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Achieving International Society for Pediatric and Adolescent Diabetes and American Diabetes Association Clinical Guidelines Offers Cardiorenal Protection for Youth with Type 1 Diabetes

Petter Bjornstad, M.D.[1], **Laura Pyle, Ph.D**[1], **Nhung Nguyen, M.P.H.**[2], **Janet K. Snell-Bergeon, Ph.D., M.P.H.**[1,2], **Franziska K. Bishop, M.S.**[2], **R. Paul Wadwa, M.D.**[1,2,*], and **David M. Maahs, M.D., Ph.D**[1,2,*]

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

[2]Barbara Davis Center for Childhood Diabetes, University of Colorado Denver, Aurora, CO

Abstract

Objective—Most youth with type 1 diabetes do not meet the American Diabetes Association (ADA) and International Society for Pediatric and Adolescent Diabetes (ISPAD) targets for HbA1c, blood pressure, lipids, and BMI. We hypothesized that ISPAD/ADA goal achievement at baseline would be associated with cardiorenal risk factors at baseline and 2 year follow-up in adolescents with type 1 diabetes.

Methods—We assessed the cross-sectional and longitudinal relationships between ISPAD/ADA goal achievement at baseline and cardiorenal health at baseline and 2-year follow-up (n=297; 15.4±2.1 years at baseline) in adolescents with type 1 diabetes. Goal achievement was defined as HbA1c<7.5%, BP<90th percentile for age, sex and height, LDL-C <100mg/dL, HDL-C >35mg/dL, TG <150mg/dL and BMI <85th percentile for age and sex. Cardiorenal outcomes included pulse-wave velocity (PWV), brachial distensibility (BrachD), augmentation index (AIx), and eGFR continuously and categorically as hyperfiltration (eGFR≥135mL/min/1.73m^2).

Results—Adolescents with type 1 diabetes who met 1–3 goals, had significantly greater (P<0.05) baseline PWV (5.1±0.1 vs. 5.4±0.1 m/s), follow-up PWV (5.5±0.1 vs. 5.7±0.1 m/s), greater follow-up eGFR (104±2 vs. 116±3 mL/min/1.73m^2), and greater odds of renal hyperfiltration at follow-up (OR: 20.0, 95% CI 3.8–105.2) compared to those who met 4–6 goals after adjusting for Tanner stage, sex, age and diabetes duration. No statistically significant differences in the cardiorenal outcomes were observed between adolescents with type 1 diabetes who met 4–6 goals and non-diabetic controls (n=96).

Address all correspondence to: Petter Bjornstad, M.D., Barbara Davis Center for Childhood Diabetes, University of Colorado, Denver, 1775 Aurora Court, Aurora, CO 80045, Phone: 720.579.1048, Fax: 303.724.6779, Petter.Bjornstad@childrenscolorado.org.

*Co-senior authors

Drs. Bjornstad, Pyle, Snell-Bergen, Wadwa and Maahs and Ms. Nguyen and Ms. Bishop have no conflict of interest to disclose.

Author Contributions

PB researched, wrote, formulated analytic plan with LP, contributed to discussion and analytic plan, and reviewed/edited the manuscript; LP reviewed/edited the analysis plan, performed the analyses, reviewed/edited the manuscript; NN contributed to discussion and analytic plan, and reviewed/edited the manuscript; JKSB contributed to discussion and analytic plan, and reviewed/edited the manuscript; FKB researched and reviewed/edited the manuscript; RPW and DMM researched, wrote, contributed to the discussion, and reviewed/edited the manuscript as senior authors.

Conclusions—In adolescents with type 1 diabetes, baseline ADA/ISPAD goal achievement was associated with cardiorenal protection at baseline and 2-year follow-up.

Introduction

Cardiorenal complications are the leading cause of morbidity and mortality in type 1 diabetes (1, 2). While diabetic nephropathy remains the most common cause of end-stage renal disease (ESRD) in the Western world (3, 4), coronary artery disease is the single strongest determinant of mortality in type 1 diabetes (1, 5). Major determinants of cardiorenal health in type 1 diabetes include glucose, blood pressure, and lipid control, but the literature suggests significant under-treatment of these risk factors in children and adolescents with diabetes (2, 5–9). In fact, most youth with type 1 diabetes in the T1D Exchange Clinic Registry did not meet the American Diabetes Association (ADA) and International Society for Pediatric and Adolescent Diabetes (ISPAD) targets for HbA1c, systolic and diastolic blood pressure (SBP/DBP), LDL-cholesterol (LDL-C), triglycerides (TG) and body mass index (BMI) (10). In adults with type 1 diabetes, suboptimal achievement of the ADA's ABC goals (HbA1c <7%, SBP/DBP <130/80 mmHg, LDL-C <100mg/dL) is strongly associated with microvascular complications, but not with macrovascular complications to the same degree (11, 12).

Early markers of micro- and macrovascular disease can manifest in adolescents with type 1 diabetes. Measures of arterial stiffness, including pulse wave velocity (PWV), augmentation index (AIx) and brachial distensibility (BrachD), have been shown to be strong predictors of development of cardiovascular disease (CVD) (13). Hyperfiltration (glomerular filtration rate [GFR] ≥135mL/min/1.73m^2) and albuminuria are associated with renal function loss in adulthood (14–17). The aim of our study was to investigate the associations between achievement of ISPAD/ADA goals for HbA1c, SBP, DBP, LDL-C, TG, HDL-C and BMI at baseline and PWV, AIx, BrachD, eGFR, hyperfiltration and elevated albumin to creatinine ratio at baseline and 2-year follow-up. We hypothesized that ISPAD/ADA goal achievement at baseline would be associated with cardiorenal outcomes at baseline and 2 year follow-up in adolescents with type 1 diabetes.

Methods

The Determinants of Macrovascular Disease in Adolescents with type 1 diabetes study was initiated to investigate atherosclerotic disease risk in youth with type 1 diabetes (18, 19). The study enrolled 300 subjects 12–19 years old from 2008 to 2010, with type 1 diabetes and 100 non-diabetic controls of similar age. Study participants with type 1 diabetes were recruited from Barbara Davis Center for Childhood Diabetes. They were diagnosed by islet cell antibody or by provider clinical diagnosis, had diabetes duration >5 years at entry into the study (mean 8.7±3.0 years), and received care at the Barbara Davis Center for Childhood Diabetes. Non-diabetic control subjects were recruited from campus and community advertisements as well as friends of the participants with type 1 diabetes. No siblings or first-degree relatives of participants with type 1 diabetes were included. Subjects were excluded for diabetes of any other type, or for a history of abnormal cardiac anatomy or arrhythmia that would preclude the subject from vascular function measurements. A total of

297 adolescents with type 1 diabetes and 96 non-diabetic peers had data on the ISPAD goals and were eligible for inclusion in the analyses. All subjects were included in order to include as many subjects as possible and to avoid introducing bias by excluding those who did not attend follow-up visits. The study was approved by the Colorado Multiple Institution Review Board, and informed consent and assent (for subjects <18 years) were obtained from all subjects.

All subjects were requested to have Tanner stage assessed with a physical exam by a study investigator or clinical provider. Height was measured to the nearest 0.1 cm with shoes removed using a wall-mounted stadiometer, and weight was measured to the nearest 0.1 kg using a Detecto scale (Detecto, Webb City, Missouri). BMI z-score was calculated using the 2000 Centers for Disease Control and Prevention growth chart standards. Participants were asked about smoking status, and current smoking is included in the analysis. HbA1c was measured on the DCA Vantage by Siemens (Princeton, New Jersey) at the Children's Hospital Colorado main clinical lab. Total cholesterol, high-density lipoprotein cholesterol (HDL-C) and TG were performed in the Clinical Translational Research Core lab using a Beckman Coulter AU system (Beckman Coulter Inc, Brea, CA). LDL-C was calculated using the Friedewald formula (no subjects had TG >400mg/dL). After subjects had been laying supine for a minimum of 5 minutes, blood pressure measurements were obtained using a Dynapulse Pathway (Pulse Metric, San Diego, California), and 3 measurements were averaged.

ISPAD/ADA goals

Participants were categorized according to the following ADA and ISPAD targets: HbA1c <7.5%, BMI <85th percentile for age and sex, SBP and/or DBP <90th percentile for age, sex, and height, LDL-C <100mg/dL, HDL-C > 35mg/dL and TG <150mg/dL (20–22). Each subject was categorized by whether the above goals were attained, and grouped into those who met 1–3 goals or 4–6 goals (i.e. more than half or less or equal to half of the goals). The cut-offs were determined to ensure sufficient observations for meaningful statistical analyses.

Measures of vascular stiffness

All subjects fasted overnight (≥8 hours) and were asked to refrain from caffeine intake and smoking within 8 hours prior to the study visit (due to potential effects on vascular measures). Brachial artery distensibility (BrachD) was obtained with a DynaPulse Pathway instrument (Pulse Metric, Inc., San Diego, CA). Pulse wave velocity (PWV) was measured in the carotid-femoral segment using arterial tonometry with the Sphygmocor Vx (AtCor Medical, Lisle, IL). The carotid to femoral path length was measured from the reference point of the lowest portion of the sternal notch to the femoral pulse. The average of three measurements was entered into the SphygmoCor software. While recording a 3-lead ECG, pulse wave was recorded using arterial tonometry, first at the carotid pulse, followed by recording of pulse wave at the femoral pulse. The two pulse waves are subsequently compared using the R-wave as a reference, allowing us to compare the time from the R-wave to the foot of pulse waves, and to calculate PWV in meters per second (m/s).

Augmentation Index (AIx), which is influenced by arterial stiffness and provides additional information concerning wave reflections, was also collected. The SphygmoCor tonometer was placed over the right radial artery and 3 measures of AIx were collected. The pressure waves were calibrated using mean arterial pressure (MAP) and DBP obtained in the same arm. The device then analyzed the pulse wave using a validated generalized transfer function. AIx is affected by heart rate (HR) and height, and therefore values were adjusted to a standard HR of 75 beats per minute and individual heights.

Markers of early diabetic nephropathy

Urine samples were collected and urine creatinine and albumin were measured (RIA, Diagnostic Products) at both visits. Elevated albumin to creatinine ratio was defined as albumin-creatinine ratio (ACR) ≥30mg/g. Serum creatinine was measured at baseline and 2-year follow-up, and cystatin C in a subset of participants at baseline in the University of Colorado Hospital clinical lab using commercially available assays (19).

eGFR (mL/min/1.73m^2) was determined at baseline and follow-up using the Schwartz 2009 equation (36.5 * height (cm)/serum creatinine (μmol/L) (23). Baseline analyses were repeated in a subset of subjects (n=254) who had serum cystatin C measured and eGFR calculated by Bouvet equation (63.2 *[1.2/cystatin C]$^{0.56}$ * [(96/88.4)/serum creatinine]$^{0.35}$ * [weight/45]$^{0.30}$ * [age/14]$^{0.40}$) (23). Cystatin C data was not available at follow-up. Hyperfiltration was defined as eGFR ≥135mL/min/1.73m^2 (24).

Statistical analysis

Analyses were performed in SAS (version 9.3 or higher; SAS Institute, Cary, NC). Variables were checked for the distributional assumption of normality using normal plots. The distribution of ACR was skewed and, therefore, natural log transformed for analyses.

Each subject was categorized based on ADA/ISPAD goals attainment, and stratified by whether 1–3 goals or 4–6 goals were met (there were no subjects that met no goals).

We employed linear regression models to compare PWV, AIx, BrachD, ACR, eGFR by Schwartz and Bouvet at baseline and follow-up between participants who met 1–3 vs. 4–6 goals at baseline, unadjusted and adjusted for age, sex, and type 1 diabetes duration. We also compared these variables between non-diabetic controls and participants with type 1 diabetes who met 4–6 goals at baseline.

Logistic regression models were used to examine whether attaining 1–3 goals vs. 4–6 goals at baseline was associated with hyperfiltration (eGFR≥135 mL/min/1.73m^2) and albuminuria (ACR≥30 mg/g) at baseline and follow-up. Linear models were used to assess the association of eGFR by creatinine and Schwartz at baseline with PWV, AIx, and BrachD at baseline and follow-up. Analyses were considered exploratory and hypothesis generating and adjustments for multiple comparisons were not employed. Linear regression results are presented as β estimate ± standard errors (SE) and logistic regression presented as odds ratios (OR) and 95% confidence intervals (CI). Significance was based on an α-level of 0.05.

Results

Characteristics and ISPAD and ADA goal achievement

At baseline, 15% of participants had HbA1c <7.5%, 73% had BP < 90th percentile for age, sex and height, 73% had LDL-C <100mg/dL, 94% had HDL-C > 35mg/dL, 91% had TG <150mg/dL and 69% had BMI <85th percentile for age and sex. At follow-up, 12% of participants achieved HbA1c <7.5%, 55% achieved BP <90th percentile for age, sex and height, 64% achieved LDL-C < 100mg/dL, 96% achieved HDL-C >35mg/dL, 87% achieved TG<150mg/dL and 71% achieved BMI <85th percentile for age and sex. We further stratified the cohort into participants who met 4–6 goals and those that met 1–3 goals (Table 1). Almost seventy percent (69.6%) of patients who achieved 4–6 goals at baseline achieved 4–6 goals at follow-up. Similarly, seventy-nine percent of patients who achieved 1–3 goals at baseline achieved 1–3 goals at follow-up (79.3%) (Kappa of 0.40, 95% CI 0.28–0.52). Participants who achieved 4–6 goals at baseline were younger (15.1±2.0 vs. 16.5±2.2 years, p<0.0001) and had less advanced pubertal status at baseline (Tanner 4–5: 74.8 vs. 92.0%, p=0.002) (Table 2).

Individual goal achievement and vascular stiffness

Achievement of HbA1c < 7.5% was associated with significantly lower AIx at follow-up (2.8 vs. 6.7%, p=0.03). Achievement of BP <90th percentile for age, sex and height was associated with significantly lower PWV at follow-up (5.5 vs. 5.7 m/s, p=0.04). Achievement of BMI <85th percentile for age and sex was associated with significantly greater BrachD (6.9 vs. 6.4 %/mm Hg, p=0.01). Achievement of LDL-C, HDL-C or TG goals were not independently associated with improvement in markers of arterial stiffness.

Goal achievements and vascular stiffness

Subjects who attained 4–6 goals at baseline compared to those who met 1–3 goals had lower PWV at baseline (5.2±0.6 vs. 5.7±0.7 m/s, p<0.0001) and follow-up (5.7±0.7 vs. 6.1±0.8 m/s, p=0.0001) and greater baseline brachD (6.9±1.3 vs. 6.4±1.1 %/mm Hg, p=0.004) (Table 2). Moreover, when adjusting for Tanner stage, sex and diabetes duration, the adjusted means for baseline PWV and 2- year follow-up PWV remained significantly lower (p<0.05) in participants who met 4–6 goals (Table 3). Similarly, baseline BrachD was significantly higher in those who met 4–6 goals after adjusting for Tanner stage, sex and type 1 diabetes duration (Table 3). These data demonstrate associations between greater goal achievement and lower arterial stiffness (e.g. lower PWV and higher BrachD). Similar results were obtained when comparing those participants who achieved 6 goals compared to those who achieved 4 goals, and also when the 3 lipid goals were combined (data not shown).

Individual goal achievement and renal health

Achievement of BP <90th percentile for age, sex and height was associated with significantly lower eGFR by Schwartz at follow-up (105.0 vs. 113.8 mL/min/1.73m^2, p=0.004). Achievement of LDL-C <100mg/dL was associated with significantly lower follow-up ACR (9.6 vs. 13.5 mg/g, p=0.03). Achievement of HbA1c, HDL-C, BMI or TG goals were not independently associated with improvement in markers of renal function.

Goal achievements and renal health

Subjects who attained 4–6 goals at baseline had lower follow-up eGFR by Schwartz (99±15 vs. 109±23 mL/min/1.73m^2, p=0.0003) likely representing a trend towards lower incidence of hyperfiltration in participants who met 4–6 goals. When adjusting for Tanner stage, sex and diabetes duration the adjusted means for follow-up eGFR by Schwartz and change in eGFR by Schwartz were all significantly lower ($p<0.05$) in participants who met 4–6 goals (Table 3). Similar results were obtained when comparing those participants who achieved 6 goals compared to those who achieved 4 goals, and also when the 3 lipid goals were combined (data not shown).

At baseline, 11.2% of participants who attained 4–6 goals had hyperfiltration calculated by Schwartz compared to 16.2% of those who attained 1–3 goals (p=NS). At follow-up, only 1.3% of participants who attained 4–6 goals had hyperfiltration calculated by Schwartz compared to 17.0% of those who attained 1–3 goals (p=0.0006). Participants who achieved 1–3 goals vs. 4–6 goals at baseline had higher odds of having hyperfiltration calculated by Schwartz at baseline, but it did not reach statistical significance after adjusting for age, sex and diabetes duration (OR: 2.1, 95% CI 0.9–4.7, p=0.08). Repeating the analyses in the subset of participants who also had eGFR calculated by Bouvet was statistically significant, with achievement of 1–3 goals vs. 4–6 goals being associated with higher odds of hyperfiltration at baseline after adjusting for age, sex and diabetes duration (OR: 2.9, 95% CI 1.4–6.1, p=0.004). Furthermore, participants who achieved 1–3 goals vs. 4–6 goals at baseline had significantly higher odds of having hyperfiltration calculated by Schwartz at follow-up after adjusting for age, sex and diabetes duration (OR: 20.0, 95% CI 3.8–105.2).

At baseline, 9.8% of participants who attained 4–6 goals had elevated ACR compared to 9.5% of those who attained 1–3 goals (p=NS). At follow-up only 5.8% of participants who attained 4–6 goals had an elevated ACR compared to 13.2% of those who attained 1–3 goals (p=NS). There were no significant associations between goal attainment and elevated ACR at baseline and 2-year follow-up (data not shown).

Associations between renal health and vascular stiffness

Estimated GFR at baseline was associated with both baseline (β±SE: 0.10±0.03% per 1 mL/min/1.73m^2, p=0.047) and follow-up AIx (β±SE: 0.07±0.03% per 1 mL/min/1.73m^2, p=0.03). These data suggest linear relationships between eGFR and measures of vascular stiffness, with increased eGFR being associated with increased vascular stiffness. Similar results were obtained with eGFR by Bouvet in place of eGFR by Schwartz in the subset (n=254) of participants who had serum cystatin C measured (data not shown).

Cardiorenal profiles in adolescents with type 1 diabetes who met 4–6 goals vs. non-diabetic controls

Adolescents with type 1 diabetes who met 4–6 goals had similar baseline and follow-up PWV, BrachD, AIx, ACR and follow-up eGFR to non-diabetic adolescent controls of similar age and pubertal status (Table 4).

Discussion

Age-specific ADA/ISPAD target achievement was suboptimal in our cohort of adolescents with type 1 diabetes. Only 6% of participants met all of the goals, and 25% met three or less of the six ISPAD/ADA goals. Achieving 4–6 goals at baseline was associated with cardiorenal protection at baseline and 2-year follow-up with similar cardiorenal risk profiles to non-diabetic adolescent controls emphasizing the importance of aggressive risk factor control.

The mortality and morbidity of CVD are markedly increased in individuals with type 1 diabetes compared to the nondiabetic population (5, 9), with atherosclerosis beginning in childhood and adolescence (25). Measures of arterial stiffness including PWV, AIx and BrachD have emerged as useful tools to evaluate vascular health (13, 26, 27) and predict future CV events and all-cause mortality (13). It has been reported that children and adolescents with type 1 diabetes have increased arterial stiffness compared to healthy controls (28, 29). Early detection of diabetic nephropathy also has a pivotal role in the prevention of end-stage renal failure in diabetes (30). Phenotypes of early diabetic nephropathy, including albuminuria and hyperfiltration which manifest prior to renal function loss in adolescents, are thought to be strong predictors of cardiorenal complications in adulthood (14–17, 31). We employed eGFR ≥ 135mL/min/1.73m^2 to define hyperfiltration, although there is no accepted definition for hyperfiltration (32, 33). It is increasingly recognized that increased GFR is an early hemodynamic abnormality seen in diabetes that is linked with an increased risk of diabetic nephropathy (4). Adults with type 1 diabetes and elevated GFR demonstrate cardiovascular dysfunction including increases in arterial stiffness and altered flow-mediated dilatation (15, 34). These observations are consistent with our data in adolescents with type 1 diabetes where increased eGFR is associated with measures of arterial stiffness.

Contemporary cohorts of adolescents and adults with type 1 diabetes demonstrate suboptimal ADA and ADA/ISPAD goal achievements respectively (11, 12). The ISPAD and ADA target achievements in our cohort is similar to what was reported in the T1D Exchange study for their 13–20 year age group with 21% of their participants meeting the HbA1c target, 78% meeting the BP target, 62% meeting the LDL-target, 94% meeting the HDL-C target, 89% meeting the TG target and 69% meeting the BMI target (10).

The reasons for the suboptimal goal achievements remain unclear which is likely multifactorial. Lack of clinical trials with lipid-lowering medications in adolescents with type 1 diabetes(2), poor medical compliance in adolescence, and the fact that puberty may aggravate risk factor profiles, are all potential causes (35, 36). Perhaps equally important are the limited data available on associations between risk factor control and cardiorenal outcomes in adolescents with type 1 diabetes. However, there are some important landmark studies worth mentioning. For instance, intensive glycemic control conferred renal protection in adolescents in the Diabetes Control and Complications Trial (DCCT), which included 195 pubertal adolescents at baseline (37). In the DCCT adolescent cohort, intensive treatment (achieving a lower HbA1c) compared with conventional treatment, reduced the risk and progression of microalbuminuria by 54%. Moreover, the benefits of intensive

therapy persisted in the former adolescent cohort during the Epidemiology of Diabetes Interventions and Complications (EDIC) study: the previously intensively managed group had 48% less microalbuminuria and 85% less albuminuria (38). We have also previously reported an association between ABC control and vascular complications in adults with type 1 diabetes (12), but this is the first time it has been shown that attaining optimal targets for BP, lipids, BMI and HbA1c is associated with improved cardiorenal health both cross-sectionally and longitudinally in adolescents. In addition, no studies to date have examined the associations between ISPAD/ADA target attainment and PWV, AIx and BrachD in adolescents with type 1 diabetes.

There are limitations to the present study, including the observational design and lack of cystatin C data at follow-up. Although we adjusted for a variety of important confounding variables, we cannot rule out the presence of unknown risk factors that may have biased the present analyses. Our analyses were considered exploratory and hypothesis generating and adjustments for multiple comparisons were not employed. Our cohort is also predominantly non-Hispanic white (81%); however, this is similar to the type 1 diabetes population in Colorado. The majority of our subjects were post-pubertal (80%) and our findings may not be applicable to pre-pubertal adolescents with type 1 diabetes; however, we adjusted for Tanner stage in our analyses. There is also a great amount of variability in the GFR ranges reported in pediatrics and adolescents in the literature, in part due to different equations utilized and in part due to the biological variation in GFR in these age groups (39). We utilized both Schwartz (serum creatinine) and Bouvet (serum creatinine and serum cystatin C) to estimate GFR in our cohort at baseline, which is a strength of our paper. We would also like to acknowledge that the distinction between achievement of 1–3 and 4–6 ISPAD goals is somewhat arbitrary, and was decided on *a priori* to ensure adequate observations for sufficiently powered analyses.

Suboptimal ISPAD/ADA target control in our cohort was associated with worse cardiorenal outcomes at baseline and 2-year follow-up, supporting the importance of achieving ISPAD/ADA clinical targets. Additional efforts and better therapies are required to help adolescents achieve these important goals. ISPAD/ADA target attainment was also associated with pubertal status in our cohort, with participants with less advanced pubertal status attaining more targets. The effects of hormonal changes on body shape, size and puberty, including the induction of insulin resistance, requires greater attention for self-monitoring and insulin adjustments (35, 36). Puberty is also recognized to be an accelerator for vascular complications (40).

In summary, in our cohort of pubertal adolescents with suboptimal ISPAD and ADA goal achievement, we report significantly higher measures of arterial stiffness and prevalence of hyperfiltration in adolescents with type 1 diabetes who attained 1–3 goals compared to those who met 4–6 goals. The association of meeting ISPAD and ADA goals with cardiorenal risk factors emphasizes the importance of improving pediatric diabetes care to prevent future vascular complications of type 1 diabetes.

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Drs. Bjornstad and Pyle are guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table 1

Frequency of ISPAD Goal Achievement at Baseline and Follow-up

Number of ISPAD goals achieved	At baseline (n=297)	At follow-up (n=211)
0	0%	1%
1	1%	3%
2	5%	15%
3	19%	23%
4	33%	31%
5	35%	25%
6	7%	1%

Table 2

Clinical characteristics of adolescents with type 1 diabetes

Variables	ISPAD/ADA goals attained at baseline		p-value
	1–3 goals (n=75)	4–6 goals (n=222)	
Age (years)	16.5±2.2	15.1±2.0	<0.0001
Male sex (%)	44.0% (32.6%–56.0%)	53.2% (46.4%–60.0%)	NS
Race-Ethnicity (% NHW)	76.0% (64.8%–85.1%)	87.8% (82.8%–91.8%)	NS
Duration (years)	8.7±3.0	8.7±3.0	NS
BMI (percentile)	86±19	65±22	<0.0001
SBP (mm Hg)	118±8	111±8	<0.0001
DBP (mm Hg)	73±7	67±6	<0.0001
HbA1c (%)	9.6±1.7	8.7±1.5	<0.0001
HbA1c (mmol/mol)	81.4±16.2	71.6±14.0	<0.0001
Tanner stage (% 4–5)	92.0% (83.4%–97.0%)	74.8% (68.5%–80.4%)	0.0015
PWV at baseline (m/s)	5.7±0.7	5.2±0.6	<0.0001
PWV at follow-up (m/s)	6.1±0.8	5.7±0.7	0.0001
BrachD at baseline (%/mm Hg)	6.4±1.1	6.9±1.3	0.004
BrachD at follow-up (%/mm Hg)	6.6±1.2	6.7±1.2	NS
AIx * **HR75 at baseline** (%)	2.0 (−2.7–9.0)	2.7 (−3.0–9.0)	NS
AIx * **HR75 at follow-up** (%)	6.5 (−0.8–10.5)	4.7 (−2.2–10.0)	NS
Baseline ACR * (mg/g)	7.0 (4.9–14.6)	7.3 (4.3–12.7)	NS
Follow-up ACR * (mg/g)	7.2 (4.1–15.7)	5.8 (4.2–13.1)	NS
Baseline eGFR by Schwartz (mL/min/1.73m^2)	109±21	108±20	NS
Follow-up eGFR by Schwartz (mL/min/1.73m^2)	109±23	99±15	0.0003
Baseline eGFR by Bouvet (mL/min/1.73m^2)	134±22	116±17	<0.0001

Data are presented as mean ± SD or % (95% CI).

* Median and interquartile range (IQR)

Table 3

Adjusted means for variables statistically different by group in Table 1

Variables	Model adjusted for baseline age, sex, and baseline type 1 diabetes duration			Model adjusted for baseline Tanner stage, sex, and baseline type 1 diabetes duration		
	1–3 goals attained at baseline	4–6 goals attained at baseline	P-value	1–3 goals attained at baseline	4–6 goals attained at baseline	P-value
Baseline PWV (m/s)	5.6±0.1	5.2±0.0	0.0001	5.4±0.1	5.1±0.1	0.0001
Follow-up PWV (m/s)	5.9±0.1	5.7±0.1	0.04	5.7±0.1	5.5±0.1	0.03
Baseline BrachD (%/mm Hg)	6.4±0.2	6.9±0.1	0.007	6.9±0.2	7.3±0.1	0.02
Baseline eGFR Bouvet (mL/min/1.73m^2)	129±2	118±1	<0.0001	127±3	114±2	<0.0001
Follow-up eGFR Schwartz (mL/min/1.73m^2)	110±2	99±1	<0.0001	116±3	104±2	<0.0001

Data are presented as least-squares means±standard error (SE).

Table 4

Clinical characteristics of adolescents with type 1 diabetes who attained 4–6 goals at baseline and non-diabetic adolescents

Variables	Non-diabetic adolescents (n=96)	Adolescents with type 1 diabetes who attained 4–6 goals (n=222)	p-value
Age (years)	15.3±2.0	15.1±2.0	NS
Male sex (%)	49.0% (38.6%–59.4%)	53.2% (46.4%–59.9%)	NS
Race-Ethnicity (% NHW)	82.1% (69.6%–91.1%)	92.0% (86.4%–95.8%	0.04
Duration (years)	–	8.7±3.0	–
BMI (percentile)	59±29	65±22	NS
SBP (mm Hg)	109±9	111±8	0.02
DBP (mm Hg)	64±6	67±6	<0.0001
HbA1c (%)	5.3±0.3	8.7±1.5	<0.0001
HbA1c (mmol/mol)	34.4±2.1	71.6±14.0	<0.0001
Tanner stage (% 4–5)	72.3% (62.2%–81.1%)	74.7% (68.5%–80.4%)	NS
PWV at baseline (m/s)	5.2±0.6	5.2±0.6	NS
PWV at follow-up (m/s)	5.5±0.7	5.7±0.7	NS
BrachD at baseline (%/mm Hg)	6.9±1.4	6.9±1.3	NS
BrachD at follow-up (%/mm Hg)	6.7±1.5	6.7±1.2	NS
AIx * **HR75 at baseline** (%)	1.7(−5.3–9)	2.7 (−3.0–9.0)	NS
AIx * **HR75 at follow-up** (%)	2.7 (−2.7–8)	4.7 (−2.2–10.0)	NS
Baseline ACR * (mg/g)	7.6 (4.2–16.0)	7.3 (4.3–12.7)	NS
Follow-up ACR * (mg/g)	6.3 (3.6–14.5)	5.8 (4.2–13.1)	NS
Baseline eGFR by Schwartz (mL/min/1.73m^2)	100±17	108±20	0.0005
Follow-up eGFR by Schwartz (mL/min/1.73m^2)	96±14	99±15	NS
Baseline eGFR by Bouvet (mL/min/1.73m^2)	113±16	116±17	NS

* Median and interquartile range (IQR) or % (95% CI).