A REVIEW OF SARS-COV-2 INFECTION IN CYSTIC FIBROSIS

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Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and the development of life-threatening COVID-19 is believed to disproportionately affect certain at-risk populations. However, it is unknown whether this is true for cystic fibrosis (CF) patients, who commonly experience recurrent viral infections of the respiratory tract, resulting in direct and indirect morbidity from the inflammatory response.

Objective

This study reviewed reports of CF patients who developed COVID-19 and compared infection rates in CF patients to the general population.

Methods

A literature search was conducted using PubMed (April 28 to June 12, 2020). Publications were selected by their relevance to CF, especially regarding COVID-19. Both primary and secondary literature were included. Key search terms included "cystic fibrosis", "CFTR", "SARS-CoV-2", "COVID-19" and "ACE".

Results and Discussion

- 22 reports were included

CF and COVID-19

- Two studies identified 117 CF patients who developed SARS-CoV-2
- Incidence of SARS-CoV-2 infection was 0.07% in CF, compared to the 0.15% in the general population (Cosgriff et al., 2020)
- Clinical features of COVID-19 in CF was comparable to the general population exposed to SARS-CoV-2

Potential Protective Mechanisms

- Increased concentrations of neutrophil elastase (NE) are linked to enhanced lung damage and a decline in pulmonary function in CF
  - Pro-inflammatory imbalance of NE is involved in the development of acute respiratory distress syndrome, a severe complication of COVID-19 (Polverino et al., 2017)
  - NE inhibitors may be a potential prophylactic treatment for COVID-19. Therefore, an infected CF patient may be on medications that mitigate clinical features of viral (e.g. SARS-CoV-2) infections; however, there has been no explicit use of these medications in any of the included studies
- Angiotensin-converting enzyme 2 (ACE2) is the host cell receptor required for cell entry of SARS-CoV-2
  - SARS-CoV-2 infection is associated with ACE2 transcriptional downregulation, resulting in an excessive synthesis of angiotensin II by angiotensin-converting enzyme (ACE)
  - Decreased expression of ACE2 is a potential factor for exacerbated lung damage (Sarzi-Puttini et al., 2020)
  - A study on an ACE biallelic polymorphism in 180 CF patients, termed I (insertion) and D (deletion), reported that subjects with the ACE D/D polymorphism were associated with an earlier appearance of clinical symptoms and higher risks of lung deterioration than those with I/I or D/I polymorphisms

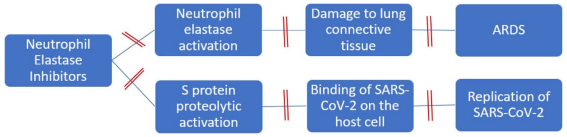

Fig 1. Action of NE inhibitors in COVID-19; red bars indicate blocks (Mohamed et al., Critical Care 2020).

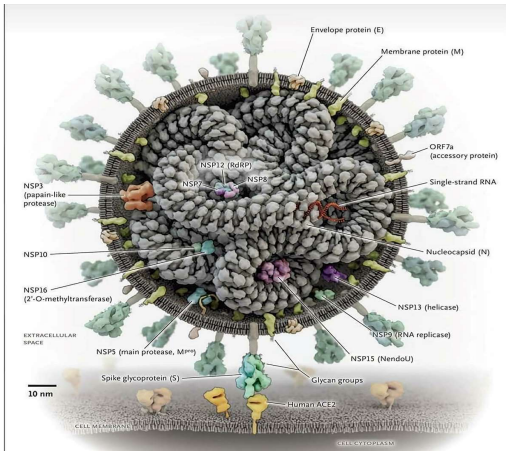

Fig 2. Interaction between SARS-CoV-2 and ACE2 receptor (Parks and Smith, NEJM 2020).

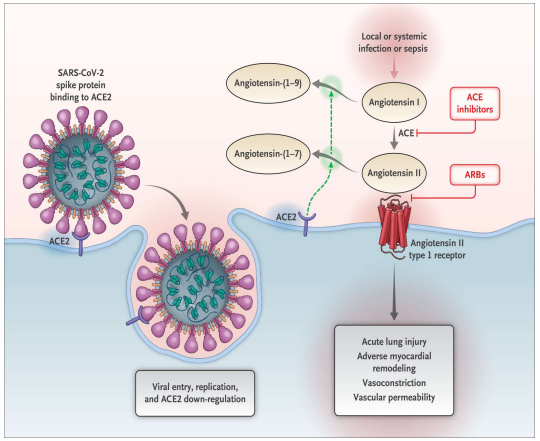

Fig 3. Interactions between SARS-CoV-2 and the ACE/ACE2 system (Vaduganathan et al., NEJM 2020).

Conclusions

- Although CF patients suffer from acute exacerbations of chronic lung disease, there is no published evidence that they were disproportionally affected by SARS-CoV-2 infection or the development of COVID-19
- Low rates of SARS-CoV-2 infection in CF patients may reflect:
  - Pre-existing practices of infection prevention and control such as more stringent social isolation owing to perceived risk
  - A lower median age in the CF patient population
  - Delays in reporting COVID-19 in CF
  - Medications that mitigate clinical features of SARS-CoV-2/COVID-19 (e.g. neutrophil elastase inhibitors)
- Future studies:
  - Effect of ACE D/I biallelic polymorphism on COVID-19 severity in CF
- Limitations:
  - Limited case reports
  - Data reported by only 8 countries

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