



# Pizza Leavening Technique Influences Postprandial Glucose Response: A Randomized Controlled Trial in Patients With Type 1 Diabetes

Luisa Cavagnuolo, Lutgarda Bozzetto, Luca Franco, Giuseppina Costabile, Gabriele Riccardi, Angela Albarosa Rivellesse, and Giovanni Annuzzi

Diabetes Care 2019;42:e157–e158 | <https://doi.org/10.2337/dc19-0778>

Achieving optimal postprandial glucose control remains a major issue in people with type 1 diabetes (T1D), including those using innovative technologies (1,2). Eating pizza is challenging for patients with T1D (3) because of its high and extremely variable glycemic index (4) and prolonged postprandial hyperglycemia. Bread leavened by sourdough instead of brewer's yeast may reduce postprandial glucose response (PGR), and duration of sourdough leavening could play a beneficial role (5). Whether this holds true for pizza and in patients with T1D is unknown.

We compared PGR for pizzas differing in type and duration of dough leavening in 16 T1D patients (9 men, 7 women) on an insulin pump. The study was approved by the institutional ethics committee (reg. no. NCT03619031, ClinicalTrials.gov). According to a randomized crossover design, participants consumed—at home, on three nonconsecutive evenings over 3 weeks—a pizza prepared with 1) brewer's yeast and wheat flour, 5-h leavening (usual leavening time) (Brew5); 2) sourdough and flour mix, 5-h leavening (Sour5); or 3) sourdough and flour mix, 60-h leavening (Sour60). Premeal insulin doses, calculated by the individual insulin-to-glycemic load ratio (2) (the same for each participant on the

three occasions, range 6–14 IU) were given as an 80/20% dual-wave bolus extended for 4 h. PGR was evaluated by the real-time continuous glucose monitoring system (Dexcom, Guardian, or Freestyle) used by the participant. Six 3- to 8-h glucose incremental areas under the curve (iAUCs) (two for each type of pizza) were not analyzed due to hypoglycemic events in the periods (symptomatic, blood glucose <3.9 mmol/L, duration <30 min).

Pizza dough and topping were prepared in a specialized factory (Mediterranea Quality Food S.r.l., Praia a Mare, Italy). Pizza dough (250 g) was partially baked and kept under vacuum until use. The topping—tomato sauce (150 g) and extra-virgin olive oil (15 g)—was supplied to the participants in jars. Participants cooked the pizza in a prewarmed electric oven at 200°C for 4–5 min. The dough for Sour5 and Sour60 was prepared with refined wheat flour (111 g), soy flour (3.3 g), rice flour (3.3 g), sourdough (44 g), water (83 g), extra-virgin olive oil (1.7 g), salt (2.4 g), and dry leavening agent (0.17 g); the dough for Brew5 was prepared with refined wheat flour (157 g), brewer's yeast (1.6 g), water (86 g), extra-virgin olive oil (2.3 g), and salt (3.4 g). The three pizza meals were very similar in terms of energy (724–752 kcal) and composition

(total carbohydrates 120–127 g, total fat 19 g, saturated fat 2.8 g, monounsaturated fat 12.5–12.8 g, polyunsaturated fat 2.1–2.4 g, protein 19.0–19.3 g, fiber 5.6–5.7 g).

Postprandial iAUCs were calculated by the trapezoidal method as AUC above baseline. Differences between meals were evaluated by Friedman test and pairwise post hoc analysis adjusted for multiple comparisons.

Participants were aged  $42 \pm 3$  years (mean  $\pm$  SEM), with BMI  $25.5 \pm 0.9$  kg/m<sup>2</sup>, diabetes duration  $25 \pm 3$  years, and HbA<sub>1c</sub>  $53 \pm 3$  mmol/mol. The prespecified primary outcome, i.e., 0- to 3-h iAUC, was higher after Sour5 ( $407 \pm 101$  mmol/L  $\times$  180 min) than Brew5 ( $172 \pm 122$ ,  $P = 0.014$ ) and Sour60 ( $301 \pm 102$ ,  $P = 0.472$ ) ( $P = 0.018$ , Friedman test) (Fig. 1). Early postprandial blood glucose incremental peak was higher after Sour5 ( $6.0 \pm 1.0$  mmol/L) than Brew5 ( $3.7 \pm 0.8$ ,  $P = 0.040$ ) and Sour60 ( $4.5 \pm 0.9$ ,  $P = 0.231$ ) ( $P = 0.039$ ). Later PGR did not differ between pizza meals (3- to 8-h iAUC  $1,073 \pm 279$ ,  $891 \pm 355$ , and  $1,081 \pm 334$  mmol/L  $\times$  300 min after Sour5, Brew5, and Sour60, respectively;  $P = 0.905$ ). The 0- to 8-h iAUCs did not differ significantly between pizza meals ( $P = 0.368$ ). The postprandial (0–8 h) blood glucose coefficients of variation were

Department of Clinical Medicine and Surgery, Federico II University, Naples, Italy

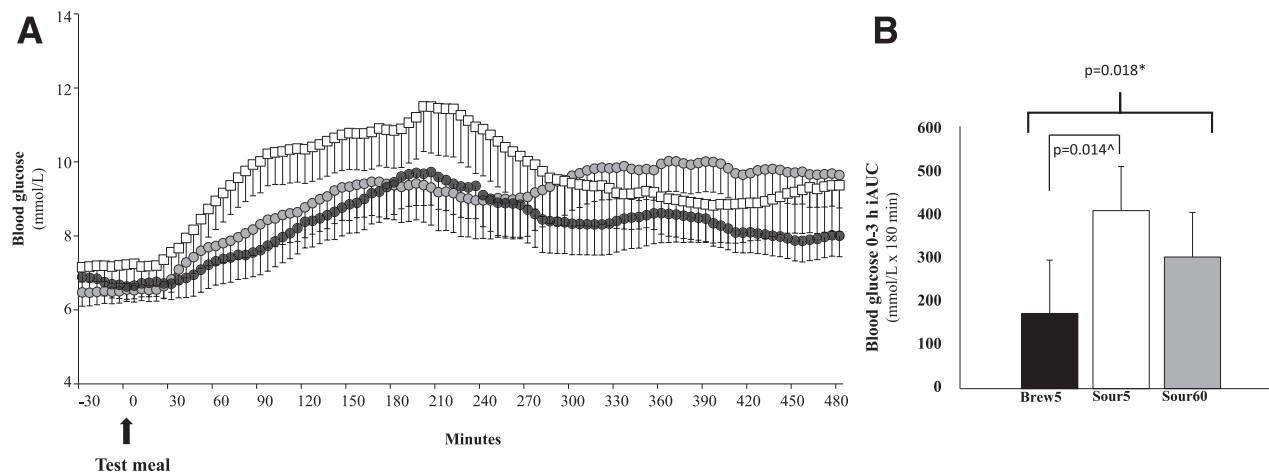
Corresponding author: Giovanni Annuzzi, [annuzzi@unina.it](mailto:annuzzi@unina.it)

Received 19 April 2019 and accepted 2 July 2019

Clinical trial reg. no. NCT03619031, [clinicaltrials.gov](http://clinicaltrials.gov)

L.C. and L.B. contributed equally to this work.

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**Figure 1**—A: Absolute changes in blood glucose concentrations after the pizza meals (Brew5, black circles; Sour5, white squares; Sour60, gray circles) (A), and 0–3 h iAUC (Brew5, black bar; Sour5, white bar; Sour60, gray bar) (B). Data are mean  $\pm$  SEM. \*Friedman test for repeated measures. <sup>A</sup>Pairwise post hoc analysis adjusted for multiple comparisons.

lower for Brew5 than Sour5 and Sour60 ( $19.8 \pm 2.3$ ,  $31.5 \pm 3.9$ , and  $28.8 \pm 3.2$ , respectively;  $P = 0.020$ ).

This study in patients with T1D on an insulin pump showed that a short-leavened sourdough pizza induces a higher early PGR than a usual brewer's yeast pizza. The long-leavened dough counterbalanced the higher PGR, which was not different between the Sour60 and Brew5 pizzas.

Therefore, we did not observe with pizza the hypoglycemic effects of sourdough shown with bread in individuals without diabetes, but our results were in line with recent findings with sourdough-fermented rye crispbread in healthy individuals (6). Factors explaining differences between bread and pizza and the effects of long sourdough fermentation, including differences in composition, leavening, cooking, storage, dough structure, and carbohydrate availability to digestion, are the object of our current investigations.

Strengths of our study are the randomized controlled design, use of continuous glucose monitoring, and the real-life experimental setting in patients with T1D. A limitation is that results are not generalizable to all

sourdough-leavened pizzas because of prevailing differences in sourdough ecosystems. Moreover, we tested an Italian “healthy” pizza with a small amount of fat and protein, two nutrients that contribute to make pizza eating so challenging.

In conclusion, there is a renewed interest in baking with sourdough owing to its favorable effects on taste, digestibility, and shelf life. With a long-leavened sourdough pizza, people with T1D might not need to modify the amount and modality of insulin bolus they use with brewer's yeast pizza, as they would need to do for a short-leavened sourdough pizza.

**Acknowledgments.** The authors thank the participants for their enthusiastic and careful cooperation in the study. The pizza meals were kindly provided by Mediterranean Quality Food S.r.l., Praia a Mare, Italy.

**Duality of Interest.** No potential conflicts of interest relevant to this article were reported.

**Author Contributions.** L.C. and L.B. conceived the study, conducted the statistical analyses, and wrote most of the manuscript. L.F. and G.C. collected data, contributed to the interpretation of data, and drafted the manuscript. G.R. and A.A.R. contributed significantly to the study design and the interpretation of data and made

substantial critical revisions. G.A. conceived the study, contributed to the analysis and interpretation of data and the development of the manuscript, and critically revised the manuscript. G.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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