

Summary

As mentioned in part I, the thesis covers many common proctology dilemmas in clinical practice. Anorectal disorders are often difficult to treat. Clinician should recognize to implement the most cost-effective evaluation and treatment. Anorectal physiology is complex. It involves the pelvic floor muscles, motor and sensory neural pathways and is intimately related to the colon physiology.

Fecal incontinence

Fecal incontinence is defined as uncontrolled passage of fecal material. In **chapter 2** we comprehensively examined the anorectal function in patients with fecal incontinence and compared these findings to patients without fecal incontinence. Incontinent and continent patients showed significant differences, but had a substantial overlap in anorectal manometry and anal endosonography results, which supported the multi-causality of fecal incontinence.

The risk factors that were evaluated in the study were appropriately selected as they usefully predict the risk of fecal incontinence. The statistical model showed which risk factor was relatively more important. The predictors in women were age, stool consistency, anal pressures, rectal capacity, and internal and external sphincter defects. The area under the ROC-curve was 0.84 ($P < 0.001$, 95%CI: 0.80-0.87). Using a cut-off point of 0.4, fecal incontinence was predicted with sensitivity, specificity, positive and negative predictive values of 86%, 68%, 74% and 82% respectively. The simplified model was practical and might be useful in counselling patients about their expected outcome after stoma closure.

Since there is an overlap in anorectal manometry and endosonography findings between incontinent and continent patients and little correlation between these tests, it is justifiable to question their utility in the routine work-up of incontinent patients. In particular as the treatment options for fecal incontinence are limited.

Assessment should begin with a thorough clinical work-up. A detailed medical history and physical examination with a digital examination are mandatory. In general, the etiology of fecal incontinence becomes obvious. Patients with diarrhea or proctitis need further evaluation and targeted treatment. Following this, conservative measures should be applied; including regulation of bowel habit with bulking agents to produce a predictable pattern may help to avoid the need for defecation at inconvenient times. If there is no improvement, the next option is physiotherapy or biofeedback with or without the use of electro-stimulation. If the patient remains incontinent after conservative treatment, further investigation by anal endosonography to exclude an anal sphincter defect would be appropriate. If a significant sphincter defect is demonstrated, the patient can be referred for surgical correction.

In **chapter 3** we showed that patients with large sphincter defects tended to have lower MBP ($P=0.09$) and shorter SL ($P=0.07$) than patients without sphincter defects, but anorectal manometry could not differentiate between patients with and without defects, therefore anal manometry is not routinely recommended in the initial evaluation of fecal incontinence. Anorectal manometry is also indicated when other surgical therapies are being considered, such as sacral nerve stimulation, gracilis plasty and artificial bowel sphincter creation.

In **chapter 4** we evaluated the efficacy and safety of a potential treatment of fecal incontinence named SECCA. The SECCA procedure provides delivery of temperature-controlled radiofrequency energy in the anal canal. It is an ambulatory procedure and can be performed using conscious sedation, which avoids the complications associated with general anaesthesia and prolonged hospitalization. In the study we included 31 patients who had failed full conservative management for fecal incontinence. The patients were followed up for 3 years. Unfortunately, the far minority of patients reported a clinically significant response. The Vaizey score of all patients was 18 (SD 3), 14 (SD 4), 14 (SD 4) and 15 (SD 4), at baseline, 6 months and 1 and 3 years. Three years after the SECCA procedure, two patients had maintained a $\geq 50\%$ decrease in Vaizey score.

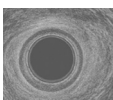
Constipation

Chronic constipation is a common disorder. Patients are usually referred for anorectal testing, because they have not responded to lifestyle measures and laxatives. While anorectal tests are necessary to diagnose defecatory disorders, recent studies highlight the utility of a careful digital rectal examination. In chapter 5 we investigate the diagnostic potential of anorectal testing in women with constipation in order to identify treatable conditions. In the study 113 women were referred and classified as idiopathic constipation (n=100), neurological disorder (n=8) and others (n=5). Of the 100 women with idiopathic constipation, clinical examination identified 25 (25%) with hypertonia of the pelvic floor (dyssynergic pelvic floor) and 15 (15%) with a rectocele. Thus, on clinical examination in 40% of women with idiopathic constipation potentially treatable conditions were found, which emphasize the importance of a careful clinical examination. In the current financial climate, with cut-backs in healthcare spending, the judicious use of technology is an important issue. Additional testing should be reserved for selected cases with constipation since childhood or patients in whom a (sub)total colectomy is being considered.

The initial management of chronic idiopathic constipation includes behaviour modification and dietary changes. For patients who do not respond to this management, laxatives represent an alternative therapy. A variety of laxatives are available for treating constipation: bulk forming, osmotic and stimulant laxatives. Osmotic laxatives, particularly polyethylene glycol (PEG) preparations are trend setting in the constipation market. PEG preparations are relatively safe, inexpensive, widely used and are even better than lactulose in improving stool frequency and consistency. In **chapter 6** three commonly used PEG 3350 preparations, often prescribed for chronic constipation, *Molaxole*[®], *Movicol*[®], and *Laxtra Orange*[®] were compared in taste and the preference was evaluated. It was a randomized, double-blind study, which involved 100 volunteers. We showed that the orange flavor of *Laxtra Orange*[®] was significantly better tasting than the lemon flavor of *Molaxole*[®] and the lime and lemon flavor of *Movicol*[®].

Perianal complaints in patients with inflammatory bowel disease

Perianal complaints and lesions are an important clinical feature of Crohn's disease and have been described to occur in a wide range of 25-80% of patients. Less is known about



the correlation between perianal lesions and ulcerative colitis.

Fecal incontinence is one of the main anorectal complaints of patients with inflammatory bowel disease (IBD). Besides attributable to diarrhea, this is often due to damage of the anal sphincter caused by perianal fistulas, anal fibrosis or surgery. Furthermore, fecal incontinence can be caused by proctitis due to a reduced rectal capacity and in patients with ileal pouch anal anastomosis. The capacity and distensibility of the pouch and the efficiency of the pouch evacuation plays a role in continence. Soiling can be caused by fistula's as well as damage to the sphincter. Pain can be due to abscesses and fissures. These burdensome clinical features of (peri)anal disease all contribute to a sizeably decrease of the overall quality of life.

In **chapter 7** we described the long-term course of anorectal complaints and function in a single centre cohort patients suffering from IBD with perianal lesions. After 14 years follow-up of IBD patients with previous anorectal complaints, approximately more than half of the patients still have mild complaints. Even the 58% patients with a deviating stoma have persisting anorectal complaints. In 25% patients, an abnormal anorectal function was found at baseline, which unfortunately persisted in the long run, negatively influencing patients' quality of life.

Perianal complaints in women after third-degree obstetric anal sphincter injury

Third-degree obstetric anal sphincter injury (OASI) is a vaginal tear with clinical disruption of the perineum with total separation of the anal sphincters, with or without a breach of the anal epithelium. Fecal incontinence is a frequent problem after childbirth. After delivery, some improvement of complaints can be expected in the first months. This is due to partial recovery of the pelvic floor muscles and pudendal nerve. However, many women will (again) develop complaints of fecal incontinence later in life attributable to OASI, aging, sphincter atrophy, or subsequent deliveries with concomitant nerve damage. Sexual complaints are associated with anal sphincter injury as well.

In **chapter 8** we evaluated clinical symptoms and anorectal function in women 5 years after they had undergone anal sphincteroplasty for third-degree OASI. Prevalence of fecal incontinence was 63% flatus, 50% liquid stool, and 20% solid stool. Sexual dysfunction, including sexual arousal, orgasm, satisfaction or pain, was present in 59%. Follow-up after third-degree OASI suggests poor anorectal and sexual function. Therefore, special attention should be paid to these women in order to mitigate these symptoms later in life.

Hemorrhoids

Hemorrhoids are the most prevalent anorectal disorder. Of all the non-surgical procedures, rubber bandligation (RBL) seems to be the preferred first-line treatment for internal hemorrhoids. Anal pain is a well-known sequel of RBL. In those situations, Sitz baths, mild analgesics and stool softeners are indicated. Unfortunately, the efficacy of those methods to alleviate pain is disappointing. In **chapter 9** we evaluated a special device, the anal cooler, in the relief of pain following RBL. The anal cooler which can be cooled in the freezer, is a cylindrical-shaped plastic device containing a mixture of glycols and has a minimum

temperature of 4 Celsius degree. In the study, 54% of the patients had a VAS-score > 6 with 55% requiring oral analgesics. The anal cooler relieved anal pain in 25% of the patients who actually used it, therefore may be worthwhile trying the anal cooler.

Future Perspective

Anorectal manometry and anal endosonography are the most widely performed test for the assessment of anal sphincter function and anorectal co-ordination. Its primary value is in fecal incontinence and constipation. There have been many developments.

Traditionally, manometry has been performed using solid-state or water-perfused catheters with a limited number of recording channels. A relatively new method, high-resolution anorectal manometry (HRAM) uses a catheter with 12 micro transducers, each of which measures circumferential pressure by means of a unidirectional pressure sensor embedded with silicone gel. Ten sensors are spaced at 6-mm intervals along the anal canal. The proximal sensor is embedded in a rectal balloon and the most distal is used as an external reference (MMS, Enschede, the Netherlands).^[1]

Another newer method which has even more sensors is high definition 3-D anorectal pressure topography. It has 256 pressure sensors that are arranged in 16 rows with each row having 16 circumferentially oriented sensors. The larger number of sensors provides more pressure recordings which can more clearly display pressures with minimal movement artefacts (Manoview™, Sierra Scientific Instruments., Los Angeles, Ca, USA).^[2]

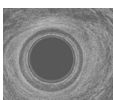
Besides a more precise measurement, the high resolution methods has been considered more easy to perform, because the conventional manometry requires placement of the recording sensors more precisely within the anal sphincter, as catheter movement with anorectal maneuvers could confound the values. Moreover, the high resolution methods use a computerized display systems with color-coded contour plots which allow intuitive visual interpretation. Finally, it has been suggested that high-resolution methods lead to shorter procedure times.^[3]

(3D) HRAM correlates well with the results obtained using a the traditional manometry catheters and provides reproducible topographic assessment of anorectal motor and sensory function.^[3,4]

Three dimensional anal endosonography is the gold standard in the morphologic evaluation of anal sphincter defects, but high resolution anorectal manometry used in combination may offer an extra dimension through functional evaluation of the sphincter. For instance, patients with perianal fistulas (3D) HRAM can be useful in selecting patients for the type of surgery and the risk of postoperative fecal incontinence.

However, is the (3D) HRAM is more expensive and fragile than the traditional technique. The (3D) HRAM probe is approximately twice the diameter and rigid and does not conform to the anorectal angle. Furthermore, some have argued that their utility may be similar but not clinically superior to conventional water perfused manometry.

New International Guidelines are being developed for standardisation of anal manometry, where the HRAM is going to be the standard because it provides so much more



information. (*Ascona II Advances in Clinical Measurement of Gastrointestinal Motility and Function, 19-24 April 2015, Ascona, Switzerland*).

Clinician should recognize to implement the most cost-effective evaluation and treatment. New methods need to be critically evaluated relative to reimbursements prior to implementing such systems into routine clinical practice. More prospective studies are needed to confirm the clinical utility in pelvic floor disorders.

References

1. Carrington EV, Brokjaer A, Craven H, Zarate N, Horrocks EJ, Palit S, Jackson W, Duthie GS, Knowles CH, Lunniss PJ, Scott SM. Traditional measures of normal anal sphincter function using high-resolution anorectal manometry (HRAM) in 115 healthy volunteers. *Neurogastroenterol Motil.* 2014 May;26(5):625-35.
2. Benezech A, Bouvier M, Grimaud JC, Baumstarck K, Vitton V. Three-dimensional high-resolution anorectal manometry and diagnosis of excessive perineal descent: a comparative pilot study with defaecography. *Colorectal Dis.* 2014 May;16(5):O170-5.
3. Kang HR, Lee JE, Lee JS, Lee TH, Hong SJ, Kim JO, Jeon SR, Kim HG. Comparison of High-resolution Anorectal Manometry With Water-perfused Anorectal Manometry. *J Neurogastroenterol Motil.* 2015 Jan 1;21(1):126-32.
4. Coss-Adame E, Rao SS, Valestin J, Ali-Azamar A, Remes-Troche JM. Accuracy and Reproducibility of High-definition Anorectal Manometry and Pressure Topography Analyses in Healthy Subjects. *Clin Gastroenterol Hepatol.* 2015 Jan 20. pii: S1542-3565(15)00041-5.

