Weight changes after initiating Elexacaftor/Tezacaftor/Ivacaftor in Patients with Cystic Fibrosis

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Abstract

Background: Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) modulators have varying levels of benefit regarding weight gain and growth, ultimately improving lung function and decreasing mortality rates in Cystic Fibrosis (CF) patients. The newly approved triple combination therapy (TCT) has shown weight gain benefits in clinical trials, but its long-term effects have yet to be studied in a site-wide setting. **Methods:** This retrospective study of 106 adult and pediatric CF patients on triple combination therapy for a year. We measured Body Mass Index (BMI) and BMI percentile changes and compared changes before and one year after initiation of TCT **Results:** TCT use showed weight gain over one year by increasing BMI in adult patients by 1.48 kg/m ^{2} (p-value < 0.0001). Pediatric patients saw significant benefit in BMI percentile with an average gain of 8.34 percentile (p-value= 0.0047). **Discussion:** The results of this study suggest that the new triple combination therapy improves BMI and BMI percentile in CF patients. This finding will help future CFF guidelines navigate the era of new modulators and the changes in baseline health that come with it.

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Discussion: The results of this study suggest that the new triple combination therapy improves BMI and BMI percentile in CF patients. This finding will help future CFF guidelines navigate the era of new modulators and the changes in baseline health that come with it.

Introduction

Cystic Fibrosis (CF) is a life-threatening, autosomal recessive disorder caused by the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene mutation. The mutation causes the absence or dysfunction of the CFTR protein that controls the movement of essential ions—mainly chloride, sodium, and bicarbonate—through the apical membrane in select epithelial cells[1]. The alteration of this protein impairs many organs, including the lungs, sinuses, pancreas, liver, and gastrointestinal tract.

While pulmonary insufficiency is the cause of death for most cystic fibrosis patients, many suffer from malnutrition[1]. This complication of CF is a multifactorial process. There is pancreatic insufficiency which can start as early as in fetal stages[2], severely impairing fat absorption[3]. Other nutrients such as carbohydrates, proteins, and fat-soluble vitamins A, D, E, and K are underutilized. Additionally, CF patients frequently have gastrointestinal problems, including cramping, bloating, and gastroesophageal reflux disease, making the consumption of extra calories painful and difficult[4].

CF patients have a higher resting energy expenditure than the non-CF population; this is more prominent in patients with advanced lung disease who consume more energy to maintain respiratory demands[5]. The

combination of inadequate nutrient absorption and calorie consumption and a higher resting energy expenditure create the persistent condition of negative energy balance and subsequent malnutrition and weight loss.

Nutritional status is assessed in many ways. In clinical practice, body mass index (BMI) strongly correlates with disease progression, as low body weight and BMI are consistently associated with increased risk of mortality and severity of pulmonary disease[6]. CF patients who maintain a high-fat diet and higher body weight have improved long-term survival[7]. Malnourished CF patients usually increase lung function–clinically monitored through the amount of forced expiratory volume in one second ($FEV_{1)}$–when they gain weight and increase their BMI[8]. Also, there is a correlation between a higher BMI and increased bone mineral density in adult CF patients; this risk factor is an important finding, as adequate nutrition and the corresponding increase in body weight could help prevent osteopenia and osteoporosis[9].

Maintaining an adequate body weight in CF patients has been traditionally difficult. The current Cystic Fibrosis Foundation (CFF) guidelines recommend that the nutrition and growth of CF patients are monitored very closely. CFF care teams keep track of nutrition in their patients by recording weight, height, and BMI quarterly. Patients 20 years and older have a BMI goal of 22 kg/m^2 for females and 23 kg/m^2 for males[10]. CF pediatric patients two years and older should remain above or equal to the 50^{th} percentile in BMI using the CDC growth charts[11]. A multi-disciplinary team consisting of a pulmonologist, dietician, gastroenterologist, endocrinologist, social worker, and psychologist ensures that each patient receives assistance for every aspect of their nutritional needs. This means actively addressing malnutrition complications, including pulmonary and GI issues, inadequate food intake, impaired glucose tolerance, and depression/anxiety. CF care teams emphasize nutrition and adequate body weight in their plan of care to preserve lung function and decrease the risk of mortality in their patients.

In recent years, the treatment of CF has focused on using CFTR modulators to restore function to the CFTR protein. Currently, there are four modulators on the market, but only two are considered highly effective modulator therapies: ivacaftor and the recently approved elexacaftor/tezacaftor/ivacaftor triple combination therapy (TCT)[12]. While increased weight gain happens with all the modulators, the extent to which the patient sees benefit is related directly to the mutation-specific modulator. Studies consistently report improved body weight and BMI in patients on ivacaftor, less significant weight gain on lumacaftor/ivacaftor, and only a modest weight promotion in patients on tezacaftor/ivacaftor. The only widely known information on the correlation of weight gain with TCT is based on two preliminary clinical trials that were relatively short-term—only 4 and 24 weeks long. The subjects enrolled in these clinical trials did see an improvement in their body weight and BMI[13]. However, long-term data are lacking.

The introduction of CFTR modulators has led to improved weight gain in CF patients, which has led to an increased opportunity for excess weight and obesity in some patients. In 2014, one CF center found that 15% of their patient population was overweight, with another 8% meeting the criteria for obesity[14]. Theoretically, the initiation of even more efficacious modulators could increase that prevalence by further improving the mechanisms of benefit. Ivacaftor has possibly induced weight gain by increasing the amount of sodium bicarbonate in the gut, which helps improve intraluminal adhesions and causes positive changes in gut flora[15]. Patients reported increased digestion and food consumption while on ivacaftor; this improvement would help patients gain weight by allowing an enhanced ability to consume more calories[16]. Lastly, other studies have shown that ivacaftor improved weight gain by decreasing resting energy expenditure and gut inflammation while increasing fat absorption[17].

The nutritional health of CF patients is a delicate balance between malnutrition and excess weight, with unique health risks presented with each situation. The introduction of the highly effective TCT modulator presents the possibility of weight gain; it is essential to be aware of these weight changes so that clinical care can be modified if needed. Our study aimed to identify the weight changes in CF patients receiving care at our CF center, after a year of taking TCT.

Methods

This study was a retrospective analysis of adult and pediatric CF patients aged 12 and above at the University of Iowa who received treatment with triple combination therapy for a year. It was approved by the Institutional Review Board. The study period was from November 2019, when the FDA approved TCT, until April 2021.

Patients included in the study had a confirmed diagnosis of CF, were on TCT, had a recorded weight within six months of TCT therapy, and had a follow-up visit approximately a year after initiation of TCT.

We excluded participants with CF-related metabolic syndrome, not on the TCT, those who did not return to the clinic for follow-up appointments, patients taken off medication one year after initiation, patients transplanted within the first year of TCT initiation, or those who were pregnant at the time of TCT initiation.

Variables studied include age at initiation, gender, race and ethnicity, CF mutations, and previous modulator taken by the subject, if applicable. Additionally, we identified the presence of pancreatic insufficiency, cystic fibrosis-related diabetes (CFRD) -identified by their use of chronic insulin-; gastroesophageal reflux disease (GERD) -identified by their use of proton pump inhibitors or H2 antagonists-. Nutritional supplementation and type (oral versus tube feeds) were also noted.

Baseline visits within six months prior to TCT initiation were captured, and the start date of TCT was used to identify follow-up visits approximately 3, 6, 9, and 12 ($\pm$3) months later. Only visits in which participants were clinically stable were chosen to represent baseline visits. Discharge from hospitalization data points was not used as baseline visits; in these cases, the prior clinic visit during which the patient was stable was chosen to represent baseline as long as it was within six months of initiation. For each visit, height, weight, and FEV_1 were recorded. BMI percentile was calculated for patients under 20 years old using the "CDC BMI Percentile Calculator for Child and Teen" [18] to account for continual growth. BMI was calculated for patients 20 years old and above by dividing weight (kg) by height (meter) squared. FEV_1 percent predicted values were calculated using the "Global Lung Function Initiative calculator for Spirometry" [19]. As they turned 20 between baseline and the post-one-year follow-up visit, five additional patients were excluded, so their BMI percentile could not be calculated at the follow-up visit. Any hospitalizations between the baseline and 12-month follow-up visits were captured, along with the length of stay and admission reasons.

The primary aim of this study was to assess the weight change in CF patients after 12 months of initiating TCT; a secondary aim was to identify potential contributing factors that may promote weight gain in combination with highly effective modulator therapy such as TCT.

The change in BMI or BMI percentile at 12 months from TCT initiation was calculated for all patients included in the analysis. A Wilcoxon signed-rank test was used to compare pre-and-post-TCT BMI or BMI percentile. We conducted the analysis using SAS version 9.4 (SAS Institute, Inc., Cary, NC). P -values less than 0.05 were considered statistically significant.

RESULTS

Study Participants

Between October 2019 and May 2020, 124 patients initiated TCT. Nine patients were excluded from the analysis for the following reasons: two patients due to pregnancy during their baseline visits; five patients aged up to 20 years old during their first year on TCT and their BMI percentile could not be calculated after their 20th birthday; and two patients underwent bilateral lung transplantation. Finally, nine patients were excluded for being lost to follow-up after a year of TCT. Ultimately, 106 patients were included in the study and analyzed for weight gain while on TCT.

Of these patients, 60.4% were male, and 39.6% were female. Sixty-eight participants were 20 years or older, and 38 were under 20 years old. Sixty-two participants had the homozygous F508del genotype, while the other 44 had a heterozygous F508del genotype. Twelve participants were previously treated with ivacaftor, 18 were previously treated with tezacaftor/ivacaftor, 48 were previously treated with lumacaftor/ivacaftor,

and the remaining 28 participants had not been previously treated with a modulator. The participants' mean (SD) FEV1 percent predicted was 74.92 (26.31)%. Of all subjects, 86.8% were pancreatic insufficient based on their pancrelipase usage. Fifteen participants were identified as having CFRD; 60 had GERD. Twenty-six patients were on calorie-boosting supplementation; 24 used oral supplementation and two used tube feed. (Table 1)

BMI and BMI Percentile after one year on TCT

Subjects > 20 years old had a mean (SD) BMI of 24.21(4.62) kg/m^2 at baseline. In participants under 20 years old, the mean BMI percentile was 49.97 (24.75) percentile. After one year on TCT, both groups increased BMI in their respective measures. The 20 years and older group had a significant mean change in BMI of 1.48 (1.63) kg/m^2 (p-value < 0.0001). The group of pediatric patients aged < 20 years significantly increased their BMI percentile by an average of 8.34 (16.98) percentile (p-value= 0.0047).

BMI and BMI Percentile Change by Gender

The female group consisted of 26 participants in the adult population, while the male group consisted of 42 participants. At the end of the first year of TCT, the female group saw a mean increase in BMI of 1.51 (1.53) kg/m^2. The male group also increased with a mean change of 1.46 (1.71) kg/m^2. In the pediatric group, there were 16 females and 22 males. Females had an average increase in BMI percentile by 1.13 (15.7) percentile, while males had an average increase in BMI percentile of 13.59 (16.23) percentile.

BMI and BMI Percentile Change by Genotype

In the adult patient group, 35 adults were identified as having the homozygous F508del genotype, while the other 33 were heterozygous F508del genotype. In the homozygous genotype group, the mean positive change in BMI was 1.46 (1.52) kg/m^2, while the average change in the heterozygous group was a gain of 1.49 (1.77) kg/m^2. In the pediatric group, there were 27 children with the homozygous genotype; they had a mean increase in BMI percentile of 9.04 (15.83). Eleven children had an F508del heterozygous genotype; they had an average increase in BMI percentile 6.63 (20.26) percentile.

BMI and BMI Percentile Change by Lung Function

Lung function classification was based on the CFF's description of lung disease severity in their latest annual report[20]**.** In the adult group, 13 participants were found to have normal lung function, defined as a percent predicted FEV_1 ($ppFEV_1$) above or equal to 90%. These patients saw an increase in BMI by 0.92 (1.34) kg/m^2. Sixteen participants had a $ppFEV_1$ between 70 and 89%, indicating mild lung disease. They were found to have an average increase in BMI of 1.45(1.87) kg/m^2. The next group of participants was defined as having moderate lung disease based on a $ppFEV_1$ between 40 and 69%. Nineteen of the adult patients had lung function values within this range. The average increase in BMI in this population was 1.5 (1.83) kg/m^2. The last 16 adults have severe lung disease as their $ppFEV_1$ was [?] 40%. This population had the most significant increase in BMI with an average change of 1.94 (1.45) kg/m^2.

In the pediatric group, 26 children had normal lung function; the mean increase of BMI percentile in this group was 7.04 (17.8) percentile. Six children fell into the mild lung disease category and had an average increase in BMI percentile of 5.83 (11.99) percentile. The moderate lung disease category for pediatric participants consisted of 6 children. This group saw an average growth of 16.5 (17.6) percentile. There were no pediatric patients that fell into the severe lung disease category.

BMI and BMI Percentile Change by Previous Modulator Usage

In the adult patient group, 20 patients had never used a CFTR modulator prior to initiating triple combination therapy; out of the remaining adult patients, ten transitioned directly from ivacaftor, 23 from lumacaftor/ivacaftor, and 15 from tezacaftor/ivacaftor. The patients who were modulator naive had an average increase in BMI of 1.97 (1.86) kg/m^2. Patients transitioning from ivacaftor had a mean increase in BMI of 0.54 (1.41) kg/m^2. In comparison, those transitioning from lumacaftor/ivacaftor had a mean increase in

BMI of 1.12 (1.31) kg/m^{2,} and those transitioning from tezacaftor/ivacaftor experienced an average increase in BMI of 1.99 (1.60) kg/m^2.

In the pediatric group, eight patients were modulator naive, two were previously on ivacaftor, 25 were on lumacaftor/ivacaftor, and three were on tezacaftor/ivacaftor. The modulator naive group saw an average increase of the BMI percentile of 10.13 (23.01). Patients previously on lumacaftor/ivacaftor and tezacaftor/ivacaftor experienced a mean increase in BMI percentile of 9.32(4.95) and 4 (16.7) percentile, respectively. The group with two pediatric patients who were previously on ivacaftor alone saw an average decrease in the BMI percentile of 4.5 (4.95).

Discussion

Gaining and maintaining an appropriate weight has traditionally been a challenge for patients with CF. Malnourishment and underweight correlate with reduced lung function, the main contributor to death in CF patients. As a result, the CFF created guidelines on nutrition and growth to address inadequate weight and malnutrition. TCT showed great promise during clinical trials in boosting weight gain and resolving malnutrition; however, long-term data is necessary to understand its long-term effects better.

This study was a retrospective chart review that analyzed how BMI and BMI percentile changed over a year of TCT therapy in patients at our CF center. The results showed that, on average, TCT leads to a significant increase in BMI and BMI percentile in adult and pediatric patients, respectively. Our study included a heterogeneous group of CF patients followed at the University of Iowa Cystic Fibrosis Center, including those with significant lung disease and other conditions that may have been excluded from the trials. Additionally, we describe the modulator effect on weight over a more extended period than previously reported.

In order to better identify other variables that may play a role in weight gain, several subgroups were studied. In the adult population, male and female patients had a similar increase in weight with almost the same average increase in BMI. Surprisingly, the male and female pediatric groups experienced very different changes in BMI percentile after a year on TCT. While the female pediatric group only saw an average increase of BMI percentile of 1.13 percentile, male participants had a much higher increase in BMI percentile at 13.59 in comparison. These results suggest that some gender-specific differences in the young adult population need to be further explored

In the adult population, patients with the homozygous and heterozygous F508del genotypes had a similar average increase in BMI. In contrast, the homozygous F508del had a slightly higher increase in BMI percentile compared to the heterozygous genotype population.

Patients with more severe lung disease in the adult population had a more pronounced increase in their BMI. Patients with moderate lung disease saw the most significant change in BMI percentile in the pediatric population, followed by normal lung function. Patients with mild lung disease saw the most negligible benefit.

Finally, adult patients who were previously on tezacaftor/ivacaftor saw the most significant weight change, followed closely by modulator naive patients. Patients previously on lumacaftor/ivacaftor experienced less benefit on average, and patients on ivacaftor saw the slightest BMI change. In the pediatric population, modulator naive children saw the most significant weight change, followed by patients who were previously on lumacaftor/ivacaftor and then patients who were previously on tezacaftor/ivacaftor. The pediatric subgroup of patients who were previously using ivacaftor was the only population to show a decrease in BMI percentile; however, this group included only two patients.

There were a few limitations to this study. The COVID-19 pandemic reduced the number of in-person follow-up visits, as many quarterly clinic visits were converted to telehealth visits that excluded the possibility of collecting height and weight. Additionally, the retrospective aspect of this study led to the inability to assess some complications in a nuanced way. Our small cohort also made it challenging to explore other

relevant outcomes, including the impact of TCT on weight in CFRD patients. It is essential to mention that compliance to all therapies could only be assessed by the documentation in medical records.

While this study helped build a more comprehensive understanding of weight gain in all types of CF patients, future more extensive studies will be needed to explore the mechanisms behind these changes. Additionally, with the recent FDA approval of TCT in 6–12-year-old children, the effect of TCT on BMI percentile will need to be evaluated in this population.

Overall, this study helped assess if TCT increases BMI in CF patients. More importantly, this study quantified the BMI gains on average that patients could expect to see after a year on the medication. This work allows for a greater understanding on an individual and systematic level. New information regarding the weight gain associated with HEMT allows patients to make more educated decisions about their nutrition while taking TCT and allows their providers to adjust recommendations and shift their focus to the possibility of excess weight gain in some patients. Ultimately, the consistent monitoring of nutritional needs is essential to build upon and correct CFF guidelines to fit the needs of all CF patients as their baseline health changes in the era of new modulators.

References

Uncategorized References

1. Cohen-Cymberknoh M, Shoseyov D, Kerem E. Managing cystic fibrosis: Strategies that increase life expectancy and improve quality of life.*American Journal of Respiratory and Critical Care Medicine.*2011;183(11):1463-1471.

2. Sturgess JM. Structural and developmental abnormalities of the exocrine pancreas in cystic fibrosis. *J Pediatr Gastroenterol Nutr.* 1984;3 Suppl 1:S55-66.

3. Pencharz PB, Durie PR. Pathogenesis of malnutrition in cystic fibrosis, and its treatment. *Clinical Nutrition.*2000;19(6):387-394.

4. Scott RB, O'Loughlin EV, Gall DG. Gastroesophageal reflux in patients with cystic fibrosis. *The Journal of Pediatrics.*1985;106(2):223-227.

5. Vaisman N, Pencharz PB, Corey M, Canny GJ, Hahn E. Energy expenditure of patients with cystic fibrosis. *J Pediatr.* 1987;111(4):496-500.

6. Calella P, Valerio G, Brodlie M, Donini LM, Siervo M. Cystic fibrosis, body composition, and health outcomes: a systematic review.*Nutrition.* 2018;55-56:131-139.

7. Corey M, McLaughlin FJ, Williams M, Levison H. A comparison of survival, growth, and pulmonary function in patients with cystic fibrosis in Boston and Toronto. *Journal of Clinical Epidemiology.*1988;41(6):583-591.

8. Kastner-Cole D, Palmer CNA, Ogston SA, Mehta A, Mukhopadhyay S. Overweight and Obesity in ΔF508 Homozygous Cystic Fibrosis. *The Journal of Pediatrics.* 2005;147(3):402-404.

9. Grey AB, Ames RW, Matthews RD, Reid IR. Bone mineral density and body composition in adult patients with cystic fibrosis. *Thorax.*1993;48(6):589.

10. Stallings VA, Stark LJ, Robinson KA, Feranchak AP, Quinton H. Evidence-Based Practice Recommendations for Nutrition-Related Management of Children and Adults with Cystic Fibrosis and Pancreatic Insufficiency: Results of a Systematic Review. *Journal of the American Dietetic Association.* 2008;108(5):832-839.

11. Sullivan JS, Mascarenhas MR. Nutrition: Prevention and management of nutritional failure in Cystic Fibrosis. *J Cyst Fibros.* 2017;16 Suppl 2:S87-s93.

12. Egan ME. Cystic fibrosis transmembrane conductance receptor modulator therapy in cystic fibrosis, an update. *Curr Opin Pediatr.* 2020;32(3):384-388.

13. Bailey J, Rozga M, McDonald CM, et al. Effect of CFTR Modulators on Anthropometric Parameters in Individuals with Cystic Fibrosis: An Evidence Analysis Center Systematic Review. *J Acad Nutr Diet.*2020.

14. Hanna RM, Weiner DJ. Overweight and obesity in patients with cystic fibrosis: A center-based analysis. *Pediatric Pulmonology.*2015;50(1):35-41.

15. Gelfond D, Heltshe S, Ma C, et al. Impact of CFTR Modulation on Intestinal pH, Motility, and Clinical Outcomes in Patients With Cystic Fibrosis and the G551D Mutation. *Clinical and Translational Gastroenterology.* 2017;8(3).

16. Edgeworth D, Keating D, Ellis M, et al. Improvement in exercise duration, lung function and well-being in G551D-cystic fibrosis patients: A double-blind, placebo-controlled, randomized, cross-over study with ivacaftor treatment. *Clinical Science.*2017;131(15):2037-2045.

17. Stallings VA, Sainath N, Oberle M, Bertolaso C, Schall JI. Energy Balance and Mechanisms of Weight Gain with Ivacaftor Treatment of Cystic Fibrosis Gating Mutations. *Journal of Pediatrics.*2018;201:229-237.e224.

18. https://www.cdc.gov/healthyweight/bmi/calculator.html.

19. http://gli-calculator.ersnet.org/

20. *Cystic Fibrosis Foundation Patient Registry 2020 Annual Data Report.* Cystic Fibrosis Foundation;2021.

Table 1. General characteristics of study participants

Characteristic	Patients (N=106) (% of total)
Gender	
Female	42 (39.6)
Male	64 (60.4)
Age	
[?] 20 years	68 (64.2)
< 20 years	38 (35.8)
Race	
White	97 (91.5)
Black	2 (1.9)
Multi-Racial	2 (1.9)
Declined/Unavailable	5 (4.7)
Ethnicity	
Hispanic or Latino	4 (3.8)
Genotype	
Homozygous F508del	62 (58.5)
Heterozygous F508del	44 (41.5)
Lung Function[1]	
Normal (FEV_1 [?] 90% Percent Predicted)	39 (31.5)
Mild (70-89%)	22 (17.7)
Moderate (40-69%)	25 (20.2)
Severe (<40%)	16 (12.9)
Previous Modulator Use	
Ivacaftor	12 (11.3)
Lumacaftor/Ivacaftor	48 (45.3)
Tezacaftor/Ivacaftor	18 (17.0)
None	28 (26.4)
Pancreatic Insufficient	92 (86.8)
CFRD[2]	15 (14.2)

Characteristic	Patients (N=106) (% of total)
GERD[3]	60 (56.6)
Consuming Nutritional Supplements	26 (24.5)
Oral	24 (19.4)
Tube	(1.6)

1 FEV^1 data were available for 102 of the 106 subjects at baseline.

2 CFRD: Cystic fibrosis-related diabetes.

3 GERD: Gastroesophageal reflux disease.