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A single bout of exercise and postprandial hyperglycemia caused by high-fat diet

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Abstract

Postprandial hyperglycemia is associated with an increase in cardiovascular disease risk. Therefore, it is important to prevent postprandial hyperglycemia. Both daily diet and exercise are important factors to control postprandial hyperglycemia. The short-term intake of a high-fat diet worsens postprandial glucose metabolism. Although a single bout of exercise can improve postprandial glucose metabolism, a single bout of moderate-continuous exercise has less effect on the impact of the short-term intake of a high-fat diet on postprandial glucose metabolism, probably because this type of intake impairs the effect of a single bout of moderate-continuous exercise. Further studies are required to determine the exercise regimen that effectively ameliorates the worsening of postprandial glucose metabolism.

Keywords: impaired glucose tolerance, insulin, glucagon-like peptide 1

Introduction

Postprandial hyperglycemia is an early feature of glucose metabolic disorder and appears to occur earlier than fasting hyperglycemia\(^1\). In addition, postprandial hyperglycemia is a better predictor of mortality and metabolic disorders, including cardiovascular disease (CVD), than fasting blood glucose concentration, as supported by the findings of several large prospective cohort studies. The Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe study group investigated associations between 2-h blood glucose concentration after the 75-g oral glucose tolerance test (OGTT) and mortality and the risk of CVD\(^2,3\). High 2-h blood glucose concentration, indicating impaired glucose tolerance (IGT), was associated with an increased risk of all-cause mortality and CVD, independent of fasting glucose concentration and other well-known CVD risk factors. Data from an Asian population also showed similar results\(^4\). Follow-up studies of a population with type 2 diabetes and IGT showed that IGT at baseline was associated with higher all-cause and cardiovascular–related mortality rates and CVD events after 7 and 14 years\(^5,6\). Furthermore, clinical studies of postprandial glucose-lowering medication, an alpha-glucosidase inhibitor, reported that attenuation of postprandial hyperglycemia decreased the incidence of diabetes and CVD\(^7,9\). Moreover, postprandial blood glucose concentration contributes to hemoglobin A1c level, which represents the mean daily blood glucose concentration over the past 2-3 months and is an important clinical marker for blood glucose monitoring, because the postprandial state accounts for 75% of the day. Fasting glucose and postprandial glucose concentration constitute 30.3% and 69.7%, respectively, of hemoglobin A1c in patients with type 2 diabetes and hemoglobin A1c <7.3%\(^10\). Moreover, repeated acute high concentration of and fluctuations in blood glucose increase oxidative stress\(^11\), inflammation\(^12\), and platelet hyperaggregability\(^13\) and suppress endothelial cell dysfunction\(^14,15\). Because postprandial hyperglycemia increases the risk of CVD, it is important to control postprandial hyperglycemia for prevention of CVD.

High-fat diet and postprandial hyperglycemia

Diet is one factor that directly affects postprandial hyperglycemia. Therefore, it is necessary to determine the specific dietary component that induces postprandial hyperglycemia. Although dietary fat does not directly increase postprandial blood glucose concentration, several studies using a hyperinsulinemic-euglycemic glucose clamp or intravenous glucose tolerance test reported that consuming a high-fat diet over a certain period of time decreases blood glucose disposal and insulin sensitivity\(^16,19\). Although controversy still exists regarding the effects of long-term intake of a high-fat diet on postprandial glucose metabolism in humans\(^20\), short-term intake of a high-fat diet appears to aggravate the subsequent postprandial glucose metabolism. However, limited data are available regarding the effect of short-term intake of a high-fat diet on postprandial blood glucose metabolism under physiological conditions (i.e., using an oral ingestion test). Because insulin secretion and incretins (GLP-1 and GIP) influence the postprandial glucose metabolism,
a hyperinsulinemic-euglycemic glucose clamp or intravenous glucose tolerance test may not accurately detect insulin action and glucose dynamics under postprandial physiological conditions. Studies using an oral ingestion test would be more appropriate to observe postprandial glucose metabolism. Several studies have been reported to determine the effect of short-term intake of a high-fat diet on postprandial blood glucose metabolism using an oral ingestion test. A ~2-day eucaloric high-fat diet intake (protein, fat, and carbohydrate [PFC] ratio = 17-22%:70-73%:5-13%) induced abnormally high postprandial blood glucose concentration during an oral glucose load compared to a eucaloric control diet (PFC ratio = 9-20%:16-29%:51-75%) in healthy young men and exercise-trained young men. We also determined the effect of short-term intake of a 3-day high-fat diet on postprandial blood glucose metabolism including GLP-1 and GIP using a 75-g OGTT. In our study, despite no effect on fasting glucose concentration, a 3-day eucaloric high-fat diet (PFC ratio = 11%:69%:20%) increased postprandial blood glucose concentration (Fig. 1A) and decreased first-phase insulin secretion (Fig. 1B) during a 75-g OGTT compared with a standardized eucaloric control diet (PFC ratio = 11%:22%:67%) in healthy young men. It should be noted that a short-term high-fat diet intake enhances blood glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinoceptive polypeptide (GIP) both during fasting and in the postprandial state. Although GLP-1 and GIP are hormones that promote insulin secretion, an increase in postprandial insulin concentration was suppressed after short-term high-fat diet intake. Although the underlying mechanisms for these GLP-1 and GIP responses remain uncertain, we believe that they imply a compensatory response to promote insulin secretion and replenish various tissues with glucose due to the restriction of the dietary carbohydrate supply. Nevertheless, short-term intake of a eucaloric high-fat diet aggravates postprandial glucose and insulin responses. Because people have a greater opportunity to habitually consume a high-fat diet in developed countries, it is possible that postprandial hyperglycemia induced by the intake of a high-fat diet repeatedly occurs. Therefore, it is necessary to consider a prevention approach for postprandial hyperglycemia caused by short-term intake of a high-fat diet.

**Single bout of exercise and postprandial hyperglycemia caused by high-fat diet**

It is well established that a single bout of physical exercise improves glucose uptake during both exercise and the post-exercise period. Therefore, exercise can be one approach to improve postprandial hyperglycemia. In fact, experimental studies have found that a single bout of exercise during the postprandial period significantly decreases postprandial blood glucose and insulin concentration, compared to no exercise. Recently, several studies using a continuous glucose monitoring system reported the continuous effects of a single bout of exercise on postprandial glucose response in free-living conditions. A single bout of moderate (~50% watt max and 60% heart rate reserve) and continuous exercise (45-60 min) decreased the average 24-h post-exercise blood glucose concentration and frequency of hyperglycemia (glucose concentration >10 mmol)32-36. However, the glucose-lowering effect of exercise on blood glucose concentration disappeared 48 h post-exercise. In one study, the glucose-lowering effect of a single bout of exercise was greater with 60-min of low-intensity, continuous exercise.

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**Fig. 1** Incremental areas under the curve (iAUC) of blood glucose concentrations (A) and first-phase insulin secretion (insulinogenic index) (B) during a 75-g oral glucose tolerance test after a 3-day standardized control diet (C) or a 3-day high-fat diet (HF). * significantly different from C (P < 0.05). (Data from reference 23)
watt max) than with 30 min of high-intensity continuous exercise (70% watt max)\(^{32}\). Moreover, despite a shorter duration than continuous exercise, a single bout of high-intensity interval exercise has positive effects on 24-h post-exercise blood glucose concentration and frequency of hyperglycemia\(^{37-41}\). With matched oxygen consumption during exercise and exercise duration, the blood glucose-lowering effect is higher with high-intensity interval exercise than with continuous exercise\(^{40}\). Thus, a single bout of low-moderate, continuous exercise, and high-intensity, interval exercise effectively control at least the 24-h post-prandial blood glucose response. However, little is known regarding the interaction between the effect of exercise and a high-fat diet on postprandial glucose metabolism.

In our study of the effect of moderate and continuous exercise on postprandial hyperglycemia caused by short-term intake of a high-fat diet\(^{42}\), a single bout of moderate and continuous exercise (200 kcal expended at 50% peak oxygen uptake) was performed on the last day of a 3-day high-fat diet intake (PFC ratio = 11%:69%:20%) period, and postprandial glucose metabolism was assessed using a 75-g OGTT the next morning. A single bout of moderate and continuous exercise did not improve the aggravation of postprandial blood glucose concentration (Fig. 2A) and first-phase insulin release (Fig. 2B) induced by the high-fat diet intake in healthy young men\(^{42}\). However, it suppressed the increased postprandial GLP-1 concentration caused by the high-fat diet intake. The underlying mechanisms for this GLP-1 response remain uncertain. Moreover, another study demonstrated that a single bout of high-intensity combined exercise (80% maximal heart rate, 30-min bicycle ergometer + resistance training using a rubber band + 90% maximal heart rate, and repeated 2-min bicycle ergometer followed by 2-min rest until exhaustion) did not ameliorate the aggravation of postprandial blood glucose concentration induced by a 36-h high-fat diet intake in healthy young men\(^{31}\). Thus, the effects of a single bout of exercise on postprandial glucose metabolism induced by short-term intake of a high-fat diet might be poor. Moreover, a high-fat diet intake might eliminate the improved glucose metabolism that occurs with a single bout of exercise, which is potentially mediated by several mechanisms: 1) a high-fat diet reduces 5’adenosine monophosphate-activated protein kinase, a signaling intermediary leading to insulin-independent glucose transport\(^{43}\); 2) exposure to a high level of blood-borne free fatty acids over several hours with a high-fat diet\(^{23,32,40}\) results in impaired insulin sensitivity and responsiveness in peripheral tissues\(^{45}\); and 3) exposure to a high level of free fatty acids impairs b-cell function in the pancreas\(^{46}\).

Our and other findings have indicated that a single bout of exercise does not compensate for the negative effect on postprandial glucose metabolism caused by the short-term intake of a high-fat diet; therefore, exercise programs should be developed to target this effect. However, owing to the limited available data in humans, further studies are required. First, the comprehensive effects of exercise, including exercise mode (continuous, interval, resistance, or intermittent), exercise intensity (low, moderate, or high),

![Fig. 2](image-url)

**Fig. 2** Incremental areas under the curve (iAUC) of blood glucose concentrations (A) and first-phase insulin secretion (insulinogenic index) (B) during a 75-g oral glucose tolerance test after a 3-day standardized control diet (C), a 3-day high-fat diet (HF), or a 3-day HF + a single bout of exercise (HFEx). * significant difference between C and HF trials (P < 0.05). † significant difference between C and HFEx trials (P < 0.05). (Data from reference 42)
exercise timing (preprandial or postprandial), and energy expenditure (upper and lower limit) should be determined. Second, future studies should include individuals with impaired glucose tolerance or diabetes, because the effects might differ from those for healthy individuals.

Conclusion

Postprandial hyperglycemia is associated with an increased risk of diabetes and CVD. A high-fat diet is one factor that can negatively affect postprandial glucose metabolism. Even the short-term intake of a high-fat diet excessively increases postprandial glucose concentration and inhibits insulin secretion. Because a single bout of exercise can improve glucose uptake and insulin sensitivity, it was considered a potential strategy for attenuating the effects of the short-term intake of a high-fat diet on postprandial glucose metabolism. However, the evidence does not support this hypothesis, suggesting that a high-fat diet inhibits the effects of a single bout of exercise. Future studies from many different perspectives are required to elucidate the effects of exercise on postprandial hyperglycemia.

Conflict of Interests

The author declare that there is no conflict of interests regarding the publication of this article.

References

1) Tabák AG, Jokela M, Akbaraly TN, Brunner EJ, Kivimäki M and Witte DR. 2009. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet 373: 2215-2221.

2) DECODE Study Group, the European Diabetes Epidemiology Group. 1999. Glucose tolerance and mortality: comparison of WHO and American Diabetes Association diagnostic criteria. Lancet 353: 617-621.

3) DECODE Study Group, the European Diabetes Epidemiology Group. 2001. Glucose tolerance and cardiovascular mortality: comparison of fasting and 2-hour diagnostic criteria. Arch Intern Med 161: 397-405.

4) Nakagami T; DECODA Study Group. 2004. Hyperglycaemia and mortality from all causes and from cardiovascular disease in five populations of Asian origin. Diabetologia 47: 385-394.

5) Tominaga M, Eguchi H, Manaka H, Igarashi K, Kato T and Sekikawa A. 1999. Impaired glucose tolerance is a risk factor for cardiovascular disease, but not impaired fasting glucose. The Funagata Diabetes Study. Diabetes Care 22: 920-924.

6) Cavalet F, Pagliarino A, Valle M, Di Martino L, Bonomo K, Massucco P, Anfossi G and Trovati M. 2011. Postprandial blood glucose predicts cardiovascular events and all-cause mortality in type 2 diabetes in a 14-year follow-up: lessons from the San Luigi Gonzaga Diabetes Study. Diabetes Care 34: 2237-2243.

7) Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A and Laakso M; STOP-NIDDM Trial Research Group. 2002. Acarbose for prevention of type 2 diabetes mellitus: the STOP-NIDDM randomised trial. Lancet 359: 2072-2077.

8) Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A and Laakso M; STOP-NIDDM Trial Research Group. 2003. Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial. JAMA 290: 486-494.

9) Kawamori R, Tajima N, Iwamoto Y, Kashiwagi A, Shimamoto K and Kaku K; Voglibose Ph-3 Study Group. 2009. Voglibose for prevention of type 2 diabetes mellitus: a randomised, double-blind trial in Japanese individuals with impaired glucose tolerance. Lancet 373: 1607-1614. doi: 10.1016/S0140-6736(09)60222-1.

10) Monnier L, Lapinski H and Colette C. 2003. Contributions of fasting and postprandial plasma glucose increments to the overall diurnal hyperglycaemia of type 2 diabetic patients: variations with increasing levels of HbA1c. Diabetes Care 26: 881-885.

11) Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP and Colette C. 2006. Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycaemia in patients with type 2 diabetes. JAMA 295: 1681-1687.

12) Esposito K, Nappo F, Marfella R, Giugliano G, Giugliano F, Ciotola M, Quagliaro L, Ceriello A and Giugliano D. 2002. Inflammatory cytokine concentrations are acutely increased by hyperglycaemia in humans: role of oxidative stress. Circulation 106: 2067-2072.

13) Sakamoto T, Ogawa H, Kawano H, Hirai N, Miyamoto S, Takazoe K, Soejima H, Kugiyama K, Yoshimura M and Yasue H. 2000. Rapid change of platelet aggregability in acute hyperglycaemia. Detection by a novel laser-light scattering method. Thromb Haemost 83: 475-479.

14) Williams SB, Goldfine AB, Timimi FK, Ting HH, Roddy MA, Simonson DC and Creager MA. 1998. Acute hyperglycaemia attenuates endothelium-dependent vasodilation in humans in vivo. Circulation 97: 1695-1701.

15) Kawano H, Motoyama T, Hirashima O, Hirai N, Miyao Y, Sakamoto T, Kugiyama K, Ogawa H and Yasue H. 1999. Hyperglycaemia rapidly suppresses flow-mediated endothelium-dependent vasodilation of brachial artery. J Am Coll Cardiol 34: 146-154.

16) Bachmann OP, Dahl DB, Brechtlel K, Machenh J, Haap M, Maier T, Loviscach M, Stumvoll M, Clausen CD, Schick F, Häring HU and Jacob S. 2001. Effects of intravenous and dietary lipid challenge on intramyocellular lipid content and the relation with insulin sensitivity in humans. Diabetes 50: 2579-2584.

17) Bisschop PH, de Metz J, Ackermans MT, Endert E, Pijl H, Kuipers F, Meijer AJ, Sauerwein HP and Romijn JA. 2001. Dietary fat content alters insulin-mediated glucose metabolism in healthy men. Am J Clin Nutr 73: 554-559.

18) Johnson NA, Stannard SR, Rowlands DS, Chapman PG, Thompson CH, O’Connor H, Sachinwalla T and Thompson MW. 2006. Effect of short-term starvation versus high-fat diet on intramyocellular triglyceride accumulation and insulin resistance in physically fit men. Exp Physiol 91: 693-703.

19) Bruns C, Jensen CB, Storgaard H, Hiscock NJ, White A, Appel JS, Jacobsen S, Nilsson E, Larsen CM, Astrup A, Quis-
torff B and Vaag A. 2009. Impact of short-term high-fat feeding on glucose and insulin metabolism in young healthy men. *J Physiol* 587: 2387-2397.

20) Hu T, Mills KT, Yao L, Demanelis K, Eloutzaz M, Yancy WS Jr, Kelly TN, He J and Bazzano LA. 2012. Effects of low-carbohydrate diets versus low-fat diets on metabolic risk factors: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 176 Suppl 7: S44-S54. doi: 10.1093/aje/kws264.

21) Sparti A and Décombaiz J. 1992. Effect of diet on glucose tolerance 36 hours after glycogen-depleting exercise. *Eur J Clin Nutr* 46: 377-385.

22) Pehleman TL, Peters SJ, Heigenhauser GJ and Spriet LL. 2005. Enzymatic regulation of glucose disposal in human skeletal muscle after a high-fat, low-carbohydrate diet. *J Appl Physiol* 98: 100-107.

23) Numao S, Kawano H, Endo N, Yamada Y, Konishi M, Takahashi M and Sakamoto S. 2012. Short-term low carbohydrate/high-fat diet intake increases postprandial plasma glucose and glucagon-like peptide-1 levels during an oral glucose tolerance test in healthy men. *Eur J Clin Nutr* 66: 926-931. doi: 10.1038/ejcn.2012.58.

24) Rose AJ and Richter EA. 2005. Skeletal muscle glucose uptake during exercise: how is it regulated? *Physiology* 20: 260-270.

25) Garetto LP, Richter EA, Goodman MN and Ruderman NB. 1984. Enhanced muscle glucose metabolism after exercise in the rat: the two phases. *Am J Physiol* 246: E471-E475.

26) Richter EA, Garetto LP, Goodman MN and Ruderman NB. 1984. Enhanced muscle glucose metabolism after exercise: modulation by local factors. *Am J Physiol* 246: E476-E482.

27) Houmard JA, Tanner CJ, Slentz CA, Duscha BD, McCartney JS and Kraus WE. 2004. Effect of the volume and intensity of exercise training on insulin sensitivity. *J Appl Physiol* 96: 101-106.

28) Hayashi Y, Nagasaka S, Takahashi N, Kusaka I, Ishibashi S, Numao S, Lee DJ, Taki Y, Ogata H, Tokuyama K and Tanaka K. 2005. A single bout of exercise at higher intensity enhances glucose effectiveness in sedentary men. *J Clin Endocrinol Metab* 90: 4035-4040.

29) Larsen JJ, Dafa L, Kjaer M and Galbo H. 1997. The effect of moderate exercise on postprandial glucose homeostasis in NIDDM patients. *Diabetologia* 40: 447-453.

30) Larsen JJ, Dafa L, Madsbad S and Galbo H. 1999. The effect of intense exercise on postprandial glucose homeostasis in type II diabetic patients. *Diabetologia* 42: 1282-1292.

31) Colberg SR, Zarrabi L, Bennington L, Nakave A, Thomas Somma C, Swan DP and Schrist SR. 2009. Postprandial walking is better for lowering the glycemic effect of dinner than pre-dinner exercise in type 2 diabetic individuals. *J Am Med Dir Assoc* 10: 394-397. doi: 10.1016/j.jamda.2009.03.015.

32) Manders RJ, Van Dijk JW and Van Loon LJ. 2010. Low-intensity exercise reduces the prevalence of hyperglycemia in type 2 diabetes. *Med Sci Sports Exerc* 42: 219-225.

33) van Dijk JW, Tummers K, Stehouwer CD, Hartgens F and van Loon LJ. 2012. Exercise therapy in type 2 diabetes: is daily exercise required to optimize glycemic control? *Diabetes Care* 35: 948-954.

34) van Dijk JW, Manders RJ, Canfora EE, Mechelen WJ, Hartgens F, Stehouwer CD and van Loon LJ. 2013. Exercise and 24-h glycemic control: equal effects for all type 2 diabetes patients? *Med Sci Sports Exerc* 45: 628-635.

35) van Dijk JW, Venema M, van Mechelen W, Stehouwer CD, Hartgens F and van Loon LJ. 2013. Effect of moderate-intensity exercise versus activities of daily living on 24-hour blood glucose homeostasis in male patients with type 2 diabetes. *Diabetes Care* 36: 3448-3453.

36) Oberlin DJ, Mikus CR, Kearney ML, Hinton PS, Manrique C, Leidy HJ, Kanaley JA, Rector RS and Thyfault JP. 2014. One bout of exercise alters free-living postprandial glycemia in type 2 diabetes. *Med Sci Sports Exerc* 46: 232-238.

37) Praet SF, Manders RJ, Lieveerse AG, Kuipers H, Stehouwer CD, Keizer HA and van Loon LJ. 2006. Influence of acute exercise on hyperglycemia in insulin-treated type 2 diabetes. *Med Sci Sports Exerc* 38: 2037-2044.

38) Gillen JB, Little JP, Punthakee Z, Tarnopolsky MA, Riddell MC and Gibala MJ. 2012. Acute high-intensity interval exercise reduces the postprandial glucose response and prevalence of hyperglycaemia in patients with type 2 diabetes. *Diabetes Obes Metab* 14: 575-577.

39) Francois ME, Baldi JC, Manning PJ, Lucas SJ, Hawley JA, Williams MJ and Cotter JD. 2014. Exercise snacks’ before meals: a novel strategy to improve glycemic control in individuals with insulin resistance. *Diabetologia* 57: 1437-1445.

40) Karstoft K, Christensen CS, Pedersen BK and Solomon TP. 2014. The acute effects of interval- vs continuous-walking exercise on glycemic control in subjects with type 2 diabetes: a crossover, controlled study. *J Clin Endocrinol Metab* 99: 3334-3342.

41) Little JP, Jung ME, Wright AE, Wright W and Manders RJ. 2014. Effects of high-intensity interval exercise versus continuous moderate-intensity exercise on postprandial glycemic control assessed by continuous glucose monitoring in obese adults. *Appl Physiol Nutr Metab* 39: 835-841.

42) Numao S, Kawano H, Endo N, Yamada Y, Konishi M, Takahashi M and Sakamoto S. 2013. Effects of a single bout of aerobic exercise on short-term low-carbohydrate/high-fat intake-induced postprandial glucose metabolism during an oral glucose tolerance test. *Metabolism* 62: 1406-1415. doi: 10.1016/j.metabol.2013.05.005.

43) Tanaka S, Hayashi T, Toyoda T, Hamada T, Shimizu Y, Hirata M, Ebihara K, Masuzaki H, Hosoda K, Fushiki T and Nakao K. 2007. High-fat diet impairs the effects of a single bout of endurance exercise on glucose transport and insulin sensitivity in rat skeletal muscle. *Metabolism* 56: 1719-1728.

44) Bisschop PH, Ackermans MT, Endert E, Ruiter AF, Meijer AJ, Kuipers F, Sauerwein HP and Romijn JA. 2002. The effect of carbohydrate and fat variation in euenergetic diets on postabsorptive free fatty acid release. *Br J Nutr* 87: 555-559.

45) Ferrarinni E, Barrett EJ, Bevilacqua S and DeFronzo RA. 1983. Effect of fatty acids on glucose production and utilization in man. *J Clin Invest* 72: 1737-1747.

46) Leung N, Sakaue T, Carpentier A, Uffelman K, Giacca A and Leidy HJ. 2009. Impact of short-term high-fat feeding on beta-cell function in obese men. *Diabetologia* 52: 204-213.