

# Postprandial Blood Glucose, Cardiovascular Events, and All-Cause Mortality: How Do We Use Postprandial Glucose in Clinical Practice?

Reviewed by Nathaniel G. Clark, MD, MS, RD

## STUDY

Cavalot F, Pagliarino A, Valle M, Di Martino L, Bonomo K, Massucco P, Anfossi G, Trovati M: 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, 2011

## SUMMARY

**Objective.** To evaluate whether postprandial blood glucose (PPG) levels predicted cardiovascular disease (CVD) events and all-cause mortality in people with type 2 diabetes in a long-term follow-up study.

**Design.** Consecutive patients with type 2 diabetes ( $n = 505$ ; age  $62 \pm 10$  years, diabetes duration  $9 \pm 8$  years) were followed for 14 years. The relationship between CVD events and five glycemic control parameters (fasting blood glucose [FBG], blood glucose 2 hours after breakfast and lunch, pre-dinner blood glucose, and A1C) were analyzed looking at all-cause mortality and first cardiovascular event during the 14-year follow-up period.

**Results.** Cardiovascular events occurred in 34% and death occurred in 29% of the study population. When the five glycemic control parameters were considered together, the major predictor of cardiovascular events was blood glucose measured 2 hours after lunch. That measurement and A1C were the strongest predictors

of all-cause mortality. When blood glucose level 2 hours after lunch and A1C were considered together with the main CVD risk factors, the results were the same.

**Conclusion.** Both PPG and A1C predicted cardiovascular events and mortality in this long-term follow-up study.

## COMMENTARY

This study, a follow-up to an earlier report,<sup>1</sup> is important because it examined the effect of PPG (i.e., blood glucose measured 2 hours after a meal) compared to blood glucose measured 2 hours after the administration of an oral glucose load as part of an oral glucose tolerance test (OGTT).

There has been an ongoing debate regarding whether hyperglycemia after an oral glucose load carries the same risk as hyperglycemia resulting from a mixed meal. Most of the data that support the connection between CVD risk and PPG come from studies using 2-hour OGTT data. Thus, the current study, which examined the effect of true postprandial hyperglycemia, is an important study in this research area.

## Some Limitations

As noted in the editorial that accompanied this study's publication,<sup>2</sup> important limitations of the study are that the researchers did not examine the effect of post-dinner glycemia, which is often when the highest blood glucose values of the

day occur. Post-dinner (or pre-bed-time) blood glucose is often an initial target of blood glucose control when determining the need for or use of rapid-acting insulins or rapid-acting insulin secretagogues.

In addition, there was no description of what specific kinds of therapeutic agents were used during the study. This is relevant because how the study population was treated compared to what one might expect in the United States may influence the general applicability of their findings.

Compared to data from the Centers for Disease Control and Prevention and the American Diabetes Association (ADA) regarding how diabetes is treated in the United States, in this study, the percentage of patients being treated through diet alone was much higher (45 vs. 16%), and the percentage using insulin either alone or combined with oral agents was much lower (12 vs. 26%). It may well be that how glycemic control was achieved was an important unexamined variable in this study.

## Relationship Between PPG and CVD

It has been stated that PPG has a noxious effect on the vascular endothelium that is mediated by oxidative stress. This summarizes the current concept regarding why one might be concerned about and target postprandial hyperglycemia. Two excellent reviews in this area are those

by Beisswenger et al.<sup>3</sup> and Ceriello et al.<sup>4</sup> These authors review the evidence that PPG plays an independent and modifiable role in CVD. They cite the epidemiological data showing that high PPG is an independent risk factor more powerful than fasting glucose or A1C.

Hypotheses discussed regarding the connection between PPG and CVD risk include the contribution of PPG to A1C, PPG as a marker for other CVD risk factors (serum lipid and triglyceride levels, in particular), and the direct toxicity of spikes in glucose concentration after meals. As noted, PPG is one component of glucose variability that is also believed to have a negative effect on the vascular system.

#### Contribution of PPG to A1C

A1C is the measure of glycemia that has been used in all studies examining the relationship between glycemic control and the complications of diabetes. The major studies on which we base current A1C target recommendations (ADA target < 7.0%; American Association of Clinical Endocrinologists target ≤ 6.5%) include the Diabetes Control and Complications Trial and the U.K. Prospective Diabetes Study, as well as the more recent ACCORD (Action to Control Cardiovascular Risk in Diabetes), ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicon Modified Release Controlled Evaluation), HEART2D (Hyperglycemia and Its Effect After Acute Myocardial Infarction on Cardiovascular Outcomes in Patients With Type 2 Diabetes), and VADT (Veterans Affairs Diabetes Trial) studies. All have all used A1C as the major measure of glycemic control.

A1C is a measure of mean glucose level over the preceding 2–3 months. It is a composite of fasting, preprandial, and postprandial values. In

looking at the relative contribution of fasting versus postprandial blood glucose levels to A1C, Monnier et al.<sup>5</sup> found that, at A1C values well above target (mean 11%), FBG had the greater effect, whereas at A1C values close to target (mean 6.5%), PPG became more important.

This suggests that, as patients move toward to their glycemic target, the relative importance of targeting FPG versus PPG shifts. This fits with the current approach to insulin use, through which we begin with basal insulin targeting FBG and then add rapid-acting insulin to control PPG. Emphasizing the need to follow and treat PPG, Woerle et al.<sup>6</sup> found that, when PPG goals (< 140 mg/dl) were achieved, 94% of patients reached the ADA A1C goal of < 7%, compared to only 64% when FBG goals (< 100 mg/dl) were attained.

#### Realities of Monitoring PPG in the Practice of Diabetes Care

Ideally, we would like to know what our patients' blood glucose pattern is throughout the day. To achieve this, we can ask patients to monitor their blood glucose before and after meals or to use a continuous glucose sensor. We need to consider, however, the burden we place on patients when we ask them to test before and after meals, as well as the related expense to patients and the health care system. We must make sure that the data obtained are clinically useful.

Current Medicare guidelines state that testing should be done only once per day for patients who are not on insulin and three times per day for those who are on insulin. Only in the care of women with gestational diabetes has pre- and postmeal testing been shown to be of benefit.

#### When Should PPG Be Monitored and Targeted?

The ADA 2012 standards of care guidelines<sup>7</sup> state that, in general,

preprandial blood glucose testing is recommended. If patients are meeting the target for premeal values but A1C remains above target, monitoring PPG with a target of < 180 mg/dl 1–2 hours after meals is reasonable. This approach (i.e., to use PPG testing when there is a specific diabetes management need) seems to make good sense. Examples of when monitoring PPG makes sense include instances when premeal blood glucose targets are met but A1C remains high or patients are using a therapy targeting postprandial hyperglycemia (e.g., a rapid-acting insulin or rapid-acting insulin secretagogue). The goal should be to prevent hyperglycemia and not simply to treat it.

Because premeal hyperglycemia contributes to postprandial hyperglycemia, a focus on PPG to the exclusion of preprandial hyperglycemia is inappropriate. To help our patients reach their glycemic targets, we must consider both pre- and postprandial hyperglycemia.

This study contributes important data supporting the importance of PPG.

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<sup>6</sup>Woerle HJ, Neumann C, Zschau S, Tenner S, Irsigler A, Schirra J, Gerich JE, Goke B: Impact of fasting and postprandial glycemia on overall glycemic control in type 2 diabetes: importance of postprandial

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<sup>7</sup>American Diabetes Association: Standards of medical care in diabetes—2012. *Diabetes Care* 35 (Suppl. 1):S11–S63, 2012

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