CYSTIC FIBROSIS (CF) COMPLICATIONS BEYOND THE LUNGS

A Resource for the CF Center Care Team
Overview:

CF complications beyond lung disease continue to emerge as patients age

- Patients require care from CF multidisciplinary teams and their complications change over time\(^1\)\(^-\)\(^3\)

- Such complications include\(^1\)\(^-\)\(^3\):
  - Loss of pancreatic exocrine and endocrine function
  - CF-related diabetes
  - CF liver disease
  - CF-related bone disease
  - Depression and anxiety

- Monitoring for these complications can help detect their emergence and progression\(^1\)\(^-\)\(^5\)

- Other less prevalent complications may also occur such as pancreatitis in 10-15\% of pancreatic-sufficient patients\(^1\),\(^2\)

CFTR protein abnormalities begin a cascade leading to structural damage in several organs\textsuperscript{1-4}

CF affects both the exocrine and endocrine functions of the pancreas

- In the healthy pancreas, CFTR channels regulate chloride and bicarbonate secretion, which, in turn, affects the composition of pancreatic fluids that carry enzymes into the intestine\(^1\)
- In CF, these processes are altered due to CFTR dysfunction\(^1\)

Exocrine: CFTR dysfunction causes clogged pancreatic ducts. Enzymes to digest food are unable to pass into the intestines, and instead they break down the pancreas itself\(^1,2\)

Endocrine: Islet \(\beta\) cells, which regulate insulin secretion, are largely spared early in life but can be lost over time due to a variety of mechanisms, leading to CF-related diabetes\(^1,3\)

CF-related diabetes may occur as the pancreas is progressively damaged

- β-cells in the pancreas regulate insulin production, carbohydrate metabolism, and blood sugar levels\(^1,2\)
- β-cell dysfunction and destruction can occur in CF through a variety of mechanisms, many of which are mediated by CFTR function\(^1,2\)
- The result can be a range of blood sugar problems and, eventually, CF-related diabetes\(^1\)

The prevalence of CF-related diabetes increases with age\(^3,4\)

Patients with CF-related diabetes can experience more rapid declines in lung function compared with those who do not\(^5,6\)

CF liver disease is associated with scarring, inflammation, and abnormal liver function.

- Altered secretions due to CFTR dysfunction can clog small bile ducts, reduce gallbladder size, increase bile viscosity, and increase the risk of gallstones.

References:

Liver transplants can be necessary beginning in childhood.
Low bone mineral density (BMD) increases in prevalence with age

The risk of fractures also increases\(^1-3\)

- 1.5% of patients with CF <18 years and 21% ≥18 years have osteopenia\(^3\)
- 0.6% of patients with CF <18 years and 8.9% ≥18 years have osteoporosis\(^3\)
- Poor nutritional status along with chronic infections and inflammation due to CF disease, among other factors, can affect bone formation and resorption\(^4\)
- Patients with CF may have insufficiencies of essential vitamins (such as vitamin D), as well as calcium malabsorption, which contribute to low BMD\(^4\)
- Delayed puberty and physical inactivity, amongst others, may also contribute towards low BMD\(^4\)
- CFTR dysfunction also affects the process of bone remodeling\(^5,6\)

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Rates of anxiety and depression are high among adolescents and adults with CF

Prevalence peaks in early adulthood\(^1\)

- In ages <18, the prevalence of depression is 3.3\(^1\)
- In ages ≥18, the prevalence of depression is 25.3\(^1\)
- In ages <18, the prevalence of anxiety is 3.2\(^1\)
- In ages ≥18, the prevalence of anxiety is 17.6\(^1\)
  - Of patients reporting anxiety or depression, 36% report both
- Depression and anxiety symptoms have been associated with\(^2\):
  - Decreased lung function
  - Lower BMI
  - Worse adherence
  - Reduced health-related quality of life
  - Increased hospitalizations

Tests are available to detect and monitor CF-related complications that emerge as a patient ages

<table>
<thead>
<tr>
<th>Organs</th>
<th>Selected Tests</th>
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<tbody>
<tr>
<td><strong>Pancreas</strong>¹⁻³</td>
<td>• Nutritional status (e.g., BMI, overall health)</td>
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<td>• Glucose monitoring (beginning at age 10)</td>
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<tr>
<td><strong>Liver</strong>⁴⁻⁶</td>
<td>• Liver function blood tests</td>
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<td>• Physical examination</td>
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<td>• Ultrasound</td>
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<td><strong>Bone</strong>²</td>
<td>• Bone mineral density scan (every adult with CF should be screened once, subsequent follow-up depends on the baseline scan)</td>
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<td>• Vitamin D levels</td>
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<tr>
<td><strong>Depression/Anxiety</strong>²,⁷</td>
<td>• Annual depression and anxiety screenings (age 12 and older)</td>
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</tbody>
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CF complications beyond lung disease emerge as patients age

- Systems and organs affected include:
  - The pancreas (CF-related diabetes, pancreatitis in pancreatic sufficient patients)\(^1,2\)
  - The liver (biliary cirrhosis)\(^3\)
  - The bones (low bone mineral density, risk of fractures)\(^1,4\)
  - The mental health (anxiety, depression)\(^5\)

Patients require care from CF multidisciplinary teams as their complications evolve over time\(^1-3\)