

## 6.5 Intestinal obstruction syndromes

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### 1. INTRODUCTION

- Patients with CF are prone to develop intestinal obstruction syndromes, including meconium ileus in neonates, constipation and distal intestinal obstruction syndrome (DIOS).
- These clinical entities are the result of increased viscosity of intestinal content, dysmotility and pancreatic insufficiency.
- Meconium ileus, occurs in up to 20% of newborns with CF and it is caused by accumulation of inspissated meconium leading to complete small bowel obstruction during the neonatal period. The predictive value of meconium ileus for long-term outcomes in CF is not clearly established.
  - Regarding nutritional outcomes, nowadays, these tend to be similar in patients with and without a history of meconium ileus.
  - Regarding pulmonary outcomes, a few studies reported worse pulmonary function in patients with a history of meconial ileus but literature is not conclusive.
- The following paragraphs focus on constipation and DIOS which are observed in adults.

### 2. CONSTIPATION

- Being the most common digestive complaint in the general population, constipation, appears to be even more frequent in CF, affecting more than 40% of patients.
- **Table 1** summarizes the diagnostic criteria of functional constipation according to Rome IV.
- Constipation remains a clinical diagnosis, with careful history and physical examination. In contrast to DIOS, constipation has a gradual onset and, if a plain abdominal radiograph is performed, accumulation of stool throughout the colon can be observed, with only mild signs of small bowel dilatation.
- Management of constipation in patients with CF consists of
  - Macrogol 3350 or 4000 with electrolytes (Movicol®, Molaxole®, Moviprep®, Klean-Prep®, Laxipeg®, Cololyt®, Isocolan®, Transipeg®).
  - In some cases, stimulant laxatives such as senna and bisacodyl can be added intermittently.
  - A pilot study suggested that lubiprostone may be used as a second-line therapy in adults CF patients with severe refractory constipation. Lubiprostone activates alternative type-2 chloride channels, thus increasing ion transport despite the nonfunctional CFTR. Although data on its use in CF are limited, it may be considered in selected cases in collaboration with the GI specialist.
- Concerning constipation, there are some misconceptions commonly held by CF patients, which are important to explain:
  - Indeed, despite regular bowel movements, a large intracolonic fecal load can develop.
  - CF patients are prone to constipation due to relatively dehydrated bowel, independently of pancreatic sufficiency or insufficiency.

- Furthermore, although constipation has been attributed to either inadequate or excessive doses of pancreatic enzyme replacement therapy (PERT), no correlation could be found between PERT dosage and constipation.

**Table 1:** Rome IV diagnostic criteria of functional constipation

**At least 2 of the following, for more than 25% of defecations**

- <3 spontaneous bowel movements per week
- Straining during defecation
- Lumpy or hard stools (Bristol stool scale 1-2)
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction/blockage
- Manual maneuvers to facilitate defecation

### 3. DISTAL INTESTINAL OBSTRUCTION SYNDROME (DIOS)

- Previously known as meconium ileus equivalent, Distal Intestinal Obstruction Syndrome (DIOS) refers to a range of clinical conditions resulting from complete or partial bowel obstruction by inspissated intestinal contents in the distal ileum, caecum and ascending colon.
- The definitions of complete and incomplete DIOS, according to ESPGHAN are:
  - **Complete DIOS:**
    - 1) Complete intestinal obstruction as evidenced by vomiting of bilious material and/or fluid levels in small intestine on an abdominal radiography AND
    - 2) Fecal mass in ileo-caecum AND
    - 3) Short history (days) of abdominal pain and/or distension
  - **Incomplete or impending DIOS:** Criteria 2 and 3, but not 1
- The incidence of DIOS is 23.3-35.5 episodes per 1000 patient-years and the lifetime prevalence is 14-16%.
- **Table 2** summarizes the risk factors for DIOS.

**Table 2:** Risk factors for DIOS (adapted from<sup>1</sup>)

Genotype associated with severe clinical manifestations  
 Pancreatic insufficiency  
 Poorly controlled fat malabsorption  
 Dehydration  
 History of meconium ileus / DIOS  
 CF-related diabetes  
 After transplantation\*

\*DIOS is seen in up to 10-20% of CF lung-transplant patients in the early post-transplant period due to dehydration, immobility and opiate use. In high-risk patients: preoperative bowel preparation, early postoperative use of laxatives and enteral feeding with immediate, adequate pancreatic enzyme substitution should be considered.

### 3.1 Diagnosis and differential diagnosis of DIOS

- **Table 3** presents symptoms, physical examination and imaging findings suggestive of DIOS.
  - In the majority of cases, a typical history combined with a palpable right lower quadrant mass and characteristic abdominal radiograph (**Figure 1**) are sufficient to establish the diagnosis.
  - Protracted and/or uncharacteristic symptoms or atypical radiograph should prompt re-evaluation to exclude another diagnosis.
- The **differential diagnosis** of DIOS is summarized in **Table 4** and includes
  - **Constipation**
  - **Atypical presentation of *Clostridium difficile* colitis:** Patients with CF have a high incidence of colonic colonization with *C. difficile* due to the frequent use of antibiotics. A few cases have been reported in the literature of patients presenting with a picture of stool impaction with abdominal distension, tenderness and decreased stooling, treated unsuccessfully with enema. Worsening clinical status led to CT-scan that revealed colitis, suggestive of *C. difficile* infection.
  - **Fibrosing colonopathy:**
    - Only a few cases of fibrosing colonopathy have been reported since the early 1990s, especially in children under very high doses of PERT (> 50000 U lipase/kg/jour).
    - Although its pathogenesis remains unclear, fibrosing colonopathy is a severe sub-mucosal fibrotic process resulting in colonic strictures. Symptoms are often similar to DIOS and this diagnosis should be considered when patients do not respond to typical DIOS treatment. Diagnostic procedures include ultrasonography, CT-scan, MRI or endoscopy. Surgical resection is usually needed.
  - Mechanical ileus may develop in patients with a previous history of abdominal surgery due to adhesions. Other causes of mechanical ileus include intussusception, volvulus, as well as tumoral processes, with a higher risk in CF patients compared to the general population.
  - As mentioned in **Table 4**, other conditions, including surgical ones such as appendicitis, appendicular abscess or mucocele of the appendix, as well as stenotic Crohn's disease may present as bowel obstruction and should be considered in the differential diagnosis. Sometimes, establishing the diagnosis may be challenging due to the overlap of symptoms but it is important to allow timely management. In these cases, ultrasonography, CT-scan or other radiologic imaging is needed.

**Table 3:** Diagnosis of DIOS

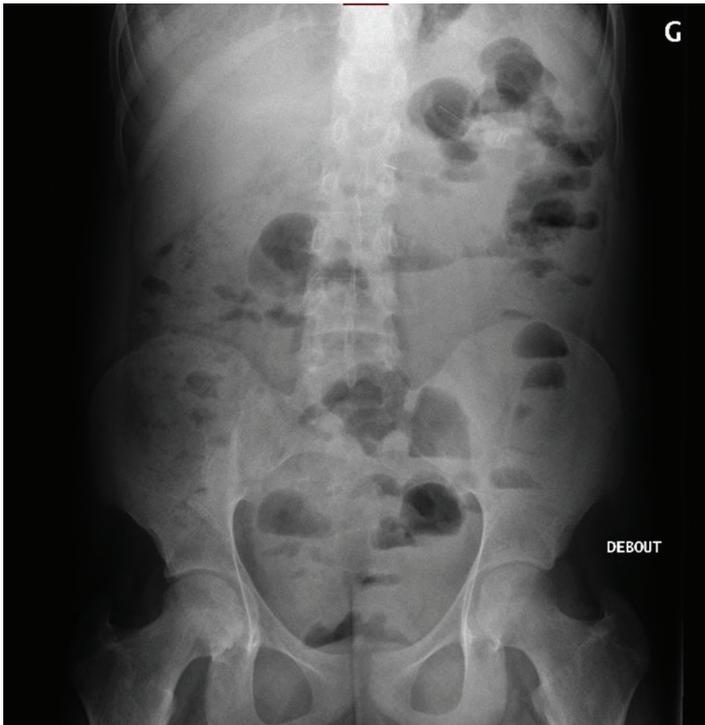
<b>Symptoms</b>	Acute onset of periumbilical colicky and/or right lower quadrant abdominal pain Nausea Anorexia Bilious vomiting (in complete DIOS)
<b>Physical examination</b>	Abdominal distension Palpable mass in the right lower quadrant

(continued)

**Plain abdominal radiograph**

Granular fecal loading in the right lower quadrant  
Sometimes, multiple air-fluid levels in the dilated small bowel (complete DIOS)

**Figure 1:** Plain abdominal radiograph in a patient with DIOS. Granular fecal loading of the right lower quadrant and the ascending colon. Multiple air-fluid levels in the small bowel.



**Table 4:** Differential diagnosis of DIOS

Constipation (most common)

Appendicitis, appendiceal abscess, mucocele of the appendix

Intussusception

Volvulus

Adhesions

*(continued)*

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*Clostridium difficile* colitis

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Malignancy\*

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Crohn's disease\*

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Fibrosing colonopathy

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\* See Chapter "CF and aging"

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### 3.2 Treatment of acute episodes of DIOS

- Largely empirical, treatment of DIOS is mostly medical and requires surgery only in a minority of cases.
- **Incomplete DIOS:**
  - Oral rehydration, correction of electrolyte abnormalities (K, Mg).
  - **Macrogol 3350 or 4000 with electrolytes** (Movicol®, Molaxole®, Moviprep®, Klean-Prep®, Laxipeg®, Cololyt®, Isocolan®, Transipeg®): 1.5-2 g/kg/day, max. 80-100 g/day, orally or by naso-gastric tube (rate of 20 to 40 ml/kg per hour, max. 1 l/hour, over 8 hours).
    - The aim is to achieve fecal effluent consisting of clear fluid and resolution of pain, abdominal distension and vomiting. Generally, patients require 5 to 6 liters.
    - Ondansteron (Zofran®) IV can be added in the case of nausea.
  - Alternative:
    - Sodium meglumine diatrizoate (**Gastrografin**), orally or by naso-gastric tube: 100 ml diluted in 400 ml of water or juice on day 1 and half doses on subsequent days until clean-out.
    - In the past, N-acetylcysteine was used in a similar fashion, but has shown to be less effective than gastrografin.
    - In refractory cases not responding to medical therapy, case series evidence suggests that emergency colonoscopy with instillation of gastrografin may be effective and may avoid the need for a surgical intervention.
- **Complete DIOS with severe intestinal obstruction, bilious vomiting or failure of previous measures:**
  - Hospitalization with IV rehydration, correction of electrolytes abnormalities and naso-gastric aspiration.
  - **Hyperosmolar enema (Gastrografin):** 100 ml diluted in 400 ml of water, under fluoroscopic guidance, performed by an experienced radiologist. By reaching terminal ileum, gastrografin enema allows clearance of the obstruction as well as exclusion of another cause of intestinal obstruction.
    - CAVE: Complications include hypotension and shock due to considerable fluid shift, perforation, necrotizing entero-colitis.
  - Other causes of bowel obstruction should be considered in patients not responding to medical management.
  - As mentioned previously, in refractory cases not responding to medical therapy, emergency colonoscopy with instillation of gastrografin may be effective.

- Surgery: required in a few patients
  - Laparotomy with washout by enterostomy
  - Ileo-caecal resection
- In transplanted, immunosuppressed patients consider also administration of antibiotics to prevent infection due to transmural migration of intestinal bacteria.
- **Prophylaxis:**
  - Prevention of dehydration.
  - Reassessment of adequate pancreatic enzyme dosage.
  - **Macrogol 3350 or 4000**, 0.5-1 g/kg/day, max. 40 g per day, for 6-12 months.

## 4. REFERENCES

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