

# Adults With Type 2 Diabetes Mellitus Exhibit a Greater Exercise-Induced Increase in Arterial Stiffness and Vessel Hemodynamics

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## ONLINE SUPPLEMENT

### **Adults with Type 2 Diabetes Exhibit a Greater Exercise-Induced Increase in Arterial Stiffness and Vessel Hemodynamics**

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**Table S1. Between-group differences in arterial stiffness and hemodynamics in response to exercise included two cfPWV outliers removed from main analysis**

Variable	Without T2DM (n=61) Mean (95% CI)	With T2DM (n=68) Mean (95% CI)	Mean difference (with-without T2DM) (95% CI)
<b>Arterial Stiffness and Hemodynamic Measures at 3 minutes</b>			
<b>Brachial Systolic BP (mmHg)</b>	164.5 (159.1, 169.9)	173.1 (168.1, 178.2)	<b>8.7 (0.9, 16.5)</b>
<b>Brachial Diastolic BP (mmHg)</b>	82.7 (80.6, 84.8)	84.3 (82.4, 86.2)	1.6 (-1.4, 4.6)
<b>Brachial PP (mmHg)</b>	81.9 (77.2, 86.5)	88.8 (84.5, 93.1)	<b>6.9 (0.3, 13.6)</b>
<b>cfPWV (m/s)</b>	13.0 (12.0, 14.0)	15.1 (14.2, 16.0)	<b>2.1 (0.7, 3.6)</b>
<b>Aortic stiffness <math>\beta_0</math></b>	34.4 (27.5, 41.4)	48.3 (41.9, 54.8)	<b>13.9 (3.8, 24.0)</b>
<b>HR (beats/min)</b>	98.3 (94.7, 101.8)	98.9 (95.6, 102.2)	0.6 (-4.5, 5.7)
<b>Arterial Stiffness and Hemodynamic Measures at 5 minutes</b>			
<b>crPWV (m/s)</b>	8.7 (8.3, 9.0)	8.9 (8.6, 9.2)	0.2 (-0.3, 0.7)
<b>Central Systolic BP (mmHg)</b>	118.3 (115.1, 121.5)	121.1 (118.1, 124.1)	2.9 (-1.7, 7.5)
<b>Central Diastolic BP (mmHg)</b>	79.6 (77.6, 81.6)	81.3 (79.4, 83.2)	1.7 (-1.2, 4.6)
<b>Central PP (mmHg)</b>	38.6 (36.3, 41.0)	39.9 (37.6, 42.1)	1.2 (-2.2, 4.6)
<b>AIx75 (%)</b>	25.9 (24.3, 27.6)	24.4 (22.8, 26.0)	-1.6 (-4.0, 0.8)

AIx75, augmentation index corrected for a heart rate of 75 beats/minute; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; PP, pulse pressure.

Bolded values indicate a significant absolute difference between groups.

cfPWV, crPWV, and Augmentation Index are adjusted for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, HR, and MAP.

Aortic stiffness  $\beta_0$  is adjusted for for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, and HR.

Blood pressure is adjusted for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, and HR.

HR and AIx75 at 3 minutes are adjusted for the pre-exercise value, age, sex, waist:hip ratio, and ACEi/ARB use.

**Table S2. Characteristics of participants excluded from analyses based on failure to meet criteria for exhaustion during maximal exercise**

<b>Variable</b>	<b>Included in Analysis (n=127)</b>	<b>Did not meet criteria for exhaustion (n=80)</b>	<b>P-value</b>
Age, years	59.3±10.6	59.8±11.4	0.767
Women, no (%)	63 (49.6%)	49 (61.3%)	0.102
Body mass index, kg/m <sup>2</sup>	31.2±3.9	31.9±4.2	0.207
Waist circumference, cm	102.6±9.8	104.2±11.5	0.228
Hip circumference, cm	109.4±8.6	111.9±9.6	0.053
Waist to hip circumference	0.94±0.07	0.93±0.08	0.584
Duration, years	10.5±7.5	10.2±8.0	0.829
<b>Arterial Stiffness and Hemodynamics</b>			
cfPWV (m/s)	9.8±2.4	9.7±1.9	0.851
Brachial Systolic BP (mmHg)	130±14	129±15	0.542
Brachial Diastolic BP (mmHg)	80±9	81±9	0.735
Brachial PP (mmHg)	50±12	49±12	0.632
Resting HR (beats/minute)	67.4±10.6	67.9±12.9	0.737
<b>Exercise Parameters</b>			
Exercise time (minutes)	14.9±2.4	13.0±3.3	<b>&lt;0.001</b>
VO <sub>2peak</sub> (mL/kg/min)	24.3±6.2	19.3±5.6	<b>&lt;0.001</b>
Peak HR (beats/minute)	153.7±23.9	138.6±23.7	<b>&lt;0.001</b>

Values expressed as mean ± standard deviation or number (%) as appropriate.

BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; HR, heart rate; MAP, mean arterial pressure; PP, pulse pressure; VO<sub>2peak</sub>, peak oxygen consumption.

**Table S3. Unadjusted values of post-exercise arterial stiffness, hemodynamics, and exercise parameters**

<b>Variable</b>	<b>Without T2DM (n=61) Mean±SD</b>	<b>With T2DM (n=66) Mean±SD</b>	<b>Mean difference (with-without T2DM) (95%CI)</b>
<b>Exercise time (minutes)</b>	14.8±5.3	15.1±2.4	0.2 (-0.6, 1.1)
<b>VO<sub>2peak</sub> (mL/kg/min)</b>	24.3±6.5	24.2±6.0	-0.1 (-2.3, 2.1)
<b>Max HR (beats/min)</b>	154±22	153±25	-1 (-9, 8)
<b>Peak SBP (mmHg)</b>	171±27	185±30	<b>14 (4, 25)</b>
<b>Peak DBP (mmHg)</b>	80±17	73±13	<b>-7 (-12, -2)</b>
<b>Brachial SBP (mmHg)</b>	164±22	173±26	<b>10 (1, 18)</b>
<b>Brachial DBP (mmHg)</b>	84 ±11	83±10	-2 (-5, 2)
<b>Brachial PP (mmHg)</b>	79±18	90±22	<b>11 (4, 18)</b>
<b>cfPWV (m/s)</b>	12.5±3.3	14.9±4.7	<b>2.4 (0.9, 3.8)</b>
<b>Aortic stiffness β<sub>0</sub></b>	32±16	47±29	<b>15.2 (6.9, 23.6)</b>
<b>HR (beats/min)</b>	98±17	99±17	1 (-5, 7)
<b>crPWV (m/s)</b>	8.6±1.3	8.9±1.5	0.4 (-0.1, 0.9)
<b>Central SBP (mmHg)</b>	119±16	121±14	2 (-4, 8)
<b>Central DBP (mmHg)</b>	81±10	80±9	-1 (-5, 2)
<b>Central PP (mmHg)</b>	37±11	41±14	3 (-1, 8)
<b>AIx75 (%)</b>	27.3±8.8	24.0±9.4	-2.3 (-5.7, 1.0)
<b>Ejection duration (ms)</b>	303.9±24.6	303.1±29.5	-0.8 (-10.7, 9.1)

AIx75, augmentation index corrected for a heart rate of 75 beats/minute; cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; DBP, diastolic blood pressure; PP, pulse pressure; SBP, systolic blood pressure; VO<sub>2peak</sub>; peak oxygen consumption.

**Table S4. Mean difference in cfPWV at 3 minutes post-exercise between adults with and without T2DM in univariate, partially adjusted, and fully adjusted models**

<b>Model</b>	<b>Included Variables</b>	<b>Mean Difference (with-without T2DM) (95% CI)</b>
1	Unadjusted	<b>2.37 (0.93, 3.81)</b>
2	Pre-exercise value	<b>1.21 (0.02, 2.40)</b>
3	Model 2 and age, sex	<b>1.32 (0.11, 2.52)</b>
4	Model 3 and WHR, ACEi/ARB use	<b>1.38 (0.05, 2.71)</b>
5	Model 4 and HR at 3 minutes	<b>1.40 (0.11, 2.69)</b>
6a	Model 5 and diastolic BP at 3 minutes	<b>1.59 (0.34, 2.85)</b>
6b	Model 5 and MAP at 3 minutes	<b>1.36 (0.13, 2.59)</b>
6c	Model 5 and systolic BP at 3 minutes	1.17 (-0.08, 2.43)
6d	Model 5 and systolic and diastolic BP at 3 minutes	<b>1.36 (0.09, 2.63)</b>
7a	Model 6a and statin use	<b>1.35 (0.01, 2.70)</b>
7b	Model 6b and statin use	1.14 (-0.18, 2.47)
7c	Model 6c and statin use	1.01 (-0.34, 2.36)
7d	Model 6d and statin use	1.15 (-0.20, 2.51)

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; HR, heart rate; MAP, mean arterial pressure; T2DM, type 2 diabetes mellitus.

**Table S5. Mean difference in aortic stiffness  $\beta_0$  at 3 minutes post-exercise between adults with and without T2DM in univariate, partially adjusted, and fully adjusted models**

<b>Model</b>	<b>Included Variables</b>	<b>Mean Difference (with-without T2DM) (95% CI)</b>
1	Unadjusted	<b>15.2 (6.92, 23.55)</b>
2	Pre-exercise value	<b>7.93 (0.95, 14.92)</b>
3	Model 2 and age, sex	<b>9.05 (1.96, 16.15)</b>
4	Model 3 and WHR, ACEi/ARB use	<b>8.61 (0.81, 16.42)</b>
5	Model 4 and HR at 3 minutes	<b>8.67 (0.96, 16.37)</b>
6	Model 5 and SBP at 3 minutes	<b>7.70 (0.05, 15.34)</b>
7	Model 5 and statin use	7.22 (-1.02, 15.46)

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; HR, heart rate; MAP, mean arterial pressure; T2DM, type 2 diabetes mellitus; SBP, systolic blood pressure.

**Table S6. Central Blood Pressure Parameters Calibrated with Brachial Mean Arterial Pressure and Diastolic Blood Pressure**

<b>Variable</b>	<b>Without T2DM (n=61)</b>	<b>With T2DM (n=66)</b>	<b>Mean difference (with-without T2DM) (95% CI)</b>
	<b>Mean (95% CI)</b>	<b>Mean (95% CI)</b>	
<b>Resting</b>			
<b>Central SBP (mmHg)</b>	117.9 (115.0, 120.9)	117.0 (113.7, 120.3)	-1.0 (-5.4, 3.4)
<b>Central DBP (mmHg)</b>	82.8 (80.6, 85.1)	79.3 (77.0, 81.5)	<b>-3.5 (-6.7, -0.4)</b>
<b>Central PP (mmHg)</b>	35.1 (32.8, 37.5)	37.7 (34.8, 40.7)	2.6 (-1.2, 6.3)
<b>5min post-exercise</b>			
<b>Central SBP (mmHg)</b>	115.1 (112.0, 118.1)	119.5 (116.6, 122.5)	4.4 (-0.02, 8.9)
<b>Central DBP (mmHg)</b>	79.5 (77.5, 81.5)	81.0 (79.1, 82.9)	1.5 (-1.5, 4.5)
<b>Central PP (mmHg)</b>	28.9 (27.0, 30.9)	30.5 (28.6, 32.3)	1.5 (-1.3, 4.4)

DBP, diastolic blood pressure; PP, pulse pressure; SBP, systolic blood pressure.

Pre-exercise measures are unadjusted. Post-exercise central SBP and DBP is adjusted for for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, and HR at the time of measurement. Adjusted means are presented.



**Table S7. Between-group differences in arterial stiffness and hemodynamics at 5, 10, 15, and 20 minutes post-exercise**

Variable	Without T2DM (n=61) Mean (95% CI)	With T2DM (n=66) Mean (95% CI)	Mean difference (with-without T2DM) (95% CI)
<b>Arterial Stiffness and Hemodynamic Measures at 5 minutes</b>			
Brachial SBP (mmHg)	131.8 (128.4, 135.2)	136.5 (133.3, 139.7)	4.7 (-0.2, 9.7)
Brachial DBP (mmHg)	77.2 (75.3, 79.1)	79.3 (77.5, 81.1)	2.1 (-0.8, 4.9)
Brachial PP (mmHg)	54.6 (51.7, 57.4)	57.2 (54.5, 59.9)	2.6 (-1.5, 6.8)
Central SBP (mmHg)	118.2 (115.0, 121.4)	121.1 (118.0, 124.2)	2.9 (-1.7, 7.7)
Central DBP (mmHg)	79.6 (77.6, 81.6)	81.2 (79.3, 83.1)	1.6 (-1.4, 4.6)
Central PP (mmHg)	38.6 (36.2, 41.0)	40.0 (37.7, 42.2)	1.36 (-2.1, 5.0)
cfPWV (m/s)	11.9 (11.3, 12.5)	12.4 (11.8, 13.1)	0.5 (-0.4, 1.5)
crPWV (m/s)	8.7 (8.3, 9.0)	8.9 (8.5, 9.2)	0.2 (-0.3, 0.7)
Aortic stiffness $\beta_0$	31.7 (27.9, 35.5)	32.6 (29.0, 36.3)	0.9 (-4.7, 6.6)
HR (beats/min)	89.5 (87.0, 92.1)	88.8 (86.4, 91.2)	-0.7 (-4.4, 3.0)
AIx75 (%)	26.0 (24.3, 27.7)	24.4 (22.8, 26.8)	-1.6 (-4.1, 0.91)
<b>Arterial Stiffness and Hemodynamic Measures at 10 minutes</b>			
Brachial SBP (mmHg)	122.5 (119.7, 125.3)	125.6 (122.9, 128.2)	3.1 (-1.0, 7.2)
Brachial DBP (mmHg)	77.2 (75.5, 79.0)	79.5 (77.8, 81.1)	2.2 (-0.4, 4.9)
Brachial PP (mmHg)	44.9 (42.5, 47.2)	46.4 (44.2, 48.6)	1.5 (-1.9, 5.0)
Central SBP (mmHg)	110.8 (108.1, 113.5)	113.1 (110.6, 115.7)	2.3 (-1.6, 6.3)
Central DBP (mmHg)	78.9 (77.0, 80.8)	80.5 (78.8, 82.2)	1.6 (-1.1, 4.3)
Central PP (mmHg)	31.5 (29.6, 33.4)	32.9 (31.2, 34.7)	1.4 (-1.3, 4.2)
cfPWV (m/s)	10.1 (9.5, 10.6)	11.3 (10.8, 11.8)	<b>1.3 (0.4, 2.1)</b>
crPWV (m/s)	8.4 (8.1, 8.7)	8.7 (8.4, 8.9)	0.3 (-0.2, 0.7)
Aortic stiffness $\beta_0$	22.0 (19.0, 24.9)	27.4 (24.7, 30.2)	<b>5.5 (1.1, 9.8)</b>
HR (beats/min)	87.0 (84.7, 89.4)	86.1 (83.9, 88.4)	-0.9 (-4.4, 2.5)
AIx75 (%)	22.5 (21.0, 23.9)	22.6 (21.2, 24.0)	0.1 (-2.0, 2.3)
<b>Arterial Stiffness and Hemodynamic Measures at 15 minutes</b>			
Brachial SBP (mmHg)	122.6 (119.8, 125.5)	124.8 (122.1, 127.5)	2.2 (-2.0, 6.3)
Brachial DBP (mmHg)	77.8 (76.1, 79.5)	79.4 (77.7, 81.0)	1.5 (-1.0, 4.1)
Brachial PP (mmHg)	44.4 (42.0, 46.9)	45.8 (43.5, 48.2)	1.4 (-2.3, 5.0)
Central SBP (mmHg)	110.1 (107.7, 112.6)	112.1 (109.7, 114.5)	1.9 (-1.7, 5.6)
Central DBP (mmHg)	79.5 (77.7, 81.2)	80.5 (78.8, 82.2)	1.0 (-1.6, 3.6)
Central PP (mmHg)	30.3 (28.4, 32.2)	32.0 (30.1, 33.9)	1.7 (-1.2, 4.5)
cfPWV (m/s)	9.8 (9.3, 10.4)	10.3 (9.8, 10.8)	0.4 (-0.3, 1.2)
crPWV (m/s)	8.7 (8.4, 9.0)	8.7 (8.4, 9.0)	0.1 (-0.4, 0.5)
Aortic stiffness $\beta_0$	20.9 (18.6, 23.2)	22.3 (20.1, 24.5)	1.4 (-2.1, 4.8)
HR (beats/min)	85.6 (83.3, 87.9)	84.2 (82.0, 86.4)	-1.3 (-4.7, 2.0)

<b>AIx75 (%)</b>	20.5 (19.1, 21.8)	21.1 (19.7, 22.5)	0.6 (-1.4, 2.7)
<b>Arterial Stiffness and Hemodynamic Measures at 20 minutes</b>			
<b>Brachial SBP (mmHg)</b>	122.6 (119.8, 125.5)	124.1 (121.4, 126.8)	1.5 (-2.6, 5.6)
<b>Brachial DBP (mmHg)</b>	78.5 (76.7, 80.2)	80.0 (78.3, 81.6)	1.5 (-1.1, 4.0)
<b>Brachial PP (mmHg)</b>	43.8 (41.2, 46.4)	44.5 (42.0, 46.9)	0.7 (-3.1, 4.5)
<b>Central SBP (mmHg)</b>	109.9 (107.3, 112.5)	111.2 (108.8, 113.6)	1.3 (-2.4, 5.1)
<b>Central DBP (mmHg)</b>	80.4 (78.6, 82.2)	80.9 (79.2, 82.5)	0.5 (-2.1, 3.1)
<b>Central PP (mmHg)</b>	29.2 (27.2, 31.2)	30.6 (28.7, 32.4)	1.3 (-1.6, 4.2)
<b>cfPWV (m/s)</b>	10.1 (9.7, 10.6)	10.8 (10.4, 11.3)	0.7 (-0.02, 1.4)
<b>crPWV (m/s)</b>	8.5 (8.1, 8.9)	8.7 (8.3, 9.1)	0.2 (-0.4, 0.8)
<b>Aortic stiffness <math>\beta_0</math></b>	23.0 (20.5, 25.4)	25.0 (22.7, 27.4)	2.1 (-1.5, 5.7)
<b>HR (beats/min)</b>	84.3 (82.1, 86.6)	83.7 (81.6, 85.8)	-0.6 (-3.9, 2.6)
<b>AIx75 (%)</b>	19.4 (17.9, 20.9)	19.1 (17.7, 20.5)	-0.3 (-2.5, 1.9)

AIx75, augmentation index corrected for a heart rate of 75 beats/minute; BP, blood pressure; cfPWV, carotid-femoral pulse wave velocity; crPWV, carotid-radial pulse wave velocity; PP, pulse pressure.

Bolded values indicate a significant absolute difference between groups.

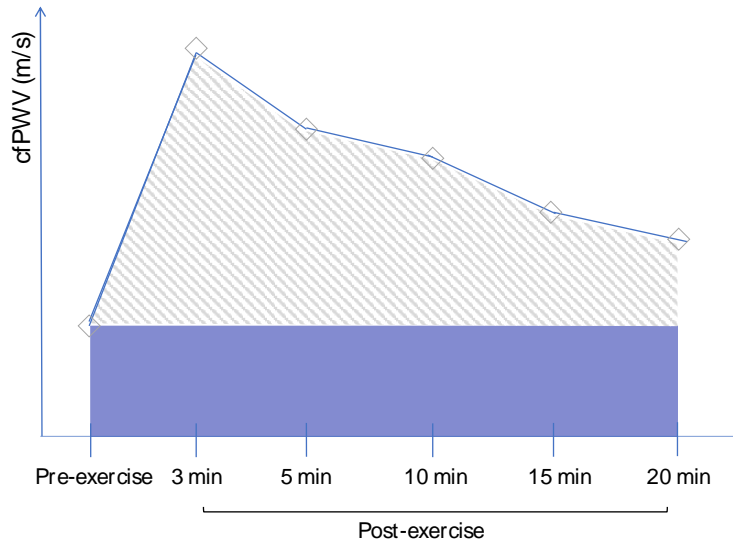
cfPWV, crPWV, and Augmentation Index are adjusted for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, HR, and MAP.

Aortic stiffness  $\beta_0$  is adjusted for for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, and HR.

Blood pressure is adjusted for the pre-exercise value, age, sex, waist:hip ratio, ACEi/ARB use, and HR.

HR and AIx75 at 3 minutes are adjusted for the pre-exercise value, age, sex, waist:hip ratio, and ACEi/ARB use.

**Figure S1. Area under the curve formula**



$$\text{cfPWV AUC} = \text{Total AUC} - \text{Baseline AUC}$$

$$\text{cfPWV AUC} = \text{pre\_cfPWV} \cdot 2 + \frac{(\text{3min\_cfPWV} - \text{pre\_cfPWV}) \cdot 2}{2} + \text{3min\_cfPWV} \cdot 3 + \frac{(\text{5min\_cfPWV} - \text{3min\_cfPWV}) \cdot 3}{2} + \text{5min\_cfPWV} \cdot 5 + \frac{(\text{10min\_cfPWV} - \text{5min\_cfPWV}) \cdot 5}{2} + \text{10min\_cfPWV} \cdot 5 + \frac{(\text{15min\_cfPWV} - \text{10min\_cfPWV}) \cdot 5}{2} + \text{15min\_cfPWV} \cdot 5 + \frac{(\text{20min\_cfPWV} - \text{15min\_cfPWV}) \cdot 5}{2} - \text{pre\_cfPWV} \cdot 20;$$