than previously reported. Based on our limited experience, sweat chloride testing may be useful to identify potential adherence problems and to emphasize the importance of consistent ELX/TEZ/IVA use to achieve the best outcomes.

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GI/NUTRITION

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Body mass index versus mid-upper arm circumference: Can we replace the gold standard?

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Background: Body mass index (BMI) has long been used as a measure and predictor of health in the general population. For people with cystic fibrosis (PwCF), it has been established as the gold standard for nutrition assessment because optimal BMI correlates with better lung function, measured according to forced expiratory volume in 1 second (FEV_1), although as in the general population, BMI use in PwCF has limitations, because it does not distinguish lean body mass from fat mass [1]. The rise in obesity in PwCF prompted our search for a better predictor of nutritional status in the pediatric CF population [2]. Mid-upper arm circumference (MUAC) is an established measure of pediatric nutrition status and predictor of fat mass [3]. In 2021, our care center began including MUAC measurements as part of our nutrition assessment in children with CF. The objective of this study was to compare BMI and MUAC nutrition assessment methods in children with CF.

Methods: An institutional review board–approved, single-center retrospective analysis was performed on 87 patients with an average age of 10.7 ± 4.2. Data were collected on BMI, MUAC, and FEV_1 from April 2021 to March 2022. Correlation was assessed between BMI Z-scores and MUAC Z-scores, between MUAC Z-scores and FEV_1, and between BMI Z-scores and FEV_1. Subsequent-visit BMI, MUAC, and FEV_1 measurements were obtained in 34 patients.

Results: BMI and MUAC Z-scores had a statistically significant positive linear correlation. MUAC Z-scores identified more patients as malnourished than BMI Z-scores. At the baseline visit, MUAC Z-score identified 12 of 75 children (16%) with CF who were identified as well nourished according to BMI Z-score as having mild or moderate malnutrition (Cohen kappa statistic=0.46, 95% CI, 0.27-0.65). FEV_1 did not differ significantly between those who BMI and MUAC identified as well-nourished and those who only MUAC identified as malnourished. Of the three values (BMI, MUAC, FEV_1), FEV_1 at baseline remained the best predictor of FEV_1 at the subsequent visit.

Conclusions: Based on our review, these results lend support to prior evidence that more patients were identified as malnourished according to MUAC than BMI, but because of the small sample size and retrospective nature of this review, a larger, multicenter study on MUAC as a nutrition assessment method in children with CF is necessary to determine correlation between MUAC and lung function.

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Impact of elexacaftor/tezacaftor/ivacaftor on body composition in a small cohort of youth with cystic fibrosis

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Background: The triple combination cystic fibrosis (CF) transmembrane conductance regulator (CFTR) modulator elexacaftor/tezacaftor/ivacaftor (ELX/TEZ/IVA) has been shown to be highly effective in improving pulmonary function, increasing body mass index (BMI), and reducing pulmonary exacerbations [1,2]. With increases in BMI and recent reports of obesity in the CF population, closer evaluation of the impact of ELX/TEZ/IVA on body composition may inform metabolic disease risk.

Methods: This was a secondary analysis of a prospective observational study assessing annual, frequently sampled oral glucose tolerance tests (OGTTs) and dual-energy X-ray absorptiometry (DXA) in people with CF aged 6 and older. Inclusion criteria were confirmed diagnosis of CF treated with ELX/TEZ/IVA and available DXA scan results before and after triple combination therapy. Exclusion criteria were use of medications affecting glucose homeostasis, including insulin; pulmonary exacerbations or admissions in the 8 weeks before the study visit; and pregnancy. Paired *t*-tests were used to compare normally distributed variables and Wilcoxon signed rank tests for non-normally distributed variables. Measurements of body composition using DXA included body free fat mass adjusted for height (FFMI) and total body fat mass adjusted for height (FMI). OGTTs with sampling at 0, 10, 30, 60, 90, and 120 minutes for glucose, insulin, and c-peptide were obtained. Integrated area under the curve (iAUC) for each was calculated. Homeostatic model assessment of insulin resistance (HOMA2 IR) was calculated as an estimate of insulin sensitivity. Spirometry data from the most-recent clinic visit were obtained through chart review.

Results: Eight participants (median age 22.1, interquartile range (IQR) 16.2–28.2; 87.5% male were included in the analysis. Mean weight z-score was −0.52 (IQR −1.51 to −0.31), and mean BMI z-score was −0.11 (IQR −0.7–0.87). Median time on ELX/TEZ/IVA was 11 months (IQR 10.8–11.3). All participants were pancreatic insufficient, and 50% were homozygous F508del. Table 1 presents clinical outcomes before and after ELX/TEZ/IVA. Weight increased from 58.6 kg to 68.9 kg ($p = 0.01$), whereas BMI z-score did not change. FMI increased ($p = 0.04$), but FFMI did not change. Glucose iAUC did not change ($p = 0.23$). Insulin secretion measured according to iAUC and C-peptide iAUC increased ($p = 0.02$), and HOMA2 IR, as an index of insulin resistance, increased ($p = 0.01$).

Conclusions: In a small cohort of people with CF treated with ELX/TEZ/IVA for less than 1 year, weight and FMI increased, whereas FFMI did not change. OGTT-derived estimates of insulin secretion (iAUC) and insulin resistance (HOMA2 IR) increased. Larger studies are needed to evaluate the effects of highly effective triple therapy on body composition, particularly body fat distribution, and its association with insulin resistance in subjects with CF.

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Table 1 (abstract 189):
Order and test adherence rates according to gender, race, age range, and age group

Table 1: Outcomes Before and After ELX/TEZ/IVA (N=8)				
Outcome measure	**Visit 1**	**Visit 2**	**Difference**	**P-value**
Weight z-score	-0.52 (-1.51, -0.31)	0.18 (-1.27, 0.66)	0.52 (0.27, 1.09)	**0.014**
BMI z-score	-0.11 (-0.69, 0.86)	0.89 (0.06, 1.46)	0.35 (0.21, 1.11)	0.18
FEV1 % predicted	79 (5, 101.75)	86 (57.5, 102.25)	3 (1, 8)	**0.076**
FVC % predicted	80 (62, 104.25)	88.5 (73.5, 104.5)	6 (0.5, 14.5)	0.09
% fat mass	19.9 (17.6, 28.57)	25.7 (19.52, 28.95)	4.75 (0.92, 5.77)	**0.03**
% fat free mass	0.8 (0.71, 0.82)	0.74 (0.71, 0.81)	-0.048 (-0.05, -0.01)	**0.03**
Fat mass index	4.12 (3.07, 6.67)	6.29 (4.08, 7.49)	1.55 (0.48, 2.11)	**0.014**
Fat free mass index	17.4 (15.73, 17.77)	17.71 (16.53, 18.01)	0.43 (0.05, 1.008)	**0.14**
Glucose iAUC	6668.8 (4850.7, 8548.8)	5760.7 (4269.6, 8459.2)	-1021.3 (-2935.1, -244.0)	**0.23**
Insulin iAUC	701.37(198.1, 2103.1)	1652.1 (929.8, 3228.5)	962.5 (522.3, 2217.5)	**0.021**
Cpeptide iAUC	46537.65 (36232.73, 62363.49)	83660.81 (66735.62, 121036.69)	36330.73 (25330.39, 46849.99)	**0.021**
HOMA2 IR	0.73 (0.61, 0.78)	1.25 (0.83, 1.61)	0.46 (0.35, 0.92)	**0.014**
*Data presented as median (IQR)				

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[1] Middleton PG, Mall MA, Drevinek P, McKone EF, Polineni D, *et al.* Elexacaftor/tezacaftor/ivacaftor for cystic fibrosis with a single Phe508del allele. *N Engl J Med* 2019;381(19):1809–19.

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Hyperosmolar salt concentrations slow digestion of milk and meconium by pancreatic enzymes

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Background: Meconium ileus (MI) is a life-threatening presentation of cystic fibrosis (CF) that occurs in approximately 20% of newborns with CF [1]. Current treatments with hyperosmolar or N-acetylcysteine (NAC) enemas often fail to relieve MI. Approximately 75% of newborns with MI ultimately require surgery [2]. Most newborns with MI have pancreatic insufficiency, indicating a possible role for pancreatic enzymes in the pathogenesis and treatment of MI. We find that meconium from CF pigs is digestible with pancreatic enzymes, but it does not break down in NAC or hypertonic solutions. Because hypertonic solutions are often used to treat MI, our goal was to determine how salt concentration affects pancreatic enzyme function using milk and meconium as substrates.

Methods: To compare digestion kinetics at different salt concentrations, we used powdered milk in water at 31.9 g/L. We added different NaCl concentrations over a range of doses with a maximum range of 333 mM. Because pH influences pancreatic enzyme function, we buffered the solutions at pH = 7.0 with 3.3 mM piperazine-N, N′-bis. We added 4.2 units of lipase/mL of mixed pancreatic enzymes (Epizyme) and then assessed the digestion of milk at 37°C kinetically by measuring absorbance at 600 nm every 5 minutes with a plate reader. In ongoing studies, we are digesting 0.7-g pieces of CF pig meconium with 10 mg/mL of mixed pancreatic enzymes in different NaCl concentrations at 37°C with constant agitation. We measure meconium digestion at 16 hours by comparing release of pigments (A_{405}) and residual weight of meconium solids.

Results: In the absence of added salt, pancreatic enzymes rapidly clarified powdered milk, decreasing the A_{600}. Increasing NaCl concentrations at doses above 0.0833 M decreased the rate of enzymatic digestion in a dose-dependent manner. At 0.166 M NaCl, enzymatic digestion of milk was approximately half as fast as the samples without added salt (Figure 1). We compared digestion of CF meconium pieces by pancreatic enzymes in normal saline (0.15 M) and 7% NaCl (1.1 M) and found that residual meconium was lower in normal saline.

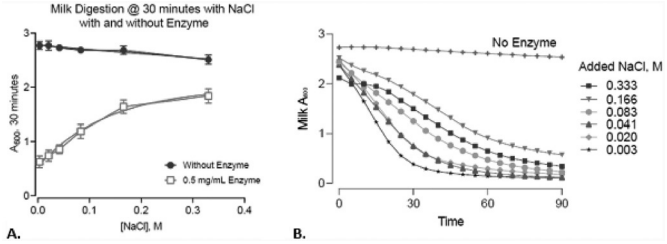

Figure 1. Pancreatic enzyme function is optimal in low salt. Dry powdered milk was dissolved in different [NaCl]. We measured milk digestion by decreasing absorbance at 600 nm using a plate reader at 37°C. Epizyme 4.2 units of lipase/mL was added to wells unless indicated. A. Residual milk signal at 30 minutes was lowest with low NaCl concentrations. Symbols represent means and standard deviations for three experiments. B. Milk digestion kinetics were faster at lower NaCl concentrations. Representative experiment, symbols are the mean from three wells.