Published in final edited form as:
J Pediatr Endocrinol Metab. 2012 ; 25(0): 717–721. doi:10.1515/jpem-2012-0070.

Adiponectin and arterial stiffness in youth with type 1 diabetes: the SEARCH for Diabetes in Youth Study

Amy S. Shah[1,*], **Lawrence M. Dolan**[1], **Abigail Lauer**[2], **Cralen Davis**[2], **Dana Dabelea**[3], **Stephen R. Daniels**[5], **Richard F. Hamman**[3], **Santica Marcovina**[4], **R. Paul Wadwa**[5], and **Elaine M. Urbina**[1]

[1]Department of Pediatrics, Cincinnati Children's Hospital, University of Cincinnati College of Medicine, Cincinnati, OH, USA

[2]Department of Biostatistical Sciences, Wake Forest University School of Medicine, Winston-Salem, NC, USA

[3]Department of Epidemiology, Colorado School of Public Health, University of Colorado, Aurora, CO, USA

[4]Northwest Lipid Research Laboratories, University of Washington, Seattle, WA, USA

[5]Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA

Abstract

Persons with type 1 diabetes are at increased risk of developing vascular disease. Adiponectin concentrations may play an intermediate role in this process. We sought to determine whether adiponectin is correlated with vascular stiffness in adolescents with type 1 diabetes. Plasma adiponectin, pulse wave velocity (PWV), augmentation index (AIx-75), and brachial distensibility (BrachD) were collected in 225 adolescents. Outcomes were evaluated by sex, and regression models were used to determine whether adiponectin was an independent determinant of arterial stiffness. Males had lower adiponectin levels and stiffer vessels (lower BrachD, $p<0.01$) than females. Unadjusted correlations revealed that adiponectin was correlated with BrachD ($p<0.01$) but not PWV and AIx-75. After adjustment, adiponectin was not a significant predictor of BrachD. The most consistent predictors of increased stiffness were age, male sex, blood pressure, obesity, and total cholesterol ($p<0.05$). Adiponectin's contributions to arterial stiffness appear to be masked by other cardiovascular risk factors in persons with type 1 diabetes.

Keywords

adiponectin; arterial stiffness; diabetes; pediatrics

[*]Corresponding author: Amy S. Shah, MD MS, Division of Endocrinology, ML 7012, Cincinnati Children's Hospital, 3333 Burnet Avenue, Cincinnati, OH 45229, USA Phone: +1-513-636-4744, Fax: +1-513-636-7486, amy.shah@cchmc.org.

Conflict of interest statement

Disclosure statement: The authors have no conflict of interest to declare.

The contents of this paper are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases.

Introduction

Vascular disease is common in persons with type 1 diabetes (1). Increased arterial stiffness is one mechanism that may explain this finding, as vascular dysfunction is linked with higher rates of cardiovascular disease (2). Reproducible non-invasive methods for assessing atherosclerosis-related increases in arterial stiffness include pulse wave velocity (PWV), augmentation index (AIx-75) (3) and brachial arterial distensibility (BrachD) (4). Prior work has found that adolescents with type 1 diabetes have increased vascular stiffness as evidenced by increased PWV and AIx-75, and decreased BrachD, compared with healthy controls (5). Despite this finding, the pathophysiologic factors that contribute to vascular stiffness are poorly understood.

Prior work has suggested adiponectin may play a protective role in the development of vascular disease (6). Adiponectin is a 244-amino acid protein secreted by the adipose tissue that is believed to have some anti-inflammatory (7) and anti-atherosclerotic properties (8).

To date, most studies in persons with type 1 diabetes have evaluated adiponectin in the setting of advanced arterial disease. Only one study has evaluated the association between adiponectin and early vascular changes. Using aortic ultrasound imaging to assess arterial stiffness, distensibility, and compliance, Galler et al. found no relationship between serum adiponectin levels and these functional measures (9). Given the paucity of studies in this area, we sought to evaluate the relationship between adiponectin and early arterial disease using PWV, AIx-75, and BrachD (three non-ultrasound measures of arterial stiffness) in adolescents with type 1 diabetes who participated in the SEARCH for Diabetes in Youth Study.

Materials and methods

Participants

Data for these analyses come from a sub-study of the multicenter SEARCH for Diabetes in Youth study. A detailed description of SEARCH study methods has been published (10). SEARCH participants were recruited between September 2004 and October 2005 from two of the six SEARCH study sites (Colorado and Ohio) to participate in a sub-study to examine determinants of arterial stiffness. Participants included in the analysis had a diagnosis of type 1 diabetes from a health care provider and were aged > 10 years at the study visit. The study was reviewed and approved by local institutional review boards. Informed consent and assent, where applicable, were obtained from all participants and their parent/guardian if aged < 18 years at the time of the visit.

Study measures

Youth with diabetes, or their parent/guardian, completed an initial survey on demographic factors. Diabetes type was reported by health care providers or abstracted from medical records. A provider report of type 1 diabetes has been shown to be consistent with clinical and biochemical characteristics of type 1 diabetes, including the presence of diabetes autoantibodies (11).

After an overnight fast, blood was drawn to measure adiponectin, hemoglobin A_{1c} (HbA_{1c}), lipids [total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) cholesterol, and triglycerides], and C-reactive protein (CRP). Analysis of plasma adiponectin was performed using a commercial radioimmunoassay kit [Linco Research, St Charles, MO, USA (now Millipore)] (12). This assay uses ^{125}I-labeled murine adiponectin and a multispecies anti-adiponectin polyclonal antibody. It has a sensitivity of 1 ng/mL and the standard curve range is 1–200 ng/mL. Analysis of each sample is performed in duplicate. The intra- and inter-assay coefficients of variation were 6.21 % and 9.25 %, respectively. The specific methods for the other laboratory tests (HbA_{1c}, lipids, and CRP) have been described previously (10, 13).

Height, weight, and waist circumference were measured for all participants and body mass index (BMI) was calculated (10). Weight and height were compared with 2000 Centers for Disease Control and Prevention standards for the Unites States to calculate normalized BMI z-scores. The average of two anthropometric measures was used in the analyses.

Arterial function testing

At a separate cardiovascular disease visit, three arterial function measurements were obtained after 5 min of rest in the supine position: PWV, AIx-75, and BrachD. PWV was measured with a SphygmoCor SCOR-PVx System (Atcor Medical, Sydney, Australia). Three separate recordings were taken and averaged. Distance from the proximal (carotid) to the distal (femoral) artery recording site was measured to the nearest 0.1 cm and entered into the software. A tonometer was used to collect proximal and distal arterial waveforms gated by the R-wave on a simultaneously recorded ECG. PWV was then calculated as the carotid-to-distal path length divided by the time delay measured between the feet of the two waveforms and reported in milliseconds (3). A higher PWV indicates stiffer vessels. Repeat measures of PWV have demonstrated a coefficient of variability of < 7% (5).

AIx-75, which provides information about arterial stiffness and pulse wave reflections (3) was also collected. AIx-75 was collected when the SphygmoCor tonometer was placed over the right radial artery. The device analyzes pulse waves using a generalized transfer function validated in a catheterization laboratory to calculate a central aortic pressure wave (14). AIx-75 was derived from the central pressure waveform by calculating the difference between the main outgoing wave and the reflected wave of the central arterial waveform, expressed as a percentage of the central pulse pressure. As AIx is affected by heart rate, values were adjusted to a standard heart rate of 75 beats per minute (AIx-75). A higher AIx-75 implies stiffer vessels. Reproducibility studies have demonstrated intraclass correlation coefficients between 0.7 and 0.9 (5).

Three measures of BrachD were obtained with a DynaPulse Pathway instrument (Pulse Metric, San Diego, CA, USA) as previously described (4). This device derives brachial artery pressure curves from arterial pressure distensibility signals obtained from a standard cuff sphygmomanometer. A lower BrachD indicates stiffer vessels. Repeat measures have shown a coefficient of variability of < 9% (5).

Statistical analyses

Statistical analyses were performed using SAS software version 9.2 (SAS Institute, Cary, NC, USA). Comparisons of demographic and clinical characteristics by sex were examined using χ^2-tests for categorical variables and t-tests for continuous variables. Log transformations were used for non-normal continuous variables (duration of diabetes, triglycerides, and CRP). Simple correlations were examined to determine the association between adiponectin and the three arterial stiffness outcomes (PWV, AIx-75 and BrachD). Multiple linear regression models were then constructed using a manual stepwise process to elucidate independent determinants of each arterial stiffness measure after adjustment for potential covariates on this relationship. Variables included in this process were: age, race, sex, BMI z-score, duration of diabetes, mean arterial pressure (MAP, to control for background distending pressure), lipid parameters (total cholesterol, LDL and HDL cholesterol, and triglycerides), CRP, waist circumference, HbA_{1c}, and heart rate (except for AIx-75, which is already adjusted to a standard heart rate of 75 beats per minute). Height was added to the model for AIx-75 as height directly influences wave reflections from the heart. All models were adjusted for clinic site and the time difference between drawing blood and measuring arterial function. Before variables were added to the models, collinearity between variables was assessed. p-Values of < 0.05 were deemed significant in these analyses.

Results

The study population consisted of 225 participants with type 1 diabetes who were a mean age of 14.7 ± 2.9 years; 53 % male and 86 % non-Hispanic white. There were no differences in age, race, BMI distribution, waist circumference, or duration of diabetes by sex (Table 1). Females had worse cardiovascular risk factors, with higher total and LDL cholesterol, triglycerides, HbA_{1c}, and CRP levels ($p < 0.05$), whereas males had lower adiponectin levels ($p < 0.05$).

The hemodynamic data are presented in Table 2. Heart rate was lower in males than females ($p < 0.01$), and males had marginally higher systolic blood pressure ($p = 0.052$). AIx-75 was higher in females than males ($p < 0.01$) but after adjustment for height, AIx-75 was no longer significantly different by sex ($p = 0.38$). BrachD was lower in males ($p < 0.01$).

Unadjusted correlations revealed that higher adiponectin levels were associated with a higher BrachD (less arterial stiffness) ($r = 0.167$, $p = 0.02$). There was no correlation between adiponectin and PWV and AIx-75 ($r = 0.081$, $p = 0.23$ and $r = -0.096$ $p = 0.16$, respectively). After adjustment for covariates, adiponectin was not a significant independent predictor of BrachD. The final regression models for each of the three arterial stiffness measures are listed in Table 3. Only significant variables are listed. Older age, male sex, higher MAP, higher heart rate, and larger waist circumference were associated with a higher PWV ($p < 0.05$). Total cholesterol and higher MAP were associated with higher AIx-75 and lower BrachD was associated with male sex, higher BMI, and higher heart rate ($p < 0.05$).

Discussion

Our findings demonstrate that in a large population of adolescents with type 1 diabetes plasma adiponectin concentrations are not independently associated with non-ultrasound measures of arterial stiffness. This paper supports findings published on a similar but smaller cohort, which evaluated the relationship between adiponectin and abdominal aortic stiffness, compliance, and distensibility (9). Confirmation is important because of the lack of reports in the literature regarding the relationship between adiponectin and early arterial disease in the setting of type 1 diabetes.

Adiponectin is widely regarded as an anti-atherogenic, antioxidant, and anti-inflammatory molecule (7, 8, 15). In the setting of type 1 diabetes, plasma adiponectin is paradoxically increased (16–20). Hypotheses to explain these higher concentrations have included: 1) adiponectin mediates vascular damage in the setting of type 1 diabetes (21), 2) higher levels reflect a compensatory response to vascular injury (18, 22), 3) adiponectin levels are dependent on renal clearance; thus higher levels reflect renal compromise (23), and 4) higher levels are caused by subcutaneous insulin treatment (24).

Supporting adiponectin's role as a protective molecule, two large prospective case-control studies in adults have shown that low levels of adiponectin predict the risk of coronary artery disease and progression of coronary artery calcification (17, 20). By contrast, a recent study conducted by Forsblom et al. found higher adiponectin levels to be associated with increased cardiovascular and all-cause mortality in persons with type 1 diabetes (21). Discrepant findings are postulated to be due to the confounding effects of renal dysfunction in persons with type 1 diabetes because renal function is a major determinant of adiponectin concentrations (25) and renal disease is strongly associated with cardiovascular risk (26). These studies clearly suggest that the role of adiponectin as a marker or mediator of vascular disease remains to be established.

Studies in adolescents have also demonstrated higher adiponectin concentrations in persons with type 1 diabetes compared with healthy controls (9, 16, 27). Using ultrasound measures of aortic stiffness, distensibility, and compliance, Galler et al. found no relationship between plasma adiponectin and these arterial function measures (9). The authors postulated this lack of association could be due to the small number of subjects in their study. Using a larger sample (n = 225) we confirm no relationship between adiponectin and AIx-75 and PWV. We did find a univariate association between adiponectin and BrachD suggesting a protective relationship. However, after adjustment for other covariates, this relationship was no longer significant. We therefore speculate that this relationship is mediated through gender and BMI, as suggested by our regression models and by others (4). Thus, in youth with type 1 diabetes these cardiovascular risk factors are more strongly associated with arterial stiffness.

Limitations of this study include its cross-sectional design, as this limits our ability to assess causality. Longitudinal studies are needed in adolescents with type 1 diabetes to fully understand the role of adiponectin in early arterial stiffness. In this study we measured total adiponectin. Studies in adults suggest high molecular weight adiponectin or the ratio of high

molecular weight to total adiponectin may better predict changes in the vasculature and, ultimately, coronary artery disease (28–30).

In summary, this study extends a previous report of a lack of an independent association between plasma adiponectin concentrations and arterial stiffness by using alternative measures of arterial stiffness in a large population of youth with type 1 diabetes. These data strengthen the argument that adiponectin concentration does not play an independent role during the early stages of the development of arterial disease in youth with type 1 diabetes.

Acknowledgments

The SEARCH for Diabetes in Youth Study is indebted to the many young people, their families, and their health care providers, whose participation made this study possible.

Grant support: SEARCH for Diabetes in Youth is funded by the Centers for Disease Control and Prevention (PA numbers 00097, DP-05-069, and DP-10-001) and supported by the National Institute of Diabetes and Digestive and Kidney Diseases. Site Contract Numbers: University of Colorado, Denver (U48/CCU819241-3, U01 DP000247, and U18DP000247-06A1), Children's Hospital Medical Center, Cincinnati (U48/CCU519239, U01 DP000248, and 1U18DP002709).

The authors wish to acknowledge the involvement of General Clinical Research Centers at the South Carolina Clinical & Translational Research Institute at the Medical University of South Carolina (NIH/NCRR Grant Number UL1RR029882); Children's Hospital and Regional Medical Center (Grant Number M01RR00037); Colorado Pediatric General Clinical Research Center (Grant Number M01 RR00069), and the Barbara Davis Center at the University of Colorado at Denver (DERC NIH P30 DK57516); and the Institutional Clinical and Translational Science Award at the University of Cincinnati (NIH/NCRR Grant Number 1UL1RR026314-01).

References

1. Stehouwer CD, Henry RM, Ferreira I. Arterial stiffness in diabetes and the metabolic syndrome: a pathway to cardiovascular disease. Diabetologia. 2008; 51:527–39. [PubMed: 18239908]
2. Cruickshank K, Riste L, Anderson SG, Wright JS, Dunn G, et al. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? Circulation. 2002; 106:2085–90. [PubMed: 12379578]
3. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. Eur Heart J. 2006; 27:2588–605. [PubMed: 17000623]
4. Urbina EM, Brinton TJ, Elkasabany A, Berenson GS. Brachial artery distensibility and relation to cardiovascular risk factors in healthy young adults (The Bogalusa Heart Study). Am J Cardiol. 2002; 89:946–51. [PubMed: 11950433]
5. Urbina EM, Wadwa RP, Davis C, et al. Prevalence of increased arterial stiffness in children with type 1 diabetes mellitus differs by measurement site and sex: the SEARCH for Diabetes in Youth Study. J Pediatr. 2010; 156:731–7. 737 e1. [PubMed: 20097360]
6. Mahmud A, Feely J. Adiponectin and arterial stiffness. Am J Hypertens. 2005; 18:1543–8. [PubMed: 16364823]
7. Ouchi N, Walsh K. Adiponectin as an anti-inflammatory factor. Clin Chim Acta. 2007; 380:24–30. [PubMed: 17343838]
8. Ouedraogo R, Wu X, Xu SQ, Fuchsel L, Motoshima H, et al. Adiponectin suppression of high-glucose-induced reactive oxygen species in vascular endothelial cells: evidence for involvement of a cAMP signaling pathway. Diabetes. 2006; 55:1840–6. [PubMed: 16731851]
9. Galler A, Heitmann A, Siekmeyer W, Gelbrich G, Kapellen T, et al. Increased arterial stiffness in children and adolescents with type 1 diabetes: no association between arterial stiffness and serum levels of adiponectin. Pediatr Diabetes. 2010; 11:38–46. [PubMed: 19496970]
10. SEARCH for Diabetes in Youth: a multicenter study of the prevalence, incidence and classification of diabetes mellitus in youth. Control Clin Trials. 2004; 25:458–71. [PubMed: 15465616]

11. Dabelea D, Pihoker C, Talton JW, D'Agostino RB Jr, Fujimoto W, et al. Etiological approach to characterization of diabetes type: the SEARCH for Diabetes in Youth Study. Diabetes Care. 2011; 34:1628–33. [PubMed: 21636800]
12. Diez JJ, Iglesias P, Fernandez-Reyes MJ, Aguilera A, Bajo MA, et al. Serum concentrations of leptin, adiponectin and resistin, and their relationship with cardiovascular disease in patients with end-stage renal disease. Clin Endocrinol (Oxf). 2005; 62:242–9. [PubMed: 15670203]
13. Kershnar AK, Daniels SR, Imperatore G, Palla SL, Petitti DB, et al. Lipid abnormalities are prevalent in youth with type 1 and type 2 diabetes: the SEARCH for Diabetes in Youth Study. J Pediatr. 2006; 149:314–9. [PubMed: 16939739]
14. O'Rourke MF, Gallagher DE. Pulse wave analysis. J Hypertens Suppl. 1996; 14:S147–57. [PubMed: 9120672]
15. Fantuzzi G. Adiponectin and inflammation: consensus and controversy. J Allergy Clin Immunol. 2008; 121:326–30. [PubMed: 18061654]
16. Barnes MM, Curran-Everett D, Hamman RF, Maahs D, Mayer-Davis EJ, et al. Determinants of adiponectin levels in young people with Type 1 diabetes. Diabet Med. 2008; 25:365–9. [PubMed: 18307464]
17. Costacou T, Zgibor JC, Evans RW, Otvos J, Lopes-Virella MF, et al. The prospective association between adiponectin and coronary artery disease among individuals with type 1 diabetes. The Pittsburgh Epidemiology of Diabetes Complications Study. Diabetologia. 2005; 48:41–8. [PubMed: 15616802]
18. Frystyk J, Tarnow L, Hansen TK, Parving HH, Flyvbjerg A. Increased serum adiponectin levels in type 1 diabetic patients with microvascular complications. Diabetologia. 2005; 48:1911–8. [PubMed: 16078018]
19. Hadjadj S, Aubert R, Fumeron F, Pean F, Tichet J, et al. Increased plasma adiponectin concentrations are associated with microangiopathy in type 1 diabetic subjects. Diabetologia. 2005; 48:1088–92. [PubMed: 15875155]
20. Maahs DM, Ogden LG, Kinney GL, Wadwa P, Snell-Bergeon JK, et al. Low plasma adiponectin levels predict progression of coronary artery calcification. Circulation. 2005; 111:747–53. [PubMed: 15699257]
21. Forsblom C, Thomas MC, Moran J, Saraheimo M, Thorn L, et al. Serum adiponectin concentration is a positive predictor of all-cause and cardiovascular mortality in type 1 diabetes. J Intern Med. 2011; 270:346–55. [PubMed: 21615808]
22. Schalkwijk CG, Chaturvedi N, Schram MT, Fuller JH, Stehouwer CD, EURODIAB Prospective Complications Study Group. Adiponectin is inversely associated with renal function in type 1 diabetic patients. J Clin Endocrinol Metab. 2006; 91:129–35. [PubMed: 16219717]
23. Zoccali C, Mallamaci F, Panuccio V, Tripepi G, Cutrupi S, et al. Adiponectin is markedly increased in patients with nephrotic syndrome and is related to metabolic risk factors. Kidney Int Suppl. 2003:S98–102. [PubMed: 12694320]
24. Havel PJ. Update on adipocyte hormones: regulation of energy balance and carbohydrate/lipid metabolism. Diabetes. 2004; 53(Suppl 1):S143–51. [PubMed: 14749280]
25. Lin J, Hu FB, Curhan G. Serum adiponectin and renal dysfunction in men with type 2 diabetes. Diabetes Care. 2007; 30:239–44. [PubMed: 17259488]
26. Groop PH, Thomas MC, Moran JL, Wadèn J, Thorn LM, et al. FinnDiane Study Group. The presence and severity of chronic kidney disease predicts all-cause mortality in type 1 diabetes. Diabetes. 2009; 58:1651–8. [PubMed: 19401416]
27. Galler A, Gelbrich G, Kratzsch J, Noack N, Kapellen T, et al. Elevated serum levels of adiponectin in children, adolescents and young adults with type 1 diabetes and the impact of age, gender, body mass index and metabolic control: a longitudinal study. Eur J Endocrinol. 2007; 157:481–9. [PubMed: 17893263]
28. Aso Y, Yamamoto R, Wakabayashi S, Uchida T, Takayanagi K, et al. Comparison of serum high-molecular weight (HMW) adiponectin with total adiponectin concentrations in type 2 diabetic patients with coronary artery disease using a novel enzyme-linked immunosorbent assay to detect HMW adiponectin. Diabetes. 2006; 55:1954–60. [PubMed: 16804063]

29. Kato A, Odamaki M, Ishida J, Hishida A. Association of high-molecular-weight to total adiponectin ratio with pulse wave velocity in hemodialysis patients. Nephron Clin Pract. 2008; 109:c18–24. [PubMed: 18493156]

30. von Eynatten M, Humpert PM, Bluemm A, Lepper PM, Hamann A, et al. High-molecular weight adiponectin is independently associated with the extent of coronary artery disease in men. Atherosclerosis. 2008; 199:123–8. [PubMed: 18021784]

Table 1

Characteristics of the study population.

Variable	Males	Females	p-Value
n, %[a]	120 (53)	105 (47)	0.32
Race[a]			
Non-white %	17 (14)	14 (13)	0.856
White, %	103 (86)	91 (87)	
Age[b]	147±2.7	14.8±3.1	0.71
Height, m[b]	172±012	163±0.07	<0.01
Height SDS[b]	052±0.90	0.34±0.96	0.17
Weight, kg[b]	683±1.6	63.7±1.4	0.03
Body mass index, kg/m^2[b]	2.29±4.2	23.8±4.6	0.12
Body mass index z-score[b]	052±0.96	0.56±0.94	0.73
Waist circumference, cm[b]	780±113	798±127	0.27
Duration of diabetes, months[c]	222±229	297±313	0.34
Total cholesterol, mmol/L[b]	4.11±0.71	4.37±078	0.01
High density lipoprotein, mmol/L[b]	136±027	141±0.29	0.15
Low density lipoprotein, mmol/L[b]	239±0.56	2.53±0.63	0.07
Triglycerides, mmol/L[c]	079±0.38	093±0.45	0.01
Hemoglobin A_{1c}, %[b]	77±1.3	8.1±1.5	0.01
C-reactive protein, mmol/L[c]	010±0.3	0.17±0.3	<0.01
Adiponectin, μg/mL[b]	154±5.5	17.8±7.2	<0.01

Values are mean±SD or n (%).

[a] p-Value from χ^2-test.

[b] p-Value from t-test.

[c] t-test on log transformed values. No SI units available for adiponectin.

Table 2

Mean hemodynamic and arterial stiffness values by sex.

Variable	Males	Females	p-Value
Heart rate, beats per minute[a]	69±1	76±1	<0.01
Systolic BP, mm Hg	118±11	115±10	0.052
Diastolic BP, mm Hg	69±10	69±9	0.82
Mean arterial pressure, mm Hg[a]	83±1	83±1	0.70
PWV, ms[a]	546±009	536±0.74	0.40
AIx-75, % (unadjusted)[a]	−239±092	123±0.98	<0.01
BrachD, %/mm Hg[a]	576±119	620±1.03	<0.01

Values are mean ± SD.

[a] p-Value from t-tests. Alx-75, augmentation index; BrachD, brachial distensibility; PWV, pulse wave velocity.

Table 3

Determinants of arterial stiffness among youth with type 1 diabetes mellitus.

Region	PWV femoral	AIx-75	BrachD
Intercept			7.92 (5.48, 10.36)
Age (baseline)	0.10 (0.05, 0.15)		
Gender (female vs. male)	−0.23 (−0.43, −0.04)		0.52 (0.22, 0.82)
BMI, kg/m^2			−0.41 (−0.67, −0.16)
Height, cm		−0.34 (−0.50, −0.17)	
MAP, mm Hg	0.03 (0.01, 0.04)	0.32 (0.13, 0.51)	
Total cholesterol, mg/dL		0.08 (0.03, 0.13)	
Heart rate, beats per minute	0.01 (3.61E-03, 0.02)		−0.02 (−0.03, −0.01)
Waist circumference, cm	0.02 (0.01, 0.04)		
Model R^2	0.51	0.30	0.31

Multiple linear regression with β coefficient and confidence intervals for β. All covariates were allowed to enter the model except height but not heart rate for AIx-75. Only significant covariates are listed above, $p < 0.05$. Models were adjusted for clinic site and time difference between visits. Alx-75, augmentation index; BMI, body mass index; BrachD, brachial distensibility; MAP, mean arterial pressure; PWV, pulse wave velocity.