An evaluation of colorectal diseases: surgical aspects and new insights into the mechanisms of fecal continence
Jonker, Jara

DOI:
10.33612/diss.131938980

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:
2020

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the “Taverne” license. More information can be found on the University of Groningen website: https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment.

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
1

General introduction and aims of the thesis
Colorectal diseases cover a wide spectrum of dysfunctions in modern-day society irrespective of age, sex, or social status. They may be inborn, such as congenital anorectal malformations (CARMs), or they may appear later in life, such as ulcerative colitis. Patients suffering from colorectal diseases can experience symptoms including abdominal pain, rectal bleeding, constipation, or fecal incontinence. Some colorectal diseases can be treated conservatively while others are so severe that surgical intervention is required to save a patient’s life. Mild forms of CARM can be treated adequately with laxatives, while more severe CARMs require surgery within 48 hours after birth.\textsuperscript{1} At a later stage, corrective surgery of the patient’s abnormal anatomy is required, like repositioning the anal canal to enable the patient to defecate.\textsuperscript{2} Ulcerative colitis is another example of a colorectal disease that can be treated either conservatively or surgically depending on its severity. If patients do not, or do not longer, respond to medical treatment, surgery is required to resect the severely damaged colon.\textsuperscript{3, 4} For patients suffering from familial adenomatous polyposis, surgical resection of the colon is always required to prevent them from eventually developing colorectal carcinoma.\textsuperscript{5} If such surgery involves removal of the colon an end ileostomy is required. By constructing an ileal pouch that functions as a collection reservoir for feces, the ileostomy can be reversed, and this enables patients to defecate through the anus once again.\textsuperscript{6}

After surgical correction, patients usually expect optimal clinical outcomes. Clinicians too seek to provide the best improvement possible, which we will address in the last part of this thesis. Surgery may, however, turn out less than optimal, rendering some patients incontinent. Fecal incontinence could be an accidental side effect of rigorous surgical interventions, while at the same time these interventions are instrumental in saving patients’ lives. Put differently, even though surgical correction may cause fecal incontinence, it cannot be predicted beforehand which patients will suffer from fecal incontinence. Many factors are involved, all of which have not yet been revealed to date. To fully comprehend the pathophysiology of fecal incontinence it is, first and foremost, necessary to achieve a thorough understanding of its physiology. We address this issue in the first part of this thesis.

**Fecal Continence**

The colon is part of the large intestine and its main function is to absorb any remaining water, nutrients, and vitamins and to pass waste material into the rectum.\textsuperscript{7} The rectum functions as a collection reservoir for the storage of feces. Different mechanisms, regulated by the internal and external anal sphincter that surround the anal canal, control the feces reservoir and prevent untimely expulsion of feces. The internal anal sphincter is an extension of the circular smooth muscle of the rectal wall and is surrounded by the external anal sphincter (Figure 1). The latter generates anal pressure that prevents uncontrolled loss of stool.\textsuperscript{8, 9} In addition, the puborectal muscle, one of the muscles in the pelvic floor, forms a sling around the rectum. When it contracts it maintains anorectal angulation that prevents involuntary loss of feces.\textsuperscript{10, 11} When it relaxes the anorectal angle increases to facilitate defecation (Figure 2).
To date, the notion persists that the internal anal sphincter contracts involuntarily and that the external anal sphincter and the puborectal muscle can only contract voluntarily. Our research group, however, demonstrated that the external anal sphincter also contracts involuntarily. Involuntary contraction of this muscle is regulated by a spinal reflex known as the anal-external sphincter continence reflex (Figure 3). It maintains continence during most of the day and night. We observed patients who suffered functional impairments of the
continence mechanisms, who still remained continent. For example, we observed patients with severe sphincter defects who did not experience fecal incontinence. Similar observations are reported in the literature and point to the existence of additional mechanisms for fecal continence to date unknown.\textsuperscript{13, 14} We postulate that the puborectal muscle plays an important role in the fecal continence mechanisms, an issue we address in detail in this thesis.

Proper regulation of the fecal continence mechanisms enabled by the nervous system is required to ensure that feces remains in the rectum, the fecal collection reservoir. The pudendal nerve is a major nerve of the pelvic floor. Among others, it innervates the perineum, anus, external anal sphincter, and urethral sphincter.\textsuperscript{15} To date, there is no consensus concerning the question whether the puborectal muscle is also innervated by the pudendal nerve.\textsuperscript{16-19} The next step toward investigating the innervation of the puborectal muscle is reported in this thesis.

\textbf{Figure 3} \hspace{1em} The pathway of the anal-external sphincter continence reflex. 1) Feces in the rectum stimulates the stretch receptors, which in turn relax the internal anal sphincter. 2) Feces enters the anal canal and stimulates contact receptors in the anal mucosa. 3) This results in activation of the anal-external sphincter continence reflex. 4) The external anal sphincter contracts and prevents accidental loss of feces.

Fecal incontinence occurs when the above mentioned muscles do not function properly on account of anatomical abnormalities, impaired innervation, or damage to the rectum. It is a debilitating condition that significantly impairs patients’ quality of life. Its prevalence is reported to be around 8% in the normal population and varies from 2% to 20%. In nursing homes for the elderly it can be as high as 50%. Fecal incontinence is often multifactorial. One dysfunction will not necessarily lead to immediate incontinence because other mechanisms are able to compensate.

Obstetric trauma, which may cause damage to the anal sphincter, has often been considered a risk factor for fecal incontinence. No consensus, however, prevails in the literature regarding the contribution of sphincter trauma to fecal incontinence. Moreover, as already mentioned, we found patients with severe sphincter defects who were continent. Other risk factors for fecal incontinence are diseases relating to inadequate innervation, such as diabetes mellitus or multiple sclerosis. Fecal incontinence can also be associated with urinary incontinence and other anorectal problems, such as hemorrhoids or constipation. Stool consistency, in particular liquid stool or diarrhea, can dispose a person to becoming fecal incontinent. Figure 4 depicts seven different types of stool in accordance with the Bristol Stool Form Scale. Types 1 and 2 represent abnormal hard stool and types 6 and 7 represent abnormal liquid stool. Types 3 up to and including 5 are considered normal stool. In general, people suffer from liquid stool incontinence more often than from solid stool incontinence, with a prevalence of approximately 6% versus 1.5%. Although many researchers have attempted to explain the mechanisms underlying the difference between solid and liquid stool incontinence, no satisfactory explanation has been provided as yet. We make an effort to explain the difference in this thesis.

CLINICAL ASSESSMENT

As a result of the taboo surrounding fecal incontinence almost half the people who suffer from fecal incontinence do not discuss their problems with anyone; not with family or friends, nor with their physicians. It is, therefore, important for doctors to broach the subject during consultations, especially with patients at risk of fecal incontinence, like patients who have other anorectal problems or who suffer from diabetes. To decrease embarrassment on the part of the patients, their medical history can be recorded by means of a questionnaire.
In addition, a questionnaire helps to classify and objectify patients' fecal incontinence complaints. Several classification systems are available, each with their own merits and drawbacks. The Rome IV criteria, for example, define fecal continence as the *recurrent uncontrolled passage of fecal material for at least three months.*[^35][^36] This score can only be noted as a 'yes' or a 'no' for incontinence complaints. The Jorge-Wexner score also allows for estimating the severity of fecal incontinence (Table 1).[^37] A merit of using these scores is that it is quick and easy to complete. A drawback is that it does not cover all the different aspects of the pathophysiology of fecal incontinence. This shortcoming was overcome in our research group. We developed the Groningen Defecation and Fecal Continence Questionnaire (added as appendix) that although it takes longer to complete, it includes both the scores mentioned above. In addition, it contains questions about constipation and in so doing it covers all the different aspects of fecal incontinence.[^38] The Groningen DeFeC Questionnaire consists of 88 questions divided into nine categories. The first category consists of demographic

[^14]: Chapter 1
[^34]: JaraJonkers_BNW.indd   14
[^35]: 17/07/2020   09:57:01

Figure 4 | The Bristol Stool Form Scale. Seven types of stool consistencies ranging from hard stool to completely liquid stool. Types 3, 4, and 5 are considered normal stool. Distributed with the kind permission of Dr K. W. Heaton; formerly reader in Medicine at the University of Bristol. Reproduced as a service to the medical profession by Norgine Ltd. ©2017 Norgine group of companies.
questions. The second category deals with basic questions regarding defecation, such as stool form classified according to the Bristol Stool Scale and defecation frequency. The third category includes constipation-related questions. The first question in this category is on incomplete bowel emptying. In case of an affirmative response, questions about the complaints follow. The fourth category concerns diet, including water intake and eating habits, both of which are factors that also influence bowel function. In the fifth category, the focus is on fecal incontinence and the severity thereof that is frequency, pad use, and the burden on daily activities. The sixth category comprises questions about defecation urge and the ability to postpone defecation. Because urinary incontinence often occurs together with fecal incontinence and constipation, the questions in the seventh category deal with bladder function. The eighth category only applies to women and consists of obstetric questions, including types of delivery and complications during delivery. The ninth category includes questions about the patient’s abdominal medical history, such as surgery and other factors that could influence bowel function.

Besides recording the patient’s medical history, a physical examination is required to look for the possible causes of fecal incontinence. Abdominal palpation, perineal inspection, and digital rectal examination are part of the physical examination. Sensitivity and specificity of assessing the anal sphincter function digitally is, however, low and more physiological tests are required to analyze fecal incontinence in detail.39

**Table 1** | The Jorge-Wexner continence grading scale

<table>
<thead>
<tr>
<th>Type of incontinence</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Never</td>
</tr>
<tr>
<td>Solid</td>
<td>0</td>
</tr>
<tr>
<td>Liquid</td>
<td>0</td>
</tr>
<tr>
<td>Gas</td>
<td>0</td>
</tr>
<tr>
<td>Wears pad</td>
<td>0</td>
</tr>
<tr>
<td>Lifestyle alteration</td>
<td>0</td>
</tr>
</tbody>
</table>

0 = perfect, 20 = complete incontinence. Never = 0 (never); Rarely = < 1/month; Sometimes = <1/week, ≥1/month; Usually = <1/day, ≥1/week, Always = ≥1/day

**ANORECTAL MANOMETRY**

Anorectal manometry visualizes the underlying pathophysiology of fecal incontinence by measuring the pressures along the rectum and the anal canal created by anal sphincter contraction and the pelvic floor muscles. Changes in pressure can be registered during different physiological conditions, such as squeezing, coughing, or pushing. Pressure can also be measured at rest when the patient is relaxed and not performing any of the above mentioned actions. Based on the changes in pressure, anorectal features, such as anorectal sensations, anal sensitivity, rectal compliance, are visualized, as are the anorectal reflexes, thus allowing abnormalities to be detected.40,41 Skeptics of anorectal manometry consider it
outdated, while in fact the method has undergone continuous development. High resolution manometry was introduced in about 2007 and has been used increasingly to assess fecal problems.40 The difference between high resolution manometry and the previous version is the increased number of sensors and the smaller distance between the sensors.40, 42 Moreover, the registration is not represented by pressure lines. Rather, it is visualized graphically by different colors for different pressures so as to facilitate comparison between pressures.

Because the etiology of fecal incontinence is multifactorial, different anorectal features need to be examined when diagnosing its cause and this involves several tests. Different anorectal function tests are performed at our Anorectal Physiology Laboratory. For the studies in this thesis we use four different tests: the anorectal pressure test, the anal electrosensitivity test, the balloon retention test, and the rectal infusion test.41 During the anorectal pressure test the person tested, either a patient or a healthy subject, lies in the left lateral recumbent position. The test is performed with a catheter brought into the lower rectum and anal canal that is fitted with sensors every 8 mm and covers a total of 6.8 cm. Pressure at rest is first measured to establish a baseline and subsequently the person is asked to squeeze so we can measure the maximum voluntary pressure. The anal electrosensitivity test measures anal sensitivity by applying superficial anal electrical stimulation.43 A catheter with electrodes is used and stimulated from 1 mA to 20 mA and we record the threshold. This test provides information about the sensory condition of the anal canal. To date, it was known to be innervated by the pudendal nerve, thus providing information about the sensory condition of this nerve. The third test we use is the balloon retention test to measure involuntary contractions of the external anal sphincter.41 During this test the person tested sits upright on a commode while a balloon inserted into the rectum is gradually filled with water of body temperature (1mL/second). The person is instructed to retain the balloon for as long as possible while we measure the pressures along the anal canal. We use this test to estimate rectal volumes and rectal compliance and to determine the presence of the anal-external sphincter continence reflex.43 This test mimics solid stool because the water remains in the rectal balloon. The fourth test is the rectal infusion test. The person tested sits upright on a commode while water of body temperature is injected directly into rectum at a speed of 1mL/second. The test is completed if 1000mL water has been injected. During the test the pressures along the anal canal can be measured. This test mimics liquid stool because the water is injected directly into the rectum.44 It is part of standard care procedures at our laboratory, but it is not always used elsewhere. Although variations of this test are described, like using mashed potato to mimic mild diarrhea or soft stool (Bristol Stool Scores 5 or 6, Figure 4), we only use water, without any thickening agent, in our laboratory.
COLORECTAL DISEASES

Congenital anorectal malformations
Sometimes, fecal problems can occur as a result of congenital abnormalities of the anorectal anatomy. Congenital anorectal malformations (CARMs) are examples of such deviations from the normal anatomy of the anorectum. Originally, a male preponderance for CARMs was reported in the literature, but subsequently other studies reported an equal distribution among the sexes.45-49 There are different forms of CARM and four examples are illustrated in Figure 5. Some occur in one sex only, while others can be present in both sexes.2 Naturally, patients with the most severe forms, such as cloaca, are unable to expel feces normally and are prone to bladder infections or abdominal infections. Such patients require a colostomy within 48 hours after birth.1 Subsequently, at approximately the age of three to six months, surgical correction of CARMs can take place, which includes replacement of the anal canal in such a way that it is surrounded by the external anal sphincter. On account of the fact that there are different forms of CARM, there are also different surgical procedures.2 In 1982, and currently still in use, deVries and Peña introduced posterior sagittal anorectoplasty, a surgical procedure applicable to all the forms of CARM irrespective of severity.50 About ten years later, Okada and colleagues introduced a less invasive approach, anterior sagittal anorectal plasty.51, 52 The latter procedure is suitable only for mild forms of CARM. The idea behind both these surgical procedures is that the surgeon dissects in the median sagittal plane. This causes less damage to the neurovascular structures because the nerves and vascularization run from lateral to medial.53 In this way, the pudendal nerve is not damaged and voluntary contractions remain adequate. The exact neural pathway of the anal–external sphincter continence reflex is unknown and it thus remains unclear whether this fecal continence reflex is inadvertently damaged during corrective surgery for CARMs.

Congenital anorectal malformations and congenital heart defects
If patients with CARMs undergo corrective surgery they need to be anesthetized. CARMs can occur together with congenital heart defects and this can be part of the VACTERL association (vertebral defects, anal atresia, cardiac defects, trachea-esophageal fistula, renal anomalies, and limb abnormalities).54 Heart defects can cause complications if the anesthesiologist is unaware of such problems prior to surgery.55-58 We also know that patients with congenital heart defects who undergo non-cardiac surgery have an increased risk of suffering cardiac arrest and increased mortality.59-62 The literature reports a prevalence of between 9% and 37% for congenital heart defects in patients with CARMs, varying from minor defects like a small atrial septum defect to major defects like tetralogy of Fallot.54, 56-58 Previous reports stated that children with severe forms of CARM are at greater risk of major congenital hearts defects.54, 57 In our clinical practice, however, we observed an equal distribution, an issue that we address in this thesis.
Figure 5 | Different forms of congenital anorectal malformations in male and female patients. A) Recto-perineal fistula in a female patient. B) Recto-vestibular fistula in a female patient. The fistula ends between the major labia. C) Cloaca malformation in which the urethra, the vagina, and the rectum have one and the same opening. D) Rectoprostatic fistula in a male patient. The meconium leaves the body through the urethra. Adapted from Anorectal malformations, by Marc A. Levitt and Alberto Peña, Orphanet Journal of Rare Disorders, July 2007.

Fecal continence in patients with congenital anorectal malformations

Even though the condition of patients with CARMs can be improved by surgery, they still have more fecal problems in comparison to healthy peers. They can suffer from constipation, increased stool frequency, and abdominal pain or they may experience different forms of fecal incontinence, including solid, liquid, or flatus incontinence, or soiling.\textsuperscript{63–65} Constipation is mainly an issue in patients with mild CARMs that can for example be caused by dyssynergic defecation. Dyssynergic defecation is defined as paradoxical contractions of the anal sphincter and/or pelvic floor muscles, which occur while one is trying to defecate.\textsuperscript{66} Additionally, patients with CARMs can suffer from fecal incontinence, up to as much as 60%, and it remains a challenge to predict which patients will suffer from fecal incontinence.\textsuperscript{67} To date, the only true predictor is the form of CARM; patients with mild anorectal malformations have better fecal continence outcomes in comparison to patients with severe CARMs.\textsuperscript{67,68} No consensus exists regarding the optimal treatment of patients with CARMs with fecal incontinence.\textsuperscript{69–71}
Proctocolectomy with ileal pouch-anal anastomosis
In approximately 15% of the patients suffering from ulcerative colitis, a total colectomy, the removal of the severely affected colon, is required because they do not respond to medical treatment. In patients with familial adenomatous polyposis, a colectomy is also required because such polyps could eventually lead to colorectal cancer around the age of 39 years. A consequence of colectomy is that patients require an ileostomy. This may be experienced as inconvenient and some people find it embarrassing. To remove the ileostomy and to expel the feces through the anus once again, Parks and Nicholls described a proctocolectomy with ileal pouch-anal anastomosis (IPAA) in 1978. During this procedure, a pouch reservoir of the ileum is created to store the feces. It is the surgical procedure of choice for patients with ulcerative colitis who do not respond to medical treatment as well as for patients with familial adenomatous polyposis.

Although proctocolectomy with IPAA seems a fair solution, patients do not function the same way as people with a healthy colon. The main function of the colon is to extract any remaining water from the stool and to solidify it, hence patients who underwent proctocolectomy with IPAA have more watery stool than people with a colon. In addition, stool frequency is higher, around six times a day, compared to once every two days to twice a day in healthy individuals. Sometimes stool frequency can be even higher - up to twelve times a day. This can cause daily recurring problems regarding any activities outside the home and for leading a normal social life. Nevertheless, many patients have accepted living with an IPAA and correspondingly experience good quality of life.

Surgical characteristics of proctocolectomy with ileal pouch-anal anastomosis
Different types of ileal pouches exist for proctocolectomy with IPAA (Figure 6). There are J-, S-, or W- pouches, depending on the number of loops the surgeon creates of the ileum, and they can be associated with different outcomes regarding fecal continence. The ileal pouch needs to be attached to the distal anorectum. This can be done in two ways. One option is mucosectomy of the rectal tissue followed by a hand-sewn anastomosis at the dentate line (Figure 7A). The other option is a stapled anastomosis whereby some rectal cuff is retained (Figure 7B). The idea behind mucosectomy is to remove all remaining mucosa because patients with familial adenomatous polyposis can still form polyps from remaining mucosa in the last section of the rectum. In patients with ulcerative colitis and severe inflammation in the last section of the rectum, it may be preferable to remove that mucosa too. During the last decades, however, stapled anastomoses are increasingly performed. A stapled anastomosis is quicker and results in better fecal continence outcomes, possibly thanks to better preservation of the anal canal and/or the anal transition zone. To date, the height of the IPAA has never been fully inventoried with regard to functional outcome.

The proctocolectomy with IPAA can be performed in different stage procedures, in a one-stage, a two-stage and a three-stage procedure. During the one-stage procedure, all
aspects of the surgical procedure are performed during one operation. Two options exist for the two-stage procedure, one with and one without a diverting ileostomy. In case of the option with the diverting ileostomy, proctocolectomy is first performed and IPAA is created with a diverting ileostomy. At a later stage the ileostomy is reversed and continuity restored. During the two-stage procedure without a diverting ileostomy, colectomy is first performed and an end ileostomy created. At a later stage the IPAA is created and continuity is restored. During the three-stage procedure, first colectomy with end ileostomy is performed, during the second stage the IPAA and a diverting ileostomy are created, and during the third stage the diverting ileostomy is reversed and continuity is restored. To date, no consensus exists in the literature as to which stage procedure is the most optimal option as far as post-operative outcomes are concerned, and whether a diverting ileostomy is actually required.89-91

Figure 6  |  The J-, W- and S-pouches, depending on the number of loops the surgeon creates of the ileum. Adapted from *Judging the J Pouch: a pictorial review*, by Sheedy et al., *Abdominal Radiology (NY)*, March 2019.
Figure 7  | Anastomotic techniques of the ileal pouch-anal anastomosis. A) Mucosectomy followed by a hand-sewn anastomosis at the dentate line. B) Stapled anastomosis with a rectal cuff remained, thus proximal of the dentate line.

Adapted from Judging the J Pouch: a pictorial review, by Sheedy et al., Abdominal Radiology (NY), March 2019.

AIMS OF THE THESIS
We postulate that an additional mechanism exists that controls fecal continence. In addition, to improve the diagnostics and treatment strategies for patients who suffer from incontinence, a better understanding of the mechanisms underlying this disorder is crucial.
The first part of the thesis focuses on the mechanisms that control fecal continence. Previously, our research group described the involuntary contractions of the external anal sphincter that are regulated by the anal-external sphincter continence reflex. In Chapter 2, we present a study on 23 healthy subjects in which we investigated fecal continence mechanisms in detail; specifically the question whether involuntary contractions of the puborectal muscle occur. In this study we proposed a to date unknown regulatory mechanism for fecal continence: the puborectal continence reflex. This reflex regulates fecal continence by mediating involuntary contractions of the puborectal muscle in addition to the known voluntary contractions. Then, because fecal continence is facilitated by the cooperation of different mechanisms, and our research group has described the anal-external sphincter continence reflex earlier, we aimed to investigate in detail the characteristics of both fecal continence reflexes on solid as well as liquid stool in healthy subjects. This study is presented in Chapter 3. To date, no explanation is available as to why there is a difference between the prevalence of liquid and solid stool. We attempted to explain this issue with the study mentioned above. To investigate the regulation of the puborectal continence reflex in more detail, specifically to find out which nerves regulate these involuntary contractions, we present the study in Chapter 4. In this study, we aimed to investigate whether the involuntary contractions of the puborectal muscle are regulated by the pudendal nerve. We included all patients who had undergone anorectal function tests in our hospital and analyzed whether the condition of the pudendal nerve was associated with voluntary and involuntary contractions of the puborectal muscle.

In the second part of the thesis we investigate clinical and fecal continence outcomes in patients with different colorectal diseases, including patients with congenital anorectal malformations (CARMs) as well as patients who underwent proctocolectomy with ileal pouch-anal anastomosis (IPAA). CARM is a rare disorder with a male preponderance according to the literature. In Chapter 5, however, we aim to confirm our clinical observation that the distribution of CARMs is equally distributed between the sexes. We also analyzed the form and severity of CARMs in relation to patients’ sex. CARMs can occur together with congenital heart defects. Nevertheless, there is no consensus regarding the prevalence of these heart defects in patients with CARMs, nor whether they need additional examination for the heart defects. With this aim in mind we performed the study we present in Chapter 6. Fecal incontinence too occurs more often in patients with CARMs in comparison to healthy controls. This could be a consequence of surgery, which changes the anatomy and the innervation, and might therefore impair the functions of certain pelvic floor muscles. Therefore, in Chapter 7, we present our investigation of the cohort of patients with CARMs who underwent anorectal function tests in our laboratory. Our aim was to find out whether anal-external sphincter continence reflex and the puborectal continence reflex were present in these patients and whether this had an influence on their fecal continence outcomes. In other patients with colorectal diseases, fecal incontinence can be a major issue. This leads us to Chapter 8 in which we present our investigation of the association between several surgical characteristics of proctocolectomy with IPAA and fecal continence outcomes, and combining these results with patients’ quality of life.
REFERENCES

Fecal continence mechanisms