

University of Groningen

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

Sun, Ge

DOI:
[10.33612/diss.556158163](https://doi.org/10.33612/diss.556158163)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2023

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Sun, G. (2023). *Towards an understanding of defecation disorders: pathophysiology, epidemiology, and clinical implications*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.556158163>

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Chapter 9

General discussion and future perspective

The high prevalence of constipation, fecal incontinence, and irritable bowel syndrome in general and patient populations strongly points out how important it is to provide the patients and their doctors with knowledge and tools that allow optimal diagnosis and treatment of these bowel disorders. Additionally, due to the improvement of living standards and economic development, our society's expectations regarding the quality of life have increased. At the same time, defecation disorders can severely decrease the quality of life. Unfortunately, both recognition of the disorders, diagnosing the causes, and treatment are still suboptimal, as indicated by the high prevalence of these problems, their chronic nature, and the high recurrence rate observed after treatment. Different factors contribute to suboptimal care, among which is that the *status quo* regarding anorectal physiology has not been completed. In other words, to properly diagnose a cause of bowel dysfunction, i.e., to recognize which element failed in the anorectal physiology, we first need to be able to identify the "healthy pattern" constituted by all the fecal continence mechanisms. Multiple studies have been performed to unravel these mechanisms, of which some yielded clear and convincing findings, while others presented ambiguous outcomes. To enable researchers to get a comprehensive and focused overview of these mechanisms, we summarized and critically evaluated the already proposed mechanisms of fecal continence in a descriptive review (**Chapter 2**). In this review, we also concluded that despite long-term research on anorectal physiology about fecal continence, it is still challenging to translate the current knowledge to the recognition, prevention, and treatment of problems resulting from altered anorectal physiology.

In the last decade, new diagnostic instruments, such as anorectal manometry and dynamic MR defecography, have been applied to clinical work. These instruments enable comprehensive investigation of various defecation disorders, including their presence, causes, and even anatomical and physiological consequences. In **Chapter 3** of this thesis, we present how valuable a combination of the outcomes of these two methods can be. Using the results of both anorectal manometry and dynamic MR defecography, we postulate our theory regarding rectocele formation. We compare our theory with two other theories regarding rectocele formation, which is proposed to be correlated with high puborectal pressure during defecation (1-3) and rectovaginal septum defect (4) in Table 1. But these other two theories have shortcomings compared to our approach. The theory regarding high puborectal pressure during defecation can only explain the rectocele formation above the puborectal muscle. Still, it cannot explain the formation of the rectocele below the puborectal muscle. The theory regarding the rectovaginal septum defect can explain the rectocele formation above or below the puborectal muscle. Still, it cannot explain the recurrence of the rectocele after the operation. Our theory regarding the mechanism of rectocele formation, i.e., that the increased anal basal pressure triggers patients to strain hard during defecation, thus generating pressure on the anal canal and elongated anal canal, which in turn would lead to bulging of the wall of the anal canal and rectocele formation. This may explain the high recurrence rate of rectocele after the operation. Also, when recurrent after the operation, rectocele often co-occurs with constipation (5-8) which corroborates our theory, as it is known that constipation is often associated with increased anal basal pressure. Keeping this theory in mind, we propose that

only surgery is insufficient to treat patients with rectocele. It is the cause of the rectocele, i.e., increased anal basal pressure, which should be treated. Consequently, anal basal pressure should be decreased, and not only anatomical correction of the anal canal should be applied. Therefore, the diagnostic process in patients suspected of rectocele should include not only MR defecography, which provides information about anatomical alterations, but also anorectal function tests, which provide quantitative outcomes regarding anal basal pressure. Also, comprehensive anamnesis involving questions about defecation habits, and symptoms associated with increased anal basal pressure, such as dyssynergic defecation and constipation, should be performed. This can help to recognize and further adequately treat the cause of the rectocele. This theory should be further investigated in a prospectively designed clinical trial, during which efficacy in terms of a decreased postoperative recurrence rate of rectocele would be investigated. The study described in **Chapter 3** illustrates our concept regarding rectocele development and indicates the importance of multidisciplinary cooperation between medical specialists, including gastroenterologists, radiologists, and surgeons. It also points out the relevance of using and combining different methods for obtaining a complete diagnostic view.

Table 1. Comparison of three theories about rectocele formation

	High anal sphincter pressure just before defecation proposed by us	High puborectal pressure during defecation (1-3)	Rectovaginal septum defect (4)
Rectocele position according to the presumption	Below or above the puborectal muscle	Only above the puborectal muscle	Below or above the puborectal muscle
Explains the high recurrence rate after resection	Yes	Yes	No

Despite almost unlimited diagnostic options, doctors' time nowadays is unfortunately limited, negatively influencing the time to interview a patient. Moreover, patients are ashamed to talk in detail about their defecatory problems. Consequently, the primary attention is given solely to this symptom, which patients report, which can also contribute to an incomplete view of the symptoms, suboptimal diagnosis, and treatment. Therefore, the DeFeC questionnaire, which comprehensively approaches a broad spectrum of symptoms, especially when taken off digitally, i.e., in a patient-friendly way, is of great value for doctors and patients. Questions included in this questionnaire not only allow identification of a bowel dysfunction according to validated scores and criteria but also indicate other co-existing bowel problems of which the patients are often unaware and thus do not report them to the doctor. Moreover, the DeFeC questionnaire contains questions about symptoms associated with possible causes of

these bowel dysfunctions. Therefore, we have translated the DeFeC questionnaire to Chinese and validated it for the Chinese population, as shown in **Chapter 4**. This step adds to better health care for Chinese patients. Notably, the translation and validation of the DeFeC questionnaire also meet the currently important need to standardize and unify the design of epidemiological studies. The need is urgent, as indicated by many studies presenting broadly ranging and thus ambiguous prevalence of defecation problems in different countries and populations. The inconsistent prevalence often results from other study designs and data collection methods. A standardized data collection will allow unbiased comparison between studies performed in China, the Netherlands, and countries where English is the leading language, as DeFeC is already available in three languages.

Of note, Hippocrates saw illness in the context of a person's whole body, not merely the affected part. Results described in **Chapter 5** resemble the philosophy of Hippocrates as we show that also defecatory problems should be diagnosed and treated in the context of a dysfunction of the whole anorectum, and not merely one symptom, for instance, just the one symptom, which was bothering a patient, and therefore reported to a doctor. **Chapter 5** shows that fecal incontinence can result from different defecation disorders, such as constipation or IBS, and should not be treated uniformly. We found that the co-occurrence of fecal incontinence and constipation or IBS is present even in the general population without organic diseases, which might influence the defecation function. We also 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. Based on these findings, we propose that the treatment of fecal incontinence should be based on a classification of fecal incontinence, which considers other co-occurring symptoms, such as constipation or IBS. The efficacy of such a treatment should be investigated in a follow-up study.

In addition to the maintenance of fecal continence, anorectal physiology also regulates the defecation process. It seems that there is nothing easier than going to the toilet, as the first evacuation of stool happens on average spontaneously within 24 hours after the birth of a child. For becoming fecal continent, toddlers are trained for months, but for defecation not. However, the high prevalence of troublesome defecation, i.e., constipation, as well as a high number of adults with dyssynergic defecation we found in the Chinese population, and which has also been reported in other populations (9)(**Chapter 6**) indicates that training for proper defecation habits and correct usage of the muscles of the pelvic floor would probably not be such a bad idea. Furthermore, we found that constipated patients frequently show a normal defecation frequency, i.e., no less than three times per week, and normal stool consistency, i.e., type 3-4, according to the Bristol stool chart (10). Thus, it is surprising that questions about the frequency of defecation and stool consistency belong to the first questions included in the anamnesis for constipation and that treatment targeting these symptoms is primarily applied without a broader investigation of other possible causes that could lead to constipation. This hinders the proper diagnosis and treatment of constipation. In **Chapter 6**, we also describe

these risk factors of constipation, which can help doctors give appropriate suggestions to constipated patients regarding lifestyle adjustments and pharmacological treatment. Interestingly, the current study found spicy food positively and strongly correlated with constipation. This is consistent with the literature (11, 12). This gives implications to relieving constipation by eating less spicy food, which is very easy to undertake without any extra expenses.

As mentioned above, dynamic MR defecography is used to evaluate anatomical parameters of the anorectum in patients with defecation disorders. This diagnostic procedure has been applied for several reasons. Firstly, dynamic MR defecography has got popular, as it is relatively easy to use and broadly available. Secondly, the anatomical parameters of the anorectum obtained with dynamic MR defecography seem relatively easy to interpret. Finally, it has been assumed that anatomical impairments in the pelvic region can indicate the cause of the underlying defecatory problems. Also, despite the dynamic MR defecography providing multiple parameters, it was unknown whether they reflect the anorectal pathophysiology and, thus, whether they detect the pathophysiological cause underlying specific defecation problems. Consequently, it was questionable whether the parameters were valuable when choosing the most optimal treatment. H- and M-lines, which are frequently determined by radiologists in patients undergoing dynamic MR defecography due to defecation problems reflect the anatomy of the pelvic floor (13). Elongated H- and M-line indicate the presence and severity of descending perineum, thus an anatomic alteration in the pelvic floor. In the study presented in **Chapter 7**, we show that the H- and M-line lengths correspond respectively to the severity of fecal incontinence and the severity of constipation (Table 2). With this study, we also show the complementary value of the dynamic MR defecography and anorectal manometry, where the first one can diagnose the anatomical alterations and the second technic can diagnose the pathophysiological cause, such as increased anal basal pressure or dyssynergic defecation often observed in constipated patients. However, as these anatomic changes detected with dynamic MR defecography are usually late-stage and irreversible without surgical intervention, we think that anorectal manometry should be the diagnostic tool of the first choice at the early stage, which allows for detecting early and potentially reversible symptoms in patients with defecation disorders. Unfortunately, despite being a gold standard for evaluating defecation disorders (14), anorectal manometry is not widely available in all hospitals (14). In addition, the interpretation of the manometry results can vary between different hospitals. Because the M line length during defecation is correlated with the constipation severity and the increased anal sphincter pressure during defecation, increased M line length might be indicating biofeedback therapy to help the anal sphincter to relax during defecation. The H line length during rest and squeezing is correlated with fecal incontinence severity but not with the anal sphincter pressure in the corresponding phase; this indicates that fecal incontinence at the end stage of constipation cannot efficiently be treated by improving the strength of the anal sphincter squeezing. Instead, constipation should be treated beforehand if fecal incontinence is to be treated. Proper diagnosis and

evaluation of defecation disorders with H and M line length can further help surgeons treat defecation disorders in a more personalized way.

Table 2. The application of the H and M line in evaluating the severity of defecation disorders

		H line	M line
Comparison	Definition	The distance between the inferior margin of the pubic symphysis and the posterior aspect of the anorectal junction (13).	The distance between the pubococcygeal line and the posterior aspect of the anorectal junction (13).
	Defecation disorder to be evaluated	Fecal incontinence	Constipation
	Relationship with the severity of defecation symptoms	Positive	Positive
	MR defecography phase to be utilized	Rest and squeezing	Defecation

Also, the study presented in **Chapter 8** confirms the diagnostic value of anorectal manometry in testing anal basal pressure in chronically constipated children who had been referred for treatment. Injections of botulinum toxin into the anal sphincter are prescribed to patients who did not respond to the first-line treatment and whose constipation does not result from organic reasons, such as Hirschsprung’s disease. The idea behind such treatment is that botulinum toxin can force relaxation of the anal sphincter and, in this way, enable defecation. The magnitude of anal sphincter relaxation can be quantified by testing anal basal pressure. Such evaluation of treatment efficacy with botulinum toxin does not belong to current standard procedures, as noticeably in literature where primarily symptomatic improvement has been reported. Although patients' self-perception regarding symptomatic improvement is essential, such outcomes, especially in pediatric patients, are often subjective, and the scientific value of such results can be questionable. Notably, not all patients report symptomatic improvement. Our findings in **Chapter 8** explain where the suboptimal efficacy of treatment involving botulinum toxin injections in chronically constipated children comes from. By monitoring the anal basal pressure before and after botulinum toxin injections, we found that the anal basal pressure must be sufficiently increased before the treatment to respond adequately. Specifically, we determined a cut-off point regarding the pre-injection anal basal pressure, and that is 70 mmHg, which should be used to select these patients who might profit from the botulinum toxin injection, i.e., whose anal basal pressure will decrease after the injection. This finding again illustrates that anorectal manometry should not only be utilized to analyze the physiological improvement after injection but also to determine the pre-treatment pathophysiological conditions. With the study described in Chapter 8, we contribute to the improved efficacy of botulinum toxin treatment in constipated patients. The cut-off value can also prevent patients with insufficiently increased pre-injection anal basal

pressure from unnecessary intervention, such as general anesthesia, which is required to inject botulinum toxin into the anal sphincter. Finally, our findings will prevent unnecessary financial costs in patients who cannot benefit from the botulinum toxin injection.

In summary, our findings in this thesis broaden our knowledge of the physiological mechanisms of various defecation disorders and their correlation with each other. This knowledge contributes to the optimization of diagnosis and treatment of defecation disorders by emphasizing the importance of, firstly, performing an objective diagnosis of pathophysiological causes that underlay the disorders and, secondly, treating the causes instead of symptoms only.

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