Influence of menopause and Type 2 diabetes on pulmonary oxygen uptake kinetics and peak exercise performance during cycling

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1School of Medicine, Department of Physiology, Trinity College Dublin, Dublin, Ireland; 2Endocrinology, St. Columcille’s and St. Vincent’s Hospitals, Dublin, Ireland; and 3School of Science and Health and School of Medicine, University of Western Sydney, Sydney, Australia

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Kiely C, Rocha J, O’Connor E, O’Shea D, Green S, Egaña M. Influence of menopause and Type 2 diabetes on pulmonary oxygen uptake kinetics and peak exercise performance during cycling. Am J Physiol Regul Integr Comp Physiol 309: R875–R883, 2015. First published August 12, 2015; doi:10.1152/ajpregu.00258.2015.—We investigated if the magnitude of the Type 2 diabetes (T2D)-induced impairments in peak oxygen uptake (V\(^\text{O}_2\)) and V\(^\text{O}_2\) kinetics was affected by menopausal status. Twenty-two women with T2D (8 premenopausal, 14 postmenopausal), and 22 non-diabetic (ND) women (11 premenopausal, 11 postmenopausal) matched by age (range = 30–59 yr) were recruited. Participants completed four bouts of constant-load cycling at 80% of their ventilatory threshold for the determination of V\(^\text{O}_2\) kinetics. Cardiac output (CO) (inert gas rebreathing) was recorded at rest and at 30 s and 240 s during two additional bouts. Peak V\(^\text{O}_2\) was significantly (P < 0.05) reduced in both groups with T2D compared with ND counterparts (premenopausal, 1.79 ± 0.16 vs. 1.55 ± 0.32 l/min; postmenopausal, 1.60 ± 0.30 vs. 1.45 ± 0.24 l/min). The time constant of phase II of the V\(^\text{O}_2\) response was slowed (P < 0.05) in both groups with T2D compared with healthy counterparts (premenopausal, 29.1 ± 11.2 vs. 43.0 ± 12.2 s; postmenopausal, 33.0 ± 9.1 vs. 41.8 ± 17.7 s). At rest and during submaximal exercise absolute CO responses were lower, but the “gains” in CO larger (both P < 0.05) in both groups with T2D. Our results suggest that the magnitude of T2D-induced impairments in peak V\(^\text{O}_2\) and V\(^\text{O}_2\) kinetics is not affected by menopausal status in participants younger than 60 yr of age.

cycling; V\(^\text{O}_2\) kinetics; women; age; cardiac output

It is well established that endogenous estrogen confers a cardioprotective effect in healthy premenopausal women compared with age-similar men and postmenopausal women (19, 40). After menopause, however, women have a marked increase in the incidence of cardiovascular disease (CVD) (3, 25) with this risk increasing to levels similar to those in men (5, 34). On the other hand, the greater cardioprotective effects and lower likelihood of developing CVD observed in healthy premenopausal women compared with men are tempered by the presence of Type 2 diabetes (T2D), so that the risk of CVD is similar between premenopausal women and age-similar men with T2D (12, 31).

The enhanced endothelium-dependent vascular function referred to as the “female advantage” (34, 44) is one of the cardioprotective effects of estrogen in healthy premenopausal women which is tempered by the presence of T2D (44). Thus it would be reasonable to think that T2D impairs the vasodilatory function and possibly oxygen delivery and exercise tolerance in premenopausal women to a greater extent than in age-similar men or postmenopausal women. This would suggest that the sex-specific influence of T2D on exercise tolerance would be more pronounced between premenopausal women and age-similar men (i.e., greater exercise intolerance in women with and without T2D than in men) than among postmenopausal women and their age-similar counterparts.

In fact, Regensteiner et al. (36) have recently reported that the differences in the magnitude of the T2D-induced impairments in peak oxygen uptake (V\(^\text{O}_2\)) are significantly larger between premenopausal women with T2D and healthy controls than between men with and without T2D of similar ages although no differences in V\(^\text{O}_2\) kinetics at moderate submaximal intensities due to T2D or sex were observed (36). In contrast, O’Connor et al. (33) showed that these sex-specific differences were not apparent in middle-aged participants (where the majority of women were postmenopausal) as the T2D-induced significant reductions in peak V\(^\text{O}_2\) and V\(^\text{O}_2\) kinetics were similar between men and women with T2D compared with nondiabetic counterparts (33). However, it should be noted that study participants with T2D of O’Connor et al. (33) had been diagnosed with T2D for longer than participants in the study of Regensteiner et al. (36) (mean time since diagnosis = ~5 vs. ~3 yr, respectively) and a larger proportion of them were taking diabetes medications (~70% vs. ~35%, respectively), suggesting potential additional cardiovascular abnormalities. In addition, the inclusion of some study participants older than 60 yr of age in the study by O’Connor et al. (33) may have affected the outcomes given that the diabetes-induced impairments in exercise performance appear to be masked by older age (between 60 and 70 yr) at least in men (32, 47). Thus it is relevant to investigate if the T2D-induced impairments in exercise performance are affected by menopausal status while participants with T2D are matched by time since diagnosis and disease severity and older study participants (> 60 yr) are excluded.

The main aim of the present study was to explore the menopause-dependent influence on the T2D-induced impairments on peak exercise performance during a graded exercise and V\(^\text{O}_2\) kinetics during submaximal exercise. Subordinate aims of the study were to test the effect of menopause in healthy women on these outcomes. We hypothesized that the magnitude of the T2D-induced reduction in peak V\(^\text{O}_2\) responses during a graded cycling exercise would be larger among premenopausal women than in postmenopausal women, due to a larger influence of menopause on peak performance in healthy women. We also hypothesized that menopausal status would not influence the T2D-induced effects on V\(^\text{O}_2\) kinetics during submaximal cycling. To explore the mechanistic basis...
of any menopausal status-specific effects in $\dot{V}O_2$ kinetics the rates of changes in cardiac output (CO), heart rate (HR), and stroke volume (SV) during submaximal cycling exercise were also assessed.

**METHODS**

**Subjects**

Forty-four women took part in this study. Twenty-two of the participants were being treated for Type 2 diabetes (8 premenopausal, 14 postmenopausal) and 22 were sex- and body mass index (BMI)-matched healthy controls (11 premenopausal, 11 postmenopausal) (Table 1). The time since diagnosis of diabetes (means ± SD) for premenopausal participants was 4.3 ± 2.2 yr and for postmenopausal participants 5.0 ± 3.3 yr. To avoid the effects of age previously established in men (see above; 32, 47) we limited the age of postmenopausal women to <60 yr, so that all premenopausal women were between the ages of 30 and 46 yr, whereas all postmenopausal women were between the ages of 46 and 59 yr. Women were premenopausal based upon regular menstrual cycles. Subjects with type 2 diabetes were recruited from the Diabetes Day Care centers at St. Columcille’s and St, Vincent’s University Hospitals, Dublin, following a chart review. Subjects with T2D were treated by diet (n = 7) or oral hypoglycemic agents (metformin monotherapy, n = 12; metformin and sulfonylurea, n = 3) and at the start of this study displayed no clinical evidence of ischemic heart disease (normal electrocardiogram, ECG, during treadmill stress test), peripheral arterial disease (0.9 mm Hg or higher in a major artery during exercise at a specified workload), or left ventricular dysfunction (la\[300\]Beck Index < 2.0) or liver dysfunction (urea or creatinine levels > 2.2 mg/dl). Controlled hypertensives were admitted to the study but participants taking β-blockers were excluded. All subjects were sedentary (<1 h/wk of moderate-intensity exercise) for the previous 6 mo, as confirmed by the Low Level Physical Activity Recall (LOPAR) (37) (Table 1). All subjects provided written informed consent prior to participation, and the study was approved by the Faculty of Health Science Research Ethics Committee and conducted in accordance with the Declaration of Helsinki (2008).

**Study Protocol**

In an initial visit to the laboratory participants performed a forearm reactive hyperemia protocol in the supine position by venous occlusion strain-gauge plethysmography (Hokanson EC-6), using calibrated mercury-in-Silastic strain gauges as shown elsewhere (14). This test was performed to explore vascular dysfunction in T2D was present in the upper limb. Peak forearm blood flow (FFB, ml/100 ml·1·min$^{-1}$) and forearm vascular conductance (FCV, ml/100 ml·1·min$^{-1}$·mmHg$^{-1}$) measurements recorded at the start of the postocclusion hyperemic response were compared.

**Exercise testing.** The full exercise testing protocol has been previously performed and is fully described elsewhere (33). Briefly, each subject was tested on two occasions, separated by 72 h, and at the same time of day. For all premenopausal women testing dates were scheduled to occur during the midfollicular phase of their menstrual cycle (days 5–12). Subjects refrained from consuming caffeine and alcohol in the 24 h prior to testing and limited their exercise to normal activities of daily living. All exercise testing was performed on an electrically braked cycle ergometer (Excalibur Sport, Lode, Groningen, Netherlands).

On exercise testing *day 1*, subjects completed a graded cycling exercise test to failure to determine the first ventilatory threshold (VT) and peak $\dot{V}O_2$. After a 3-min period of seated rest, all subjects began the graded test by cycling at an initial power output of 40 W for 3 min using a fixed cadence (60 rpm). Therefore, the power output was increased by 20 W every 3 min until the required cadence could not be maintained (i.e., task failure) (9). The VT was determined using the V-slope method by identifying the power output at which a clear steeper increase of CO$_2$ output (V$\dot{CO}_2$) compared with $\dot{V}O_2$ occurs (1, 7), peak $\dot{V}O_2$ was the highest 30-s mean $\dot{V}O_2$ value recorded before the subject’s volitional termination of the test, and peak workload was the highest workload sustained for at least 1 min. On testing *day 2*, subjects performed six, 6-min bouts of cycling at 80% VT, with each bout separated by 12 min of rest and preceded by a 3-min cycling period at 10 W. $\dot{V}O_2$ and heart rate (HR) were recorded during the first four bouts, and CO was measured during the last two bouts. The resting periods applied between bouts were sufficient for HR (n = 44) and blood lactate (measured in a subgroup of n = 20) to return to baseline levels. $\dot{V}O_2$ kinetics parameter estimates have been shown to be similar when calculated from repeated trials performed on the same day or on separate days (42).

**Measurements**

During exercise subjects wore a facemask to continuously collect expired air using an online metabolic system (Innocor, Innovision A/S, Odense, Denmark) that measured airflow using a pressure transducer and expired air using an online metabolic system (Innocor, Innovision A/S, Odense, Denmark) that measured airflow using a pressure transducer.
difference pneumotach. Carbon dioxide analysis was performed by using a photoacoustic gas analyzer and oxygen was analyzed using an oxygen sensor (Oxigraf) based on the principle of laser diode absorption spectroscopy. The volume was calibrated with a 3-liter syringe, and the oxygen sensor was calibrated (against room air) prior to each test by the researcher. Both the oxygen sensor and photoacoustic gas analyzer require multipoint calibration performed by the manufacturer periodically (6–12 mo). Analysis of expired air allowed determination of pulmonary O2 uptake (VO2), VCO2, minute ventilation (Ve), and the respiratory exchange ratio (RER) breath by breath. CO was measured using the same system by the inert gas (sulfur hexafluoride and nitrogen oxide) rebreathing technique at rest, 30 s, and 240 s (11, 21), HR was recorded every 5 s (S610i, Polar Electro Oy, Finland), and stroke volume (SV = CO/HR) and arteriovenous O2 difference (a-vO2 = VO2/CO) were estimated from these measurements. Final values for all variables were averaged from responses during the final two submaximal exercise bouts.

Data Analysis

To determine the kinetic parameters of VO2 at 80% VT, VO2 responses during the first four bouts were linearly interpolated to 1-s intervals, time aligned and averaged and finally smoothed using a 5-s moving average filter (13). While when exercising below the VT the responses during the first four bouts were linearly interpolated to 1-s intervals (17), and thus only its mean duration is presented.

Cardiodynamic phase cannot be always described by an exponential function (Eq. 1) or triexponential function (Eq. 2) as follows:

\[
V_{O2}(t) = baseline_VO2 + A_s \left(1 - e^{-(t-TD_s)\tau_c}\right)U_c + A_p \left(1 - e^{-(t-TD_p)\tau_p}\right)U_p
\]

\[
V_{O2}(t) = baseline_VO2 + A_s \left(1 - e^{-(t-TD_s)\tau_c}\right)U_c + A_p \left(1 - e^{-(t-TD_p)\tau_p}\right)U_p + A_d \left(1 - e^{-(t-TD_d)\tau_d}\right)U_d
\]

Either one or the other function was selected for fitting on the basis of comparing the goodness-of-fit of these functions (26) and only its mean duration is presented.

Statistical Analysis

Physical characteristics and activity levels, peak physiological responses, and kinetic parameters were compared using a two-way (diabetic status vs. menopausal status) ANOVA (PRISM, Version 5.03, GraphPad Software). Cardiovascular responses were assessed using a three-way (diabetic status vs. menopausal status vs. time of measurement) repeated-measures ANOVA (Datadesk Version 6.2.1 OS X, Data Description). Differences between groups were detected using Bonferroni’s post hoc test. Significance was set at \( P < 0.05 \). All values are expressed as means ± SD.

RESULTS

Physical Characteristics and Activity Levels

There were no significant differences in BMI or activity levels between groups. Premenopausal women were significantly younger than postmenopausal participants. HbA1c and fasting glucose levels were significantly higher for individuals with T2D than controls but similar between the two groups with T2D. Peak forearm blood flow and forearm vascular conductance responses were not significantly different among groups (main effect = diabetes status, \( P = 0.49 \) for FBF and \( P = 0.12 \) for FVC).

Graded Test

Peak VO2 (l/min and ml·kg\(^{-1}\)·min\(^{-1}\)) were significantly lower in both groups with T2D compared with their respective nondiabetic counterparts (Table 2). The magnitude of the reduction in relative peak VO2 (ml·kg\(^{-1}\)·min\(^{-1}\)) was numerically higher among premenopausal women (~25%) than among postmenopausal women (~8%) (diabetes status \( \times \) menopausal status interaction, \( P = 0.11 \)) whereas this magnitude was similar (~13% among premenopausal groups and ~9% among postmenopausal groups) when absolute values (l/min) were analyzed (diabetes status \( \times \) menopausal status interaction, \( P = 0.57 \)). Peak HR responses were significantly (\( P < 0.05 \)) lower in premenopausal women with T2D than controls. This was influenced at least in part by the fact that nondiabetic premenopausal controls were numerically younger and they reached higher mean age-predicted peak HR levels (~100%, range = 98–102%) than premenopausal women with T2D (~90%, range = 83–102%, where 5 of 8 participants reached an age-predicted peak HR value > 90%). Importantly, RER responses were similar among the four groups suggesting comparable peak exercise effort. All but one woman in each group reached peak RER values ≥ 1.1.

\( V_{O2} \) Kinetics

\( V_{O2} \) responses during moderate exercise for representative individuals are presented in Fig. 1. The time constant for \( V_{O2} \) phase II (\( \tau_p \)) was significantly slowed in both pre and postmenopausal women with T2D compared with healthy counter-
parts (Table 3). The rest of the parameters were not affected by T2D or menopausal status.

Cardiovascular Responses

Cardiovascular responses at rest and during cycling exercise are shown in Fig. 2 and their gains relative to workload at 30 s and 240 s are shown in Table 4. Absolute CO responses were significantly lower in both groups of T2D compared with controls, while absolute HR responses were significantly lower only in premenopausal women with T2D than controls but not among postmenopausal women (Fig. 2). However, when the change in absolute workload was taken into account the gains

Table 2. Peak physiological responses during incremental cycling exercise

<table>
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<tr>
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<th>Premenopausal Women</th>
<th>Postmenopausal Women</th>
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<tbody>
<tr>
<td></td>
<td>Controls (n = 11)</td>
<td>Type 2 diabetes (n = 8)</td>
</tr>
<tr>
<td>VO2peak, l/min</td>
<td>1.79 ± 0.16</td>
<td>1.55 ± 0.32†</td>
</tr>
<tr>
<td>VO2peak, ml·min⁻¹·kg⁻¹</td>
<td>23.8 ± 2.9</td>
<td>17.9 ± 5.9†</td>
</tr>
<tr>
<td>Peak HR, beats/min</td>
<td>179 ± 7.1</td>
<td>155 ± 15†</td>
</tr>
<tr>
<td>Peak RER</td>
<td>1.13 ± 0.05</td>
<td>1.13 ± 0.06</td>
</tr>
<tr>
<td>Peak workload, W</td>
<td>125 ± 14</td>
<td>105 ± 28†</td>
</tr>
<tr>
<td>Workload at VT, W</td>
<td>89 ± 16</td>
<td>74 ± 29†</td>
</tr>
<tr>
<td>VO2 at VT, ml·min⁻¹·kg⁻¹</td>
<td>15.7 ± 3.6</td>
<td>14.0 ± 5.7</td>
</tr>
<tr>
<td>Workload at 80% VT, W</td>
<td>71 ± 13</td>
<td>60 ± 23†</td>
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</table>

Data are means ± SD. VO2peak, peak oxygen consumption; HR, heart rate; RER, respiratory exchange ratio; VT, ventilatory threshold. *P < 0.05 vs. premenopausal women within same diabetes-status group (i.e., within controls or within Type 2 diabetes). †P < 0.05 vs. women with Type 2 diabetes within same menopausal status group.

Fig. 1. Oxygen uptake responses during cycling exercise at intensities equivalent to 80% ventilatory threshold (VT) in representative premenopausal (A and C) and postmenopausal (B and D) women with Type 2 diabetes (T2D) and nondiabetic counterparts. The continuous lines of best fit illustrate the primary phase of the oxygen uptake (VO2) response. A and B show oxygen uptake values expressed in absolute units with the residuals (black crosses for the women with T2D and gray crosses for the nondiabetic women shown below profiles) demonstrating that the data were well fit. C and D show oxygen uptake values relative to the end-exercise amplitude to facilitate comparisons between participants with T2D and nondiabetic controls. Note the relatively slower response of the primary phase of the VO2 response in both pre- and postmenopausal women with T2D compared with the nondiabetic women.
in CO, HR, and SV at 240 s were significantly larger in both groups with T2D (Table 4). The absolute changes in a-V̇O₂ or their gains were not significantly affected by T2D. The relative change in CO from baseline (%ΔCO) was not significantly affected by diabetes (data not shown).

DISCUSSION

To our knowledge, the present study is the first to compare effects of T2D on peak exercise performance and V̇O₂ kinetics in pre- and postmenopausal women. Importantly, participants with T2D had similar diabetes severity and all participants were younger than 60 yr. The main findings of the present study were that peak V̇O₂ and peak power output were significantly reduced and V̇O₂ kinetics significantly slowed in pre- and postmenopausal women with T2D compared with their respective healthy controls and that the magnitude of these impairments was not affected by menopausal status. In addition, while the absolute responses of CO during submaximal exercise were lower in women with T2D, when taking into account the changes in absolute workload, the gains of CO were larger in both groups with T2D compared with controls suggesting that the observed impairments in V̇O₂ kinetics during exercise are not likely due to abnormal CO responses.

Maximum or “peak” V̇O₂ levels have generally been reported as being reduced in people with T2D compared with age- and sex-matched healthy controls by an average of 12–15% (21, 32, 33, 36, 38), and this is of particular importance because in the present study women had higher BMIs, which have been suggested to have differential effects on the magnitude of the T2D-induced impairments between pre- and postmenopausal women (8%) (diabetes status × menopausal status interaction, P = 0.11). However, of the bias introduced by consistently higher body weights (and BMI) of participants with T2D compared with control subjects in the literature, peak V̇O₂ values should be expressed in liters per minute rather than normalized to body weight (10). When the absolute peak V̇O₂ values were analyzed, contrary to our main hypothesis, there were no differences in the magnitude of the T2D-induced impairments between pre- and postmenopausal (~9%) women (diabetes status × menopausal status interaction, P = 0.57), suggesting that menopausal status does not affect the extent to which T2D impairs peak exercise responses in women. Despite this it is still worth noting that there was a tendency for a menopausal effect on absolute peak V̇O₂ (main effect = menopausal status, P = 0.11) which was ~11% lower in healthy post- than premenopausal women whereas it was ~6% lower among T2D patients. However, this lack of significant reduction due to menopause in our healthy participants is also in contrast with our secondary hypothesis, and it is somewhat surprising given that natural menopause has been shown to significantly reduce exercise tolerance and peak V̇O₂ by 17–25% in healthy sedentary women relative to premenopausal women of the same age (20, 23, 24).

Table 3. Dynamic response characteristics of V̇O₂ during cycling at 80% VT

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<td>Controls (n = 11)</td>
<td>Type 2 diabetes (n = 8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Controls (n = 11)</td>
</tr>
<tr>
<td>V̇O₂ baseline, l/min</td>
<td>0.55 ± 0.11</td>
<td>0.55 ± 0.19</td>
</tr>
<tr>
<td>V̇O₂ TDp, s</td>
<td>27.5 ± 8.4</td>
<td>24.8 ± 6.2</td>
</tr>
<tr>
<td>V̇O₂ Ap, l/min</td>
<td>0.50 ± 0.21</td>
<td>0.44 ± 0.28</td>
</tr>
<tr>
<td>V̇O₂ TDp, s</td>
<td>32.6 ± 11.2</td>
<td>26.4 ± 5.9</td>
</tr>
<tr>
<td>V̇O₂ Ap, s</td>
<td>29.1 ± 11.2</td>
<td>43.0 ± 12.2†</td>
</tr>
<tr>
<td>V̇O₂ End A, l/min</td>
<td>1.29 ± 0.25</td>
<td>1.17 ± 0.31</td>
</tr>
<tr>
<td>V̇O₂ gain, ml·min⁻¹·W⁻¹</td>
<td>11.2 ± 1.9</td>
<td>11.5 ± 1.4</td>
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</table>

Data are means ± SD. V̇O₂, oxygen consumption; A, amplitude; TD, time delay; r, time constant; subscript c, cardiodynamic phase; subscript p, primary phase. †P < 0.05 vs. women with Type 2 diabetes within same menopausal status group.
without accompanying analysis of hormone levels and the participants’ onset age of menopause was not known it is also possible that discrepancies between studies are due to differences in the time course of menopausal onset and duration because emerging evidence indicates that these factors affect cardiovascular parameters (30). Furthermore, in contrast to the above-mentioned studies (23, 24) our study groups were not matched by age (i.e., postmenopausal women were ~12 yr older than premenopausal women), so, it appears that neither age nor female hormonal differences
were sufficiently powerful to affect the magnitude of the diabetes-induced impairments in exercise performance. In addition to examining the maximum responses of pulmonary VO₂, the present study also measured the VO₂ dynamic responses during submaximal exercise, i.e., the rate of adjustment of oxygen uptake to steady-state exercise. The time constant for VO₂ phase II (τₚ) was significantly slowed in both pre- and postmenopausal women with T2D compared with their healthy counterparts, a finding that is consistent with most previous studies examining their healthy counterparts, a finding that is consistent with most pre- and postmenopausal women with T2D compared with healthy controls; however, CO is a function of absolute workload which revealed significantly larger gains in both groups with T2D compared with healthy controls. These findings are in agreement with previous studies using noninvasive (4, 22, 32, 33) as well as invasive methods to measure CO (39) and suggest that cardiac responses do not contribute to the observed diabetes-induced impairments in the dynamic response of VO₂, at least in patients with uncomplicated T2D. The latter study, even if it explored a graded exercise test, is particularly important since despite not observing differences in CO, HR, and SV taking into account the change in absolute workload which revealed significantly larger gains in both groups with T2D compared with healthy controls. These findings are in agreement with previous studies using noninvasive (4, 22, 32, 33) as well as invasive methods to measure CO (39) and suggest that cardiac responses do not contribute to the observed diabetes-induced impairments in the dynamic response of VO₂, at least in patients with uncomplicated T2D. The latter study, even if it explored a graded exercise test, is particularly important since despite not observing differences in CO, HR, and SV, Regensteiner and colleagues (39) reported that pulmonary capillary wedge pressure was abnormally increased during graded exercise in recently diagnosed type 2 diabetes within same menopausal status group.

### Table 4. Gains of cardiac output and related variables during cycling at 80% VT

<table>
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<tr>
<td></td>
<td></td>
<td>Controls (n = 11)</td>
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<tr>
<td>Gain at 30 s</td>
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<tr>
<td>CO, ml·min⁻¹·W⁻¹</td>
<td>43 ± 22</td>
<td>56 ± 19</td>
</tr>
<tr>
<td>HR, beats·min⁻¹·W⁻¹</td>
<td>0.33 ± 0.16</td>
<td>0.45 ± 0.28</td>
</tr>
<tr>
<td>SV, ml/W</td>
<td>0.20 ± 0.22</td>
<td>0.28 ± 0.20</td>
</tr>
<tr>
<td>a-VO₂ diff, ml O₂·100 ml·blood⁻¹·W⁻¹</td>
<td>0.055 ± 0.021</td>
<td>0.057 ± 0.055</td>
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<tr>
<td>Gain at 240 s</td>
<td></td>
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<tr>
<td>CO, ml·min⁻¹·W⁻¹</td>
<td>65 ± 16</td>
<td>87 ± 27†</td>
</tr>
<tr>
<td>HR, beats·min⁻¹·W⁻¹</td>
<td>0.57 ± 0.23</td>
<td>0.69 ± 0.18†</td>
</tr>
<tr>
<td>SV, ml/W</td>
<td>0.24 ± 0.19</td>
<td>0.41 ± 0.16†</td>
</tr>
<tr>
<td>a-VO₂ diff, ml O₂·100 ml·blood⁻¹·W⁻¹</td>
<td>0.094 ± 0.032</td>
<td>0.105 ± 0.053</td>
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Data are means ± SD. CO, cardiac output; HR, heart rate; SV, stroke volume; a-VO₂ diff, arterial-venous oxygen difference. †P < 0.05 vs. women with Type 2 diabetes within same menopausal status group.
affected by menopausal status in participants of <60 yr. Future studies should examine larger sample sizes, assess cardiac responses more frequently, and take into consideration the onset age and duration of menopause.

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AUTHOR CONTRIBUTIONS

REFERENCES


