CF RD AND SW CONSORTIUM

February Newsletter

Special thanks to our sponsors:

- MVW Nutritionals
- Alcresta
- Callion Pharma
- Nestle

Updates from CFF:

Exercise Program at No Cost Through June 2023

The CF Foundation is extending their support for free access to Beam, an online exercise, education, and well-being platform. People with CF ages 18 and older in the United States can continue to enjoy a variety of on-demand and live classes at no cost through June 2023. No promo code necessary.

Join Beam today »

CF Foundation External Racial Justice Working Group Releases New Recommendations

To work toward addressing health inequities in cystic fibrosis, the Foundation's External Racial Justice Working Group has been focusing on the unique challenges Black people with CF face. The group, comprising Foundation staff and external advisors from the broader CF community, including people with CF, family members, researchers, and care team members, has released its recommendations in two key focus areas: health equity and outcomes and diverse workforce development.

Read the recommendations »

CF Foundation Applauds Reintroduction of HELP Copays Act

This week, we issued a statement supporting the reintroduction of the Help Ensure Lower Patient (HELP) Copays Act, urging Congress to pass the bill swiftly. This bipartisan bill requires copay assistance to be applied to patient cost-sharing requirements and closes a loophole in private employer health plan essential health benefits coverage.

Read our statement »

Resource for navigating insurance denials and appeals:

Navigating CF is a series of short videos, about 2–6 minutes long, from Compass that helps people with cystic fibrosis, their families, and care teams navigate complex issues. The videos can help you explain to patients why insurance claims are denied and what their options are based on their type of insurance. For assistance navigating a specific denial or appeal, care teams and their patients can contact Compass at 844-COMPASS (1-844-266-7277). For questions, contact Azi Kaider.

ICER Barriers to Fair Access Report and Webinar:

The CF Foundation participated in a webinar with the Institute for Clinician and Economic Review (ICER) to discuss their barriers to fair access report, which assessed payer coverage policies for CFTR modulators. Real-world experiences from Compass callers and clinicians were shared during the webinar. We reiterated access challenges not included in the report, including copay accumulator programs and the totality of the cost burden people with CF experience. For questions, contact Olivia Dieni.

Medicaid redeterminations:

Starting April 1, states will be allowed to terminate Medicaid coverage for people who are no longer eligible, which had been prevented during the public health emergency. Encourage your patients on Medicaid to update their contact information with their plan so they will receive information about renewing their coverage. For more information, contact Azi Kaider.

Daily care check-in webinar:

On Thurs., Jan. 26, 12 – 1 p.m. ET, the Partnerships for Sustaining Daily Care team hosted the Daily Care Check-In Webinar. All care team members were invited to participate in this introduction to a **new tool** intended to support conversations with people with CF and their families about maintaining their daily care regimen. Topics include development of the tool and resources for its successful use in clinic. For questions contact PSDCteam@cff.org

Updates from CFRI

New Podcast: Rise Up For A Dream

Nicholas Kelly, dietitian, motivational speaker, author, DJ, artist, poet, dancer, advocate, and CF Warrior, shares the secrets to his freestyling "sauce." Enjoy his inspirational freestyle artistry entitled "Rise Up For A Dream," and learn how you can empower and express your unique voice. **Watch this episode on our YouTube channel**. **Watch/download this episode on Podbean**. *CF Community Voices is made possible to date through grants from Chiesi USA, Genentech, and Viatris.*

Support Group For Adults with CF Meets Online third Mondays.

The group, facilitated by Meg Dvorak, LCSW, is open to participants nationwide, and meets from 6:00 pm PST to 7:30 pm (9:00 pm – 10:30 pm EST). To receive the link to the registration page, please email Sabine Brants (sbrants@cfri.org). If you registered before, you don't need to do it again.

CF Caregivers Support Groups Third Tuesday

Parents of Children third Tuesday from 5:00 pm – 6:00 pm PST; **Parents/ Spouses/ Partners of Adults** meet from 6:00 pm – 7:00 pm PST. To receive the link to the registration page, please email Sabine Brants (sbrants@cfri.org). If you registered before, you don't need to do it again.

Monthly Support Group for Teenagers with CF Meets Online third Wed

Addresses the unique issues faced by teenagers (aged 13 – 18) living with CF. This peer-to-peer support group is facilitated by Deborah Menet, LCSW, social worker at the Stanford CF Center. Parents must provide consent for their teenagers to attend. **Register for the teen support group.**

Parents, Students with CF, and CF Social Workers: Order Free Copies of Updated "CF In the Classroom"

CFRI's recently updated "CF in the Classroom" and "Fibrosis Quística en la CLase" booklets were developed to help teachers, school administrators and other educators to better understand cystic fibrosis, and the CF-related issues they should be aware of. They are useful for educating family and friends as well! Available in English and Spanish, in single copies and in bulk. To order your free copies, please email cfri@cfri.org. *Made possible through educational grants from Viatris and Vertex.*

CFRI's Counseling Program Offers Financial Support for Therapy Sessions:

Children and adults with CF and family members (parents, siblings, spouses/ partners) are eligible to receive financial support for six individual sessions with their licensed provider of choice. CFRI may cover up to $120 per session for six sessions. Participants must live in the United States. **Find more information on CFRI's counseling support program here**,or email Sabine at sbrants@cfri.org for any questions.

A Wealth of Information on Our YouTube and Podbean Channels!

Get information about scholarships, patient assistance, hemoptysis, CF and mental health, bone health, advocacy, CF and COVID-19, and much more. Our CF Community Voices podcast series covers it all! Many recordings on YouTube are available with Spanish and Hindi captions. **Watch or download CFRI's podcasts on our Podbean channel. Watch CFRI's podcasts on our YouTube channel.**

Lipid Monitoring and Cystic Fibrosis: A Review of Current Research

by Shari R. Willy, RD, LDE, CACFD

How often and when should people with cystic fibrosis (PwCF) have their lipid panel checked? If you ask your past self, you might come up with an answer similar to the findings of Slesinski and colleagues in their 1994 publication on the topic of lipid levels and adults with CF:

> **The [study] findings indicate that a high-energy, high-fat diet does not raise serum lipid levels in those patients with cystic fibrosis and pancreatic insufficiency. However, those individuals with cystic fibrosis and normal pancreatic function may be at the same risk as the general population for developing high serum lipid levels. They should have their serum lipid levels monitored and be given appropriate recommendations (p.402).**

However, your current self is working in the era of highly effective modulators (HEMTs) which challenges the legacy of care models developed before HEMTs were introduced to the plan of care for PwCF. You need answers to this question. Therefore, this article aims to evaluate the current research on dietary intake and lipid profiles in PwCF and provide guidance for lipid monitoring in this new era of care.

In a poster discussed at the North American Cystic Fibrosis Conference in 2022, Sundaram and authors presented their findings on the impact of modulator therapies in 30 adults with CF. Using MRI imaging and lab data from each subject before and after use of modulators, an increase in both high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), and body mass index (BMI) were noted in subjects using the HEMT elexacaftor/tezacaftor/ivacaftor (ETI). It should be noted the research did not find a statistically significant change in protein density fat fraction (PDFF) and triglycerides. As well, hepatic steatosis was not consistently changed with modulator use. In closing the authors question if modulator treatment in PwCF increases the risk for cardiovascular disease.

Bailey and colleagues discuss in their 2022 paper comorbidities associated with overweight and obesity in PwCF, including the propensity for higher total cholesterol and LDL-C when compared to normal weight counterparts. The authors summarize previous research which revealed the use of ETI was shown to increase total cholesterol, HDL-C, and LDL-C in PwCF who also carried the diagnosis of CF-related diabetes. Again, it is concluded that more research is needed to understand the relationship between the CF specific care plan including HEMT use, dietary intervention, and the risk of metabolic and cardiovascular disorders in PwCF who are overweight or obese.

Just as in the examples above, review of the literature acknowledges the prevalence and risk of dyslipidemia in PwCF whose weight has increased to overweight or obese categories. Furthermore, no specific guidance on timing of and frequency of lipid monitoring in PwCF with or without modulator use is reported. The National Heart, Lung, and Blood Institute (NHLBI) recommends for the general population, the following guide for fasting lipid panel (total cholesterol, HDL-C, LDL-C, and triglycerides) testing, noting exceptions for personal risk factors and family history of cardiovascular disease.

Age 19 years or younger	Screening begins at 9-11 years (can screen as young as 2 depending upon risk factors)	Repeat every 5 years
Age 20-65 years	Frequency depends upon age and presence of risk factors and/or family history	Younger adults every 5 years Men 45-55 years every 1-2 years Women 55-65 years every 1-2 years
Older than 65 years	No current exceptions	Every year

It is well established that the advent of HEMTs has changed the trajectory of care for PwCF. We are seeing gains in weight, increasing prevalence of metabolic and cardiovascular disease, and even encouraging some patients to stray from the legacy CF diet as a direct result of HEMT use. The NHLBI guidelines provide a starting point for implementation in the CF care center as our future self awaits specific guidance on timing and frequency of lipid monitoring for PwCF.

References:

Bailey, J., Krick, S., & Fontaine, K. R. (2022). The changing landscape of nutrition in cystic fibrosis: The emergence of overweight and obesity. Nutrients, 14, 1216. https://doi.org/10.3390/nu14061216

National Heart, Lung, and Blood Institute (NHLBI). (n.d.). Blood Cholesterol. https://www.nhlbi.nih.gov/health/blood-cholesterol/diagnosis

Slesinski, M. J., Gloninger, M. F., Costantino, J. P., & Orenstein, D. M. (1994). Lipid levels in adults with cystic fibrosis. Journal of the American Dietetic Association, 94(4), 402–408. https://doi.org/10.1016/0002-8223(94)90095-7

Sundaram, K., McBennett, K, Flask, C., & Kutney, K. (2022). Impact of cystic fibrosis transmembrane conductance regulator modulator therapy on nutrition status, hepaticsteatosis, and dyslipidemia. Journal of Cystic Fibrosis, 2152, S1-S378.

Shari R. Willy holds a Bachelor of Science degree in Dietetics and is currently pursuing the Master of Public Health, both from Purdue University. In 2007 she joined the University of Louisville Pediatric Cystic Fibrosis Program after spending the early years of her dietetics career in hematology, oncology, and critical care nutrition as well as food service management. Ms. Willy is active in the Cystic Fibrosis Foundation – Kentucky/West Virginia Chapter serving as a board member and sponsorship chair for the annual gala committee. Professional interests include the care of the cystic fibrosis newborn, optimization of pancreatic enzyme replacement therapy, nutrition concerns in the age of highly effective modulator therapy, and nutrition specific research in cystic fibrosis. Ms. Willy resides in Louisville, Kentucky and enjoys spending time with her family, hiking, and traveling.

***Are you interested in writing an article for our newsletter? Send us an email: rdswconsortium@gmail.com**

We provide an honorarium for your article!

CME/CE Resource

CF and Diet and Nutrition: The Changing Paradigm

Katie McDonald, PhD, Megan Gabel, MD, Amanda Leonard, MPH, RD, LD, CDE, and Alexandra Wilson, MS, RDN, CDE

For most of their lives, individuals with CF have struggled to gain weight and achieve BMI norms. Now however, a growing number of people with CF are meeting the current criteria for overweight or obesity. What changed? And without specific evidence-based guidance for managing overweight/obesity in people with CF, how should clinicians respond? Read more

Congratulations to the following dietitians who received their Advanced CF RD Credentials! They join the list of RDs from last month's newsletter.

Michelle DeGraaf	Jennifer Blair	Yajaira Pluess
Patricia Rose	Bekah Sommer	

Creative Fuel: Writing Through Suffering

Bradley Dell

Taking a therapeutic writing course helped the author cope with his cystic fibrosis, which also helped him connect more strongly to the CF community. Read more

Abstracts

General

Pediatr Pulmonol. 2023 Jan 6.
doi: 10.1002/ppul.26311.

Clinical management of pediatric patients with cystic fibrosis and autism spectrum disorder

Kimberly Pasley[1], Katelyn Krivchenia[1], Mary Lynn Dell[2], Karen S McCoy[1], Grace R Paul[1]

PMID: 36610056 DOI: 10.1002/ppul.26311

Abstract

Background: Cystic Fibrosis (CF) and autism spectrum disorder (ASD) are life-long conditions with intense treatment burdens for patients and families. Patients with a concurrent diagnosis (CF-ASD) experience unique obstacles to CF care. This study describes the experiences of our multidisciplinary CF team in caring for patients with CF-ASD and provides insight into provider and parental perspectives on clinical management.

Methods: This is a three-part qualitative study involving (1) retrospective chart review of patients with CF-ASD, (2) surveys with multidisciplinary care team members, and (3) semistructured interviews with caregivers of patients with CF-ASD. Challenges in clinical management of this specific cohort were compiled using data from chart review and care team surveys. Strategies to address these concerns were identified and rated by individual families based on relevance and practicality.

Results: Within our CF center, 12 patients have an official diagnosis of ASD. Median age of patients with CF-ASD was 8.5 years (range 3-20 years), 67% were male, and 83% were on highly effective modulator therapy. Clinical barriers included sensory processing issues, environmental overstimulation, intolerance to procedures and to disrupted routines. Potentially impactful strategies include patient-specific coping plans, guided behavioral interventions, parental advocacy, and improved communication between the family and multidisciplinary team.

Conclusion: Children with CF-ASD face extraordinary challenges beyond the experience of neurotypical children with CF. Increased awareness of this complex dual diagnosis will help providers be sensitive to the unique needs of these patients, help build consistent and trustworthy relationships with their families and deliver effective clinical care despite limitations.

Eur J Pediatr 2022 Dec 24.

Evaluation of specificity and sensitivity of IRT/IRT protocol in the cystic fibrosis newborn screening program: 6-year experience of three tertiary centers

Tugba Ramasli Gursoy[1], Pelin Asfuroglu[1], Tugba Sismanlar Eyuboglu[1], Ayse Tana Aslan[2], Asli Imran Yilmaz[3], Gokcen Unal[3], Büsra Sultan Kibar[4], Sevgi Pekcan[3], Melih Hangul[5], Mehmet Kose[5], Isil Irem Budakoglu[6], Deniz Acican[7]

PMID: 36565324 DOI: 10.1007/s00431-022-04766-4

Abstract

We aimed to evaluate cutoff values of immunoreactive trypsinogen (IRT)/IRT and determine relationship between IRT values and clinical characteristics of children with cystic fibrosis (CF). This study is cross-sectional study. Data of children with positive newborn screening (NBS) between 2015 and 2021 were evaluated in three pediatric pulmonology centers. Age at admission, sex, gestational age, presence of history of meconium ileus, parental consanguinity, sibling with CF, and doll-like face appearance, first and second IRT values, sweat chloride test, fecal elastase, fecal fat, biochemistry results, and age at CF diagnosis were recorded. Sensitivity and specificity of IRT cutoff values were evaluated. Of 815 children with positive NBS, 58 (7.1%) children were diagnosed with CF. Median values of first and second IRT were 157.2 (103.7-247.6) and 113.0 (84.0-201.5) µg/L. IRT values used in current protocol, sensitivity was determined as 96.6%, specificity as 17.2% for first IRT, and 96.6% sensitivity, 20.5% specificity for second IRT. Positive predictive value (PPV) was determined as 7.1%. When cutoff value for first IRT was estimated as 116.7 µg/L, sensitivity was 69.0% and specificity was 69.6%, and when cutoff value was set to 88.7 µg/L for second IRT, sensitivity was 69.0% and specificity was 69.0%. Area under curve was 0.757 for first and 0.763 for second IRT ($p < 0.001$, $p < 0.001$, respectively). PPV was calculated as 4.3%. Conclusion: Although sensitivity of CF NBS is high in our country, its PPV is significantly lower than expected from CF NBS programs. False-positive NBS results could have been overcome by revising NBS strategy. What is Known: • Although immunoreactive trypsinogen elevation is a sensitive test used in cystic fibrosis newborn screening, its specificity is low. • In countries although different algorithms are used, all strategies begin with the measurement of immunoreactive trypsinogen in dried blood spots. What is New: • In our study, it was shown that use of the IRT/IRT protocol for cystic fibrosis newborn screening is not sufficient for the cut-off values determined by the high number of patients. • Newborn screening strategy should be reviewed to reduce false positive newborn screening results.

Nutrients. 2023 Jan 8;15(2):314.
doi: 10.3390/nu15020314.

Can Bioactive Food Substances Contribute to Cystic Fibrosis-Related Cardiovascular Disease Prevention?

Laura Mihaela Trandafir[1], Otilia Elena Frăsinariu[1], Elena Țarcă[2], Lăcrămioara Ionela Butnariu[3], Maria Magdalena Leon Constantin[4], Mihaela Moscalu[5], Oana Raluca Temneanu[1], Alina Sinziana Melinte Popescu[6], Marian George Melinte Popescu[6], Iuliana Magdalena Stârcea[1], Elena Cojocaru[7], Stefana Maria Moisa[1]

PMID: 36678185 PMCID: PMC9860597 DOI: 10.3390/nu15020314

Abstract

Advances in cystic fibrosis (CF) care have significantly improved the quality of life and life expectancy of patients. Nutritional therapy based on a high-calorie, high-fat diet, antibiotics, as well as new therapies focused on CFTR modulators change the natural course of the disease. They do so by improving pulmonary function and growing BMI. However, the increased weight of such patients can lead to unwanted long-term cardiovascular effects. People with CF (pwCF) experience several cardiovascular risk factors. Such factors include a high-fat diet and increased dietary intake, altered lipid metabolism, a decrease in the level of fat-soluble antioxidants, heightened systemic inflammation, therapeutic interventions, and diabetes mellitus. PwCF must pay special attention to food and eating habits in order to maintain a nutritional status that is as close as possible to the proper physiological one. They also have to benefit from appropriate nutritional counseling, which is essential in the evolution and prognosis of the disease. Growing evidence collected in the last years shows that many bioactive food components, such as phytochemicals, polyunsaturated fatty acids, and antioxidants have favorable effects in the management of CF. An important positive effect is cardiovascular prevention. The possibility of preventing/reducing cardiovascular risk in CF patients enhances both quality of life and life expectancy in the long run.

Pharmaceutics. 2023 Jan 3;15(1):162.
doi: 10.3390/pharmaceutics15010162.

Current and Future Therapeutic Approaches of Exocrine Pancreatic Insufficiency in Children with Cystic Fibrosis in the Era of Personalized Medicine

Mirela-Elena Ritivoiu[1,2], Cristina Manuela Drăgoi[3], Dumitru Matei[1,2], Iustina Violeta Stan[1,2], Alina Crenguța Nicolae[3], Mihai Craiu[1,2], Ion-Bogdan Dumitrescu[3], Alina Angelica Ciolpan[1,2]

PMID: 36678791 PMCID: PMC9862205 DOI: 10.3390/pharmaceutics15010162

Abstract

This review presents current updates of pancreatic enzyme replacement therapy in children with cystic fibrosis based on literature published in the last decade and some special considerations regarding pancreatic enzyme replacement therapy in the era of new therapies, such as cystic fibrosis transmembrane conductance regulator modulator therapies. Few articles evaluate the efficacy of pancreatic enzyme replacement therapy in the pediatric population, and most studies also included children and adults with cystic fibrosis. Approximately 85% of cystic fibrosis patients have exocrine pancreatic insufficiency and need pancreatic enzyme replacement therapy. Fecal elastase is the most commonly used diagnostic test for exocrine pancreatic insufficiency, although this value can fluctuate over time. While it is used as a diagnostic test, it cannot be used for monitoring the effectiveness of pancreatic enzyme replacement therapy and for adjusting doses. Pancreatic enzyme replacement therapy, the actual treatment for exocrine pancreatic insufficiency, is essential in children with cystic fibrosis to prevent malabsorption and malnutrition and needs to be urgently initiated. This therapy presents many considerations for physicians, patients, and their families, including types and timing of administration, dose monitoring, and therapy failures. Based on clinical trials, pancreatic enzyme replacement therapy is considered effective and well-tolerated in children with cystic fibrosis. An important key point in cystic fibrosis treatment is the recent hypothesis that cystic fibrosis transmembrane conductance regulator modulators could improve pancreatic function, further studies being essential. Pancreatic enzyme replacement therapy is addressed a complication of the disease (exocrine pancreatic insufficiency), while modulators target the defective cystic fibrosis transmembrane conductance regulator protein. Exocrine pancreatic insufficiency in cystic fibrosis remains an active area of research in this era of cystic fibrosis transmembrane conductance regulator modulator therapies. This new therapy could represent an example of personalized medicine in cystic fibrosis patients, with each class of modulators being addressed to patients with specific genetic mutations.

Appl Physiol Nutr Metab. 2023 Jan 21.
doi: 10.1139/apnm-2022-0163. Online ahead of print.

Low Vitamin K Status In Adults With Cystic Fibrosis Is Associated With Reduced Body Mass Index, Insulin Secretion And Increased Pseudomonal Colonization

Cindy Bergeron[1], Kathryn Jane Potter[2], Valerie Boudreau[3], Bouchra Ouliass[4], Anne Bonhoure[5], Julie Lacombe[6], Marjolaine Mailhot[7], Annick Lavoie[8], Mathieu Ferron[9], Guylaine Ferland[10], Rémi Rabasa-Lhoret[11]

PMID: 36680800 DOI: 10.1139/apnm-2022-0163

Abstract

Patients with Cystic Fibrosis (CF) are at high risk of fat-soluble vitamin deficiencies, even with supplementation. The contribution of a suboptimal vitamin K status to respiratory and endocrine pathophysiology in CF has been inadequately characterized. Cross-sectional study in adult CF patients (≥ 18 years old) from the Montreal Cystic Fibrosis Cohort. Vitamin K1 (VK1) was measured with high performance liquid chromatography (HPLC), using fasted serum samples collected during an oral glucose tolerance test (OGTT: 2h with plasma glucose & insulin every 30 min) (n = 168). Patients were categorized according to VK1 status (suboptimal defined as <0.30 nmol/L). Suboptimal VK1 levels were observed in 66 % of patients. Patients with a suboptimal VK1 status have a higher risk of colonization with Pseudomonas aeruginosa (p=0.001), lower body mass index (BMI) (p=0.003) and were more likely to have exocrine pancreatic insufficiency (p=0.002). Using an established threshold for VK1, we did show significantly reduced OGTT-derived measures of insulin secretion in patients with a VK1 status below 0.30 nmol/L (1st and 2nd Phase AUCINS/GLU (p=0.002 and p=0.006), AUCINS (p=0.012) and AUCINS/GLU (p=0.004)). Subclinical vitamin K deficiency is more common than other fat-soluble vitamin deficiencies in patients with CF. We demonstrate an association between a suboptimal VK1 status and measures of insulin secretion. We highlight the potential associations of mild vitamin K deficiency with pseudomonal colonization and lower BMI, although these need to be validated in prospective studies.

J Cyst Fibros. 2023 Jan 22;S1569-1993(23)00009-7.
doi: 10.1016/j.jcf.2023.01.008. .

Bariatric surgery in a patient with cystic fibrosis and diabetes: A case report

N R A Bruijn[1], M A E M Wagenmakers[2], M van Hoek[2], J A Apers[3], M M van der Eerden[4], B Özcan[2]

PMID: 36693768 DOI: 10.1016/j.jcf.2023.01.008

Abstract

Cystic fibrosis (CF) is incurable and chronic, causing severe multisystemic damage and long-term complications. The most prominent extrapulmonary long-term complication is CF-related diabetes, which is the most reported form of diabetes in individuals with cystic fibrosis. Here we present the first case of an individual with cystic fibrosis who developed type 2 diabetes due to obesity rather than CF-related diabetes. The type 2 diabetes went into remission due to extreme weight loss after gastric bypass surgery. To our knowledge, this case is also the first report describing the effect of bariatric surgery in a patient with CF. This case demonstrates that patients with CF may present with type 2 diabetes instead of CF-related diabetes. Differential diagnosis of these two types of diabetes is essential for optimal treatment and quality of life.

Front Pediatr. 2023 Jan 6;10:1083155.
doi: 10.3389/fped.2022.1083155. eCollection 2022.

Case report: Cystic fibrosis with kwashiorkor: A rare presentation in the era of universal newborn screening

Annemarie G Wolfe[1], Stephanie P Gilley[1], Stephanie W Waldrop[1], Christina Olson[1], Emma Harding[1], Kaitlin Widmer[1], Lindsey B Gumer[1], Matthew Haemer[1], Jordana E Hoppe[1]

PMID: 36683818 PMCID: PMC9853421 DOI: 10.3389/fped.2022.1083155

Abstract

Background: Universal newborn screening changed the way medical providers think about the presentation of cystic fibrosis (CF). Before implementation of universal screening, it was common for children with CF to present with failure to thrive, nutritional deficiencies, and recurrent infections. Now, nearly all cases of CF are diagnosed by newborn screening shortly after birth before significant symptoms develop. Therefore, providers often do not consider this illness in the setting of a normal newborn screen. Newborn screening significantly decreases the risk of complications in early childhood, yet definitive testing should be pursued if a patient with negative newborn screening presents with symptoms consistent with CF, including severe failure to thrive, metabolic alkalosis due to significant salt losses, or recurrent respiratory infections.

Case presentation: We present a case of a 6-month-old infant male with kwashiorkor, severe edema, multiple vitamin deficiencies, hematemesis secondary to coagulopathy, and diffuse erythematous rash, all secondary to severe pancreatic insufficiency. His first newborn screen had an immunoreactive trypsinogen (IRT) value below the state cut-off value, so additional testing was not performed, and his growth trajectory appeared reassuring. He was ultimately diagnosed with CF by genetic testing and confirmatory sweat chloride testing, in the setting of his parents being known CF carriers and his severe presentation being clinically consistent with CF. Acutely, management with supplemental albumin, furosemide, potassium, and vitamin K was initiated to correct the presenting hypoalbuminemia, edema, and coagulopathy. Later, pancreatic enzyme supplementation and additional vitamins and minerals were added to manage ongoing deficiencies from pancreatic insufficiency. With appropriate treatment, his vitamin deficiencies and edema resolved, and his growth improved.
Conclusion: Due to universal newborn screening, symptomatic presentation of CF is rare and presentation with kwashiorkor is extremely rare in resource-rich communities. The diagnosis of CF was delayed in our patient because of a normal newborn screen and falsely reassuring growth, which after diagnosis was determined to be secondary to severe edematous malnutrition. This case highlights that newborn screening is a useful but imperfect tool. Clinicians should continue to have suspicion for CF in the right clinical context, even in the setting of normal newborn screen results

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Bone. 2023 Jan 20;116657.
doi: 10.1016/j.bone.2022.116657.
Development of musculoskeletal deficits in children with cystic fibrosis in later childhood
Alex Ireland[1], Amy Riddell[2], Antony Colombo[3], Robert Ross-Russell[4], Ann Prentice[5], Kate A Ward[6]
PMID: 36690166 DOI: 10.1016/j.bone.2022.116657
Abstract
Cystic fibrosis (CF) is a genetic condition primarily affecting the respiratory system, with the associated progressive lung damage and loss of function resulting in reduced lifespan. Bone health is also impaired in individuals with CF, leading to much higher fracture risk even in adolescence. However, the development of these deficits during growth and the relative contributions of puberty, body size and muscular loading remain somewhat unexplored. We therefore recruited 25 children with CF (10 girls, mean age 11.3 ± 2.9y) and 147 children without CF (75 girls, mean age 12.4 ± 2.6y). Bone characteristics were assessed using peripheral quantitative computed tomography (pQCT) at 4 % and 66 % distal-proximal tibia. Muscle cross-sectional area (CSA) and density (an indicator of muscle quality) were also assessed at the latter site. Tibial bone microstructure was assessed using high-resolution pQCT (HR-pQCT) at 8 % distal-proximal tibial length. In addition, peak jump power and hop force were measured using jumping mechanography. Group-by-age interactions and group differences in bone and muscle characteristics were examined using multiple linear regression, adjusted for age, sex and pubertal status and in additional models, height and muscle force. In initial models group-by-age interactions were evident for distal tibial total bone mineral content (BMC) and trabecular volumetric bone mineral density (vBMD), with a lower rate of age-related accrual evident in children with CF. In assessments of distal tibial microstructure, similar patterns were observed for trabecular number and thickness, and cortical CSA. In the tibial shaft, group-by-age interactions

indicating slower growth in CF were evident for total BMC and cortical CSA, whilst age-independent deficits in CF were observed for several other variables. Peak jump power and hop force also exhibited similar interactions. Group-by-age interactions for bone were partially attenuated at the distal tibia and fully attenuated at the tibial shaft by adjustment for muscle force. These results suggest that bone and muscle deficits in children with CF develop throughout later childhood, independent of differences in pubertal stage and body size. These diverging growth patterns appear to be mediated by differences in muscle function, particularly for bone characteristics in the tibial shaft. Given high fracture risk in this population from childhood onwards, development of interventions to improve bone health would be of substantial clinical value.

GI

J Pediatr (Rio J). 2022 Dec 20;S0021-7557(22)00133-4.
doi: 10.1016/j.jped.2022.11.007.

Combined multi-channel intraluminal impedance measurement and pHmetry in the detection of gastroesophageal reflux disease in children with cystic fibrosis

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PMID: 36564006 DOI: 10.1016/j.jped.2022.11.007

Abstract

Objective: To assess the prevalence of GERD exclusively by means of multichannel intraluminal impedanciometry associated with pH monitoring (MIIpH) and compare it with respiratory symptoms in children with CF. To compare MIIpH with pHmetry alone to perform GERD diagnosis.

Methods: An analytical cross-sectional study was conducted with children diagnosed with CF who underwent MIIpH. Clinical and laboratory markers, including respiratory and digestive symptoms, were used for comparative analyses. High-resolution chest computed tomography was performed on patients with symptoms of chronic lung disease. Severity was classified according to the Bhalla score.

Results: A total of 29 children < 10 yo (18 girls) were evaluated; 19 of whom with physiological GER and 10 with GERD. Of the children with GERD, seven had predominantly acid GER, two acid+non-acid GER, and one non-acid GER. Three patients had GERD diagnosed only by MIIpH. Bhalla scores ranged from seven to 17.75 with no significant relationship with GERD. The number of pulmonary exacerbations was associated with a decrease in esophageal clearance regardless of the position in pHmetry and MIIpH.

Conclusions: The prevalence of GERD was 34% in children with CF. There was no association between respiratory disease severity and GER types. MIIpH detected 30% more patients with GERD than pHmetry.

J Cyst Fibros. 2022 Dec 28;S1569-1993(22)01434-5.
doi: 10.1016/j.jcf.2022.12.014. Online ahead of print.

Prevalence, Risk Factors, and Sequelae of Asymptomatic Clostridioides difficile Colonization in Children with Cystic Fibrosis

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PMID: 36585317 DOI: 10.1016/j.jcf.2022.12.014

Abstract

Patients with CF (pwCF) have high antibiotic use and an altered intestinal microbiome, known risk factors for infection with Clostridioides difficile. However, in adults with CF, C. difficile infection (CDI) is uncommon and asymptomatic colonization with C. difficile occurs frequently, for reasons that remain unclear. We investigated the rate, risk factors, and sequelae of asymptomatic C. difficile colonization in children with CF (cwCF). We identified that 32% of cwCF were colonized with C. difficile without acute gastrointestinal symptoms. Higher BMI and exposure to specific antibiotic classes (cephalosporins, fluoroquinolones, and vancomycin) were significantly associated with C. difficile colonization. No children developed symptomatic CDI in 90-days following enrollment.

Gut Microbes. 2023 Jan-Dec;15(1):2156254.
doi: 10.1080/19490976.2022.2156254.

Diet and the gut-lung axis in cystic fibrosis - direct & indirect links

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PMID: 36573804 PMCID: PMC9809969 DOI: 10.1080/19490976.2022.2156254

Abstract

Cystic fibrosis (CF) is a multisystem, autosomal, recessive disease primarily affecting the lungs, pancreas, gastrointestinal tract, and liver. Whilst there is increasing evidence of a microbial 'gut-lung axis' in chronic respiratory conditions, there has been limited analysis of such a concept in CF. We performed a comprehensive dietary and microbiota analysis to explore the interactions between diet, gastrointestinal microbiota, respiratory microbiota, and clinical outcomes in children with CF. Our results demonstrate significant alterations in intestinal inflammation and respiratory and gastrointestinal microbiota when compared to age and gender matched children without CF. We identified correlations between the gastrointestinal and respiratory microbiota, lung function, CF pulmonary exacerbations and anthropometrics, supporting the concept of an altered gut-lung axis in children with CF. We also identified significant differences in dietary quality with CF children consuming greater relative proportions of total, saturated and trans fats, and less relative proportions of carbohydrates, wholegrains, fiber, insoluble fiber, starch, and resistant starch. Our findings position the CF diet as a potential modulator in gastrointestinal inflammation and the proposed gut-lung axial relationship in CF. The dietary intake of wholegrains, fiber and resistant starch may be protective against intestinal inflammation and should be explored as potential therapeutic adjuvants for children with CF.

J Cyst Fibros2022 Dec 24;S1569-1993(22)01431-X.
doi: 10.1016/j.jcf.2022.12.011.

Impaired distal colonic pH in adults with cystic fibrosis

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PMID: 36572613 DOI: 10.1016/j.jcf.2022.12.011

Abstract

Previous wireless motility capsule (WMC) studies demonstrated decreased small intestinal pH in people with CF (PwCF) however the data is lacking on the colonic pH profile. We re-analyzed previously published WMC data to determine colonic pH/bicarbonate concentration and single cell RNA sequencing (sc-RNAseq)

to examine the normal expression of acid-base transporters in the colon/rectum.CF patients showed significantly lower pH and bicarbonate concentration values, particularly in the distal rectosigmoid region. There was no difference in colonic motility parameters between CF and non-CF subjects. SLC26A3 is highly expressed bicarbonate transporter in the colon and rectum, more so than CFTR. While dysmotility can alter intraluminal pH, observed changes likely originate from alterations in intestinal ion transport rather than colonic dysmotility. SLC26A3 is abundantly expressed in the human colon and rectum and may be a therapeutic target for restoration of bicarbonate transport. These findings may help better understand the gastrointestinal symptoms in PwCF.

Colorectal Dis. 2023 Jan 4.
doi: 10.1111/codi.16472. Online ahead of print.
"A systematic review of the colorectal microbiome in adult cystic fibrosis patients."
Brent Gilbert[1,2], Gerard Kaiko[1,3], Stephen Smith[1,3,4], Peter Wark[1,2,3]
PMID: 36598333 DOI: 10.1111/codi.16472
Background: Cystic Fibrosis (CF) is a hereditary, life-limiting, multi-system condition that results in chronic respiratory infections, pancreatic insufficiency and intestinal inflammation. Evidence indicates that CF patients develop colorectal cancer (CRC) earlier and more often than the general population. Intestinal dysbiosis resulting from genetics and CF treatment is a contributing factor. This systematic review aims to evaluate the literature to compare the microbiome of adult CF patients to non-CF patients and to assess if these changes correspond with known CRC microbiome alterations.
Methods: A systematic review across five databases was performed according to PRISMA guidelines. Studies focusing on adult CF patients, using next generation sequencing and had appropriate non-CF controls were included. Two reviewers independently screened results and assessed study quality using the Newcastle-Ottawa scale.
Results: The search generated 2757 results. 118 studies were retained after reviewing the title/abstract and full article review found five studies met the inclusion criteria. All studies consistently showed reduced microbial diversity in CF patients and unique clustering between CF and control cohorts. 34 genera and 27 species were differently expressed between CF and controls. The CF cohort had a reduced number of short-chain fatty acid (SCFA) producing bacteria and a higher abundance of bacteria associated with CRC compared to controls.
Conclusion: There was substantial heterogeneity across all the studies with regards to methodologies and reporting. However, all studies consistently found CF patients had reduced microbial diversity, fewer SCFA producing bacteria and increased CRC associated bacteria. Further prospective studies employing consistent multi-omics approaches is needed to improve our understanding of the CF gut microbiome and its involvement in early onset CRC.
Significance statement: This is the first systematic review to assess adult CF colorectal microbiome changes. This study shows CF patients have reduced SCFA producing bacteria and increased CRC associated bacteria compared to non-CF patients and may help to explain the increased risk of CRC in the CF cohort.

Dig Dis Sci. 2023 Jan 4.
doi: 10.1007/s10620-022-07812-1.
Cystic Fibrosis-Related Gut Dysbiosis: A Systematic Review
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PMID: 36600119 DOI: 10.1007/s10620-022-07812-1
Background and aims: Cystic Fibrosis (CF) is associated with gut dysbiosis, local and systemic inflammation, and impaired immune function. Gut microbiota dysbiosis results from changes in the complex gut milieu in response to CF transmembrane conductance regulator (CFTR) dysfunction, pancreatic malabsorption, diet, medications, and environmental influences. In several diseases, alteration of the gut microbiota influences local and systemic inflammation and disease outcomes. We conducted a systematic review of the gut microbiota in CF and explored factors influencing dysbiosis.
Methods: An electronic search of three databases was conducted in January 2019, and re-run in June 2021. Human, animal, and in vitro studies were included. The primary outcome was differences in the gut microbiota between people with CF (pwCF) and healthy controls. Secondary outcomes included the relationship between the gut microbiota and other factors, including diet, medication, inflammation, and pulmonary function in pwCF.
Results: Thirty-eight studies were identified. The literature confirmed the presence of CF-related gut dysbiosis, characterized by reduced diversity and several taxonomic changes. There was a relative increase of bacteria associated with a pro-inflammatory response coupled with a reduction of those considered anti-inflammatory. However, studies linking gut dysbiosis to systemic and lung inflammation were limited. Causes of gut dysbiosis were multifactorial, and findings were variable. Data on the impact of CFTR modulators on the gut microbiota were limited.
Conclusions: CF-related gut dysbiosis is evident in pwCF. Whether this influences local and systemic disease and is amenable to interventions with diet and drugs, such as CFTR modulators, requires further investigation.

J Cyst Fibros. 2023 Jan 18;S1569-1993(23)00008-5.
doi: 10.1016/j.jcf.2023.01.007.
Longitudinal effects of elexacaftor/tezacaftor/ivacaftor on liver tests at a large single adult cystic fibrosis centre
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PMID: 36669962 DOI: 10.1016/j.jcf.2023.01.007
Background: Elexacaftor/tezacaftor/ivacaftor (E/T/I) therapy has resulted in substantial improvements in health status for many with cystic fibrosis. Monitoring of liver tests is recommended due to observed rises in transaminases in trials and cases of hepatotoxicity. Comprehensive data in large populations of unselected individuals and those with established CF related liver disease (CFLD) is lacking.
Methods: Patients prescribed E/T/I at a large, adult centre had liver tests monitored at least 3 monthly for 12 months. Changes in individual liver tests were analysed and abnormalities were compared in those with and without CFLD.
Results: 255 of 267 eligible patients were included. Mild rises in median ALT, AST and bilirubin from baseline to 3 months (all $p < 0.001$) within normal limits were noted which were sustained. There were no differences in changes in liver tests between those with or without CFLD. There was a significant difference in alkaline phosphatase for those with raised levels at baseline versus those with normal baseline level (-18.5 vs +2.0 IU/L, $p = 0.002$). Clinically significant rises in ALT and AST occurred in 8 (3.1%) and 6 (2.4%) cases respectively, with derangements in 2 individuals attributed to therapy.
Conclusions: E/T/I leads to a mild, likely clinically insignificant increase in ALT, AST and bilirubin after 3 months which is sustained but does not appear to increase further in the vast majority. Underlying CFLD should not be a barrier to treatment. Although there was a reduction in ALP when elevated at baseline, this was not unique to those with pre-existing CFLD.

Microorganisms. 2022 Dec 20;11(1):9.
doi: 10.3390/microorganisms11010009.
Gut Dysbiosis in Children with Cystic Fibrosis: Development, Features and the Role of Gut-Lung Axis on Disease Progression
Ilaria Testa[1], Oliviero Crescenzi[2], Susanna Esposito[3]
PMID: 36677301 PMCID: PMC9865868 DOI: 10.3390/microorganisms11010009
Abstract
Cystic fibrosis (CF) is the most common autosomal recessive disease among Caucasians. Over the last 20 years, culture-independent analysis, including next-generation sequencing, has paired with culture-based microbiology, offering deeper insight into CF lung and gut microbiota. The aim of this review is to analyse the features of gut microbiota in patients with CF and its possible role in the progression of the disease, establishing the basis for a potential role in microbe-based therapies. The literature analysis showed that the gut environment in CF patients has unique features due to the characteristics of the disease, such as decreased bicarbonate secretion, increased luminal viscosity, and an acidic small intestinal environment, which, due to the treatment, includes regular antibiotic use or a high-energy and fat-dense diet. As a result, the gut microbial composition appears altered, with reduced richness and diversity. Moreover, the population of pro-inflammatory bacteria is higher, while immunomodulatory genera, such as *Bacteroides* and *Bifidobacterium*, are scarcer. The imbalanced gut microbial population has a potential role in the development of systemic inflammation and may influence clinical outcomes, such as respiratory exacerbations, spirometry results, and overall growth. Although a better understanding of the pathophysiology behind the gut-lung axis is needed, these findings support the rationale for considering gut microbiota manipulation as a possible intervention to regulate the severity and progression of the disease.

Cureus. 2022 Dec 9;14(12):e32340.
doi: 10.7759/cureus.32340. eCollection 2022 Dec.
The Usefulness of Combining Noninvasive Methods for Early Identification and Potential Prevention of Cystic Fibrosis-Associated Liver Disease
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PMID: 36628032 PMCID: PMC9826601 DOI: 10.7759/cureus.32340
Abstract
Cystic fibrosis-associated liver disease is the third leading cause of morbidity and mortality in patients with cystic fibrosis (CF). Liver damage in the course of CF ranges from biochemical abnormalities to full-blown cirrhosis and may involve complicated processes like inflammation, fibrogenesis, remodeling, apoptosis, and cholestasis. Despite robust research in the field of CF, its complex pathogenesis is not fully understood. Because of the unknown pathogenesis, it is difficult to develop a highly sensitive and specific test or technology that is standardized, acceptable, and available at most pediatric institutions. The Cystic Fibrosis Foundation (CFF) recommends annual blood tests to screen for liver pathology, which often fails to identify early-onset liver disease. In this review article, we present the use of different liver indices and imaging modalities that can help identify liver disease at the onset and may help in its prevention. Although the disease is commonly diagnosed in the pediatric population, due to increased life expectancy, there is increasing evidence of liver disease in adults too. We believe that the tools we present in this review will help in the prevention of liver disease and thereby reduce the associated morbidity and mortality.

Endocrine

Paediatr Respir Rev. 2022 Dec 5;S1526-0542(22)00086-0.
doi: 10.1016/j.prrv.2022.11.005. Online ahead of print.
Cystic fibrosis related diabetes (CFRD) in the era of modulators: A scoping review
Bernadette Prentice[1], Mike Nicholson[2], Grace Y Lam[3]
PMID: 36581478 DOI: 10.1016/j.prrv.2022.11.005
Abstract
Cystic fibrosis-related diabetes (CFRD) is a common complication of CF that increases in incidence as patients age. Poor glycemic control has been shown to negatively impact lung function and weight, resulting in higher risk of recurrent pulmonary exacerbations. With the advent of highly effective modulator therapies (HEMT), patients with CF are living longer and healthier lives. Consequently, CFRD and its microvascular complications are rising in prominence, becoming one of the most urgent clinical concerns. As HEMT were developed with the primary focus of improving pulmonary outcomes, it is not clear from the original phase III studies what the short- or long-term benefits of modulators might be on CFRD development and trajectory. In this review, we will examine the pathophysiology of CFRD, summarize and synthesize the available evidence of HEMT impact on CFRD and describe the emerging research needs in this field.

Pediatr Pulmonol. 2023 Jan 2.
doi: 10.1002/ppul.26304. Online ahead of print.
The use of DXA for early detection of pediatric cystic fibrosis-related bone disease
Christina Chadwick[1], Renallie Arcinas[2], Melissa Ham[3], Rong Huang[4], Stacie Hunter[5], Megha Mehta[1], Preeti Sharma[6], Prigi Anu Varghese[6], Kelli Williams[7], David M Troendle[1], Meghana Sathe[1]
PMID: 36593123 DOI: 10.1002/ppul.26304
Abstract
Background: Cystic fibrosis (CF)-related bone disease (CFBD) is seen in adults and can be associated with respiratory illness and malnutrition. There is limited and conflicting data regarding CFBD in pediatric CF. With longer life expectancy and promotion of disease prevention, pediatric CFBD demands further investigation.
Methods: Our center initiated a quality improvement (QI) project from April 2016 to December 2018 to improve CFBD screening in patients 8 years or older, per current CF Foundation (CFF) guidelines. Our team formulated a dual-energy X-ray absorptiometry (DXA) scan algorithm based upon degree of bone mineral density (BMD); shared CFBD guideline recommendations in our quarterly newsletter; and ordered scans for eligible patients at weekly review meetings. We reviewed DXA results from 141 patients after institutional review board approval and gathered data including comorbidities, genetics, anthropometric measures, medication exposure, and relevant serum studies.
Results: Fifty-three percent of our patients had normal BMD (n = 75). Seventeen patients (12%) had a Z score ≤ -2. Patients with lower BMD also had lower mean forced expiratory volume (FEV_1) percent predicted (FEV_1 %) ($p < 0.001$) as well as lower body mass index % ($p = 0.001$). Patients with lower BMD were overall older at time of DXA ($p = 0.016$). During study duration, 13 patients who had abnormal DXA results underwent repeat DXAs after physical therapy; 11 of the 13 showed improvement in DXA results.
Conclusions: A DXA scan is a useful screening tool and can be used to identify pediatric patients who could benefit from further therapy and interventions to preserve adequate bone health and avoid further loss. QI initiatives can lead to improved screening and diagnosis and earlier intervention such as physical therapy. Further studies are needed to better understand the utility of physical therapy in children with CF.

Medicine (Baltimore). 2023 Jan 6;102(1):e32227.
doi: 10.1097/MD.0000000000032227.
Clinical relevance of low bone density in cystic fibrosis adult patients: A pilot study
Sandra Dury[1,2], Julien Ancel[1], Bruno Ravoninjatovo[1], Isabelle Lambrecht[3], Jeanne-Marie Perotin[1,4], Pauline Mulette[1], François Lebargy[1,2], Jean-Hugues Salmon[3], Gaëtan Deslée[1,4], Claire Launois[1]
Affiliations expand
PMID: 36607849 PMCID: PMC9829254 DOI: 10.1097/MD.0000000000032227
Abstract
Survival improvement in cystic fibrosis (CF) is associated with more frequent long-term complications, including CF related bone disease (CFBD). Impact of CFBD on global health outcome remains poorly described. We aimed to assess the relationship between low bone mineral density (BMD) and spinal pain, disability, and quality of life in CF adult patients. This monocentric cross-sectional study with prospective data collection was conducted from November 2016 to December 2019 in the Department of Respiratory Diseases at the University Hospital of Reims (NCT02924818). BMD was assessed by X-ray absorptiometry (DXA). Disability was assessed by the Health Assessment Questionnaire (HAQ). Quality of life was assessed by both the St George's Respiratory Questionnaire and the Cystic Fibrosis Questionnaire for teenagers and adults (CFQ 14+). Forty patients were analyzed, 68% of men, with a median age of 25 years, a median body mass index of 21 kg/m² and a median FEV1% of 54%. Nine patients (23%) had spinal pain. Ten patients (25%) had a low BMD. Compared with patients with normal BMD, patients with low BMD had a significantly lower BMI (22 vs 19 kg/m²; P = .006) and less vitamin D supplementation (33% vs 0%; P = .035). Low BMD was not associated with spinal pain, disability and quality of life. Low BMD is frequent in CF, affecting 1-quarter of adult patients. No significant association was found between low BMD and spinal pain, disability or quality of life.

Pancreas. 2022 Sep 1;51(8):1029-1036.
doi: 10.1097/MPA.0000000000002134.
Association of Islet Amyloid Polypeptide to C-Peptide Ratio With Cystic Fibrosis-Related Diabetes: A Prospective Cross-sectional Study
Rohith N Thota, Katie Wynne, Shyamala Pradeepan, Peter A B Wark, Manohar L Garg
PMID: 36607950 DOI: 10.1097/MPA.0000000000002134
Abstract
Objectives: Early detection of cystic fibrosis (CF) related diabetes (CFRD) improves health outcomes and reduces CF-related mortality. The study aims to evaluate the ratio of islet amyloid polypeptide (IAPP) to C-peptide in CF patients with diabetes and without diabetes.
Methods: Cross-sectional analysis was carried out in a prospective cohort of 33 participants (CF [n = 16] and CFRD [n = 18]). We examined the association of plasma IAPP:C-peptide ratio with clinical information, including glycated hemoglobin, and lung function markers.
Results: The median (interquartile range) IAPP:C-peptide ratio was significantly (P = 0.004) higher in people with CFRD (4.8 [4.5]) compared with participants without CFRD (12.1 [19.7]). The ratio of IAPP to C-peptide significantly accounted for a 38% variation in the diabetes status in patients with CF (r2 = 0.399, P < 0.001). Islet amyloid polypeptide is strongly correlated with serum ferritin levels (r = 0.683, P = 0.005) and forced expiratory volume in CFRD, but not in nondiabetic participants with CF.
Conclusions: Islet amyloid polypeptide:C-peptide ratio could be a potential marker of CFRD in adults with CF. Further research requires validation of this marker in longitudinal cohort studies to confirm the capability of IAPP:C-peptide to predict CFRD.

J Cyst Fibros. 2023 Jan 18;S1569-1993(23)00005-X.
doi: 10.1016/j.jcf.2023.01.003. Online ahead of print.
Bone health outcomes in post-lung transplant patients with cystic fibrosis
Triet Vincent M Tran[1], Xilong Li[2], Naim M Maalouf[3]
PMID: 36669961 DOI: 10.1016/j.jcf.2023.01.003
Abstract
Background: Osteoporosis is a common comorbidity in patients with cystic fibrosis (CF). Although lung transplantation (LTx) improves quality of life of CF patients, there is little research examining long-term bone health outcomes following LTx in these patients.
Methods: Data were collected on 59 patients who underwent LTx between 2006 and 2019, including 30 with CF and 29 without CF. We compared baseline characteristics, long-term bone mineral density (BMD) trends, and fracture incidence between the two patient populations, and examined factors associated with post-LTx fractures in CF patients.
Results: Compared with non-CF patients, patients with CF were younger, had lower body mass index, and lower baseline BMD Z-scores at the lumbar spine, femoral neck, and total hip (all p<0.001). BMD at all sites declined in both groups in the first year post-LTx. In subsequent years, CF patients exhibited better BMD recovery relative to pre-transplantation, but continued to have lower BMD post-LTx. Post-transplant fractures occurred in 30% and 34% of CF and non-CF patients, respectively. CF patients who developed fractures after LTx had significantly lower BMD and lower pre-transplantation percent predicted forced expiratory volume in one second (FEV1%).
Conclusions: Although CF patients exhibit better BMD recovery following LTx compared to their non-CF counterparts, CF patients start with significantly lower pre-LTx BMD and experience a similarly high rate of post-LTx fractures. These findings highlight the unique contribution of the CF disease process to bone health, as well as a clear need for better prevention and treatment of osteoporosis in CF patients before and after LTx.

Cochrane Database Syst Rev. 2023 Jan 10;1(1):CD002010.
doi: 10.1002/14651858.CD002010.pub5.
Bisphosphonates for osteoporosis in people with cystic fibrosis
Tomas C Jeffery[1], Anne B Chang[2], Louise S Conwell[3,4]
PMID: 36625789 PMCID: PMC9831115 DOI: 10.1002/14651858.CD002010.pub5
Abstract
Background: Osteoporosis is a disorder of bone mineralisation occurring in about one third of adults with cystic fibrosis. Bisphosphonates can increase bone mineral density and decrease the risk of new fractures in post-menopausal women and people receiving long-term oral corticosteroids. This is an updated version of a previous review.
Objectives: To assess the effects of bisphosphonates on the frequency of fractures, bone mineral density, quality of life, adverse events, trial withdrawals, and survival in people with cystic fibrosis.
Search methods: We searched the Cystic Fibrosis and Genetic Disorders Group's Trials Register of references (identified from electronic database searches and hand searches of journals and abstract books) on 5 May 2022. We performed additional searches of PubMed, clinicaltrials.gov and the WHO ICTRP (International Clinical Trials Registry Platform) on 5 May 2022.
Selection criteria: Randomised controlled trials of at least six months duration studying bisphosphonates in people with cystic fibrosis.

Data collection and analysis: Authors independently selected trials, extracted data and assessed risk of bias in included studies. Trial investigators were contacted to obtain missing data. We judged the certainty of the evidence using GRADE.
Main results: We included nine trials with a total of 385 participants (272 adults and 113 children (aged five to 18 years)). Trial durations ranged from six months to two years. Only two of the studies were considered to have a low risk of bias for all the domains. Bisphosphonates compared to control in people with cystic fibrosis who have not had a lung transplant Seven trials included only adult participants without lung transplants, one trial included both adults and children without lung transplantation (total of 238 adults and 113 children). We analysed adults (n = 238) and children (n = 113) separately. Adults Three trials assessed intravenous bisphosphonates (one assessed pamidronate and two assessed zoledronate) and five trials assessed oral bisphosphonates (one assessed risedronate and four assessed alendronate). Bisphosphonates were compared to either placebo or calcium (with or without additional vitamin D). Data showed no difference between treatment or control groups in new vertebral fractures at 12 months (odds ratio (OR) 0.22, 95% confidence interval (CI) 0.02 to 2.09; 5 trials, 142 participants; very low-certainty evidence) and two trials (44 participants) reported no vertebral fractures at 24 months. There was no difference in non-vertebral fractures at 12 months (OR 2.11, 95% CI 0.18 to 25.35; 4 trials, 95 participants; very low-certainty evidence) and again two trials (44 participants) reported no non-vertebral fractures at 24 months. There was no difference in total fractures between groups at 12 months (OR 0.57, 95% CI 0.13 to 2.50; 5 trials, 142 participants) and no fractures were reported in two trials (44 participants) at 24 months. At 12 months, bisphosphonates may increase bone mineral density at the lumbar spine (mean difference (MD) 6.31, 95% CI 5.39 to 7.22; 6 trials, 171 participants; low-certainty evidence) and at the hip or femur (MD 4.41, 95% 3.44 to 5.37; 5 trials, 155 participants; low-certainty evidence). There was no clear difference in quality of life scores at 12 months (1 trial, 47 participants; low-certainty evidence), but bisphosphonates probably led to more adverse events (bone pain) at 12 months (OR 8.49, 95% CI 3.20 to 22.56; 7 trials, 206 participants; moderate-certainty evidence). Children The single trial in 113 children compared oral alendronate to placebo. We graded all evidence as low certainty. At 12 months we found no difference between treatment and placebo in new vertebral fractures (OR 0.32, 95% CI 0.03 to 3.13; 1 trial, 113 participants) and non-vertebral fractures (OR 0.19, 95% CI 0.01 to 4.04; 1 trial, 113 participants). There was also no difference in total fractures (OR 0.18, 95% CI 0.02 to 1.61; 1 trial, 113 participants). Bisphosphonates may increase bone mineral density at the lumbar spine at 12 months (MD 14.50, 95% CI 12.91 to 16.09). There was no difference in bone or muscle pain (MD 3.00, 95% CI 0.12 to 75.22), fever (MD 3.00, 95% CI 0.12 to 75.22) or gastrointestinal adverse events (OR 0.67, 95% CI 0.20 to 2.26). The trial did not measure bone mineral density at the hip/femur or report on quality of life. Bisphosphonates compared to control in people with cystic fibrosis who have had a lung transplant One trial of 34 adults who had undergone lung transplantation compared intravenous pamidronate to no bisphosphonate treatment. It did not report at 12 months and we report the 24-month data (not assessed by GRADE). There was no difference in the number of fractures, either vertebral or non-vertebral. However, bone mineral density increased with treatment at the lumbar spine (MD 6.20, 95% CI 4.28 to 8.12) and femur (MD 7.90, 95% CI 5.78 to 10.02). No participants in either group reported either bone pain or fever. The trial did not measure quality of life.
Authors' conclusions: Oral and intravenous bisphosphonates may increase bone mineral density in people with cystic fibrosis, but there are insufficient data to determine whether treatment reduces fractures. Severe bone pain and flu-like symptoms may occur with intravenous bisphosphonates. Before any firm conclusions can be drawn, trials in larger populations, including children, and of longer duration are needed to determine effects on fracture rate and survival. Additional trials are needed to determine if bone pain is more common or severe (or both) with the more potent zoledronate and if corticosteroids can ameliorate or prevent these adverse events. Future trials should also assess gastrointestinal adverse effects associated with oral bisphosphonates.