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## Constipation and cystic fibrosis

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## Journal of Cystic Fibrosis

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## Editorial

## Constipation and cystic fibrosis. Slow movement



Constipation is a gastro-intestinal problem that is frequently seen in cystic fibrosis (CF) patients. As both the symptoms of constipation and the pathophysiology are different from patients without CF, the Rome criteria cannot be applied. Therefore an ESPGHAN working group gathered in 2010 to decide on the diagnostic requirements of constipation in CF patients. The subsequent definition for constipation in CF patients encompassed abdominal pain and/or abdominal distention, or a reduced frequency of bowel movements or an increased consistency of stools, as observed in the last few weeks to months. Finally and importantly these symptoms should be relieved by the use of laxatives [1].

Only a few studies have described the prevalence of constipation in a non-selected and non-admitted cohort of CF patients. The actual period prevalence, i.e. having or ever having had symptoms of constipation, varied from 32%–57% [2–5]. So far the ESPGHAN criteria were used in only two studies. In a small study 15 out of 34 patients, aged 3–20 years, turned out to be constipated (44%) [6], while in a study amongst 230 patients, aged 0–18 years, a period prevalence of 47% (107/230) was found [5]. At the moment of this survey 46 out of the 230 patients were constipated, amounting to a point prevalence of 20% [5].

The survey by Stefano et al. published in this journal [7] is a welcome addition to these studies. It showed that 43 out of 105 (41%) CF patients between 6 and 21 years of age had, according to the ESPGHAN criteria, symptoms of constipation, with relief of these problems after the initiation of laxatives, which, as pointed out above, is an essential component of these criteria. The higher point prevalence in this study might be due to the age of the patients included, as opposed to the 0–18 year group in the article by van der Doef [5], as it is known that, although constipation can be present in this younger age group, it is more rare [2]. The article by Stefano [7] also once again highlights the differences between constipation in CF and non-CF patients, with the vast majority (86%) of constipated CF patients having a normal frequency of bowel movements (i.e. daily or each other day), while pain or discomfort when passing stools is infrequent, although abdominal pain in general is frequent. The increased stool consistency as seen in this study, however, is a feature that is present in constipated patients both with and without CF.

The pathophysiology of constipation in CF is likely to be multifactorial, with a slower small intestinal transit and a different composition of intestinal contents with more “sticky” mucus probably being the most important, although a different pH, low grade intestinal inflammation, as evidenced by increased calprotectin levels, and an abnormal composition of the microbiome can have an

additional contribution. The latter is described by Marsh et al. in this issue of the journal [8]. They found that the microbiome was significantly less diverse in a group of 12 CF patients as compared to 12 healthy controls. Further analysis revealed that antibiotic use was the most important contributor to this difference, as was, not surprisingly, the presence of CF disease. Other factors that influenced this difference were small bowel water content, a slower oral-caecal transit time, and colon fasting volume.

These latter three aspects of gastrointestinal disease in CF patients have been described recently, partly by the same authors [9]. As studied by MRI they found that oral-caecal transit time in CF patients was longer, and that CF patients had a larger colonic volume. Interestingly small intestinal water content in fasting conditions was higher in CF patients, which was suggested to be caused by stasis in the terminal ileum, a well recognized problem in CF. A subsequent article from the same group confirmed these findings, but also showed that after a meal the increase in small bowel water content is reduced in CF patients [10]. In the current issue of the Journal of Cystic Fibrosis the same authors now extend these observations [11]. When comparing a group of 12 CF patients with 12 controls, and using MRI, they found a reduced small bowel motility, especially when fasting. In addition the texture of bowel contents, both in the small and large intestine were different, which was hypothesized to be due to gas bubbles (small intestine), likely related to bacterial overgrowth and a more pasty stool texture (colon) probably due to some residual fat malabsorption.

So where does this lead us? Importantly these and earlier studies confirm the high prevalence of constipation in CF. As this condition substantially reduces quality of life [12], improving its treatment and prevention is essential, with a first step being a better understanding of its pathophysiology. However there is only slow movement in this realm. Obviously the basic defect in CF, the abnormal electrolyte and water transport due to CFTR mutations, is a likely root cause of the problem. Nevertheless the exact steps that explain the stasis of faecal material in the gut remain unclear. Many of the observed differences between CF patients and controls, such as the low grade inflammation of the gut, as evidenced by an increased faecal calprotectin and the abnormal composition of microbiota, are likely to be secondary to the water and electrolyte transport problems, but could also be an additional factor to the faecal stasis.

It is unclear at present whether the new modulator/potentiator combinations will influence the prevalence and clinical course of constipation in CF patients. However this therapy does reduce fae-

cal calprotectin levels [13] and thus might also positively affect other aspects of the disturbed intestinal physiology, including intestinal flow. Nevertheless starting laxatives, preferably Macrogol, in CF patients who have symptoms of constipation, remains essential. According to a recent survey this was indeed the preferred therapy, both in children and adults [14].

#### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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