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Original Research

## Glucose Fluctuations are Not Modulated by the Proportion of Calories from Macronutrients or Spontaneous Total Energy Expenditure in Adults with Cystic Fibrosis

Sophie Ziai PhD <sup>a,b</sup>, Adèle Coriati MSc <sup>a,b</sup>, David St-Pierre <sup>a</sup>, Katherine Chabot RD, MSc <sup>a,b</sup>,  
Katherine Desjardins RD, MSc <sup>a</sup>, Catherine Leroux RD <sup>a,b</sup>, Martin V. Richter PhD <sup>c</sup>,  
Rémi Rabasa-Lhoret MD, PhD <sup>a,b,d,e,\*</sup>

<sup>a</sup> Institut de Recherches Cliniques de Montréal (IRCM), Montréal, Québec, Canada

<sup>b</sup> Nutrition Department, Pavillon Liliane-de-Stewart, Université de Montréal, Montréal, Québec, Canada

<sup>c</sup> Department of Medicine, Étienne-Lebel Clinical Research Center, Sherbrooke, Québec, Canada

<sup>d</sup> Montreal Diabetes Research Centre (MDRC), Montréal, Québec, Canada

<sup>e</sup> Cystic Fibrosis Clinic, Centre Hospitalier de l'Université de Montréal (CHUM), Montréal, Québec, Canada

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### ABSTRACT

**Objectives:** To determine the modifiable factors affecting glucose variability in people with cystic fibrosis (CF). CF-related diabetes (CFRD) is the most common complication of CF, and its presence increases morbidity and mortality in patients. Patients with CF (with and without CFRD) have potentially harmful glucose fluctuations and glucose excursions when compared to healthy adults. Carbohydrate intake and exercise have been shown to affect glycemia. Therefore, our hypothesis was that the proportion of energy from carbohydrates and total energy expenditure (TEE) would influence glucose fluctuations in adults with CF.

**Methods:** A cross-sectional study involved 36 patients with CF, in whom continuous glucose monitoring systems were installed. Glucose fluctuations were then quantified using 3 indexes: mean amplitude of glucose excursions, standard deviation and coefficient of variation. Patients filled out a 3-day food diary to quantify energy intake and the proportions of calories from carbohydrates, fats and proteins, and they wore Sensewear Armbands to estimate spontaneous TEE and footsteps walked. Glucose tolerance status was determined using oral glucose tolerance tests.

**Results:** Patients with CF with normal and impaired glucose tolerance had fewer glucose fluctuations than patients with CFRD ( $p < 0.05$ ). However, linear regression models used to determine whether nutrition or energy expenditure affects glucose fluctuations demonstrated that energy, the proportion of carbohydrates, of fat and of protein, TEE or the number of footsteps walked did not affect glucose fluctuation indexes ( $p > 0.05$ ).

**Conclusions:** TEE and the proportion of energy from carbohydrates did not affect glucose fluctuations in adults with CF.

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### R É S U M É

**Objectifs :** Déterminer les facteurs modifiables qui affectent la variabilité glycémique chez les personnes atteintes de la fibrose kystique (FK). Le diabète associé à la fibrose kystique (DAFK) est la complication la plus fréquente de la FK, dont la présence augmente la morbidité et la mortalité chez les patients. Les patients atteints de la FK (DAFK ou non) montrent potentiellement des fluctuations glycémiques nuisibles et des excursions glycémiques comparativement aux adultes en santé. Il a été démontré que l'apport en glucides et l'exercice affectent la glycémie. Par conséquent, notre hypothèse était que le pourcentage de l'apport énergétique provenant des glucides et la dépense énergétique totale (DÉT) influençaient les fluctuations glycémiques chez les adultes atteints de FK.

#### Mots clés :

diabète associé à la fibrose kystique  
fluctuations glycémiques  
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provenant des glucides  
dépense énergétique totale

\* Address for correspondence: Rémi Rabasa-Lhoret, MD, PhD, IRCM, 110, avenue des Pins Ouest, Montréal, Québec H2W 1R7, Canada.

E-mail address: [Remi.Rabasa-Lhoret@ircm.qc.ca](mailto:Remi.Rabasa-Lhoret@ircm.qc.ca)

**Méthodes :** Une étude transversale regroupait 36 patients atteints de la FK, chez qui des systèmes de surveillance de la glycémie en continu étaient installés.

Les fluctuations glycémiques étaient ensuite quantifiées à l'aide de 3 indices : l'amplitude moyenne des excursions glycémiques, l'écart type et le coefficient de variation. Les patients remplissaient un journal alimentaire de 3 jours pour quantifier l'apport énergétique et les pourcentages des calories provenant des glucides, des lipides et des protéines, et portaient un SenseWear pour estimer la DÉT et le nombre de pas effectués. La tolérance au glucose était déterminée à l'aide d'hyperglycémie provoquée par voie orale.

**Résultats :** Les patients atteints de la FK ayant une tolérance normale ou intolérants au glucose montraient moins de fluctuations glycémiques que les patients atteints de DAFK ( $p < 0,05$ ). Cependant, les modèles de régression linéaire utilisés pour déterminer si l'alimentation ou la dépense énergétique affectent les fluctuations glycémiques démontraient que l'énergie, le pourcentage de glucides, de lipides et de protéines, la DÉT ou le nombre de pas effectués n'affectaient pas les indices de fluctuations glycémiques ( $p > 0,05$ ).

**Conclusions :** La DÉT et le pourcentage d'énergie provenant des glucides n'affectaient pas les fluctuations glycémiques chez les adultes atteints de FK.

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## Introduction

Cystic fibrosis (CF) is the most common autosomal recessive genetic disease among Caucasians. CF is characterized by an accumulation of thick mucus in various organs, including the lungs and the pancreas. Consequently, patients with CF often have recurrent lung infections and exocrine pancreatic insufficiency (1). The most common complication of CF is CF-related diabetes (CFRD), and its presence increases morbidity and mortality in patients (1). The pathophysiology of this complication is not completely understood, but it is known that it is caused mainly by a decrease in insulin secretion (2–7). Also, our group and others have demonstrated that patients with CF, with and without CFRD, have increased glucose excursions and/or glucose fluctuations when compared to healthy subjects (7–9).

Studies have established that glucose fluctuations and hyperglycemia are possibly harmful (10–12). A study published in 2006 demonstrated that glucose fluctuations were positively associated with levels of a marker of oxidative stress, 8-iso prostaglandin F<sub>2</sub> alpha, in patients in type 2 diabetes (10). In addition, Meugnier et al. observed that in healthy adults, hyperglycemia increased gene expression of FOXO1A and other proteins involved in scavenging reactive oxygen species, including metallothioneins (11). In the same population, hyperglycemia and glucose fluctuations have been shown to increase the production of inflammatory markers, such as interleukin-6 and C reactive protein (12). CF is a disease associated with decreased insulin secretion (2–7) and increased inflammation (1), so determining the modifiable factors affecting glucose variability is crucial.

Therefore, the aim of this study was to quantify glucose fluctuations using mathematically calculated indexes in adults with CF and to determine whether they are modulated by total energy consumption, by the proportions of calories from carbohydrates, fat and protein as well as by total energy expenditure (TEE) and/or the number of footsteps. Because carbohydrate intake is one of the leading factors affecting blood glucose values (13), and because physical activity can affect glycemic control (14,15), we hypothesized that the proportion of calories from carbohydrates and TEE would modulate glucose fluctuations in patients with CF. To our knowledge, no published reports explore the effects of modifiable factors on glucose fluctuations in persons with CF.

## Methods

This cross-sectional study included 36 adults with CF (18 men and 18 women) and is a subanalysis of a larger project studying CFRD. The protocol was approved by the Research Ethics Committees of

the Centre Hospitalier de l'Université de Montréal (CHUM) and the Institut de recherches cliniques de Montréal (IRCM). This work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). Informed consent was obtained from all human subjects. All CF subjects were recruited from the CHUM and tested at the IRCM. Participants were excluded if they were taking medication affecting metabolism, were pregnant or were experiencing pulmonary exacerbations diagnosed by a CF pulmonologist of the CHUM in the previous month.

All patients with CF had continuous glucose monitoring systems (CGMSs) (Gold, Medtronic; Pointe-Claire, Québec, Canada) installed for 72 hours. The CGMS allows the measurement of interstitial glucose values every 5 minutes and was calibrated using capillary blood glucose levels, according to the manufacturer's recommendations. The accuracy of CGMSs in CF has been previously established (16).

Glucose fluctuations were quantified using 3 indexes: mean amplitude glucose excursion (MAGE), standard deviation (SD) and coefficient of variation (%CV) (GStat, University of Cambridge, Cambridge, UK). The MAGE calculates the average amplitude of glucose excursions (increase or decrease in blood glucose) of more than 1 SD from the mean. SD is the standard deviation of the glucose values obtained during the 3-day period and %CV is the coefficient of variation (SD/mean) of those values (17).

All patients also filled out 3-day food diaries for the same days during which they wore the CGMS. Using Food Processor SQL (Esha Research, Salem, Oregon, USA) and the 2007 Canadian Nutrient File as well as food labels, if needed, a registered dietitian analyzed 3-day food diaries, and these analyses were reviewed by a trained second person. Average daily proportions of calories from carbohydrates (% carbohydrates), fat (% fat) and protein (% protein) as well as the average daily energy consumed (kcal/day) were used for our analysis.

The average daily spontaneous (nonstructured physical activity) TEE (kcal/day) and the average number of footsteps (steps/day) walked during the 3-day period when the CGMS was worn were estimated by using a Sensewear Armband (SWA) (Sensewear Pro3 Armband; BodyMedia, Pittsburgh, Pennsylvania, USA). This biaxial accelerometer has been validated to estimate these 2 parameters in CF (18).

Patients without CFRD who were included in the present study underwent oral glucose tolerance tests within 4 months of the beginning of their participation to determine their glucose tolerance according to the guidelines of the Canadian Diabetes Association (19). Patients with CFRD underwent different treatments. Of that group, 5 patients took insulin, 2 patients took sitagliptin and 9 were treated with dietary intervention alone. Lung function (forced expiratory volume in 1 second [FEV<sub>1</sub> L]) was also measured using the National Health and Nutrition Examination Survey (NHANES III)

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