Alterations in left ventricular, left atrial, and right ventricular structure and function to cardiovascular risk factors in adolescents with type 2 diabetes participating in the TODAY clinical trial

Data on cardiovascular disease (CVD) risk in adolescents with type 2 diabetes (T2D) are limited. Echocardiography was performed in the last year of the Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) clinical trial (median 4.5/2 yr from diagnosis of T2D, average age 18 yr), including MMode and 2D measurements of left ventricular (LV) and left atrial (LA) dimensions, LV tissue Doppler imaging (TDI), and tricuspid annular plane systolic excursion (TAPSE). Relationships between cardiac structure and function with demographic characteristics and baseline and change-from-baseline in CVD risk factors were examined in 455 participants. Mean LV mass (LVM) was high/normal and 16.2% had adverse LV geometry (8.1% concentric geometry, 4.5% LV hypertrophy, and 3.6% both). Determinants of higher LVM were male gender, black race, baseline and increasing body mass index (BMI), baseline and increasing systolic blood pressure (SBP), use of blood pressure (BP) medications, maintenance of glycemic control, and smoking; heart rate (HR) was inversely related. LV shortening fraction was high/normal and related to increasing BMI and higher baseline SBP. LV relative wall thickness was related to race–ethnicity, change in BMI, baseline glycated hemoglobin (HbA1c), and baseline and change in SBP. Mean LA internal dimension was high/normal and gender, baseline and increasing BMI, increasing SBP, and HR (inverse) were related. LV TDI was positively related to obesity (higher with adverse geometry). TAPSE was normal and related to higher BMI and lower HR. There was no effect of T2D treatment on cardiac target organ injury. Adolescents with T2D have adverse measures of cardiac structure and function positively related to BMI and BP.
disease. Left ventricular (LV) mass, relative wall thickness, and shortening fraction and left atrial (LA) size may provide predictive power in addition to conventional risk factors regarding cardiovascular morbidity and mortality (6). Right ventricular (RV) dysfunction or pulmonary hypertension could be present secondary to obesity.

The Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) randomized clinical trial assembled the largest group of children and adolescents with T2D to date (7). The youth in TODAY were well characterized with reliable objective measurements of traditional markers of cardiovascular risk that predict CVD in adults. Echocardiograms were performed in the last year of the study to (1) characterize LV and LA structure in the TODAY cohort; (2) determine relationships with cardiovascular risk factors at the baseline examination, changes in those risk factors over time, or assigned treatment group; and (3) analyze whether optimal control of T2D and cardiovascular risk factors were associated with better LV and LA structure and function and RV function. Analyses also examined the relationships between echocardiography outcomes and race–ethnicity, gender, duration of diabetes, time in study, and failure to maintain glycemic control (defined as HbA1c ≥8% for 6 months or acute metabolic decompensation with failure to wean insulin therapy within 90 days).

Methods

TODAY sample, study design, and primary results

The TODAY study design has been reported (7) and is briefly described. Inclusion criteria for the 699 youth were ≥85th percentile for body mass index (BMI), aged 10–17, diagnosed with T2D ≤2 yrs, and negative for diabetes antibodies. Participants were randomized to one of three treatment arms (1) metformin alone (M), (2) metformin plus rosiglitazone (M + R), and (3) metformin plus an intensive lifestyle program (M + L). Treatment with M + R was superior to M in preventing loss of glycemic control in youth with T2D; M + L was not different from M or M + R (8).

The protocol was approved by the Institutional Review Boards for the Protection of Human Subjects of each participating institution. All participants provided informed consent and minor children confirmed assent according to local guidelines.

Cardiovascular risk assessment and treatment

All physical measurements were made by trained staff according to a study-wide protocol. BMI was calculated from height and weight (weight in kg divided by height in m²). Blood pressure (BP) was taken using a CAS 740 monitor (CAS Medical, Branford CT, USA) with standardized oscillometric cuff sizes. Participants with high blood pressure (defined as BP ≥95th percentile for age, sex, and height or ≥130/80, whichever was lower) received dietary counseling on a low salt diet. If values remained elevated, study-supplied lisinopril was initiated and titrated to achieve target goals according to an algorithm. Fasting lipids were measured yearly and analyzed by a central lab. American Diabetes Association guidelines for treatment of dyslipidemia were used.

Echocardiography

Echocardiograms were performed on participants in the last year of the study. Equipment used was site specific. At each site, certified cardiac ultrasound technicians performed scans according to a predetermined protocol that included a total of 34 separate image acquisitions. All technicians underwent a web-based tutorial administered by the TODAY Echocardiography Reading Center and protocol certification that required completion of both a knowledge-based examination and satisfactory completion of test studies.

Standard LV long axis, short axis, and apical imaging planes were obtained and appropriate 2-dimensional and 2-dimensional guided MMode images were saved digitally (minimum of two beats, each image was repeated so that two clips of each view were stored). Images were transmitted electronically to the TODAY Echocardiography Reading Center. MMode and 2D measurements of LV and LA dimensions were made according to American Society of Echocardiography guidelines (9–11). LA dimension was described as the measure of LA size. LV mass, LV ejection fraction, and LV relative wall thickness were calculated according to standard formulae. Tissue Doppler imaging (TDI) analysis of the lateral mitral valve annulus during diastole was performed and values from sequential beats were averaged; diastolic function was calculated as TDI = E/Em. RV function was assessed by tricuspid annular plane systolic excursion (TAPSE); RV pressure was assessed by tricuspid regurgitation velocity when a sufficient jet was identified (12, 13).

All studies were graded for quality according to a 4 point scale (3=all measurements easily made to 0=unmeasurable). Only studies with grades 1 and above were included in this report. All studies were read by one reader. Intra- and inter-observer variability was assessed by random re-reading of 30 studies (about 6% of the total) by the primary reader and by a second reader at the Echocardiography Reading Center working on a different study with a similar
scanning protocol. For LV mass, LA diameter, and LV diastolic dimension, correlation coefficients for intra-reader repeat measurements were 0.97, 0.94, and 0.96, respectively, and for inter-reader repeat measurements were 0.77, 0.67, and 0.82.

Statistical analysis
Descriptive statistics presented are percent or mean and standard deviation. General linear models were used to assess relationships among echocardiography outcomes and independent predictors including gender, race–ethnicity, reaching the primary study outcome of glycemic failure, treatment group, age at echocardiogram, time on assigned treatment, and cardiovascular risk factors measured at baseline and follow-up [BMI, systolic blood pressure (SBP), HbA1c, BP medication use, and cigarette use]. Heart rate (HR) was measured as part of the echocardiogram. At every visit, use of or prescription for BP medications was indicated. Participants self-reported cigarette use, categorized as either used within the past month or never used/not used within the past month. Follow-up BMI, HbA1c, and SBP had to be collected 3 months of the echocardiogram, and change was follow-up minus baseline.

With regard to LV geometry, the cohort was stratified into four groups according to LV mass (cut-off at 51 g/m2.7) and relative wall thickness (cut-off at 0.41): (1) normal, (2) eccentric LV hypertrophy (increased LV mass only), (3) concentric remodeling (increased relative wall thickness only), and (4) concentric LV hypertrophy (14). Categories were tested between gender and across the three major race–ethnicities using chi-square.

Results
Echocardiograms were performed at a median ∼4 1/2 yr from diagnosis of T2D and an average age of 18 yr. At this point in the trial (2–6 yr after randomization), we were able to schedule and obtain echocardiograms on 542 participants of 699 in the randomized cohort; 3 were of unacceptable quality and were repeated. The current analysis presents data for those participants who also had cardiovascular risk factors measured within 3 months of the echocardiogram (n = 455). Comparison of the analysis sample with the remaining 244 TODAY participants showed no significant difference for gender, race–ethnicity, baseline BMI, baseline HbA1c, treatment group assignment, or study outcome; those not in the analysis sample had slightly higher SBP (by 2.5 mmHg) and age (by 0.3 yr).

Demographic and risk information at the baseline visit and the visit within 3 months of the echocardiogram are shown in Table 1 by treatment group. There were no significant differences in baseline characteristics among treatment groups. As the initial analysis revealed no relationship between lipid level (at baseline and over time) with echocardiography outcomes, lipids were not included in subsequent analysis models. Over time HbA1c increased and the number of subjects taking BP medications increased 5–7-folds. At the time of echocardiogram, 215 of the 455 (47.3%) participants had failed to maintain glycemic control.

Table 1. Mean (SD) or percent with explanatory factors by treatment group at baseline and at follow-up

| Factor                        | Baseline | Time of echocardiography |
|-------------------------------|----------|--------------------------|
|                               | M        | M + L                    | M        | M + R     | M + L     |
| Female                        | 63.9%    | 66.0%                    | 62.0%    |           |           |
| Race–ethnicity                |          |                          |          |           |           |
| NHB                           | 34.2%    | 27.9%                    | 32.7%    | 37.0 (8.4)| 37.7 (8.2)| 35.1 (7.5)|
| Hispanic                      | 37.3%    | 44.9%                    | 42.0%    | 8.44 (2.64)| 7.71 (2.83)| 7.93 (2.70)|
| NHW                           | 22.8%    | 20.4%                    | 19.3%    | 116.5 (12.0)| 116.2 (11.7)| 115.3 (10.1)|
| Other                         | 5.7%     | 6.8%                     | 6.0%     | 38.0%     | 32.7%     | 28.7%     |
| BMI                           | 35.7 (8.5)| 34.7 (7.3)               | 33.8 (7.4)|           |           |           |
| HbA1c                         | 6.10 (0.74)| 5.95 (0.71)              | 5.95 (0.76)|           |           |           |
| Systolic BP                   | 112.5 (11.1)| 112.7 (10.1)             | 112.0 (10.6)|           |           |           |
| BP medication use             | 7.6%     | 6.1%                     | 2.7%     | 38.0%     | 32.7%     | 28.7%     |
| Cigarette use                 | 1.3%     | 2.0%                     | 2.0%     | 5.1%      | 4.8%      | 2.7%      |
| Failed to maintain glycemic control |      |                          |          | 55.7%     | 40.1%     | 45.3%     |
| Age (yr)                      |          |                          |          | 18.7 (2.3)| 18.2 (2.7)| 18.3 (2.4)|
| Time in study (mos)           |          |                          |          | 76.2 (53.9)| 90.6 (51.7)| 88.0 (56.3)|
| HR by echo                    |          |                          |          | 78.7 (14.2)| 76.5 (11.5)| 73.5 (12.6)|

M, metformin only; M + R, metformin + rosiglitazone; M + L, metformin + lifestyle program; NHB, non-Hispanic Black; NHW, non-Hispanic White; BMI, body mass index; BP, blood pressure; SD, standard deviation.
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**Table 2. Mean (SD) of echocardiography outcomes by treatment group within gender**

| Outcome                          | Female M | Female M+R | Female M+L | Male M | Male M+R | Male M+L |
|----------------------------------|----------|------------|------------|--------|----------|----------|
| LV mass (g)*                     | 138.1 (35.3) | 144 (35.0) | 132.7 (34.4) | 181.0 (44.3) | 185.0 (42.7) | 186.5 (55.4) |
| LV mass/height^{2.7} (g/m^{2.7})*| 36.5 (8.2) | 37.4 (8.0) | 36.1 (9.1) | 39.8 (8.7) | 40.1 (7.6) | 40.7 (11.5) |
| LV relative wall thickness       | 0.33 (0.06) | 0.34 (0.06) | 0.33 (0.06) | 0.34 (0.06) | 0.34 (0.06) | 0.35 (0.06) |
| LV fractional shortening (%)    | 38.1 (5.1) | 37.7 (4.8) | 38.7 (4.8) | 39.3 (6.1) | 37.1 (4.8) | 37.0 (5.1) |
| LA internal dimension (cm)^*     | 3.56 (0.41) | 3.63 (0.48) | 3.46 (0.43) | 3.66 (0.42) | 3.85 (0.43) | 3.65 (0.51) |
| LA internal dimension/height (cm/m)^* | 2.18 (0.25)  | 2.21 (0.29)  | 2.14 (0.27)  | 2.09 (0.23)  | 2.19 (0.25)  | 2.08 (0.28)  |
| TAPSE (cm)                       | 2.16 (0.33) | 2.18 (0.35) | 2.17 (0.41) | 2.12 (0.35) | 2.20 (0.27) | 2.17 (0.35) |

**Doppler diastology**

| Outcome              | Female M | Female M+R | Female M+L | Male M | Male M+R | Male M+L |
|----------------------|----------|------------|------------|--------|----------|----------|
| LV E (cm/sec)^*      | 95.7 (19.2) | 93.6 (17.9) | 96.0 (18.8) | 88.3 (18.7) | 89.6 (18.4) | 87.2 (16.0) |
| LV Em (cm/sec)       | 16.6 (3.9) | 16.6 (3.9) | 16.4 (4.4) | 16.0 (4.2) | 16.8 (4.0) | 16.2 (5.6) |
| E/Em ratio           | 6.10 (1.93) | 5.89 (1.61) | 6.24 (1.93) | 5.84 (1.67) | 5.56 (1.60) | 5.90 (2.13) |

M, metformin only; M+R, metformin + rosiglitazone; M+L, metformin + lifestyle program; LV, left ventricular; LA, left atrial; TAPSE, tricuspid annular plane systolic excursion; SD, standard deviation.

*Females significantly different from males, p < 0.05.

### Echocardiography outcomes

Echocardiographic outcome data are shown in Table 2 by treatment group within gender. Mean LV mass in this cohort was 154.7 (standard deviation or SD 45.6) g and 37.9 (9.0) g/m².7 when indexed for height, which is ~90th percentile for the gender-specific population mean (10) (see Fig. S1, Supporting Information in on-line appendix). LV wall thickness ratio was 0.33 in girls and 0.34 in boys. LV shortening fraction was high normal (38%). Mean LA internal dimension was 3.61 (0.46) cm and 2.15 (0.27) cm/m², which is ~75th percentile for the healthy weight population mean (11) (see Fig. 1-S in on-line appendix). LV diastolic function measures were within the normal range, with females having slightly higher LV E velocities. There were no significant differences related to treatment group with the exception of slightly higher LA diameter in the M+R group compared to the M+L group (p < 0.05). Mean TAPSE was 2.17 (0.35) cm.

The cohort was classified according to LV geometry and by race–ethnicity and gender (Fig. 1) using cut-offs of 51 g/m².7 for LV mass (14). Overall, 83.8% had normal LV geometry with concentric remodeling found in 8.1%, eccentric LV hypertrophy in 4.5%, and concentric LV hypertrophy in 3.6%. Males and non-Hispanic Blacks had a greater prevalence of abnormal geometry. LV diastolic function was significantly different...
across LV geometry groups, with EM velocity lower and E/Em ratio higher in all three adverse geometry groups (see Table 1-S in on-line appendix). If the 95th percentile for LV mass was chosen, the percent with abnormal geometry would have been much higher (10).

A total of 91 study participants were referred for cardiology evaluation because of significant or incidental echocardiographic findings (ectopy, bicuspid aortic valve, etc.). This included increased LV mass (n = 44) as well as outcomes related to cardiac function: 12 for increased LV internal dimension diastole, 1 for increased internal ventricular septum diastole, 1 for decreased LV ejection fraction, and 7 for LA enlargement. There were no significant differences in cardiac referrals across treatment groups.

Determinants of LV, LA, and RV outcomes

Regression models of echocardiographic outcomes analyzed the contribution of cardiovascular risk factors at entry into the TODAY study as well as changes in these risk factors at time of echocardiogram (Table 3). HR displayed a negative relationship with echocardiographic outcomes in all models except LV shortening fraction and relative wall thickness where it was not significantly related. Predictors of higher LV mass were male gender, race–ethnicity (non-Hispanic Black), baseline and change in BMI, baseline SBP, and higher SBP when treatment group was only significant for MMODE LA internal dimension (higher in the M + R group). Age at time of echocardiogram, time in study, cigarette use at baseline, and BP medication use during follow-up were not significant.

LV diastolic function measures were related to both BMI at baseline and change in BMI. HbA1c was weakly related to E/Em ratio. HR was negatively related to both LV E and LV Em with no effect on the ratio. The M + R group had slightly lower E/Em ratio.

RV assessment revealed that three participants had predicted RV pressure >35 mmHg. Mean TAPSE values were within the range reported for this age group; however, 13.1% had values <1.8 reflecting diminished RV function. TAPSE was positively related to BMI at baseline and inversely related to HR.

Table 3. Significant p-values (p < 0.05) for explanatory factors* in models of echocardiography outcomes

| Factors                      | LV mass (g) | LV mass/ht^2.7 (g/m^2.7) | LV relative wall thickness | LV fractional shortening (%) | LA internal dimension (cm) | LA internal dimension/height (cm/m) | LV E (cm/sec) | LV Em (cm/sec) | E/Em ratio | TAPSE (cm) |
|------------------------------|-------------|----------------------------|----------------------------|-------------------------------|---------------------------|------------------------------------|---------------|---------------|-------------|------------|
| Gender                       | <0.0001     | <0.0001                   | ns                         | ns                           | <0.0061                   | 0.0118                            | ns             | ns             | ns          | ns         |
| Race–ethnicity               | ns          | ns                        | ns                         | ns                           | <0.0001                   | <0.0001                          | ns             | ns             | ns          | ns         |
| BMI at baseline              | <0.0001     | <0.0001                   | <0.0088                    | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| BMI change†                  | <0.0001     | <0.0001                   | 0.0045                     | 0.0067                       | <0.0001                   | <0.0001                          | 0.0010         | 0.0022         | 0.0001      | 0.0009     |
| HbA1c at baseline            | ns          | 0.0056                    | 0.0091                     | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| SBP at baseline              | 0.0009      | 0.0121                    | 0.0338                     | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| SBP change†                  | <0.0001     | 0.0026                    | 0.0126                     | ns                           | 0.0385                    | ns                                 | ns             | ns             | ns          | ns         |
| BP medication use at baseline| 0.0138      | 0.0081                    | ns                         | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| Cigarette use during follow-up| 0.0273     | ns                        | ns                         | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| Treatment group              | ns          | ns                        | ns                         | ns                           | 0.0427                    | ns                                 | ns             | ns             | 0.0313      | ns         |
| Failed to maintain glycemic control | 0.0082 | 0.0065 | ns | ns | ns | ns | ns | ns | ns | ns |
| Age at time of echo          | ns          | ns                        | ns                         | ns                           | ns                        | ns                                 | ns             | ns             | ns          | ns         |
| Heart rate by echo‡          | 0.0005      | 0.0008                    | ns                         | ns                           | 0.0219                    | 0.0478                            | <0.0001        | 0.0015         | ns          | 0.0141     |

BMI, body mass index; BP, blood pressure; HbA1c, hemoglobin A1c; LV, left ventricular; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion.

*Factors included if significant in any multivariate model of the echo outcomes.
†Change was determined as the difference of follow-up value at time of echo minus baseline value.
‡‡Negative slope for all.
Discussion

In the largest study of adolescents with T2D to date, we showed significant LV and LA target organ abnormalities that are predicted by obesity and elevated BP in both adults (15) and children (16, 17). Changes in BMI and BP continued to drive changes in LV and LA structure. The prevalence of abnormal LV structure across the cohort was 16.2%, with non-Hispanic Blacks and males disproportionately affected, compared to 3% in non-diabetic non-obese children (18). These results are comparable to the few studies of youth with T2D (3–5), including one that compared individuals with T2D with obese and lean controls (3). These studies have shown that children with T2D have increased LV mass, abnormal LV geometry, and perhaps a hyperkinetic circulation (4, 5). Because children and adolescents with T2D have chronic exposure to obesity and frequently hypertension as well, the cardiac findings in this study reflect the importance of these exposures early in childhood on LV geometry. In adults (mean age 50.1, SD 3.6 yr) in the Coronary Artery Risk Development in Young Adults (CARDIA) study, longstanding but not recent onset T2D is associated with cardiac structural changes assessed by echocardiography (19). This may indicate significant future increase in risk for adverse cardiac structural abnormalities in children with T2D.

LV mass is an important independent risk factor for cardiovascular morbidity and mortality (20, 21), and the risk from increased LV mass is independent of conventional risk factors in both non-Hispanic Whites and Blacks (22, 23). The threshold for LV hypertrophy (51 g/m².7) is associated with a 2–4-fold increase in cardiovascular events independent of other risk factors (24). In our large cohort of youth with T2D the association of LV mass with obesity and BP was consistent with reports in non-diabetic youth (14, 25, 26). Longitudinal data in non-diabetic youth show that LV mass tracks over 5 yr and is predicted by excess weight (27). The fact that longitudinal changes in BMI and BP in TODAY impacted LV mass suggests that control of these risk factors might substantially improve future risk of CVD events.

LV shortening fraction was in the high normal range (28) in this cohort and these findings are similar to those reported by Shah et al. in 157 youth with T2D (3). Change in BMI and baseline SBP were associated with higher LV shortening, consistent with the hypothesis that a hyperkinetic circulation is an early finding in the development of longstanding hypertension (29). Although decreased cardiac function is commonly hypothesized in studies of obese children, increased systolic function secondary to increased sympathetic tone and a higher cardiac output state may be more typical. It may take years of exposure to hypertension and T2D before measurable changes in systolic function are appreciated.

There has been less research on determinants of LA size in children than for LV mass. Our findings are consistent with studies in children without diabetes that show a strong relationship with obesity and a weak relationship with BP (30). LA size indexed for height in our cohort was higher than the values reported by Ayer et al. in non-diabetic youth (11). LA size also predicts future CVD (31).

In adults, diastolic dysfunction is linked to the development of heart failure in those with T2D (32). Shah et al. (3) found that youth with T2D and obesity had worse diastolic function than lean controls. In American Indians without diabetes, Em velocity was decreased and consequently E/Em ratio was increased in those with adverse LV geometry, with increasing E/Em ratio at high BMI despite the fact that this cohort had severe obesity (33). The relationship of diastolic function to LV geometry suggests that a subgroup of adolescents with T2D at risk for early heart failure may be identifiable.

With regard to the RV, we did find evidence for pulmonary hypertension in three participants (<1%) by tricuspid regurgitation velocity, and about one-eighth of the cohort had TAPSE values that suggest RV dysfunction. Our average values for TAPSE were slightly lower than those reported in healthy children (12, 13), suggesting the need for longitudinal assessment of RV function in those with T2D. TAPSE has been thought to be independent of HR (34), but not in our analyses.

Measures of diabetes severity, treatment, and control had little effect on echocardiographic measures in this large group of youth with early onset T2D. Baseline HbA1c was related to higher LV mass after indexing for height. Baseline HbA1c was also associated with increased LV relative wall thickness. Paradoxically, loss of glycemic control was associated with lower LV mass. This finding may be because of the acute metabolic effect of poor glucose control (reflected in higher HbA1c) at the time of echocardiogram (data not shown), with glycosuric-related vascular volume contraction resulting in a reduction of LV cavity size and lower calculated LV mass. Shah et al. (3) did not find an independent effect of diabetes control on LV geometry and function in individuals with T2D compared to a control group matched for BMI but did not look at treatment effects.

Our study shows that significant cardiac end organ injury, caused by pre-existing cardiovascular risk factors such as BP and obesity, is present early in the course of T2D. In adults, T2D has an independent effect on LV geometry (13). In a small study comparing T2D adolescents with obese controls, Cerutti et al. (4) found higher LV wall thickness in those with T2D.
Because duration of T2D in all of these cohorts was relatively short, chronic effects of diabetes may have not yet emerged. Our results are also consistent with longitudinal data from the CARDIA study where longstanding T2D but not new onset T2D adversely impacted LV hypertrophy (19).

Adult trials of aggressive hypertension control in T2D have had disappointing results with regard to coronary artery disease, perhaps because the intervention was too late to reverse vascular injury (35). It is possible that early intervention in youth with T2D may reverse this injury, and trials using cardiac function as endpoints to determine optimal strategies for management to control obesity and hypertension in youth with T2D are needed. The TODAY study utilized currently recommended management protocols for both BP control and weight management yet echocardiographic outcomes were adverse.

There are some limitations to this study. Because non-examined subjects have slightly higher SBP than the examined cohort, this analysis may slightly underestimate the severity of outcomes. Because echocardiograms were performed at only one time point, changes in echocardiographic endpoints over time could not be assessed. Because all participants had T2D, only severity of T2D and associated comorbidities can be assessed as predictors of outcomes rather than T2D itself. Echocardiograms performed on children with this degree of obesity are technically challenging, and the relevance of current methods for adjusting for body size developed in healthy populations to youth with severe obesity is unclear. Cohorts of healthy children of similar racial composition were not available for comparison. As our cohort had near normal HbA1c at baseline, long-term follow-up of the cohort including an echocardiogram will evaluate implications of diabetes and glycemic control over time.

In conclusion, this study of the largest group of youth with T2D to date showed adverse distributions of measures of cardiac structure and function and a hypertensive circulation related mostly to cardiovascular risk factors (hypertension and obesity). Our data indicate that obesity and hypertension are paramount in this population, so meticulous attention to BP and weight management is key to risk control. Whereas the effects of diabetes control and treatment had little impact in this cohort with relatively recent onset of T2D, longitudinal study of these youth will better detect the contribution of diabetes to these outcomes. Because of the high likelihood of future cardiovascular morbidity and mortality, assessment of right and left heart structure and function is required in the management of T2D, particularly in those with hypertension.

Acknowledgements

The writing group was: Lorraine Levitt Katz (chair), MD, Children’s Hospital of Philadelphia, University of Pennsylvania School of Medicine; Samuel S. Gidding, MD, Nemours Cardiac Center, A. I. DuPont Hospital for Children; Fida Bacha, MD, Children’s Nutrition Research Center, Baylor College of Medicine; Kathryn Hirst, PhD, Biostatistics Center, George Washington University; Sriroopan McKay, MD, Texas Children’s Hospital, Baylor College of Medicine; Laura Pyle, PhD, Biostatistics Center, George Washington University; Joao A. C. Lima, MD, Johns Hopkins University.

This work was completed with funding from NIDDK/NIH grant numbers U01-DK61212, U01-DK61230, U01-DK61239, U01-DK61242, and U01-DK61254; from the National Center for Research Resources General Clinical Research Centers Program grant numbers M01-RR0036 (Washington University School of Medicine), M01-RR0043-45 (Children’s Hospital Los Angeles), M01-RR00639 (University of Colorado Denver), M01-RR00884 (Children’s Hospital of Pittsburgh), M01-RR10166 (Massachusetts General Hospital), M01-RR00125 (Yale University), and M01-RR14467 (University of Oklahoma Health Sciences Center); and from the NCRR Clinical and Translational Science Awards grant numbers UL1-RR024134 (Children’s Hospital of Philadelphia), UL1-RR024139 (Yale University), UL1-RR024153 (Children’s Hospital of Pittsburgh), UL1-RR024989 (Case Western Reserve University), UL1-RR024992 (Washington University in St Louis), UL1-RR025758 (Massachusetts General Hospital), and UL1-RR025780 (University of Colorado Denver).

The TODAY Study Group thanks the following companies for donations in support of the study’s efforts: Becton, Dickinson and Company; Bristol-Myers Squibb; Eli Lilly and Company; GlaxoSmithKline; LifeScan, Inc.; Pfizer; Sanofi Aventis. We also gratefully acknowledge the participation and guidance of the American Indian partners associated with the clinical center located at the University of Oklahoma Health Sciences Center, including members of the Absentee Shawnee Tribe, Cherokee Nation, Chickasaw Nation, Choctaw Nation of Oklahoma, and Oklahoma City Area Indian Health Service; the opinions expressed in this paper are those of the authors and do not necessarily reflect the views of the respective Tribal and Indian Health Service Institution Review Boards or their members. Materials developed and used for the TODAY standard diabetes education program and the intensive lifestyle intervention program are available to the public at https://today.bsc.gwu.edu/. Clinical trial reg. no. NCT0081328, clinicaltrials.gov

Conflict of interests

None of the members of the writing group have a conflict to disclose. The study was funded by NIDDK/NIH, and the scientific program officer was involved in all aspects of the design and development of TODAY but is not a member of the writing group for this manuscript. Donations from the following companies in support of the study’s efforts are acknowledged, but none participated in study design, conduct, data analysis, or report: Becton, Dickinson and Company; Bristol-Myers Squibb; Eli Lilly and Company; GlaxoSmithKline; LifeScan, Inc.; Pfizer; Sanofi Aventis. Lorraine Levitt Katz and Samuel S. Gidding wrote the first draft of the manuscript. All members of the writing group had levels of effort on
the study grant for responsibilities that did not include producing the manuscript.

Supporting Information
Additional Supporting Information may be found in the online version of this article:
Appendix S1. Listing of the TODAY Study Group.
Figure S1. Indexed LV mass (by gender) and LA diameter by treatment group [mean, 95% (confidence interval) CI] compared to healthy population norms*.

Table S1. Doppler diastology mean standard deviation (SD) by LV geometry categories

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