Cystic Fibrosis: Literature Review

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Cystic fibrosis affects more than 30,000 children and adults in the US and 70,000 people worldwide. Cystic fibrosis is one of the leading causes of death among various lung diseases (Endres & Konstan, 2022). Early detection and optimal treatment are the goals of preventing a decline in the patient's health. A literature review on cystic fibrosis may enhance the body of knowledge on the subject in question (Houser, 2023). This literature review will go over the general overview of cystic fibrosis, its diagnosis, and treatment of the disease.

Quantitative multivolume proton-magnetic resonance imaging in patients with cystic fibrosis lung disease: Comparison with clinical indicators

Pennati et al. (2019) dive into magnetic resonance imaging (MRI) and its relationship with cystic fibrosis (CF). MRI has the advantage over global measures of functional impairment that it can identify local structural and functional alterations in CF lung disease (Pennati et al., 2019). As a non-ionizing imaging technique, MRI may be lovely in CF care for longitudinal evaluation, providing a new imaging biomarker to detect early ventilatory abnormalities (Pennati et al., 2019). Other diagnostic tests are mentioned throughout this article, identifying different CF variabilities.

Key Points

Pennati et al. (2019) used a cross-sectional study. Patients with CF were participants in their annual review in stable clinical condition. For their annual review, a sweat chloride test confined the diagnosis of CF. In total, 28 consecutively selected patients (mean age 18 years,

range 10–27 years, 14 males) enrolled in the study. All patients underwent a chest MRI, spirometry, and multiple breath washout test (MBW). This study was approved by the local ethics committee and conducted in compliance with the guidelines of the institutional review board.

The lungs were divided into six lobar regions (five lobes plus lingula) and assessed for 1) bronchiectasis/bronchial wall thickening (bronchial wall abnormalities); 2) mucus plugging; 3) abscesses/sacculations; 4) consolidations; and 5) remarkable findings. The findings assessed each lobe as 0 (no lobe involvement), 1 (less than half a lobe involved), and 2 (more than half a lobe involved) (Pennati et al., 2019). Pennati et al. (2019) found a strong correlation between quantitative multi-volume MRI, spirometry, and MBW and a clear structure-function relationship in CF lung disease. A p-value <0.05 was considered statistically significant.

Pennati et al. (2019) emphasize that these results support the further investigation of multi-volume MRI to detect and regionally monitor disease progression and quantify individual response to treatment. MRIs have proven sensitivity to structural changes at various stages of CF lung disease. Because the present study is cross-sectional, we can only speculate that MRI ventilation measures will worsen with advancing structural alterations and that ventilation defects can anticipate morphological changes (Pennati et al., 2019). Future longitudinal studies using multi-volume MRI may elucidate local structure-function relationships in patients followed over several years (Pennati et al., 2019). The authors also explain the study's limitations and concerns regarding the lack of patients and the fact that it is cross-sectional.

Assumptions

Pennati et al. (2019) assumed that breath-hold multivolume 1H-MRI would provide quantitative biomarkers in CF lung disease capable of detecting functional impairment. In

particular, they aimed to verify the correlation between multivolume H-MRI biomarkers and standard clinical parameters and to investigate the relationship between functional impairment and structural damage quantified by a specific CF-scoring system (Pennati et al., 2019). The authors also assume that the MRI is the only diagnostic tool to visualize early deficits in CF patients. After the study came out with the results, results showed that the other diagnostic tools mentioned in the article also helped visualize lung deficits (Pennati et al., 2019).

Deficit/Conclusion

The reader accepts the authors' line of reasoning because, in the article, the authors' study shows that an MRI is essential in finding a deteriorating factor in CF patients. Pennati et al. (2019) state that imaging function and structure are essential in CF because functional lung changes are dissociated from structural changes; imaging may reveal the structure-function relationship at the regional and whole lung. If nursing fails to accept this line of reasoning, preventing further complications of CF will be harder to catch. As mentioned earlier, the reasoning behind the imaging is to ensure that if the patients are deteriorating, this is a way to know to catch and fix it. The outcome would be catastrophic, leading to more deaths among CF patients.

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

Hart et al. (2018) discuss the relationship between CF and diabetes. Cystic fibrosis-related (CF-related) diabetes (CFRD) is an increasingly common and devastating comorbidity of CF, affecting approximately 35% of adults with CF (Hart et al., 2018). Studies have shown that patients with CF have a higher chance of developing diabetes because of pancreatic beta cells.

The authors 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 (Hart et al., 2018). Furthermore, the authors realized that the cause of CFRD was inflammation and the loss of islet cells.

Key Points

Hart et al. (2018) elucidated the underlying causes of CFRD and the role of CFTR in islet cell function, generated acute and chronic models of β cell-specific CFTR deletion, and investigated the effect(s) of CFTR loss on glucose tolerance or β cell function. The authors used ten male and female mice to conduct their research along with CF donor patients. The authors established a nationwide network to obtain and study pancreas and islets and identified medical records from CF donors and healthy age-matched donors to examine the effect of CF-causing mutations on insulin secretion. Hart et al. (2018) developed a protocol to obtain pancreatic tissue and isolated islets from a single CF organ to maximize the data collected from CF pancreata. This approach allowed for an integrated investigation of pancreatic tissue, CFTR mutations, islet function, gene expression, and immune activity (Hart et al., 2018). First, the healthcare worker takes an oral glucose test after a 6-hour fast on conscious animals. The plasma glucose is taken for whole blood from the tail, with an Accu-chek glucose meter (Roche Diagnostics) prior to and 15, 30, 60, 90, 120, and 150 minutes after oral gavage of a 2 g/kg glucose bolus (Hart et al., 2018). A p-value of less than 0.05 was considered significant.

Pancreatic sections were stained with H&E or labeled with insulin and visualized using a DAB (Vector Laboratories) stain with a hematoxylin counterstain. Analysis of β cell area was

performed on whole pancreatic sections using customized Tissue Classifiers (Indica Labs) generated in Halo (Leica Biosystems). β Cell area was determined by dividing the β cell classified area by the total classified area. These results indicate that the deletion of CFTR from murine β cells did not affect glucose homeostasis. The studies indicate that the remaining islets in CF/CFRD are functional, highlighting the importance of efforts to limit pancreatic destruction and inflammation.

Additionally, treatment with agents that improve β cell function and islet health, such as GLP1R agonists, might be considered to prevent and treat CFRD. The studies also suggest that new modulators of CFTR function do not directly affect β cell function. However, their ability to improve overall health or limit pancreatic exocrine inflammation and pathology may lead to improved diabetes management (Hart et al., 2018).

Assumptions

Hart et al. (2018) assume that there is no underlying cause for the development of diabetes in cystic fibrosis patients and that the destruction of the beta cells is the only plausible explanation. The authors tested this theory by destroying the beta cells of the pancreas and seeing the effect on the patient's glucose. With further evaluation, they predicted that this had no effect and that it had also to be followed by islet inflammation. Specific deletion of CFTR from murine β cells did not affect β cell function. CFTR mRNA is in human islets, and CFTR protein and electrical activity were not detected (Hart et al., 2018). Isolated CF/CFRD islets demonstrated appropriate insulin and glucagon secretion, with few changes in vital islet-regulatory transcripts. Approximately 65% of β cell area was lost in CF donors, compounded by pancreatic remodeling and immune infiltration of the islet (Hart et al., 2018). These results indicate that CFRD happens

because of β cell loss and intra- islet inflammation in a complex pleiotropic disease setting and not by intrinsic islet dysfunction from CFTR mutation (Hart et al., 2018).

Deficit/Conclusion

The reader accepts the author's reasoning because the research is accurate and shows proof that islet loss and inflammation cause CFRD. Hart et al. (2018) present, for the first time to our knowledge, a detailed characterization of an increased inflammatory potential within the human CF islet by increased expression of several cytokines/chemokines and high levels of TNF-α and IFN-γ production by stimulated T cells isolated from CF islets. The authors postulate that islet isolation from the CF pancreas removes the islet from the inflammatory environment, limiting the effect of cytokines/chemokines and allowing for relatively normal in vitro islet secretion of insulin and glucagon (Hart et al., 2018). If nursing fails to accept this line of reasoning, nurses will not be ready to determine the comorbidities that cystic fibrosis patients may have. With the knowledge from the article, the nurses would not be aware that diabetes is a comorbidity and would be unable to determine the best course of action, such as checking blood glucose levels at the bedside.

Identification of novel blood biomarkers of treatment response is cystic fibrosis pulmonary exacerbations by label-free quantitative proteomics

Dong et al. (2019) studied pulmonary exacerbations in patients with cystic fibrosis. Unfortunately, many CF individuals with PEx fail to regain their baseline lung function despite treatment. Biomarkers that are measured objectively and reproducibly help guide therapeutic

interventions (Dong et al., 2019). In CF, blood-based biomarkers that reflect systemic inflammation, such as C-reactive protein and calprotectin, decrease significantly following PEx treatment (Dong et al., 2019). However, for a biomarker to aid in clinical decision-making, an early change is potentially more informative in assisting treatment decisions as it allows CF physicians to modify treatments (Dong et al., 2019).

Key Points

In this study, Dong et al. (2019) recruited adult CF subjects diagnosed with PEx and required hospitalization for IV antibiotic treatment. The authors collected blood, symptom diaries, and spirometry within 24 hours of admission, day 5, day 10, and IV antibiotic treatment completion. The objective of this study was to identify blood protein biomarkers associated with early response to IV antibiotics and to determine if early changes correlate with clinical outcomes by the end of IV antibiotic treatment in terms of improved lung function and symptoms (Dong et al., 2019). A total of 25 PEx events from 22 unique CF subjects were eligible for this study. Statistical significance when two-sided p-values are ≤ 0.05.

Dong et al. (2019) explain that using label-free LC-MS/MS quantitative proteomics, the authors identified several blood proteins involved in complement activation and inflammatory and immune-related pathways that changed in response to IV antibiotic treatment. Early change in IGFR2 correlated with symptom improvement by the end of treatment and requires further validation as an early marker of symptomatic treatment response in individuals with CF (Dong et al., 2019). For 25 PEx

events, the median duration of IV antibiotic treatment was 14 days (ranging from 13 to 24 days). Most PEx events recovered 90% of baseline lung function, but fewer recovered to ≥100% of their baseline lung function (Dong et al., 2019).

Assumptions

Dong et al. (2019) assumed that prophylactic antibiotic treatment for patients with cystic fibrosis would prevent pulmonary exacerbations and even more lung dysfunction. The authors also assumed that suboptimal PEx outcomes might be due to delayed recognition and treatment, widely varied treatment decisions, and differences in the approach to monitoring treatment response, including recovery in lung function and resolution in signs and symptoms (Dong et al., 2019). Despite the potential lung protective effects of downregulating the complement system early during PEx treatment, the authors did not observe a more significant recovery of lung function in such individuals. However, this study was small, which warrants further study (Dong et al., 2019). However, as mentioned above, Dong et al. (2019) did identify several blood proteins involved in complement activation and inflammatory/immune-related pathways that changed in response to IV antibiotic treatment. With these discoveries, they can expand their research and get effective results.

Deficit/Conclusion

The reader accepts the authors' line of reasoning. However, there is more research to be done on this particular topic. Dong et al. (2019) prove significant points about pulmonary exacerbations and cystic fibrosis but need more volunteers to prove their point. Dong et al. (2019) also

mentioned that as this was an untargeted discovery study, many proteins were identified with LC-MS/MS proteomics and found to change significantly following treatment, but the multiple statistical comparisons performed could have inflated the type 1 error. As such, the Benjamini-Hochberg method is, in effect, adjusted for multiple testing with a cut-off q-value of ≤0.10 (Dong et al., 2019). However, this approach may have been too stringent and resulted in false negatives at this discovery stage (Dong et al., 2019).

If nursing fails to accept this line of reasoning, the implications would not be significant. Since Dong et al. (2019) need more time to understand their theory with more research, nurses should not use this in practice. Giving prophylactic antibiotics to CF patients undergoing pulmonary exacerbations with no benefit could do more harm than good. Nurses can use this in practice until the authors understand what is happening and expand their research. The authors are going in the right direction and can improve treatment and lung function in these patients.

Conclusion

Overall, these three articles explained the overall view of cystic fibrosis, the diagnosis, and the treatment. The authors emphasized the importance of ensuring that the care of patients with cystic fibrosis is studied. Pennati et al. (2019) emphasized the importance of using MRI screenings to catch other lung deficits early and efficiently to treat patients ahead of time. Hart et al. (2018) discussed cystic fibrosis-related diabetes and the reasoning behind why this is a

comorbidity for these patients. Lastly, Dong et al. (2019) discussed blood biomarkers and antibiotic treatment to lessen the chances of cystic fibrosis patients on lung declination.

The improvement of patient outcomes will increase since the authors researched the different ways to care for cystic fibrosis patients and how these diagnostics and treatments will benefit their future. For nursing practice, it allows nurses to take care of their patients before they get worse proactively. The research also allows nurses to acquire additional knowledge about the disease and the types of things that may happen in cystic fibrosis patients. The evidence-based practice holds great promise for moving care to a high likelihood of producing the intended health outcome. That is why healthcare, as a whole, benefits from the information that Pennati et al. (2019), Hart et al. (2018), and Dong et al. (2019) discussed. This information improves the outcomes of the patient, as mentioned before since cystic fibrosis is a disease that drastically affects lung function. Additional treatments and diagnostics that may delay further decreased lung function improve the mortality rate the healthcare industry may see in cystic fibrosis patients.

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