SUPPLEMENTARY DATA

Participant characteristics at baseline

We compared characteristics of women who were premenopausal at baseline by diabetes status; specifically, we compared demographic characteristics, measures of ovarian dysfunction, measures of cardiovascular risk, anthropometric measures, clinical measures, and laboratory results by diabetes status. The mean values of all normally distributed continuous variables were compared by diabetes status using independent two-sample t-tests. The median values of all non-normally distributed continuous variables (i.e., triglycerides) were compared by diabetes status using the Kruskal-Wallis non-parametric test. All categorical variables were compared by diabetes status using the $\chi^2$ test for independence.

Calculation of the American College of Cardiology’s atherosclerotic cardiovascular (ASCVD) risk

The 10-year risk of a cardiovascular event as estimated by ASCVD risk was calculated for each study participant (1). Although this measure is validated for use in adults over the age of 40, we calculated it for the full study sample as limiting the sample to only those individuals over 40 did not appreciably change the estimates.

Comparison of participant characteristics at the final study visit

We examined demographic, menopause, and cardiovascular characteristics of women by diabetes and menopause status at their final study visit. Specifically, we calculated the mean age at the last study visit and the proportion of women in each CAC score category by menopause and diabetes status. Among women who were postmenopausal at their last study visit, we also summarized the proportion that underwent natural menopause as opposed to surgical menopause, and the mean age of natural menopause.

Comparison of women who completed 4 vs. <4 study visits

To examine whether there was differential loss to follow-up that could potentially bias our results, we used the same methods described above to compare baseline characteristics of women who completed all 4 study visits to those of women who completed <4 study visits.

Repeated measures mixed models

We examined CAC as our primary outcome by applying a square root transformation to CAC volume (2). We used repeated measures mixed modeling for all statistical analyses to account for within-subject correlation of repeated measures taken at each of the 4 study visits. All longitudinal models used a spatial power covariance structure to model within-subject correlation over time and to account for unequal spacing of study visits. All models specified visit number as the repeated variable, and were adjusted for age in years at each visit.

The base model specifically tested whether CAC differed by diabetes and menopause status over time. We used a repeated measures model examining square root-transformed CAC volume and testing the interactions between diabetes and visit and between diabetes and menopause. This model was further adjusted for time-varying age and baseline CAC.

Modeling cardiovascular risk factors

We tested the following variables for their relationships with diabetes and menopause status: waist and hip circumference, body mass index (BMI), systolic and diastolic blood pressure, pulse pressure (i.e., the difference between systolic and diastolic blood pressure), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, total cholesterol, and triglycerides. These risk factors were examined as the outcomes of separate repeated measures models in which we again tested the interactions between diabetes and visit number and diabetes and menopause. All models were adjusted for age, visit, menopause and diabetes status, baseline values of the risk factor of interest, the interaction between diabetes and visit, and the interaction between diabetes and menopause. In the models that examined blood pressure and pulse pressure as outcomes we further adjusted for antihypertensive medication use; similarly, in the model that examined LDL cholesterol as the outcome, we further adjusted for statin use.
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We retested Model 1 with the addition of all risk factors where there was a significant statistical interaction between diabetes and menopause status, as well as a variable for ovarian dysfunction. Women with type 1 diabetes have previously reported increased prevalence of amenorrhea and irregular menstrual cycles than women without diabetes (3), and we explored whether accounting for the risk factors known to change with menopause and ovarian dysfunction changed the relationship between diabetes, menopause, and CAC. In the CACTI study, women self-reported their history of ovarian dysfunction at Visit 2.

Statistical interaction between diabetes, menopause, visit number

In all repeated measures models, we also tested the three-way interaction between diabetes, menopause, and visit number. This alternate model allowed for the comparison of mean CAC volume by each stratum over time. Least squares means from the model containing the three-way interaction were used to generate the figures included in the manuscript.

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### SUPPLEMENTARY TABLE S1. Participant characteristics at the last study visit.

|                                      | Premenopausal women with diabetes (n=236) | Postmenopausal women with diabetes (n=75) | Premenopausal women without diabetes (n=228) | Postmenopausal women without diabetes (n=97) |
|--------------------------------------|------------------------------------------|------------------------------------------|---------------------------------------------|---------------------------------------------|
| **Demographic information**          |                                          |                                          |                                             |                                             |
| Age (years)                          | 39 ± 8                                   | 55 ± 8                                   | 39 ± 10                                     | 57 ± 6                                      |
| **Menopause information**            |                                          |                                          |                                             |                                             |
| Natural menopause (n [%])            | --                                       | 63 [84%]                                 | --                                          | 78 [80%]                                    |
| Age of natural menopause (years)     | --                                       | 50 ± 6                                   | --                                          | 50 ± 8                                      |
| **Measures of cardiovascular risk**  |                                          |                                          |                                             |                                             |
| CAC score (Agatston units)           |                                          |                                          |                                             |                                             |
| 0 Agatston units (n [%])             | 154 [65%]                                | 20 [27%]                                 | 187 [82%]                                   | 59 [61%]                                    |
| 1-100 Agatston units (n [%])         | 54 [23%]                                 | 26 [35%]                                 | 39 [17%]                                    | 31 [32%]                                    |
| 101-300 Agatston units (n [%])       | 15 [6%]                                  | 11 [15%]                                 | 1 [0.4%]                                    | 5 [5%]                                      |
| >300 Agatston units (n [%])          | 13 [6%]                                  | 18 [24%]                                 | 1 [0.4%]                                    | 2 [2%]                                      |
SUPPLEMENTARY TABLE S2. Baseline characteristics by whether participants completed 4 vs. <4 study visits.

|                                | Completed 4 study visits (n=414) | Completed <4 study visits (n=222) | p-value |
|--------------------------------|----------------------------------|-----------------------------------|---------|
| **Demographics**               |                                  |                                   |         |
| Age (years)                    | 36 ± 8                           | 33 ± 8                            | <0.0001 |
| Type 1 diabetes (n [%])        | 208 [50%]                        | 103 [46%]                         | 0.36    |
| **Measures of ovarian dysfunction** |                                  |                                   |         |
| Irregular menstrual cycles (n [%]) | 69 [18%]                    | 25 [17%]                          | 0.72    |
| Amenorrhea (n [%])             | 39 [10%]                         | 22 [15%]                          | 0.15    |
| **Measures of cardiovascular risk** |                                  |                                   |         |
| CAC score (Agatston units)     |                                  |                                   |         |
| 0 Agatston units (n [%])†      | 337 [81%]                        | 184 [83%]                         | 0.92    |
| 1-100 Agatston units (n [%])   | 64 [15%]                         | 33 [15%]                          |         |
| 101-300 Agatston units (n [%]) | 8 [2%]                           | 3 [1%]                            |         |
| >300 Agatston units (n [%])    | 5 [1%]                           | 2 [1%]                            |         |
| ASCVD risk (%)                 | 0.86 ± 1.52                      | 1.20 ± 2.48                       | 0.08    |
| **Anthropometry**              |                                  |                                   |         |
| BMI (kg/m²)                    | 25.3 ± 4.9                       | 25.5 ± 5.4                        | 0.60    |
| Waist circumference (cm)       | 79.1 ± 12.0                      | 79.3 ± 12.9                       | 0.87    |
| Waist-to-hip ratio             | 0.77 ± 0.06                      | 0.77 ± 0.07                       | 0.91    |
| **Clinical information**       |                                  |                                   |         |
| Systolic blood pressure (mmHg) | 110 ± 12                         | 112 ± 12                          | 0.32    |
| Diastolic blood pressure (mmHg)| 74 ± 8                           | 76 ± 8                            | 0.04    |
| Pulse pressure (mmHg)          | 36 ± 10                          | 36 ± 10                           | 0.61    |
| **Laboratory results**         |                                  |                                   |         |
| Fasting glucose (mmol/L)       | 7.4 ± 4.4                        | 7.8 ± 4.7                         | 0.30    |
| HbA1c (% [mmol/mol])           | 6.6 ± 1.6 [49 ± 18]              | 6.7 ± 1.8 [50 ± 20]               | 0.70    |
| HDL cholesterol (mmol/L)       | 1.54 ± 0.39                      | 1.47 ± 0.36                       | 0.04    |
| LDL cholesterol (mmol/L)       | 2.7 ± 0.7                        | 2.7 ± 0.8                         | 0.69    |
| Triglycerides (mmol/L)         | 0.89 [0.70, 1.20]                | 0.89 [0.71, 1.23]                 | 0.48    |
| Total cholesterol (mmol/L)     | 4.7 ± 0.9                        | 4.6 ± 0.8                         | 0.27    |
| Estimated insulin sensitivity (mg/dL) | 11.9 ± 8.4          | 13.0 ± 9.3                        | 0.17    |
| Estimated glomerular filtration rate (mL/min/1.73m²) | 105.6 ± 24.1 | 110.1 ± 24.6 | 0.03 |

All variables are presented as the mean value ± SD with the exceptions of triglycerides, which is presented as the median value [IQR], and the following categorical measures: ovarian dysfunction and the 4 CAC score categories. These are presented as the number of women reporting each measure of dysfunction or their category based on their CAC score, respectively, and the percent they make up in that group.

*The measures of ovarian dysfunction are based on participant responses at Visit 2, not baseline. For this reason, the number of women in each group are as follows: 271 premenopausal women with diabetes, 27 postmenopausal women with diabetes, 279 premenopausal women without diabetes, and 46 postmenopausal women without diabetes.

†Due to rounding, percentages may not add to 100%.