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Cystic fibrosis–related diabetes—adherence to screening at a large clinical center

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Background: Cystic fibrosis (CF)-related diabetes (CFRD) is increasing in incidence in people with CF (PwCF) as life expectancy increases with the advent of CF transmembrane conductance regulator (CFTR) modulator treatments. Current Cystic Fibrosis Foundation screening guidelines, last updated in 2010, recommend screening for CFRD with a 2-hour oral glucose tolerance test (OGTT) annually starting at 10 years of age [1]. Prior studies have demonstrated that centers with higher rates of screening with OGTTs diagnose CFRD earlier and have slower rates of pulmonary decline [2]. Questions remain as to the best way to screen for diabetes in PwCF given their complexity. The aim of our study was to describe adherence rates of ordering OGTTs and completion rates of OGTTs at Michigan Medicine in CF populations.

Methods: The cohort was defined as PwCF who were eligible for screening with an OGTT between 2010 and 2021. We excluded patients with a diagnosis code of CFRD. We defined screen-eligible years as number of years between 2010 and 2021 in which the CF patient should have been screened with an OGTT. We defined number of OGTT tests ordered per patient by summing number of OGTT orders performed per year over the period. We defined number of OGTT tests completed per patient by summing number of completed OGTT tests for the period. We defined order adherent as having a percentage ordered per patient of 75% or greater. We defined test adherent as having a percentage performed per patient of 75% or greater. We analyzed the differences in these measures based on race, gender, and age and examined the outcomes of screening (pre-diabetes or diabetes) based on OGTT results and glycosylated hemoglobin (HbA1c).

Results: At Michigan Medicine, in all patients eligible for screening with an OGTT, there was a 16.5% center-level rate of ordering OGTTs and a 13.8% rate of screening with completed OGTTs. Patients completed 83% of OGTTs and 100% of HbA1c tests ordered. Of OGTTs completed, 24% screened positive for pre-diabetes and 3.4% for diabetes. Of HbA1c performed, 31% screened positive for pre-diabetes, and 1.2% screened positive for diabetes. There were significant differences according to age in screening ($p < 0.01$) and completion ($p < 0.01$) rates, with higher rates of screening in younger than older patients, but not according to gender or race (Table 1).

Conclusions: Overall, adherence rates to OGTT ordering and completion were suboptimal. Patients had a higher adherence rate to diabetes screening with HbA1c than to OGTTs, and ordering adherence was higher for pediatric than adult patients. Although current CFF guidelines recommend the OGTT as the standard of screening for CFRD, oral glucose tolerance testing is more burdensome and takes more time to complete than HbA1c testing in a patient population that already has high health care use. Continued analysis of our data is needed to determine outcomes of screening, specifically trends in body mass index, pulmonary function tests (forced expiratory volume in 1 second, forced expiratory flow at 25% and 75% of pulmonary volume), number of hospitalizations, and variations in insulin use.

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Table 1 (abstract 3):
Order and test adherence rates according to gender, race, age range, and age group

	Order Adherent (>/= 75%)	Order Non-Adherent (< 75%)	p-value	Test Adherent (>/= 75%)	Test Non-Adherent (< 75%)	p-value
Overall Adherence	12.9 (60)	87.1 (405)		71.8 (135)	28.2 (53)	
Gender			p = 0.636			
Female	51.7 (31)	48.4 (196)		45.2 (61)	47.2 (25)	p = 0.535
Male	48.3 (29)	51.6 (209)		54.8 (74)	52.8 (28)	
Race			p = 0.511			p = 0.152
Caucasian	100 (60)	91.9 (372)		97 (131)	94 (50)	
African American	0 (0)	2.7 (11)		0.7 (1)	6 (3)	
Asian	0 (0)	1.0 (4)		0 (0)	0 (0)	
American Indian or Alaska Native	0 (0)	0.5 (2)		0 (0)	0 (0)	
Other or Unknown	0 (0)	3.9 (16)		0 (0)	0 (0)	
American Indian or Alaska Native	0 (0)	0.5 (2)		0 (0)	0 (0)	
Other or Unknown	0 (0)	3.9 (16)		0 (0)	0 (0)	
Age Group (yrs)			p < 0.01			p < 0.01
10-19	80 (48)	24 (97)		52.6 (71)	64.2 (34)	
20-29	20 (12)	27.4 (111)		45.2 (61)	35.9 (19)	
30-39	0 (0)	14.8 (60)		2.2 (3)	0 (0)	
40-49	0 (0)	14.3 (58)		0 (0)	0 (0)	
50+	0 (0)	19.5 (79)		0 (0)	0 (0)	
Adult vs. Pediatrics			p < 0.01			p < 0.01
Adult (>/= 18 yrs)	31.7 (19)	80.5 (326)		59.3 (80)	39.6 (21)	
Pediatrics (< 18 yrs)	68.3 (41)	19.5 (79)		40.7 (55)	60.4 (32)	

screening on clinical outcomes by center: A CF patient registry study. *J Cyst Fibros* 2020;19(2):316–20.

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Role of hyperglycemia in cystic fibrosis pulmonary exacerbations

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Background: Hyperglycemia could affect treatment response during cystic fibrosis (CF) pulmonary exacerbations (PEx). We aimed to evaluate hyperglycemia prevalence during CF PEx, associations between hyperglycemia and PEx outcomes, and feasibility of continuous glucose monitoring (CGM) during PEx.

Methods: This was an ancillary study to the STOP2 study—a multicenter randomized clinical trial evaluating the efficacy and safety of different durations of intravenous (IV) antibiotics for PEx in adults with CF [1]. Random glucose levels measured clinically during the first 7 to 10 days of PEx treatment were captured. A subset of participants at four sites also consented to undergo CGM for 5 days, beginning at IV antibiotic day 1 to 4. Associations between hyperglycemia, defined as random glucose greater than140 mg/dL, and changes in weight and lung function between baseline (initiation of IV treatment), visit 2 (day 7–10), and visit 3 (14 days after completion of IV treatment) were evaluated using linear regression after adjustment for confounders.

Results: Random glucose measurements were available for 182 STOP2 participants (18.6% of 982 randomized in STOP2). Of these participants, 37% had CF-related diabetes (CFRD), 27% were taking insulin, mean ± SD age was 31.6 ± 10.8 years, and mean ± SD baseline percentage predicted forced expiratory volume in 1 second (FEV1pp) was 53.6 ± 22.5. Hyperglycemia was detected in 44% of these participants, and 61% of those with hyperglycemia had a diagnosis of CFRD. Table 1 shows the mean estimated differences in changes in FEV1pp and weight from baseline to visit 2 and visit 3 between those with and without hyperglycemia and taking and not taking insulin. No differences were detected according to hyperglycemia or insulin use at visit 2 or visit 3. Ten participants who were not taking insulin or oral hypoglycemic agents in the 4 weeks before study underwent CGM. Mean ± SD age was 30.1 ± 6.5 years, 70% were female, and mean ± SD baseline FEV1pp was 48.9 ± 21.0 L. Mean time at greater than 140 mg/dL was 24.6 ± 12.5%, and 9/10 participants spent more than 4.5% of the time at more than 140 mg/dL.

Conclusions: Hyperglycemia identified using random glucose testing was prevalent during CF PEx in patients with and without CFRD, but we did not detect an association between hyperglycemia and changes in lung function or weight with treatment. CGM is feasible and may be a useful tool in the inpatient setting.

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Comparison of meal-time dosing of rapid-acting insulin using carbohydrate counting versus fixed doses using continuous glucose monitoring in patients with cystic fibrosis–related diabetes

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Background: Optimizing prandial bolus insulin dosing is essential for cystic fibrosis (CF)-related diabetes (CFRD) management but the traditionally high-calorie diet prescribed to maintain ideal body mass index and the demands of close glucose monitoring make this difficult. This study leveraged continuous glucose monitoring (CGM) to compare fixed meal dosing with carbohydrate count–based insulin dosing.

Methods: People with CFRD treated with meal-time rapid-acting insulin were recruited. A dietician provided carbohydrate counting education, and insulin carbohydrate ratio was determined according to total daily insulin dose at the study start. Abbott Freestyle Flash Libre continuous glucose monitors were worn for 14 days. Participants used fixed mealtime insulin dosing for the first 7 days (fixed dosing week, FDW) and carbohydrate counting–based insulin dosing for the second 7 days (carbohydrate count week, CCW) using the 'rule of 500' to calculate insulin-to-carbohydrate ratio. We also compared the frequency and duration of hypo- and hyperglycemia of the two insulin delivery methods.

Results: Six (3 female, 3 male; aged 65 ± 7.7; 2 F508del homozygous, 2 F508del heterozygous, 2 with unknown mutation status) of the nine recruited participants had complete data (3 dropped out or had CGM malfunction). All subjects were on triple modulator therapy for at least 12 months. Average CFRD duration was 8.6 ± 2.9 years, glycosylated hemoglobin was 7.3 ± 0.5%, and weight was 55 ± 5.4 kg. Insulin to carbohydrate ratio ranged from 1:10 grams to 1:17 grams Average sensor glucose was not significantly different between FDW (7.27 ± 0.83 mmol/L) and CCW (7.04 ± 0.88 mmol/L) ($p = 0.8$). There were no differences in time in range (CCW, 984 ± 86 minutes; FDW, 919 ± 110 minutes; $p = 0.6$) or number of low-glucose events (FDW, 11; CCW, 9; $p = 0.6$).

Conclusions: Few studies have compared the efficacy of carbohydrate counting for dosing mealtime insulin with that of fixed pre-meal insulin doses. Larger studies that use CGM to optimize insulin to carbohydrate-

Table 1. (abstract 4):
Mean estimated difference (95% confidence interval) in changes in lung function and weight from baseline to visit 2 and visit 3 according to hyperglycemia and insulin use

	Change in ppFEV1 at visit 2	P value	Change in ppFEV1 at visit 3	P value	Change in weight at visit 2	P value	Change in weight at visit 3	P value
Hyperglycemia vs. no hyperglycemia	1.34 (-1.39, 4.08)	0.37	-1.15 (-4.01, 1.71)	0.43	0.33 (-0.11, 0.78)	0.15	0.34 (-0.31, 0.99)	0.31
On insulin vs. no insulin	0.41 (-2.33, 3.14)	0.77	-1.71 (-4.36, 0.94)	0.2	0.27 (-0.21, 0.75)	0.27	0.05 (-0.70-0.80)	0.89