Patient-Reported Outcomes of COVID-19 Vaccine Breakthrough Infection–Associated Changes in Glucose Control in Subjects With Type 1 Diabetes (PRO-VACS 2 Study)

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Despite the effectiveness of mRNA vaccines in preventing severe coronavirus disease 2019 (COVID-19) (1), infections (particularly with Omicron variant) occur in vaccinated individuals (2), especially in the case of hyperglycemia (3). Although COVID-19–related inflammation, even in its mild forms, could increase glycemia, glucose control during breakthrough infection in type 1 diabetes (T1D) has not been studied so far. The aim of this study is the assessment of short-term COVID-19 effects on glucose variability in fully vaccinated patients with T1D.

This observational retrospective study (Florence Ethical Board approval no. 21911_oss) was performed on a consecutive series of adults with T1D, attending the Diabetes Unit of Careggi Hospital, with use of interstitial flash or continuous glucose monitoring, with COVID-19 infection reported (confirmed by either molecular or antigen testing) after 15 December 2021.

Mean glucose, time with glucose in range (TIR) (70–180 mg/dL and 3.9–10 mmol/mol), time in a state of hypoglycemia, time in a state of hyperglycemia, and glucose coefficient of variation in the 7 days following the detection of COVID-19 infection (if asymptomatic) or the onset of symptoms were compared for the 2 weeks preceding and the 2 weeks after. Separate analyses were performed for vaccinated and nonvaccinated individuals, and for those with hybrid closed loop (HCL); for the latter, data on mean insulin daily dose (boluses and basal units) were also collected. We used Student paired *t* tests for comparison of means at different time points after checking for normal distribution for the variable considered. All analyses were performed on SPSS 28.

Of 25 enrolled patients, 24 had received a two-dose primary series and one booster of COVID-19 vaccine (mRNA, Moderna or Pfizer-BioNTech), and one had not been vaccinated. The unvaccinated patient, a 43-years-old woman on multiple daily injections (MDI), experienced a severe form of COVID-19 requiring artificial ventilation. Her mean glucose and TIR were 119 mg/dL (6.6 mmol/L) and 86%, respectively, before infection and 211 mg/dL (11.7 mmol/mol) and 26% during the first week of infection. Of the 24 vaccinated individuals (15 women; mean ± SD age 38 ± 13 years, duration of diabetes 24 ± 10 years, and A1C 7.0 ± 2.8% (53.5 ± 6.8 mmol/mol), 12 and 8 were on MDI and continuous subcutaneous insulin infusion (CSII), respectively; of those, one used Tandem Diabetes Care t:slim X2, two used A7 TouchCare MEDTRUM, two used Accu-Chek Solo, and three used mylife YpsoPump. Four patients used an HCL system (Accu-Chek Solo/Dexcom G6 with DBLG1 technology). All of the 24 cases of vaccine-breakthrough COVID-19 were mild (2 asymptomatic and 22 with mild symptoms: cold [*N* = 12], cough [*N* = 13], fever [*N* = 13], and sore throat [*N* = 10]). No patients was treated with corticosteroids. No significant change in mean glucose or glucose variability was observed in patients on MDI/CSII or in those with HCL (Table 1); in the latter, mean daily insulin doses transiently increased during infection.

Although COVID-19–related inflammation could produce a pronounced impairment of glucose control, the current study does not show any major effect on mean glucose and glucose variability, at least in fully vaccinated patients. In the few patients with HCL, a significant increase in insulin dose was observed during breakthrough infection, suggesting that the adjustment of insulin doses prevented a relevant increase of blood glucose. Unfortunately, the retrospective nature of the study did not allow the collection of reliable data on insulin doses in the whole sample. Notably, COVID-19 vaccination, which also stimulates inflammation, did not appear to modify glucose control in patients with T1D (4).

In the only unvaccinated patient, the deterioration of glucose control during COVID-19 could have been determined by the severity of disease or by specific treatments (e.g., corticosteroids); alternatively, vaccination could have reduced COVID-19–induced inflammation (5).

The limited sample size suggests caution in the interpretation of results, particularly for patients on HCL. In addition,

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Table 1—Glucose variability and insulin doses and COVID-19

	Before COVID-19	During COVID-19	After COVID-19
Patients on MDI/CSII (*n* = 20)			
Glucose, mg/dL (mmol/L)	153 ± 25 (8.5 ± 1.4)	158 ± 27 (8.8 ± 1.5)	153 ± 27 (8.5 ± 1.5)
% TIR	61.4 ± 16.7	62.7 ± 19	65.9 ± 17.3
Glucose CV (%)	37 ± 7.1	35.2 ± 7.1	35 ± 6.1
Patients on HCL (*n* = 4)			
Glucose, mg/dL (mmol/L)	155 ± 11 (8.6 ± 0.6)	166 ± 4 (9.2 ± 0.2)	160 ± 4 (8.9 ± 0.2)
% TIR	70.2 ± 4	65.5 ± 5.8	66.5 ± 4.3
Glucose CV (%)	31.3 ± 3.7	28.4 ± 3.0	29 ± 5
Daily insulin dose (IU/die)	44.8 ± 17.8	51.6 ± 20.2*	47.4 ± 23.1
Basal insulin dose (IU/die)	16.2 ± 3.3	15.8 ± 4.1	15.4 ± 4.2
Boluses insulin dose (IU/die)	28.2 ± 14.8	35.8 ± 19.3	32 ± 22.3

Data are means ± SD. Before COVID-19: mean of the 2 weeks preceding diagnosis. During COVID-19: mean of the 1st week following diagnosis. After COVID-19: mean of the 2 weeks following testing negative. Glucose CV, glucose coefficient of variation. *Before vs. during, $P = 0.048$.

subjects in the MDI/CSII group used two different types of devices for glucose monitoring. All cases were recorded after 15 December 2021, when Omicron was the dominant variant in the country; however, no molecular characterization of individual cases was performed. In any case, data collected in a predominantly Omicron-infected sample cannot be extended to other variants. Furthermore, enrolled patients, who all attended the same Diabetes Unit and had received extensive education on the management of insulin therapy, cannot be considered representative of all patients with T1D.

Despite these limitations, the present data suggest that the impact of COVID-19 on glucose control in fully vaccinated individuals with T1D could be smaller than expected, provided that the patients have received adequate instruction for insulin adjustment during sick days; however, further data on larger samples should be collected to obtain reliable estimates of the glycemic impact of COVID-19 in vaccinated individuals.

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References

1. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. N Engl J Med 2021;384:1412–1423

2. Brosh-Nissimov T, Orenbuch-Harroch E, Chowers M, et al. BNT162b2 vaccine breakthrough: clinical characteristics of 152 fully vaccinated hospitalized COVID-19 patients in Israel. Clin Microbiol Infect 2021;27:1652–1657

3. Basso P, Negro C, Cegolon L, Larese Filon F. Risk of vaccine breakthrough SARS-CoV-2 infection and associated factors in healthcare workers of Trieste teaching hospitals (North-Eastern Italy). Viruses 2022;14:336

4. Dicembrini I, Vitale V, Cosentino C, et al. Interstitial glucose monitoring, type 1 diabetes and COVID-19 vaccine: the patient-reported outcomes and vaccine-associated changes in glucose and side effects (PRO-VACS). Acta Diabetol 2022;59:435–438

5. Zambrano LD, Newhams MM, Olson SM, et al.; Overcoming COVID-19 Investigators. Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA vaccination against multisystem inflammatory syndrome in children among persons aged 12–18 years - United States, July-December 2021. MMWR Morb Mortal Wkly Rep 2022;71:52–58