CF RD AND SW CONSORTIUM

Winter Newsletter

Special thanks to our sponsors:

- **MVW Nutritionals**
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Save the date!

Our annual meeting will be held in Louisville, KY April 3rd-5th at the historic and beautiful Brown Hotel brownhotel.com

Registration will be limited to the first 150 registrants, so plan ahead!

Registration opens Monday, January 9th at 12 pm EST

Body Image Resources:

- Perspectives on body image from people with CF (U.K. Trust)

https://www.cysticfibrosis.org.uk/what-is-cystic-fibrosis/how-does-cystic-fibrosis-affect-the-body/body-image

- Training video for discussing weight during medical visits (*non-CF specific*).

https://www.youtube.com/watch?v=lZLzHFgE0AQ

- Article from adult with CF about Trikafta weight gain

https://cystic -fibrosis.com/living/trikafta-weight-gain?utm_source=facebook.com&utm_medium=organic&fbclid=IwAR1XlqzVy58RqkglyVXMSY7LY_dBkc6R1NFJlFExwPlF-PfcrkYl6vonGNg

- GI Symptom trackers (with body image questions):

https://www.chiesicfportal.com/SymptomTracker/teenandadult

Social Risk Factors

Check out the new CF Social Determinants of Health (SDOH) toolkit available in the CF Resource Library

https://my.cff.org/cfx-docrep/document/detail/CF%20SDOH%20Toolkit.pdf

Insurance Resources

Find Modules from CFF Compass related to Insurance denials and insurance appeals - including commercial insurance, Medicare and Medicaid:

https://www.youtube.com/playlist?list=PLhoQ6vyZhgqpycN_-mYIbioKVamOPcuYL

RDs!

Certified Advanced CF Dietitian (CACFD) applications opened on December 1st! Applications and information is posted on our website:

https://www.cfrdswconsortium.com/s-projects-side-by-side

Congratulations to the RDs that have been approved for their Advanced CF Certification so far during this round of applications:

Kimberly Altman
Kelly Baumberger
Nicole Benesh
Molly Bigford
Courtney Busby
Tara Griffin
Sara Hendrix
Courtney Iwanicki
Amanda Leonard
Catherine McDonald
Clarissa Morency
Leann Mullens
Tammy Petrossian
Theresa Schindler
Bekah Sommer
Kimberly Stephenson
Kay Vavrina
Shari Willy

Applications will be accepted again in the summer with a deadline of July 15th

4th Quarter 2022 Abstracts

NUTRITION

The relationship between weight and pulmonary outcomes in overweight and obese people with cystic fibrosis: A retrospective observational study

John J Welter[1], Alison T Lennox[1], Sankaran Krishnan[1], Christy Kim[1], Sheila Krishnan[2], Haley Thompson[1], Emily McAllister[1], Kristen Huang[1], Kasiemobi Nwaedozie[1], Allen J Dozor[1]
Health Sci Rep. 2022 Oct 28;5(6):e910.
doi: 10.1002/hsr2.910. eCollection 2022 Nov.

- PMCID: PMC9616171
- DOI: 10.1002/hsr2.910

Background: A major focus in cystic fibrosis (CF) care aims to increase weight gain. Rates of overweight and obese people with CF have gradually increased over the past decade. Obesity could be a risk for restriction of lung volumes and airway obstruction as well as increase rates of pulmonary exacerbations in people with CF.

Aim: To assess the relationship between weight categories and pulmonary outcomes in children and adults with CF.

Methods: Patients 6 years of age and older were categorized into weight categories based on the Centers for Disease Control and Prevention (CDC) definitions. A retrospective chart review was conducted to obtain lung function testing and other outcomes.

Results: One hundred five patients with a median age of 20.6 years were included in this analysis. 8.4%, 64%, 18%, and 10% of patients were underweight, normal/healthy weight, overweight, and obese, respectively. Forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) (% predicted) did not differ between patients with weights in the normal range versus patients in the overweight/obese categories. Linear regression analysis showed a direct correlation between body mass index (BMI) and FEV_1 that continued as BMI entered overweight and obese categories in both pediatric and adult patients. Overweight/obese patients did not have increased rates of pulmonary exacerbations compared to those in the normal/healthy weight category.

Conclusion: As CF therapies continue to improve, an increasing number of people with CF are exceeding the CDC's normal-weight range. Gaining weight past the normal range does not appear to negatively impact pulmonary health of people with CF. If this trend of increased weight gain continues, it remains to be seen if it will eventually negatively affect lung health

Trajectories of early growth and subsequent lung function in cystic fibrosis: An observational study using UK and Canadian registry data

Amy Macdougall[1], Deborah Jarvis[2], Ruth H Keogh[3], Cole Bowerman[4], Diana Bilton[5], Gwyneth Davies[6], Siobhán B Carr[7], Sanja Stanojevic[4]
J Cyst Fibros. 2022 Sep 7;S1569-1993(22)00658-0.
doi: 10.1016/j.jcf.2022.09.001. Online ahead of print.

- PMID: 36088206
- DOI: 10.1016/j.jcf.2022.09.001

Background: Understanding the pulmonary impact of changes in early life nutritional status over time in a paediatric CF population may help inform how to use nutritional assessment to guide clinical care. National registry data provides an opportunity to study patterns of weight gain over time at the level of the individual, and thus to gain detailed understanding of the relationship between early weight trajectories and later lung function in children with Cystic Fibrosis (CF).

Methods: Using data from the United Kingdom (UK) and Canadian CF Registries, a mixed effects linear regression model was used to describe children's weight and BMI z-score trajectories from age 1 to 5 years. The intercept (weight-for-age at age 1) and slope (weight-for-age trajectory) from this model were then used as covariates in a linear regression of first lung function measurement at age 6 years.

Results: In both the UK and Canadian data, greater weight-for-age z-score at age 1 year and greater change in weight-for-age over time were associated with higher FEV_1%

predicted. A greater weight-for-age z-score at age 1 year was associated with a higher FEV_1% predicted (UK: 3.78% (95% CI: 1.76; 4.70); Canada: 3.20% (95%CI: 1.76, 4.70)). These associations were reproduced for BMI z-scores and FVC% predicted.

Conclusions: Early weight-for-age, specifically at age 1 year, and weight-for-age trajectories across early childhood are associated with later lung function. This relationship persists after adjustment for potential confounders. Current guidelines may need to be updated to place less emphasis on a specific cut-off (such as the 10th percentile) and encourage tracking of weight-for-age over time.

Obesity in Cystic fibrosis: prevalence, trends and associated factors data from the US cystic fibrosis foundation patient registry

Sylvia Szentpetery[1], Gabriela S Fernandez[2], Michael S Schechter[3], Raksha Jain[4], Patrick A Flume[5], Aliza K Fink[2]
J Cyst Fibros. 2022 Sep;21(5):777-783.
doi: 10.1016/j.jcf.2022.03.010. Epub 2022 Apr 5.

- PMID: 35396178
- PMCID: PMC9509402
- DOI: 10.1016/j.jcf.2022.03.010

Strong emphasis has been placed historically on increasing weight and improving nutritional status in cystic fibrosis patients. Due to correlation between nutritional indices (e.g. BMI) and lung function, CF Nutrition Guidelines have recommended BMI percentile goals at the 50th percentile or higher. Trends in increasing BMI across CF programs suggest significantly increasing proportions of overweight and obese status in recent years. We identify that between 2000 and 2019 there has been a relative decrease in underweight status by ~40%, simultaneously with a > 300% increase in overweight status, and >400% increase in obesity. Patient specific factors associated with higher prevalence of obesity included age ≥46, living in a zip code where the median income was < $20,000, having at least one allele with a class IV or V mutation, a $ppFEV_1$ >90 prescribed ivacaftor, and not prescribed pancreatic enzymes. Program specific factors were not identified.

Updates in Nutrition Management of Cystic Fibrosis in the Highly Effective Modulator Era

Alexandra Wilson[1], Kimberly Altman[2], Terri Schindler[3], Sarah Jane Schwarzenberg[4]
Clin Chest Med 2022 Dec;43(4):727-742.
doi: 10.1016/j.ccm.2022.06.012.

- PMID: 36344077
- DOI: 10.1016/j.ccm.2022.06.012

Attainment and maintenance of good nutrition has been an important aspect of management in cystic fibrosis (CF) for decades. In the era of highly effective modulator therapy for CF, the quality of the nutrients we recommend is increasingly important. Our therapy must support our patients' health for many years beyond what we previously thought. Preventing cardiovascular disease, reducing hyperlipidemia, and optimizing lean body mass for active, longer lives now join the long-standing goal of promoting lung function through nutrition. This chapter summarizes recent developments in nutrition in people with CF, with an eye to the evolution of our practice.

An unusual case of cystic fibrosis with pancytopenia due to copper deficiency and blindness caused by vitamin A deficiency: A case-report

Hesamedin Nabavizadeh[1,2], Leila Johari[1], Rafat Noeiaghdam[1], Soheila Alyasin[1,2], Hossein Esmaeilzadeh[1,2], Zahra Kanannejad[2], Maryam Emaminia[1]
Affiliations expand
Respir Med Case Rep. 2022 Nov 7;40:101774.
doi: 10.1016/j.rmcr.2022.101774. eCollection 2022.

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- PMCID: PMC9650065
- DOI: 10.1016/j.rmcr.2022.101774

Cystic fibrosis (CF) is a multi-systemic autosomal recessive disease which mostly involves the respiratory, digestive, and reproductive systems, but it can present with various clinical presentations, especially in adulthood. We describe a 19-year-old boy, a known case of CF who presented with less known clinical presentations of CF, blindness, liver cirrhosis, vitamin A deficiency, and pancytopenia.

Experience to date with CFTR modulators during pregnancy and breastfeeding in the British Columbia Cystic Fibrosis clinic

Jodi Goodwin[1], Bradley S Quon[1], Pearce G Wilcox[1]
Respir Med Case Rep 2022 Nov 8;40:101778.
doi: 10.1016/j.rmcr.2022.101778. eCollection 2022.

- PMID: 36386290
- PMCID: PMC9649942
- DOI: 10.1016/j.rmcr.2022.101778

The introduction and rapid uptake of CFTR modulator therapy, in addition to other treatments, has significantly increased life expectancy in CF and provided more women the opportunity to consider and successfully be managed throughout pregnancy. There is however limited evidence to guide patient management and enable informed decision making. Here we report the experience to date from a large multidisciplinary Cystic Fibrosis quaternary referral center in managing patients on CFTR modulators in the peri- and post-partum periods. While women in this case series were advised to discontinue CFTR modulators during pregnancy, they would likely receive a very different message today.

Cystic Fibrosis Patients with F508del/Minimal Function Genotype: Laboratory and Nutritional Evaluations after One Year of Elexacaftor/Tezacaftor/Ivacaftor Treatment

Vincenzo Carnovale[1], Filippo Scialò[2,3], Monica Gelzo[3,4], Paola Iacotucci[5], Felice Amato[3,4], Federica Zarrilli[3,4], Assunta Celardo[1], Giuseppe Castaldo[3,4], Gaetano Corso[6]
J Clin Med 2022 Nov 22;11(23):6900.
doi: 10.3390/jcm11236900.

- PMID: 36498475
- PMCID: PMC9735556
- DOI: 10.3390/jcm11236900

The last ten years have been characterized by an enormous step forward in the therapy and management of patients with Cystic Fibrosis (CF), thanks to the development and combination of *Cystic Fibrosis Transmembrane Receptor* (*CFTR*) correctors and potentiators. Specifically, the last approved triple combination elexacaftor/tezacaftor/ivacaftor has been demonstrated to improve lung function in CF patients with both homozygous Phe508del and Phe508del/minimal function genotypes. Here we have assessed the effect of elexacaftor/tezacaftor/ivacaftor in patients carrying the Phe508del/minimal function genotype (*n* = 20) after one year of treatments on liver function and nutrient absorption with a focus on lipid metabolism. We show that weight, BMI, and albumin significantly increase, suggesting a positive impact of the treatment on nutrient absorption. Furthermore, cholesterol levels as a biomarker of lipid metabolism increased significantly after one year of treatment. Most importantly, we suggest that these results were not dependent on the diet composition, possibly indicating that the drug improves the hepatic synthesis and secretion of proteins and cholesterol.

GASTROINTESTINAL

Multicenter prospective study showing a high gastrointestinal symptom burden in cystic fibrosis

Baha Moshiree[1], A Jay Freeman[2], Phuong T Vu[3], Umer Khan[3], Carmen Ufret-Vincenty[3], Sonya L Heltshe[4], Christopher H Goss[5], Sarah Jane Schwarzenberg[6], Steven D Freedman[7], Drucy Borowitz[8], Meghana Sathe[9]; GALAXY Study Group
J Cyst Fibros 2022 Oct 29;S1569-1993(22)01388-1.
doi: 10.1016/j.jcf.2022.10.006.

- DOI: 10.1016/j.jcf.2022.10.006

Background and aims: People with cystic fibrosis (PwCF) suffer from gastrointestinal (GI) symptoms affecting their quality of life (QOL). Despite the relevance of GI symptoms to the overall health of PwCF, a paucity of studies only have comprehensively assessed the prevalence, severity and QOL of GI symptoms in both children and adults with Cystic Fibrosis (CF).

Methods: Eligible participants ≥2 years of age across 26 US CF centers were followed for 4 weeks. Three validated GI electronic patient-reported outcome measures (ePROMs) with a recall period of 2 weeks and a stool-specific questionnaire were

administered weekly over four weeks. Total and domain scores of ePROMs were evaluated overall and in subgroups using linear mixed-effect models.

Results: Of 402 enrolled, 58% were ≥ 18 years of age (52% male). The mean (SD) of the total score for PAC-SYM was 0.52 (0.55), for PAGI-SYM was 0.63 (0.67), and for PAC-QOL was 0.67 (0.55). For specific ePROM questions, prevalence of moderate to very severe symptoms were as follows: straining (20.3%), fullness (18.3%), incomplete bowel movements (17.1%), bloating (16.4%), distension (16.4%), abdominal pain (upper-5.1%, lower-7.5%). Comparing participants ≥18 versus <18, a higher prevalence of bloating (63.7% versus 27.3%), lower abdominal pain (39.8% vs 26.2%), stomach fullness (75.6% versus 56.2%), and abdominal distension (60.2% versus 34.9%) was found. Both age groups reported high treatment dissatisfaction as measured with PAC-QOL, mean 1.39 (95% CI: 1.30, 1.47).

Conclusion: GI symptoms were reported in all age ranges irrespective of gender, with higher prevalence observed amongst older and female subgroups. Dissatisfaction with GI targeted treatments were reported in a large proportion of participants despite therapy, highlighting an unmet need for clinical interventions.

Gastrointestinal consequences of lipopolysaccharide-induced lung inflammation

Rachel M McQuade[1,2,3], Methma Bandara[4], Shanti Diwakarla[4,5], Lauren Sahakian[4], Myat Noe Han[4,6], Maryam Al Thaalibi[7], Madeleine R Di Natale[6,8], Marsha Tan[9], Kiera H Harwood[9], Elena K Schneider-Futschik[#9], Andrew Jarnicki[#10]
Inflamm Res 2022 Nov 2;1-18.
doi: 10.1007/s00011-022-01657-0.

- PMID: 36322182
- PMCID: PMC9628607
- DOI: 10.1007/s00011-022-01657-0

Background: Respiratory inflammation is the body's response to lung infection, trauma or hypersensitivity and is often accompanied by comorbidities, including gastrointestinal (GI) symptoms. Why respiratory inflammation is accompanied by GI dysfunction remains unclear. Here, we investigate the effect of lipopolysaccharide (LPS)-induced lung inflammation on intestinal barrier integrity, tight-junctions, enteric neurons and inflammatory marker expression.

Methods: Female C57bl/6 mice (6-8 weeks) were intratracheally administered LPS (5 µg) or sterile saline, and assessed after either 24 or 72 h. Total and differential cell counts in bronchoalveolar lavage fluid (BALF) were used to evaluate lung inflammation. Intestinal barrier integrity was assessed via cross sectional immunohistochemistry of tight junction markers claudin-1, claudin-4 and EpCAM. Changes in the enteric nervous system (ENS) and inflammation in the intestine were quantified immunohistochemically using neuronal markers Hu + and nNOS, glial markers GFAP and S100β and pan leukocyte marker CD45.

Results: Intratracheal LPS significantly increased the number of neutrophils in BALF at 24 and 72 h. These changes were associated with an increase in CD45 + cells in the ileal mucosa at 24 and 72 h, increased goblet cell expression at 24 h, and increased expression of EpCAM at 72 h. LPS had no effect on the expression of GFAP, S100β, nor the number of Hu + neurons or proportion of nNOS neurons in the myenteric plexus.

Conclusions: Intratracheal LPS administration induces inflammation in the ileum that is associated with enhanced expression of EpCAM, decreased claudin-4 expression and increased goblet cell density, these changes may contribute to systemic inflammation that is known to accompany many inflammatory diseases of the lung.

Update in Advancing the Gastrointestinal Frontier in Cystic Fibrosis

Christopher Vélez[1], Steven D Freedman[2], David N Assis[3]
Clin Chest Med 2022 Dec;43(4):743-755.
doi: 10.1016/j.ccm.2022.07.001.

- PMID: 36344078
- DOI: 10.1016/j.ccm.2022.07.001

Clinical complications of cystic fibrosis (CF) include a variety of gastrointestinal (GI) and hepatobiliary manifestations. Recent years have witnessed several advances in the understanding and management of these complications, in addition to opportunities for therapeutic innovations. Herein we review the current understanding of these disorders and also discuss the management of the GI and hepatobiliary complications experienced by persons with CF.

Higher mortality rates associated with Clostridioides difficile infection in hospitalized children with cystic fibrosis

Prathipa Santhanam[1], Matthew Egberg[1,2,3], Michael D Kappelman[1,2,3]
Pediatr Pulmonol 2022 Nov 9.
doi: 10.1002/ppul.26214.

- PMID: 36349995
- DOI: 10.1002/ppul.26214

Objective(s): To determine the association of Clostridioides difficile Infection (CDI) with in-hospital mortality, Length of Stay (LOS), and hospital charges among pediatric Cystic Fibrosis (CF) hospitalizations using a large nationally representative pediatric hospital database.

Study design: We identified Cystic Fibrosis-related hospitalizations during the years 1997 to 2016 in the Kids' Inpatient Database (KID) and compared in-hospital mortality, LOS, and hospital charges among hospitalizations with and without a coexisting diagnosis of C. difficile using logistic regression models for mortality and general linear models with gamma distribution and logarithmic transformation for LOS and hospital charges. We also evaluated temporal trends in the proportion of CF hospitalizations with concomitant CDI using data published triennially RESULTS: We analyzed 21,616 pediatric CF hospitalizations between the years 1997 to 2016 and found a total of 240 (1.1%) hospitalizations with concurrent CDI diagnosis. Adjusted analyses demonstrated an association of CDI with increased mortality (OR 5.2, 95% CI 2.5-10.7), longer LOS (46.5% increment, 95% CI 36.0-57.1), and higher charges (65.8% increment, 95% CI 53.5-78.1) for all comparisons. The proportion of CF hospitalizations with CDI increased over time from 0.64% in 1997 to 1.73% in 2016 ($p < 0.001$).

Conclusion(s): As CDI is associated with excess mortality, LOS, and cost in children hospitalized for CF, a healthy level of suspicion for CDI may be needed in patients with CF in the appropriate clinical context. Efforts to prevent, diagnose, and treat CDI may improve hospital outcomes among children with CF.

Personalized medicine approaches in cystic fibrosis related pancreatitis

Kyu Shik Mun[1,2], Jaimie D Nathan[3,4], Anil G Jegga[5,6], Kathryn A Wikenheiser-Brokamp[7,8], Maisam Abu-El-Haija[5,9], Anjaparavanda P Naren[1,10]
Am J Transl Res 2022 Oct 15;14(10):7612-7620.
eCollection 2022.

- PMID: 36398272
- PMCID: PMC9641468

We report a rare case of a patient with cystic fibrosis suffering from debilitating abdominal pain due to chronic pancreatitis. This 13-year-old patient was evaluated for surgical intervention to relieve pain from chronic pancreatitis and to improve quality of life. The patient carried two mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene; the most common ΔF508 variant and a second variant, p.Glu1044Gly, which has not been previously described. The patient's condition did not improve despite medical management and multiple endoscopic interventions, and therefore total pancreatectomy with islet autotransplantation and a near-total duodenectomy was offered for definitive management. Patient-derived duodenal crypts were isolated and cultured from the resected duodenum, and duodenal organoids were generated to test CFTR function. Our studies demonstrate that this novel mutation (ΔF508/p.Glu1044Gly) caused severely impaired CFTR function *in vitro*. The Food and Drug Administration (FDA)-approved drug ivacaftor, a CFTR potentiator, was identified to robustly improve CFTR function in the context of this novel mutation. Herein, we describe a personalized medicine approach consisting of performing drug testing on individual patient derived organoids that has potential to guide management of patients with novel CFTR genetic mutations. Identified effective medical therapeutics using this approach may avoid irreversible surgical treatments such as total pancreatectomy with islet autotransplantation in the future.

The association of fecal calprotectin and respiratory exacerbation in cystic fibrosis patients

Farid Imanzadeh[1], Fatemeh Kerami[2], Maryam Hassanzad[3], Amirhossein Hosseini[4], Mahmoud Hajipour[1], Ghamartaj Khanbabaee[5], Naghi Dara[1], Katayoun Khatami[1], Nazanin Farahbakhsh[5], Aliakbar Sayyari[1]
BMC Gastroenterol 2022 Nov 28;22(1):494.
doi: 10.1186/s12876-022-02553-x.

- PMID: 36443671
- PMCID: PMC9707052
- DOI: 10.1186/s12876-022-02553-x

Background: CF patients experience several episodes of pulmonary exacerbations and reduction in their lung function progressively. Lung function is not the only diagnostic index by physicians to decide if CF patients require antibiotic therapy following pulmonary exacerbations. Non-invasive fecal indicators are increasingly being used to assess intestinal inflammation. Calprotectin is the most extensively utilized fecal biomarker in recent CF researches.

Methods: In this longitudinal study, 30 CF patients (1-18 years) without current infectious gastroenteritis were recruited from Mofid Children's Hospital and Masih Daneshvari Hospital, Tehran, Iran. Then, fecal calprotectin levels were evaluated before treatment, two weeks after systemic antibiotic administration, as well as recurrence of pulmonary exacerbation after first post-hospital discharge.

Results: The initial fecal calprotectin level in CF patients receiving antibiotics was 651.13 ± 671.04, significantly decreasing two weeks after antibiotic therapy and following recurrence (171.81 ± 224.40, 607.93 ± 549.89, respectively; $P < 0.01$). Following systemic antibiotic treatment, the patient's respiratory and GI symptoms improved ($P < 0.01$).

Conclusion: Our findings revealed that fecal calprotectin modifications are associated with CF pulmonary exacerbations and antibiotic treatment could reduce calprotectin levels. Therefore, the fecal calprotectin level could be considered as a diagnostic tool and an index to follow the response to treatment in CF pulmonary exacerbations

Need to study simplification of gastrointestinal medication regimen in cystic fibrosis in the era of highly effective modulators

Meghana Sathe[1], Baha Moshiree[2], Enid Aliaj[3], MinJae Lee[4], Jessica Hudson[3], Alex Gifford[5,6], Susan Attel[7], Breck Gamel[7], Steven D Freedman[8], Sarah Jane Schwarzenberg[9], A Jay Freeman[10]
Pediatr Pulmonol 2022 Nov 30.
doi: 10.1002/ppul.26257. .

- PMID: 36448312
- DOI: 10.1002/ppul.26257

Introduction: The success of highly effective modulator therapy (HEMT) has led to consideration of simpler regimens for people with CF (PwCF) with opportunities to modify burdensome regimens. Despite the intuitive appeal of discontinuing chronic therapies no longer necessary, this process should be pursued systematically to ensure safety, adherence, and validate patient-centered preferences. We designed a questionnaire to determine the state of use of acid-suppressive medications (ASM) and pancreatic enzyme therapy (PERT), current self-withdrawal and provider-directed withdrawal practices, and interest in a standardized withdrawal study.

Methods: In collaboration with CF Foundation (CFF), a questionnaire was developed and distributed to members of Community Voice (CV, comprised of PwCF and their loved ones), and CF providers regarding the need to study simplifying the gastrointestinal (GI) regimen for PwCF on HEMT.

Results: Approximately 20-40% of CV or CF providers have decreased or stopped ASM for those on HEMT. For PERT, CV and CF providers have decreased dose (34%-48% and approximately 25%, respectively) more often than having stopped it altogether (13%-24% and 3%-12%, respectively). Cumulatively, there is interest in pursuing research in this area (86% CV and 89% CF providers) and willingness to enroll in such a study (80% CV and 89% CF providers).

Conclusion: Systematically studying the withdrawal of common GI medications, ASM and PERT, is important to CV and CF providers. Decreases in dosing and withdrawal are already taking place without evidence to support this practice. This questionnaire is the first step in designing a GI medication simplification study in PwCF on HEMT.

Case Series of Acute Meconium Peritonitis Secondary to Perforation of the Ileum in the Antepartum Period

Maria Grazia Piccioni[1], Lucia Merlino[1], Giulia D'Ovidio[1], Federica Del Prete[1], Valerio Galli[1], Lucia Petrivelli[1], Flaminia Vena[1], Valentina D'Ambrosio[1], Antonella Giancotti[1], Roberto Brunelli[1]
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doi: 10.3390/jcm11237127.

- PMID: 36498701
- PMCID: PMC9740722
- DOI: 10.3390/jcm11237127

Perforation of the ileum in the antepartum period resulting in meconial peritonitis is a condition that, although rare, is burdened by several complications. In 80-90% of cases, meconial ileus is the first manifestation of a disease, cystic fibrosis. In the remaining 10-20% of cases, it is caused by other situations, such as prematurity. In most cases, the diagnosis of meconial ileus occurs after birth, although in some cases it can be suspected prenatally, with the finding of a hyperechoic intestine on second trimester ultrasound. The prognosis depends on the gestational age, the location of the obstruction and the presence of fetal abnormalities. Mortality is very high and the recovery of intestinal function in the postoperative course is very high risk. In this case series, we describe two meconial peritonitis and our experience at the center.

PSYCHOSOCIAL

Management of Mental Health in Cystic Fibrosis

Christina Jayne Bathgate[1], Michelle Hjelm[2], Stephanie S Filigno[3], Beth A Smith[4], Anna M Georgiopoulos[5]
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doi: 10.1016/j.ccm.2022.06.014.

- PMID: 36344081
- DOI: 10.1016/j.ccm.2022.06.014

This article is intended for use among all cystic fibrosis care team members. It covers common mental health concerns and their unique presentations in persons with cystic fibrosis (pwCF) in areas such as depression, anxiety, trauma, behavioral disorders emerging in childhood, sleep, problematic eating patterns, and the impact of substance use. Furthermore, the authors address ways to manage these mental health symptoms through risk assessment, psychological interventions, and/or psychotropic medications. Quick reference tables are provided for evidence-based psychological interventions and medications often used for mental health conditions in pwCF.

Mental Health of Cystic Fibrosis Patients and the COVID-19 Pandemic in Poland: A Single-Center Comparative Study

Magdalena Humaj-Grysztar[1], Marta Rachel[2,3], Olga Śmiech-Michalec[4], Joanna Bonior[4]
Int J Environ Res Public Health 2022 Nov 30;19(23):16056.
doi: 10.3390/ijerph192316056.

- PMID: 36498128
- PMCID: PMC9736216
- DOI: 10.3390/ijerph192316056

Research shows that people with cystic fibrosis are more prone to suffer from psychological problems than healthy people; thus, the outbreak of the COVID-19 pandemic in Poland could have had an impact on their mental health. To assess this impact, we examined the mental health of patients before and during the pandemic. Survey participants were asked to fill in questionnaires that consisted of Beck Depression Inventory (BDI), 12-Item General Health Questionnaire (GHQ-12) and Cystic Fibrosis Questionnaire-Revised (CFQ-R; for the purpose of the study, an emotional functioning domain was used) during their hospital visits. A total of 81 patients took part in the study: 39 before the COVID-19 pandemic (BP) and 42 during the COVID-19 pandemic (DP). Patients' medians were lower for the BDI, GHQ-12 and higher for the emotional domain of CFQ-R during the pandemic (3, 6, 75 vs. 4, 10, 73.33). Fewer patients felt that their mental health had deteriorated during the pandemic ($\Delta\chi^2$ = 7.723; p = 0.005), and GHQ-12 scores were lower in the DP group (Z = -3.044; p = 0.002). No significant differences were found between groups in terms of experiencing depressive symptoms ($\Delta\chi^2$ = 1.036; p = 0.309). It was found that patients with cystic fibrosis from our study group not only maintained but also improved their mental health state during the COVID-19 pandemic.

Clinician perspectives on assessing for disordered eating and body image disturbance in adolescents and young adults with cystic fibrosis

Alexandra P Kass[1], Traci M Kazmerski[2], Elana Bern[3], Sabina Sabharwal[3], Jessica Leonard[3], Moira Harrison[3], Katherine Barnico[3], Tracy Richmond[3], Gregory S Sawicki[3]
J Cyst Fibros
2022 Dec 2;S1569-1993(22)01416-3.
doi: 10.1016/j.jcf.2022.11.006. Online ahead of print.

- PMID: 36470797
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Background: Maintaining a healthy weight is a focus of Cystic Fibrosis (CF) care. With the increased use of highly effective CFTR modulators, many people with CF are gaining weight more easily, which may affect eating habits and body image. This study investigates providers' understanding and current practices surrounding body image disturbance and disordered eating in people with CF.

Methods: We distributed a one-time web-based survey to United States (U.S.)-based CF healthcare providers via CF Foundation list servs. The survey investigated providers' understanding and perceived importance of issues surrounding disordered eating and body image disturbance in adolescent and young adults (AYA) with CF as well as current screening practices. We used descriptive statistics to analyze participants' characteristics and practices.

Results: A total of 232 healthcare providers completed the survey. While most participants felt that screening for both body image disturbance and disordered eating should be standardized in CF care (79% and 82%, respectively), fewer than one third felt comfortable screening, and only one quarter actually screened for various eating disordered behaviors in daily practice. Only 2.7% reported using a formal screening tool. Participants reported provider assessment tools (86%), standardized partnerships with eating disorder specialists (80%), and CFF or national guidelines (79%) would be helpful to improve screening and counseling.

Conclusion: While most CF providers believe that body image disturbance and disordered eating are important topics in AYA with CF, few address these topics with their patients. The development of educational sessions and national guidelines may improve screening and counseling practices.

ENDOCRINE

Endocrine Complications of Cystic Fibrosis

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Endocrine comorbidities have become increasingly important medical considerations as improving cystic fibrosis (CF) care increases life expectancy. Although the underlying pathophysiology of CF-related diabetes remains elusive, the use of novel technologies and therapeutics seeks to improve both CF-related outcomes and quality of life. Improvements in the overall health of those with CF have tempered concerns about pubertal delay and short stature; however, other comorbidities such as hypogonadism and bone disease are increasingly recognized. Following the introduction of highly effective modulator therapies there are many lessons to be learned about their long-term impact on endocrine comorbidities.

Carbohydrate metabolism impairment in children and adolescents with cystic fibrosis

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Introduction: Development of cystic fibrosis-related diabetes (CFRD) is associated with worsening of nutritional status and lung function, as well as increased mortality. The relevance of diagnosing the «pre-diabetic» status in these patients has not been addressed and the utility of HbA1c measurement in these patients is under discussion.

Aim: To study and characterise the different categories of carbohydrate metabolism impairment in paediatric patients with cystic fibrosis.

Patients and methods: A transversal study for characterisation of carbohydrate metabolism impairment according to clinical and anthropometric status and genetic

background in 50 paediatric patients with cystic fibrosis (CF) was undertaken. Oral glucose tolerance tests (OGTT) for determination of glucose and insulin levels measurement and continuous subcutaneous glucose monitoring (CSGM) were performed.

Results: 6% of patients presented with CFRD, 26% impaired glucose tolerance, 10% an indeterminate glucose alteration and 2% impaired fasting glucose. The severity of glycaemic impairment correlated positively with age and negatively with standardised height ($p < 0.05$) with intergroup differences in HbA1c levels ($p < 0.01$), with the latter correlating with the duration of hyperglycaemia throughout CSGM. No intergroup differences in mutation prevalence, pulmonary function test, nutritional status or disease exacerbations in the previous year were found. The daily enzyme replacement dose correlated with the glucose area under the curve (AUC, $p < 0.05$) but not with insulin-AUC.

Conclusions: An older age and greater enzyme replacement need are correlated with more severe carbohydrate metabolism impairment and lower standardized height in paediatric CF patients, with HbA1c correlating with the duration of hyperglycaemia. The study of the full glucose/insulin AUCs throughout the OGTT affords no additional information compared to glucose determination at 120 min in these patients

Prevalence and Risk Factors for Low Bone Mineral Density in Adults With Cystic Fibrosis

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Single-center studies have suggested that up to 70% of adults with cystic fibrosis (CF) have lower than expected bone mineral density (BMD), substantially higher than the 25% prevalence reported from national registries. We determined the prevalence of low BMD in CF adults at our center and assessed risk factors for low BMD. This retrospective cohort study was conducted in all CF patients ≥18 years of age who had a dual-energy X-ray absorptiometry (DXA) scan performed at the Johns Hopkins Adult Cystic Fibrosis center between 2010 and 2018. Prevalence and incidence of low BMD during the study period were determined. Poisson regression based on generalized estimating equations and robust standard errors were used to evaluate selected risk factors and risk of disease progression. A total of 234 individuals underwent an initial DXA scan. At this scan, prevalence of low BMD was 52.6% (95% confidence interval [CI] 46.0-59.1). A total of 43.6% were at risk for CF-related low BMD (AR-CFLBMD) (95% CI 37.1-50.2) and 9.0% had CF-related low BMD (CFRLBMD) (95% CI 5.6-13.4). Of the 25 with normal BMD at initial scan and a subsequent follow-up scan, 8 (32.0%) progressed to AR-CFLBMD. Of the 53 with AR-CFLBMD on initial scan and a subsequent scan, 6 (11.3%) progressed to CFLBMD, 9 (17.0%) returned to normal BMD, and 38 (71.7%) remained AR-CFLBMD. Older age (relative risk [RR] = 1.01; 95% CI 1.00-1.01) and male sex (RR = 1.32; 95% CI 1.04-1.66) were associated with increased risk of low BMD, while higher forced expiratory volume over 1 second (FEV_1%) predicted (RR = 0.99; 95% CI 0.99-1.00) and body mass index (BMI; RR = 0.97; 95% CI 0.94-1.00) were associated with lower risk for low BMD. The fact that more than half of all individuals were found to have lower than expected BMD suggests that the actual prevalence may be higher than currently reported in national registries. This supports the importance of universal bone health screening of all CF adults.

OTHER

Clearing up the smoke: Physical and mental health considerations regarding cannabis use in adolescents with cystic fibrosis

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The cannabis plant is the most used federally illegal drug in the United States and is widely used by adolescents. Cannabis has complex effects on the body and mind. All health professionals who take care of adolescents with cystic fibrosis (CF) should be aware of the factors impacting cannabis use in CF. Given limited evidence regarding the benefits of cannabis and the significant risks, clinicians have the responsibility to identify risk of cannabis use early, counsel patients about the risks, provide a safe space for ongoing conversations about cannabis use in the context of CF care, and deliver evidence-based interventions.

Steps Ahead: Optimising physical activity in adults with cystic fibrosis: A pilot randomised trial using wearable technology, goal setting and text message feedback

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Background: Regular participation in physical activity (PA) is encouraged for people with Cystic Fibrosis (CF). This study aimed to assess the effectiveness of an intervention using wearable technology, goal setting and text message feedback on PA and health outcomes in people with CF.

Methods: This was a pilot randomised trial conducted at University Hospital Limerick. Participants were randomly assigned to the intervention (INT) or active comparator (AC). The 12-week intervention consisted of wearable technology (Fitbit Charge 2) which was remotely monitored, and participants set step count goals. Participants were sent a one-way text message once a week over 12 weeks to positively reinforce and encourage PA participation. The AC group received the wearable technology alone. Follow up was assessed at 24 weeks. Outcomes assessed were PA, aerobic capacity, lung function, sleep, quality of life and wellbeing.

Results: Step count increased significantly for the INT group over 12 weeks when compared to the AC group (p=0.019). The INT group had a 28% week-to-week percentage change (Weeks 1-12), while the AC group reduced by 1%, p=0.023. Within group changes demonstrated that VO2 peak (ml/kg/min) significantly increased for the INT group at 12 weeks (24.4 ±7.65 to 26.13 ±7.79, p=0.003) but not at 24 weeks (24.45 ±7.05, p=0.776). There were no significant differences observed for VO2 peak (ml/kg/min) for the AC group. There was no significant effect on lung function, sleep, well-being, or quality of life for either group.

Conclusions: A personalised PA intervention using wearable technology, goal setting and text message feedback increased PA and aerobic capacity in people with CF. Integration of this intervention into usual care may encourage regular PA participation for people with CF.

Manuka honey in combination with azithromycin shows potential for improved activity against *Mycobacterium abscessus*

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Mycobacterium abscessus is an increasingly prevalent opportunistic pathogen causing both pulmonary and skin and soft tissue infections. It is of increasing concern for immunocompromised individuals, such as those with cystic fibrosis, due to its highly drug resistant nature and ability to evade the host immune system. Current treatments for *M. abscessus* pulmonary infections are largely ineffective and treatment outcomes are generally poor, thus we urgently require new treatments to combat these infections. Recently, it has been demonstrated that manuka honey is effective against *M. abscessus* and can improve the inhibitory effect of amikacin. Here, we explore the potential improvement of both azithromycin and tobramycin with the addition of manuka honey against *M. abscessus* complex. Improved growth inhibition was observed for azithromycin with manuka honey against all *M. abscessus* subspecies. Improved bactericidal activity was also observed. Importantly, the macrolide resistant *M. abscessus* subsp. *bolletii* showed improved inhibition and bactericidal

activity was obtained in response to 0.117 g/mL manuka honey MGO40 with 16 µg/mL azithromycin. No improved activity was observed for tobramycin and manuka honey against any of the *M. abscessus* isolates tested. This demonstrates the potential for antibiotic enhancement by the addition of manuka honey, furthering the applications of therapeutic manuka honey.

Cancer incidence and prevalence in cystic fibrosis patients with and without a lung transplant in France

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Background: Cystic fibrosis (CF) care and the life expectancy of affected patients have substantially improved in recent decades, leading to an increased number of patients being diagnosed with comorbidities, including cancers. Our objective was to characterize the epidemiology of cancers between 2006 and 2017 in CF patients with and without a lung transplant.

Methods: Medical records of CF patients from 2006 to 2016 in the French CF Registry were linked to their corresponding claims data (SNDS). The annual prevalence and incidence rates of cancers were estimated from 2006 to 2017 in CF patients without lung transplant and in those with lung transplant after transplantation.

Results: Of the 7,671 patients included in the French CF Registry, 6,187 patients (80.7%) were linked to the SNDS; among them, 1,006 (16.3%) received a lung transplant. The prevalence of any cancer increased between 2006 and 2017, from 0.3 to 1.0% and from 1.3 to 6.3% in non-transplanted and transplanted patients, respectively. When compared to the general population, the incidence of cancer was significantly higher in both non-transplanted [Standardized Incidence Ratio (SIR) = 2.57, 95%CI 2.05 to 3.17] and transplanted (SIR = 19.76, 95%CI 16.45 to 23.55) patients. The median time between transplant and the first cancer was 3.9 years. Among the 211 incident cancer cases, the most frequent malignant neoplasms were skin neoplasm (48 cases), lung cancers (31 cases), gastro-intestinal (24 cases), and hematologic cancers (17 cases).

Conclusion: The overall burden of cancer in CF patients is high, particularly following lung transplantation. Therefore, specific follow-up, screening and cancer prevention for CF patients with transplants are necessary.

The influence of exocrine pancreatic function on the exposure and pharmacokinetics of ivacaftor in people with cystic fibrosis

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Background: Cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies target the underlying cause of cystic fibrosis (CF), and show robust treatment effects at group level. The individual effect however, is variable which might be (partially) related to differences in drug exposure. The profound influence of fat containing food compared to fasting on drug exposure gives need to investigate if the exocrine pancreatic function changes the degree and rate of absorption of ivacaftor and thereby may contribute to differences in drug exposure.

Methods: Pharmacokinetic parameters of ivacaftor were measured in 10 pancreatic sufficient (PS) and 10 pancreatic insufficient (PI) patients with CF on current treatment with tezacaftor/ivacaftor and compared between both groups. In PI patients pharmacokinetic parameters were investigated with and without the use pancreatic enzymes and compared in each individual.

Results: We demonstrated that the pharmacokinetic parameters of ivacaftor did not differ significantly between PS and PI people with CF (pwCF). Pancreatic enzymes did not significantly change the absorption or exposure to ivacaftor in PI pwCF using tezacaftor/ivacaftor.

Conclusion: The exocrine pancreatic function of pwCF does not significantly influence the absorption and exposure of ivacaftor. The use of pancreatic enzymes in PI pwCF does not change the absorption and exposure of ivacaftor. Therefore, the dosing advice as mentioned in the SmPC for ivacaftor can be maintained independent of the exocrine pancreatic function.

Approaches to the management of haemoptysis in young people with cystic fibrosis

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Haemoptysis occurs in up to 25 % of young people with Cystic fibrosis (CF) [1]. We undertook a literature review and described the management approach to haemoptysis in CF between 2010 and 2020 at an Australian tertiary paediatric centre, The Children's Hospital Westmead, Sydney, New South Wales, using a retrospective review of the medical records which identified 67 episodes. Sixty episodes met inclusion criteria, including 31 patients. Using the US CF Foundation guidelines, episodes were classified as scant (53.3 %), moderate (38.3 %) or massive (8.3 %). Fifty-two percent of patients were female, mean age at presentation was 15.4 years (SD+/- 2.4) and 58 % were homozygous for the Fdel508 genotype. Twelve episodes (9 patients) required bronchial artery embolization (BAE). BAE was used in all cases of massive haemoptysis 5/5 (100 %), 6/23 (22 %) episodes of moderate and 1/32 (3 %) episode of scant haemoptysis as an elective procedure for recurrent haemoptysis. Our literature review and institutional experience highlights the need for up-to-date management guidelines in the management of haemoptysis in Cystic Fibrosis. Based on our experience, we provide a proposed algorithm to help guide the management of haemoptysis in CF.