

Aspects of the primary assessment and management of anal incontinence

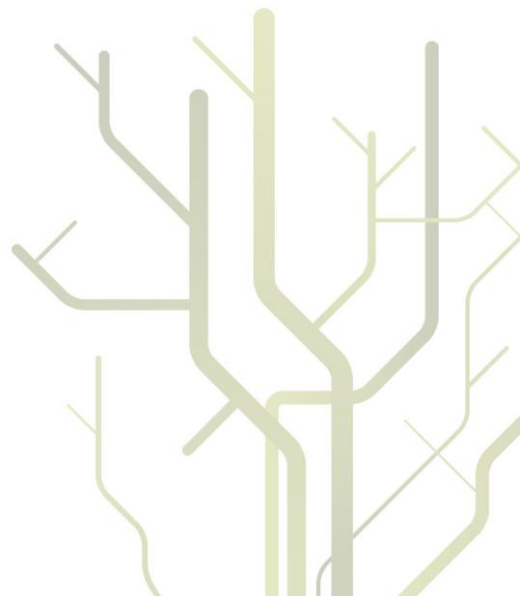
Evaluation of a new treatment



Trond Dehli

A dissertation for the degree of
Philosophiae Doctor

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2. List of papers

1. Norderval S, Dehli T, Vonen B. Three-dimensional endoanal ultrasonography: intraobserver and interobserver agreement using scoring systems for classification of anal sphincter defects. *Ultrasound Obstet Gynecol.* 2009; 33 (3): 337-43.
2. Dehli T, Martinussen M, Mevik K, Stordahl A, Sahlin Y, Lindsetmo RO, Vonen B. Translation and validation of the Norwegian version of the fecal incontinence quality-of-life scale. *Scand J Surg.* 2011; 100 (3): 190-5.
3. Dehli T, Stordahl A, Vatten LJ, Romundstad PR, Sahlin Y, Lindsetmo RO, Vonen B. Sphincter training with biofeedback or anal injections of dextranomer in hyaluronic acid for treatment of anal incontinence: a randomised, controlled trial. *Scand J Gastroenterol.* 2013 Jan 8. [Epub ahead of print]

3. Introduction

After birth, there is an increasing control over our muscles and movements as we grow older. It takes about one year from birth to learn how to walk. At the age of three we start to gain control over urinary output and bowel movements, suggesting that this might be more difficult than to walk. Later in life, some women lose control over their bowel movements and leak, often due to a rupture in their anal sphincter during delivery.

Leakage of gas and stool often has a great impact on the quality of life for the affected patients, influencing both their professional life and personal life. The fear of other people smelling their stool is often prominent. The research here presented is a small contribution in order to improve the first line assessment and management of anal incontinent patients.

4. Background

Definition of anal incontinence

In scientific reports, the most often used definition of anal incontinence is “anal incontinence is the involuntary leakage of stool and gas”. Urge is sometimes included in the definition, as “loss of ability to defer defecation until a socially acceptable time”. Some reports do not present a definition of anal or fecal incontinence, even if they present therapy for the condition¹.

Some other conditions have features in common with anal incontinence and can be confused with incontinence. Perianal skin tags are remnants from external hemorrhoids. These might impair personal hygiene, as small samples of stool can be retained around them despite normal personal hygiene. Skin tags can therefore lead to skin soreness around the anus. Anal incontinence in the presence of skin tags might increase the skin problem. Removing the skin tags is a simple surgical procedure that can be helpful for both incontinent and continent patients.

Soiling is commonly defined as minor incontinence² and can be described as the discharge of small amounts of brown mucus, which stains underwear or pads. It mainly affects middle-aged men, who often use toilet paper in their underpants as a way of coping. Traditional treatment has been aimed at drying the area to reduce mucus formation. There is no clear consensus in the distinction between soiling and incontinence, but soiling is usually not included in the anal incontinence definition.

Urge, as described above, does not have a specific time limit coupled to it. St. Mark's score define urge incontinence as an inability to defer defecation for 15 minutes³.

Several symptom-scores assess anal incontinence³, but so far these have not been used to define anal incontinence. In several of these, it is plausible that normal, continent people do not score 0. If you involuntarily let out gas once in one month, it gives a score of 1. If you do it once a week, you score even higher. There is no point limit in the symptoms scores to divide between what is considered as incontinence and what is considered within normal range.

A recent study describes fecal incontinence as the involuntary leakage of feces, and anal incontinence as involuntary leakage of gas and feces⁴.

A viral gastroenteritis could in most people lead to several occasions of stool and gas leakage, and a moderate to high score of incontinence, but episodes like this are not considered as incontinence. In epidemiological publications with postal questionnaires, the questions on anal incontinence vary, from simple questions like "Have you experienced uncontrolled leakage of stool" to the similar questions including frequency as well^{5,6}. To my knowledge, no epidemiological publication has used a symptom score for the grading of the severity, but some take into consideration the frequency of incontinence^{4,6}.

In the International classification of diseases, ICD-10, anal incontinence has been placed in the R-chapter, under symptoms, sign, abnormal clinical and laboratory findings, not classified elsewhere⁷. "R15 Involuntary defecation" does not have an explanatory text following it, implying a lack of a clear definition.

In conclusion regarding the definition of anal incontinence, it seems to be consensus in reports that it constitutes the involuntary leakage of stool and gas. However, several questions remain;

- How much leakage is required to be defined as incontinence?
- What frequency of leakage is required to be defined as incontinence?
- Should urge be included in the definition of anal incontinence (or maybe defined as a separate condition)?
- If urge is included, what is the time limit of urge?
- Should soiling be included?
- Should lifestyle or quality of life be part of the definition?

The differences in the definition of anal incontinence have several implications for research. The study population will vary with the definition, which makes it difficult to compare different studies. This applies especially to epidemiological studies, which might overestimate the incidence and prevalence of incontinence. It might also have clinical consequences with both over- and under-treatment according to what the local center define as incontinence. Studies on assessment of treatment might be difficult to compare, due to variations in inclusion criteria and outcome parameters.

When trying to define anal incontinence, there are at least two factors to assess; type of leakage (gas or stool) and frequency of leakage. There seem to be a tendency among people to accept gas leakage several times a week, and they seek help first when there is daily leakage. Leakage of stool is less tolerated, and people seek help even with leakage of stool once or twice a month. There should also be room for a certain range of normal variance before leakage is considered pathological.

With the experience from patients in the randomized trial presented in this thesis (paper 3), I would suggest that the definition of anal incontinence uses the St. Mark's score, and that the definition of incontinence requires at least four points for gas leakage (gas leakage once a day or more) or two points for stool leakage (leakage of loose or solid stool once a week or more).

There is also a need to assess the severity of incontinence, for instance in mild, moderate and severe incontinence. The use of St. Mark's score (or a different symptom score) could serve this purpose also, letting the sum of points define the grading of severity. A consensus in both definition and grading of severity would improve many aspects in both management and research on this condition.

Epidemiology

The incidence and prevalence of anal incontinence vary with definitions and between populations studied. The prevalence varies from 2 to 18 % for people living at home, for patients living in institutions the prevalence is higher.

A Norwegian study reports that in a population of women with a repaired anal sphincter tear after vaginal delivery, as many as 45 % had persisting anal incontinence⁸. With approximately 60.000 births in Norway pr year, and 1.5 % sphincter tears, a conservative estimate is approximately 400 new patients pr year with perineal rupture at birth.

A French population survey on defecation disorders reveals a gas leakage (defined as a yes answer to the following question: "During the previous 12-month period, have you ever experienced an uncontrolled leakage of gas?") in 40 % of the people, and fecal leakage (defined as a yes answer to the following question: "During the previous 12-month period, have you ever experienced an uncontrolled leakage of stool?") in 17 %. The survey was done among people >15 years living at home⁵.

In a similar survey from Great Britain among people <40 years living at home or in a primary care facility, a prevalence of fecal incontinence of 3.3 % was observed. Major fecal incontinence was defined as "*soiling* of underwear, outer clothing, furnishing, or bedding several times a month or more often." Minor incontinence was defined as "*staining* of underwear several times a month or more often." There was no difference between the sexes⁶.

A Swiss survey among women in the community and women seeking medical help in obstetrics and gynecology outpatient clinics, showed a prevalence of anal incontinence of 4.4 % in the general population⁹.

A literature review on the prevalence of incontinence in the community showed that the prevalence of anal incontinence (including flatus incontinence) varied from 2 to 24 percent, and the prevalence of fecal incontinence (excluding flatus incontinence) varied from 0.4 to 18 percent, summing up the results from 16 studies¹⁰.

A recent Norwegian study among women >30 years in a Norwegian county reported incontinence for stool in 3.0 %, and incontinence for gas 19.1 %⁴. They used questions similar to the St. Marks score to assess incontinence for stool and gas: "Have you been experiencing involuntary leakage of stool from the bowels in the last month?" and "Have you been experiencing involuntary leakage of gas from the bowels in the last month?" Both questions could be answered with one of the three alternatives: Never/rare, every week or every day.

The prevalence in institutions is high. Most papers report a prevalence of 50 % for patients in nursing homes^{11,12}. Immobility and dementia are risk factors for incontinence in this part of the population; both factors might disable the patients from going to the toilet on their own and therefore increase incontinence.

Clinical series often report female patients, with focus on child delivery and sphincter injuries. This might give the impression that female patients dominate within this condition. However, the epidemiological studies mentioned, show no clear differences between the sexes^{5,6,10}.

The latest Norwegian study from 2012, reporting prevalence only in women, shows a weaker correlation between fecal incontinence and childbirths than expected, indicating that other causes are plausible. The same study indicates a strong relationship between anal incontinence and the symptoms urge and diarrhea, suggesting that the gastrointestinal tract might contribute strongly to incontinence⁴.

Still, more than 90 % of patients in our incontinence clinic are female, and we believe this reflects a real incidence difference between the sexes. It is difficult to imagine that men tolerate anal incontinence any better than women; we think men would to the same extent as women seek help if they had anal incontinence. Also, according to some of the epidemiological studies here mentioned, almost 20 % of the population is incontinent. It is difficult to believe that one person in five has pathological leakage; it is simply too many.

The difference between epidemiological and clinical data is more likely caused by differences in the definition of anal incontinence (ref. section 2.2), and hence, the definitions in epidemiological studies might include too many patients. Epidemiological studies often have one or only a few questions to assess if there is incontinence, and often without any grading of the severity. There seems to be a

need for more questions or the use of a symptom-score in epidemiological studies to more precisely assess incidence and prevalence of anal incontinence.

Diagnostic overview and strategy

Incontinent patients can experience change in their bowel pattern, like more frequent emptying or looser stool, which also can be symptoms of cancer in the digestive tract or elsewhere. Cancer disease should therefore be considered, and further examinations like colonoscopy or CT scan of the abdomen and pelvis might be considered.

Loose stool or diarrhea is strongly associated with anal incontinence⁴. It is more difficult to stay continent with loose or liquid stool than with solid stool. Many conditions can give loose stool, like inflammatory bowel disease, pancreatic failure, removal of the gallbladder, hyperthyreosis and more. The patients might benefit from investigations and, if possible, treatment of the diarrhea first, as this also might help the incontinence.

The evaluation of an anal incontinent patient starts with an anamnesis focused on frequency and type of incontinence (gas or stool), and how this affects the professional, private and social life. The anamnesis should include incontinence score (see below) and try to find a cause of the incontinence. It may be caused by many different conditions, like sphincter injury from birth or surgery, rectal prolaps, radiation and more. Clinical examination includes inspection, palpation and exploration of the pelvic floor, and might show scars from trauma, sphincter defects, fistula, and more. The examination should include an anorectoscopy to assess the anal canal and rectum for marisks and hemorrhoids, proctitis, anal/rectal prolapse and more. Many centers do an anal ultrasound at the first visit in order to assess the sphincter and potential sphincter defects. Further investigations include defecography and/or MRI of the pelvic floor, anal manometry, rectal capacity measurement and neurophysiologic tests. These further investigations are done in selected patients, and rarely at the first visit to the center.

Next, some of the methods mentioned here will be discussed more closely.

How to measure

Incontinence scores

Grading of the severity of anal incontinence is necessary in order to assess the condition, choose treatment and to evaluate treatment effect. There is no physiological or otherwise objective measurement that reflects the severity of incontinence accurately, and scoring systems based on patient reports have been developed. Pescatori published the first in 1992¹³. Several scoring systems have been published since, and the two most used are the Wexner score (1993) and the St. Mark's score (1999)^{3,14}. The most widely used is the Wexner score (Wexner score has 187 hits in

Pubmed on the name; St. Mark's score has 97 hits in Pubmed on the name). The Wexner score and the St. Mark's score are as follows:

Wexner score

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pads	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Never, 0; rarely, <1/month; sometimes,<1/week, ≥1 month; usually,<1/day, ≥1 week, always, ≥1 day
0= perfect continence; 20=complete incontinence

St. Mark's score:

	Never	Rarely	Sometimes	Weekly	Daily
Incontinence for solid stool	0	1	2	3	4
Incontinence for liquid stool	0	1	2	3	4
Incontinence for gas	0	1	2	3	4
Alteration in lifestyle	0	1	2	3	4

	No	Yes
Need to wear a pad or plug	0	2
Taking constipating medicine	0	2
Lack of ability to defer defecation for 15 minutes	0	4

Never, 0; rarely, <1/month; sometimes,<1/week, ≥1 month; usually,<1/day, ≥1 week, always, ≥1 day
0=perfect continence; 24=complete incontinence

The Wexner and St. Mark's score are similar; the most important difference is that St. Mark's score assess the last four weeks only (Wexner score has no time limitation) and St. Mark's score includes urge (urge is not part of the Wexner score).

Earlier scores, like Pescatori, did not take into account lifestyle alterations; this was introduced first with the Wexner score in 1993.

All these symptom scores depend on the patients' recall, which might be biased. A different method for grading the severity of incontinence is to make the patients keep a diary over their daily bowel movements and leakage. This opens for several data or parameters to be extracted, and W. Graf et.al. highlights the number of incontinence-free days and the number of incontinence episodes to be sensitive to change, in their randomized, sham-controlled study of anal injections¹⁵. Keeping a diary has also become the standard evaluation when treating patients with sacral nerve modulation. A 50 % reduction in number of incontinence periods in the test-period, is by many required for permanent implantation of the nerve modulator¹⁶.

The study by Graf et. al. showed there can be a significant difference in one assessment method and not in the other when using two different assessment methods simultaneously¹⁵. The study reported a significant difference in incontinence episodes and incontinence-free days as recorded in the patients' diary, but this difference did not result in a significant difference in the Wexner score. This implies that the different methods for assessing anal incontinence have different sensitivity for change, some assessment methods manage to detect a smaller change. How small the change in incontinence is allowed to be and still be clinically relevant is not clear.

Quality of life

Many clinical studies today include a patient-related outcome variable. It is important in order to change clinical guidelines on treatment of different conditions. It is of great value in the assessment of anal incontinence, where there are no objective measures of incontinence available¹⁷.

To identify change in anal incontinence, there has to be a grading of the severity of the condition, and the symptom scorings like St. Marks's score is important in this regard. However, there are situations where the symptom scoring alone does not give an adequate assessment. If a patient cannot hold his bowel movements for more than one minute, it would result in leakage in most situations where a toilet is not in the immediate surroundings. However, if the same patient does not work, and stays at home almost all the time with a toilet within reach, the resulting incontinence and symptom score might be very little, but the quality of life would be poorer due to an involuntary "isolation" at home.

Health-related quality-of-life questionnaires (HR QoL) are an important part in the assessment of incontinent patients. There are several hundred different questionnaires available. Most of them are developed to describe a specified condition or groups of conditions, and some cover general quality of life.

For the general health-related quality-of-life, two of the most widely used questionnaires are Short Form 36 (SF-36) and the EQ-5D^{18,19}. A table of the most often used is:

Name	No. of hits in Pubmed on the name
SF 36	10 953
SF 12	6 194
SF 6D	266
EQ-5D	1 815
Nottingham Health Profile	1 008
Sickness Impact Profile	5 719

The EQ-5D was chosen in our study on the basis that it was available in Norwegian, widely used and with few questions. Our experience in a pilot study implied that it was an advantage to keep the number of questions low, in order to improve the quality in the answers²⁰.

In order to increase the likelihood of registering changes in quality-of-life, there is a need for using a condition-specific questionnaire in addition to the general quality of life questionnaire. The most widely used is the Fecal Incontinence Quality of Life Scale, FIQLS²¹, which is also used in this study to be able to compare the results with other studies. The questions in FIQLS describe quite well how fecal incontinence might affect everyday life.

Because it was not formally translated and validated in Norwegian, we did this as an integrated part of the randomized trial²²(paper2). The FIQLS is presented in the appendix.

Quality of life-questionnaires are important tools to assess the patients' view of health related issues, but they have several possibilities for bias. Problems in filling out the questionnaires (for instance due to dyslexia, impaired vision, language difficulties) might result in incorrect answers or no answers. Chronic conditions with varying severity (for instance rheumatoid arthritis) might lead to varying assessments and difficulties in interpretation of the results. Some patients might overestimate their problems in order to justify the right to treatment. Answering the questionnaires in different situations, for instance in a hospital or at home, might also give different answers related more to the situation and not the health issue. Good care and good communication with health personnel might give a placebo effect and improved HRQoL, unrelated to the condition in question. In some areas of medical research, like research on cancer and heart disease, there is an emphasis on hard endpoints in assessing treatment, like 5-year survival, recurrence and complications. These areas of medicine have clear pathologic-anatomical definitions of disease and complications, with

well defined outcome parameters for research. These hard endpoints will probably continue to be the most important in the assessments of different treatments, leaving little emphasis on HRQoL. For other research, like palliative chemotherapy in cancer patients, hard end-points like length of survival assess treatment effect, but do not necessarily show the whole picture. If the chemotherapy gives serious side-effects, the gained survival time might not be worth the patient's effort in enduring therapy.

The usefulness of quality of life-questionnaires will vary with the disease in question. For functional conditions with symptom-scores as the primary assessment, like anal incontinence, HR QoL is of high value. However, the most important evaluation of the condition should still be the disease itself and the change in disease, even if it is difficult to measure.

Classification of anal sphincter defects, ultrasound score

A gynecologist classify injuries to the anal sphincter during vaginal deliveries²³. The classification is based upon perioperative findings. The development of two-dimensional endoanal ultrasound gave a new and improved modality for assessing the anal sphincter. The 2D ultrasound gives an exact projection where it is used, but is dependent of the location of the probe in the sphincter. The 2D ultrasound therefore has an intra- and inter-observer agreement varying from poor to very good for axial still frames²⁴⁻²⁶. When combining axial pictures with video recording, the agreement improved²⁷. Ultrasound can identify defects in the internal and external anal sphincter in women with sphincter defects from vaginal deliveries²⁸. If there is a defect, the size might influence the decision to offer the patient a sphincteroplasty in order to repair the defect, or other treatment^{29,30}. There is, however, no international or national consensus on which patients should be offered a sphincteroplasty and who should not. Some studies have shown a correlation between the size of the defect and the severity of the incontinence, but there is also a recent Norwegian study that suggests that childbirth and perineal injuries are not strongly associated with incontinence^{4,30}. An anatomical evaluation of the anal sphincter is none the less clinically relevant in patients with anal incontinence. In 1996 the possibility to take three dimensional pictures of the anal sphincter emerged. Based on this new technology, two different classification systems were presented, the Starck Score and the Norderval Score.

The Starck Score was the first to be published³¹. It assesses the external and internal sphincter separately in regards of defect length, depth and size. No defect has a score of 0; maximal defect has a score of 16. Note that the scores of one and two are not in use, the lowest scoring possible for a small defect is three: the smallest possible defect is less than half the length of the sphincter, partial in thickness and less than 90°. Each of these features gives a score of 1, giving the sum of three points for the smallest defect.

The Starck Score

Defect characteristics	Score 0	Score 1	Score 2	Score 3
External sphincter				
Length of defect	None	Half or less	More than half	Whole
Depth of defect	None	Partial	Total	-
Size of defect*	None	≤90°	91–180°	>180°
Internal sphincter				
Length of defect	None	Half or less	More than half	Whole
Depth of defect	None	Partial	Total	-
Size of defect*	None	≤90°	91–180°	>180°

*Radial extension/radial size of defect.

The Norderval Score is somewhat simpler, and ranges from 0 (no defect) to 7 (maximal defect) using all whole numbers in between³⁰. Contrary to the Starck Score, the partial defect in the internal sphincter has been omitted, mainly because this muscle layer is so thin that a partial defect is difficult to identify.

The Norderval Score:

Defect characteristics	Score 0	Score 1	Score 2	Score 3
External sphincter				
<i>Length of defect</i>	≤50%	<50%		
<i>Depth of defect</i>	None	Partial	Total and ≤90° radial extension	Total and >90° radial extension
Internal sphincter				
<i>Length of defect</i>	≤50%	<50%		
<i>Depth of defect</i>	None	Total and ≤90° radial extension	Total and >90° radial extension	

The following pictures are examples of endoanal ultrasound showing a normal anal sphincter (fig 1), a defect in the external sphincter (fig 2) and a defect in both the external and internal sphincter (fig 3).

Fig 1 Normal sphincter

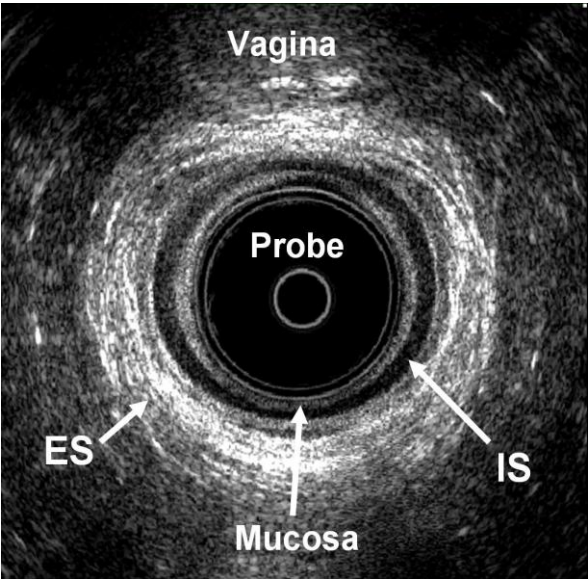


Fig 2 Defect in the external sphincter

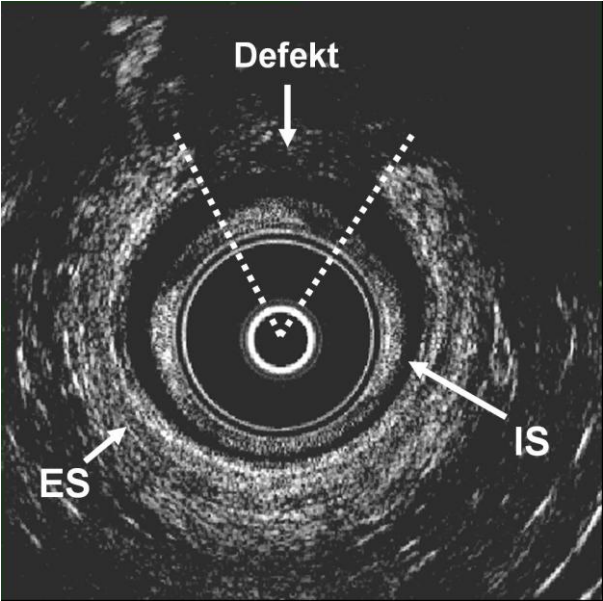
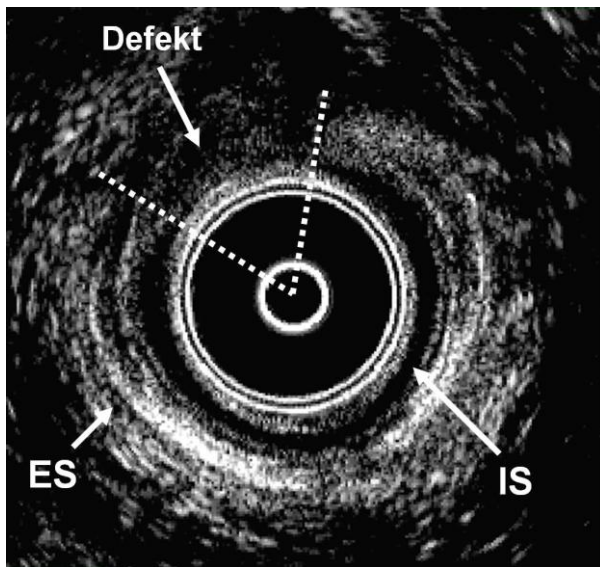


Fig 3 Defect in both external and internal sphincter



(Photo: Dehli et al 2008³²)

ES=external sphincter, IS=internal sphincter

The ultrasound assessment gives the clinician a possibility to assess the anal sphincter better than with other imaging techniques, like magnetic resonance imaging (MRI). However, an assessment using a scoring system is time consuming, both in learning the assessment method and using it in clinical practice. Ultrasound imaging of the sphincter is widely used in centers receiving patients with pelvic floor problems, but it is the author's impression that the scorings systems presented here, have not been taken into clinical practice to the same degree.

Physiological measurements

Functional changes have been studied in order to explore possible mechanisms to explain change in incontinence. However, changes in physiological measurements do not always correlate with change in incontinence after sphincter training with biofeedback³³. Physiological changes after anal injections have been sparsely studied, and overall, the physiological assessments of the sphincter have limited implications in the management of anal incontinence.

There are several different physiological assessments of the sphincter, and a short version of three methods are presented below:

Anal manometry

Anal manometry describes the pressure in the anal sphincter at rest and at voluntary sphincter contraction. It was performed in this study with an 8 channel water perfused catheter on a motor device to move the catheter through the anal canal and coupled to a computer, to give pressures in

the full length of the anal canal at rest and during sphincter contraction (Medtronic, Skovlunde, Denmark). It has been showed that biofeedback can give a significant increase in squeeze pressure, but this improved strength has only a weak correlation to improved continence, limiting the clinical importance of this measurement³³.

Rectal capacity (Balloon test)

To examine the association between volume and anal perception, a balloon can be placed in the lower rectum in anal incontinent patients. The balloon is then filled with water in 10 ml steps, and the volume for first sensation, the volume at the first wish to defecate, and the volume at first pain is recorded³⁴. An increase in volume at urge and first pain can be seen after biofeedback³³. In clinical use, the test can identify severely impaired rectal sensitivity associated with some neurological conditions (like spinal injuries) giving very high volumes. Selected patients can therefore benefit from this test.

Pudendal nerve latency test

The Pudendal nerve latency test is performed using a small electric stimulator placed on the tip of a gloved finger, and a sensor placed at the base of the same finger. With the finger in the anal canal and the fingertip placed against the nervus pudendus close to the tuber ischiadicum, an electric current is given to the nerve, and the time to contraction of the sphincter around the sensor at the base of the finger, is registered. The method has been widely criticized. It measures only intact nerves, possibly overlooking nerve damage. It has no prognostic value on effect of treatment, and no association with other variables, and is not recommended in use³⁵⁻³⁷.

Treatment

Conservative treatment

Conservative treatment includes a variety of measures. Most patients use different pads or absorbent bandages to avoid staining of their clothes. Different creams are available to protect the skin, also different wet tissues for both cleaning and protection. A spongy plug placed in the anal canal can be used to avoid leakage.

Changes in the diet might also influence the continence. Foods that might cause loose stools or diarrhea should be avoided. Supplementation of fiber or bulking agents like lactulosis is often recommended because solid stool is easier to control than liquid stool.

Constipating medicine like loperamid, decreases intestinal motility and secretion, and increases sphincter pressure. It can be used constantly or intermittently³⁸. Many patients reserve this medication for special occasions like travelling or social events.

Bowel habit training is an option, but is more often used in children.

Most incontinent patients experience improvements with conservative treatment, of which pads and constipating medicine often are the most effective. When these measures do not suffice, sphincter training with biofeedback is very often a natural next step in the treatment algorithm.

Sphincter training with biofeedback

Biofeedback is a learning strategy based on “operant conditioning” or “learning through reinforcement”³⁹. It is based on using equipment in order to enhance and feed back to the patient activities of the body. It was first used in anal incontinent patients by Engel, who presented the results from the first seven patients in 1974⁴⁰. Several reports up until about 1990 presented high success rates⁴¹⁻⁴⁵, measured as >75 % decrease in number of incontinence episodes⁴⁶. A symptom score was not used, as the first symptom score was published in 1992¹³. However, a Cochrane report reviewing studies up until 2006 did not find this treatment better compared to other conservative methods⁴⁷. After 2006, four randomized trials have been reported. Two trials did not show any difference between electro-stimulation vs. biofeedback, and between two different sphincter exercise programs^{48,49}. The two other trials showed a superior effect of adding biofeedback to sphincter training, and superior effect of a more comprehensive training program including electro-stimulation compared to an ordinary program^{1,50}.

There are three principally different methods of training with biofeedback in anal incontinent patients⁴⁶.

- Strength training of the sphincter muscle. The external sphincter consists of striated muscle cells, which respond to training with increased strength and endurance, just as striated musculature anywhere in the body. The internal sphincter consists of smooth muscle cells, which is classically perceived as not responsive to training. The internal sphincter is responsible for the resting pressure in the anal canal, while the sum of both sphincters gives the squeeze pressure, the major contribution coming from the external sphincter. With electromyography skin electrodes or an anal probe, the electric current resulting from use of muscles is enhanced and fed back to the patient with sound or a graph on a screen. This way improvement of muscle performance can be recorded.
- Rectal sensitivity. One method of biofeedback training involves placing a balloon in the rectum and record the first volume the patient can discriminate. The aim is to decrease the volume the patient can register, and then contract the sphincter early and avoid leakage.
- Coordination. One might use several balloons in the rectum and anal canal. One balloon is placed in the rectum and distends it. The distension of the rectum triggers a reflex that relaxes the sphincter recorded by balloons placed in the anal canal, and which might lead to

leakage. The training teaches the patients to contract the anal sphincter to counteract this recto-anal inhibitory reflex.

Biofeedback might combine two or three of the elements here listed. Sphincter training with biofeedback is offered in many centers, often in combination with conservative measures. The goal of using biofeedback in our study (paper 3) is two-fold; to increase the strength in the external sphincter in order to better avoid leakage, and to improve the voluntary control of the sphincter. Both aspects are important, strength to better close the anus and avoid leakage, and voluntary control to contract the sphincter when needed, and relax if there is no gas or stool in the ampulla recti or when emptying the bowels. Many patients contract their entire pelvic floor constantly in order to avoid leakage and the smell of stool from them, and have more or less lost the ability to relax the sphincter when appropriate.

Training programs vary between institutions. It is normally done several times a week over a period of 10 to 26 weeks. The number and frequency of recommended guided training vary between several times per week, to once or twice pr month.

The picture shows the device used in sphincter training with biofeedback. The probe is placed in the anal canal, and the metallic sides detect current in the sphincter muscle. The patient can see changes in a graph on the screen while contracting and relaxing the sphincter.



(Photo: Dehli)

Anal injections

The injection of bulking agents in the anal canal for treatment of anal incontinence is a relatively new treatment. The technique has been used in urinary incontinence to close down the bladder neck, and it was a natural next step to try the same with the anal sphincter. The first report on using a bulking agent to “close down” the anal canal was published in 1993, where all 11 patients injected with polytetrafluoroethylene (“Teflon”) showed improvement⁵¹. Several reports using 10-20 patients followed, using different substances like autologous fat(1998)⁵², collagen (1999)⁵³, silicone (2001)⁵⁴, and carbon-coated zirconium oxide beads (2003)⁵⁵. The bulking agent has been placed submucosally, intersphincteric and extraasphincteric, and injected through the mucosa in the anal canal or percutaneously⁵⁶. To achieve the right placement of the bulking agent, the injection has been guided by sight through an anoscope (most often submucosal placement of the bulking agent), with a finger in the anal canal (percutaneous injection and intersphincteric placement) or with an ultrasound probe in the anal canal (percutaneous injection and intersphincteric placement)⁵⁷.

Injecting in the intersphincteric space using a percutaneous needle route might require general anesthesia. Submucosal placement is a simpler procedure and do not require any anesthesia.

Extrasphincteric placement of the bulking agent is not often used.

Side-effects of the treatment in the referred reports are few. Some patients experience pain and discomfort the first days after injection, some might experience leakage of the bulking agent, and a few develop infections. A review summing up results on 420 patients injected with different techniques and different agents reports only one infection requiring drainage⁵⁷. Perhaps a little surprising is the lack of reports of chronic pain following injection⁵⁷.

A curiosity from the literature is worth mentioning, because there is an overall agreement that injection treatment is safe. In 1997 the first and so far only death was reported following a periurethral injection of autologous fat due to urinary incontinence⁵⁸. The post-mortem showed pulmonary adipose tissue and lipid droplet embolism.

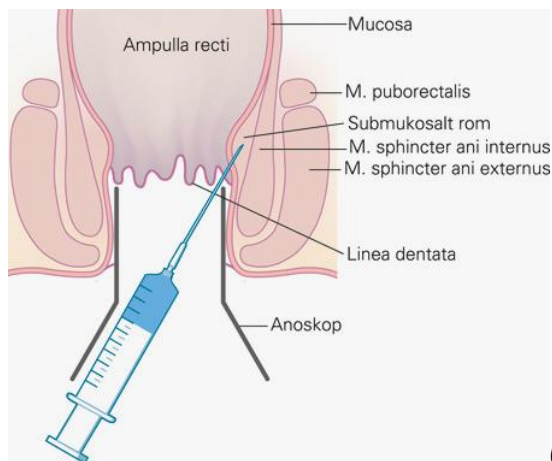
There have been several reviews of the technique, both on the effect of the treatment and safety^{56, 57, 59}. The conclusions in the report from Luo et al in 2009 and the Cochrane report from 2010 are that the treatment is safe, but has no effect. The same reports also points to the lack of large and well designed studies. However, the trial presented by Graf et al in 2011 showed that the injection of dextranomer in stabilised hyaluronic acid was superior to sham injection¹⁵.

Solesta (Q-Med, Uppsala, Sweden) consist of dextranomer microspheres in hyaluronic acid and saline. It does not induce tissue changes in the surrounding environments or migrate in animal studies^{60, 61}. It is used in the treatment of vesico-ureteral reflux in children, as an augmenting agent in the bladder wall close to the ureteral orifice⁶².

Solesta with the submucosal placement technique was chosen in this study. The method had a promising effect in a Swedish trial (presented as a poster at the 37th Annual Meeting of the International Continence Society, Rotterdam 20-24 August 2007. Abstract No. 280), and a pilot study related to this thesis showed promising results^{20, 63}.

Solesta was injected 4 x 1 ml submucosally in the anal canal 5 mm above the dentate line (see figure below). The procedure is performed in an outpatient setting, without any anesthesia. Three of the first ten patients experienced infections. Adding antibiotic prophylaxis resulted in no infections in the next over fifty patients (paper 3).

The picture shows the injection technique and the submucosal placement of the bulking agent in the anal canal.



(Dehli et al 2007²⁰)

Other treatment modalities

When conservative treatment and sphincter training with biofeedback fail to relieve symptoms sufficiently, more invasive procedures are considered. These procedures include sacral nerve modulation, surgical repair of sphincter defects, artificial sphincter implantation and electrostimulated graciloplasty⁶⁴. Sacral nerve modulation has been more widely used the last ten years, but is very expensive (approx.20 000 euro pr patient). Sphincter repair is decreasing, as long term results are failing, and some reports suggest a poorer outcome when the procedure is done in patients over 40 years of age⁶⁵⁻⁶⁷. However, it is still an important option in patients with larger sphincter defects. A last possible alternative is colostomy, an option not often chosen by patients or surgeons.

5. Aim of the study

The main aim in this thesis has been the primary assessment and management of anal incontinent patients. With improved assessment of the condition, one can better evaluate treatment effect, and also better evaluate the severity of the condition, in both clinical practice and in research. Thus, the Norderval score for classification of sphincter defects was tested for reliability in clinical use (paper 1) and a symptom-score and a condition-specific quality-of-life questionnaire were translated and validated in Norwegian (paper 2). It was also a goal to introduce and evaluate a new treatment option, in the hope of improving first line therapy of anal incontinent patients (paper 3).

Questions for each paper:

- Paper 1:
 - Reproducibility, or inter- and intra-observer agreement in two different grading systems for classification of sphincter defects
 - How many assessments must be done by an inexperienced ultrasonographer in order to achieve acceptable intra-observer agreement

- Paper 2:
 - o Formal translation of the St. Mark's score and the FIQLS
 - o Psychometric testing of the FIQLS
- Paper 3:
 - o Primary question: How effective is the anal injection compared to sphincter training with biofeedback?
 - o Secondary questions:
 - How long does each treatment work?
 - How does each treatment work?
 - How is the quality of life affected during treatment?
 - Are there side effects in either treatment?

6. Materials and methods

Patients

In paper 1, the sample was from a total of 55 ultrasound datasets from all women aged 20 to 40 years investigated in the outpatient clinic of the Department of Gastrointestinal Surgery, University Hospital of North Norway, Tromsø from January 2003 to December 2005 with recorded three dimensional ultrasound of the full sphincter length.

In paper 3 a total of 126 patients were actively recruited to participate in a randomized controlled trial, if they fulfilled the following criteria: adults (> 18 years of age) with a St. Mark's score of 4 or higher, no previous treatment for anal incontinence, and able to understand and fulfil the requirements of the study. Exclusion criteria were inflammatory bowel disease, pregnancy, anal or rectal prolapse, irritable colon according to ROME II criteria, neurological disease disabling them from sphincter training, previous surgery in the upper anal canal or lower rectum, and a total anal sphincter defect > 150 degrees. Study participants were recruited from three specialised outpatient centres for anal incontinence in Norway, located in Hamar, Sarpsborg and Tromsø.

In paper 2, 76 of the same patients as in paper 3 were used, if they have filled in the translated FIQLS form twice within 2-4 weeks without any intervention.

All recruited patients provided written, informed consent, and all three studies were approved by the Regional Committee for Medical Research Ethics, North Norway. The randomised trial is registered at www.clinicaltrial.gov with registration number NCT00303030.

Classification of sphincter defect and intra- and inter-observer agreement

Both the classifications according to Starck and Norderval were used^{27, 30}. One experienced ultrasonographer (Stig Norderval), with more than 400 assessments with anal ultrasound performed, and one inexperienced ultrasonographer (Trond Dehli) both assessed the same set of pictures. Assessment was done blinded to other patient data, and each ultrasonographer assessed the pictures twice with eight weeks between the first and second evaluation. If the first and second assessment disagreed, a third and final evaluation was performed four weeks after the last evaluation.

Translation

Translation was done first from English to Norwegian by three independent translators with Norwegian as their mother tongue; two surgeons and one professional translator. A common Norwegian version was then established by the authors. Translation back into English was then done by two new independent translators speaking Norwegian but with English as their mother tongue. Permission was obtained from the original authors to translate and validate the FIQLS and St. Mark's score into Norwegian.

Testing of psychometric properties

Patients answered the translated questionnaire twice with 1-8 (average 3) weeks in between, and all patients were in a stable condition without any interventions during this period.

Interventions

Biofeedback

The sphincter training with biofeedback was done once a day for five days weekly over a period of six months. The patients were instructed by a specialized nurse or physiotherapist five to six times during this period. The main part of the training was done at home. A device was used to give the patients feedback on the strengths of their contractions, and to measure improvement (NeuroTrac ETS, Verity Medical Limited, Hampshire, United Kingdom). A typical training session consisted of 4 series of 5 contractions in each series, with one contraction lasting 5-10 seconds. In some patients, the same device was used to stimulate the sphincter electrically to help the patients identify and contract their sphincter. Electro-stimulation was used if the patients had difficulties with voluntary control with their sphincter.

Anal injections

Solesta was injected 4 x 1 ml submucosally in the anal canal 5 mm above the dentate line. The procedure was performed in an outpatient setting, without any anesthesia. We used antibiotic prophylaxis after 3 infections among the first ten patients injected, with no subsequent infection in the next over fifty patients. Patients had no limitations after injections except to avoid pressure to their pelvis, like when riding a bicycle, for two weeks.

Assessment of a new treatment

A randomized, controlled study design was chosen in order to assess the new treatment. A pragmatic approach was chosen by comparing the new treatment, anal injections, against an existing, widely offered conservative treatment; sphincter training with biofeedback. The patients were randomized by a computer program, performed by a person outside the study, who was reached by telephone. The randomization was done in blocks with the size unknown to the study coworkers, and stratified according to St. Mark's score in order to have equal severity of anal incontinence in both groups at baseline. The primary outcome variable, St. Mark's score, was assessed by telephone by a blinded coworker, all other assessments was done by none-blinded coworkers. The study period was set to two years, with six months treatment period followed by 18 months of follow-up. The patients with no effect of the treatment after the end of the treatment period, were offered alternative treatment and removed from further follow-up, as it was unethical to keep other treatment from them.

Statistical analyses

Statistical analyses were done with SPSS version 11, 15 and 18, STATA version 11.1 and Medcalc version 9.3. Two tailed $p < 0.05$ was considered significant.

Paper 1

Inter- and intra-observer agreement for categorical and numeric data were expressed with kappa and weighted kappa respectively. Agreement was rated very good (kappa 0.81-1.00), good (kappa 0.61-0.80), moderate (kappa 0.41-0.60), fair (kappa 0.21-0.40), slight (kappa 0.0-0.20) and poor (kappa < 0). Correlations were assessed by Pearson's test (normal distribution of data) and Spearman's test (not normal distribution of data).

Paper 2

Internal consistency was tested with Cronbach's alpha, and intra-class correlations (single measure) for stability over time. These two reliability tests were considered acceptable with a coefficient of 0.70-0.80, good with 0.80-0.90 and excellent if >0.90.

Pearson correlation was calculated for correlation between subscales of the FIQLS, and construct validity was assessed with correlations between the FIQLS-subscales and the St. Mark's score. Correlations were considered large when >0.50 , medium $0.30-0.50$ and small when <0.10 .

Paper 3

The outcome parameters in the two groups were compared using the student t-test, mixed models and analysis pr protocol. Within each group, data was analyzed with mixed models and the student t-test. Missing data was estimated with the last value carried forward-method, or estimated as an integral part in the mixed model-analysis.

7. Summary of papers

Paper 1

All 55 women between 20 and 40 years of age, and who had been investigated in our outpatient clinic with a complete three-dimensional EAUS in the period from January 2003 to December 2005 comprise the sample of this study. The EAUS datasets were assessed twice independently by both an experienced and an inexperienced ultrasonographer, blinded for all other patient data. Cases with intraobserver disagreement were resolved by a third (final) assessment. Sphincter defects were classified according to the EAUS defect score and the Starck score. Incontinence was graded according to the St. Mark's score at the time for the EAUS recording.

Intraobserver agreement for the experienced ultrasonographer was good for the EAUS defect score (weighted *kappa* 0.75) and the Starck score (weighted *kappa* 0.73). Intraobserver agreement for the inexperienced ultrasonographer was moderate for the EAUS defect score (weighted *kappa* 0.58) and good for the Starck score (weighted *kappa* 0.62). Interobserver agreement was good for both the EAUS defect score (weighted *kappa* 0.65) and the Starck score (weighted *kappa* 0.74). The degree of incontinence correlated significantly to the extent of sphincter defects expressed by the Starck score and the EAUS defect score for both ultrasonographers.

In conclusion, the two score systems are reliable for classification of anal sphincter defects using three-dimensional EAUS. The extent of sphincter defects correlates to the degree of incontinence.

Paper 2

The FIQLS and the St. Mark's score were formally translated. The retranslation back to English did not reveal any major inconsistency in the Norwegian versions.

76 patients recruited in the randomised study comparing anal injections against sphincter training with biofeedback (paper 3) and who had filled in the FIQLS twice with an average of three weeks in between, comprised the study sample.

The analysis show a good to excellent internal consistency for three of four subscales in the FIQLS, and a high stability over time with coefficients >0.74 for all subscales. A student t-test showed no difference between the baseline and retest. Correlations were high between all of the subscales and the St. Mark's score.

In conclusion, the FIQLS and the St. Mark' score have both been successfully translated to Norwegian, and the psychometric analyses of the FIQLS indicate that the Norwegian version is valid.

Paper 3

Using a single-blind, controlled design, 126 patients with anal incontinence (St. Mark's score >3) were randomly allocated to sphincter training with biofeedback or anal injections. The treatment period was six months, and the total follow-up time from start of the treatment was two years.

For the 62 patients allocated to biofeedback, the St. Mark's score improved from 12.6 (95 % CI 11.4-13.8) at baseline to 7.2 (95 % CI 7.2-8.8). Patients receiving anal injections had a change in St. Mark's score from 12.9 (95 % CI 11.8-14.0) to 8.3 (95 % CI 6.7-9.8). There was no significant difference between the groups. Quality of life measured with the FIQLS showed a significant improvement in both group from baseline to two years, but again no difference between the groups. Physiological measurements showed an increase in the rectal sensitivity for small volumes in both groups, and increased sphincter squeeze pressure in those patients who trained.

In conclusion, the treatment effect of anal injection and biofeedback did not differ in this randomised trial. Both treatments gave a significant improvement of incontinence and quality of life.

8. Main results and discussion

Intra-observer and inter-observer agreement

Intraobserver and interobserver agreement were determined for an experienced and an inexperienced ultrasonographer using the EAUS defect score and the Starck score.

In general, the interobserver agreement between an experienced and an inexperienced ultrasonographer using the Norderval score and the Starck score was good with weighted *kappa* between 0.62 and 0.75 for both scores. The experienced ultrasonographer obtained a higher degree of intraobserver agreement compared with the inexperienced for both scores.

The intraobserver agreement for the inexperienced ultrasonographer was better between the second and the final assessment than between the first and the final assessment for both the Starck score and for the EAS defect score. This improvement in intraobserver agreement may reflect a learning curve for the inexperienced ultrasonographer. The results indicate that an examiner unaccustomed to ultrasonography of the anal sphincter has to perform at least 100 three-dimensional EAUS-assessments in order to achieve a high degree of repeatability when using the score systems described.

This implies that the ultrasound scoring is difficult, and accurate assessment of the sphincter using endoanal ultrasound requires a considerable amount of time to learn thoroughly. Hence, the scoring systems of the anal sphincter might not be widely used in the clinic. A simpler classification could accomplish a greater acceptance.

Translation

After translation of the FIQLS and the St. Mark's score from English into Norwegian by three independent translators, a common Norwegian version was established by the authors without any disagreements. The reverse translation back into English yielded no major inconsistencies. A pilot test with ten patients was performed, and resulted in minor changes to clarify the questions in Norwegian. In addition, for the item "Need to wear a pad or plug" in St. Mark's score, it was useful to add "because of faecal leakage" to avoid adding points from the use of pads for other reasons, like coexistent urinary incontinence. With these changes, the final versions were established.

Psychometric testing

The FIQLS questionnaire was answered twice by 76 patients participating in the randomised study (paper 3). The internal consistency analysed with Cronbach's alpha showed good to excellent values (0.83 and higher) except for the subscale embarrassment (0.64) (table 2 paper 2). The poor performance of the embarrassment subscale might be caused by limited items in the subscale (three). The intra-class correlation with coefficients ranging between .74 and .86 for the four scales indicated a high stability over time (table 2 paper 2). The correlations between each of the subscales and the St. Marks score, were generally high, ranging from 0.46 to 0.92, indicating that a high severity of faecal incontinence correlates with a low quality of life.

Assessment of the new treatment

Of the 126 randomly allocated patients, 61 completed 24 months. The majority of the discontinuing patients had no effect of treatment, and were dismissed from the study and offered a new assessment and treatment.

The three different statistical approaches (1. mixed models, 2. student t-test with missing data estimated with the last value carried forward-method and 3. Student t-test in patients completing and not completing the study separately) showed that there were no differences in change of St. Mark's score between treatments. However, they also showed a significant and equal improvement of incontinence for both treatment groups. The FIQLS also showed an improvement in quality of life, parallel to the improved continence.

Physiological measurements showed an increase in the rectal sensitivity for small volumes in both groups, and increased sphincter squeeze pressure in those patients who trained. This might be part of the mechanism of effect.

Patients with a neurological cause of their incontinence and without ability to do sphincter training, were excluded from the study. Otherwise a large fraction of the patients agreed to participate in the study, with a wide range of incontinence severity. This indicates that the results are valid for the major part of incontinent patients without a neurological cause to their condition.

It was also attempted to show a correlation between the change in severity of St. Mark's score with treatment and different baseline parameters, in order to identify predictors for success or failure for the treatments. No predictors were found. It was also attempted to show a correlation between the severity of incontinence (St. Mark's score) and the degree of sphincter damage (Norderval score), but again no correlation was found.

To assess a new treatment, the randomized, controlled trial (RCT) is the best choice of study design when possible. An RCT has several challenges to overcome in order to be accomplished. Some challenges are more prominent in surgical trials compared to other interventions⁶⁸. The following is a discussion of some important methodological aspects related to the present study:

RCT and surgery

First of all, it must be considered if it is necessary to do a randomized trial. It is probably better done early rather than later during the development of a new intervention. If the new intervention has been assessed in several cohort studies, or been widely implemented, the RCT might be of lesser value. An example is the worldwide implementation of laparoscopic cholecystectomy instead of open cholecystectomy without any RCT. On the other hand, if it is done too early, and the intervention is further refined, it might not reveal the full potential of the new intervention. The time window for an evaluation might be narrow, as Buxton observed: "It's always too early until, unfortunately, it's suddenly too late".⁶⁹

New surgical procedures has a learning curve, a surgeon can expect better results with more experience. In a trial involving a difficult procedure with a long learning curve, the results might

improve with experience during the trial itself, and the interventions early and late in the study is not necessarily identical. Interventions requiring a skill, like in surgery, psychiatry or physiotherapy, all might have difficulties in standardizing the intervention⁷⁰. In our trial, the doctors all had performed at least 5 injections each before the trial, which we considered to be sufficient to learn the procedure. The physiotherapists varied in experience with spincter training with biofeedback, from no experience to several years of practice, but unfortunately, we have not registered these data. There are different aims with an RCT. It can be pragmatic, by comparing different treatments in order to find the better of the two (or more). It can also be explanatory, by assessing if an intervention has effect. Explanatory trials often compare an intervention against a sham intervention¹⁵ or no intervention.

RCT's in surgery have traditionally been regarded as difficult to manage and time consuming, with uncertain results. Surgeons also have to spend a lot of time doing clinical work, which might make it unattractive to invest the time and energy an RCT requires. Still, it is the best design for assessment of interventions, and should be considered when assessing interventions.

Blinding

It is difficult to blind both patients and surgeons to which interventions is given. Most often a wound or other signs make it obvious to the patient, and the surgeon has to know which intervention to perform. However, it is most often possible to assess the outcome blinded, which means that someone other than the surgeon should do the assessment, blinded to the treatment given. This is important in order to avoid a biased outcome assessment. In several of the studies published on anal incontinence, blinding of the evaluator has not been used^{35, 48, 50, 65}.

Patient and doctor expectations

Expectations in both surgeons and patients are probably mostly influenced by the two interventions in the study. Both surgeons and patients might have strong preference for one over the other. This can be based on a great difference in the interventions (surgery vs. sham-surgery, major surgery vs. watchful waiting) or different profiles of effect and side-effects. Our study had only minor differences between the two treatments, and was well received by patients and doctors.

Placebo

A Cochrane review assessing the placebo effect across clinical conditions, states that placebo does not have clinically important effect in general. However, patient-reported effects of placebo might be greater than observer-related outcomes⁷¹. In a study with two active interventions and a symptom score as the primary outcome measure, the effect of the interventions and placebo is difficult to

distinguish. It is theoretically possible that all the effect is from placebo. To evaluate the placebo effect, a third treatment with sham- or no treatment should be included. In a pragmatic trial, this is most often not done, and it might also raise ethical questions about keeping treatment from the patients. In this study, the placebo effect might have had an impact on the results. However, Graf et al have shown that anal injections are superior to placebo, showing that the treatment has an effect¹⁵.

Patients reluctance to participate

There are several reasons for patients not to participate in RCT's. A major cause for patients' reluctance to participate in a RCT is the differences in the interventions offered. Examples are surgery vs. non-surgery, placebo vs. active intervention, open surgery vs. minimally invasive procedures, intervention vs. no intervention and so on. Data on participating patients and patients who declined to participate, cannot be assumed to be identical, and hence, might influence the results⁷². In our study, a large fraction of the eligible patients participated, which strengthens the study.

Interventions might also be available outside the study, which could impair the motivation for participation if the patient is not randomised to the wanted intervention. These factors may also influence the drop-out rate in the study. If the effect of one intervention is none or only limited, the risk of discontinuing the study might increase, like in our study. This might compromise the power calculation, of which the statistical analysis is based.

Missing data

A randomised study is dependent upon patients concluding the study to high degree. Missing data might seriously jeopardize the analysis, because the power calculation is not valid with fewer patients. Every possible measure is therefore recommended to make the completion rate as high as possible⁷³. It is the author's impression that a completion rate of < 90 % might cause problems in the analysis, and the problems are more serious with decreasing completion rate.

This study chose a design that allowed the patients to leave the study at a defined time point, if they had no effect of treatment. It was found unethical to keep other treatment modalities from the patients, when both the patient and the author know alternatives to the given therapy. Clinically this makes sense, it is what is done in normal practice (if something doesn't work, one tries something else to help the patient). However, statistically this is not feasible, and might compromise the study to the point where the results are not interpretable. There is a limit to what the statistical methods can yield in a normal clinical practice. The solution might be to make shorter studies to avoid missing data, and/or to follow the patients even if they discontinue the treatment. There are also several

statistical methods which can be used to “salvage” the study, using different ways of estimating the missing data, like the last-observation-carried-forward-method or mixed models as used in this study. These estimations are all inferior to real data⁷⁴.

Intervention related factors

Surgical procedures can be complex, with many factors influencing the outcome. These factors are the surgeon, the surgical team, the anesthesiological team, preoperative and postoperative care, patient factors (other diseases, age, and medication) and so on. In addition, the surgical skills in the procedures offered might vary among the surgeons in a study. The sum of all this makes it difficult to compare two different interventions, and those interventions only. In studies with very different interventions, this becomes more prominent.

In this study, the main difference between the treatments in this regard, was the repeated follow-up by physiotherapists in the biofeedback group, giving this group more attention and care than the anal injections group. It is difficult to assess if this have influenced the outcome.

This study was aimed at treating patients in the same way they would have received treatment in everyday practice. A treatment given under ideal conditions, with carefully selected patients and specially trained personnel, might not give an answer to the effect of the treatment in everyday practice. Trials such as this study, with emphasis on an assessment of the interventions close to normal practice, are called “pragmatic” or “practical” trials⁷⁵.

Outcome assessment

Traditionally, health personnel assess the effect of a treatment by mortality and morbidity rates. Patient often assess other factors as well, described with the terms patient-related outcome measures and/or health-related quality-of-life. Therefore, clinical trials today often include one or more questionnaires, to assess quality-of-life before and after the intervention.

Mortality and morbidity rates will probably continue to be the most important factors when deciding between different interventions. However, with otherwise similar results, patient related outcome measures might influence this decision.

The results in this study were similar in all outcomes, suggesting that both treatments can be used, in accordance with patients’ and doctors’ preference.

Mechanism of action in two treatment modalities

In the sphincter training group, we found that the patients got stronger after training, their squeeze pressure increased significantly (table 3 paper 3). This might be part of the mechanism of action for biofeedback, and has also been found by others³³.

For both groups, there was an increase in the sensitivity threshold of small volumes in the lower rectum (table 3 paper 3). This might also be part of the mechanism of action for both treatments. One could speculate that it is necessary to feel that there is something in the ampulla recti in order to keep it there, and not leak. It is also possible that the effect of sphincter training with biofeedback is related to increased sensitivity, and not increased sphincter strength. The equal improvement in incontinence for these two treatments might support such a correlation, but this is speculation.

9. Main conclusions

- Interobserver agreement is good for the Norderval score and the Starck score, and both score systems are reliable for classification of anal sphincter defects using three-dimensional endoanal ultrasound
- This study suggests a learning curve of approximately 100 three-dimensional EAUS investigations for an observer unaccustomed with ultrasonography to obtain a high degree of repeatability when assessments are performed according to the two scoring systems.
- The St. Mark's score is formally translated and available in Norwegian
- The FIQLS has been successfully translated and psychometrically tested, and is available in its Norwegian version
- In a single-blind, randomised trial, both sphincter training with biofeedback and anal injections gave a significant improvement in severity of incontinence and in quality of life in patients with anal incontinence
- There was no difference between the two treatment modalities in the trial.
- Increased sensitivity for small volumes in the lower rectum might be part of the mechanism of action for both treatments. In addition, increased sphincter strength after training might also contribute to improved continence.

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11. Appendix

FIQLS consists of four subscales which all ranges from 1.0 (lowest quality-of-life) to 4.0 (best quality-of-life). The value in each scale is the mean of the answers:

Scale 1 Lifestyle: Question 2a, 2b, 2c, 2d, 2e, 2g, 2h, 3b, 3l, 3m

Scale 2 Coping/behavior: Question 2f, 2i, 2j, 2k, 2m, 3c, 3h, 3j, 3n

Scale 3 Depression/self-perception: Question 1, 3d, 3f, 3g, 3i, 3k, 4(question 1 is reversely coded)

Scale 4 Embarrassment: Question 2l, 3a, 3e

Fecal Incontinence Quality of Life Scale (FIQLS) – original version

Q 1: In general, would you say your health is:

- 1 Excellent
- 2 Very good
- 3 Good
- 4 Fair
- 5 Poor

Q2: For each of the items, please indicate how much of the time the issue is a concern for you due to accidental bowel leakage. (If it is a concern for you for reasons other than accidental bowel leakage then check the box under Not Apply, (N/A))

Q2. Due to accidental bowel leakage	Most of the time	Some of the time	A little of the time	None of the time	N/A
a. I am afraid to go out	1	2	3	4	<input type="checkbox"/>
b. I avoid visiting friends	1	2	3	4	<input type="checkbox"/>
c. I avoid staying overnight away from home	1	2	3	4	<input type="checkbox"/>
d. It is difficult for me to get out and do things like going to a movie or to church	1	2	3	4	<input type="checkbox"/>
e. I cut down on how much I eat before I go out	1	2	3	4	<input type="checkbox"/>
f. Whenever I am away from home, I try to stay near a restroom as much as possible	1	2	3	4	<input type="checkbox"/>
g. It is important to plan my schedule (daily activities) around my bowel pattern	1	2	3	4	<input type="checkbox"/>
h. I avoid travelling	1	2	3	4	<input type="checkbox"/>
i. I worry about not being able to get to the toilet in time	1	2	3	4	<input type="checkbox"/>
j. I feel I have no control over my bowels	1	2	3	4	<input type="checkbox"/>
k. I can't hold my bowel movement long enough to get to the bathroom	1	2	3	4	<input type="checkbox"/>
l. I leak stool without even knowing it	1	2	3	4	<input type="checkbox"/>
m. I try to prevent bowel accidents by staying very near a bathroom	1	2	3	4	<input type="checkbox"/>

Q3: Due to accidental bowel leakage, indicate the extent to which you AGREE or DISAGREE with each of the following items. (If it is a concern for you for reasons other than accidental bowel leakage then check the box under Not Apply, N/A).

Q3. Due to accidental bowel leakage:	Strongly agree	Some what agree	Some what dis-agree	Strongly dis-agree	N/A
a. I feel ashamed	1	2	3	4	<input type="checkbox"/>
b. I can not do many of things I want to do	1	2	3	4	<input type="checkbox"/>
c. I worry about bowel accidents	1	2	3	4	<input type="checkbox"/>
d. I feel depressed	1	2	3	4	<input type="checkbox"/>
e. I worry about others smelling stool on me	1	2	3	4	<input type="checkbox"/>
f. I feel like I am not a healthy person	1	2	3	4	<input type="checkbox"/>
g. I enjoy life less	1	2	3	4	<input type="checkbox"/>
h. I have sex less often than I would like to	1	2	3	4	<input type="checkbox"/>
i. I feel different from other people	1	2	3	4	<input type="checkbox"/>
j. The possibility of bowel accidents is always on my mind	1	2	3	4	<input type="checkbox"/>
k. I am afraid to have sex	1	2	3	4	<input type="checkbox"/>
l. I avoid travelling by plane or train	1	2	3	4	<input type="checkbox"/>
m. I avoid going out to eat	1	2	3	4	<input type="checkbox"/>
n. Whenever I go someplace new, I specifically locate where the bathrooms are	1	2	3	4	<input type="checkbox"/>

Q 4: During the past month, have you felt so sad, discouraged, hopeless, or had so many problems that you wondered if anything was worthwhile?

- 1 Extremely So - To the point that I have just about given up
- 2 Very Much So
- 3 Quite a Bit
- 4 Some - Enough to bother me
- 5 A Little Bit
- 6 Not At All

12. Paper 1-3

