Effect of exercise timing on elevated postprandial glucose levels

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Effect of exercise timing on elevated postprandial glucose levels. J Appl Physiol 123: 278–284, 2017. First published April 13, 2017; doi:10.1152/japplphysiol.00608.2016.—There is no consensus regarding optimal exercise timing for reducing postprandial glucose (PPG). The purpose of the present study was to determine the most effective exercise timing. Eleven participants completed four different exercise patterns (no exercise; 2) preprandial exercise (jogging); 3) postprandial exercise; and 4) brief periodic exercise intervention (three sets of 1-min jogging + 30 s of rest, every 30 min, 20 times total) in a random order separated by a minimum of 5 days. Preprandial and postprandial exercise consisted of 20 sets of intermittent exercise (1 min of jogging + 30 s rest per set) repeated 3 times per day. Total daily exercise volume was identical for all three exercise patterns. Exercise intensities were 62.4 ± 12.9% VO2 peak. Blood glucose concentrations were measured continuously throughout each trial for 24 h. After breakfast, peak blood glucose concentrations were lower with brief periodic exercise (99 ± 6 mg/dl) than those with preprandial and postprandial exercise (109 ± 10 and 115 ± 14 mg/dl, respectively, P < 0.05, effect size = 0.517). After lunch, peak glucose concentrations were lower with brief periodic exercise than those with postprandial exercise (97 ± 5 and 108 ± 8 mg/dl, P < 0.05, effect size = 0.484). After dinner, peak glucose concentrations did not significantly differ among exercise patterns. Areas under the curve over 24 h and 2 h postprandially did not differ among exercise patterns. These findings suggest that brief periodic exercise may be more effective than preprandial and postprandial exercise at attenuating PPG in young active individuals.

NEW & NOTEWORTHY This was the first study to investigate the effect of different exercise timing (brief periodic vs. preprandial vs. postprandial exercise) on postprandial glucose (PPG) attenuation in active healthy men. We demonstrated that brief periodic exercise attenuated peak PPG levels more than preprandial and postprandial exercise, particularly in the morning. Additionally, PPG rebounded soon after discontinuing postprandial exercise. Thus, brief periodic exercise may be better than preprandial and postprandial exercise at attenuating PPG levels.

Higher postprandial glucose (PPG) concentration is a risk factor for cardiovascular disease (CVD) (27), mortality (34), and cognitive performance impairment (30) in patients with Type 2 diabetes. In addition, in nondiabetic populations, elevated PPG is a risk factor for coronary heart disease, ischemic stroke (24), and CVD (21). Endothelial dysfunction, which is predictive of a future cardiovascular event, is caused by hyperglycemia through oxidative stress (4). Furthermore, oscillating glucose levels increase oxidative stress more than constant high glucose levels and have a deleterious effect on endothelial dysfunction (3). For these reasons, controlling PPG levels may prevent cardiovascular disease events.

A single bout of aerobic exercise has been demonstrated to reduce PPG levels (26, 31, 32). In particular, the issue of exercise timing around meals to attenuate PPG concentrations has been widely discussed (5, 15). Many previous studies have reported that postprandial aerobic exercise effectively lowers PPG concentrations (15, 17, 19, 20, 26, 29, 35, 38). Larsen et al. (19) reported that postprandial cycling exercise (52 ± 2% VO2max) for 45 min reduced the incremental area under the curve (AUC) of glucose for 240 min after breakfast.

A review of exercise timing also reported that postprandial exercise is more effective at lowering PPG levels than preprandial exercise in healthy individuals and patients with diabetes (15). However, recent studies have reported that preprandial aerobic exercise can effectively lower PPG concentrations (10, 32). To date, there is little research directly comparing the effects of preprandial vs. postprandial aerobic exercise on PPG concentrations at one meal (dinner) (7), and there are no studies comparing all three meals throughout the same day. Moreover, it has been recently demonstrated that sitting interspersed with brief bouts of light-to-moderate intensity exercise attenuates PPG levels, indicating that frequent physical activity potentially increases glucose uptake (1, 2, 9, 28).

Thus, although postprandial exercise is considered to be ideal timing for attenuating PPG concentrations, the question has been raised as to whether preprandial and frequent aerobic exercise attenuate PPG to the same extent as postprandial exercise. To the best of our knowledge, there has been no research comparing the effects of preprandial, postprandial, and frequent aerobic exercise on PPG levels for every meal of the day (breakfast, lunch, and dinner). We hypothesized that all exercise approaches would improve PPG equally on the basis of previous evidence. The purpose of the present study was to determine the most effective exercise timing (preprandial vs. postprandial vs. brief periodic moderate exercise intensity) on PPG concentrations throughout the day in healthy men using a continuous glucose monitoring system.

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Table 1. Participant characteristics and energy balance of the experiments

<table>
<thead>
<tr>
<th>Participant characteristic</th>
<th>Means ± SD</th>
</tr>
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<tbody>
<tr>
<td>Age, yr</td>
<td>23 ± 2</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172 ± 7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>63.6 ± 4.8</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>21.5 ± 1.0</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>16.0 ± 4.2</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.3 ± 0.3</td>
</tr>
<tr>
<td>( \dot{V}O_2 \text{peak}, \text{ml·kg}^{-1} \cdot \text{min}^{-1} )</td>
<td>51.0 ± 5.9</td>
</tr>
<tr>
<td>%( \dot{V}O_2 \text{peak} ), %</td>
<td>66 ± 13</td>
</tr>
<tr>
<td>Running speed at LT, m/min</td>
<td>161 ± 34</td>
</tr>
<tr>
<td>Energy intake in each trial, kcal/day</td>
<td>2,299 ± 153</td>
</tr>
<tr>
<td>Estimated energy expenditure in control trial (no exercise) day, kcal/day</td>
<td>1,741 ± 107</td>
</tr>
<tr>
<td>Estimated energy expenditure during exercise, kcal/60 min</td>
<td>2,389 ± 218</td>
</tr>
<tr>
<td>Estimated energy balance in control trial kcal/day</td>
<td>571 ± 163</td>
</tr>
<tr>
<td>Estimated energy balance for each exercise trial day, kcal/day</td>
<td>530 ± 33</td>
</tr>
<tr>
<td>Estimated energy balance for each exercise trial day, kcal/day</td>
<td>-117 ± 159</td>
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</table>

METHODS

Study Participants

Eleven comparatively active (not necessarily trained in any particular sport) healthy men participated in the present study. Participants were recruited through a poster on the laboratory information board at the Faculty of Sports and Health Science at Fukuoka University. Participant characteristics are displayed in Table 1. All subjects gave informed consent after reviewing the purpose, methods, and significance of the study. The study was approved by the Ethics Committee of Fukuoka University (no. 140601).

Baseline Testing

Aerobic capacity exercise test. The participants fasted for 12 h before baseline testing. Participants completed the multistage aerobic capacity test using a treadmill. This test had two purposes: 1) to determine peak oxygen consumption (\( \dot{V}O_2 \text{peak} \)); and 2) to determine the lactate threshold (LT) of running speed (this value was used in trials). After a 1-min rest, the multistage exercise tolerance test was initiated at each subject’s running speed, according to individual fitness levels. The speed was increased in increments of 10 m/min with each load (4 min/load), with 1-min rest sessions between each load. Blood lactate concentrations (LA; Lactate Pro 2LT-1730 ARKRAY, Kyoto, Japan) were measured immediately after the earlobe after each load (1-min rest) until levels of 4 mmol/l were reached. Heart rate (HR; Polar RS800CX) was measured during the final 30 s of each stage. Participants were asked for their rating of perceived exertion (RPE) during the rest period of each stage. Once LA levels exceeded 4 mmol/l, the treadmill incline was increased 2% per minute until the participant was completely exhausted. During the exercise test, the concentration of expired gas was measured continuously every 12 s by a mixing chamber method using a mass spectrometer for respiratory analysis (ARCO-2000; Arco System, Chiba, Japan).

Determination of LT. The LT is the initial breakpoint in the elevation of blood lactate concentrations. The LT was determined by measuring blood lactate concentrations during each stage of the aerobic capacity test until 4 mmol/l was reached. The LT was based on visual inspection by five trained staff members, and the mean LT was calculated from three of the five results (40). The multistage exercise test was completed more than 4 days before the first trial. In the present study, the LT intensity was used for the following reasons: 1) if exercise intensity is based on % \( \dot{V}O_2 \text{peak} \), some subjects will perform below the LT, but others will perform above the LT, 2) exercise above the LT intensity acutely increases catecholamine release (36), which influences glucose metabolism during and after exercise (39), 3) the LT intensity improves insulin sensitivity (25), and 4) the LT intensity would be expected to activate glucose uptake, because LT may activate AMPK by decreasing phosphocreatine and ATP and increasing AMP. This increase in AMPK levels increases glucose transport by stimulating GLUT4 translocation to the cell surface in the muscle (11, 18) and, thereby, lowering blood glucose concentrations (33). Thus, LT intensity exercise should be effective at attenuating PPG concentrations and is a practical exercise method.

Body composition. Body composition was estimated using the underwater weighing method, and body density was calculated after correction for residual air by the O₂ rebreathing method. Body fat...
Basal metabolic rate (BMR) \( \times \) 1.5 [physical activity level (PAL)] was used to standardize meal composition and volume. BMR was estimated in the participants by the formula for Japanese individuals (12). We used BMR \( \times \) 1.5 to calculate energy intake to roughly adjust for energy balance in exercise interventions. We calculated total energy expenditure as PAL \( \times \) 1.2 [total energy expenditure with sedentary activity in a day (37)] + estimated energy expenditure during exercise. The energy intake and estimated energy expenditure profiles are displayed in Tables 1 and 2. The timing of meals was identical among all trials, and participants were asked to consume the meal within 15 min and in the same order. The only beverage allowed on the experiment day was water.

**Glucose Monitoring**

Glucose was measured using a continuous glucose monitoring (CGM; iPro2, Medtronic, Northridge, CA) device. The CGM was placed on each participant’s abdomen 1 day before the experiment. Participants were asked to record their blood glucose concentrations more than four times by finger-stick on the day before the experiment for calibration purposes. The coefficient of variance for 14.5-h blood glucose AUCs was 2.8% by CGM when compared with paired self-monitoring of blood glucose at 18 time points.

**Evaluation of PPG Elevation**

Glucose AUCs were calculated from the start of every meal to 120 min after using the trapezoidal method. The postmeal 120 min AUC was calculated using absolute values. Peak PPG values were obtained from the highest value recorded within 120 min of meal onset. We think that exercise timing is particularly important for preventing elevated postprandial glucose values. Thus, we focused on the 120-min postprandial period for each meal.

**Statistical Analysis**

Data are reported as means ± SD. Glucose AUCs and average glucose values over 24 h were compared. Postprandial glucose levels over 6 h were calculated as the sum of the three postprandial 2-h AUCs for each trial. Additionally, peak PPG values and absolute 120-min AUCs after every meal were compared. All analyses were conducted using one-way repeated-measures ANOVA with Bonferroni post hoc test (SPSS version 23, IBM Corporation). A P value <0.05 was considered to be statistically significant.

**RESULTS**

All participants successfully completed the experiment. The mean HbA1c of participants was 5.3 ± 0.3, and all participants were healthy. The mean HRs and RPEs after the first preprandial exercise were 134 ± 17 beats/min and 11.9 ± 1.2, respectively. The postprandial exercise HRs and RPEs were 136 ± 15 beats/min and 12.7 ± 0.8, respectively. The peak PPG values were 117 ± 20 and 10.5 ± 1.3 mmHg for the preprandial and postprandial exercise periods, respectively.

### Table 3. Heart rate and RPE after first exercise

<table>
<thead>
<tr>
<th></th>
<th>Preprandial Exercise</th>
<th>Postprandial Exercise</th>
<th>Brief Periodic Exercise</th>
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<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>134 ± 17</td>
<td>136 ± 15</td>
<td>117 ± 20</td>
</tr>
<tr>
<td>RPE</td>
<td>11.9 ± 1.2</td>
<td>12.7 ± 0.8</td>
<td>10.5 ± 1.3</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SD. RPE, rate of perceived exertion.
dial, postprandial, and brief periodic exercises are displayed in Table 3. Mean HRs and RPEs after the first preprandial and postprandial exercises were not significantly different, but HRs and RPEs after brief periodic exercise were significantly lower ($P < 0.05$). The mean CGM results for all four exercise patterns throughout the day and after the morning meal are displayed in Figs. 2 and 3, respectively. The mean glucose values and AUCs recorded over 24 h were not significantly different among the four exercise patterns (data not shown, continuous 24-h glucose values are displayed in Fig. 2). The PPG AUCs for 120 min after the onset of each meal (i.e., breakfast, lunch, and dinner) were not significantly different among the four trials (Fig. 4). Similarly, 6-h AUCs, which were calculated as the sum of the three postprandial AUCs, were not significantly different.

Peak PPG values were significantly lower at breakfast for brief periodic exercise compared with the other exercise patterns ($P < 0.05$, effect size = 0.517) and significantly lower at lunch for brief periodic exercise compared with postprandial exercise ($P < 0.05$, effect size = 0.484, Fig. 5). There were no significant differences among the peak PPG values for preprandial exercise, postprandial exercise, and controls at any meal.

**DISCUSSION**

Elevated PPG is a risk factor, especially for CVD, in both patients with diabetes and nondiabetic individuals. One reason for this is that high blood glucose levels, and particularly oscillating glucose levels, increase oxidative stress, leading to endothelial dysfunction. The present study examined whether preprandial exercise and brief periodic exercise are as effective as postprandial exercise at improving blood glucose control throughout the day using CGM. To our knowledge, there have been no studies comparing the effect of preprandial and postprandial and brief periodic exercise on blood glucose control. This study demonstrated that brief periodic exercise may be more effective at blunting PPG compared with preprandial and postprandial exercise, particularly at breakfast.

Recent studies have examined the effect of sitting interrupted by walking on PPG levels for 5 h in the morning after an overnight fast in obese and healthy individuals (1, 9). They reported that sitting interrupted with 2 min of walking every 20 min for 5 h (total exercise bouts and duration were 14 times and 28 min, respectively) reduced the 5-h PPG AUC compared with no exercise. Peddie et al. (28) reported that a regular-

![Fig. 2. Mean variation of glucose associated with different exercise timings until immediately before sleep ($n = 11$). CON, black line; preprandial exercise, gray line; postprandial exercise, gray dashed line; and brief periodic exercise, black dotted line.](Image)

![Fig. 3. Mean variation of glucose associated with different exercise timings before and after breakfast. Preprandial exercise started 45 min before breakfast. Postprandial exercise started 30 min after breakfast. The small black box on the graph depicts the timing of brief periodic exercise.](Image)
activity break intervention, which included walking for 1 min 40 s every 30 min, reduced 9-h blood glucose AUCs. The present study compared the effect of brief periodic exercise with postprandial exercise on PPG levels. Although postprandial continuous exercise is generally thought to be effective at lowering PPG concentrations, the present result demonstrated that brief bouts of exercise of only 3 min every 30 min are better than postprandial exercise at attenuating PPG levels especially at breakfast and lunch. As fluctuating blood glucose levels increase oxidative stress (3, 23), attenuating peak PPG may protect endothelial function. However, as our participants were young, healthy, and active, it is likely that statistical significance might not always equal clinical significance.

An effect of brief periodic exercise in the evening was not observed. A possible reason is that the brief periodic exercise volume was less around dinner compared with that at breakfast and lunch. Thus, there may have been an insufficient exercise volume to lower peak PPG. The present study did not elucidate the mechanism by which brief periodic exercise was effective at lowering PPG levels. One potential reason could be that frequent brief exercise (frequent muscle contraction) may maintain stimulation of blood glucose uptake into skeletal muscle, which would increase GLUT4 translocation to the cell surface, resulting in continuous increased glucose uptake from the blood (16, 31).

Interestingly, in the present study, postprandial exercise reduced PPG levels during exercise, but PPG levels rebounded soon after discontinuing exercise, attaining peak PPG and PPG AUC levels comparable to those of the control pattern. Our participants were comparatively active men with good glucose metabolism, as indicated by HbA1c values of 5.3 ± 0.3. Thus, as blood glucose levels did not elevate abnormally without exercise, peak PPG levels and AUCs would not be expected to differ between the control and postprandial exercise trials. However, it is unclear whether blood glucose values would rebound similarly after short continuous aerobic exercise in obese individuals or those with diabetes. In a few studies, blood glucose levels appeared to rebound after discontinuing postprandial continuous aerobic exercise (17, 19, 38). The glucose kinetics associated with postprandial exercise may be due to a relationship between glucose uptake in muscles and hepatic glucose output.

For this phenomenon, exercise duration may be important in sustaining the effect of PPG lowering associated with postprandial continuous exercise. Nygaard et al. (26) compared the effects of 15 min and 40 min of walking immediately after breakfast on PPG levels. Both exercise durations reduced the 2-h AUCs compared with those with no exercise, although 40 min of exercise was superior to 15 min. Walking for only 15 min did not blunt peak PPG levels. A review analyzing exercise timing reported that 60 min of cycling at 60% V\textsuperscript{\textcircled{max}} is most effective at lowering blood glucose when performed postprandially. Although light-to-moderate exercise for 45–60 min would lower PPG levels, it is difficult to exercise for this duration around every meal, particularly for those who work throughout the day. The present results indicated that for individuals who do not have time to exercise after every meal, brief physical activity durations surrounding the meal may be effective at blunting PPG elevation. As previous studies have
Exercise Timing for Decreasing Postprandial Glucose • Hatamoto Y et al.

suggested (8, 10), more feasible exercise timing and duration are needed for effective integration into daily life.

The present results revealed no significant differences in peak PPG levels and PPG AUCs between preprandial and postprandial exercise. Preprandial exercise stimulates glucose uptake and, therefore, would be expected to lower PPG concentrations (13). Colberg et al. (7) compared the effects of preprandial and postprandial self-paced walking (40.3 ± 2.7% heart rate reserve) for 20 min on glycemic responses. They reported that postprandial walking blunted peak PPG levels compared with those following rest and preprandial exercise. However, recent studies have reported that preprandial exercise lowered PPG levels using exercise intensities above the LT (10, 32). The exercise intensity performed by Colberg’s study could not attain the LT. Although preprandial exercise may stimulate glucose uptake, the intensity of preprandial exercise may result in prolonged lower PPG levels because of activation of GLUT4, which increases glucose transport by stimulating GLUT4 translocation in the muscle (6, 11). There are few studies directly comparing the glycemic responses between preprandial and postprandial exercise, and further research is needed in the future.

There are some limitations to the present study. First, there were no significant differences, particularly in PPG AUC values, between exercise trials and control conditions. The participants in the present study were comparatively healthy, active, young men without insulin resistance, as indicated by HbA1c values, which would explain why PPG levels were similar among all four trials. Brief periodic exercise lowered peak PPG levels compared with prepostprandial exercise at breakfast. However, we do not know whether this phenomenon leads to positive effects on health outcomes, particularly cardiovascular disease. On the basis of evidence indicating that within-day glucose fluctuations are an independent risk factor for cardiovascular disease (23) and increased oxidative stress, we believe that lowering peak glucose levels should positively impact endothelial dysfunction. In addition, it is unclear whether brief periodic exercise is the ideal exercise pattern for the general population, obese individuals, or those with diabetes, because the participants were comparatively young active men. Future experiments should include individuals with insulin resistance or diabetes. Furthermore, the present study did not measure hormones related to glucose metabolism, which may further clarify the mechanisms underlying the effects of exercise timing on PPG control.

In conclusion, we examined the effect of exercise timing on PPG control and found that brief periodic exercise attenuated peak PPG levels compared with longer bouts of preprandial or postprandial exercise in young comparatively active healthy men. In addition, our results revealed that brief bouts (within 20 min) of postprandial continuous exercise were not likely to mitigate acute blood glucose elevation. This information may be helpful to people who do not have much time to exercise around a meal, such as young to middle-aged workers.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

Y. Hatamoto and H. Tanaka conceived and designed the study; Y. Hatamoto, R.G., and S.N. performed experiments; Y. Hatamoto, R.G., and S.N. analyzed data; Y. Hatamoto, Y.Y., E.Y., and Y. Higaki interpreted results of experiments; Y. Hatamoto, Y.Y., and E.Y. drafted manuscript; Y. Hatamoto, Y.Y., E.Y., and H.T. edited and revised manuscript; Y. Hatamoto, Y.Y., E.Y., Y. Higaki, and H.T. approved final version of manuscript; R.G. prepared figures.

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