11

Preliminary feasibility and value of home fertility testing for men with cystic fibrosis

A. Szczepanski[1], V. Vincent[1], A. Wardyn[1], L. Christon[2], K. Foil[3]. *[1]School of Medicine, University of South Carolina, Columbia, SC; [2]Department of Psychiatry, Medical University of South Carolina, Charleston, SC; [3]Department of Medicine, Medical University of South Carolina, Charleston, SC*

Background: An estimated 98% of men with cystic fibrosis (CF) are infertile because of congenital absence of the vas deferens [1], although most studies were conducted before wide recognition of milder genotypes and phenotypes. Limited data suggest that infertility rates may vary according to genotype [1,2]. Semen analysis is indicated for all men with CF [3], but barriers include pressing care needs, that some labs do not process semen, and that referrals may burden patients. The Food and Drug Administration–approved SpermCheck Fertility Home Test for Men is 96% accurate at detecting normal sperm count (>20 000 000 sperm/mL). This rapid qualitative immunodiagnostic test detects sperm using antibodies against sperm acrosome-specific protein analyte SP10. At-home semen analysis may be a valuable, feasible, cost-effective ($25/test) option for men with CF. This descriptive study aimed to assess feasibility and patient perceptions.

Methods: Men with CF who completed an online fertility survey were invited to receive a test kit and complete an interview about ease of use, interpretation, perceived accuracy and benefit, and feelings about results. With permission, interviews were recorded and transcribed; descriptive results are presented.

Results: Four men participated (Table 1). All had negative test results consistent with CF-related infertility. All found following instructions and reading results to be easy, believed results were accurate, and felt this type of test would be helpful to the CF community. None intended to alter family plans based on results. Several expressed relief that assumed infertility was confirmed. Descriptive feedback included:

P1: "It's nice to officially know. I guess there's less doubt in my head, like, "well, you know, I technically don't know." So now I believe it. For what it's worth I thought I had to go to a professional agency to get this done. Had I known this was so affordable and I could do it from home I probably would have done it back in my early 20 s."

P2: "I mean, I kind of expected the results that I got, but at the same time, it made me feel sad for a few seconds. Like the realization of it, but then like… ehh, well, I expected it."

P3: "I'm married… I had a pretty good idea I wasn't fertile, but it's good to have information on stuff and be able to pass information along."

P4: "I think it's just a way to confirm things. Because, you know, within clinic and stuff they talk about it but there's no real way of testing. They don't give you any options as far as how to test certain things."

Conclusions: These perspectives support continued investigation of home fertility tests for men with CF. Formal qualitative analysis was not completed because the number of participants was small. Future directions include a larger study, results correlation with conventional semen analysis and patient genotypes, and potential use of the SpermCheck Vasectomy kit, which detects lower sperm concentration (250 000 sperm/mL). Such tests may contribute to modern fertility insights and improve patient care.

Acknowledgements: This work was supported by the National Society of Genetic Counselors CF Special Interest Group.

References

[1] Ahmad A, Ahmed A, Patrizio P. Cystic fibrosis and fertility. *Curr Opin Obstet Gynecol* 2013;25(3).

[2] Dreyfus DH, Bethel R, Gelfand EW. Cystic fibrosis 3849+10 kbC >T mutation associated with severe pulmonary disease and male fertility. *Am J Respir Crit Care Med* 1996;153(2):858–60.

[3] Taussig LM, Lobeck CC, di Sant Agnese PA, Ackerman DR, Kattwinkel J. Fertility in males with cystic fibrosis. *N Engl J Med* 1972;287(12):586–9.

12

Using continuous glucose monitoring to predict disease progression and development of diabetes in youth with cystic fibrosis

A. Lorenz[1], L. Pyle[2], E. Towler[3], T. Vigers[3], S. Sagel[3], C. Chan[3]. *[1]University of Colorado School of Medicine, Aurora, CO; [2]Department of Biostatistics, University of Colorado Anschutz Medical Campus, Aurora, CO; [3]Department of Pediatrics, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO*

Background: Cystic fibrosis (CF)-related diabetes (CFRD) is one of the most common complications of CF and is associated with undernutrition, poor pulmonary function, and mortality. Clinical decline has been described up to 5 years before the diagnosis of CFRD and may be related to early dysglycemia. Continuous glucose monitoring (CGM) can detect early glucose abnormalities before they develop during a 2-hour oral glucose tolerance test, but no clear CGM based cut-points for predicting clinical decline in people with CF have been defined. Our aim was to explore CGM as a tool for prospectively predicting CF-relevant clinical outcomes in youth with CF.

Methods: This was a single-center, prospective analysis of data collected as part of the GlycEmic Monitoring in CF (GEM-CF) Study. Participants were aged 6 and older, diagnosed with CF, and followed at Children's Hospital of Colorado CF Center. Participants wore a CGM (iPro®2) between 2014 and 2018. Participants with diagnoses of CFRD taking insulin or other medications affecting glucose metabolism at time of CGM wear were excluded from this analysis. Information on the following variables was collected at baseline (time of CGM wear) and prospectively through early 2020: forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), body mass index z-score (BMI-z), time to diagnosis of CFRD, and time to insulin start. Mixed-effects models were used to test association between baseline CGM variables and change in BMI-z, FEV_1 percentage predicted (FEV_1pp), and FVC percentage predicted (FVCpp) over 1 and 3 years. Cox proportional hazards models were used to test the associations between baseline CGM variables and time to diagnosis of CFRD and time to insulin start.

Results: Seventy-five individuals with CF were included. Baseline age was 13.36 ± 3.48 years, 42 (56%) participants were female, and five (6.7%) were pancreatic sufficient. Baseline mean BMI-z was –0.04 ± 0.80, mean FEV_1pp was 95.9 ± 14.7%, and mean FVCpp was 102.7 ± 13.2%. Mean ± SD for the following CGM variables were average sensor glucose, 112 ± 15 mg/dL; percentage of time spent at greater than 140 mg/dL, 13.1 ± 13.2%;

Table 1 (abstract 11):
Participant characteristics

Table 1. Participant Characteristics

Participant	Age	Race	Genotype	Pancreatic Insufficient	Modulator	Prior semen analysis
1	29	Caucasian	F508del, not reported	N	Y	N
2	39	Caucasian	F508del homozygous	Y	Y	N
3	24	Caucasian	F508del homozygous	Y	Y	N
4	25	Caucasian	F508del, 2789+5G>A	N	Y	N

Table (abstract 12):

Table 1. Predictive value of CGM variables and outcomes of interest

CGM Variables	BMI Z-Score (3 year) †	FEV1 (3 year) †	FVC (3 year) †	Time to CFRD Dx ‡	Time to Insulin Start ‡
Mean Glucose	0.008	-0.027	-0.027	1.23 (1.03, 1.47)*	1.20 (1.05, 1.36)**
% Time Spent >140 mg/dL	0.007	-0.072	-0.089	1.22 (1.03, 1.44)*	1.16 (1.04, 1.29)**
% Time Spent >200 mg/dL	-0.016	0.109	-0.048	1.40 (0.78, 2.50)	1.53 (0.96, 2.42)
Coefficient of Variation	-0.015	0.152	0.056	1.06 (0.68, 1.65)	1.19 (0.85, 1.68)
MAGE	0.001	0.074	0.042	1.03 (0.95, 1.11)	1.09 (1.02, 1.16)*

†Value presented is the slope derived from fixed-effects models.
‡Value presented is the hazard ratio (95% confidence interval) for a 5-unit increase in the CGM variable.
*$p < 0.05$ ** $p < 0.01$.

percentage of time spent at greater than 200 mg/dL,1.3 ± 3.1%; coefficient of variation, 20 ± 6; and mean amplitude of glycemic excursion, 72 ± 35 mg/dL. CGM variables did not predict change in BMI-z, FEV_1pp, or FVCpp at 1 or 3 years after baseline (Table 1). For every 5-unit increase in CGM mean glucose and CGM percentage of time spent at greater than 140 mg/dL, there was a 22% to 23% greater risk of developing CFRD ($p < 0.05$). The odds of insulin start was also greater with every 5-unit increase in these CGM parameters ($p < 0.01$, Table 1). A 5-unit change in CGM mean amplitude of glycemic excursion, a measure of glycemic variability, was also associated with greater risk of starting insulin ($p < 0.05$, Table 1).

Conclusions: The CGM variables explored in this group of relatively healthy, young individuals with CF who were not yet on insulin did not predict clinical decline as measured according to 1- and 3-year changes in BMI z-score, FEV_1pp, or FVCpp, although mean glucose, percentage of time spent at greater than 140 mg/dL, and mean amplitude of glycemic excursion on CGM were associated with greater odds of developing CFRD and requiring insulin over the study period.

Acknowledgements: This study was supported by funding from Cystic Fibrosis Foundation (CFF) grant CHAN16A0, CFF Student Traineeship Award LORENZ22H0, and UL1 TR001082 (CCTSI and REDCap).

13

A North American provider survey of cystic fibrosis–related diabetes screening practices

R. Hicks[1,2], K. Larson Ode[3], T. Vigers[4], A. Martinez[5], C. Chan[4]. *[1]Pediatric Endocrinology, University of California Los Angeles, Los Angeles, CA; [2]Pediatric Endocrinology, Miller Children's and Women's Hospital, Long Beach, CA; [3]Pediatric Endocrinology, University of Iowa, Iowa City, IA; [4]Department of Pediatrics, Children's Hospital Colorado, University of Colorado Anschutz Medical Campus, Aurora, CO; [5]Pediatric Neurology, University of California Los Angeles, Los Angeles, CA*

Background: Cystic fibrosis (CF)-related diabetes (CFRD) is highly prevalent in approximately 15% of teens and 50% of adults with CF. CFRD is associated with declining pulmonary function, pulmonary exacerbations, poor nutritional status, and greater risk of mortality; its onset is often insidious. Guidelines recommend a 2-hour oral glucose tolerance test (OGTT) annually for people with CF aged 10 and older, but Cystic Fibrosis Foundation patient registry data have demonstrated consistently low OGTT screening rates (<30% of adults, <60% of youth nationally). Our aims were to conduct a survey of U.S. CF center directors and endocrinologists affiliated with the EnVision program to characterize CFRD screening practices, better understand provider perceived barriers to screening, and identify potential strategies to increase CFRD screening.

Methods: Two REDCap surveys consisting of 23 questions pertaining to CFRD screening practices were developed. Questions were asked regarding CF center practice settings and population demographic characteristics, details about how OGTTs were performed, use of alternate diabetes screening strategies, and perceived barriers. The endocrinologist survey included additional questions regarding interpretation and practice management based on OGTT results and other measures of glycemia. The link to survey 1 was emailed to CF center directors, who could designate an alternate individual at their discretion. The link to survey 2 was sent out via group email distribution to mentors and mentees within EnVision I and II, a CFF program to foster endocrinologists in the care of CF-related endocrinopathies. Survey responses were summarized using means and standard deviations or medians and first and third quartiles for continuous variables and frequencies with percentages for categorical variables. Practices were compared using t-tests or chi-square tests depending on distribution of variables. Data were summarized and analyzed in R.

Results: The survey response rate was 20.3% (59/290) for CF centers and 62.5% (25/40) for endocrinologists. Fifty-seven percent of CF centers surveyed obtain 0- and 120-minute glucose values; 38% obtain 0-, 60-, and 120-minute values; and 4% obtain additional values. Of endocrinologists surveyed, 20% obtain 0- and 120-minute glucose values, 72% obtain 0-, 60-, and 120-minute values, and 8% obtain additional values. Forty-nine percent of CF centers reported greater than 50% OGTT completion in the previous year. Centers that always or almost always provide reminders to patients are about 5 times as likely to have OGTT completion rates greater than 50% ($p = 0.02$). CF centers and endocrinologists reported using alternative strategies to evaluate for diabetes, such as glycosylated hemoglobin (23.0%, 28.6%), fasting plasma glucose (17.7%, 20.8%), continuous glucose monitoring (10.8%, 18.2%), and fingerstick monitoring (20%, 15.6%), respectively.

Conclusions: Although OGTT is considered the gold standard screening method for CFRD, practice variation exists, completion rates are suboptimal, and many providers are using alternate glycemia screening methods. Having a reminder system for scheduling OGTTs may increase completion rates. Studies to improve our approach to CFRD screening are urgently needed.

Acknowledgements: This work was supported by the Cystic Fibrosis Foundation (grants HICKS19GE0, MORAN19GE3) and STATNET (grant ZEMANI20Y7).