% to 11.6% for point-to-point for the 3 carotid segments; unpublished data, Urbina, MD, 2008). Three segments were imaged with right and left sides averaged for the common carotid artery, the bifurcation (carotid bulb), and the internal carotid artery.

M-mode measurements of the common carotid artery were also performed.11 An optimal 2-dimensional image of the common carotid artery was obtained, and the M-mode cursor was placed ~1 cm proximal to beginning of the carotid bulb. The maximal and minimal lumen diameters were read from the M-mode tracing for calculations of carotid stiffness.11 Calculations included the Young elastic modulus (YEM) and beta stiffness index (β).12

Statistical Analysis

All analyses were performed with Statistical Analyses Software (SAS, version 9.1.3)13 Average values for demographic, anthropometric, and laboratory data were obtained by group. Variance stabilizing measures to transform nonnormal values were performed as needed. ANOVA was performed to look for differences by BMI group, with Bonferroni correction for multiple comparisons as appropriate. Bivariate correlations were calculated between carotid outcome variables and all covariates overall and by BMI group. General linear models were constructed with the use of important covariates from correlation analyses to elucidate independent determinants of cIMT and carotid stiffness.

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Table 1. Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Variables</th>
<th>Lean (n=182)</th>
<th>Obese (n=136)</th>
<th>T2DM (n=128)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>17.8 (3.5)</td>
<td>17.9 (3.3)</td>
<td>18.8 (3.2)</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>59</td>
<td>67</td>
<td>60</td>
</tr>
<tr>
<td>Race, % nonwhite</td>
<td>62</td>
<td>65</td>
<td>63</td>
</tr>
<tr>
<td>Height, m†</td>
<td>165.7 (10.8)</td>
<td>167.1 (10.3)</td>
<td>169.7 (10.2)</td>
</tr>
<tr>
<td>Weight, kg‡</td>
<td>59.5 (11.9)</td>
<td>102.6 (21.2)</td>
<td>105.8 (29.9)</td>
</tr>
<tr>
<td>BMI, kg/m²†‡</td>
<td>21.4 (2.6)</td>
<td>36.5 (6.5)</td>
<td>36.4 (9.4)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg††</td>
<td>110.2 (9.5)</td>
<td>119.1 (10.4)</td>
<td>124.6 (12.5)</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg††</td>
<td>66.2 (6.9)</td>
<td>68.7 (7.3)</td>
<td>73.3 (8.8)</td>
</tr>
<tr>
<td>Mean pressure, mm Hg††</td>
<td>77.6 (7.8)</td>
<td>83.6 (7.6)</td>
<td>88.3 (9.9)</td>
</tr>
<tr>
<td>Pulse pressure, mm Hg‡</td>
<td>44.0 (7.0)</td>
<td>50.4 (7.3)</td>
<td>51.3 (9.1)</td>
</tr>
<tr>
<td>Heart rate, bpm†‡</td>
<td>63.7 (11.3)</td>
<td>67.4 (10.2)</td>
<td>72.3 (11.7)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL††</td>
<td>159.6 (27.7)</td>
<td>174.3 (35.5)</td>
<td>186.2 (39.7)</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL†‡</td>
<td>88.5 (23.3)</td>
<td>108.6 (32.1)</td>
<td>113.8 (37.3)</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL*†‡</td>
<td>57.0 (13.1)</td>
<td>46.3 (9.6)</td>
<td>45.1 (11.7)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL*†‡</td>
<td>69.8 (32.2)</td>
<td>100.9 (62.8)</td>
<td>145.5 (100.9)</td>
</tr>
<tr>
<td>Glucose, mg/dL*†‡</td>
<td>89.7 (6.4)</td>
<td>93.8 (8.9)</td>
<td>160.9 (89.9)</td>
</tr>
<tr>
<td>Insulin, µmol/L*†‡</td>
<td>11.5 (4.7)</td>
<td>23.9 (18.3)</td>
<td>29.9 (23.5)</td>
</tr>
<tr>
<td>HbA1c, %*†</td>
<td>5.4 (0.4)</td>
<td>5.0 (0.7)</td>
<td>8.5 (3.3)</td>
</tr>
<tr>
<td>CRP, mg/L*‡</td>
<td>1.10 (3.49)</td>
<td>5.41 (6.39)</td>
<td>6.27 (7.74)</td>
</tr>
</tbody>
</table>

LDL indicates low-density lipoprotein; HDL, high-density lipoprotein. Variance stabilizing transformations were applied as needed before ANOVA was conducted. Values are mean (SD) unless otherwise indicated.

P<0.05 for *lean < T2DM; †obese < T2DM; ‡lean < obese.

Results

Groups did not differ by age, race, or sex distribution. Traditional cardiovascular risk profile (weight, BP, heart rate, lipids, glucose, insulin, inflammation) worsened from lean to obese to T2DM (probability values in Table 1). The proportion of subjects with BP in the prehypertensive or true-hypertensive range differed significantly among groups when evaluated by ANOVA. However, the absolute number of subjects with abnormal BP levels was low in the lean (3.9% prehypertensive, 2.8% true hypertensive) and obese groups (8.1% prehypertensive, 13.2% true hypertensive), with the T2DM group having higher prevalence (10.5% prehypertensive, 26.6% true hypertensive). The prevalence of abnormal diastolic BP was lower (lean: 2.8% prehypertensive, 2.2% true-hypertensive; obese: 2.9% prehypertensive, 7.4% true hypertensive; T2DM: 5.7% prehypertensive, 14.5% true hypertensive). For all carotid segments, T2DM subjects had significantly greater cIMT than lean subjects. T2DM subjects had thicker cIMT than obese participants for the common carotid artery and bulb but did not differ for the internal carotid artery, where both obese and T2DM subjects were thicker than lean subjects (Table 2 and Figure 1; all P<0.05). Obese and T2DM groups had stiffer carotid arteries with higher YEM and β than the lean group (Table 2 and Figure 2).

Correlation analyses revealed that age, BP, and low-density lipoprotein cholesterol correlated with all outcome measures. BMI was significant for all but YEM. Glucose was significant for all cIMT segments. CRP correlated with stiffness measures and all cIMT but the common carotid artery. High-density...
lipoprotein cholesterol only correlated with internal cIMT. Triglycerides correlated with internal cIMT and YEM (all \( P<0.05 \)). Correlations did not differ substantially by group.

Multivariate linear regression was performed for all carotid outcome variables against the covariates of group, race, sex, age, height, BMI, heart rate, systolic BP, diastolic BP, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, glucose, insulin, and high-sensitivity CRP (Table 3). Independent determinants of cIMT were group, age, group \( \times \) age interaction, sex, systolic BP for the common carotid artery \( (r^2=0.17) \); age, race, and systolic BP for the bulb \( (r^2=0.15) \); and age, race, sex, systolic BP, and total cholesterol for the internal carotid artery \( (r^2=0.21) \), respectively. When stratified by group, general linear models and simple plots (Figure 3) revealed that the slope for the regression of age on common carotid IMT was flat for lean subjects, indicating no significant increase over the age range in our study \( (\text{lean } \text{cIMT}=0.49+0.0017 \times \text{age}; P=\text{NS}) \). However, there was a significant increase in cIMT with age for obese and T2DM groups, with the slope of the regression steepest for T2DM \( \text{obese } \text{cIMT}=0.41+0.0051 \times \text{age}; \text{T2DM } \text{cIMT}=0.38+0.0083 \times \text{age}; \text{both } P<0.002 \), suggesting an increased effect of age on cIMT progression in the presence of obesity or T2DM. Age and BP were determinants of all measures of carotid stiffness with group, age, and group \( \times \) age interaction contributing to \( \beta \) \( (r^2 \text{ for YEM}=0.23, \beta=0.31; \text{all } P<0.0001) \).

Table 2. Carotid Ultrasound Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lean ( (n=182) )</th>
<th>Obese ( (n=136) )</th>
<th>T2DM ( (n=128) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>cIMT, mm( ^{\dagger} )</td>
<td>0.52 (0.08)</td>
<td>0.50 (0.09)</td>
<td>0.54 (0.10)</td>
</tr>
<tr>
<td>Bulb cIMT, mm( ^{\dagger} )</td>
<td>0.47 (0.08)</td>
<td>0.48 (0.11)</td>
<td>0.52 (0.13)</td>
</tr>
<tr>
<td>Internal cIMT, mm( ^{\dagger} )</td>
<td>0.39 (0.08)</td>
<td>0.42 (0.09)</td>
<td>0.44 (0.10)</td>
</tr>
<tr>
<td>( \beta ), unitless( ^{\ddagger} )</td>
<td>0.96 (0.27)</td>
<td>1.12 (0.44)</td>
<td>1.08 (0.48)</td>
</tr>
<tr>
<td>YEM, mm Hg/mm( ^{\dagger} )</td>
<td>83.8 (24.6)</td>
<td>105.2 (40.5)</td>
<td>100.8 (47.1)</td>
</tr>
</tbody>
</table>

Variance stabilizing transformations were applied before ANOVA was conducted. Values are mean (SD).

\( P<0.05 \) for \( \ast \text{lean } \text{cIMT}<\text{T2DM}; \ast \text{obese } \text{cIMT}<\text{T2DM}; \dagger \text{lean } \text{cIMT}<\text{obese}; \ddagger \text{obese } \text{cIMT}<\text{T2DM}; \| \text{lean } \text{cIMT}<\text{T2DM}.\)

Figure 1. cIMT by group. \( \ast P<0.05, \text{lean and obese } \text{T2DM}; \dagger P<0.05, \text{lean } \text{obese and T2DM}.\)

Figure 2. Carotid stiffness by group. \( \ast P<0.05, \text{lean } \text{T2DM}; \dagger P<0.05, \text{lean } \text{obese}; \ddagger P<0.1, \text{lean } \text{T2DM}.\) YEM (mm Hg/mm) is divided by 100 for graphing purposes. \( \beta \) is unitless.

Modeling was repeated with BP category (normal, prehypertensive, or true hypertensive) instead of continuous BP variables. The results did not change substantially, although the models tended to explain a smaller proportion of the variability in cIMT and carotid stiffness. The importance of group as a covariate did not change except that group entered the model for the internal carotid artery. Because of the small number of subjects in some of the BP category by group cells, it was believed that modeling with BP as a continuous variable was more robust.

Discussion

Our study showed that adolescents and young adults with T2DM have significantly thicker cIMT than lean controls for all the carotid artery segments. This is not surprising because our subjects with T2DM had higher cardiovascular risk factor levels. More important is the confirmation that increased thickness of the common carotid artery and bulb can also be found in uncomplicated obesity. Furthermore, \( \beta \) and YEM were higher in both obese and T2DM subjects compared with lean subjects when examined by ANOVA. These data demonstrate that early changes in vascular structural and function can be demonstrated in youth with obesity before the development of carbohydrate intolerance. Additional compromise is demonstrated in patients with established T2DM.

As expected, levels of cardiovascular risk factors increased from the lean to obese to T2DM groups, and traditional cardiovascular risk factors correlated with cIMT and stiffness. In multivariate analyses, group was an independent determinant of cIMT for the common carotid artery and \( \beta \). Classification as obese or T2DM was not an independent determinant of cIMT in the bulb or internal carotid artery or YEM. This suggests that the effect of obesity and T2DM may impart additional influences on common carotid structure and some measures of carotid function that are not entirely explained by traditional cardiovascular risk factors. In addition, obesity and T2DM may be modifying the effect of risk factors as seen by the greater effect of age on common carotid cIMT in the obese and T2DM groups compared with the lean group.
Adult studies have demonstrated a strong association between obesity and cIMT. The Multi-Ethnic Study of Atherosclerosis examined a large cohort (n=6814; age 45 to 84 years) of cardiovascular disease–free subjects and found that obese subjects of both sexes were more likely to have common and internal carotid cIMT greater than the 80th percentile. Although the obese subjects were more likely to report hypertension or diabetes, the association between adiposity and cIMT persisted after adjustment for traditional cardiovascular risk factors. Developing adiposity in childhood has also been linked to having increased carotid thickness as an adult. In the Muscatine Study, childhood BMI was a significant determinant of cIMT measured as an adult (age 3 to 42 years) for women. The Bogalusa Heart Study found that cumulative levels of BMI in childhood were associated with adult cIMT in both sexes even after controlling for adult BMI.

Cross-sectional studies have demonstrated a relationship between obesity and common carotid IMT during childhood. Iannuzzi et al studied 100 children with BMI >95th percentile (Centers for Disease Control and Prevention) who were healthy without any obesity-related comorbidities (hypertension, dyslipidemia, glucose intolerance, or diabetes). Common carotid IMT was thicker in obese youth compared with age-matched controls even after controlling for traditional cardiovascular risk factors. However, when glucose was entered into the model instead of homeostatic model assessment, the difference in cIMT by obesity group reached only marginal significance. In a similar study, Reinehr et al found glucose to be an independent determinant of cIMT in obese and lean children along with BMI, systolic BP, and high-sensitivity CRP. These data suggest a relationship between worsening carbohydrate intolerance and thicker cIMT similar to that seen in adults. Mangge et al studied a larger cohort (n=228) and also found increased cIMT in obese compared with lean children. However, only the common carotid was evaluated, and no multivariate modeling was performed. In a study of Chinese youth, both the internal and common carotid arteries were thicker in obese subjects. However, the bulb was not examined in the study, nor was multivariate regression performed. Furthermore, the average BMI in this small study (n=61; BMI 27.7 kg/m²) was lower than in our cohort (BMI 36.5 kg/m²), suggesting that their findings may not be generalizable to more obese American youth. One recent study measured all 3 carotid segments in lean and obese youth but only on the left side. Furthermore, their multivariate models contained incomplete lipid data (only 12 of 30 controls) and did not include BP as a covariate. Our data extend the observations

![Figure 3. cIMT by age and group. P for slope not equal to 0 was <0.002 for obese and T2DM; P=NS for lean group.](image-url)
on the effect of obesity on all segments of the carotid artery and provide insight on independent determinants of cIMT in youth with the use of multivariable models containing all traditional cardiovascular risk factors.

Similar to data on cIMT, truncal subcutaneous fat accumulation measured as an adolescent was associated with increased carotid stiffness in adulthood (average age, 36 years). In a larger study of healthy adults (n=2255; age 24 to 39 years), the relationship remained even after adjustment for number of cardiovascular risk factors. Cross-sectional studies of children have also demonstrated increased carotid stiffness in obese subjects with the metabolic syndrome compared with obese children without this cardiovascular risk factor clustering even after adjustment for age, sex, and CRP. Tounian et al found obese youth to have stiffer carotid arteries than lean controls, but they did not find a significant relationship between carotid stiffness and cardiovascular risk factors. Our data include a larger cohort than the study by Tounian, which may explain our ability to demonstrate relationships between cardiovascular risk factors and carotid stiffness in both univariate and multivariate models. These data suggest that a spectrum of vascular abnormalities may develop as an individual develops obesity before progressing to metabolic derangement and final development of T2DM.

Substantial data are available describing vascular changes in adults with T2DM. Diabetic subjects have both thicker and stiffer carotid arteries than healthy controls. Thickness is affected by BP, age, duration of diabetes, glycemic control, and degree of adiposity. Insulin resistance modifies carotid stiffness in adults with T2DM. Arterial stiffness is also affected by carbohydrate intolerance. Data from the Atherosclerosis Risk in Communities Study show higher carotid stiffness with increasing concentrations of fasting glucose in nondiabetic middle-aged subjects. This was also seen in the Rotterdam Study of older adults. Our observation of increasing severity of carotid abnormalities across the obese to the diabetic subjects also suggests a graded effect of diminishing metabolic control on vascular damage.

In youth, substantial evidence is available demonstrating abnormalities on carotid ultrasound in subjects with type 1 diabetes mellitus. Most are small studies with <100 subjects, and the majority image only the common carotid artery. Although the majority demonstrate significantly thicker cIMT in youth with type 1 diabetes mellitus compared with controls, many are unable to demonstrate relationships between cardiovascular risk factors and cIMT. This may be due to the absence of risk factor data or study designs in which subjects were intentionally or coincidentally matched by risk factor levels. Similar to our data, a few studies found univariate correlations between cIMT and BMI, BP, and lipids but did not perform multivariate analyses to evaluate independent determinants. The narrow range of differences in BP and cholesterol levels between controls and children with type 1 diabetes mellitus is not surprising given the normal, low BMI levels in cases and controls in these articles. Our data are the first to examine the effect of T2DM on cIMT. Furthermore, our study includes 2 controls (1 lean and 1 obese) for each subject with T2DM, providing a wider range of cardiovascular risk factor levels and increasing our power to demonstrate independent associations between T2DM, cardiovascular risk factors, and cIMT.

Stiffer vessels are also found in youth with type 1 diabetes mellitus. Poor glycemic control, as manifest by higher HbA1c levels, correlated with carotid distensibility in 1 study. Another found environmental agents such as exposure to tobacco or frequent respiratory infections to be related to carotid compliance. Our data are unique in showing the effect of T2DM on vascular compromise in a larger group of adolescents and young adults.

Limitations
Our cross-sectional design does not allow us to determine the time sequence for development of vascular changes as an individual progresses from uncomplicated obesity to metabolic syndrome and finally to T2DM. This cohort also has a somewhat narrow age range, which may have limited our ability to detect increases in common carotid cIMT in the lean subjects. The T2DM group was also slightly older and had higher BP and cholesterol levels than the lean and obese groups. However, multivariate analyses controlling for these covariates were performed to statistically control for these disparities. Although we found a significant difference in cIMT between groups, the absolute magnitude of the differences was small. Therefore, the utility of cIMT measurement for risk stratification for pediatric patients may be diminished by imprecision of the methodology and biological variability. Furthermore, use of ultrasound screening is limited by lack of normative data across ages, sexes, and race/ethnicity. Further refinement of ultrasound techniques and collection of additional data in normal children are needed to advance the field.

Conclusions
We conclude that adolescents and young adults with obesity and T2DM are at risk for early atherosclerotic changes in the carotid arteries. The abnormalities are only partially explained by traditional cardiovascular risk factors such as age and BP because the presence of obesity or diabetes mellitus contributed independently to carotid structure and function. These findings are particularly disturbing because the prevalence of obesity-related metabolic syndrome and T2DM in youth is increasing across the globe and may lead to a parallel increase in adverse cardiovascular outcomes. Therefore, pediatric healthcare practitioners should continue to screen for abnormalities in cardiovascular risk factors, especially in children with elevated BMI or T2DM. Comprehensive lifestyle interventions to reduce obesity must be applied now if we are to prevent a projected decline in life expectancy for our youth.

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We would like to acknowledge the work of the entire Cardiovascular Disease in Type 2 Diabetes Study team. We would also like to thank the participants of the Cardiovascular Disease in Type 2 Diabetes Study and their families, without whose support this study would not be possible.

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Disclosures

None.

References


Clinical Perspective

Adults with obesity or type 2 diabetes mellitus (T2DM) are at higher risk for stroke and myocardial infarction. Many of these high-risk individuals demonstrate evidence of target organ damage in the carotid arteries (increased carotid intima-media thickness and carotid stiffness) well before the adverse cardiovascular outcomes occur. Whether similar changes in the carotid arteries occur in youth with obesity or T2DM is not known. Therefore, we compared carotid intima-media thickness and carotid stiffness in high-risk youth with lean controls. We found that youth with T2DM had significantly greater carotid intima-media thickness than lean subjects for all carotid segments (common, bulb, and internal), and their carotid intima-media thickness was thicker than in obese participants for the common carotid artery and bulb (all \( P < 0.05 \)). Obese and T2DM groups had stiffer carotid arteries with higher Young elastic modulus and beta stiffness index than the lean group. We conclude that youth with T2DM demonstrate significant abnormalities in carotid structure and function, and, in obese youth, changes are present well before progression to overt T2DM. The abnormalities are only partially explained by traditional cardiovascular risk factors such as age and blood pressure because the presence of obesity or diabetes mellitus contributed independently to carotid structure and function. The increasing prevalence of obesity across the globe may lead to a parallel increase in cardiovascular diseases. Therefore, pediatric healthcare practitioners should continue to screen for abnormalities in cardiovascular risk factors, especially in children with elevated body mass index or T2DM. Comprehensive lifestyle interventions to reduce obesity must be applied now to prevent a projected decline in life expectancy for our youth.
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