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Short Communication
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One-Year Assessment of Body Composition in Cystic Fibrosis Patients on Elexacaftor-Tezacaftor-Ivacaftor

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Short Communication

Cystic Fibrosis (CF) is a life-threatening autosomal recessive genetic disease caused by a mutation of the Cystic Fibrosis Transmembrane Regulator (CFTR) gene that encodes a chloride-conducting transmembrane channel, leading to dysregulation of electrolytes transport, thick fluid secretions, and severe impacts on the respiratory and gastrointestinal systems [1].

CF has always been related to poor nutritional status and, in children, stunted growth and development linked directly by factors related to the underlying genetic mutation, as well as indirectly by factors such as energy losses, decreased nutrient intake and absorption, and higher energy needs due to increased work of breathing and chronic inflammation [2].

There is a clear link between nutritional status and respiratory function in both children and adults with CF: A low Body Mass Index (BMI) is associated with low Forced Expiratory Volume in the 1st second (FEV1%), and poor survival; on the other hand, a BMI in the normal range correlates with better clinical outcomes [3].

For this reason, aggressive dietary interventions have always focused attention on increasing BMI to avoid or prevent malnutrition and promote adequate growth and development. However, although the BMI is more often clinically used to define nutritional status, it does not differentiate between specific body-composition components. In addition, recent studies analyzed that the Fat Free Mass (FFM) is more strongly associated with lung function in CF compared to the BMI, and an abnormal or excessive accumulation of Fat Mass (FM), according to World Health Organization (WHO), places the individual at risk of cardiovascular and chronic lifestyle diseases [4].

New therapeutic advancements have shown favorable effects on the quality of life and longevity among CF patients (pts). The advent of CFTR modulators, especially the most recent one, i.e., the Elexacaftor-Tezacaftor-Ivacaftor (ETI), has been demonstrated to reduce sweat chloride levels and risk of pulmonary exacerbations and improve respiratory function and nutritional status. This results in an increase in weight and BMI and, therefore, overweight and obesity, which are becoming areas of interest among clinical care and researchers for the first time in CF history [5].

Currently, CFTR modulators are known to improve nutritional status and increase anthropometric parameters, but very little is known about how they affect body composition over time [6]. Hence, the objective of this study was to assess the body composition of CF pts on ETI during their first year of treatment at Ancona CF center in order to prevent obesity and chronic diseases through adequate dietetic interventions.

At Ancona CF center, the nutritional status of CF pts who started the commercial triple combination ETI was monitored at fixed times (T0, T1, T3, T6, T12). In this study, we analyzed the weight and body composition of F508del/Minimal Function (F/MF) (n=15) and F508del/F508del (F/F) (n=12) pts over 12 years of age who completed the assessment at 12 months (T12). Weight, BMI, and body composition parameters, in particular FM and FFM, were analyzed using a Bioelectrical Impedance Analysis (BIA).

What about results? Variations (Δ) (T0-T6; T12-T6) in weight and body composition parameters of CF pts on ETI were outlined in the following graphs.

Despite the limited number of pts, this monocentric study showed a consistent increase at T6 and a moderate increase at T12 in weight, BMI, and FM in pts on ETI. The lowest increment in weight, BMI, and FM and the highest increment in FFM in the second semester are determined by a personalized dietary intervention and increased physical activity.

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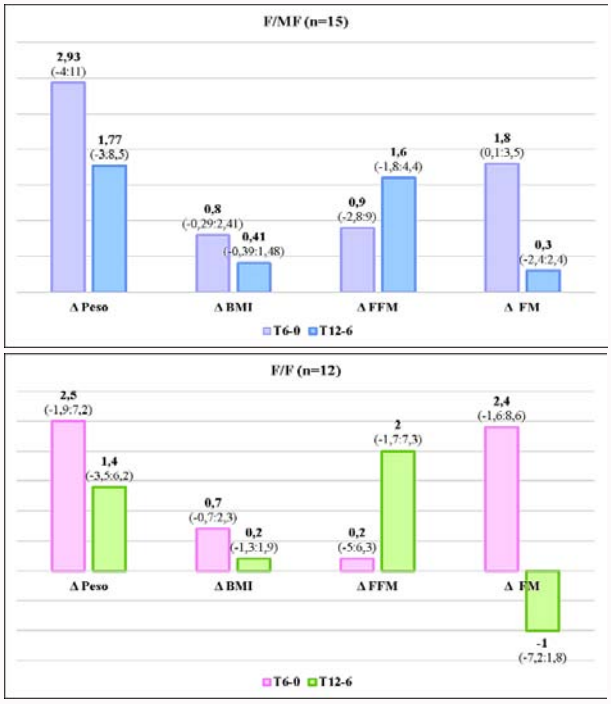

Graphs: Variations (Δ) (T0-T6; T12-T6) in weight and body composition parameters of CF pts on ETI were outlined in the graphs.

The results of this study show that pts on ETI appear to have an increased risk of developing overweight or obesity and, consequently, cardiovascular and metabolic diseases, especially if not properly followed by a specialized CF dietitian.

The effects of CFTR modulators on the increasing weight, height, and BMI in individuals with CF are known and highly dependent on therapy formulation (single or combined therapy), clinical conditions, and targeted CFTR mutation. However, current evidence regarding the impact of CFTR modulation therapy, particularly ETI, on body composition remains undefined.

The advent of CFTR modulation therapy has revolutionized CF care, in terms of less-severe symptoms, higher quality of life, longer survival, lower rates of hospitalization, and better nutritional status in eligible pts. Many studies have shown how these drugs improve the nutritional status of CF pts by increasing weight, height, and BMI, while only a few of them have assessed the impact of CFTR modulators on body composition. Although BMI is commonly used as an indicator of nutritional status in clinical practice, it is not able to provide information regarding body composition parameters. Indeed, a BMI in the normal range can hide a condition of "sarcopenia" or "normal weight obesity" [7]. Despite the strong correlation between BMI and lung function in CF, recent studies have demonstrated that a high content of FM is inversely associated with pulmonary function and, on the other hand, FFM positively impacts respiratory strength and lung function [8,9].

As therapeutic advancements have significantly improved, longevity has increased and overweight and obesity have become emerged issues among the CF population. The implications of excessive weight gain and adiposity on CF clinical outcomes are unknown but may produce similar health consequences and chronic diseases as those observed in the general population [5,10].

According to the scientific literature, our study showed that pts on ETI increased FM more than FFM, but this increment can be identified through regular body-composition assessment and controlled by individualized dietary intervention, constant physical activity, and correct lifestyle.

Current nutritional guidelines state that individuals with CF may need a higher energy intake than the general population through a high calorie and fat diet. Nevertheless, these recommendations may no longer be appropriate, especially in the era of CFTR modulators. Moreover, it is important to consider that the nutritional status of many CF pts remains suboptimal, even after starting CFTR modulation therapy, and, thus, a more energy-dense diet may be necessary [11].

In conclusion, the CF nutritional approach should meet each individual's dietetic requirements and focus on diet quality in order to promote optimal health outcomes and prevent other chronic lifestyle diseases. Further research is needed to understand which method of body-composition assessment can be recommended in CF clinical care and analyze longer-term metabolic consequences of ETI [12].

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