Towards an understanding of defecation disorders: pathophysiology, epidemiology, and clinical implications

Sun, Ge

DOI:
10.33612/diss.556158163

Summary

Defecation disorders, such as constipation, i.e., troublesome defecation or fecal incontinence (FI), i.e., involuntary loss of feces, are common diseases troubling the general population. They have an extremely negative impact on the quality of life and socioeconomic status. Despite recent improvements in techniques that can be profitable for patients with defecatory problems, the recognition, diagnosis, and treatment of these dysfunctions remain troublesome, as indicated by the high prevalence and posttreatment recurrence of the defecation disorders. The suboptimal treatment possibly results from the knowledge gap, which still exists in the field of anorectal pathophysiology. Also, the current state of the art, which approves symptom-based approaches to treat diseases, instead of targeting the cause of the disease, hampers the efficacy of the treatment.

Different factors can lead to fecal incontinence, but in general, the involuntary loss of feces appears when some fecal continence mechanisms fail. Fortunately, as indicated in **Chapter 2** of this thesis, fecal continence is maintained through multiple physiological processes, which cooperate in a healthy subject. These processes involve, in addition to the function of the colon and rectum, voluntary and involuntary contractions of the external anal sphincter and puborectal muscle and the involuntary contraction of the internal anal sphincter. In this review, we also concluded that despite long-term research on anorectal physiology underlying fecal continence, it is still challenging to translate the current knowledge to the recognition, prevention, and treatment of problems resulting from altered anorectal physiology.

To provide a patient with adequate treatment, first, the problem needs to be diagnosed, and second, the cause underlying this problem should be found. However, the ideal situation would be to prevent disease development as long-lasting, severe fecal problems, especially constipation, can lead to unreversible consequences, for instance, anatomical changes. One common anatomical alteration observed in the anorectal part of patients with defecatory problems is the rectocele. Rectocele is an bulging of the wall of the anal canal. It has been believed that the presence of a rectocele can result in defecation problems, for instance, constipation. Therefore, operations are performed to remove the rectocele, i.e., to correct the anatomy of the anal canal. In contrast to the belief above, we hypothesize that it is the other way around: the troublesome defecation prone patients to strain, which generates pressure that possibly gradually weakens the anterior side of the anal canal. This, in turn, leads to an bulging of the wall of the anal canal (**Chapter 3**). This finding is supported by the fact that the constipation severity is correlated with anal sphincter pressure just before defecation. It is not surprising, as the anal sphincter in a healthy subject relaxes before defecation, as reflected by temporarily decreasing anal basal pressure, which prevents the subject from straining. In constipated subjects, the anal basal pressure does not decrease, the anal sphincter cannot relax, defecation is therefore troublesome, and then patients strain to enforce defecation. This indicates that the etiology of the symptomatic rectocele might be due to the paradoxical contraction of the anal sphincter, i.e., the dyssynergic defecation, instead of the previously proposed theory about the rectovaginal septum defect. It would be more efficient to prevent patients from developing rectoceles by treating the increased anal

basal pressure in time than by treating the rectoceles with surgical procedures after waiting a long time. Moreover, our findings conclude that only operation of the rectocele is insufficient and should be accompanied by treatment of the increased anal basal pressure to prevent postoperative recurrence of the rectocele.

Furthermore, we investigated the epidemiology of defecation disorders and associated symptoms in the Chinese population. We used the Defecation and Fecal Continence questionnaire (DeFeC), developed in the Anorectal Physiology Laboratory and used initially for the Dutch people. To use this questionnaire in the Chinese population, we translated the Dutch version of DeFeC to Chinese and validated it in the Chinese population as described in **Chapter 4**. We found that the Chinese version of DeFeC had high feasibility and reproducibility, indicating that it can be used for scientific research and clinical setting. Using the questionnaire, we found that fecal incontinence can co-occur with constipation and irritable bowel syndrome. Based on this finding, we distinguished three forms of fecal incontinence, i.e., IBS-associated FI, constipation-associated FI, and isolated FI with comparably high prevalence (**Chapter 5**). The fact that fecal incontinence can be associated with constipation or irritable bowel syndrome (IBS) points out the importance of diagnosing and targeting the cause of FI to provide personalized care instead of addressing only the FI symptoms. Moreover, with this study, we found that more than half of the respondents suffering from fecal incontinence coexisting with constipation were treated with anti-diarrhea medicine, which indicates that the treatment was not adequately targeting the cause of the incontinence and undermines the suboptimal treatment of fecal incontinence. This knowledge provides fundaments for future research on treatment efficacy when the cause of FI, instead of only the symptom, is treated.

Furthermore, using the Chinese version of the DeFeC questionnaire, we also confirmed the previous reports that the prevalence of constipation with a predominance of dyssynergic defecation-associated symptoms is high in the Chinese population (**Chapter 6**). Importantly, we found that symptoms such as hard stool and decreased defecation frequency, frequently investigated by doctors when diagnosing constipation, are unreliable indicators of constipation. Thus, the current way of constipation diagnosis is too limited and therefore suboptimal, which can lead to overlooking constipation. The DeFeC questionnaire allows more detailed consultation and identifies other constipation-related symptoms, such as straining during defecation, incomplete defecation, pain, or bleeding during defecation. Indeed, with the study described in **Chapter 6**, we show that a majority of the constipated Chinese respondents did experience the symptoms above. Importantly, we also found that respondents who frequently eat spicy food have a higher prevalence of constipation. This can help prevent and treat constipation by adjusting lifestyle, i.e., reducing spicy food intake.

To further improve the diagnosis of defecation disorders, we investigated the value of the dynamic MR defecography in evaluating constipation and fecal incontinence (**Chapter 7**). Dynamic MR defecography is often used to diagnose anatomical changes of the pelvic floor in patients with defecation problems. This method can, for instance, indicate elongation of the

so-called M- line and H- line. Although the elongation is typical for patients with long-term defecation problems, it has never been investigated which alteration manifests these pathophysiological features. Therefore, it was impossible to pinpoint the underlying cause that led to the M- and H- line elongation and *vice versa*. It was impossible to determine what kind of pathophysiological impairments are demonstrated by a certain length of these lines. In contrast to the dynamic MR defecography, anorectal manometry does not illustrate the anorectal anatomy but measures pressures along the rectum and anal canal. This way, anorectal manometry provides comprehensive information about anorectal (patho)physiology. By comparing the outcomes of the dynamic MR defecography and anorectal manometry, we found that the M- line reflects the constipation severity, while the H- line during rest and squeezing reflects the fecal incontinence severity. This observation let us conclude that the anatomical changes in the pelvic floor, demonstrated by M- and H- lines, indicate the long-term consequence of the defecation problem but not the cause. Therefore, this study again emphasizes the need to treat defecatory problems in their early phase before irreversible changes, for instance, anatomical changes, will be reached.

In the above-summarized chapters, we presented outcomes of studies on etiology, clinical characteristics, and diagnosis of fecal problems. To complete this thesis, we also added to the optimization of treating severe and chronic constipation in children who do not respond to treatment with botulinum toxin (**Chapter 8**). In general, botulinum toxin should lead to the relaxation of the anal sphincter, which would be demonstrated by decreased anal basal pressure. As explained above, the increased anal basal pressure is the cause that makes it impossible to open the anal canal during defecation, which leads to troublesome defecation. From clinical experience, we knew that not all patients positively react to the treatment with botulin toxin. Thus, one might think that botulinum toxin did not relax the anal canal sufficiently in some patients. Interestingly, by measuring the anal basal pressure before and after injections, we found that the anal canal will only relax upon botulin toxin if it has a problem with relaxation before the injection. Specifically, we found that if the anal basal pressure is not higher than approximately 70 mmHg, then the injection of botulinum toxin is useless. Our finding is logical because the pressure of 70 mmHg is present in healthy, non-constipated subjects and therefore does not require treatment. Thus, constipation in patients with normal anal basal pressure results thus from a different factor and should not be treated with botulinum toxin. With the study described in **Chapter 8,** we highlight the importance of utilizing the anorectal physiology test before injecting botulinum toxin to decide whether the injection will be profitable for patients. This finding has significant clinical relevance for patients, as it can prevent them from unnecessary anesthesia and intervention. This finding also has economic importance as it will avoid unnecessary medical costs.

In summary, with the findings described in this thesis, we contributed to improved knowledge of anorectal physiology and the optimization of different facets of medical care in patients with defecatory problems.

*