University Hospitals Bristol NHS
NHS Foundation Trust

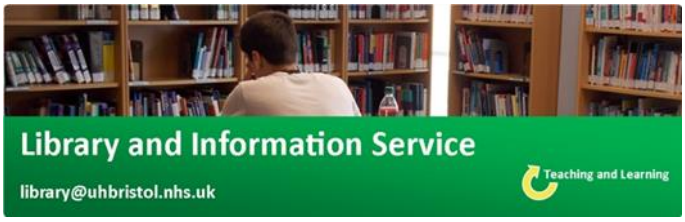
Cystic Fibrosis

Evidence Update

May 2018

(Quarterly)

Respecting everyone
Embracing change
Recognising success
Working together
Our hospitals.



Training Sessions 2018

All sessions are one hour

May (13.00-14.00)
3rd (Thu) Critical Appraisal
11th (Fri) Statistics
14th (Mon) Literature Searching
22nd (Tue) Critical Appraisal
30th (Wed) Statistics

June (12.00-13.00)
7th (Thu) Literature Searching
11th (Mon) Critical Appraisal
20th (Wed) Statistics
28th (Thu) Literature Searching

Your Outreach Librarian: Jo Hooper

Whatever your information needs, the library is here to help. We offer **literature searching services** as well as training and guidance in **searching the evidence** and **critical appraisal** – just email us at library@uhbristol.nhs.uk

Outreach: Your Outreach Librarian can help facilitate evidence-based practice for all in the restorative dentistry team, as well as assisting with academic study and research. We can help with **literature searching, obtaining journal articles and books**. We also offer one-to-one or small group training in **literature searching, accessing electronic journals, and critical appraisal**. Get in touch: library@uhbristol.nhs.uk

Literature searching: We provide a literature searching service for any library member. For those embarking on their own research it is advisable to book some time with one of the librarians for a one-to-one session where we can guide you through the process of creating a well-focused literature research and introduce you to the health databases access via NHS Evidence. Please email requests to library@uhbristol.nhs.uk

Contents

Training Sessions 2018 ..... **2**

..... **2**

Your Outreach Librarian: Jo Hooper **2**

Updates **5**

NICE National Institute for Health and Care Excellence **5**

Cochrane Library **6**

UpToDate® **7**

Journal Tables of Contents **9**

Journal of Cystic Fibrosis 10

American Journal of Respiratory and Critical Care Medicine 10

Thorax 10

Chest 10

Database Articles on Cystic Fibrosis **11**

Medical 11

Microbiological 22

Psychological 29

Nutritional 30

Other 31

Library Opening Times **32**

Library Clinic

Stop by and find out more about our services. We will be here to answer any questions you may have!

June 6th: **Terrace (Level 4, Education Centre)** *12.00-14.00*

June 19th: **Welcome Centre, BRI** *10.00-16.00*

July 3rd: **Welcome Centre, BRI** *10.00-16.00*

July 4th: **Canteen (Level 9, BRI)** *12.00-14.00*

August 8th: **Foyer, Education Centre** *12.00-14.00*

August 29th: **Foyer, St Michael's Hospital** *12.00-14.00*

September 5th: **Canteen (Level 9, BRI)** *12.00-14.00*

September 11th: **Welcome Centre, BRI** *10.00-16.00*

October 3rd: **Terrace (Level 4, Education Centre)** *12.00-14.00*

November 7th: **Canteen (Level 9, BRI)** *12.00-14.00*

December 5th: **Foyer, Education Centre** *12.00-14.00*

December 11th: **Welcome Centre, BRI** *10.00-16.00*

Updates

NICE National Institute for Health and Care Excellence

Cystic fibrosis - quality standard (QS168)
Source: National Institute for Health and Care Excellence - NICE - 18 May 2018 Read Summary

BNF

Mucolytics for cystic fibrosis | Treatment summary Source: British National Formulary - BNF - 12 April 2018

BNF for Children

Mucolytics for cystic fibrosis | Treatment summary
Source: British National Formulary for Children - BNFc - 12 April 2018

Risk of gastrointestinal cancers in patients with cystic fibrosis: a systematic review and meta-analysis
26 April 2018 - Publisher: The Lancet Oncology

Six-minute walk test as a determinant of the functional capacity of children and adolescents with cystic fibrosis: A systematic review Source: PubMed - 01 April 2018 - Publisher: Respiratory Medicine Read Summary

Clinical consequences of Aspergillus disease in cystic fibrosis Source: UK Clinical Trials Gateway - UKCTG - 22 March 2018

Safety, Tolerability, and Pharmacokinetics of PTI-808, PTI-801, and PTI-428 Combination Therapy in Subjects With Cystic Fibrosis Source: UK Clinical Trials Gateway - UKCTG - 09 April 2018

Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with cystic fibrosis
Source: Cochrane Database of Systematic Reviews - 18 March 2018 - Publisher: Cochrane Database of Systematic Reviews Read Summary

Inhaled anti-pseudomonal antibiotics for long-term therapy in cystic fibrosis
Source: Cochrane Database of Systematic Reviews - 30 March 2018 - Publisher: Cochrane Database of Systematic ReviewsRead Summary

Ivacaftor for cystic fibrosis
17 May 2018 - Publisher: British Medical JournalRead Summary

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis
Source: Cochrane Database of Systematic Reviews - 09 March 2018

Prevention of exacerbations in patients with stable non-cystic fibrosis bronchiectasis: a systematic review and meta-analysis of pharmacological and non-pharmacological therapies
Source: PubMed - 20 April 2018 - Publisher: Bmj Evidence-based MedicineRead Summary

QS168 Cystic fibrosis: Tools and resources
Source: National Institute for Health and Care Excellence - NICE - 18 May 2018

Data from the US and UK cystic fibrosis registries support disease modification by CFTR modulation with ivacaftor
10 May 2018 - Publisher: ThoraxRead Summary

Marketing Authorisation Application submitted EMA for Linhaliq (liposome encapsulated/unencapsulated ciprofloxacin) in non-cystic fibrosis bronchiectasis
09 March 2018 - Publisher: Biospace Inc.Read Summary

Cochrane Library

Inhaled anti-pseudomonal antibiotics for long-term therapy in cystic fibrosis
Online Publication Date: March 2018

Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with cystic fibrosis Online Publication Date: March 2018

Preconception risk assessment for thalassaemia, sickle cell disease, cystic fibrosis and Tay-Sachs disease
Online Publication Date: March 2018

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis
Online Publication Date: March 2018

Anti-IgE therapy for allergic bronchopulmonary aspergillosis in people with **cystic fibrosis**
Online Publication Date: March 2018

Standard (head-down tilt) versus modified (without head-down tilt) postural drainage in infants and young children with cystic fibrosis
Online Publication Date: March 2018

Preconception risk assessment for thalassaemia, sickle cell disease, **cystic fibrosis** and Tay-Sachs disease
Online Publication Date: March 2018

Inhaled anti-pseudomonal antibiotics for long-term therapy in **cystic fibrosis** Online Publication Date: March 2018

Inhaled corticosteroids for bronchiectasis Online Publication Date: May 2018

Physical therapies for postural abnormalities in people with **cystic fibrosis**

Online Publication Date: April 2018

Strategies to prevent kidney injury from antibiotics in people with **cystic fibrosis**
Online Publication Date: May 2018

UpToDate®

OpenAthens login required. Register here: https://openathens.nice.org.uk/

Practice Changing UpDate

PEDIATRICS; PRIMARY CARE (ADULT); PULMONARY AND CRITICAL CARE MEDICINE
(December 2017)

Tezacaftor-ivacaftor approved for cystic fibrosis

●For patients 12 years and older with cystic fibrosis who are homozygous for the F508del mutation, we recommend treatment with tezacaftor-ivacaftor (Grade 1B). We also suggest tezacaftor-ivacaftor for patients who have one of several specific residual function mutations (Grade 2B).

Cystic fibrosis transmembrane regulator (CFTR) modulators are a new class of drugs that improve production, intracellular processing, and/or function of the defective CFTR protein. Tezacaftor-ivacaftor, a new combination of CFTR modulators, was approved by the US Food and Drug Administration (FDA) in February 2018 for patients 12 years or older who have homozygous mutations of F508del (the most common CFTR genotype and associated with severe disease), or who have at least one "residual function" mutation as listed in the table (table 2). The approval for F508del homozygotes was based upon a randomized trial that reported modest improvement in pulmonary function and lower risk of pulmonary exacerbations over the duration of the trial, and a good safety profile [14]. Similar findings were reported in a second trial in patients with compound heterozygosity for F508del and a residual function mutation [15]. Expansion of the FDA approval to include patients with a residual function mutation was based upon in vitro data [16]. Selection of CFTR modulators depends upon the patient's genotype and age, as summarized in the table (table 3). (See "Cystic fibrosis: Overview of the treatment of lung disease", section on 'Tezacaftor-ivacaftor for homozygous F508del and residual function mutations'.)

(Listen to UpToDate Talk podcast.)

Cystic fibrosis: Overview of the treatment of lung disease
Literature review current through: Apr 2018. | **This topic last updated:** Mar 02, 2018.

Cystic fibrosis: Overview of gastrointestinal disease
Literature review current through: Apr 2018. | **This topic last updated:** May 03, 2018.

Cystic fibrosis: Genetics and pathogenesis
Literature review current through: Apr 2018. | **This topic last updated:** May 15, 2018.

Cystic Fibrosis Trust @cftrust

CF healthcare professionals push for progress in precision medicine talks

News - 02/05/2018

Doctors group write to Vertex Pharmaceuticals, politicians and decision-makers offering support in making breakthrough in negotiations. *** Updated 11/05/18 ***

Sign up to our e-newsletter

Blog - 01/05/2018 So, now what can I eat? Food post-transplant

News - 23/04/2018 NHS England and Vertex Pharmaceuticals to meet

News - 13/04/2018 Making mucus manageable

News - 11/04/2018 NIHR to fund CF community's research priorities

Clinical Trials Accelerator Platform

With more advances in cystic fibrosis care and treatment than ever before, and a host of new treatments in the pipeline, this is an exciting time for the cystic fibrosis community. However, a lack of capacity and awareness of clinical trials is preventing people with cystic fibrosis from having timely access to cutting-edge therapies and treatments through participation in clinical trials.

The Clinical Trials Accelerator Platform is a UK-wide initiative to bring together cystic fibrosis (CF) centres, to increase participation and improve access to CF clinical trials. We are building a network of CF centres that will collectively lead in the delivery of high-impact clinical trials. Each participating centre will be awarded funding for a Trial Coordinator or Research Nurse to provide much-needed extra capacity to support the delivery of CF clinical trials.

To find out more about clinical trials, visit our Clinical Trials Digital Hub. Here you will find an array of information about taking part in clinical trials, as well as our very own CF Trials Tracker; a CF clinical trials database to help you find suitable clinical trial opportunities.

Focus Group

Are you interested in sharing your unique perspectives of life with CF to ensure that what really matters to people living with the condition is incorporated into research? Join our Focus Group as part of our Clinical Trials Accelerator Platform.

What's involved?

Register your details with us today and you may be called upon without obligation, to:

- Complete questionnaires, surveys or comment forms relating to clinical trials or research as they arise
- Join digital forums, webinars or live social media feeds, providing engagement with researchers or pharmaceutical companies

- Join Q&A sessions on proposed studies

We want the voices of the entire CF community to be represented, from youngest to oldest, which is why we are excited to be offering this opportunity to get involved to people and children with CF and their families.

Contact clinicaltrials@cysticfibrosis.org.uk for a registration form

KnowledgeShare

What is KnowledgeShare?

Provides regular, targeted, personalised evidence updates to staff, based on their specific professional interests. Subject-specific bulletins can also be produced.

Targeted evidence updates

These are individualised, based on a staff member's interest in particular conditions or lifestyle factors, age groups, settings of care, interventions and management topics.

Collaboration and knowledge sharing

As more library and knowledge services join KnowledgeShare it becomes more powerful for sharing evidence and generating communities of practice.

To register, click the logo

Or email library@uhbristol.nhs.uk

Journal Tables of Contents

The most recent issues of the following journals:

- **Journal of Cystic Fibrosis**
- **American Journal of Respiratory and Critical Care Medicine**
- **Thorax**
- **Chest**

Click on the links for abstracts. If you would like any of these papers in full text then get in touch: library@uhbristol.nhs.uk

Journal of Cystic Fibrosis

May 2018 Volume 17, Issue

American Journal of Respiratory and Critical Care Medicine

May 2018 Volume 197, Issue 10

Thorax

June 2018 Volume 73 - 6

Chest

May 2018, Volume 153, Issue 5

Database Articles on Cystic Fibrosis

Below is a selection of articles on cystic fibrosis recently added to the healthcare databases, grouped in the following categories:

- **Medical**
- **Microbiological**
- **Psychological**
- **Nutritional**
- **Other**

If you would like any of the following articles in full text, or if you would like a more focused search on your own topic, then get in touch: library@uhbristol.nhs.uk

Medical

Pulmonary exacerbations and acute declines in lung function in patients with cystic fibrosis

Author(s): Wagener J.S.; Williams M.J.; Millar S.J.; Pasta D.J.; Morgan W.J.; Konstan M.W.

Source: Journal of Cystic Fibrosis; 2018

Publication Type(s): Article In Press

Abstract: Background: Patients with cystic fibrosis (CF) who experience acute declines in percent predicted FEV1 (ppFEV1 decreased >=10% relative to baseline) are often not treated with antibiotics for pulmonary exacerbations (PEx), whereas other patients are treated even when they have not experienced a decline in lung function. Methods: We analyzed 2 patient cohorts using 3 years of Epidemiologic Study of CF data. Cohort 1 (12,837 patients) experienced a >=10% acute decline in ppFEV1 (n = 22,898) and Cohort 2 (10,416 patients) had a clinician-diagnosed PEx (n = 20,731). Results: 70.7% of >=10% decline events were treated with antibiotics; with intravenous antibiotics used 67.1% of the time. 32.0% of clinician-diagnosed PEx declined <10%; with intravenous antibiotics used 36.9% of the time. Conclusions: A clinician's decision to diagnose a PEx and treat with antibiotics often is not defined by measured lung function: a >=10% FEV1 decline is not considered an absolute indication of a PEx and the lack of a decline does not contraindicate a PEx. Clinicians appear to use the history of prior PEx plus other variables as factors for diagnosing PEx.

Metabolomic responses to lumacaftor/ivacaftor in cystic fibrosis

Author(s): Kopp B.T.; Sarzynski L.; Woodley F.W.; Hayes D.; Shrestha C.L.; Zhang S.; McCulloch S.

Source: Pediatric Pulmonology; May 2018; vol. 53 (no. 5); p. 583-591

Publication Type(s): Article

Abstract: Background: Cystic fibrosis (CF) is a life-limiting disease caused by a defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Lumacaftor/Ivacaftor is a novel CFTR modulator approved for patients that are homozygous for Phe508del CFTR, but its clinical effectiveness varies amongst patients, making it difficult to determine clinical responders. Therefore, identifying biochemical biomarkers associated with drug response are clinically important for follow-up studies. Methods: Serum metabolomics was performed on twenty patients with CF pre- and 6-month post-Lumacaftor/Ivacaftor response via Ultrahigh Performance Liquid Chromatography-Tandem Mass Spectroscopy (UPLC-MS/MS). Correlation with clinical variables was performed. Results: Metabolomics analysis demonstrated 188 differentially regulated metabolites between patients pre- and post-Lumacaftor/Ivacaftor initiation, with a predominance of lipid and amino acid

alterations. The top 30 metabolites were able to differentiate pre- and post-Lumacaftor/Ivacaftor status in greater than 90% of patients via a random-forest confusion matrix. Alterations in bile acids, phospholipids, and bacteria-associated metabolites were the predominant changes associated with drug response. Importantly, changes in metabolic patterns were associated with clinical responders. Conclusions: Selected key lipid and amino acid metabolic pathways were significantly affected by Lumacaftor/Ivacaftor initiation and similar pathways were affected in clinical responders. Targeted metabolomics may provide useful and relevant biomarkers of CFTR modulator responses.

Mechanical insufflation-exsufflation for airway clearance in adults with cystic fibrosis.

Author(s): Gaynor, Madeline; Wood, Jamie

Source: Respirology case reports; May 2018; vol. 6 (no. 4); p. e00307

Publication Type(s): Journal Article

Available at Respirology Case Reports - from PubMed Central

Abstract: In cystic fibrosis (CF), acute exacerbations can decrease the effectiveness of patients' usual airway clearance techniques (ACT). In order to maintain effective airway clearance and preserve lung function, these ACT must be adapted to prevent further dyspnoea and fatigue and improve ease of expectoration. Mechanical insufflation-exsufflation (MI-E) is widely used in neuromuscular disorders to facilitate airway clearance and augment cough but has rarely been used in CF despite potential indications. The NIPPY Clearway, an airway clearance device with multiple modes including MI-E, can be set to deliver multiple insufflations prior to a single exsufflation. We present two cases where this modified version of MI-E was used as an adjunct to traditional ACT in adults during an acute exacerbation of CF.

Clinical Model of Exercise-Related Dyspnea in Adult Patients With Cystic Fibrosis.

Author(s): Stevens, Daniel; Neyedli, Heather F

Source: Journal of cardiopulmonary rehabilitation and prevention; May 2018; vol. 38 (3); p. 187-192

Publication Type(s): Journal Article

Abstract:PURPOSEDyspnea is a highly distressing symptom of pulmonary disease that can make performing physical activities challenging. However, little is known regarding the strongest predictors of exercise-related dyspnea in adult cystic fibrosis (CF). Therefore, the purpose of the present study was to determine the best clinical model of exercise-related dyspnea in this patient group.METHODSA retrospective analysis of pulmonary function and cardiopulmonary exercise testing data from patients with CF being followed up at the Adult CF Program at St Michael's Hospital, Toronto, Canada, from 2002 to 2008 were used for the analysis.RESULTSPatients (n = 88) were male 66%; aged 30.4 ± 9.4 years; body mass index (BMI) 23.1 ± 3.3 kg/m; forced expiratory volume in 1 second (FEV1) 70% ± 19% predicted; and peak oxygen uptake 74% ± 20% predicted. A multivariate linear regression model assessing the effects of age, sex, BMI, airway obstruction (FEV1), perceived muscular leg fatigue, and dynamic hyperinflation explained 54% of the variance in dyspnea severity at peak exercise ($P < .01$). Relative importance analysis showed that the presence of dynamic hyperinflation and perceived muscular leg fatigue were the largest contributors.CONCLUSIONSPulmonary rehabilitation programs may consider strategies to reduce dynamic hyperinflation and promote muscular function to best improve exercise-related dyspnea in this patient group.

Cystic fibrosis transmembrane conductance regulator-emerging regulator of cancer.

Author(s): Zhang, Jieting; Wang, Yan; Jiang, Xiaohua; Chan, Hsiao Chang

Source: Cellular and molecular life sciences : CMLS; May 2018; vol. 75 (no. 10); p. 1737-1756

Publication Type(s): Journal Article Review

Abstract: Mutations of cystic fibrosis transmembrane conductance regulator (CFTR) cause cystic fibrosis, the most common life-limiting recessive genetic disease among Caucasians. CFTR mutations have also been linked to increased risk of various cancers but remained controversial for a long time. Recent studies have begun to reveal that CFTR is not merely an ion channel but also an important regulator of cancer development and progression with multiple signaling pathways identified. In this review, we will first present clinical findings showing the correlation of genetic mutations or aberrant expression of CFTR with cancer incidence in multiple cancers. We will then focus on the roles of CFTR in fundamental cellular processes including transformation, survival, proliferation, migration, invasion and epithelial-mesenchymal transition in cancer cells, highlighting the signaling pathways involved. Finally, the association of CFTR expression levels with patient prognosis, and the potential of CFTR as a cancer prognosis indicator in human malignancies will be discussed.

Association between body composition and pulmonary function in children and young people with cystic fibrosis

Author(s): Calella, Patrizia; Valerio, Giuliana; Thomas, Matt; McCabe, Helen; Taylor, Jake;

Source: Nutrition; Apr 2018; vol. 48 ; p. 73

Publication Type(s): Journal Article

Abstract: Objectives Body mass index (BMI) has significant limitations when assessing nutritional status in pediatric patients with cystic fibrosis (CF). We evaluated whether measurements of lean body mass (LBM) and fat mass (FM) are more sensitive nutritional parameters by testing their association with pulmonary function in adolescent patients with CF. Methods Sixty-nine male and female adolescents with CF were studied (age: 14.5 ± 2.3, BMI: 19.5 ± 2.3 kg/m2). Dual-energy x-ray absorptiometry (DXA) was used to measure total and segmental (appendicular, truncal) body composition (FM, LBM bone mineral density, and content) as routine care to monitor bone health. Correlation and multiple regression analyses were performed to assess the association among body composition variables and forced expiratory volume in 1 s (FEV1). We also evaluated the influence of the F508del mutation on body composition. Results FEV1was significantly associated with total (r= 0.68,P<0.001), truncal (r= 0.71,P<0.001), and appendicular (r= 0.67,P<0.001) LBM, whereas it was not associated with total (r= 0.02,P= 0.89) and truncal (r= 0.04,P= 0.77) FM. BMI had a significant but weaker correlation with FEV1(r= 0.52,P<0.001) compared with LBM. LBM was the only significant predictor of FEV1in fully adjusted regression models. Conclusions LBM is a significant predictor of pulmonary function in CF adolescent patients. DXA scanning performed as part of routine bone health monitoring in CF can provide important body composition data relevant to clinical interventions that optimize nutritional status. DXA reference data for LBM in non-adult populations are needed to enhance diagnostic assessment and monitor clinical progression of CF.

Prevalence of Fecal Incontinence in Adults with Cystic Fibrosis.

Author(s): Benezech, Alban; Desmazes-Dufeu, Nadine; Baumstarck, Karine; Bouvier, Michel

Source: Digestive Diseases & Sciences; Apr 2018; vol. 63 (no. 4); p. 982-988

Publication Type(s): Academic Journal

Abstract: Background: Patients with cystic fibrosis (CF) are deemed at risk of developing urinary incontinence (UI) due to repeated coughing and other factors causing increased pressure on the pelvic floor. Fecal incontinence (FI) is probably derived from the same mechanism, but only very few data are available on its frequency.Aims: The aim of this study was to determine the prevalence of FI in an adult population with CF.Methods: This retrospective study was conducted from January 2012

to June 2014. Patients were recruited from Marseille referral center for adult CF. They were asked to fill in a self-completed anonymous questionnaire for symptom assessment of UI and FI. Clinical data and a detailed history of CF were also recorded.Results: A total of 155 out of 190 patients (92 females) of mean age 30.5 ± 11 years completed the survey. Seventy-three patients (47%) were lung transplanted. Forty patients (25.8%) reported FI with a mean St Mark's score of 4.9 ± 2. Thirty-five patients (22.6%) reported UI. Eighteen patients (11.6%) reported both FI and UI. FI was significantly more frequent in older patients (34.27 vs. 29.54 years, p = 0.03) and in patients with associated UI (p = 0.001). No relationship was found between respiratory, bacterial, nutritional status, transplantation, pancreatic status, practice of physiotherapy, delivery history, and FI.Conclusions: The high prevalence of FI in CF and its negative impacts need to integrate this symptom in the overall treatment of this pathology. The systematic early detection of FI may allow its rapid management and limit their consequences.

Non-contrast enhanced magnetic resonance imaging detects mosaic signal intensity in early cystic fibrosis lung disease.

Author(s): Leutz-Schmidt, Patricia; Stahl, Mirjam; Sommerburg, Olaf; Eichinger, Monika

Source: European Journal of Radiology; Apr 2018; vol. 101 ; p. 178-183

Publication Type(s): Academic Journal

Abstract: Objectives: To determine if morphological non-contrast enhanced magnetic resonance imaging (MRI) of the lung is sensitive to detect mosaic signal intensity in infants and preschool children with cystic fibrosis (CF).Materials and Methods: 50 infant and preschool CF patients (mean age 3.5 ± 1.4y, range 0-6y) routinely underwent morphological (T2-weighted turbo-spin echo sequence with half-Fourier acquisition, HASTE) and contrast-enhanced 4D perfusion MRI (gradient echo sequence with parallel imaging and echo sharing, TWIST). MRI studies were independently scored by two readers blinded for patient age and clinical data (experienced Reader 1 = R1, inexperienced Reader 2 = R2). The extent of lung parenchyma signal abnormalities on HASTE was rated for each lobe from 0 (normal), 1 (<50% of lobe affected) to 2 (≥50% of lobe affected). Perfusion MRI was rated according to the previously established MRI score, and served as the standard of reference.Results: Inter-method agreement between MRI mosaic score and perfusion score was moderate with κ = 0.58 (confidence interval 0.45-0.71) for R1, and with κ = 0.59 (0.46-0.72) for R2. Bland-Altman analysis revealed a slight tendency of the mosaic score to underestimate perfusion abnormalities with a score bias of 0.48 for R1 and 0.46 for R2. Inter-reader agreement for mosaic score was substantial with κ = 0.71 (0.62-0.79), and a low bias of 0.02.Conclusions: This study demonstrates that non-contrast enhanced MRI reliably detects mosaic signal intensity in infants and preschool children with CF, reflecting pulmonary blood volume distribution. It may thus be used as a surrogate for perfusion MRI if contrast material is contra-indicated or alternative techniques are not available.

Innovative therapeutic strategies for cystic fibrosis: Moving forward to CRISPR technique

Author(s): Marangi M.; Pistritto G.

Source: Frontiers in Pharmacology; Apr 2018; vol. 9

Publication Type(s): Short Survey

Available at Frontiers in Pharmacology - from Europe PubMed Central - Open Access

Abstract: One of the most revolutionary technologies in recent years in the field of molecular biology is CRISPR-Cas9. CRISPR technology is a promising tool for gene editing that provides researchers the opportunity to easily alter DNA sequences and modify gene function. Its many potential applications include correcting genetic defects, treating and preventing the spread of diseases. Cystic fibrosis (CF) is one of the most common lethal genetic diseases caused by mutations in the CF transmembrane

conductance regulator (CFTR) gene. Although CF is an old acquaintance, there is still no effective/resolutive cure. Life expectancy has improved thanks to the combination of various treatments, but it is generally below average. Recently, a significant number of additional key medications have become licensed in Europe for the CF treatment including CFTR modulators. But innovative genomically-guided therapies have begun for CF and it is predictable that this will lead to rapid improvements in CF clinical disease and survival in the next decades. In this way, CRISPR-Cas9 approach may represent a valid tool to repair the CFTR mutation and hopeful results were obtained in tissue and animal models of CF disease.

Exploring Opportunities for Primary Outpatient Palliative Care for Adults with Cystic Fibrosis: A Mixed-Methods Study of Patients' Needs.

Author(s): Hobler, Mara R.; Engelberg, Ruth A.; Curtis, J. Randall; Ramos, Kathleen J.

Source: Journal of Palliative Medicine; Apr 2018; vol. 21 (no. 4); p. 513-521

Publication Type(s): Academic Journal

Abstract: Background: Persons with cystic fibrosis (CF) experience high morbidity and mortality, yet little is known about their palliative care needs and how clinicians may address these needs. Objectives: (1) To identify palliative care and advance care planning needs of patients with CF and their families; and (2) to identify clinicians' potential roles in meeting these needs. Methods: A mixed-methods study of adult patients (age ≥18 years) with moderate-to-severe CF [forced expiratory volume in the first second (FEV1) <65% predicted] were recruited from a CF Center. Semi-structured interviews (30–60 minutes) and questionnaires were administered in person or by phone. Grounded theory was used to analyze the interviews. Questionnaires were analyzed descriptively. Results: Forty-nine patients (FEV1 % range = 19%–63%) participated; the participation rate was 80% for eligible patients. Three main domains of palliative care needs were identified: (1) to be listened to, feel heard, and be "seen"; (2) understanding the context around CF and its trajectory, with the goal of preparing for the future; and (3) information about, and potential solutions to, practical and current circumstances that cause stress. In questionnaires, few patients (4.3%) reported talking with their clinician about their wishes for care if they were to become sicker, but mixed-methods data demonstrated that more than half of participants were willing to receive palliative care services provided those services were adapted to CF. Conclusion: Patients expressed a need for and openness to palliative care services, as well as some reluctance. They appreciated clinician communication that was open, forthcoming, and attuned to individualized concerns.

Evaluating Changes in Handgrip Strength in Children With Cystic Fibrosis: A Pilot Study.

Author(s): Gibson, Hannah T.; McDonald, Catherine M.; Derrick, Jennifer Willahan; Eggett, Dennis L.

Source: Nutrition in Clinical Practice; Apr 2018; vol. 33 (no. 2); p. 261-267

Publication Type(s): Academic Journal

Abstract: Abstract: Background: Body mass index (BMI) is used to determine nutrition status in children with cystic fibrosis (CF); however, lean body mass (LBM) is more strongly associated with pulmonary function. Handgrip strength (HGS) measures muscle function and is reflective of LBM. The aims of this study were to assess relationships among HGS, nutrition status, and pulmonary function; changes in HGS posthospitalization; and any relationship between HGS and nutrient intake. Methods: Twenty-three children with CF aged 6–18 years participated. BMI z scores, nutrition risk scores, and pulmonary function were assessed about 5 months before, days 5–7 of hospitalization, and about 6 weeks posthospitalization. HGS z scores and arm anthropometrics were measured during and after hospitalization. Nutrient intakes were assessed during hospitalization. Results: Mean HGS z score at hospitalization was −1.95 ± 0.92 and posthospitalization was −1.59 ± 1.06 (P = .007). Mean BMI z score prehospitalization was −0.17 ± 0.63, at hospitalization was −0.09 ± 0.64, and

posthospitalization was 0.06 ± 0.54 (P = .065). Mean forced expiratory volume in 1 second (FEV1) prehospitalization was 93.52 ± 17.35, at hospitalization was 85.65 ± 21.57, and posthospitalization was 95.63 ± 18.18 (P = .001). No significant relationship was found between HGS z scores and BMI z scores (P = .892) or HGS z scores and FEV1 (P = .340). Conclusions: HGS z scores and FEV1 significantly increased at follow-up. HGS z scores were lower than the standard even though mean BMI z scores classified participants as normal nutrition status.

Combined Pancreatic Islet-Lung-Liver Transplantation in a Pediatric Patient with Cystic Fibrosis-Related Diabetes

Author(s): Klee P.; Dirlewanger M.; Schwitzgebel V.M.; Lavallard V.; Pernin N.; McLin V.A.

Source: Hormone Research in Paediatrics; Apr 2018

Publication Type(s): Article In Press

Abstract: Background: Cystic fibrosis-related diabetes (CFRD) is the most frequent extrapulmonary complication of cystic fibrosis (CF). Methods: We report the first combined pancreatic islet-lung-liver transplantation in a 14-year-old adolescent. CFTR was analyzed by Sanger sequencing. Further genes were analyzed by high-throughput sequencing. Results: The patient was diagnosed with CF at the age of 14 months. Nine years later, after diagnosis of CFRD, the patient's BMI and lung function began to decline. Bilateral lung transplantation with simultaneous liver transplantation was performed at the age of 14.5 years. The first islet transplantation (IT) was carried out 10 days later. Six months later, C-peptide secretion after arginine stimulation showed peak values of 371 pmol/L (vs. 569 pmol/L before IT) and insulin doses had slightly increased (1.40 vs. 1.11 units/kg/day before IT). A second IT was performed at the age of 15 years, a third at 16 years. Two years after the first IT, arginine-stimulated C-peptide secretion increased to 2,956 pmol/L and insulin doses could be reduced to 0.82 units/kg/day. HbA1c decreased from 7.3% (57.4 mmol/mol) to 5.9% (41.0 mmol/mol). Conclusion: IT following lung and liver transplantation, with injection of islets into a transplanted organ, is feasible. It improves C-peptide secretion, decreases insulin needs, and lowers HbA1c.

Predictors of long term survival in patients with cystic fibrosis following lung transplantation

Author(s): Robinson C.A.; Deibel A.; Schuurmans M.M.; Benden C.; Inci I.

Source: Journal of Heart and Lung Transplantation; Apr 2018; vol. 37 (no. 4)

Publication Type(s): Conference Abstract

Abstract: Purpose: Lung transplantation (LTX) is the ultimate therapy for end-stage cystic fibrosis (CF) lung disease; however, morbidity and mortality are considerable. CF patients achieve the best overall outcome post LTX. We investigated a subgroup of CF-patients and a minimum of 10 years post-LTX survival, aiming to determine possible predictors of long-term survival and characterize comorbidities. Methods: All CF-patients undergoing LTX with a survival > 10 years were included. Clinical endpoints: development of chronic lung allograft dysfunction (CLAD) and CLAD-free survival and lung allograft failure. Additional endpoints: acute cellular rejection (ACR, ISHLT> 1), chronic pulmonary infection (CPI), rehospitalization rate and extra-pulmonary comorbidities. Results: 146 patients with CF underwent LTX; 39 CF patients showed post-tranplant survival > 10 years. Median age at LTX was 25 years (range 16-52). Median BMI at time of listing was 17.4kg/m2 (13.4-22.8). 51% (n= 20) had CF-related diabetes mellitus, 21% (n= 8) had CF-related liver disease. 77% (n= 30) had CPI with pseudomonas aeruginosa, 5% (n= 2) staphylococcus aureus and 5% (N= 2) with burkholderia cepacia complex. All were double transplanted, no patient was bridged to transplantation by using mechanical ventilation or extracorporeal membrane oxygenation (ECMO) systems. 51% (n= 20) patients were CMV high risk. Median survival was 14 years (10.1-22.2). By June 30th 2017, 31% of patients (n= 13) had died (CLAD= 5, cardiovascular disease= 2, infection= 1, cancer= 1 and other

reasons= 2). 60% (N= 25) had developed CLAD. Median time to CLAD diagnosis was 3864 days (1480-6069). 38% (n= 15) had minimum 1 ACR episode. 10 years following LTX, 82% (n= 32) had hypertension, 72% (n= 28) had chronic kidney disease, n= 5 were on dialysis. 26% (n= 10) had undergone kidney transplant, 23% (n= 9) had coronary arterial or peripheral vascular disease. 13% (n= 5) have had skin cancer, no other forms of malignancy were observed. Hospitalization rate per year was median 1.1. Conclusion: Possible predictors of long-term survival after LTX are bilateral transplantation, no need for mechanical ventilation or ECMO, low incidence of ACR (ISHLT> 1), low incidence of malignancy and low frequency of hospitalization. Prevalence of chronic pulmonary infection with PSA, diabetes mellitus, hypertension and CKD appear unrelated to long-term survival.

The top 10 research priorities in cystic fibrosis developed by a partnership between people with CF and healthcare providers

Author(s): Rowbotham N.J.; Smith S.; Hurley M.N.; Smyth A.R.; Leighton P.A.; Rayner O.C

Source: Thorax; Apr 2018; vol. 73 (no. 4); p. 388-390

Publication Type(s): Article

Available at Thorax - from BMJ Journals - NHS

Abstract: There remain many treatment uncertainties in cystic fibrosis (CF). With limited resources, research should focus on questions which are most important to the CF community. We conducted a James Lind Alliance Priority Setting Partnership in CF. Research questions were elicited and then prioritised in successive surveys. A workshop agreed the final top 10. Online methods avoided cross infection and widened participation. The elicitation survey had 482 respondents (1080 questions) and prioritisation survey 677 respondents. Participants were drawn equally from the patient and clinical communities globally. We have achieved a consensus on 10 research priorities which will be attractive to funders.

Impact of home spirometry on medication adherence among adolescents with cystic fibrosis

Author(s): Shakkottai A.; Kasmikha L.; Nasr S.Z.; Kaciroti N.

Source: Pediatric Pulmonology; Apr 2018; vol. 53 (no. 4); p. 431-436

Publication Type(s): Article

Abstract: Objective: Medication adherence among adolescents with cystic fibrosis (CF) is often suboptimal and this has significant impact on their health and quality of life. The purpose of the study was to evaluate the impact of frequent home pulmonary function (PFT) monitoring on medication adherence among adolescents with CF. Hypothesis: We hypothesized that weekly home PFT monitoring will improve adherence while not significantly adding to the treatment burden. Methods: Individuals aged 12-21 years with CF were provided a spirometer to measure PFTs weekly for 1 year. Results were reviewed weekly via telephone. PFT data were downloaded from the device during quarterly clinic visits. Adherence was calculated from prescription refill data and compared to the previous year. Perceptions of treatment burden were assessed using the CF questionnaire-revised (CFQ-R) quality of life measure. Health outcome measures including nutritional status and PFTs from clinic were collected for the study period and the year prior. Results: Thirty-nine subjects participated in the study. Mean age was 15.89 +/- 2.18 years and 54% were female. Mean adherence to weekly spirometry monitoring was 59.47 +/- 24.60%. Values generated on the device showed good correlation with those obtained in clinic. Mean medication possession ratio (MPR) was 60% in the previous year and 65% during the study (P = 0.04). Mean treatment burden scaled score on the CFQ-R was 68 at enrollment and 66 at study completion (P = 0.14). Conclusions: Frequent home PFT monitoring is feasible in CF adolescents and could successfully improve medication adherence without significantly impacting treatment burden.

Long term extra pulmonary comorbidities after lung transplantation in cystic fibrosis: update of specificities.

Author(s): Jardel, Sabine; Reynaud, Quitterie; Durieu, Isabelle

Source: Clinical transplantation; Apr 2018 ; p. e13269

Publication Type(s): Journal Article Review

Abstract: Lung transplantation (LT) is the standard therapeutic option for cystic fibrosis (CF) patients with end-stage lung disease. Both conditions lead to extra-respiratory complications, such as diabetes, renal insufficiency, bone disease, and cancer. The purpose of the present paper is to provide an update of the non-respiratory comorbidities following LT in adult patients with CF and their specificities regarding their multi-systemic underlying condition despite their younger age compared to other patients undergoing LT. Diabetes, renal insufficiency, metabolic bone disease, hypertension, liver disease and cancer are the comorbidities considered in this review. The increase of CF adults living with a lung transplant justifies an update of knowledge for this specific situation (prevalence of these complications, underlying risk factors), in order to provide better medical care and establish early diagnosis strategies. This article is protected by copyright. All rights reserved.

eHealth in Cystic Fibrosis: Promising, but Proof of Concept is Still Needed.

Author(s): Martelli, Vanessa; Stanbrook, Matthew; Anand, Anju

Source: American journal of respiratory and critical care medicine; Apr 2018

Publication Type(s): Journal Article

Decreasing the Time to Insulin Administration for Hospitalized Patients With Cystic Fibrosis-Related Diabetes.

Author(s): Smego, Allison; Lawson, Sarah; Courter, Joshua D; Warden, Deborah; Corathers, Sarah

Source: Hospital pediatrics; Apr 2018

Publication Type(s): Journal Article

Abstract:OBJECTIVESChildren with cystic fibrosis-related diabetes (CFRD) represent a commonly hospitalized pediatric population whose members require insulin for blood glucose (BG) control. The aim of this quality improvement initiative was to increase the proportion of hospitalized patients with CFRD receiving insulin within 30 minutes of a BG check while decreasing severe hypo- and hyperglycemia episodes.METHODSQuality improvement methodology (gathering a team of stakeholders, identifying metrics, implementing iterative plan-do-study-act cycles and analysis of data over time) was applied in the setting of a cystic fibrosis unit in a tertiary care children's hospital. The percentage of patients with CFRD who received rapid-acting insulin within 30 minutes of a BG check and the rates of hypoglycemia (BG 200 mg/dL) were measured. Improvement interventions were focused on efficient communication among patients, nurses and providers; refining carbohydrate calculation; and sharing expectations with patients and caregivers.RESULTSThe proportion of rapid-acting insulin doses given within 30 minutes increased from a baseline mean 40% to a sustained mean of 78%. During active improvement interventions, success rates of 100% were achieved. Hyperglycemic events (BG >200 mg/dL) decreased from 125 events to 85 events per 100 rapid-acting insulin days. Hypoglycemic events (BG <70 mg/dL) remained low at <5 events per 100 rapid-acting insulin days.CONCLUSIONSSystematic implementation of low-cost interventions successfully resulted in measurable improvement in timely rapid-acting insulin administration for hospitalized patients with CFRD and lower rates of severe hypo- and hyperglycemia on the unit.

Future efforts will be directed to increase the reliability of interventions to maintain optimal performance and outcomes.

Effects of an Antioxidant-enriched Multivitamin in Cystic Fibrosis: Randomized, Controlled, Multicenter Trial.

Author(s): Sagel, Scott D; Khan, Umer; Jain, Raksha; Graff, Gavin; Daines, Cori L; Dunitz, Jordan M

Source: American journal of respiratory and critical care medicine; Apr 2018

Publication Type(s): Journal Article

Available at American journal of respiratory and critical care medicine - from EBSCO (MEDLINE Complete)

Abstract:RATIONALECystic fibrosis (CF) is characterized by dietary antioxidant deficiencies, which may contribute to an oxidant-antioxidant imbalance and oxidative stress.OBJECTIVESEvaluate the effects of an oral antioxidant-enriched multivitamin supplement on antioxidant concentrations, markers of inflammation and oxidative stress, and clinical outcomes.METHODSIn this investigator-initiated, multicenter, randomized, double-blind, controlled trial, 73 pancreatic insufficient CF subjects 10 years of age and older with an FEV1 between 40-100% predicted were randomized to 16 weeks of an antioxidant-enriched multivitamin or control multivitamin without antioxidant enrichment. Endpoints included systemic antioxidant concentrations, markers of inflammation and oxidative stress, clinical outcomes (pulmonary exacerbations, anthropometric measures, pulmonary function), safety and tolerability.MEASUREMENTS AND MAIN RESULTSChange in sputum myeloperoxidase concentration over 16 weeks, the primary efficacy endpoint, was not significantly different between the treated and control groups. Systemic antioxidant concentrations (β-carotene, CoQ10, γ-tocopherol, lutein) significantly increased in the antioxidant treated group ($p<0.001$ for each), while circulating calprotectin and myeloperoxidase decreased in the treated group compared to the control group at week 4. The treated group had a lower risk of first pulmonary exacerbation requiring antibiotics than the control group (adjusted hazard ratio=0.50, $p=0.04$). Lung function and growth endpoints did not differ between groups. Adverse events and tolerability were similar between groups.CONCLUSIONSAntioxidant supplementation was safe and well tolerated, resulting in increased systemic antioxidant concentrations and modest reductions in systemic inflammation after 4 weeks. Antioxidant treatment was also associated with a lower risk of first pulmonary exacerbation. Clinical trial registration available at www.clinicaltrials.gov, ID NCT01859390.

A smartphone application for reporting symptoms in adults with cystic fibrosis: protocol of a randomised controlled trial.

Author(s): Wood, Jamie; Jenkins, Sue; Putrino, David; Mulrennan, Siobhain; Morey, Sue

Source: BMJ open; Apr 2018; vol. 8 (no. 4); p. e021136

Publication Type(s): Journal Article

Available at BMJ open - from Europe PubMed Central - Open Access

Abstract:INTRODUCTIONIn people with cystic fibrosis (CF), exacerbations have been shown to have profound and prolonged negative effects such as reducing physical activity and health-related quality of life, increasing the rate of decline of lung function and healthcare costs, and ultimately increasing the risk of mortality. Delayed initiation of treatment following the signs of an exacerbation has been shown to be associated with failure to recover to baseline. Therefore, the late identification and treatment of an exacerbation due to delayed presentation will potentially worsen short-term and long-term outcomes. We have developed a smartphone application, containing questions which require yes or no responses relating to symptoms suggestive of a respiratory exacerbation. Its use is intended to facilitate the early identification of symptoms

suggestive of a respiratory exacerbation, and allow the CF team to initiate treatment sooner, thereby potentially reducing the risk of severe exacerbations which require intravenous antibiotics (IVAB) and often a hospital admission.METHODSWe will undertake a randomised controlled trial. 60 adults with CF will be recruited and randomised to either the intervention or control group. The intervention group will use the smartphone application weekly for 12 months, or earlier than the next weekly reporting time if they feel their symptoms have worsened. The control group will continue to receive usual care, involving regular (approximately 3 monthly) CF outpatient clinic appointments. The primary outcome measure will be courses and days of IVAB.ETHICS AND DISSEMINATIONApproval was obtained from the Sir Charles Gairdner Group Human Research Ethics Committee for WA Health (2015-030) and Curtin University Human Research Ethics Committee (HR212/2015), and has been registered with the Australian and New Zealand Clinical Trials Registry. Results of this study will be presented at international conferences and published in peer-reviewed journals in accordance with the Consolidated Standards of Reporting Trials statement.TRIAL REGISTRATION NUMBERACTRN12615000599572.

Cystic fibrosis-related diabetes is caused by islet loss and inflammation.

Author(s): Hart, Nathaniel J; Aramandla, Radhika; Poffenberger, Gregory; Fayolle, Cody;

Source: JCI insight; Apr 2018; vol. 3 (no. 8)

Publication Type(s): Journal Article

Available at JCI insight - from Europe PubMed Central - Open Access

Abstract: Cystic fibrosis-related (CF-related) diabetes (CFRD) is an increasingly common and devastating comorbidity of CF, affecting approximately 35% of adults with CF. However, the underlying causes of CFRD are unclear. Here, we examined cystic fibrosis transmembrane conductance regulator (CFTR) islet expression and whether the CFTR participates in islet endocrine cell function using murine models of β cell CFTR deletion and normal and CF human pancreas and islets. Specific deletion of CFTR from murine β cells did not affect β cell function. In human islets, CFTR mRNA was minimally expressed, and CFTR protein and electrical activity were not detected. Isolated CF/CFRD islets demonstrated appropriate insulin and glucagon secretion, with few changes in key islet-regulatory transcripts. Furthermore, approximately 65% of β cell area was lost in CF donors, compounded by pancreatic remodeling and immune infiltration of the islet. These results indicate that CFRD is caused by β cell loss and intraislet inflammation in the setting of a complex pleiotropic disease and not by intrinsic islet dysfunction from CFTR mutation.

Hemoglobin A1c Accurately Predicts Continuous Glucose Monitoring-Derived Average Glucose in Youth and Young Adults With Cystic Fibrosis.

Author(s): Chan, Christine L; Hope, Emma; Thurston, Jessica; Vigers, Timothy; Pyle, Laura

Source: Diabetes care; Apr 2018

Publication Type(s): Journal Article

Available at Diabetes care - from EBSCO (MEDLINE Complete)

Abstract:OBJECTIVEIn cystic fibrosis (CF), HbA1c is thought to underestimate glycemia. However, few studies have directly assessed the relationship between HbA1c and average glucose in CF. We determined the relationships among glycemic markers-HbA1c, fructosamine (FA), glycated albumin (%GA), and 1,5-anhydroglucitol (1,5-AG)-and continuous glucose monitoring (CGM) in CF, hypothesizing that alternate markers would better predict average sensor glucose (ASG) than HbA1c.RESEARCH DESIGN AND METHODSCF participants and a group of healthy control subjects (HC), ages 6-25 years, wore CGM for up to 7 days. Pearson correlations assessed the relationships between CGM variables and HbA1c, FA, %GA, and 1,5-AG. The regression line between HbA1c and

ASG was compared in CF versus HC. Linear regressions determined whether alternate markers predicted ASG after adjustment for HbA1c.RESULTSCF (n = 93) and HC (n = 29) groups wore CGM for 5.2 ± 1 days. CF participants were 14 ± 3 years of age and 47% were male, with a BMI z score -0.1 ± 0.8 and no different from HCs in age, sex, or BMI. Mean HbA1c in CF was 5.7 ± 0.8% (39 ± 9 mmol/mol) vs. HC 5.1 ± 0.2% (32 ± 2 mmol/mol) (P < 0.0001). All glycemic markers correlated with ASG (P ≤ 0.01): HbA1c (r = 0.86), FA (r = 0.69), %GA (r = 0.83), and 1,5-AG (r = -0.26). The regression line between ASG and HbA1c did not differ in CF versus HC (P = 0.44). After adjustment for HbA1c, %GA continued to predict ASG (P = 0.0009) in CF.CONCLUSIONSHbA1c does not underestimate ASG in CF as previously assumed. No alternate glycemic marker correlated more strongly with ASG than HbA1c. %GA shows strong correlation with ASG and added to the prediction of ASG beyond HbA1c. However, we are not advocating use of HbA1c for diabetes screening in CF based on these results. Further study will determine whether glycemic measures other than ASG differ among different types of diabetes for a given HbA1c.

Aminoglycoside exposure and renal function before lung transplantation in adult cystic fibrosis patients.

Author(s): Novel-Catin, Etienne; Pelletier, Solenne; Reynaud, Quitterie; Nove-Josserand, Raphaele

Source: Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; Apr 2018

Publication Type(s): Journal Article

Abstract: BackgroundPatients with cystic fibrosis (CF) are at risk of kidney injury even before undergoing lung transplantation, because of prolonged exposure to aminoglycosides (AGs), chronic dehydration and complications of diabetes mellitus. The usual equations estimating the glomerular filtration rate (GFR), such as Cockcroft-Gault and Modification of Diet in Renal Disease, are not adapted to the CF population due to patients' low body weight and reduced muscle mass. The aim of this study was to precisely measure GFR in adult CF patients and to see whether repeated AG treatment would impair renal function before lung transplantation.MethodsInulin or iohexol clearances were performed in 25 adult CF patients when they entered the lung transplant waiting list. No patient was treated with AGs at the time of GFR measurement. Body mass index (BMI), history of diabetes mellitus and blood pressure were recorded. Exposure to intravenous (IV) AGs within 5 years prior to the GFR measurement was obtained from the patient's medical files. Urine samples were collected to check for albuminuria and proteinuria.ResultsThe population was predominantly female (67%). The mean age was 32 years, the mean BMI was 19 kg/m2 and 28% had CF-related diabetes. Median exposure to IV AG within 5 years before GFR measurement was 155 days with a mean dosage of 7.7mg/kg/day. The mean measured GFR was 106 mL/min/1.73 m2 and the mean estimated GFR according to the Chronic Kidney Disease Epidemiology Collaboration formula was 124 mL/min/1.73 m2.ConclusionDespite prolonged exposure to high-dose IV AG, no decline in GFR was observed in these patients

Intravenous fosfomycin for pulmonary exacerbation of cystic fibrosis: Real life experience of a large adult CF centre.

Author(s): Spoletini, G; Kennedy, M; Flint, L; Graham, T; Etherington, C; Shaw, N; Whitaker, P

Source: Pulmonary pharmacology & therapeutics; Apr 2018

Publication Type(s): Journal Article

Abstract:BACKGROUNDThe increased prevalence of multi-drug resistant strains of P.aeruginosa and allergic reactions among adult patients with cystic fibrosis (CF) limits the number of antibiotics available to treat pulmonary exacerbations. Fosfomycin, a unique broad spectrum bactericidal antibiotic, might offer an alternative therapeutic option in such cases.AIMTo describe the clinical

efficacy, safety and tolerability of intravenous fosfomycin in combination with a second anti-pseudomonal antibiotic to treat pulmonary exacerbations in adult patients with CF.METHODA retrospective analysis of data captured prospectively, over a 2-years period, on the Unit electronic medical records for patients who received IV fosfomycin was performed. Baseline characteristics in the 12 months prior treatment, lung function, CRP, renal and liver function and electrolytes at start and end of treatment were retrieved.RESULTS54 patients received 128 courses of iv fosfomycin in combination with a second antibiotic, resulting in improved FEV1 (0.94 L vs 1.24 L, p < 0.01) and reduced CRP (65 mg/L vs 19.3 mg/L, p < 0.01). Renal function pre- and post-treatment remained stable. 4% (n = 5) of courses were complicated with AKI at mid treatment, which resolved at the end of the course. Electrolyte supplementation was required in 18% of cases for potassium and magnesium and 7% for phosphate. Nausea was the most common side effects (48%), but was well controlled with anti-emetics.CONCLUSIONAntibiotic regimens including fosfomycin appear to be clinically effective and safe. Fosfomycin should, therefore, be considered as an add-on therapy in patients who failed to respond to initial treatment and with multiple drug allergies.

Microbiological

Eradication of early P. aeruginosa infection in children <7years of age with cystic fibrosis: The early study

Author(s): Ratjen F.; Moeller A.; McKinney M.L.; Asherova I.; Alon N.; Maykut R.; Angyalosi G.;

Source: Journal of Cystic Fibrosis; 2018

Publication Type(s): Article In Press

Abstract: Objective: Antibiotic eradication treatment is the standard-of-care for cystic fibrosis (CF) patients with early Pseudomonas aeruginosa (Pa)-infection; however, evidence from placebo-controlled trials is limited. Methods: This double-blind, placebo-controlled trial randomised CF patients <7 years (N = 51) with early Pa-infection to tobramycin inhalation solution (TOBI 300 mg) or placebo (twice daily) for 28 days with an optional cross-over on Day 35. Primary endpoint was proportion of patients having throat swabs/sputum free of Pa on Day 29. Results: On Day 29, 84.6% patients in the TOBI versus 24.0% in the placebo group were Pa-free (p < 0.001). At the end of the cross-over period, 76.0% patients receiving TOBI in the initial 28 days were Pa-free compared to 47.8% receiving placebo initially. Adverse events were consistent with the TOBI safety profile with no differences between TOBI and placebo. Conclusion: TOBI was effective in eradicating early Pa-infection with a favourable safety profile in young CF patients. Trial registration number: NCT01082367

Occurrence of Pseudomonas aeruginosa in waters: Implications for patients with cystic fibrosis (CF)

Author(s): Caskey S.; Moore J.E.; Rendall J.C.; Stirling J.

Source: Letters in Applied Microbiology; 2018

Publication Type(s): Article In Press

Abstract: Chronic Pseudomonas aeruginosa infection is associated with increased morbidity and mortality in patients with cystic fibrosis (CF). Current understanding of risk factors for acquisition is limited and so the aim of this study was to examine a large sample of environmental waters from diverse sources. Environmental water samples (n = 7904) from jacuzzis, hydrants, swimming pools, hot tubs, plunge pools, bottled natural mineral water, taps, springs, ice machines, water coolers, bores and showers were examined for the presence of P. aeruginosa. Pseudomonas aeruginosa was detected in 524/7904 (6.6%) waters examined. Hot tubs (51/243; 20.9%), tap water (3/40; 8%) and jacuzzis (432/5811; 7.4%) were the most likely environments where P. aeruginosa was isolated.

Pseudomonas aeruginosa was isolated from bottled water (2/67; 3%). Our study highlights the ubiquitous nature of P. aeruginosa in the environment. Given CF patients are frequently counselled to make lifestyle changes to minimize P. aeruginosa exposure, these results have important implications. In particular, the occurrence of P. aeruginosa in tap water highlights the need to disinfect the CF patients' nebulizer after each use. Significance and Impact of the Study: This study examined a large number of water sources (n = 7904) over a 9-year period for the presence of Pseudomonas aeruginosa. The study highlighted that jacuzzis (n = 5811; 7% positive) and hot tubs had the highest occurrence of this organism (n = 243, 21% positive). Patients with cystic fibrosis (CF) are interested in knowing what water environments are likely to be contaminated with this organism, as this bacterium is an important cause of increased morbidity and mortality in such patients. With such information, CF patients and parents may make informed decisions about lifestyle choice and water environment avoidance.

Ozone disinfection of home nebulizers effectively kills common cystic fibrosis bacterial pathogens

Author(s): Towle D.; Baker V.; Schramm C.; Collins M.S.; O'Brien M.; Feinn R.; Murray T.S.

Source: Pediatric Pulmonology; May 2018; vol. 53 (no. 5); p. 599-604

Publication Type(s): Article

Abstract: Objective: The Cystic Fibrosis Foundation (CFF) recommends routine nebulizer disinfection for patients but compliance is challenging due to the heavy burden of home care. SoClean is a user friendly ozone based home disinfection device currently for home respiratory equipment. The objective of this study was to determine whether SoClean has potential as a disinfection device for families with CF by killing CF associated bacteria without altering nebulizer output. Hypothesis: Ozone based disinfection effectively kills bacterial pathogens inoculated to home nebulizer equipment without gross changes in nebulizer function. Study Design: Common bacterial pathogens associated with CF were inoculated onto the PariLC jet nebulizer and bacterial recovery compared with or without varied ozone exposure. In separate experiments, nebulizer output was estimated after repeated ozone exposure by weighing the nebulizer. Results: Ozone disinfection was time dependent with a 5 min infusion time and 120 min dwell time effectively killing >99.99% bacteria tested including Pseudomonas aeruginosa and Staphylococcus aureus. Over 250 h of repeat ozone exposure did not alter nebulizer output. This suggests SoClean has potential as a user-friendly disinfection technique for home respiratory equipment.

Experience of using non-invasive ventilation as an adjunct to airway clearance techniques in adults with cystic fibrosis–A qualitative study.

Author(s): Rodriguez Hortal, Maria Cecilia; Hedborg, Anna; Biguet, Gabriele; Nygren-Bonnier, Malin

Source: Physiotherapy Theory & Practice; Apr 2018; vol. 34 (no. 4); p. 264-275

Publication Type(s): Academic Journal

Abstract: Background: Adults with cystic fibrosis (CF) suffer from abnormally thick mucus that is difficult to clear from the airways. Different airway clearance techniques (ACTs) can be used to clear secretions and non-invasive ventilation (NIV) can be used as an adjunct to these techniques. ACTs are ideally introduced at the time of diagnosis and thereafter modified throughout the patient's lifespan and disease progress.Purpose: The research aim was to describe adult patients' views and experiences with using NIV as an adjunct to ACT.Method: Eighteen adults with CF were interviewed about their experiences with using NIV during ACT. Semi-structured interviews were conducted and analyzed in accordance with qualitative content analysis.Results: The results gave rise to the overall theme 'Becoming Friends with NIV' and six associated categories: 1) getting a sense of control and feedback; 2) getting support; 3) dealing with doubt; 4) finding the rhythm; 5) feeling the effects; and

6) finding their own motivation. The findings represent a learning process for adults during the implementation stages of NIV; the physiotherapist was found to play a key role in this process.Conclusion: 'Becoming Friends with NIV' involves a learning process for adults with CF. To facilitate this learning process, different aspects should be taken into account so as to promote independence and self-management, which in turn allows the patient to experience the treatment as meaningful. The findings are relevant to physiotherapists working with adults and NIV, as improved insight into and understanding of the relationship may have a positive influence on the outcome and success of NIV usage.

Vx-809/Vx-770 treatment reduces inflammatory response to Pseudomonas aeruginosa in primary differentiated cystic fibrosis bronchial epithelial cells

Author(s): Ruffin M.; Maille E.; Brochiero E.; Roussel L.; Rousseau S.

Source: American Journal of Physiology - Lung Cellular and Molecular Physiology; Apr 2018; vol. 314 (no. 4)

Publication Type(s): Article

Abstract: Cystic fibrosis patients exhibit chronic Pseudomonas aeruginosa respiratory infections and sustained proinflammatory state favoring lung tissue damage and remodeling, ultimately leading to respiratory failure. Loss of cystic fibrosis transmembrane conductance regulator (CFTR) function is associated with MAPK hyperactivation and increased cytokines expression, such as interleukin- 8 [chemoattractant chemokine (C-X-C motif) ligand 8 (CXCL8)]. Recently, new therapeutic strategies directly targeting the basic CFTR defect have been developed, and ORKAMBI (Vx-809/Vx-770 combination) is the only Food and Drug Administration-approved treatment for CF patients homozygous for the F508del mutation. Here we aimed to determine the effect of the Vx-809/Vx-770 combination on the induction of the inflammatory response by fully differentiated primary bronchial epithelial cell cultures from CF patients carrying F508del mutations, following exposure to P. aeruginosa exoproducts. Our data unveiled that CFTR functional rescue with Vx-809/Vx-770 drastically reduces CXCL8 (as well as CXCL1 and CXCL2) transcripts and p38 MAPK phosphorylation in response to P. aeruginosa exposure through a CFTR-dependent mechanism. These results suggest that ORKAMBI has anti-inflammatory properties that could decrease lung inflammation and contribute to the observed beneficial impact of this treatment in CF patients.

Procalcitonin, erythrocyte sedimentation rate and C-reactive protein in acute pulmonary exacerbations of cystic fibrosis

Author(s): Loh G.; Skabelund A.; Ryaboy I.; French A.

Source: Clinical Respiratory Journal; Apr 2018; vol. 12 (no. 4); p. 1545-1549

Publication Type(s): Article

Abstract: Introduction: Acute pulmonary exacerbations of cystic fibrosis (APECF) are a leading cause of morbidity and mortality among patients with cystic fibrosis (CF). APECF require frequent administration of antibiotics and subsequently lead to development of resistant organisms. Objectives: The aim of this study was to identify inflammatory markers that may be help identify need for antibiotics and exacerbation as well as predict risk of exacerbations. Methods: A total of 17 patients were enrolled, and baseline erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and procalcitonin levels were obtained in addition to obtaining these levels during admissions for APECF. Results: A total of 28 APECF were recorded. ESR and CRP significantly increased during exacerbation (P <.01 for both). Procalcitonin did not increase during exacerbations. Baseline elevations in ESR and CRP increased risk of an exacerbation (RR = 2.3 and 4.5, respectively). Conclusions: ESR and CRP are useful markers for CF exacerbations, as levels rise with exacerbations.

Baseline elevations in ESR and CRP were noted to show an increased risk for CF exacerbations. Procalcitonin, in contrast, is not a useful inflammatory marker.

Mortality outcomes related to multi-drug resistant organisms in cystic fibrosis lung transplant recipients: An international society of heart and lung transplantation (ISHLT) registry study

Author(s): Lay C.; Law N.; Aslam S.; Holm A.M.; Benden C.

Source: Journal of Heart and Lung Transplantation; Apr 2018; vol. 37 (no. 4)

Publication Type(s): Conference Abstract

Abstract: Purpose: Patients with cystic fibrosis (CF) may have pulmonary infection with multi-drug resistant organisms (MDRO) potentially impacting post-transplant mortality. Our objective was to study 1-year mortality in CF patients with MDRO compared to those without MDRO lung transplant recipients (LTR) querying the largest international registry. Methods: We used the ISHLT Thoracic Transplant Registry dataset to identify all CF adult, first-time, double LTR from 1999-2015. Extracted data: recipient baseline demographics and clinical characteristics especially pertaining to infection; donor characteristics; overall mortality and infection-related mortality. We analyzed categorical data using chi-square and continuous data using student's t-test. We created a multivariate (MV) binary logistic regression model with 1-year mortality as the primary outcome. Results: Among 3256 CF LTRs, there were significant baseline differences between those with pre-transplant MDRO infection and those without (CF+MDRO vs. CF-MDRO), as noted in Table 1. Prior to transplant, CF+MDRO group was more likely to be on ventilator support and suffering with an infection requiring intravenous (IV) antibiotics within 2 weeks of transplant. Despite this, 1-year mortality was similar between both groups (18.6% vs. 16%, p= NS) and presence of MDRO was not a predictor of 1-year mortality in MV analysis. However, infection-related death within the 1st year post-transplant was higher in the CF+MDRO group (6.6% vs. 4.6%, p< 0.001). Conclusion: Patients with CF chronically infected with MDRO prior to transplant have similar 1-year mortality as those without MDRO according to the largest international registry dataset. Thus, patients with CF chronically infected with MDRO should not per se be excluded from lung transplantation but undergo thorough multidisciplinary evaluation including infectious diseases specialist input (Table presented).

Lung transplantation in cystic fibrosis patients infected with B. cepacia complex: A single center experience

Author(s): Nechaev N.; Golovinskiy S.; Simonova M.; Poptsov V.; Gautier S.; Krasovskiy S.

Source: Journal of Heart and Lung Transplantation; Apr 2018; vol. 37 (no. 4)

Publication Type(s): Conference Abstract

Abstract: Purpose: Infection of B. cepacia complex (BCC) is one of the most common contraindication for LTx in cystic fibrosis(CF) patients. The reason is intrinsic resistance to multiple antibiotics and disinfectants of BCC. We report our experience of LTx for CF patients infected with BCC. Methods: 9 patients with CF underwent LTx from September 2014 to October 2017. Mean age was 24,8+/-4,0 years. 6 males and 3 females. 4 patients were infected with BCC that was confirmed with MALDI TOF test of sputum. 3 with B.cenocepacia (ST208,ST709,ST728) and 1 with B.contaminans,(ST438). Recipients with CF were divided into two groups with (A, 4 patients) and without (B, 6 patients) BCC infection. Induction immunosuppression for both groups was basiliximab (20mg i/v 0 and 4 POD) and methylprednisolone 500mg i/v 1 hour before incision. All of patients were maintained on triple immunosuppressive therapy, which included methylprednisolone 0,2 mg/kg on 4 POD and 0,1 mg/kg on 14 POD, tacrolimus on 6 POD with target C0 10-12 ng/ml and mycophenolate mofetil on 14 POD. Antibacterial therapy was combination of i/v and inhalation therapy. On 18-20 POD group A recipients received course of a hyperbaric oxygenation(HBO). Results: I/v antibacterial therapy was

ended 3 days before discharge in all patients when CRP level was less than 10 mg/l. Inhalation antibacterial therapy lasted for 1 month after discharge. There was noted 1 infection complication in group A (phlegmon of the chest wall) and 2 in group B (pneumonia, persisted bronchitis, p> 0,99). 1 patient in group B died of multiple organ failure on 5 POD. There was one intolerance to HBO in patient with B.contaminans which manifested as hypercapnic status. In 2 cases after course of HBO there was achieved a full eradication of BCC, in 1 case we needed 3 courses of HBO. There was not evidence of reinfection. Mechanical ventilation time, ICU stay and hospitalization time were not significantly different between groups (0,9+/-0,1 vs 11,7+/-10,1 days, p= 0,37; 4,5+/-1,1 vs 22,2+/-10,7, p= 0,19; and 56,8+/-13,3 vs 33,8+/-15,3, p= 0,31). 30-day and 1-year survival was 100%, 100% in group A, and 80%,80% in group B, that is not significantly different (p= 0,37). Conclusion: Patients with CF infected with BCC could be successfully transplanted with good results. We propose that using of HBO plays a major role in posttransplantation complex therapy, but further study is needed to explore.

Better survival post lung transplantation in cystic fibrosis despite multidrug antibiotic resistance in patients with previous achromobacter colonization

Author(s): De Verdiere S.C.; Grenet D.; De Miranda S.; Picard C.; Abdul H.; Stern M.; Roux A

Source: Journal of Heart and Lung Transplantation; Apr 2018; vol. 37 (no. 4)

Publication Type(s): Conference Abstract

Abstract: Purpose: Achromobacter colonization of cystic fibrosis (CF) patients is deemed to be associated with higher risk of graft loss and the rods are usually defined as multi or pan resistant. We aimed to evaluate if CF patients transplanted with previous Achromobacter colonization had worst clinical outcome post lung transplantation. Methods: Retrospective analysis of CF lung transplanted patients in our center between january 2007 and may 2017. After exclusion of patients colonized with Burkholderia species, patients were categorized according to pretransplant Achromobacter colonization. They were compared for baseline demographic datas and graft survival. Quantitative data were expressed as mean and CI95 and qualitative as number and %. Results: A total of 244 CF Lung transplanted patients were included in the analysis. Within this population, 61 patients had at least once positive culture with Achromobacter species before transplantation ("achromo" group). Comparison of these group with the 183 remaining patients ("no achromo" group) for baseline characteristic did not show any difference age at transplantation (30.91 years (28.5-33.3) and 31.1 (29.7- 32.5) respectively, p= 0.86) but proportion of patient transplanted before 22 years tend to be higher in "achromo" patient (13/61 vs. 23/183, p= 0.1). Sex ratio (55% vs. 51% were female, p= 0.44), type of CFTR mutation and CMV donor recipient serology status were similar between two groups. However "achromo" patients had significantly longer time on waiting list (71.9 (43-100.5) vs. 43 (33.4-52.6), p= 0.037), less frequent need for high emergency Lung Transplantation (9.8 vs. 23.5, p= 0.026) and a trend for a lower LAS (39.7 (38.1-41.22) vs. 44.1(42-46.2), p= 0.28). "Achromo" patients had significantly better graft survival with a 1000 days survival of 92.6% compare to 81.3% for "no achromo" patients (p= 0.02, log rank test). Conclusion: In these analysis, patients with colonization with achromobacter previous to lung transplantation had better graft survival. Based on these results there should not be any reluctance for considering Lung transplantation for "achromo patients" despite the multidrug resistance of the rods. The reason why youngest colonized patients tend to need earlier lung transplant require complementary studies.

Airway persistence by the emerging multi-azole-resistant Rasamsonia argillacea complex in cystic fibrosis.

Author(s): Abdolrasouli, Alireza; Bercusson, Amelia C; Rhodes, Johanna L; Hagen, Ferry

Source: Mycoses; Apr 2018

Publication Type(s): Journal Article

Abstract: Infections caused by Rasamsonia argillacea complex have been reported in various clinical settings. Cystic fibrosis (CF) is one of the main underlying conditions. An observational cohort study of CF patients with Rasamsonia in respiratory samples was conducted. Eight isolates from six patients were identified as R. argillacea complex and tested for antifungal susceptibility. All isolates had high MICs to voriconazole and posaconazole and low MECs to echinocandins. Four patients experienced lung function decline in the year preceding first Rasamsonia isolation. This continued in the year following first isolation in three out of four cases. Antifungal therapy was initiated in two patients, to which only one exhibited a clinical response. Three out of six patients died within three years of isolating Rasamsonia. Genotyping suggests that similar genotypes of Rasamsonia can persist in CF airways. Consistent with other fungi in CF, the clinical impact of airway colonization by Rasamsonia is variable. In certain patients, Rasamsonia may be able to drive clinical decline. In others, though a clear impact on lung function may be difficult to determine, the appearance of Rasamsonia acts as a marker of disease severity. In others it does not appear to have an obvious clinical impact on disease progression. This article is protected by copyright. All rights reserved.

Effectiveness of ivacaftor in cystic fibrosis patients with non-G551D gating mutations.

Author(s): Guimbellot, Jennifer; Solomon, George M; Baines, Arthur; Heltshe, Sonya L

Source: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society; Apr 2018

Publication Type(s): Journal Article

Abstract:BACKGROUNDThe cystic fibrosis transmembrane conductance regulator (CFTR) potentiator ivacaftor is approved for patients with CF with gating and residual function CFTR mutations. We report the results of an observational study investigating its effects in CF patients with non-G551D gating mutations.METHODSPatients with non-G551D gating mutations were recruited to an open-label study evaluating ivacaftor. Primary outcomes included: lung function, sweat chloride, weight gain, and quality of life scores.RESULTSTwenty-one subjects were enrolled and completed 6 months follow-up on ivacaftor; mean age was 25.6 years with 52% <18. Baseline ppFEV1 was 68% and mean sweat chloride 89.6 mEq/L. Participants experienced significant improvements in ppFEV1 (mean absolute increase of 10.9% 95% CI = [2.6,19.3], p = 0.0134), sweat chloride (-48.6 95% CI = [-67.4,-29.9], p < 0.0001), and weight (5.1 kg, 95% CI = [2.8, 7.3], p = 0.0002).CONCLUSIONSPatients with non-G551D gating mutations experienced improved lung function, nutritional status, and quality of life. This study supports ongoing use of ivacaftor for patients with these mutations.

Cystic fibrosis pathogens survive for extended periods within cough-generated droplet nuclei.

Author(s): Wood, Michelle E; Stockwell, Rebecca E; Johnson, Graham R; Ramsay, Kay A

Source: Thorax; Apr 2018

Publication Type(s): Journal Article

Available at Thorax - from BMJ Journals - NHS

Abstract: The airborne route is a potential pathway in the person-to-person transmission of bacterial strains among cystic fibrosis (CF) populations. In this cross-sectional study, we investigate the physical properties and survival of common non-Pseudomonas aeruginosa CF pathogens generated during coughing. We conclude that Gram-negative bacteria and Staphylococcus aureus are aerosolised during coughing, can travel up to 4 m and remain viable within droplet nuclei for up to 45 min. These results suggest that airborne person-to-person transmission is plausible for the CF pathogens we measured.

Impact of pharmacy services on cystic fibrosis medication adherence: Update.

Author(s): Zobell, Jeffery T; Collingridge, Dave S; Asfour, Fadi

Source: Pediatric pulmonology; Apr 2018

Publication Type(s): Letter

Timing of Spirometry May Impact Hospital Length of Stay for Cystic Fibrosis Pulmonary Exacerbation.

Author(s): Krivchenia, Katelyn; Tumin, Dmitry; Nemastil, Christopher J; Tobias, Joseph D; Hayes, Don

Source: Lung; Apr 2018; vol. 196 (no. 2); p. 207-211

Publication Type(s): Journal Article

Abstract:PURPOSEThe optimal timing of spirometry during hospitalization for acute pulmonary exacerbation (PEx) in patients with cystic fibrosis (CF) is unclear. We retrospectively evaluated whether measuring spirometry earlier during hospitalization was associated with a shorter length of stay (LOS).METHODSIn this retrospective study, we analyzed data from the electronic medical record of CF patients 6 years of age and older admitted to a single center for acute PEx requiring IV antibiotic therapy between 2009 and 2016. After excluding patient encounters with missing data on covariates, random-effects linear regression was used to predict LOS as a function of days to first pulmonary function testing (PFT), which was spirometry for our study.RESULTSOne thousand thirty-five hospitalizations of 242 patients met inclusion criteria, with 801 including complete data on covariates. Mean LOS was 10 ± 7 days, with mean time to first PFT of 4 ± 3 days after admission. In multivariable analysis, each additional day to first PFT was associated with 0.97 days longer LOS (95% CI 0.29, 1.64; p = 0.005).CONCLUSIONSAs CF researchers and clinicians work to improve management of PEx, the timing of spirometry during hospitalization remains an important question. Obtaining objective lung function data earlier during the course of therapy may provide information which can lead to reduced hospital LOS for PEx.

Understanding Pseudomonas status among adults with cystic fibrosis: a real-world comparison of the Leeds criteria against clinicians' decision.

Author(s): Hoo, Zhe Hui; Edenborough, Frank Peter; Curley, Rachael; Prtak, Laura; Dewar, Jane

Source: European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology; Apr 2018; vol. 37 (no. 4); p. 735-743

Publication Type(s): Journal Article

Abstract: Pseudomonas aeruginosa status influences cystic fibrosis (CF) clinical management but no 'gold standard' definition exists. The Leeds criteria are commonly used but may lack sensitivity for chronic P. aeruginosa. We compared clinicians' decision with the Leeds criteria in three adult CF centres. Two independent prospective datasets (Sheffield dataset, n = 185 adults; ACtiF pilot dataset, n = 62 adults from two different centres) were analysed. Clinicians involved in deciding P. aeruginosa status were blinded to the study objectives. Clinicians considered more adults with CF to have chronic P. aeruginosa infection compared to the Leeds criteria. This was more so for the Sheffield dataset (106/185, 57.3% with clinicians' decision vs. 80/185, 43.2% with the Leeds criteria; kappa coefficient between these two methods 0.72) compared to the ACtiF pilot dataset (34/62, 54.8% with clinicians' decision vs. 30/62, 48.4% with the Leeds criteria; kappa coefficient between these two methods 0.82). However, clinicians across different centres were relatively consistent once age and severity of lung disease, as indicated by the type of respiratory samples provided, were taken into account. Agreement in P. aeruginosa status was similar for both datasets among adults who predominantly provided sputum samples (kappa coefficient 0.78) or adults > 25 years old (kappa coefficient 0.82). Across three different centres, clinicians did not always agree with the

Leeds criteria and tended to consider the Leeds criteria to lack sensitivity. Where disagreement occurred, clinicians tended to diagnose chronic P. aeruginosa infection because other relevant information was considered. These results suggest that a better definition for chronic P. aeruginosa might be developed by using consensus methods to move beyond a definition wholly dependent on standard microbiological results.

Psychological

Mental Health Screening of Medically-Admitted Patients With Cystic Fibrosis.

Author(s): Garcia, Georgina; Snell, Carolyn; Sawicki, Gregory; Simons, Laura E

Source: Psychosomatics; 2018; vol. 59 (no. 2); p. 158-168

Publication Type(s): Journal Article

Abstract:BACKGROUNDMulti-national studies have identified an increased risk for depression and anxiety among the cystic fibrosis population. People with cystic fibrosis and depression have decreased lung function, adherence, and quality of life, and increased health care utilization. This is a pilot study of mental health screening and referral of patients with cystic fibrosis in a large tertiary medical center.OBJECTIVEPatients with a diagnosis of cystic fibrosis aged 8 and older, medically admitted to a tertiary hospital, were screened for eligibility and offered mental health screening for depression and anxiety.METHODSPatients indicating elevated rates of anxiety, depression, or suicidal ideation were offered a psychiatric consultation, and all participants were offered mental health referrals. Health-related outcomes were gathered via medical record review.RESULTSThe pediatric population showed elevated rates/at risk of depression (17%), anxiety (22%) and clinically-elevated depression (5%), and anxiety (11%). Twenty-two percent of the youth reported suicidal ideation. The adult population reported mild rates of depression (11%), anxiety (28%), and suicidality (11%). The mental health screening process resulted in 1 mental health referral, 16 patients eligible for psychiatric consultation, and 4 completed psychiatric consultations.DISCUSSIONThis study represents a pilot mental health screening in the inpatient medical setting. The results indicate an elevated rate of depression, anxiety, and suicidal ideation, and a protocol for responding to elevated responses via psychiatric consultation. This study indicates the need for further exploration of implementation of mental health screening, rapid response to suicidal ideation, referral process, and treatment interventions.

Living with cystic fibrosis - A qualitative study of a life coaching intervention

Author(s): Knudsen K.B.; Katzenstein T.L.; Jarden M.; Boisen K.A.; Mortensen L.H.; Pressler T.

Source: Patient Preference and Adherence; Apr 2018; vol. 12 ; p. 585-594

Publication Type(s): Article

Available at Patient Preference and Adherence - from Europe PubMed Central - Open Access

Abstract: Background: Cystic fibrosis (CF) is a chronic, life-shortening disease with a significant treatment burden. To support young adults with CF in their everyday life, we previously conducted a life coaching feasibility trial (published elsewhere). The aim of the current study was to explore how life coaching was experienced by study participants within the context of their lives with CF. Methods: A qualitative study using individual interviews. Respondents (n=14) were recruited from the intervention group after participation in life coaching. Data were analyzed from a phenomenologic-hermeneutical perspective, inspired by Ricoeur's theory. Findings: Periodic exacerbations of CF led to worry about disease progression, and interrupted the respondents' ability to fulfill daily life roles satisfactory. The treatment burden demanded self-discipline and this was sometimes at the expense of social life or career. The young adults rarely spoke to others about their situation; therefore, they valued opening up to a professional coach about life and concerns. We

identified three themes: 1) living an unpredictable life; 2) the conflict between freedom and the constraints of illness; and 3) the value of telling one's story. In relation to all three themes, coaching promoted reflection over life situations, reframed thoughts, and facilitated finding new ways to manage everyday life. Conclusion: Life coaching is an intervention that is valued for those who feel challenged by their CF disease. Coaching programs should be designed to include the participants, when they feel a need for coaching and are open for change. Screening parameters to identify persons who will most likely benefit from life coaching are needed.

Impact of social complexity on outcomes in cystic fibrosis after transfer to adult care.

Author(s): Crowley, Erin M; Bosslet, Gabriel T; Khan, Babar; Ciccarelli, Mary; Brown, Cynthia D

Source: Pediatric pulmonology; Apr 2018

Publication Type(s): Journal Article

Abstract:OBJECTIVEThis study evaluates the roles of medical and social complexity in health care use outcomes in cystic fibrosis (CF) after transfer from pediatric to adult care.METHODSRetrospective cohort design included patients with CF who were transitioned into adult care at Indiana University from 2005 to 2015. Predictor variables included demographic and comorbidity data, age at transition, treatment complexity score (TCS), and an objective scoring measure of their social complexity (Bob's Level of Social Support, BLSS). Outcome variables included outpatient visit rates and hospitalization rates. Pearson's correlations and linear regression were used to analyze the data.RESULTSThe median age of the patients (N = 133) at the time of transition was 20 (IQR 19-23) years. The mean FEV1 % predicted at transition was 69 ± 24%. TCS correlated with outpatient visit rates (r = 0.3, P = 0.003), as well as hospitalization rates (r = 0.4, P < 0.001); while the BLSS only correlated with hospitalization rates (r = 0.7, P < 0.001). After adjusting for covariates, the strongest predictors of post-transfer hospitalizations are BLSS (P < 0.0001) and pre-transfer hospitalization rate (P < 0.0001).CONCLUSIONGreater treatment complexity is associated with greater healthcare utilization overall, while greater social complexity is associated with increased hospitalizations (but not outpatient visits). Screening young adults for social complexity may identify high-risk subpopulations and allow for patient centered interventions to support them and prevent avoidable health care use.

Nutritional

Prevalence of hypoglycemia during oral glucose tolerance testing in adults with cystic fibrosis and risk of developing cystic fibrosis-related diabetes

Author(s): Mannik L.A.; Chang K.A.; Annoh P.Q.K.; Sykes J.; Gilmour J.; Robert R.; Stephenson A.L.

Source: Journal of Cystic Fibrosis; 2018

Publication Type(s): Article In Press

Abstract: Background: Hypoglycemia in cystic fibrosis (CF) patients during the oral glucose tolerance test (OGTT) has been reported; however, these patients have not been well-characterized. Few studies have examined whether hypoglycemia during the OGTT increases the risk of developing CF-related diabetes (CFRD). Objectives of this study were to describe the characteristics of CF patients with hypoglycemia during the OGTT and to determine the incidence and time to development of CFRD in those with hypoglycemia. Methods: This cohort study included 466 adults with CF at the Toronto Adult CF Clinic between 1996 and 2015. Subjects were classified into two groups based on their plasma glucose (PG) level 2 h after a 75 g OGTT: hypoglycemia (PG <= 3.9 mmol/L) or no hypoglycemia (PG > 3.9 mmol/L). Clinical and demographic data were collected from the clinic visit closest to the OGTT. Differences between groups were assessed using Fisher's exact test or Mann-

Whitney-Wilcoxon test. Results: 138 patients (29.6%) experienced hypoglycemia during the OGTT. More males experienced hypoglycemia compared to no hypoglycemia (69.6% vs. 54.6% respectively; p = 0.003). Those who were heterozygous deltaF508 were more likely to experience hypoglycemia (p = 0.006). Subjects who experienced hypoglycemia were less likely to develop CFRD at ten years compared to no hypoglycemia (12.0% vs. 42.1%, respectively; p < 0.001). Conclusions: Hypoglycemia following OGTT is common in CF however the 10 year risk of developing CFRD in these patients was low. Males and those who were heterozygous deltaF508 were at higher risk for hypoglycemia.

Other

Older Adolescent with Cystic Fibrosis: Transitioning to Adult Care

Author(s): Debiasi, Laura B; Nichols, Lynn Stover; Ladores, Sigrid

Source: Pediatric Nursing; 2018; vol. 44 (no. 2); p. 95

Difficult conversations: Discussing prognosis with children with cystic fibrosis

Author(s): Farber J.G.; Shay R.; Prieur M.G.; Roach C.; Borowitz D.; Walter M.; Dellon E.P.

Source: Pediatric Pulmonology; May 2018; vol. 53 (no. 5); p. 592-598

The experience of men and women with cystic fibrosis who have become a parent: A qualitative study

Author(s): Jessup, Melanie; Li, Anne; Fulbrook, Paul; Bell, Scott C

Source: Journal of Clinical Nursing; Apr 2018; vol. 27 (no. 7-8); p. 1702

Is daily physical activity affected by dynamic hyperinflation in adults with cystic fibrosis?

Author(s): Savi, Daniela; Di Paolo, Marcello; Simmonds, Nicholas J.; Pascucci, Chiara;

Source: BMC Pulmonary Medicine; Apr 2018; vol. 18 (no. 1)

Six-minute walk test as a determinant of the functional capacity of children and adolescents with cystic fibrosis: A systematic review

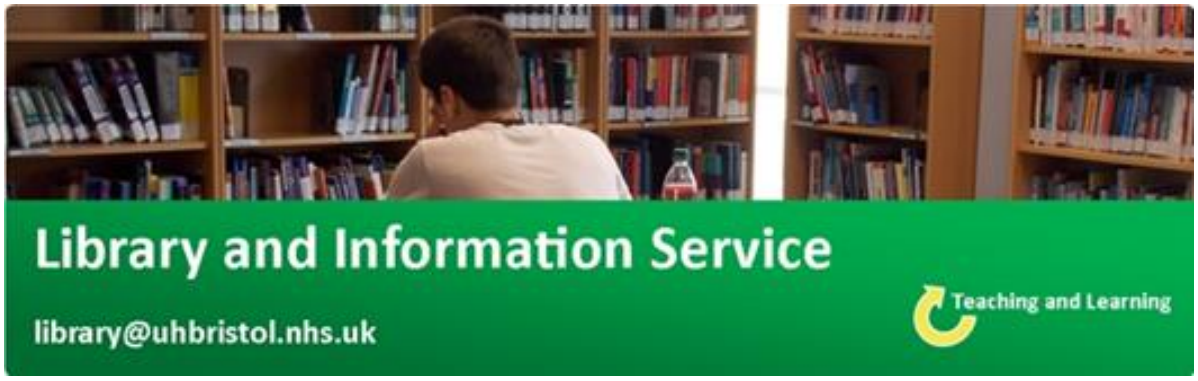
Author(s): Cibelle Andrade Lima; Armèle Dornelas de Andrade; Shirley Lima Campos; Daniella Cunha Brandão; Ianny Pereira Mourato; Murilo Carlos Amorim de Britto

Source: Respiratory Medicine; Apr 2018; vol. 137 ; p. 83

Perspectives of adolescent girls with cystic fibrosis and parents on disease-specific sexual and reproductive health education.

Author(s): Kazmerski, Traci M; Hill, Kelsey; Prushinskaya, Olga; Nelson, Eliza; Greenberg, Jonathan;

Source: Pediatric pulmonology; Apr 2018



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