Surgical treatment of defecation disorders

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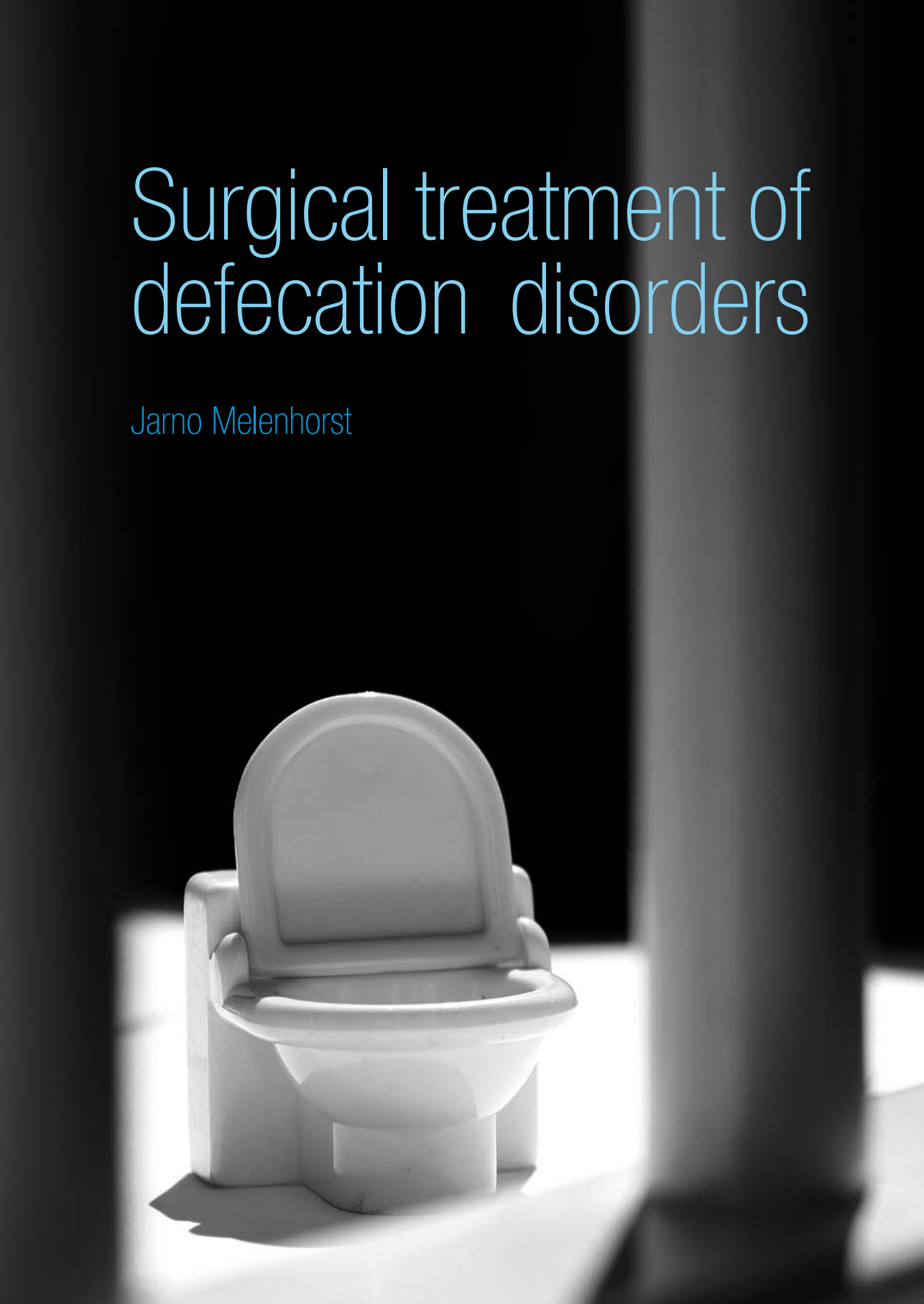
Jarno Melenhorst



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Chapter 1

Introduction

Faecal incontinence

Introduction

Faecal incontinence (FI) has gained a significant increase in treatability during the last 20 years. The introduction of the Dynamic Graciloplasty (DGP) by Baeten[1] and simultaneously by Williams[2] has made a huge impact on the whole colorectal community. Together with the Artificial Bowel Sphincter, these two surgical procedures offered patients dealing with faecal incontinence, an opportunity to augment their defective anal sphincter. Before this period of surgical innovations, the standard treatment of a defective sphincter was an anal repair, however the results of this procedure failed in time.[3] Also conservative therapy, e.g. constipating medicine and (biofeedback) pelvic behavioural therapy wasn't providing the success that patients with severe faecal incontinence needed. These patients frequently ended with a definitive stoma. The introduction of Sacral Nerve Modulation (SNM) also known as Sacral Nerve Stimulation (SNS) provided a minimal invasive procedure with less morbidity to treat faecal incontinence.[4] As a spinoff of this treatment modality it also seemed possible to treat idiopathic constipation by means of SNM. This thesis focuses on the surgical treatment of faecal incontinence and the treatment of idiopathic constipation by means of SNM.

Epidemiology and aetiology of faecal incontinence

Faecal incontinence is a common health care problem, affecting 5% to 10% of community-dwelling adults[5,6] with 1% to 2% experiencing huge impact on daily activities. It aggravates with advancing age and disability. It is a disorder, which is particularly embarrassing and socially unacceptable, and many patients do not seek professional help.[7] Therefore, a huge underestimation of the problem can be expected. The part of the population that seeks help is merely “the tip of the iceberg”.[8] Faecal incontinence has a negative impact on physical and psychological health and lifestyle, with social activity restriction in many instances.[9,10]

The aetiology of faecal incontinence is divers and multi-factorial.[11] It is a combination of sphincter pressure, anorectal sensation and compliance, rectal storage function, faecal consistence and brain function. Trauma to the sphincter complex is one of the most frequent causes of FI. It can be due to birth trauma[12] or iatrogenic trauma in anal surgery.[13,14] Bols et at found that 3rd of 4th degree ruptures contribute significantly to postpartum faecal incontinence.[15] The anorectal sensation and compliance can be altered due to inflammatory processes, as seen in Crohn’s disease and ulcerative colitis. Nerve damage post-partum can cause diminished sensation of rectal filling.[16] Altered anorectal storage function, as seen after low anterior resection for rectum carcinoma, can contribute to faecal incontinence. Due to chronic inflammatory bowel diseases the liquidity of the faeces increases, which decreases the “grip” on the faecal

matter and can lead to incontinence. Neurologic diseases, e.g. spina bifida, multiple sclerosis, can cause FI.[17] Disorders of brain function, e.g. after cerebrovacular events, can cause FI.
The above-mentioned multi-variability makes it challenging to solve the problem of FI. A holistic approach is necessary to solve every aspect of the problems encountered by FI. Preferably this should take place in specialised centres, where dedicated teams operate closely together. Such teams ideally consist of a colorectal surgeon, gynaecologist, urologist, gastro-enterologist, psychiatrist and physiotherapist.

Treatment of faecal incontinence

The first step of treatment of FI should not be surgical. Conservative therapy aims on diet modification, medication and pelvic floor rehabilitation. Diet modification can consist of additional fibres and avoiding gas-producing vegetables. Drugs (loperamide, codeine phosphate) aim to reduce colonic motility and thereby reducing the sense of urge. Bile acid binders and diphenoxylate can be added to augment the effectiveness.[18] Pelvic floor rehabilitation can be successful in as much as 72%. However, the results of a Cochrane review on the effects of biofeedback and/or pelvic floor muscle training for the treatment of FI in adults were based on eleven randomized controlled, but heterogeneous, trials and showed that some elements of biofeedback therapy and sphincter exercises have a therapeutic effect in light to moderate degrees of FI.[19] Retrograde colonic irrigation should be considered when other conservative measures are not successful. With the aid of a special pump, water is introduced trans-anally to clean the bowel and establish a form of pseudo-continence.[20] All forms of conservative therapy could be supplementary to surgical therapy.

Rectal irrigation in “the dark ages”

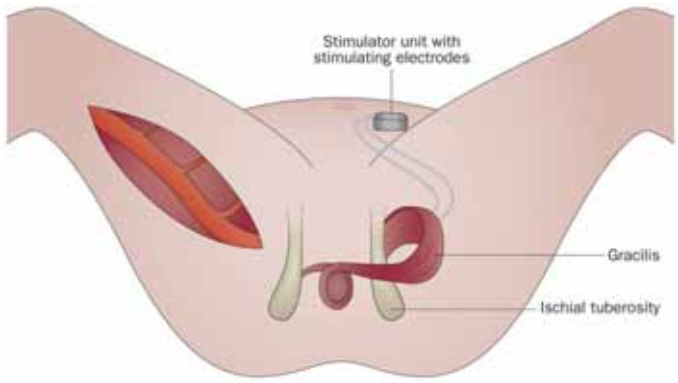
Surgery

Traditionally FI was seen as a problem of the anal sphincter complex. All therapies were aiming at restoring the anatomy of the defective sphincter. The anatomy could well be restored by directly repairing the sphincter by an overlapping sphincteroplasty. Both ends of the defective anal sphincter are surgically explored and sutured. Satisfactory results are achieved in a tension-free repair in 47-100 percent of the cases.[21] Long-term results are far less satisfying.[22]

Dynamic Graciloplasty

The Dynamic Graciloplasty (DGP) was first described in 1988.[1] In a patient with an anal atresia and an existing gracilis muscle transposition, an implantable neurostimulator was placed to augment sphincter function and overrule voluntary contraction. Hereafter, the DGP was simultaneously developed at two research sites.[1,2] Using electrical stimulation type II, fatigue-prone muscle fibres can be changed into type I, fatigue resistant fibres. This stimulation gives the transposed gracilis muscle the properties required to function as an anal sphincter. In the beginning the electrical stimulator was placed several weeks after the initial gracilis muscle transposition, to avoid infections of the electrodes and stimulator. Nowadays, the gracilis transposition and the placement of the implantable pulse generator (IPG) are done at the same time. The operative procedure will be described here.

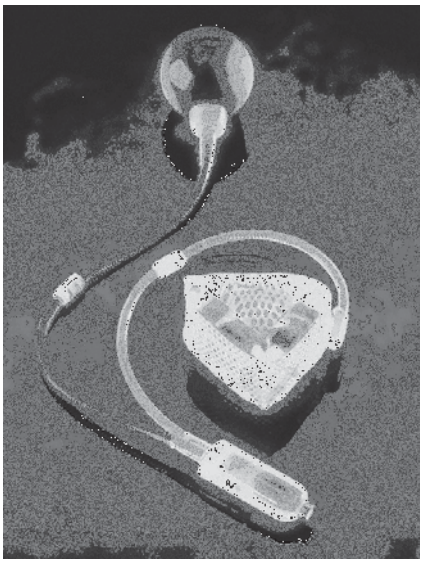
After receiving prophylactic intravenous antibiotic administration, the patient is placed in the lithotomy position. After an incision in the medial side of the upper leg, the gracilis muscle is freed without damaging the neurovascular bundle. A circular tunnel is created around the anus and a subcutaneous connection to the leg was made. The tendon of the muscle is anchored to the ramus inferior of the pubic bone after the wrapping around the anal canal.



The wrapping can be done in three different ways; gamma configuration (first turn anterior and tendon attachment at the contralateral side), epsilon configuration (first turn posterior and contralateral tendon attachment) or in an alpha configuration (ipsilateral tendon attachment). Two intramuscular electrodes (model 4350, Medtronic, USA) are placed close to the insertion of the nerve and subcutaneously tunnelled to a pocket beneath the rectus fascia at the ipsilateral side were the pulse generator (Itrell1, Itrell2, Interstim model 3023, Medtronic, USA) is placed. Telemetry is used to program the IPG. A stimulation protocol of increasing frequency is used during six to eight weeks to change the fatigable muscle to one that can sustain continuous contraction. Patients are able to switch the simulator off and thereby relaxing the muscle, allowing faeces to pass.
The initial results looked very promising.[23] After longer follow-up, this seems to decline to 50% (Melenhorst, submitted). Frequently seen complications are infection, rectal outlet obstruction and pain. Some of these complications can be treated successfully.[24]

Artificial Bowel Sphincter

The first artificial bowel sphincter for faecal incontinence was an urinary prosthesis (AMS 800, AMS) placed by Christiansen in 1987.[25] Modifications had to be made to suit the anal sphincter for the use in patients with faecal incontinence. The ABS implant consists of three parts: an inflatable balloon, a cuff and a pump. The individual components are connected by subcutaneous tubes and filled with an isotonic radiopaque fluid. The cuff is placed around the anus using two lateral incisions. The pump is placed in the labia majora or scrotum, and the pressure-regulating balloon is placed in the cavum Retzii. This pressurised balloon is responsible for the continue squeeze pressure in the cuff around the anus, thereby blocking the faecal contents by closing the anal canal. When the patient feels the need to defecate, the pump is used to deflate the cuff and actively pump the fluid to the balloon. The cuff fills passively after a couple of minutes by the pressure in the balloon. Only limited data on long-term follow-up of a sufficient number of ABS sphincters are available.
There is one multicentre study with disappointing long-term data where the initial data were promising.[26] The anal manometry data of this patient population suggest poor action of the ABS. The authors conclude that the ABS acts as a passive barrier causing a rectal outlet obstruction. The complication rate of the ABS is high and rectal outlet obstruction can be a difficult problem. However, the largest risk of ABS implantation is infection. This can be as high as 25%.[27]



Sacral Nerve Modulation

Sacral Nerve Modulation has been used in patients with urinary dysfunction for more than 20 years.[28] In 1995 Matzel et al.[29] published their results of SNM applied for faecal incontinence. Since then many studies demonstrated the efficacy of SNM for the treatment of faecal incontinence.[30-32]

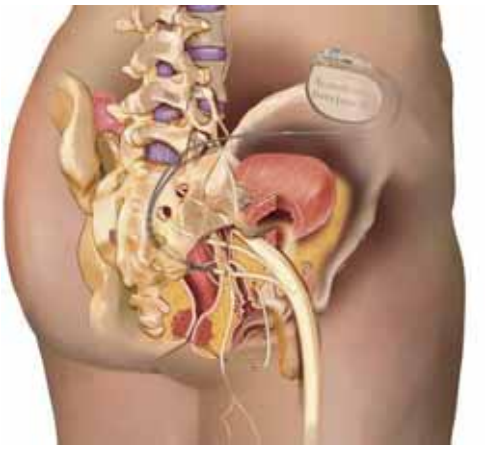
The major advantage of this treatment modality is the opportunity to perform a subchronic test-stimulation to predict the outcome.[33]

After a successful test-stimulation period, a complete system can be implanted. This system consists of an electrode and an implantable pulse generator. The patient is able to switch off the system if necessary by means of a remote control. The parameters of the system can be checked and altered in the outpatient clinic. A special physician-programming device is available.

Initially an intact anal sphincter was a prerequisite for treatment by SNM, but promising results were reported in a small group of patients with a sphincter defect treated by SNM alone.[34]

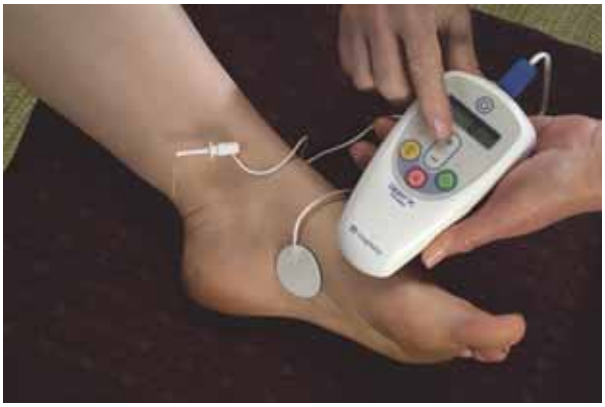
Despite a lot of effort, the working mechanism has still to be elucidated. Initially, there were publications showing an effect on the anal resting and squeeze pressures. Others however were not able to reproduce these data. It was proposed that there was more than a simple efferent motor response. An afferent sensory response could also be responsible for at least a part of the therapeutic action. Rectal sensitivity is also markedly influenced by SNM.[35] Lastly it is hypothesized that SNM alters higher cortical functions and therefore influencing anal continence in a total different matter. An extensive elaboration has been recently published, whereby it is stated that the

mechanism of action of SNM in patients with faecal incontinence almost certainly depends on the modulation of spinal and / or supra spinal afferent inputs.[36]



Peripheral Tibial Nerve Stimulation

Yet another treatment modality for faecal incontinence has its origin in the urological field. Electrical stimulation of the posterior tibial nerve results in stimulation of the sacral plexus from where this nerve arises. A fine needle is percutaneously placed in the vicinity of the posterior tibial nerve. Electrical stimulation causes the hallux to flex as an indication that the positioning of the needle is in the appropriate place. Patients are stimulated in an outpatient stetting. Not much research has been done regarding peripheral nerve stimulation for the treatment of faecal incontinence, but promising results have been published.[37] However a recent double blind randomized controlled trial show no effect on faecal incontinence compared to sham treatment.[38]



Colostomy

The diversion of faeces by the means of a colostomy should be the last surgical therapeutic option given to patients with FI. If any of the earlier mentioned options fail, this could be a way to create pseudo-continence.
The mentioning of the word “stoma” usually brings horrific thoughts to the patient’s minds, however studies assessing the quality of life of patients with a permanent stoma show that the majority of patients are satisfied.[39] This is also due to the increasing quality of stoma material and excellent support of “stoma-nurses”. Therefore, this option should be considered in patients dealing with intractable FI.

Constipation

Introduction

As mentioned before defecation is influenced by several important factors (brain, nerves, colon, rectum and muscles). Problems regarding coordination between these structures can lead to constipation. The definition of constipation is not simple. It can best be described by different objective criteria. These are mentioned in the Rome III criteria for functional bowel disorders (Table 1.1).

Table 1.1 Rome III criteria for functional constipation.

Diagnostic criteria*
1. *Must include 2 or more of the following*
- Straining during at least 25% of defecations
- Lumpy or hard stools in at least 25% of defecations
- Sensation of incomplete evacuation for at least 25% of defecations
- Sensation of anorectal obstruction/blockage for at least 25% of defecations
- Manual manoeuvres to facilitate at least 25% of defecations (e.g., digital evacuation support of the pelvic floor)
-Fewer than three defecations per week
2. Loose stools are hardly present without the use of laxatives
3. Insufficient criteria for irritable bowel syndrome

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

Epidemiology

Based on a recent systematic review, the prevalence of constipation is very variable, ranging from 2.5% to as high as 79%.[40] However, the variability in prevalence can be due to a lack of uniformity in the definition of constipation. When applying the Rome III criteria, the prevalence varies between 11% and 18%. It is present in all age groups and is most commonly seen in women and non-Caucasians. Other symptoms such as bloating and pain can be present. Different subtypes have been distinguished; colonic inertia, outlet obstruction, functional constipation. The outlet obstruction can be caused by pelvic floor dyssynergia, but also by anatomical obstructions such as a rectal prolapse, intussusception, enterocele and/or rectocele, but also by a rectum carcinoma. Thorough investigation is necessary since the treatment of the above-mentioned entities is very different.

Treatment of constipation

Conservative measurements

Since the aetiology is not clearly described the treatment is also not straightforward. Analogue to faecal incontinence the treatment should start with conservative measures. Dietary modifications and medications are started to modify the stool consistency.

Laxatives (bulk, osmotic, stimulant) have all been proven safe and effective in the past. In the recent past, a 5-HT4 receptor agonist, Cisapride, was abandoned from the medical market since it induced fatal arrhythmias. However a recently developed 5-HT4 agonist, Prucalopride, shows good clinical effect without the cardiac problems.[41]

Biofeedback therapy can be effective for constipation. A recent review[42] shows that the symptomatic improvement lies between 44% and 100% in uncontrolled trails. Controlled trails show an efficacy of 70-80%.
Retrograde colonic irrigation, as used for FI, can also be effective in treating constipation. Koch et al.[20] showed that even patients suffering from combined problems (faecal incontinence and constipation) could be helped in this matter.

Surgery

If extensive conservative treatment fails, or constipation is due to significant anatomical abnormalities, surgery may be required. However, this immediately implies the risk of complications off the surgical intervention. Grossly, the surgical options for constipation are divided between two entities; procedures for slow transit constipation (colonic inertia) and evacuation disorders.
In the early 20th century subtotal colectomy for slow transit constipation was firstly described. Segmental colectomy can also be performed, but recurrence rates are higher.[43,44] In this day and age laparoscopic total colectomy and ileorectal anastomosis are becoming the standard of care instead off open procedure.
Knowles et al.[45] performed a systematic review on colectomies. Postoperatively, the median number of bowel movements per day was 2.9. Recurrent constipation developed in 0–33% (median 9%), diarrhoea in 0–46% (median 14%), incontinence in 0–52% (median 14%), and persistent abdominal pain in 0–91% (median 41%). A permanent ileostomy was formed in a median of 5%. However not all the authors showed good results. Riss et al found that 50% of 12 patients were constipated again if one used the Rome II criteria for constipation. The history learns that abdominal pain and bloating are usually not cured by surgery alone.[46]
Surgery for evacuation disorders is a complex matter. Over 200 different operations have been described for the treatment of complete rectal prolapse alone.[47] Results and procedures vary and there is no gold standard for intussusception or rectal prolapse repair. Laparoscopic ventral rectopexy shows promising results, however studies are not randomised and extended follow-up is usually not reported.[48]
In Europe there is a growing interest for the STARR procedure. It involves circumferentially resecting a ring of internally prolapsed rectum using a circular stapling device and ideally results in resection of any redundant rectum and correction of a rectocele if present. Jayne et al. reported the one-year results from the European STARR Registry in 2009.[49] Significant improvements in symptom severity scores and quality of life were seen between baseline and 12 months. Complications occurred in 36.0% and included defecatory urgency (20%), perianal pain (7%). Long terms results from this procedure are still waiting. If all surgical procedures fail a permanent ileostomy after total colectomy can be offered.

Nederlandse introductie

Fecale incontinentie

Introductie

De chirurgische behandeling van fecale incontinentie (FI) heeft de afgelopen 30 jaar een enorme progressie gemaakt. De introductie van de Dynamic Graciloplasty [DGP] door Baeten[1] en tegelijkertijd door Williams[2] heeft een enorme impact op de hele colorectale gemeenschap gehad.
Samen met de Artificial Bowel Sphincter[25] gaf deze ingreep patiënten met fecale incontinentie de kans om hun matig functionerende sluitspier te verbeteren.
Vóór deze periode van chirurgische innovaties was de standaardbehandeling van een defecte sfincter een anal repair. De resultaten van deze procedure zijn echter op lange termijn minder succesvol dan initieel gesteld werd.[3] Ook conservatieve therapie, b.v. constiperende medicatie en (biofeedback) bekkenfysiotherapie gaf niet het succes dat patiënten met ernstige fecale incontinentie nodig hadden. Deze patiënten eindigden vaak met een definitief stoma.
De introductie van Sacrale Nerve Modulation (SNM), ook bekend als Sacrale zenuwstimulatie (SNS), bood een minimaal invasieve procedure met minder morbiditeit om fecale incontinentie te behandelen.[4]
Als spin-off van deze behandelingsmodaliteit leek het ook mogelijk om idiopathische constipatie te behandelen door middel van SNM. Dit proefschrift richt zich op de (chirurgische) behandeling van fecale incontinentie en de behandeling van de idiopathische constipatie door middel van SNM.

Epidemiologie en etiologie van fecale incontinentie

Fecale incontinentie is een veel voorkomend probleem, die 5 tot 10% van volwassenen populatie betreft,[5,6] waarbij 1 tot 2% grote invloed op de dagelijkse activiteiten bemerkt. Het komt vaker voor bij voortschrijdende leeftijd en patiënten met een locomotorische handicap. Het is een aandoening, die bijzonder belastend en maatschappelijk onaanvaardbaar is. Veel patiënten durven geen professionele hulp te zoeken.[7] Het gedeelte van de bevolking dat hulp zoekt, is slechts "het topje van de ijsberg".[8] Fecale incontinentie heeft een negatieve invloed op de lichamelijke en psychische gezondheid, met sociale activiteit beperking in veel gevallen.[9,10]
De etiologie van fecale incontinentie is divers en multifactorieel.[11] Het is een combinatie van sfincterdruk, anorectale sensatie en compliance, rectale opslagfunctie, fecale consistentie en hersenfunctie. Trauma aan het sluitspier complex is een van de meest voorkomende oorzaken van FI. Het kan te wijten zijn aan problemen tijdens de partus[12] of iatrogeen trauma tijdens anale chirurgie.[13,14] Bols et al. toonden aan dat

3de en 4de graad rupturen aanzienlijk bijdragen aan postpartum fecale incontinentie.[15] De anorectale sensatie en compliantie kan aangedaan zijn als gevolg van ontstekingsprocessen, zoals bij de ziekte van Crohn en Colitis Ulcerosa. Een zenuwbeschadiging postpartum kan verminderde gewaarwording van rectale vulling[16] veroorzaken. Een veranderde anorectale opslag functie, zoals ontstaan na een laag anterieure resectie, kan bijdragen aan fecale incontinentie. Chronische inflammatoire darmaandoeningen kunnen verantwoordelijk zijn voor toename van de vloeibaarheid van de feces. Dit kan de " grip" op de feces verminderen en kan leiden tot incontinentie. Neurologische ziekten zoals spina bifida en multiple sclerose kunnen FI veroorzaken.[17] Tevens kunnen problemen van de hersenfunctie, bijv. na cerebrovaculaire accidenten, FI veroorzaken. Bovengenoemde multifactoriële oorzaken maken het moeilijk om het probleem van FI eenvoudig op te lossen. Een holistische benadering is noodzakelijk om elk aspect van de problematiek aan te pakken. Bij voorkeur moet dit plaatsvinden in gespecialiseerde centra, waar toegewijde teams nauw samenwerken. Dergelijke teams bestaan idealiter uit een colorectaal chirurg, gynaecoloog, uroloog, gastro-enteroloog, psychiater en fysiotherapeut.

Behandeling van fecale incontinentie

Conservatief

De eerste stap van de behandeling van FI is niet-chirurgisch. Conservatieve therapie is gericht op dieet interventies, medicatie en bekkenbodem fysiotherapie. Dieet modificatie kan bestaan uit extra vezels en het vermijden van gas producerende groenten. Medicatie (loperamide, codeïne fosfaat) zorgen voor afname van de colon peristaltiek. Galzuur bindende harsen en difenoxylaat kunnen worden toegevoegd om de effectiviteit[18] te vergroten. Bekkenbodem fysiotherapie kan succesvol zijn. Echter een Cochrane review over de effecten van biofeedback en / of bekkenbodem spiertraining voor de behandeling van FI bij volwassenen, toonde slechts aan dat sommige elementen van biofeedback therapie en sluitspier oefeningen een therapeutisch effect hebben.[19] Retrograde darmspoeling moet worden overwogen wanneer andere conservatieve maatregelen niet succesvol zijn. Met behulp van een speciale pomp wordt water transanaal ingebracht om de darm te reinigen om op deze manier een vorm van pseudo- continentie te bewerkstelligen.[20] Alle vormen van conservatieve therapie kunnen later ook een aanvulling zijn op een vorm van chirurgische behandeling.

Chirurgie

Traditioneel werd fecale incontinentie gezien als een probleem van het anale sluitspier complex. Alle therapieën waren gericht op het herstellen van de anatomie van de defecte sluitspier. De anatomie kon goed worden hersteld door direct herstel van de sluitspier door een overlappende sfincterplastiek . Bevredigende resultaten werden bereikt in een tension-free herstel in 47 tot 100% van de gevallen.[21] Resultaten op lange termijn zijn echter veel minder bevredigend.[22]

Dynamische Graciloplasty

De Dynamische Gracilisplastiek werd voor het eerst beschreven in 1988.[1] Bij een patiënt met een anale atresie en een bestaande gracilisspier transpositie, werd een implanteerbare neurostimulator geplaatst om de sfincterfunctie te ondersteunen en de vrijwillige contractie te onderdrukken. Hierna werd de Dynamische Graciloplasty gelijktijdig ontwikkeld op twee onderzoek locaties.[1,2] Met behulp van elektrische stimulatie kunnen type II, vermoeibare, spiervezels worden veranderd in type I, onvermoeibare, vezels. Deze stimulatie geeft de omgezette m. gracilis de gewenste eigenschappen om te functioneren als anale sluitspier. In het begin werd de elektrische stimulator geplaatst enkele weken na de initiële m. gracilis transpositie. Dit werd gedaan om infecties van de elektroden en de stimulator te voorkomen. Tegenwoordig worden de gracilis omzetting en de plaatsing van de implanteerbare pulsegenerator (IPG) op hetzelfde moment gedaan. De operatieve procedure wordt hieronder kort beschreven.

Na toediening van profylactische intraveneuze antibiotica wordt de patiënt geplaatst in de lithotomiepositie. Na een incisie in de mediale zijde van het bovenbeen wordt de m. gracilis vrijgemaakt zonder de neurovasculaire bundel te beschadigen. Er wordt door middel van twee incisies naast de anus een cirkelvormige tunnel gecreëerd rond de anus. Tevens wordt er een subcutane verbinding met het been gemaakt. De pees van de spier wordt verankerd aan de ramus inferior van het schaambeen na het wikkelen rond het anale kanaal.

Dit wikkelen kan op drie verschillende manieren; gamma configuratie (draai eerst anterieur en peesaanhechting aan de contralaterale zijde), epsilon configuratie (draai eerst posterior en contralaterale peesaanhechting) of in een alfa-configuratie (ipsilaterale peesaanhechting). Twee intramusculaire elektroden (model 4350, Medtronic, USA) worden dicht bij de neurovasculaire bundel ingebracht in de spier en subcutaan getunneld naar een ruimte onder in de buik onder de rectus fascia aan de ipsilaterale zijde. Aldaar wordt ook de pulsegenerator (Itrell1, Itrell2, InterStim model 3023, Medtronic, USA) geplaatst. Door middel van telemetrie wordt de IPG geprogrammeerd, zodat er een stimuleringsprotocol van toenemende frequentie gedurende zes tot acht weken kan worden uitgevoerd. De m. gracilis wordt dan

getraind om continue contractie te houden. Patiënten kunnen de simulator zelf in en uit schakelen om ontlasting te laten passeren.
De eerste resultaten waren veelbelovend.[23] Na een langere follow-up, lijkt de effectiviteit te dalen tot 50% (Melenhorst, submitted). Vaak geziene complicaties zijn infectie, “rectal outlet obstructie” en pijn. Sommige van deze complicaties kunnen met succes worden behandeld.[24]

Artificial bowelsphincter

De eerste kunstmatige darmsfincter voor fecale incontinentie was een urinaire prothese (AMS 800, AMS) geplaatst door Christiansen in 1987.[5] Er moesten wijzigingen worden aangebracht in de sfincter, zodat deze gebruikt kon worden bij patiënten met fecale incontinentie. Het ABS implantaat bestaat uit drie delen : een opblaasbare ballon, een anale manchet en een pomp . De afzonderlijke onderdelen zijn verbonden door subcutane buisjes en gevuld met een isotone radio-opake vloeistof. De manchet wordt geplaatst rond de anus door middel van een tweetal incisies naast de anus. De pomp wordt in de grote schaamlippen of het scrotum geplaatst, waarbij de drukregulerende ballon in het cavum Retzii wordt gepositioneerd. Deze druk regulerende ballon is verantwoordelijk voor de knijpkracht in de manchet rond de anus, waardoor de fecale inhoud geblokkeerd wordt. Hierdoor wordt het anale kanaal mechanisch afgesloten. Wanneer de patiënt de behoefte voelt te ontlasten, wordt de pomp gebruikt om de manchet leeg te maken door actief de vloeistof naar de ballon te pompen. De manchet vult zich na een paar minuten door de overdruk in de ballon.
Slechts beperkte gegevens over de lange termijn follow -up van een voldoende aantal ABS implantaten zijn beschikbaar. Er is een multicenter studie met tegenvallende gegevens op lange termijn, terwijl de initiële gegevens veelbelovend waren.[26] De anale manometrie gegevens van deze patiëntenpopulaties suggereren echter een slechte werking van de ABS sfincters. De auteurs concluderen dat de ABS slechts werkt als een passieve barrière en niet als een actieve sfincter. De complicaties ratio van de ABS sfincters is hoog en rectal outlet obstructie kan een moeilijk probleem zijn. De grootste morbiditeit echter van ABS sfincters is postoperatieve infectie. Dit kan oplopen tot 25%.[27]

Sacrale Zenuw Modulatie

Sacrale Zenuw Modulatie (SNM) wordt reeds meer dan 20 jaar gebruikt bij patiënten met urinedysfunctie gedurende.[28] Matzel et al.[29] publiceerden in 1995 voor het eerst hun resultaten van SNM voor patiënten met fecale incontinentie. Sindsdien hebben veel studies de werkzaamheid van SNM voor de behandeling van fecale incontinentie aangetoond.[30-32] Het grote voordeel van SNM is de mogelijkheid om een teststimulatie [Percutane Nerve Evaluation, PNE] uit te voeren om de uitkomst[33] op de langere

termijn te voorspellen. Tegenwoordig wordt de subchronische teststimulatie met een lead met weerhaakjes uitgevoerd; de zogenaamde Tined Lead (Medtronic model 3889).
Na een succesvolle teststimulatie periode kan een compleet systeem worden geïmplanteerd. Dit systeem bestaat uit een elektrode en een implanteerbare pulsegenerator. De patiënt kan het systeem eventueel uit schakelen door middel van een afstandsbediening. De parameters van het systeem kunnen worden gecontroleerd en aangepast op de polikliniek.
Aanvankelijk was een intact anale sluitspier een voorwaarde voor de behandeling met SNM , maar veelbelovende resultaten werden gerapporteerd in een kleine groep patiënten met een sluitspier defect, die direct behandeld waren met SNM.[34]
Ondanks vele wetenschappelijke inspanningen, is het werkingsmechanisme nog steeds niet opgehelderd. Aanvankelijk waren er publicaties die een effect meldden op de anale rust en knijp druk. Anderen waren echter niet in staat om deze gegevens te reproduceren. De hypothese werd naar voren gebracht dat het meer dan een eenvoudige efferente motorische respons zou zijn. Een afferente respons zou ook verantwoordelijk kunnen zijn voor ten minste een deel van de therapeutische actie. Een andere studie toonde aan dat de rectale gevoeligheid ook beïnvloed wordt door continue stimulatie SNM.[35] Ten slotte is de hypothese dat SNM de hogere corticale functies beïnvloedt en dus de anale continentie op een geheel ander manier herstelt. Onlangs is er een publicatie verschenen, waarbij wordt gesteld dat het werkingsmechanisme van SNM bij patiënten met fecale incontinentie te maken heeft met modulatie van het ruggenmerg en spinale afferente inputs.[36]

Perifere Tibiale Zenuwstimulatie

Nog een andere behandelingsmodaliteit voor fecale incontinentie heeft zijn oorsprong in het urologische gebied. Elektrische stimulatie van de posterieure tibialis zenuw resulteert in stimulatie van de sacrale plexus, alwaar de origo van deze zenuw is. Tijdens de Perifere Tibiale Zenuwstimulatie (PTNS) wordt een fijne naald percutaan geplaatst in de nabijheid van de posterieur tibialis zenuw. Elektrische stimulatie veroorzaakt het buigen van de grote teen. Dit is een indicatie dat de plaatsing van de naald op de juiste plaats gepositioneerd is. Vervolgens worden patiënten gestimuleerd in een poliklinische setting voor gedurende een half uur eens in de twee weken. Nog niet veel onderzoek is gedaan naar de perifere zenuwstimulatie voor de behandeling van patiënten met fecale incontinentie, maar veelbelovende resultaten zijn gepubliceerd.[37] Een recent placebo dubbelblind gerandomiseerde studie toont echter aan dat de werking beperkt is.[38]

Colostoma

De laatste chirurgische optie voor patiënten met fecale incontinentie is het aanleggen van een permanent colostoma. Als een van de eerder genoemde mogelijkheden faalt, kan dit een manier zijn om pseudocontinentie te creëren. Echter het noemen van het woord "stoma" heeft voor de meeste patiënten een zeer negatieve bijklank, maar de kwaliteit van leven van patiënten met een permanent stoma blijkt in de meerderheid van de patiënten niet slecht te zijn.[39] Dit is ook dankzij de toenemende kwaliteit van het stomamateriaal en uitstekende ondersteuning van de stomaverpleegkundigen. Deze mogelijkheid moet altijd worden overwogen bij patiënten met FI .

Obstipatie

Introductie

Zoals eerder vermeld wordt defecatie beïnvloedt door een aantal belangrijke factoren (hersenen, zenuwen, colon, rectum en spieren). Problemen met betrekking tot de coördinatie tussen deze structuren kan leiden tot constipatie . De definitie van constipatie is niet eenvoudig. Het kan het beste worden beschreven door verschillende objectieve criteria. Deze zijn vermeld in de Rome III criteria voor functionele darmstoornissen.

Epidemiololgie

Op basis van een recente systematische review, is de prevalentie van obstipatie zeer variabel. Het varieert van 2,5% tot zo hoog als 79%.[40] Echter, de variabiliteit in prevalentie is partieel te wijten aan een gebrek aan uniformiteit in de definitie van constipatie. Bij toepassing van de Rome III criteria, varieert de prevalentie tussen 11 en 18%. Obstipatie komt voor in alle leeftijdsgroepen en wordt het meest gezien bij niet blanke vrouwen. Verschillende subtypen kunnen worden onderscheiden; colon inertie, pelvic outlet obstructie, functionele obstipatie. De pelvic outlet obstructie kan worden veroorzaakt door bekkenbodem dyssynergie, maar ook door anatomische problemen zoals een rectale prolaps, invaginatie, enterocele, rectocele, maar ook door een rectum carcinoom. Grondige anamnese, lichamelijk onderzoek en aanvullend onderzoek is noodzakelijk, omdat de behandeling van de bovengenoemde entiteiten heel anders is.

Behandeling van constipatie

Conservatieve behandeling

Omdat de etiologie niet altijd geheel duidelijk is, is de behandeling ook niet eenvoudig. Analoog aan de behandeling van fecale incontinentie moet er begonnen worden met conservatieve maatregelen. Dieetwijzigingen en medicijnen kunnen gestart worden om de consistentie van de ontlasting te wijzigen. Laxeermiddelen (bulk, osmotische, stimulerende) zijn allemaal veilig en effectief gebleken in het verleden. In het recente verleden is cisapride, een 5-HT4 receptor agonist, verlaten omdat het fatale hart ritmestoornissen veroorzaakte. Maar een recent ontwikkelde 5-HT4 agonist, Prucalopride, toont goede klinische effecten zonder hartproblemen.[4] Biofeedback therapie kan effectief zijn voor constipatie. Een recente publicatie[42] laat zien dat er een symptomatische verbetering is tussen 44% 100%. Retrograde darmspoeling, zoals gebruikt voor FI, kan ook effectief zijn bij de behandeling van obstipatie. Koch et al.[20] toonden aan dat zelfs patiënten die lijden aan gecombineerde problemen (fecale incontinentie en obstipatie) succesvol kunnen worden geholpen met retrograde darmspoelingen.

Chirurgie

Als uitgebreide conservatieve behandeling faalt , of obstipatie is te wijten aan aanzienlijke anatomische afwijkingen, kan een operatie noodzakelijk zijn. Dit impliceert echter onmiddellijk het risico van complicaties na de chirurgische handeling. Grofweg zijn de chirurgische opties voor obstipatie verdeeld tussen twee entiteiten; procedures voor slow transit obstipatie (colon inertie) en evacuatoire aandoeningen. In het begin van de 20e eeuw werd subtotale colectomie voor slow transit obstipatie voor het eerst beschreven. Segmentale colectomie kan ook worden uitgevoerd, maar het recidief percentage is hoger.[43,44] Vandaag de dag wordt de laparoscopische totale colectomie en ileorectale anastomose steeds meer als gouden standaard gezien in vergelijking met de open procedure.
Knowles et al.[45] voerden een systematische review uit. Na de operatie, was het mediane aantal darmbewegingen per dag 2.9. Terugkerende obstipatie ontwikkelde in 0-33% mediaan (9%), diarree bij 0-46% (mediaan 14%), incontinentie bij 0-52% (mediaan 14%), en aanhoudende buikpijn bij 0-91% (mediaan 41%). Een permanent ileostoma werd gevormd in van 5% van de gevallen. Echter niet alle auteurs claimen goede resultaten. Riss et al. vonden dat 50% van de 12 patiënten opnieuw obstipatie had als men de Rome criteria voor obstipatie hanteerde. De geschiedenis leert dat buikpijn en een opgeblazen gevoel meestal niet alleen chirurgisch op te lossen zijn.[46]
Chirurgie voor evacuatie stoornissen is een complexe zaak. Meer dan 200 verschillende procedures zijn beschreven alleen al voor de behandeling van rectale prolaps.[47] Resultaten en procedures variëren en er is geen gouden standaard voor

intussusceptie of rectale prolaps. Laparoscopische ventrale rectopexie geeft hoopvolle resultaten, maar studies zijn niet gerandomiseerd en lange termijn follow-up wordt meestal niet gemeld.[48]

In Europa is er een groeiende belangstelling voor de STARR procedure. Hierbij wordt met een circulair stapler device een resectie uitgevoerd van het overtollige rectum en een correctie uitgevoerd van de aanwezige rectocele.

Jayne et al. publiceerden de postoperatieve resultaten na een jaar uit de Europese STARR-register in 2009.[49] Significante verbeteringen in symptoom scores en kwaliteit van leven werden gezien tussen baseline en 12 maanden. Complicaties traden op bij 36% en omvatten onder andere fecale urgentie (20%) en perianale pijn (7%). Lange termijn resultaten van deze procedure laten nog steeds op zich wachten. Als alle chirurgische procedures gefaald hebben kan een permanent ileostoma na een totale colectomie worden aangeboden.

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Chapter 2

Dynamic Graciloplasty for fecal incontinence. Long term prospective follow-up in a single center

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Submitted

Abstract

Introduction

The Dynamic Graciloplasty (DGP) for fecal incontinence (FI) was first described in 1988. Since then a large cohort of patients has been treated with this procedure. The indication for DGP however is declining, since new, less invasive, techniques have been developed. Our institutions long term results from the DGP have already been published. We had, however, the idea that the results were decreasing in time, therefore we describe the results of the DGP's for faecal incontinence in our institution at this time.

Patient en methods

From November 1986 through January 2012 patients with faecal incontinence treated with DGP were included. All patients had received maximal conservative therapy according to the standards of that time. They have been evaluated with anal manometry, defecography and electromyography. The EMG was later replaced by the PNTML measurement. Endo-anal ultrasound was not done in the beginning, in time this was introduced as a standard examination. Patients were seen at the outpatient clinic on a predefined time path (1,3,6,12 months). After the first year, patients were seen ideally once a year. The continence score (Williams score: 1= continent, 2= incontinent to flatus, 3= incontinent for diarrhoea, 4= incontinent for solids< 5= incontinent to solids), defecation frequency, postponement of defecation, and adverse events were recorded. The IPG settings were noted and the lead impedance was calculated. If the IPG settings had to be changed this was done. The resting pressure (Smin) and stimulation pressure (Smax) was obtained through anal manometry. All the data was stored in a spreadsheet program (Excel, Microsoft, USA). Success was defined as an incontinence score of 1 or 2. Three or more was considered as failure. All data are expressed in means with range. SPSS 16.0 (SPSS inc.) and Microsoft Excel were used for the statistical analysis. A p value of 0.05 or less was regarded as significant. A Cox analysis was performed to identify factors responsible for failure in time.

Results

A total number of 326 patients (75 men) were treated with DGP. 34 patients received a DGP after Abdominal Perineal Resection and were excluded for analysis. A total of 292 patients (62 men) were available for the long-term analysis. Eight (2.5%) patients were deceased by the time of analysis. Nine (2.8%) patients were permanently lost to follow-up and were analysed with the most recent data available. The mean age was 50 (range 12-78) years at the time of surgery. The mean duration of follow-up was 8.3 (0-22.4) years. In this time the mean years of successful continence action was 4.9 years (0-15.9) years. One hundred and forty six (50%) patients had and continence score of 1 or 2 and were considered successful in the long term. The other half was

considered a failure. Of the latter half of the patients, 58 patients used augmentative retrograde colonic irrigation to empty the bowel and 52 patients were converted to a stoma after failure. Age, indication and sex were non-significant factors for failure. The resting pressure (Smin) was also not a significant factor for failure. The pressure on the moment of failure (Sfailure) significantly indicates failure.

Conclusion

DGP is an option to treat FI in seriously malformated anal sphincters due to birth trauma. It should be performed in dedicated institutions, with experience in the surgical treatment of faecal incontinence. The indication to perform a DGP is decreasing, since newer treatment options provide less morbidity and complications. The long-term results are less satisfactory then stated in earlier publications.

Introduction

The common knowledge around the topic faecal incontinence is growing. Whereas twenty years ago the surgical solution to the problem was focused on the sphincter function, nowadays the approach is much more holistic. Anal continence depends on several factors, e.g.: sphincter function, sensibility and compliance of the rectum, consistency of the faeces, peristalsis of the sigmoid colon, pelvic floor muscle and sphincter function. There is also growing evidence of cerebral control pathways.[1] The sphincter function itself may seem of less importance than it was previously assumed.
Until early 2000 all patients with intractable therapy resistant faecal incontinence where treated by means of a Dynamic Graciloplasty (DGP) in our hospital. Around 1999 sacral nerve stimulation was introduced in our institution, which led to a decrease in the number of DGP procedures. However, in the case of a major sphincter defect, such as cloaca-like deformities, the necessity of a sphincter replacing procedure still existed.
The DGP was first described in 1988.[2] In a patient with an anal atresia and an existing gracilis muscle transposition, an implantable neurostimulator was placed to augment sphincter function and overrule voluntary contraction. Hereafter, the Dynamic Graciloplasty was simultaneously developed at two research sites.[3,4] Using electrical stimulation type II, fatigue-prone muscle fibres can be changed into type I, fatigue resistant fibres.[5] This stimulation gives the transposed gracilis muscle the properties required to function as an anal sphincter. In the beginning the electrical stimulator was placed several weeks after the initial gracilis muscle transposition, to avoid infections of the electrodes and stimulator. Nowadays the gracilis transposition and the placement of the implantable pulse generator (IPG) are done at the same time.
A substantial amount of studies have already been published concerning the outcomes of the DGP.6-9 Our institutions long-term results have already been published.[10] We had, however, the idea that the results were decreasing in time, therefore we describe the results of all of the DGP's in our institution at this time.

Patients and Methods

From November 1986 through January 2012 patients with faecal incontinence treated with DGP were included. The aetiology of the incontinence varied. As stated earlier in the approximatey last 10 years, only the patients with more extensive trauma were treated with DGP, since other less invasive therapies were availiable. The largest group of patients is the group where faecal incontinence is related to a traumatic cause e.g. birth trauma. The group in which the DGP procedure is done after an abdominal perineal resection (APR) for rectum carcinoma is a special group of patients. Many of these patients received a double DGP for total perineal reconstruction.[11] We considered these patients not "regular" incontinence patients

and were excluded for functional FU analysis, since failure of the patients also reflected oncological recurrences. We only present them in the Kaplan Meier.
All other patients had received maximal conservative therapy according to the standards of that time. They have been evaluated with anal manometry, defecography and electromyography. The EMG was later replaced by the PNTML measurement. Endo-anal ultrasound was not done in the beginning, in time this was introduced as a standard examination.
Patients, who had a diverting stoma prior to the DGP, retained their stoma until the DGP was successfully trained. This was confirmed by defecography, which is standard performed in all patients after the completion of the muscle-training period. Patients were seen at the outpatient clinic on a predefined time path (1,3,6,12 months).
After the first year patients were seen ideally once a year. The continence score (Williams score: 1= continent, 2 = incontinent to flatus, 3= incontinent for diarrhoea, 4= incontinent for solids< 5= incontinent to solids), defecation frequency, postponement of defecation, and adverse events were recorded. The IPG settings were noted and the lead impedance was calculated. If the IPG settings had to be changed this was done. The resting pressure (Smin) and stimulation pressure (Smax) was obtained through anal manometry.
Patients, who prior were lost to follow-up, were invited to make an outpatient control appointment. If the patient moved to another address, the current address was found by inquiring their general physician. If the patient was not able to physically make an appointment, a questionnaire regarding the current state of DGP performance and history was filled in by telephone. In this manner we were able to trace every patient.
All the data was stored in a spreadsheet program (Excel, Microsoft, USA). Success was defined as an incontinence score of 1 or 2. Three or more was considered as failure.

Statistical analysis

All data are expressed in means with range. SPSS 16.0 (SPSS Inc.) and Microsoft Excel were used for the statistical analysis. A p value of 0.05 or less was regarded as significant. A Cox analysis was performed to identify factors responsible for failure in time.

Procedure

The operative procedure has been extensively described.[12] It will be summarized here. After receiving prophylactic intravenous antibiotic administration, the patients were placed in the lithotomic position. After an incision in the medial side of the upper leg, the gracilis muscle was freed without damaging the neurovascular bundle. A circular tunnel was created around the anus and a subcutaneous connection to the leg was made. The tendon of the muscle was anchored to the ramus inferior of the pubic bone after the wrapping. This wrapping can be done in three different ways; gamma

configuration (first turn anterior and tendon attachment at the contralateral side) epsilon configuration (first turn posterior and contralateral tendon attachmen) or in an alpha configuration (ipsilateral tendon attachment). Two intramuscular electrodes (model 4350, Medtronic, USA) were placed close to the insertion of the nerve and subcutaneously tunnelled to a pocket beneath the rectus fascia at the ipsilateral side were the pulse generator (Itrell1, Itrell2, Interstim model 3023, Medtronic, USA) was placed. Telemetry was used to program the IPG. A stimulation protocol of increasing frequency was used during six-eight weeks to change the fatigable muscle to one that can sustain continuous contraction. At every control visit anal manometry was performed to objectify the generated pressure. The voltage was increased if necessary. Patients themselves are able to switch the simulator off and thereby relaxing the muscle, allowing faeces to pass.

Results

A total number of 326 patients (75 men) were treated with DGP. Of the 34 patients who received a DGP after APR, 15 patients had undergone total perineal reconstruction with double gracilis muscle transposition. Two hundred and ninety two (292) patients (62 men) were available for the long-term analysis, after excluding the DGP after APR patients. Figure 2.1 shows a survival curve of the total patient population. Eight (2.5%) patients were deceased by the time of analysis. Nine (2.8%) patients were permanently lost to follow-up and were analysed with the most recent data available.

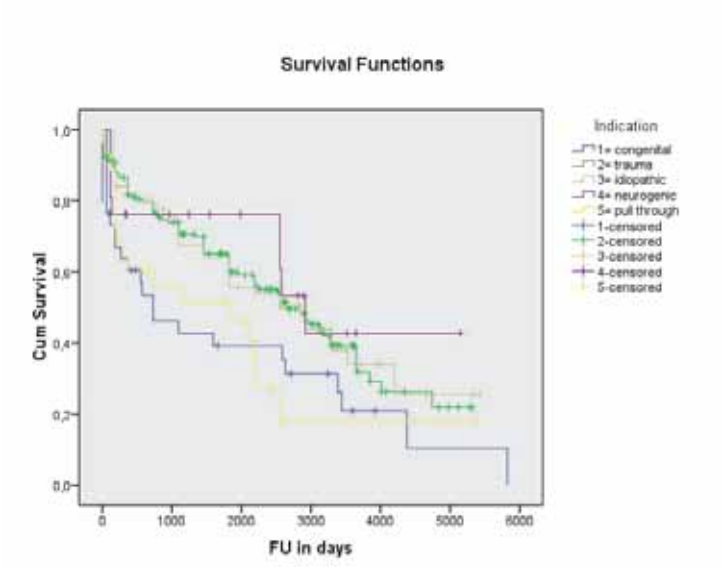

Figure 2.1 Kaplan Meier survival curve of all the DGP patients.

The mean age was 50 (range 12-78) years at the time of surgery. The mean duration of follow-up was 8.3 (0-22.4) years. In this time the mean years of successful continence action was 4.9 years (0-15.9) years.
One hundred and forty six (50%) patients had and continence score of 1 or 2 and were considered successful in the long term. The other half was considered as failures. Of the latter half of the patients, 58 patients used augmentative retrograde colonic irrigation to empty the bowel and 52 patients were converted to a stoma after failure.
Two hundred and fifty two complications occurred. Constipation occurred in 58 (19,9%) patients. Infectious problems occurred in 38 (13%) patients. 35 (11.9%) patients required explantation. 27 (9,2%) patients were permanently explanted. The mean stimulation voltage was at the last FU was 2.1 (0.2-6.5) Volt. This was not significantly different compared to the mean voltage at one year postoperative. The mean lead impedance was 422 (170-4000) Ohm at the last follow-up moment. This was not significantly different tot the values at one year. The initial IPG depleted in 97 patients leading to a mean IPG life 6.3 (0.8-11.9) years. 29 patients required a third IPG and 6 patients a fourth. The mean postoperative resting (Smin) and squeeze (Smax) pressure at the last FU was 68.1 (18-175) and 99.7 (23-333) mm Hg. The latter was significantly increased compared to baseline values ($p<0.01$). Age, indication and sex were no significant factors for failure. The resting pressure (Smin) was also not a significant factor for failure. The pressure on the moment of failure (Sfailure) significantly indicates failure. (Figure 2.2)

Cox analysis

							95,0% CI for Exp(B)	
	B	SE	Wald	df	Sig.	Exp(B)	Lower	Upper
Age	0,001	0,006	0,021	1	0,884	1,001	0,989	1,013
Indication	-0,221	0,131	2,858	1	0,091	0,802	0,621	1,036
M/V	0,018	0,205	0,008	1	0,929	1,018	0,682	1,521
Sfailure	-0,022	0,007	11,469	1	0,001	0,978	0,966	0,991
Smin	0,009	0,005	3,063	1	0,08	1,009	0,999	1,019
Smax	-0,022	0,004	37,175	1	0	0,98	0,972	0,986

Figure 2.2 Cox regression analysis.

Discussion

Since the introduction of the DGP in 1988, a way was found to create a new anal sphincter with the aid of an implantable pulse generator. The technical advancements of that time allowed surgeons to create new functional sphincters, without using the patient's own defective sphincter. This idea of a new sphincter was broadly embraced

by the colorectal surgical community as it provided a “natural” way of augmenting the existing defective sphincter in contrast to the Artificial Bowel Sphincter (ABS, American Medical Systems, Minneapolis, MN, USA), which used silicon material to do the same. Despite the fact that DGP uses the patient’s own gracilis muscle, infections of the leads and IPG’s were the main cause of failure. As the IPG’s and leads are expensive to use, infections were not only a dramatic complication for the patient, but also a costly problem to the health care system. Together with a learning curve of the procedure, this has led to a decreasing interest to use the DGP. Only in specialised colorectal centres it remained a treatment option.

Our results have always been successful, even in the long term. However not all the patients were successful. Patients with congenital anorectal malformations and patients after a low anterior resection were doing worse the patients with sphincter rupture after a birth trauma for example. Since we had the idea that also the obstetric trauma patients were doing worse in time, all the DGP’s have been analysed in this study.

Rongen et al. described an overall success rate of 72%.[13] In this analysis the total success rate was 50%. Patients who use rectal irrigation were considered as a failure, since it was frequently not clear if the patients used the irrigation for constipation and overflow incontinence or primary failure. Rongen did not mention the amount of patients who used rectal irrigation to augment their continence. A DGP can augment the ability to successfully irrigate the bowel, since a bulky sphincter can aid the prevention of leakage of water. However augmentation of rectal irrigation should never be an indication for DGP.

Technical progress has been made and understanding of the multi factorial aspect of the incontinence problem led to different therapeutic interventions. One of the most important ones is Sacral Nerve Modulation (SNM).[14] It’s a promising treatment modality, with also has good results in patients with a sphincter defect. Since its working mechanism is not elucidated to this day, a lot of research has to been done to understand the way of action.

Several studies[15-18] have shown that the action on the anal sphincter is not the most important one. This could be the reason for failure of DGP in congenital incontinence and acquired incontinence after APR, since the rectal function is different compared to a “normal” population.

The multifactor problems that are encountered treating patients with a DGP for faecal incontinence, should be dealt with in specialised centres, understanding the reason for failure of certain treatments and offering alternative treatment options. Since complications could be numerous, patients should be highly motivated and informed accordingly.

To answer the question if there still is a place for DGP in treating faecal incontinence, patient selection is the most important factor. If a patient fails conservative treatment and PNE test stimulation for SNM and not willing to be dependent of incontinence

materials or stoma problems, DGP still is a treatment entity giving 50% success in the long term.

Conclusion

DGP still is an option to treat faecal incontinence. It should be performed in dedicated institutions, capable of treating the complications and offering alternative treatment options. The indication to perform a DGP is decreasing, since newer treatment options provide less morbidity and complications. The long-term results are less satisfactory then one stated in earlier publications, but are overall 50%.

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Chapter 3

The artificial bowel sphincter for faecal incontinence: a single centre study

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Int J Colorectal Dis 2008;23:107-11

Abstract

Background and aims
Faecal incontinence (FI) is a socially devastating problem. The treatment algorithm depends on the aetiology of the problem. Large anal sphincter defects can be treated by sphincter replacement procedures: the Dynamic Graciloplasty and the artificial bowel sphincter (ABS).

Materials and methods
Patients were included between 1997 and 2006. A full preoperative workup was mandatory for all patients. During the follow-up, the Williams incontinence score was used to classify the symptoms, and anal manometry was performed.

Results
Thirty-four patients (25 women) were included, of which, 33 patients received an ABS. The mean follow-up was 17.4 (0.8–106.3) months. The Williams score improved significantly after placement of the ABS ($p<0.0001$). The postoperative anal resting pressure with an empty cuff was not altered ($p=0.89$). The postoperative ABS pressure was significantly higher then the baseline squeeze pressure ($p=0.003$). Seven patients had an infection necessitating explantation. One patient was successfully reimplanted.

Conclusion
The artificial bowel sphincter is an effective treatment for FI in patients with a large anal sphincter defect. Infectious complications are the largest threat necessitating explantation of the device.

Introduction

Faecal incontinence (FI) is a complex problem. The resulting social isolation is a major concern, which results in a reduced quality of life [1]. The real prevalence is unknown, but studies show a higher prevalence than expected [2–5]. Most patients are females with one or more vaginal deliveries in the past. Direct trauma to the anal sphincter complex can give immediate problems or problems later in life [6, 7].
The initial therapy should be conservative, e.g. diet modifications, medication, biofeedback physiotherapy or retrograde irrigation. Surgical intervention is indicated when conservative treatment fails. An anal repair is usually the first choice of treatment for a minor sphincter defect. Satisfactory results are achieved in a tension-free repair in 47–100% of the cases [8]. Long-term results are less satisfying [9]. Sacral nerve modulation (SNM) has proven to be effective for treating faecal incontinence in patients with an intact sphincter complex [10]. Sphincter replacing therapy is indicated in patients with large sphincter defects or completely disrupted sphincters and in case of SNM failure. The sphincter replacement procedures are grossly divided in the Dynamic Graciloplasty (DGP) [11, 12] or the artificial bowel sphincter (ABS). The first artificial bowel sphincter for faecal incontinence was a urinary prosthesis (AMS 800, AMS) placed by Christiansen in 1987 [13]. Modifications had to be made to suit the anal sphincter for use in patients with faecal incontinence.
Until 1997, patients with faecal incontinence due to large anal sphincter defects were treated with DGP in our institution [16]. Since then, the ABS was introduced in our institution for the same indication. Because the operating technique is similar, there was no learning curve to be dealt with. Is this study, the results of the ABS implantations for the treatment of faecal incontinence in a large volume centre are presented.

Materials and Methods

This study is a non-randomised, non-controlled, prospective single-centre study. Thirty-four patients with persisting or recurrent end-stage FI were included between 1997 and
2006.The majority of patients had large (>33% of circumference) anal sphincter defects. A sufficient length of the perineum was a prerequisite for ABS implantation. Previous sphincter replacement surgery was no exclusion criterion for implantation of an ABS. All patients underwent a full preoperative examination consisting of a defaecography, endo-anal ultrasound (SDD 2000, Multiview, Aloka, Japan,
7,5 MHz endo-anal transducer), pudendal nerve terminal motor latency measurement (St Mark's pudendal electrode) and anal manometry using a Konigsberg catheter (Konigsberg Instrument, Pasadena CA, USA) connected to a polygraph (Synectics Medical, Stockholm, Sweden). An Acticon artificial bowel sphincter (ABS, American

Medical Systems, Minneapolis, MN, USA) was used in all patients. The Williams incontinence score was used to classify the symptoms. Anal manometry was routinely performed during the follow-up and used to objectivity ABS function. The follow-up appointments were scheduled at 1, 3, 6, 12 months and annually. Infection necessitating explantation was a primary endpoint. A re-intervention was a secondary endpoint.

The system implantation has been described extensively elsewhere [14, 15], but will be summarised here. The ABS implant consists of three parts: an inflatable balloon, a cuff and a pump. Under strict systemic and local antibiotic prophylaxes, the cuff is placed around the anus using two lateral incisions. The pump is placed in the labia majora or scrotum, and the pressure-regulating balloon is placed in cavum Retzii. Care is taken not to perforate the rectum. If a perforation occurs, the procedure is stopped. After proper wound healing, the patient is eligible for another implantation procedure.

Data are expressed as the mean with the range between parentheses. Data were analysed using the commercially available GraphPad Prism 4.00 software (GraphPad Software, San Diego, USA). The Wilcoxon signed rank test was used for non-parametric paired values. Statistical significance was set at $p<0.05$.

Results

The patient population existed of 25 women and nine men. The aetiology of the faecal incontinence is shown in Table 3.1. Three patients were previously treated with a DGP. The average age was 55.3 (23.8–75.6) years. The mean period of faecal incontinence before the placement of the ABS was 11.0 (1.0–48.0) years. One patient had a rectum perforation during the initial surgery, and placement of the ABS was abandoned. She awaits a second implant attempt. Thirty-three patients were implanted. The mean follow-up was 17.4 (0.8–106.3) months. The mean procedure time was 68.1 min (38.0–105.0). In 24 patients, the length of the cuff was 11 cm, in three patients 10 cm, in two patients 13 cm, in two patients 12 cm, in one patient 14 and in one patient 9. The width of the cuff was in all, but one patient, 2.9 cm. There was one patient with a cuff off 2.0 cm. All patients received a pressure- regulating balloon of 91–100 cm H2O. The mean postoperative hospital stay was 3.5 (2.0–12.0) days. The mean preoperative Williams score of 4.8 (4–5) decreased significantly after ABS placement to 2.1 (1–5; Figure 3.1).

Table 3.1 Aetiology and pervious surgical treatment.

Number	Sex	Etiology	Previous treatment
1	F	Hysterctomy, cervix carcinoma, radiotherapy	
2	M	Anal atresia	DGP
3	F	Two breech deliveries: rupture	Anal repair, SNM
4	F	Episiotomy, hysterctomy	PNE
5	M	Pelvic trauma: urethra/rectum rupture	Repair and colostomy
6	M	Trauma, partial spinal cord lesion	PNE
7	F	Delivery trauma, total rupture, hysterectomy	Anal repair, SNM
8	F	Delivery trauma: rupture	
9	M	Anal atresia	
10	M	Classical hemorroidectomy	
11	F	Episiotomy, hysterctomy	PNE
12	F	Delivery trauma: rupture	Two anal repairs, PNE
13	F	Delivery trauma: total rupture	Two anal repairs
14	F	Delivery trauma: rupture	Anal repair
15	F	Delivery trauma: rupture, cauda syndrome	Anal repair
16	F	Delivery trauma: rupture, hysterctomy	Anal repair
17	F	Delivery trauma: rupture, hysterctomy	Anal repair
18	M	Anal atresia	DGP
19	F	Delivery trauma: rupture	Anal repair
20	F	Delivery trauma: rupture	Pre-/post-anal repair, PNE
21	F	Delivery trauma: rupture, hysterectomy	Anal repair
22	F	Delivery trauma: rupture	Post-anal repair, SNM
22	M	Low anterior resection T2NOM0	
23	F	Delivery trauma: rupture	
24	M	Pelvic crush trauma: urethra/rectum rupture	Repair and colostomy
25	F	Delivery trauma: rupture	
26	F	Delivery trauma: total rupture	12 anal repairs
27	F	Delivery trauma: rupture	Anal repair, colostomy
28	F	Delivery trauma: rupture	Anal repair
29	M	Pelvic trauma	
30	F	Delivery trauma, uterus extirpatie	DGP
31	F	Delivery trauma	PNE
32	F	Classical hemorroidectomy	SECCA
33	F	Delivery trauma, total rupture	Anal repair, Thiersch wire
34	F	Delivery trauma, hysterectomy	PNE

F= female, M=male, DGP=dynamic graciloplasty, SNM=sacral neuromodulation, PNE=percutaneous nerve evaluation.

The mean preoperative anal resting pressure was 58.1 (17.0–128.0) mmHg. This was not significantly altered after implantation (60.3 (21.0–93.0 mmHg; p=0.89). The mean preoperative squeeze pressure was 80.1(25.0–149.0) mmHg, which increased to 120.5 (65.0–154.0) mmHg after implantation (p=0.003; Figure 3.2).

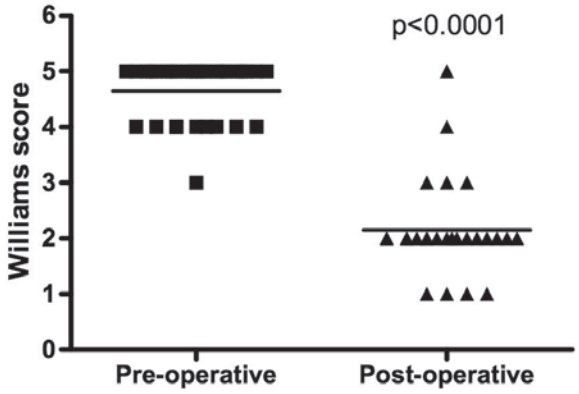

Figure 3.1 Mean pre- and postoperaive Williams score (1=continent, 2=incontonent to flatus, 3=incontinent to liquid stool, 4=occasional incontinence to normal stool <1, 5=fully incontinent).

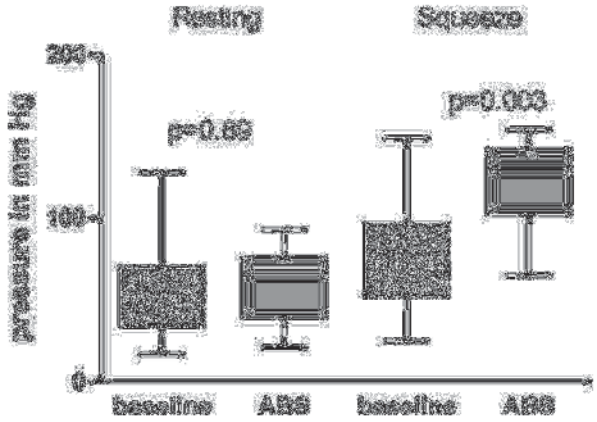

Figure 3.2 Baseline resting pressure versus deflated ABS pressure and baseline squeeze pressure versus inflated ABS pressure pre- and postoperatively (at last follow-up).

Thirteen patients (39%) complained about a rectal evacuation problem. In 12 patients, this could be managed conservatively. One patient had a revision of the system with placement of a wider anal cuff. Seven patients (21.2%) had an infection of the system, which led to seven explantations. One of these patients has been implanted successfully with a new ABS (Figure 3.3). In one patient, the ABS was successfully converted to a Dynamic Graciloplasty. In two patients, a colostomy was performed. The other three patients had no other interventions. One patient was explanted due

to persisting perianal pain without an infection. She received a colostomy. Twenty-six reinterventions (including explantations) had to be performed. This means 0.79 reintervention per implanted patient.

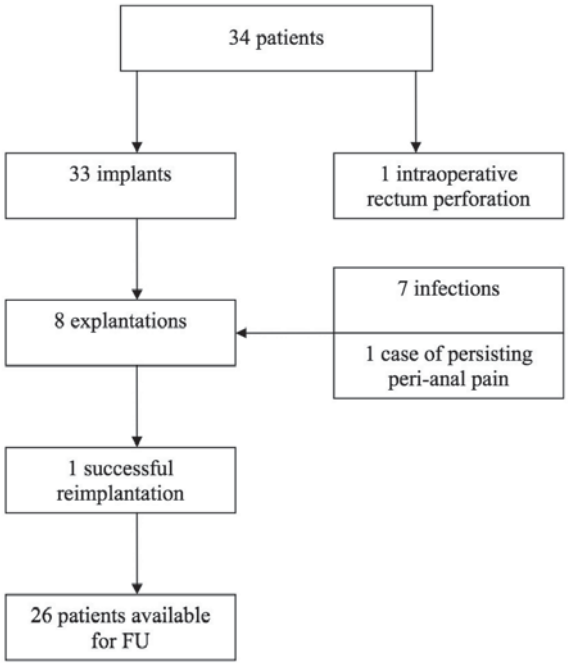

Figure 3.3 Flow chart of implanted parients.

Discussion

There is a large experience in our institution with the DGP.[16] However, since 1997, the ABS is also performed in our institution for the same area of indications as the DGP. When a patient qualifies for a sphincter replacement procedure, he or she can decide whether an ABS or DGP will be performed. Nonetheless, sufficient perineal length is a prerequisite for ABS implantation in a female patient. We believe that the risk for late erosion of the ABS is higher in the case of severe, cloaca-like malformations of the perineum. In these cases, a DGP is the preferred procedure. All patients in this study had an adequate perineal length.

In the beginning, the initial infection rate of the DGP was a problem, but improved as a result of technical modifications and the introduction of systemic and local antibiotic prophylaxis. The same prophylaxis protocol was used for the implantation of ABS. However, despite meticulous application of the antimicrobial protocol, the infection

rate of the ABS implantations in our patient population remains high and is comparable with other series.[14,15] We believe that this infection rate is likely to remain a serious problem in every attempt to place a corpus alienum around the anus through peri-anal incisions.

To overcome this problem of infection, Finlay et al.[17] have developed a new prosthetic sphincter, which is placed above the pelvic floor musculature by means of a laparotomy. It was hypothesised that this sphincter will function as a new puborectal sling in this position. Till now, 12 patients are implanted. Infectious complications, how- ever, occurred in three patients (25%), with subsequent removal of the system. Technical problems occurred in five of the nine remaining patients during follow-up. Technical failure is also one of the main problems of the ABS. Twelve of our patients had some sort of technical failure. This is also known from other studies concerning the ABS.[18] Only limited data on long-term follow-up of a sufficient number of ABS sphincters are available. There is one multicentre study with disappointing long-term data where the initial data were promising.[19] The anal manometry data of this patient population suggest poor action of the ABS. The authors conclude that the ABS acts as a passive barrier causing a rectal outlet obstruction. Our manometry data contradict with this conclusion. We strongly believe that the ABS acts as an active sphincter. In our experience, the patients need to deflate the anal cuff to defecate. Nevertheless, constipation can be a problem. Thirteen of our patients complained about constipation. This could be solved in the majority of patients by conservative means. One patient needed a wider anal cuff to treat an outlet obstruction.

The indications for sphincter replacement surgery are decreasing in our institution since the introduction of SNM. The relative numbers of DGPs and ABSs decreased, while the number of SNM has increased. This implicates that ABS and DGP are reserved for the more severe complicated cases of faecal incontinence. A higher complication rate is therefore expected. However, the placement of an ABS remains an alternative to a colostomy in the well-informed and motivated patient even if a DGP has failed.

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Chapter 4

Sacral neuromodulation in patients with faecal incontinence: results of the first 100 permanent implantations

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Abstract

Objective

Faecal incontinence (FI) is a socially devastating problem. Sacral nerve modulation (SNM) has proven its place in the treatment of patients with FI. In this study, the first 100 definitive SNM implants in a single centre have been evaluated prospectively.

Methods

Patients treated between March 2000 and May 2005 were included. Faecal incontinence was defined as at least one episode of involuntary faecal loss per week confirmed by a 3-week bowel habit diary. Patients were eligible for implantation of a permanent SNM when showing at least a 50% reduction in incontinence episodes or days during ambulatory test stimulation. Preoperative workup consisted of an X-defaecography, pudendal nerve terminal motor latency measurement, endo-anal ultra- sound and anal manometry. The follow-up visits for the permanent implanted patients were scheduled at 1, 3, 6 and 12 months and annually thereafter. The bowel habit diary and anal manometry were repeated postoperatively during the follow-up visits.

Results

A total of 134 patients were included and received a subchronic test stimulation. One hundred patients (74.6%) had a positive test stimulation and received a definitive SNM implantation. The permanent implantation group consisted of 89 women and 11 men. The mean age was 55 years (range 26–75). The mean follow-up was 25.5 months (range 2.5–63.2). The mean number of incontinence episodes decreased significantly during the test stimulation (baseline, 31.3; test, 4.4; $p<0.0001$) and at follow-up (36 months postoperatively, 4.8; $p<0.0001$). There was no significant change in the mean anal resting pressure. The squeeze pressures were significantly higher at 6 months (109.8 mmHg; $p=0.03$), 12 months (114.1 mmHg; $p=0.02$) and 24 months postoperatively (113.5 mmHg; $p=0.007$). The first sensation, urge and maximum tolerable volume did not change significantly. Twenty-one patients were considered late failures and received further treatment.

Conclusion

Sacral neuromodulation is an effective treatment for FI. The medium-term results were satisfying.

Introduction

Sacral nerve modulation (SNM) has earned its place in the treatment algorithm for faecal incontinence (FI). Since the first publication by Matzel et al.[1], many others have reported good results.[2–5] Conservative treatment, including drugs, constipating diet and biofeedback physiotherapy, remains the first-line treatment. Surgical treatment becomes an option when conservative treatment fails. Patients with large sphincter defects are suitable for sphincter repair or sphincter replacement including dynamic graciloplasty or an artificial bowel sphincter. Sacral nerve modulation is indicated in patients with an intact anal sphincter with or without a previous anal sphincter repair.[5] We report the results of the first 100 definitive SNM implants in patients with FI carried out in a single centre. This is a follow-up report of a previously published article.[4]

Methods

In a prospective single-centre study, patients with FI aged 18–75 years were included between March 2000 and May 2005. Conservative treatment had failed in all patients. An intact anal sphincter confirmed by endo-anal ultrasound with or without a previous anal sphincter repair was a prerequisite for SNM. The exclusion criteria are listed in Table 4.1.

Table 4.1 Exclusion criteria for sacral nerve medulation.

Congenital anorectal malformation
Previous rectal surgery (rectopexy and rectal resection), within last 12 months
Previous/present external rectal prolapse
Chronic inflammatory bosel disease
Chronic diarrhoea, unmanageable by drugs or diet
Severe constipation
Stoma
Neurological disease, diabetic neuropathy, Parkinson's disease, multiple sclerosi
Bleeding complications
Pregnancy
Anatomical limitations preventing placement of an electrode
Skin and perineal disease with the risk of infection
Psychiatric or physical inability to comply with the study protocol

All patients gave their informed consent. Faecal incontinence was defined as at least one episode of involuntary faecal loss per week. This was confirmed by a bowel habit diary. All patients underwent a full preoperative workup including defaecography, endo-anal ultrasound (SSD 2000, Multiview, Aloka, Japan 7.5 MHz endo-anal transducer), pudendal nerve terminal motor latency measurement (St Mark's pudendal electrode, Medtronic, Skovlunde, Denmark) and anal manometry using a

Konigsberg catheter (Konigsberg Instrument Inc., Pasadena, California, USA) connected to a polygraph (Synectics Medical, Stockholm, Sweden). The sensation, urge and maximum tolerated volumes were assessed using an inflatable rectal balloon. The technique for SNM has been described previously in detail.[1] Electrodes were placed under local anaesthesia at the S3 or S4 foramen based on the best sensory or motor response during peripheral neural evaluation (PNE). A conventional X-ray confirmed the position of the electrode after the procedure. The patients completed a bowel habit diary during the ambulatory stimulation period of 3 weeks. The patients were eligible for a definitive SNM implant when a reduction of at least 50% of incontinence episodes or days with incontinence episodes or days with incontinence was observed. Follow-up visits for patients having a permanent implant were scheduled at 1, 3, 6 and 12 months and annually thereafter. Statistical analysis was performed using Student's t-test or the Wilcoxon signed-rank test for nonparametric samples in SPSS 13.0 (SPSS, Chicago, Illinois, USA). Data are shown as the mean value with the range or with the standard error of mean (SEM) when stated. Statistical significance was set at $p<0.05$.

Results

One hundred and thirty-four patients (117 women) were included and underwent PNE testing with a subchronic period of 3 weeks. The mean age was 56 years (range 26-75). The mean preoperative period of FI was 9.1 years (range 0.5–43). The aetiology of the incontinence is shown in Table 4.2. One hundred patients proceeded to a permanent SNM implant [46, S3 right side; 33, S3 left side; 13, S4 right side; 11, S4 left side (including three bilateral implants)] giving a PNE success rate of 74.6%. The mean follow-up was 25.5 months (range 2.5–63.2). The SNM was set at a pulse width of 210 ms and a frequency of 16 Hz. During follow-up, it was sometimes necessary to alter the polarity of the electrodes. Patients were able to change the amplitude with a programmer. The mean number of incontinent episodes per 3 weeks decreased significantly from 31.3 (3.0–142.0) at baseline to 4.4 (0.0–31.0) during the testing period ($p<0.0001$). This remained stable at 4.5 (0.0–20.0) at 36 months ($p<0.0001$) (Figure 4.1).

Table 4.2 Results of the peripheral neural ecaluation related to the aetiology of faecal incontinence.

	Improvement in continence		
Origin	>50%	<50%	Total
Idiopathic (including hysterectomy)	40 (77)	12	52
Rupture or episiotomy	38 (76)	12	50
Anal repair	14 (78)	4	18
Neurologic injury	8 (73(	3	11
Low anterior resection	0 (0)	3	3
Total	100 (75)	34 (25)	134 (100)

Values in brackets are percentages.

The mean number of days with an episode of incontinence per 3 weeks also decreased significantly from 12.7 (2.0–21.0) at baseline to 3.3 at 36 months (0.0–13.0; p<0.0001) (Figure 4.2).

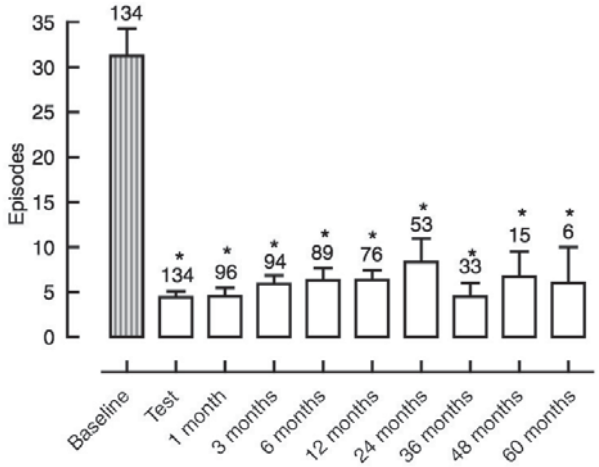

Figure 4.1 Incontinence episodes per three weeks (SEM). *bStatistically significant compared with baseline value. Numbers represented number of patients at follow-up.

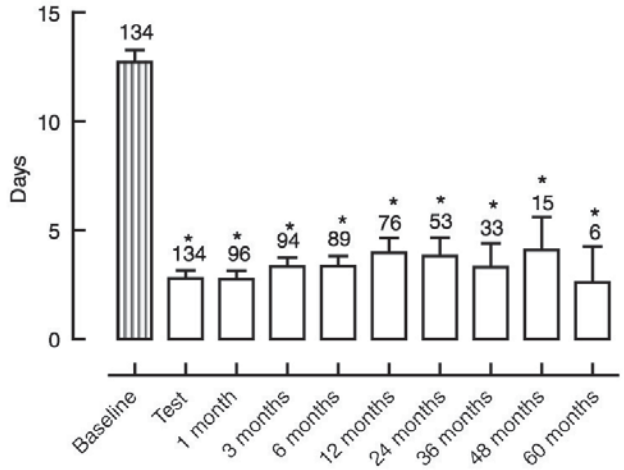

Figure 4.2 Days with an incontinent episode per three weeks (SEM). * Statistically significant compared with baseline value. Numbers represent number of patients at follow-up.

Anal manometry showed no significant alteration in mean resting pressure during stimulation (Figure 4.3). The mean squeeze pressure was significantly higher at 6, 12 and 24 months (109.8 mmHg, p=0.03; 114.1 mmHg, p=0.02; 113.5 mmHg, p=0.007) (Figure 4.4).

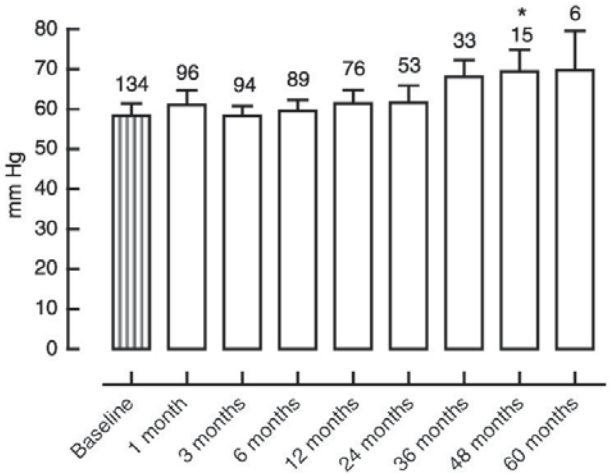

Figure 4.3 Resting anal pressure (SEM). * Statistically significant compared with baseline value. Numbers represent number of patients at follow-up.

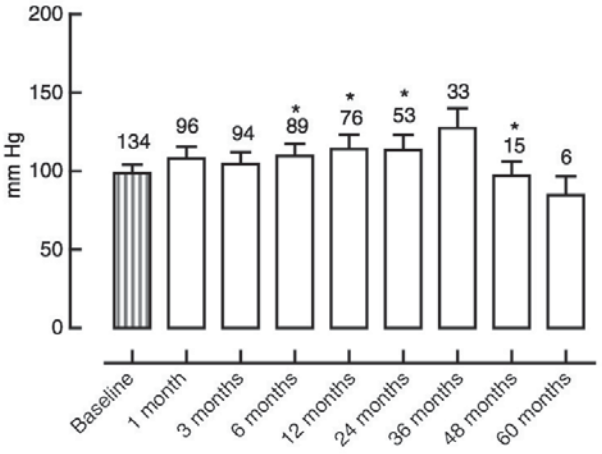

Figure 4.4 Anal squeeze anal pressure (SEM). * Statistically significant compared with baseline value. Numbers represent number of patients at follow-up.

The sensation, urge and maximum tolerable volume did not change significantly during the first year of stimulation (Table 4.3). The stimulation amplitude used during follow-up is shown in Table 4.4.

Table 4.3 Rectal volumes (ml) on balloon testing.

	Baseline	12 months	p-value
Sensation volume	50.4 (10-200)	32.2 (10-110)	0.28
Urge volume	107.2 (20-400)	75.0 (30-225)	0.39
Maximum tolerable volume	174.5 (35-400)	141.2 (60-300)	0.73

Table 4.4 Stimulation amplitude during follow-up.

	1 month	3 months	6 months	12 months	24 months	36 months	48 months
Amplitude (mV)	1.9 (0.1-3.0)	2.2 (0.1-4.6)	2.1 (0.1-4.6)	2.2 (0.4-5.8)	2.6 (0.6-6.0)	2.4 (0.4-4.9)	2.1 1.0-3.8)

Failures

Twenty-one patients (19 women) were considered late failures (Figure 4.5). There was no evidence of lead migration or breakage. The average age of these patients was 57 years (range 41–75). The mean time to definitive failure was 13.6 months (range 3–42.4).

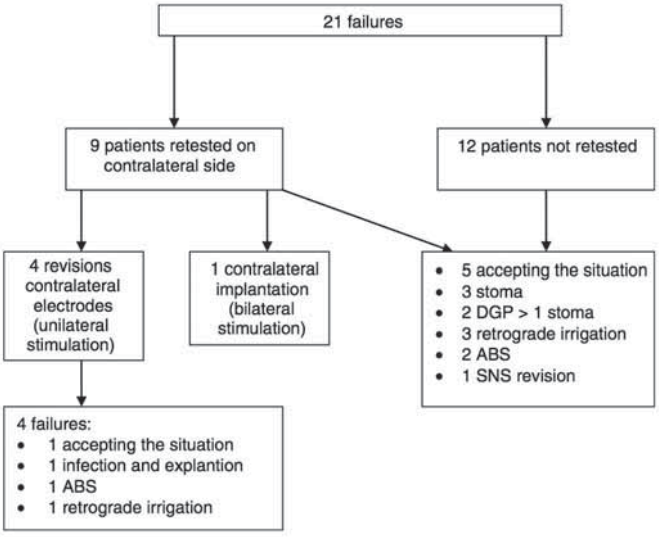

Figure 4.5 Flow chart of the late sacral nerve modulation failure. ABS=artificial bowel sphincter, DGP=dynamic graciloplasty.

The criteria for failure included relapse of symptoms to <50% improvement from baseline symptoms, implementation of another therapy for FI and patient dissatisfaction. One patient was treated for a suspected lead migration. This was, however, not confirmed by X-ray. She failed after an apparently technically successful intervention. All patients continued to feel the effects of stimulation in the anal polarity switching was tried several times in an attempt to regain effectiveness of SNM. Nine patients were retested with a new PNE applied to the contralateral side. Four of these patients received a new permanent electrode at the contralateral side. One patient received a second implant at the contralateral side. Currently, this patient is stimulated bilaterally with a fair result. The other revised patients eventually failed. All the other patients who failed without revision received further treatment as shown in Figure 4.5.

Discussion

Analogous to the treatment of urological symptoms including frequency, urinary urge incontinence and retention, the indications for SNM in the field of defaecation disorders have broadened. Constipation has been treated with promising initial results.[6,7] Early publications in the field of FI included patients with an intact anal sphincter, but recent studies show promising results in patients with an anal sphincter defect.[8,9] A major advantage of SNM is the opportunity to perform a test stimulation (PNE) to predict the outcome of a permanent SNM implant. About a quarter of patients (34/134) in our study showed <50% improvement in baseline symptoms and were not treated with a permanent SNM. The failure rate of PNE is similar to our previous report.[4] It is difficult to predict the success for an individual patient, and an analysis of possible predictive factors for a successful PNE (success rate 40.3%) in treating urinary symptoms concluded that the result of the test simulation itself remained the most valuable predictor of outcome.[10]

As the exact mechanism of SNM is not clear, the type of patient who will benefit most cannot be predicted. This means that the PNE period is essential to identify the patient suitable for SNM implantation.

There is controversy regarding the effect of SNM on anal sphincter pressures. Some studies[3,11,12] have shown an increase in both resting and squeeze pressures, while others[1,13,14] have only demonstrated an increase in squeeze pressure or no increase at all.[4,15] The results between the different research groups are often no comparable because the stimulation settings and method of measurement are not standardized. The manometric results of this study cannot clarify this problem as the squeeze pressure was significantly increased on some follow-up visits and not others.

In the past, the pathophysiology of FI has focussed on anal sphincter dysfunction and anal continence was mainly achieved by restoration of the anal sphincter

function. Nowadays, it is believed that continence is not only achieved by adequate sphincter function, but is also the result of alterations of rectal sensation, colonic and rectal motor activity, consistency of the stools and brain function. The nerve control of continence is regulated by close interaction of the autonomic and somatic nerve systems. It is generally assumed that the spinal reflex arc is modulated by supraspinal centres, as defaecation can be postponed if the time and place are not appropriate. Patients with a spinal cord lesion may experience difficulty in evacuation and continence.[16] It is also known that anorectal function is disturbed in patients with a complete supraconal spinal cord lesion. The basal anal pressure due to involuntary contraction of the internal anal sphincter is not altered but voluntary contraction of the external anal sphincter is abolished. Rectal sensation during rectal distension is absent in patients with a complete spinal cord lesion.[17]

Hobday et al.[18] were able to show the cortical processing of anorectal sensation by functional magnetic resonance imaging. These data suggest supraspinal control of anorectal function. A recent study showed changes in brain activity following SNM for patients with urinary retention. It was suggested that SNM restored the brain activity to the level of normal healthy subjects.[19] It is likely that SNM for FI produces the same intracerebral function changes. This may explain why SNM can also be successful in patients with FI who have an anal sphincter defect.[8,9] Further studies are, however, necessary to assess this hypothesis.

Twenty-one patients (21%) in the present study were considered late failures. The reason for these is not known. The patients still felt the stimulation in the perineal area. Several reprogramming sessions did not result in the same success as the initial PNE. During the reprogramming sessions the electrode configuration was changed. The frequency or pulse/width was not changed as the initial positive test stimulation was done with a fixed frequency and pulse/width setting.

In patients who appear to be failing, it is worthwhile performing a contralateral test stimulation. This offers the opportunity to do a subchronic test stimulation on the contralateral side and it also allows bilateral stimulation. When the contralateral test stimulation alone is successful, a second permanent lead can be inserted. The 'old' implantable neurostimulator can be reused. A second neurostimulator and lead have to be placed if bilateral stimulation offers success.

Studies of SNM for urological disorders show that the therapeutic response wears off in a number of patients during follow-up. Voskuilen et al. [20] published a series of 149 patients with urinary dysfunction treated by SNM, of whom 49 (32.9%) had an inadequate response to permanent implantation. In 18 explantations, it was necessary to remove the device. Analysis of the failures did not show any particular characteristics predisposing to failure. In our own study, no prognostic patient characteristics for failure were identified. False positive results may occur during the PNE phase and such when given a permanent implant may fail. The patient

should be encouraged to be as active as possible during the test period. Those who stay at home close to the toilet may deliver a false positive result leading to a permanent implant, which then fails.

Conclusion

Sacral neuromodulation is an effective treatment for FI with an overall success rate of 79% for patients undergoing a permanent implant. The medium term results are promising. Some patients will fail in the long term, the reasons for which we have not explained at present. Further neurophysiological research is necessary to understand the mechanisms of SNM.

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Chapter 5

Is a morphologically intact anal sphincter necessary for success with sacral nerve modulation in patients with faecal incontinence?

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Colorectal Dis 2008;10:257-62

Abstract

Objective

Sacral nerve modulation (SNM) for the treatment of faecal incontinence was originally performed in patients with an intact anal sphincter or after repair of a sphincter defect. There is evidence that SNM can be performed in patients with faecal incontinence and an anal sphincter defect.

Method

Two groups of patients were analysed retrospectively to determine whether SNM is as effective in patients with faecal incontinence associated with an anal sphincter defect as in those with a morphologically intact anal sphincter following anal repair (AR). Patients in group A had an AR resulting in an intact anal sphincter. Group B included patients with a sphincter defect which was not primarily repaired. Both groups underwent SNM. All patients had undergone a test stimulation percutaneous nerve evaluation (PNE) followed by a subchronic test over 3 weeks. If the PNE was successful, a permanent SNM electrode was implanted. Follow-up visits for the successfully permanent implanted patients were scheduled at 1, 3, 6 and 12 months and annually thereafter.

Results

Group A consisted of 20 (19 women) patients. Eighteen (90%) had a positive subchronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. Group B consisted of 20 women. The size of the defect in the anal sphincter varied between 17% and 33% of the anal circumference. Fourteen (70%) had a positive subchronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. In both groups, the mean number of incontinence episodes decreased significantly with SNM (test vs. baseline: $p=0.0001$, $p=0.0002$). There was no significant difference in resting and squeeze pressures during SNM in group A, but in group B squeeze pressure had increased significantly at 24 months. Comparison of patient characteristics and outcome between groups A and B revealed no statistical differences.

Conclusion

A morphologically intact anal sphincter is not a prerequisite for success in the treatment of faecal incontinence with SNM. An anal sphincter defect of <33% of the circumference can be effectively treated primarily with SNM without repair.

Introduction

The incidence of faecal incontinence is probably underestimated. Daily or weekly involuntary loss of liquid or solid stool occurs in about 2% of the adult population and in about 7% of healthy adults aged over 65 years. Few patients report incontinence of faeces spontaneously and they have often suffered several years before the first presentation.[1–4]

Faecal continence depends on several factors including intact anorectal sensation, motor innervation and an anatomically intact sphincter complex.[5] It mainly affects women after childbirth. Pudendal nerve damage and⁄or damage to the anal sphincter is thought to be the main cause of faecal incontinence.[6,7]. Surgical treatment is an option when conservative treatment, such as dietary modification, anti-diarrhoeal agents, colonic lavage and biofeedback fails. Patients with a sphincter defect are usually treated by an overlapping sphincteroplasty with satisfactory short-term results in 47–100% of the cases[8], but long-term results are less satisfactory after repair of a defect[9] or after total pelvic repair and postanal repair in patients with no structural defects.[8,10]

Sacral nerve modulation (SNM) has been used in patients with urinary dysfunction for more than 15 years.[11] In 1995, Matzel et al.[12] published their results of SNM applied to faecal incontinence. Since then, many studies demonstrated the efficacy of SNM for the treatment of faecal incontinence.[13–15]

Hitherto, an intact anal sphincter ring was a prerequisite for treatment by SNM, but promising results were reported in a small group of patients with a sphincter defect treated by SNM alone.[16] In this study, the results of SNM for the treatment of faecal incontinence in patients with and without an anal sphincter defect were compared.

Methods

Forty patients with faecal incontinence treated by SNM between 2000 and 2005 were included in the study. Two groups of patients were compared retrospectively. Patients in group A had initially undergone an anal repair (AR) to create an intact anal ring, but despite this they continued to be incontinent. Group B included patients with faecal incontinence associated with an anal sphincter defect, who were treated by SNM alone. Data were prospectively collected and all patients underwent full preoperative investigation including defaecography, endo-anal ultrasound (SDD 2000; Multiview, Aloka, Japan; 7.5 MHz endo-anal transducer), measurement of pudendal nerve terminal motor latency (PNTML) (St Mark's pudendal electrode) and anal manometry using a Konigsberg-catheter (Konigsberg Instrument Inc. Pasadena, California, USA) connected to a polygraph (Synectics Medical, Stockholm, Sweden). The sensation, urge and maximum tolerated volumes were assessed using an inflatable balloon.

Patients with a baseline bowel habit diary showing more than one incontinence episode per week were included. The exclusion criteria are shown in Table 5.1.

Table 5.1 Exclusion criteria for sacral nerve medulation.

1.	Congenital anorectal malformation
2.	Previous rectal surgery (rectopexy and rectal resection)
3.	Previous/present external rectal prolapse
4.	Chronic inflammatory bosel disease
5.	Chronic diarrhoea, unmanageable by drugs or diet
6.	Severe constipation
7.	Stoma
8.	Neurological disease, diabetic neuropathy, Parkinson's disease, multiple sclerosi
9.	Bleeding complications
10.	Pregnancy
11.	Anatomical limitations preventing placement of an electrode
12.	Skin and tissue disease with the risk of infection
13.	Psychiatric or physical inability to comply with the study protocol

The test stimulation (PNE) followed by a subchronic test during 3 weeks and definitive SNM implantation were performed as previously described.[17] The settings used during the screening and follow-up of the implant were a pulse width of 210 ms and a frequency of 16 Hz. The patients themselves were able to adjust the voltage to the level of sensory response in a pre-set range. The position of the PNE and definitive electrodes was confirmed by X-ray after the procedure. The main criterion to proceed to a permanent implant was a 50% or more decrease in the number of incontinence episodes or days.

Follow-up after the permanent implantation was scheduled at 1, 3, 6 and 12 months and annually thereafter. The bowel habit diary was collected and anorectal function tests were performed. Failure was defined as return of symptoms to baseline values. A study flow chart is presented in Figure 5.1.

Data were analysed using the paired-samples t-test or Wilcoxon signed rank test for nonparametric samples in SPSS 13.0 (SPSS, Chicago, Illinois, USA). Results are presented as mean values with standard deviation or range. Statistical significance was set at $p<0.05$.

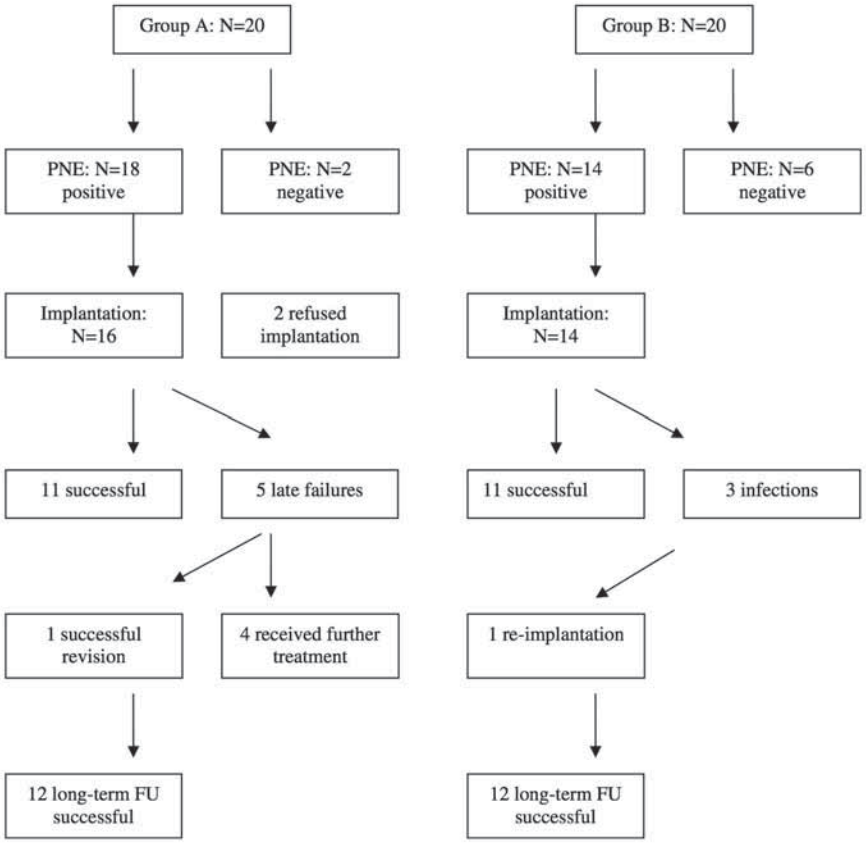

Figure 5.1 Study flow chart.

Results

There were 20 patients in group A and 20 in group B. Five (33%) patients in group B had had an unsuccessful AR with a persisting sphincter defect demonstrated on physical examination and endo-anal ultrasound. The groups were comparable regarding sex, age and duration of incontinence (Table 5.2).

Table 5.2 Patient characteristics.

	Group A	Group B	p-value
Characteristics			
Age (years)	55.8 (39.5-78.6)	52.1 (30.7-74.1)	0.35
Years of incontinence	13.8 (3.0-43.0)	7.9 (1.0-47.0)	0.08
Women/men	19/1	20/0	
Follow-up (months)	29.2 (6.5-60.0)	22.6 (4-41.9)	0.36 (Mann-Whitney)

Data were expressed as the mean value with range.

Group A

The median follow-up period was 29.2 months (range 6.5–60.0) and the median period between the last AR and the PNE was 3 years (range 1–20). All had an intact anal sphincter determined by endo-anal ultrasound. Twelve patients had a pudendopathy (PNTML>2.4 ms), which was bilateral in nine [mean latency times were 2.7 ms (range 1.4–4.8) and 2.6 ms (range 1.7–4.6) on right and left sides respectively]. Eighteen (90%) patients had a successful PNE and 16 underwent a definitive implantation (two patients who would have been suitable declined). Five (31.3%) of the 16 patients were considered late failures and received further treatment, which included a permanent electrode at the contra-lateral side in one patient. One patient died of an unrelated cause. The mean number of baseline incontinence days during 3 weeks of 11.8±5.4 was significantly reduced to 2.5±2.7 ($p<0.001$) during the test stimulation. At 24 months, the effect remained stable at 4.9±6.9 ($p=0.02$) incontinence days (Table 5.3). The mean number of incontinence episodes during 3 weeks also decreased significantly after test stimulation. The effect was sustained during follow-up [baseline: 26.6±21.1, test: 4.8±8.1, (test vs. baseline: $p=0.0001$), 24 months: 12.5±19.7, (24 months vs. baseline: $p=0.001$), (Figure 5.2). There was a significant increase in the time of deferment of defaecation, which was sustained during follow-up (Table 5.3).

Table 5.3 Incontinence days/3 weeks, urgency (minutes) and voltage.

	Baseline	24 months	p-value
Group A			
Incontinence days/3weeks (±SD)	11.8 (5.4)	4.9 (6.9)	0.02
Urgency (min) (±SD)	2.4 (6.9)	6.4 (5.8)	0.008
Voltage (V) (±SD)	1.8 (0.9)	2.2 (1.3)	0.16
Group B			
Incontinence days/3weeks (±SD)	12.5 (4.9)	2.6 (3.2)	0.008
Urgency (min) (±SD)	1.3 (2.0)	27.6 (38.8)	0.008
Voltage (V) (±SD)	1.7 (1.0)	1.8 (1.0)	0.63

Data are expressed as the mean value (±SD).

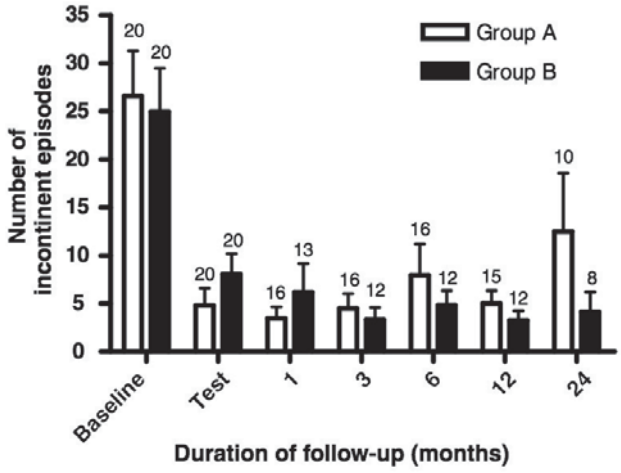

Figure 5.2 Incontinence episodes per 3 weeks (mean, SD). Numbers represent patients at indicated follow-up.

There was no significant difference between the pre- and postoperative anal resting pressures (Figure 5.3) squeeze pressures (Figure 5.4), first sensation, urge and maximum tolerable volume (Table 5.4).

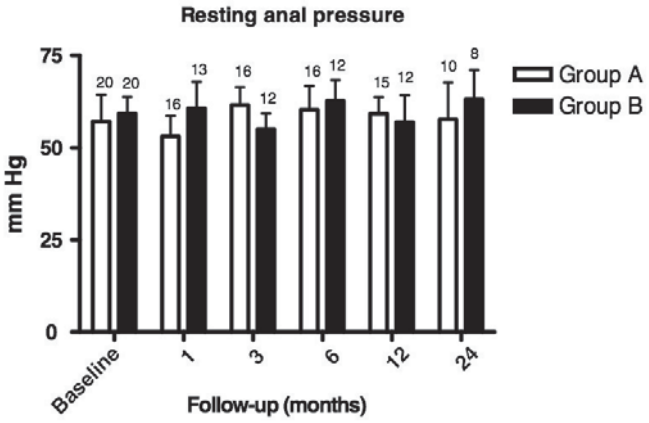

Figure 5.3 Resting pressures (mean, SD).

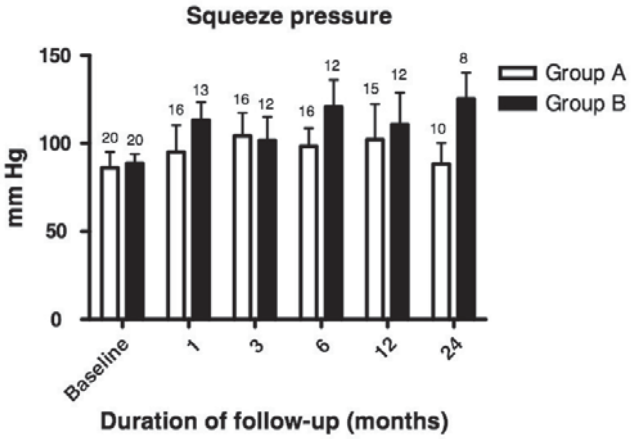

Figure 5.4 Squeeze pressures (mean, SD).

Table 5.4 Rectal volymetry (balloon volumes).

Rectal balloon testing	Baseline	12 months	p-value
Group A			
Sensation (ml)	50.8 (44.9)	38.9 (31.3)	0.06
Urge (ml)	96.1 (64.9)	83.3 (40.9)	0.31
Maximal tolerable (ml)	164 (87.6)	153.3 (38.1)	0.36
Group B			
Sensation (ml)	35.5 (29.0)	25.0 (11.4)	0.16
Urge (ml)	59.8 (31.6)	75.0 (33.5)	0.06
Maximal tolerable (ml)	125.5 (59.5)	139.1 (44.2)	0.37

Data are expressed in mean (±SD) with p-value.

Group B

The mean follow-up period was 22.6 months (range 4.0–41.9). All patients had a defect in the external anal sphincter varying from 17% to 33% of the circumference determined by endo-anal ultrasound. In one patient, the lesion extended throughout the full length of the anal canal. In all other patients, it involved the upper and middle part of the anal canal with the most distal part intact. Three patients had an internal anal sphincter defect in addition. Ten patients had a pudendopathy, which was bilateral in five (mean latency times were 2.6 (range 1.7–5.0) and 2.6 (range 1.3–5.7) on right and left sides respectively). Fourteen (70%) patients had a successful test stimulation period. Three (23.1%) patients had an infection and required subsequent removal of the device. One patient received a second implant that is still functioning well. After the test stimulation, the mean number of incontinence days during 3 weeks decreased significantly [baseline: 12.5±4.9, test: 4.3±5.2 ($p<0.001$)]. At

24 months, the effect remained stable (Table 5.3). The mean number of baseline incontinence episodes during 3 weeks decreased significantly after test stimulation. The effect was sustained during follow-up [baseline: 24.9±20.2, test: 8.1±9.4 (test vs. baseline: p=0.002), 24 months: 4.1±5.9 (24 months vs. baseline: p=0.008); Figure 5.2]. A significant improvement in defaecation postponement time was observed (Table 5.4).

No significant difference was observed between the pre-and postoperative anal resting pressures (Fig. 3). The squeeze pressure has risen significantly by 24 months of follow-up [baseline: 88.6±23.6 mmHg, 24 months: 125.3±42.1 mmHg (p=0.03) Figure 5.4]. The first sensation, urge and maximum tolerable volume were not significantly altered (Table 5.4).

Comparison between the Groups

There was no significant difference between the baseline number of incontinence episodes (p=0.61) indicating that the severity of the incontinence was similar. The reduction in incontinence episodes after stimulation was also similar (test: p=0.14) and remained stable during follow-up (24 months: p=0.63) in each group.

Although the anal sphincter was disrupted in patients in group B, there was no significant difference in the resting and squeeze pressure compared with group A during baseline (p=0.36 respectively; p=0.49). At 24 months of follow-up, there was no significant change in the resting and squeeze pressures (p=0.94 respectively; p=0.08). There was no significant difference between the groups in the baseline first sensation volume (p=0.13), which remained the same at follow-up of 12 months (p=0.31). Baseline urge volume and maximum tolerable volume were significantly higher in group A (p=0.024 and p=0.012 respectively). After implantation, the difference in urge and maximum tolerable volumes disappeared (12 months: p=0.81 and p=0.82 respectively).

Discussion

Faecal incontinence is not merely due to the sphincter disruption. Although defects after childbirth are related to faecal incontinence[18], traction and damage to the pudendal nerve[19] and rectal sensory and motor dysfunction are also contributing factors.[20] Twenty per cent of women with an occult anal sphincter defect after delivery report symptoms of faecal incontinence.[21] Treatment of incontinence is also multi-factorial and is not solely based on repairing the sphincter defect. This is supported by the fact that biofeedback therapy can improve faecal incontinence in patients with ultrasound evidence of a sphincter defect.[22]

Enhancement of residual functional capacity after biofeedback therapy may be one of the factors to explain the success of SNM, but the mechanism is still not understood.

In the beginning, it was thought that SNM directly stimulated the anal sphincter. As with dynamic graciloplasty, it was thought that stimulation induced the transformation of fast-twitch, fatigable muscle fibres (type II) into slow-twitch, fatigue-resistant fibres (type1) resulting in higher resting and squeeze pressures[12], and indeed several studies showed significant changes in resting and squeeze pressures.[23,24] There is evidence that the effect of SNM is not only motor but also sensory. Uludag et al.[25] showed that rectal volumes of first sensation, urge and maximum tolerated volume decreased significantly after SNM with no change in rectal compliance. In the present study, there was a tendency towards a decrease in rectal volumes but this did not reach statistical significance, probably because of the population size.

Sacral nerve modulation can reduce cortico-anal excitability in patients with faecal incontinence, but there is no evidence that a reduction in cortico-anal excitability improves faecal incontinence and there are no long-term data available. SNM possibly drives dynamic brain changes that play a role in influencing anal continence.[26]

Koch et al.[27] demonstrated that the therapeutic threshold is lower or equal to the sensory threshold and that the resting and squeeze pressures remain unaffected during the stimulation period. In the present study, there was no significant change in the resting and squeeze pressure in both groups during the follow-up.

As this study was not a randomized controlled trial, it is difficult to draw significant conclusions. Almost all the AR's of patients in group A were performed in other hospitals. It is possible that these were different in size from the anal sphincter defects of patients in group B.

Our treatment strategy for patients with faecal incontinence and an anal sphincter defect has changed as a result of the present study. We now start with a PNE and subchronic test stimulation regardless of the morphological state of the anal sphincter complex. If the test is positive, we proceed to the implantation of a permanent system. The data indicate that an intact anal sphincter complex is not necessary for success. A randomized controlled trial should however be carried out to be certain of this strategy.

Conclusion

The results of this study demonstrate that faecal continence acquired later in life not only depends on an anatomically intact anal sphincter. The action of SNM does not rely solely on the motor effect on the anal sphincter complex. Faecal incontinence associated with an anal sphincter defect up to 33% of the anal circumference can be directly treated with SNM with a success rate comparable to SNM after sphincter repair.

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Chapter 6

Sacral nerve stimulation for intractable constipation

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Abstract

Objective
Traditional surgical procedures for intractable idiopathic constipation are associated with a variable outcome and substantial morbidity. The symptomatic response, physiological effect and effect on quality of life of sacral nerve stimulation (SNS) were evaluated in patients with constipation (slow transit and normal transit with impaired evacuation).

Methods
In a prospective study at five European sites patients who failed conservative treatment underwent 21 days test stimulation. Patients with >50% improvement in symptoms underwent permanent neurostimulator implantation. Primary end points were increased defecation frequency, decreased straining and decreased sensation of incomplete evacuation.

Results
62 patients (55 female, median age 40 years) underwent test stimulation, of whom 45 (73%) proceeded to chronic stimulation. 39 (87%) of these 45 patients achieved treatment success. After a median 28 (range 1-55) months follow-up, defecation frequency increased from 2.3 to 6.6 evacuations per week ($p<0.001$). Days per week with evacuation increased from 2.3 to 4.8 ($p<0.001$). There was a decrease in time spent toileting (10.5 to 5.7 min, $p<0.001$), straining
(75e46% of successful evacuations, $p<0.001$), perception of incomplete evacuation (71.5-46% of successful evacuations, $p<0.001$) and subjective rating of abdominal pain and bloating ($p<0.001$). Cleveland Clinic constipation score (0=no to 30=severe constipation) decreased from 18 to 10 ($p<0.001$). Visual analogue scale (VAS) score (0=severe to 100=no symptoms) increased from 8 to 66 ($p<0.001$). Patients with slow and normal transit benefited. Quality of life significantly improved. Colonic transit normalised in half of those with baseline slow transit ($p=0.014$).

Conclusion
SNS is effective in the treatment of idiopathic slow and normal transit constipation resistant to conservative treatment.

Introduction

A minority of patients with severe constipation, including some with slow transit and some with normal transit but impaired evacuation, fail conventional pharmacological and behavioural treatments. Traditional operations are associated with substantial morbidity and a variable outcome.[1-4]

Modulation of the extrinsic neural control of the large bowel and pelvic floor may provide an alternative to direct bowel surgery for treating intractable idiopathic constipation. Continuous low-amplitude electrical stimulation of sacral nerve roots is an established treatment for urinary voiding disorders and faecal incontinence[5,6] In a combination of early studies of 250 patients undergoing sacral nerve stimulation (SNS) for urinary voiding disorders, 28 (78%) of 36 subjects with co-existing symptoms of constipation reported increased frequency of defecation at 6-months follow-up.[7-9] Other small, preliminary studies, some with limited outcome measures, have reported successful short-term SNS for treating idiopathic constipation.[10-13]

This study aimed to evaluate prospectively the therapeutic efficacy of temporary and permanent SNS in the treatment of idiopathic constipation resistant to medical and behavioural treatment.

Patients and Methods

A multicentre, prospective, consecutive cohort study was undertaken to evaluate the efficacy of SNS in patients with idiopathic constipation. Patients had a minimum 1-year history of chronic constipation, and failed treatment with laxatives, suppositories, enemas and behavioural therapy (biofeedback). Which drugs had been used, and the nature of the biofeedback, was not specified.

Constipation was defined as two or fewer bowel evacuations per week on average and/or straining to evacuate on >25% of attempts to evacuate and/or sensation of incomplete evacuation after defecation on >25% of occasions. Although some patients may have also fulfilled criteria for irritable bowel syndrome, this was not formally assessed. Dyssynergia was not assessed and was not part of the entry criteria, as we believe this pattern of muscle function to be an inconsistent and poorly reproducible finding, whose diagnosis differs according to the test being used.[14]

Baseline evaluation included patient completion of a bowel habit diary, subjective questionnaire, visual analogue scale (VAS) score, Cleveland clinic constipation score15 and SF-36 (Short-Form 36) quality of life questionnaire.[16] A physical examination, sigmoidoscopy, anorectal physiological studies, a whole gut transit study[17] and evacuation proctography[18] were performed.

The bowel habit diary was completed by the patient over 21 consecutive days, assessing the frequency of attempted and successful defecation, time spent trying to evacuate, presence of straining, need for manual digitation and medications to

stimulate defecation, sensation of incomplete evacuation, abdominal pain and bloating, and the impact symptoms had on daily activities of living. During the diary assessment period the patient was asked to abstain from using medications and rectal irrigation. If symptoms became too severe to be tolerated, up to 10 mg of bisacodyl was permitted, with use documented.

A questionnaire completed at the end of the bowel habit diary asked patients to rate subjectively the severity of their constipation, abdominal pain and bloating over the preceding week as absent, mild, moderate or severe. The need to strain to defecate, use of a finger to empty or initiate bowel emptying and feeling of bowel emptiness after defecation during the preceding week were rated as never, sometimes, frequently or always.

Grading of constipation severity was performed using the Cleveland Clinic constipation score that gives a validated, incremental score ranging from 0, equating to no symptoms, to a maximum of 30, equating to severe symptom.[15] AVAS was also completed asking patients to rate their bowel habit over the previous 3 weeks by placing a mark at an appropriate point along a horizontal line representing very poor bowel habit at one end (minimum score of 0) and very good bowel habit at the other (maximum score of 100). Impact on quality of life was assessed by the SF-36 questionnaire.[16] This consists of eight domains, each scored from 0 (poor function) to 100 (good function), which assess an individual's physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role and mental health.

Anorectal physiological assessment included anal manometry (mean resting and mean incremental squeeze pressures) recorded using a stationary pull-through technique. Rectal sensation to latex balloon distension with air, inflated at a standardised rate of 50 ml/ min, was used to measure the rectal sensory threshold, urge threshold and maximal tolerated rectal volume.[19] Anal and rectal sensitivity to low amplitude electrical stimulation was measured using a catheter-mounted ring electrode placed within the mid-anal canal and upper rectum, respectively. The sensory threshold to electrical stimulation was defined at the first sensation experienced, using stimulation performed at pulse frequency 10 Hz and pulse width 500 ms.[20]

Whole gut transit was assessed using three sets of radio-opaque markers of different geometric shapes, with one set given daily over three consecutive days. A plain abdominal radiograph was performed 5 days after the first set of markers was ingested to determine the number of retained markers. Transit was deemed to be slow if an excess of any one of the three sets of markers was retained in comparison with the previously established normal reference range for each set.[17]

Evacuation proctography was performed to assess the anorectal configuration, pelvic floor position and the presence of structural or functional abnormalities before, during and after evacuation of a barium paste enema under fluoroscopic imaging.[18]

For the purpose of analysis, patients were stratified on the basis of their transit time into one of two groups, those who demonstrated slow whole gut transit and those who had normal whole gut transit.

Statistical analysis

For all measures in this study, each patient served as his or her own control, with baseline data compared with the outcome at last follow-up. Data are presented as mean (SD), median (range) for continuous variables, and count (percentage) for categorical variables. Statistical testing was based on paired t test or Fisher exact test as appropriate, with a significance level of 0.05. The analysis was by intention to treat.
The study was designed to treat a minimum of 40 patients with permanent implantation. This was based on the number believed to be necessary to provide clear evidence of efficacy, following a result of >50% of patients responding in an earlier pilot study.

Exclusion criteria

Patients were not eligible to enter the study if they had alternating constipation and diarrhoea, congenital or organic bowel pathology, rectal prolapse, previous large bowel surgery, the presence of a stoma or co-existing neurological disease. Those with significant psychological co-morbidity, as assessed subjectively by the investigator, those who were pregnant or those attempting to become pregnant were excluded.

Operative details

The operative technique for SNS treatment has been described previously and was standardised between centres.[21] All patients underwent initial percutaneous nerve evaluation (PNE) to establish neural pathway integrity and identify the correct sacral foramen for electrode placement. If a satisfactory response, defined as pelvic floor contraction, was obtained with PNE, then a temporary stimulation wire (Medtronic InterStim model 3057, Minneapolis, Minnesota, USA) was placed and connected to an external pulse generator (Medtronic model 3625). A 3 week screening period of continuous low amplitude stimulation (pulse amplitude (0.1-10 V; 14 Hz; 210 ms) was then commenced during which each subject completed a further bowel habit diary to assess the outcome from test stimulation. At the end of the screening period the temporary wire was removed in all patients.
To be eligible for permanent neurostimulator implantation a patient had to have experienced a subjective improvement of symptoms in the absence of an increase in the use of laxatives, enemas or manual stimulation, as recorded in their bowel habit diary over the 3 week trial period. Minimal criteria for progressing to chronic stimulation were an increase in evacuation frequency to three or more bowel

movements per week, and/or a reduction by >50% in the number of episodes of straining and/or a decrease by >50% in the sensation of incomplete evacuation. The permanent implantable neurostimulator (INS; Medtronic InterStim Model 3023) was implanted under antibiotic cover in a subcutaneous gluteal pocket, and attached to a tunnelled, quadripolar tined electrode lead (InterStim model 3093/3889) via a short connecting cable (InterStim model 3095). Initial stimulation parameters for permanent stimulation were set normally at 14 Hz (range 10-21 Hz), 210 ms, continuous stimulation with the amplitude of stimulation set at just below the patient's sensory threshold.[22] A desirable electrode configuration was achieved when the patient experienced sensation localised near, or within, the anus with stimulation amplitude set at the sensory threshold.

Assessment and follow-up

Patients were reviewed, with bowel habit diary assessment, symptom questionnaires, VAS score, Cleveland Clinic constipation score and SF-36 quality of life questionnaire completed at 1, 3, 6 and 12 months following implantation of the permanent device, and at yearly intervals thereafter. The diary card evaluations were all undertaken with the patient not using laxatives. Anorectal physiological studies were performed at each follow-up. A whole gut transit study and evacuation proctography were repeated at 6 months following permanent implantation.

Undesirable symptoms occurring during the study were documented as an adverse event, regardless of whether they were considered to be related to the treatment. The severity of these events was classified as mild, moderate or severe, using standard international criteria.

The primary outcome measure of treatment success was defined in each patient as improvement in any one of: (1) bowel frequency changing from two or less to three or more evacuations per week; (2) a >50% reduction in the proportion of defecation episodes associated with straining; or (3) a >50% reduction in the proportion of defecation episodes associated with a sense of incomplete evacuation. The use of improvement of any one of the three main symptoms was designed to reflect the spectrum of symptoms that patients with this condition complain of. Assessment was also made of the number of patients who had improved all their abnormal inclusion criteria at the end of follow-up, each subject acting as their own control. The trial was performed in accordance with the 1975 Declaration of Helsinki. Ethical approval from each institution participating in the study was obtained and every patient provided written, informed consent.

Results

Sixty-two patients, 55 (89%) female, with a median age of 40 (range17-79) years were enrolled in the study. Thirty patients (48%) were recruited from St Mark's Hospital, London, UK; 17 patients (27%) from Academisch Ziekenhuis Maastricht, The Netherlands; eight patients (13%) from Aarhus University Hospital, Denmark; four patients (7%) from Danderyd University Hospital, Sweden; and three patients (5%) from Sozialmedizinisches Zentrum Ost, Vienna, Austria. All had idiopathic constipation that was refractory to maximal medical and behavioural treatment. Symptoms of constipation had been present for a median duration of 10 (range 1-60) years prior to study enrolment. Fifty patients (81%) demonstrated slow colonic transit (group 1) and 12 patients (19%) normal colonic transit (group 2). There was no significant difference in baseline demographics or severity of symptoms between the two groups of patients.

All patients completed PNE followed by insertion of a temporary stimulation electrode. Screening in all patients was performed for a median of 21 (range 1-38) days. Six patients underwent a repeat test procedure and screening evaluation due to lead damage or loss of efficacy secondary to dislocation of the temporary stimulation electrode. Three of these six subjects met the criteria for permanent implantation. A total of 45 of the 62 patients (73%) met one or more criteria to proceed to implantation of a permanent device. All 45 patients who met the implant criteria proceeded to implantation of a permanent electrode lead and INS. Of these patients, 37 (82%) had slow transit constipation and eight (18%) normal transit constipation with impaired evacuation.

The foramen for permanent lead implantation was based on the best motor response during acute operative nerve testing, being S3 in 41 (91%) patients, S2 in one (2%) patient and S4 in three (7%) patients. Median (range) initial stimulation parameter settings were: pulse amplitude 1.25 (0.3-4.0) V, pulse frequency14 Hz 10-21 and pulse width 210 ms.

Results of chronic SNS are reported at latest follow-up, median 28 (range 1e55) months following permanent implantation.

Clinical outcome

Thirty-nine (87%) of the 45 permanently implanted patients were classified as having achieved treatment success, meeting at least one primary end point, based on their inclusion criteria, at latest follow-up. Fifteen of the 45 patients (33%) improved all their abnormal inclusion criteria at latest follow-up. The number of patients enrolled by different inclusion criteria and their matched subsequent outcome from permanent SNS is illustrated in Figure 6.1.

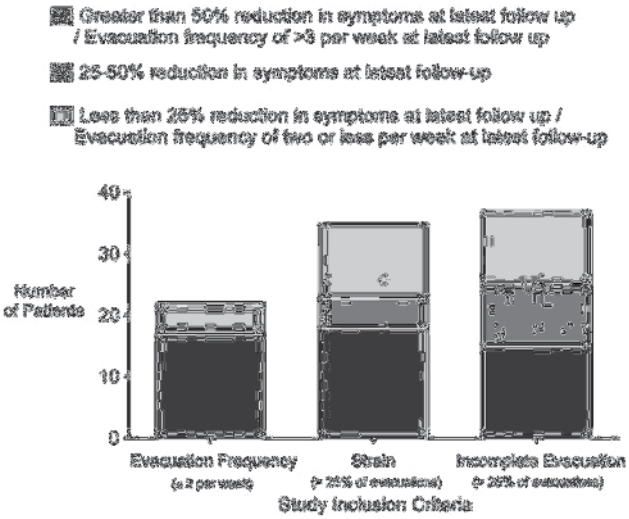

Figure 6.1 Number of patients enrolled by different inclusion criteria (evacuation frequency, straining >25% of all evacuations, sensation of incomplete evacuation >25% of all evacuations) and matched sebsequent outcome for individuals with thar criterion after chronic sacral nerve stimulation at a median of 28 (range 1-55) months follow-up.

On an intention-to-treat basis, 39 of all 62 patients (63%) enrolled in the study met the primary end point definition of a successful treatment outcome at latest follow-up.

The results of chronic stimulation at each stage of follow-up are summarised in Table 6.1. There was no significant difference in the success rate of temporary or permanent stimulation between centres.

There was a significant increase in frequency of defecation from a median (range, mean) of 2.3 (0-20, 3.6) evacuations per week at baseline to 6.6 (1-16, 6.6) evacuations per week at most recent follow-up ($p<0.001$). Spontaneous bowel movements that is, those occurring without laxatives or other stimulation increased from a median (range, mean) of 1.7 (0-14, 2.5) per week at baseline to 4.3 (0-12, 4.6) at latest follow-up ($p=0.004$). Defecation was significantly more likely to be associated with successful evacuation after permanent SNS, compared with baseline (Figure 6.2; $p=0.018$).

Table 6.1 Effects of chronic sacral nerve stimulation on the symptoms of constipation compared with prestimulation baseline severity.

	Baseline	Trial	1 month	3 months	6 months	12months	24 months	36 months	p-value
Frequency of defecation (number of episodes per week)	3.5 (3.6)	7.1 (4.3)	7.1 (3.7)	6.0 (3.4)	6.4 (3.7)	8.0 (7.3)	6.7 (2.7)	7.5 (3.7)	<0.001
Spontaneous bowel movements (numer of episodes per week)	2.5 (2.7)	6.0 (4.0)	5.8 (4.3)	5.5 (3.1)	5.4 (3.7)	6.2 (8.1)	6.9 (2.6)	3.7 (2.9)	0.004
Proportion of successful evacuations that required patient to strain (%)	75.3 (35.2)	40.5 (33.7)	40.0 (27.5)	42.3 (33.7)	49.6 (33.2)	46.0 (32.3)	38.5 (35.3)	42.0 (30.0)	<0.001
Proportion of successful evacuations associated with a sensation of incomplete emptying (%)	71.4 (32.6)	39.6 (28.7)	39.9 (30.1)	47.0 (37.5)	38.8 (30.7)	37.0 (27.5)	44.7 (31.1)	36.4 (29.5)	<0.001
Number of days per week with successful defecation	2.8 (1.8)	4.7 (1.6)	5.1 (1.3)	4.3 (1.7)	4.5 (1.6)	4.8 (1.7)	4.8 (1.5)	4.9 (2.0)	<0.001
Ratio of successful/unsuccessful defecation	1.1 (2.1)	5.1 (10.5)	6.2 (7.3)	5.3 (8.0)	5.0 (7.3)	5.1 (5.5)	5.7 (8.3)	10.6 (17)	0.018
Time on toilet (min)	16.5 (15.2)	8.4 (6.5)	7.7 (1.2)	9.9 (8.7)	8.1 (5.2)	8.4 (6.7)	8.2 (6.8)	7.7 (5.9)	0.001
Laxative, supppository or enema use during bowel diary assessment (number of days per week)	0.4 (1.5)	0.8 (2.1)	1.0 (2.0)	0.7 (1.8)	0.6 (1.9)	0.7 (1.8)	1.0 (2.4)	1.3 (2.6)	0.753
Abdominal pain (number of days per week)	4.5 (2.3)	2.4 (2.3)	2.3 (2.4)	2.5 (2.4)	2.6 (2.1)	2.8 (2.3)	2.2 (2.2)	2.4 (2.1)	<0.001
Abdominal bloating (number of days per week)	4.7 (2.3)	3.1 (2.3)	3.0 (2.5)	3.0 (2.5)	2.7 (2.5)	2.9 (2.3)	3.0 (2.5)	2.6 (2.3)	<0.0001
Limitation in daily activities (numer of days per week)	2.3 (2.3)	1.0 (2.0)	0.8 (1.8)	1.0 (1.8)	0.8 (1.6)	0.7 (1.4)	0.8 (1.4)	0.4 (0.6)	0.003

Values are expressed as mean (SD) at baseline and at each stage of follow-up.

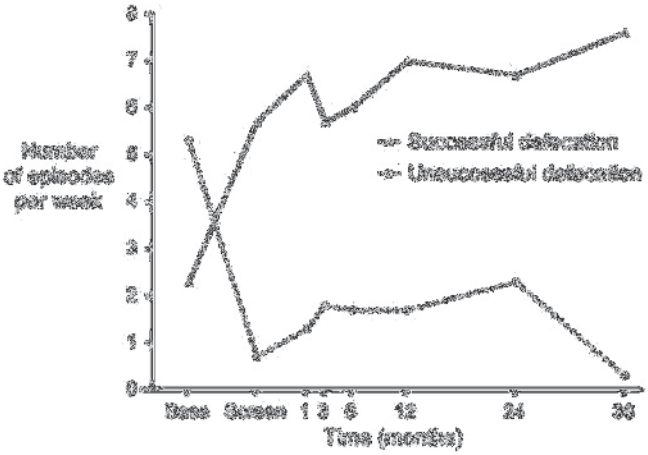

Figure 6.2 Median number of episodes of successful and unsuccessful evacuation in patients attempting to defecate, recorded by a 3 week bowel habit diary before and after chronic sacral nerve stimulation (p=0.018).

The number of days per week with successful defecation increased significantly (p<0.001) and is shown in Figure 6.3. The time spent on toileting decreased significantly (p<0.001) and is shown in Figure 6.4.

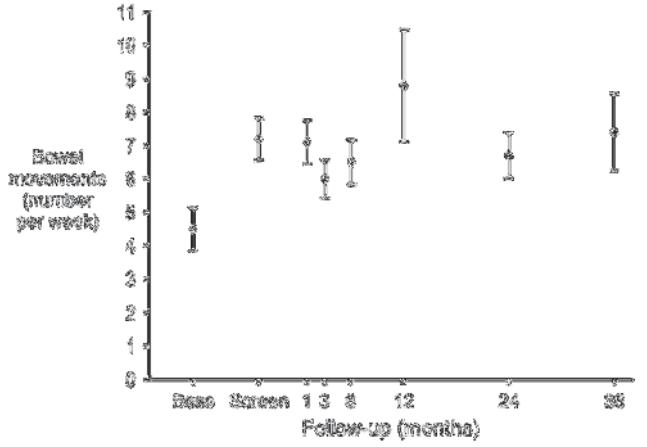

Figure 6.3 Mean (SD) number of evacuations per week in patients, recorded by a 3 week bowel habit diary before and after chronic sacral nerve stimulation.

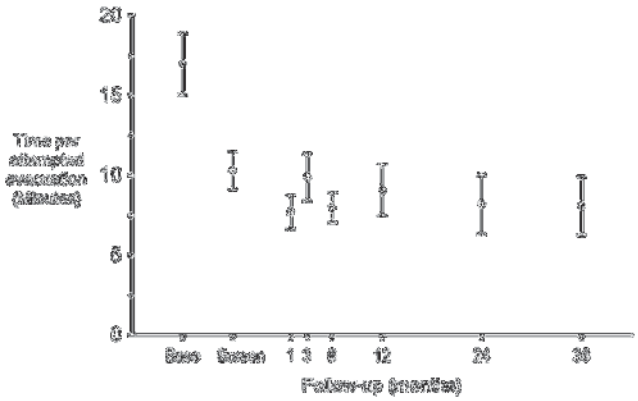

Figure 6.4 Mean (SD) duration of time spent on toileting for each arrempted bowel evacuation, recirded b bowel habit diary before and afte chronic sacral nerve stimulation.

A reduction in percentage of episodes during which straining was required to open the bowels was seen with SNS. Straining was present for 75% of all successful evacuations at baseline versus 46% of all successful evacuations at latest follow-up ($p<0.001$). There was a significant reduction in the percentage of successful evacuations associated with a sensation of incomplete evacuation, from 71% at baseline to 46% at latest follow-up ($p<0.001$).

There was an improvement in the symptoms associated with constipation. The number of days per week that abdominal pain was experienced decreased from a median (range, mean) of 5 (0-7, 4.5) at baseline to 1.7 (0-7, 2.3) days per week at latest follow- up ($p<0.001$). The number of days abdominal bloating was experienced decreased from a median of 5.7 (0-7, 4.7) to 2.3 (0-7, 2.9; $p<0.001$). On subjective rating of the overall severity of abdominal pain and bloating as absent, mild, moderate or severe, there was a significant improvement in both symptoms with chronic stimulation (Figure 6.5).

The Cleveland Clinic constipation score (0=no symptoms of constipation to 30=severe constipation) decreased significantly ($p<0.001$) and is shown in Figure 6.6.

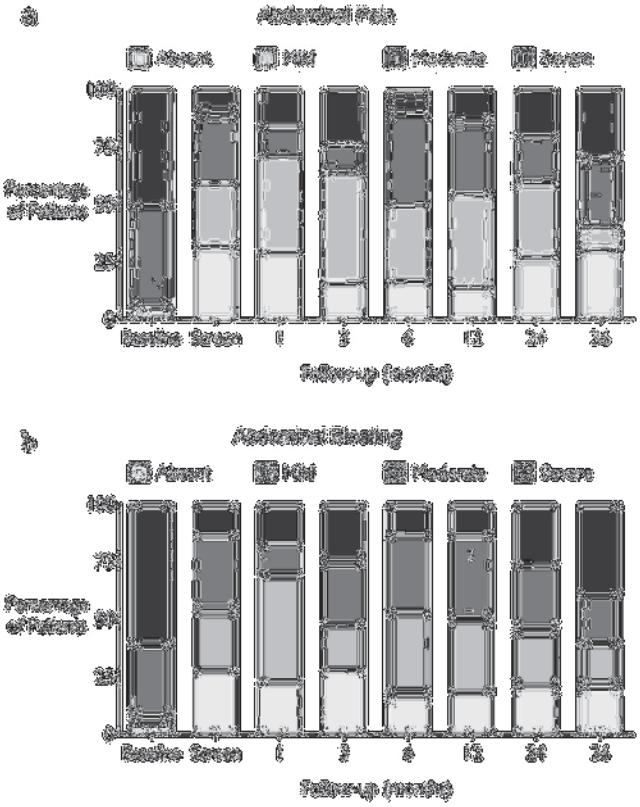

Figure 6.5 Subjective rating of (a) abdominal pain and (b) abdominal bloating at baseline and with chronic sacral nerve stimulation, as recorded by symptom questionnaire. Patients rated each of these symptoms as absent, mild, moderate or severe.

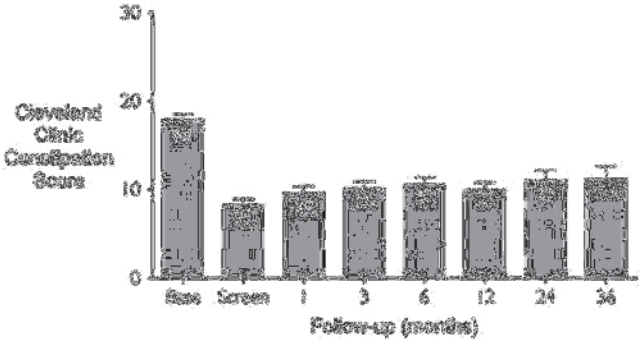

Figure 6.6 Mean (SD) Cleveland Clinic constipation score before and after chronic sacral nerve stimulation. The mean number of patients at each stage of follow-up is shown within the bars.

Grading of the severity of symptoms by VAS (0=poor function to 100=best function) demonstrated a subjective improvement in constipation with chronic stimulation, with the score increasing from a median (range) of 8 (0-100, 15) to 66 (11-100, 63; p<0.001; Figure 6.7).
Medication usage was documented and was found to be constant at each stage of follow-up (p=0.753).
Patients with both slow and normal transit achieved significant treatment success with improved defecation frequency, reduction in straining and improvement in other symptoms.

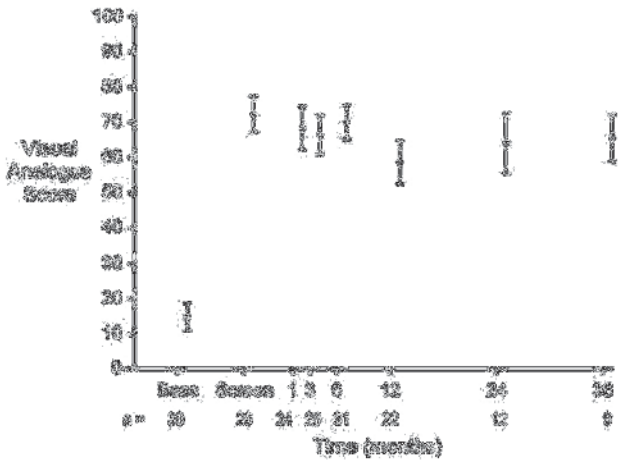

Figure 6.7 Subjective grading of the severity of constipation in those patients undergoing sacral nerve stimulation as measured by mean (SD) visual analogue score (p<0.001). Score ranging from 0=worst function to 100=best function.

Quality of life

There was significant improvement in four of the eight subsets measured by the SF-36 questionnaire. Bodily pain (median 37 at baseline vs. 49 at latest follow-up; p=0.001), mental health (39 vs. 46; p=0.027), social functioning (40 vs. 51; p=0.008) and vitality (median 36 vs. 46; 0.003) were significantly improved, while general health, physical functioning, emotional and physical role scores did not change significantly (Figure 6.8).

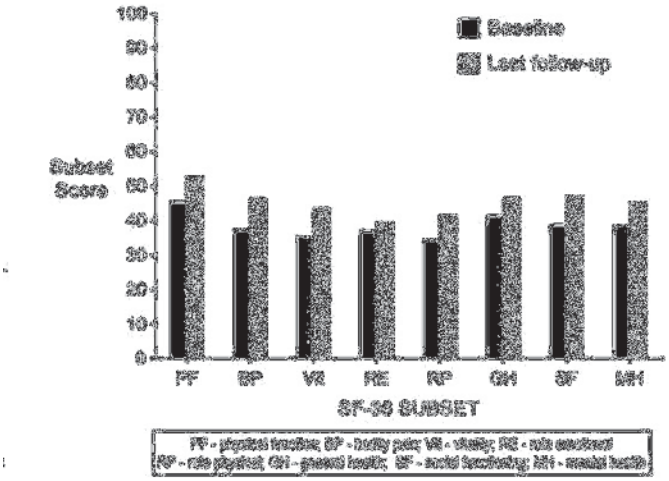

Figure 6.8 Mean Short-Form 36 (SF-36) subset scores at baseline and following chronic sacral nerve stimulation at latest follow-up.

Physiological data

There was no significant change when comparing anal manometric findings performed at baseline and after 6 months chronic stimulation.

Sensory function changed with treatment. The sensory threshold to rectal balloon distension decreased by a non-significant degree (median 30 ml at baseline vs. 29 ml at 6 months, mean 48 vs. 34 ml, p=0.09). There was a significant reduction in the urge threshold (median 76 ml at baseline vs. 74 ml at 6 months, mean 95 vs. 72 ml, p=0.007) and maximal tolerated threshold (median 138 ml at baseline vs. 103 ml at 6 months, mean 151 vs. 107 ml, p<0.001) to rectal balloon distension with chronic stimulation.

Whole gut transit

Paired whole gut transit data were available in 27 patients. Of these, 20 (74%) had delayed whole gut transit at baseline compared with 9 (33%) at 6 months of permanent chronic stimulation (p=0.014). In those subjects who normalised their whole gut transit time with SNS, frequency of defecation increased from a median (range) of 2.7 (0.5-8.7) at baseline to 6.5 (3.2-12.7) evacuations per week at 6 months (p=0.008). In those in whom no improvement in transit was observed, there was no significant change in the frequency of evacuation, from a median (range) of 3.2 (1.4-11.2) at baseline to 4.6 (2.5-8.3) at 6 months (p=0.456).

Proctogram

Paired proctogram data were available in 22 patients. Of these, 12 patients (55%) had prolonged evacuation at baseline compared with 7 (32%) at 6 months of chronic SNS (p=0.642). Six patients had complete evacuation at baseline (27%), improving to 13 patients (59%) at 6 months follow-up (p=0.046).

Adverse events

One hundred and one adverse events were reported, of which 40 (40%) were attributed to underlying constipation or a new unrelated diagnosis. Of the adverse events that were related to the treatment, over two-thirds were classified as mild, these being mainly secondary to postoperative discomfort that resolved spontaneously or adverse stimulation that was eliminated following reprogramming of the INS.

There were 11 severe adverse events related to treatment. Two patients developed a deep postoperative infection necessitating removal of the INS; in one of these patients a further device was inserted once the infection had been treated. One patient required further surgery to remove and replace a stimulation lead that had eroded superficially through the skin. Two patients experienced persistent post-operative pain at the site of INS implantation that necessitated moving the INS to a new implant site. Four patients underwent elective lead revision, three for adverse stimulation that was persistent despite reprogramming of the INS and one for suspected lead migration. Two patients experienced device failure that required further surgery to replace the defective component.

Women who were pregnant, or considering getting pregnant, were excluded from study entry. One patient, however, had two pregnancies during the course of the study. In the first pregnancy, stimulation was ceased at 9 weeks gestation and the patient had a subsequent premature delivery at 29 weeks to an infant with Down syndrome. In the second pregnancy, stimulation was stopped early in the first trimester and a healthy baby was born at 38 weeks by elective caesarean section. The patient successfully resumed treatment after these pregnancies.

Seven patients exited from the study (Figure 6.9). Three patients expressed a wish not to continue participation in the study, two patients exited due to lack of efficacy, one patient declined a further INS after their infected implant was removed and one patient underwent surgery in the form of a subtotal colectomy.

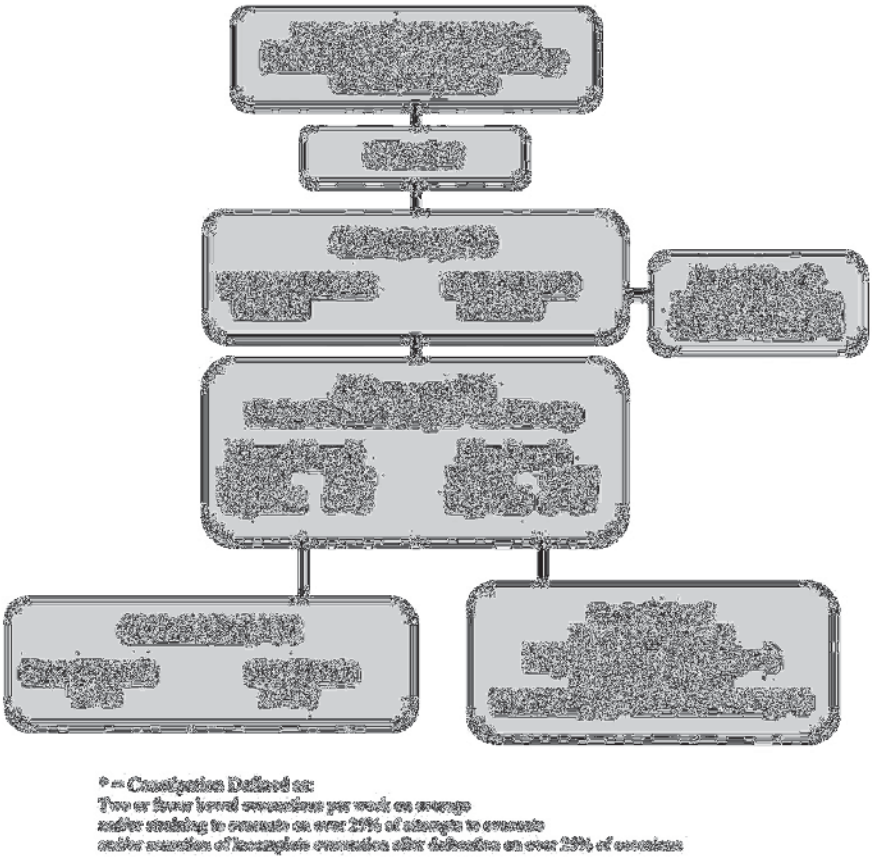

Figure 6.9 Flow diagram to show the passage of participants through each stage of the trial. SNS=sacral nerve stimulation.

Discussion

This study has demonstrated that SNS is an effective treatment for intractable idiopathic constipation in patients who have failed to respond to maximal conservative treatments. The effect of stimulation on bowel function is rapid, with a significant improvement in symptoms occurring with temporary screening. This effect is maintained in the medium to long term, with improvement in a range of outcome measures.

This was intended to be a real-life study, to include patients with a spectrum of symptoms. However, patients were classified prospectively into those with normal and slow transit, to gain some degree of homogeneity of groups. All patients had

failed full medical treatment. Patients had severe enough symptoms subjectively to pursue this intervention; the Cleveland Clinic scores were high, suggesting severe subjective symptoms. This study suggests that SNS is effective for severe idiopathic constipation.

The definition used for constipation in this study differs from that of some other pharmacological studies; direct comparisons should therefore be undertaken with caution. There are no universally accepted standardised inclusion criteria for patients undergoing clinical trials for constipation. The Rome criteria require two or more predefined symptoms to be present for a minimum of 3 months. In this study, patients had to exhibit one of three symptoms to be eligible for test stimulation. Thirty-four of the 45 patients undergoing permanent stimulation had two or more inclusion criteria and would have satisfied the Rome criteria.

Patients were deemed as having a successful response to treatment if one or more of the symptoms for which they were included in the trial significantly improved. This definition may make comparison of the results with other studies difficult to interpret. Life expectancy of the battery is 4-7 years, depending on stimulation parameters and the device used. The battery can then be changed operatively.

This was designed to be a real-life long-term evaluation in a prospective consecutive series of patients for up to 5 years, with a minimum of 1year duration. To our knowledge no previous controlled study of treatment for idiopathic constipation has been conducted over the length of time that the current study was conducted; it is therefore difficult to estimate what might be a placebo response over such a long time period. However, we believe that the therapeutic benefit demonstrated over this long time course is very unlikely to relate to a placebo effect. Furthermore, in addition to subjective improvement, there was an objective improvement in transit time and evacuation time on proctography. A previous small, double-blind, cross-over study has demonstrated that the beneficial effects of this treatment are unlikely to relate to a placebo effect.[23]

We do not have data on the exact quantity of laxatives used during follow-up, although laxative use was only a mean of 1 day per week at last follow-up.

Quality of life improved significantly in six of the eight SF-36 domains. Comparison was not made with population norms, as they were not available for all the countries in which this study took place; however, quality of life generally did not improve to the normal level of the US population (data not shown). The SF-36 is not “disease specific” and can be influenced by co-existing illness that was not relieved by SNS.

Patients with both slow and normal transit benefited from SNS. Treatment resulted in improvement of all symptoms and objective improvement in transit time and evacuation time on proctography. Slow transit and impaired evacuation often overlap.[14] Studies in healthy volunteers have shown that the suppression of defecation by pelvic floor contraction can result in the retrograde movement of

colonic contents and delayed transit.[24] In contrast, colonic transit can be normalised following pelvic floor-focused behavioural therapy ("biofeedback").[25]

At baseline the median frequency of defecation was greater than three evacuations per week, with 22 patients reporting a bowel frequency of less than twice per week. A number of patients had multiple attempts to open their bowels within a day, passing small amounts on each occasion but never completely evacuating. This was reflected in the low mean number of days of successful evacuation. Alternative inclusion criteria included an excessive proportion of evacuations during which the patient strained, or an excessive proportion of evacuations in which the patient felt symptoms of incomplete emptying. These subjective abnormalities were associated with objectively measured slow transit in the majority (80%) of patients. Some patients failed to benefit from temporary SNS. This may relate to neuromuscular pathology or psychological morbidity. There are no techniques available to indicate the former reliably. Misplacement or migration of the temporary electrode can occur and account for failure.

One in eight patients (13%) who responded to temporary screening failed to benefit from chronic stimulation. This may relate to a placebo effect during temporary screening, a positive early effect diminishing over several weeks, surgical misplacement of the quadripolar electrode lead or late lead dislocation.[26] Inaccurate patient screening diaries, unreported medication use, changes in stool consistency or persistent undesirable learned behaviour such as straining may be alternative factors. Further studies on a range of stimulation parameters may benefit patients with an incomplete or absent response.[27] Understanding of the precise mechanism of action of SNS for constipation remains incomplete. A number of different neural pathways may be involved. Stimulation is performed at a low level and continuously, in contrast to the acute intermittent high level stimulation used with the Brindley stimulator in spinal cord-injured patients.[28] Effects are seen on motor[29] sensory[12] and central neural pathways.[30] The effect is therefore not a straightforward result of acute increased peristaltic motor activity through activation of efferent nerves.

In this study transit time was seen to normalise in some patients undergoing chronic stimulation. An increase in the frequency of pan-colonic antegrade propagating sequences following high amplitude stimulation of the third sacral nerve root has previously been demonstrated.[29] Measured sensory function within the rectum also appeared to be affected by chronic SNS. This may reflect altered perception of rectal content, or may just be a surrogate marker of altered autonomic activity.

The incidence of adverse events was similar to that of previous studies.[5,6] This procedure has low morbidity and is well tolerated, in marked contrast to major resectional bowel surgery. Whether the birth of an infant with Down syndrome was related to the SNS is unknown. In one previous report of six pregnancies occurring in patients undergoing SNS for urological disorders the only adverse outcome was a premature delivery in one patient.[31]

In conclusion, SNS is an effective treatment for patients with intractable constipation unresponsive to conservative treatments. Benefit is maintained, at least in the medium term. Further randomised trial data are now awaited.

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Chapter 7

Summary and future perspectives

Summary and future perspectives

In **Chapter two** the long-term results of the Dynamic Graciloplasty (DGP) for faecal incontinence was discussed. From November 1986 through January 2012, all patients treated with DGP were included in the study. All patients had received maximal conservative therapy. They have been evaluated with anal manometry, defecography and electromyography/PNTML. Postoperatively, patients were seen at the outpatient clinic at 1, 3, 6, 12 months and annually thereafter. The Williams incontinence score was used and anal manometry was performed. Success was defined as an incontinence score of 1 or 2. A Cox analysis was performed to identify factors responsible for failure.
326 Patients were treated with DGP. 34 Patients received a DGP after Abdominal Perineal Resection and were excluded. 292 Patients (62 men) were available for the long-term analysis. Eight (2.5%) patients were deceased by the time of analysis. Nine (2.8%) patients were permanently lost to follow-up. The mean age was 50 (12-78) years at the time of surgery. The mean duration of follow-up was 8.3 (0-22.4) years. 146 (50%) Patients had a continence score of 1 or 2. 58 Patients used additional retrograde colonic irrigation and 52 patients were converted to a stoma after failure. Age, indication, gender and resting pressure were no significant factors for failure. The squeeze pressure and pressure on the moment of failure were significant factors in the Cox analysis.
We concluded that DGP is still an option to treat FI in seriously malformed anal sphincters. The indication to perform a DGP is decreasing, since newer treatment options provide less morbidity and complications. The long term results are less satisfactory then the one stated in our earlier publications.

Chapter three discusses the treatment of Faecal incontinence (FI) by means of the Artificial Bowel Sphincter (ABS). All patients were included between 1997 and 2006. The standard preoperative work-up was done for all patients, equal to the workup with the Dynamic Graciloplasty. During the follow-up, the Williams incontinence score was used to classify the symptoms and repetitive anal manometry was performed. Thirty-four patients (25 women) were included, of which 33 patients received an ABS. The mean follow-up was 17.4 (0.8-106.3) months. The Williams score improved significantly after placement of the ABS ($p<0.0001$). The postoperative anal resting pressure with an empty cuff was not altered ($p=0.89$). The postoperative ABS pressure was significantly higher then the baseline squeeze pressure ($p=0.003$). Seven patients had an infection necessitating explantation. One patient was successfully reimplanted. In this study, the artificial bowel sphincter was an effective treatment for FI in patients with a large anal sphincter defect. Infectious complications were the largest threat necessitating explantation of the device.
A review of the contemporary literature shows that most series reporting the use of the ABS are small series with a relatively short follow-up. Only limited data on long-

term follow-up of a sufficient number of ABS sphincters are available. There is one multicentre study with disappointing long-term data where the initial data were promising.
All of the series have significant infectious problems. We tried to reduce the infectious problems by means of pre-operative patient selection. Only patients with a sufficient perineal length were included to minimize the risk of (late) erosion.
Not only infectious problems are a concern also technical problems are frequently encountered. In our institution we have dealt with a special one (gigantic inflation of the balloon), as described by Van Wunnik et al.[1]
A systematic review by Mundy et al.[2] concludes the ABS to be of uncertain benefit and potentially harmful for patients. An infection rate of 22.5% and erosion rate of 17.4% was reported in 12 out of the14-included studies. This procedure should be reserved for selected patients in specialized centres with a high level of experience with sphincter replacement procedures. Patients should be very well informed prior to surgery.

Chapter four describes patients treated with SNM between March 2000 and May 2005. Faecal incontinence was defined as at least one episode of involuntary faecal loss per week confirmed by a 3-week bowel habit diary. Patients were eligible for implantation of a permanent SNM when showing at least a 50% reduction in incontinence episodes or days during ambulatory test stimulation. The standard preoperative work-up was done. The follow-up visits for the permanent implanted patients were scheduled at 1, 3, 6, 12 months and annually thereafter. The bowel habit diary and anal manometry were repeated postoperatively during the follow-up visits.
A total of 134 patients were included and received sub chronic test stimulation. One hundred patients (74.6%) had positive test stimulation and received a definitive SNM implantation. The permanent implantation group consisted of 89 women and 11 men.
The mean age was 55 years (range 26–75). The mean follow-up was 25.5 months (range 2.5–63.2). The mean number of incontinence episodes decreased significantly during the test stimulation (baseline, 31.3; test, 4.4; $p<0.0001$) and at follow-up (36 months postoperatively, 4.8; $p<0.0001$). There was no significant change in the mean anal resting pressure. The squeeze pressures were significantly higher at 6 months (109.8 mmHg; $p=0.03$), 12 months (114.1 mmHg; $p=0.02$) and 24 months postoperatively (113.5 mmHg; $p=0.007$). The first sensation, urge and maximum tolerable volume did not change significantly. Twenty-one patients were considered late failures and received further treatment.
This was the largest single centre study published on faecal incontinence treated with SNM. Similar results have been published in large series by other research groups.[2,3,4]

In **Chapter five** two groups of patients were analysed retrospectively to determine whether SNM is as effective in patients with faecal incontinence associated with an anal sphincter defect as in those with a morphologically intact anal sphincter following anal repair (AR). Patients in group A had an initial AR resulting in an intact anal sphincter ring. Group B included patients with a sphincter defect, which was not primarily repaired. Both groups were due for SNM treatment. All patients underwent a percutaneous nerve evaluation (PNE) followed by a sub chronic test over 3 weeks. If the PNE was successful, a permanent SNM electrode was implanted. Follow-up visits for the successfully implanted patients were scheduled at 1, 3, 6, 12 months and annually thereafter.

Group A consisted of 20 (19 women) patients. Eighteen (90%) had a positive sub chronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. Group B consisted of 20 women. The size of the defect in the anal sphincter varied between 17% and 33% of the anal circumference. Fourteen (70%) had a positive sub chronic test stimulation. Twelve patients had a successful SNM implant during middle-term follow-up. In both groups, the mean number of incontinence episodes decreased significantly with SNM (test vs baseline: p=0.0001). There was no significant difference in resting and squeeze pressures during SNM in group A, but in group B squeeze pressure had increased significantly at 24 months. Comparison of patient characteristics and outcome between groups A and B revealed no statistical differences. As this study was not a randomized controlled trial, it is difficult to draw significant conclusions. Almost all the ARs of patients in group A were performed in other hospitals. It is possible that the initial size of the anal sphincter defects was different compared to the patients in group B. However, the treatment strategy in our hospital for patients with faecal incontinence and an anal sphincter defect has changed as a result of the present study. We now start with a PNE and sub chronic test stimulation regardless of the morphological state of the anal sphincter complex. If the test is positive, we proceed to the implantation of a permanent system. The data indicate that an intact anal sphincter complex is not necessary for success. Others conformed these findings.[7,8]

A recent systematic review showed that quality of evidence supporting sacral nerve stimulation for faecal incontinence associated with an anal sphincter lesion was poor. As we stated in our publication a randomised trial should be conducted.[6]

Chapter six discusses a prospective study of patients who failed conservative treatment for constipation and underwent 21 days test stimulation at five European sites. Patients with >50% improvement in symptoms underwent a permanent neurostimulator implantation. Primary end points were increased defecation frequency, decreased straining and decreased sensation of incomplete evacuation.

Sixty-two patients (55 female, median age 40 years) underwent test stimulation of whom 45 (73%) proceeded to chronic stimulation. 39 (87%) Of these 45 patients

achieved treatment success. After a median 28 (range 1-55) months follow-up, defecation frequency increased from 2.3 to 6.6 evacuations per week (p<0.001). Days per week with evacuation increased from 2.3 to 4.8 (p<0.001). Cleveland Clinic constipation score (0=no constipation to 30=severe constipation) decreased from 18 to 10 (p<0.001). Quality of life significantly improved. Grading of the severity of symptoms by VAS (01⁄4poor function to 1001⁄4best function) demonstrated a subjective improvement in constipation with chronic stimulation, with the score increasing from a median (range) of 8 to 66 (p<0.001) Colonic transit normalised in half of those with baseline slow transit (p=0.014). We concluded that SNS an effectieve treatment option is in the treatment of idiopathic slow and normal transit constipation resistant to conservative treatment.
A recent study conducted by Govaert et al.[10] was unfortunately limited by a lack of consistent outcome measurements, but showed that despite of improvement in the Wexner scores, slightly more than 50% of the patients that started with permanent stimulation did not use it anymore at medium-term follow-up. They concluded that more data were necessary to establish a role for SNM for constipation. Maybe a change in the stimulation parameters could offer a solution in the long term as suprasensory stimulation produces increased frequency of colonic propagating sequences.[11,12]

Future perspectives

The classical surgical approach to functional bowel disorders is changing. The frequency of performing procedures for sphincter repair and sphincter replacement procedures is decreasing. Not only are the results decreasing in time, also numerous complications are encountered. Continuous research is therefore necessary to make sure that the current standard of care is good enough. In the Netherlands this led to several active centres with enthusiastic doctors, who made the treatment of faecal incontinence to one of their main tasks. You could see this as centralisation “avant la lettre”.
One of the major changes in the treatment of functional bowel disorders was the introduction of sacral nerve modulation by Matzel et al.[13] When he was observing a patient population with urinary incontinence that was treated with SNM, he found out that several patients with functional bowel problems were successfully treated as well. These results were confirmed in other studies.[14]
As sphincter pressure alone was not significantly altered, this led to several hypotheses concerning the mechanism of action. Sceptics indicated that it was merely a placebo effect, but long-term analysis of function and double-blinded research has shown otherwise.[15-18] As efficacy was established, the cost of the treatment of SNM was discussed. A recent study of the situation in the Netherlands confirmed several

other studies, showing that it is cost effective to treat faecal incontinence with sacral nerve modulation.[19-24]

What remains however, is the "Holy Grail" of the sacral nerve modulation: the mechanism of action. Once we can understand how it works, patient selection could be made easier.

Different ideas have been studied (rectal sensation, rectal blood flow, anal squeeze pressure, colonic propagating waves, recto-anal angle etc.). Many of these studies were not able to explain the working mechanism completely. Maybe the level of action is not only peripheral, but more centrally, in the brain itself.

Blok et al.[25] showed in urological patients that chronic sacral nerve modulation influences, presumably via the spinal cord, brain areas previously implicated in detrusor hyperactivity, awareness of bladder filling, the urge to void and the timing of micturition. Furthermore, chronic SNM affected areas involved in alertness and awareness. However, acute SN modulated predominantly areas involved in sensorimotor learning, which might become less active during the course of chronic SN. This may be the explanation of late failure during chronic stimulation after initial successful acute and sub chronic stimulation.

Duelund-Jakobsen et al.[15] showed that patients experiencing loss of efficacy could experience improvement if alternative pacemaker settings are tested.

We know that the brain plasticity is large and the brain is able to adept to new situations. The test with the prism glasses showing the world up side down is well known. The brain is able to correct for the glasses after three days.

Long term stimulated "brains" with sacral nerve modulation have not been studied yet.

A recent study by Gaini et al.[26] learned that measurement of P40 latency of somatosensory evoked potentials at baseline and at one month of sacral nerve modulation of 40 Hz may help to predict outcome of SNM and influence decision making for permanent implantation for patients with incontinence and constipation. This could means that different people respond differently to sacral nerve modulation. Functional MRI of CT-Pet studies could give the answer to patients who fail in time. This could also give insight in brain responsiveness during different stimulation parameter settings. It will take a large amount of effort of the patients and investigators, but I am looking forward to the results of these studies.

Nederlandse samenvatting en toekomstperspectieven

In hoofdstuk twee worden de resultaten op lange termijn van de Dynamic Graciloplasty (DGP) voor fecale incontinentie besproken. Van november 1986 tot en met januari 2012, werden alle patiënten, behandeld met DGP, in de studie opgenomen. Alle patiënten hadden maximale conservatieve therapie ontvangen. Ze zijn geëvalueerd met anale manometrie, defecografie en elektromyografie en/of pudenduslatentietijden. Na de operatie werden de patiënten gezien op de polikliniek op 1, 3, 6, 12 maanden en daarna jaarlijks. De Williams incontinentie score werd gebruikt en anale manometrie werd uitgevoerd. Succes werd gedefinieerd als een incontinentie score van 1 of 2. Een Cox analyse werd uitgevoerd om factoren die verantwoordelijk zijn voor het falen te identificeren.
326 Patiënten werden behandeld met DGP. 34 patiënten kregen een DGP na Abdominale Perineale resectie en werden uitgesloten. 292 patiënten (62 mannen) waren beschikbaar voor de lange termijn analyse. Acht (2,5%) patiënten waren overleden ten tijde van analyse. Negen (2,8%) patiënten zijn voor de follow-up definitief verloren gegaan. De gemiddelde leeftijd was 50 (12-78) jaar ten tijde van de operatie. De gemiddelde duur van de follow-up was 8,3 (0-22,4) jaar. 146 (50%) patiënten hadden een continentie score van 1 of 2. 58 patiënten gebruikten extra retrograde darmspoeling en 52 patiënten werden omgezet naar een stoma na falen van de DGP. Leeftijd, indicatie, geslacht en rustdruk waren geen significante factoren voor falen. De knijpkracht van de DGP en de druk op het moment van falen kwamen als significante factoren naar voren in de Cox analyse.
We concludeerden dat DGP is nog steeds een optie is bij patiënten met FI op basis van grote anale sfincter defecten. Echter, de indicatiestelling tot het uitvoeren van een DGP bij patiënten met fecale incontinentie neemt af, omdat nieuwere behandelings-opties minder morbiditeit bieden. De lange termijn resultaten zijn minder bevredigend dan degene vermeldt in onze eerdere publicaties.

Hoofdstuk drie bespreekt de behandeling van fecale incontinentie (FI) doormiddel van de Artificial Bowel Sphincter (ABS). Alle patiënten werden geincludeerd tussen 1997 en 2006. Bij alle patiënten werden de standaard preoperatieve onderzoeken gedaan, gelijk aan het opwerken voor een Dynamic Graciloplasty. Tijdens de follow-up, werd de Williams incontinentie score gebruikt om de symptomen te classificeren en anale manometrie werd uitgevoerd. Vierendertig patiënten (25 vrouwen) werden geincludeerd, waarvan 33 patiënten een ABS kregen. De gemiddelde follow-up was 17,4 (0,8-106,3) maanden. De Williams score verbeterde aanzienlijk na de plaatsing van de ABS ($p<0,0001$). De postoperatieve anale rustdruk met een lege anale cuff veranderde niet ($p=0,89$). De postoperatieve ABS druk was significant hoger dan de pre operatieve knijpkracht ($p=0,003$). Zeven patiënten hadden een infectie, die explantatie tot gevolg had. Een patiënt kreeg met succes een nieuwe implantatie. Deze studie liet zien dat de ABS een effectieve behandeling is voor FI bij patiënten met

een groot anaal sfincter defect. De postoperatieve morbiditeit bestond voornamelijk uit infecties.
Een overzicht van de hedendaagse literatuur laat met name series zien met met een relatief korte follow-up. Slechts beperkte gegevens over de lange-termijn follow-up van zijn beschikbaar. Er is een multicenter studie gepubliceerd met tegenvallende gegevens op lange termijn, waarbij de initiële uitkomsten veelbelovend waren.
In alle gekende series staan infectieuze problemen op de voorgrond als grootste postoperatieve probleem. We hebben geprobeerd om de infectieuze problemen te verminderen door middel van preoperatieve patiënt selectie. Alleen patiënten met een voldoende perianale lengte zijn opgenomen om het risico van (late) erosie te minimaliseren.
Niet alleen infectieuze problemen zijn een bron van zorg ook technische problemen worden vaak aangetroffen. Van Wunnik et al. beschreef een casus waarbij de ballon om onduidelijke reden tot een enorme omvang was gegroeid.[1] Een systematische review van Mundy et al.[2] concludeert zelfs dat een ABS schadelijk kan zijn voor patiënten. Een infectie percentage van 22,5% en erosie percentage van 17,4% werd gemeld bij 12 van de 14 geïncludeerde studies. Deze procedure moet worden gereserveerd voor geselecteerde patiënten in gespecialiseerde centra met een hoge mate van ervaring met sluitspier vervangende procedures. Patiënten moeten goed worden geïnformeerd voorafgaand aan de operatie over de te verwachten morbiditeit.

Hoofdstuk vier beschrijft de patiënten behandeld met SNM voor fecale incontinentie tussen maart 2000 en mei 2005. Ontlastingsincontinentie werd gedefinieerd als ten minste een episode van onvrijwillige fecale verlies per week bevestigd door een 3-week stoelgangsdagboek. Patiënten kwamen in aanmerking voor implantatie van een permanente SNM als ten minste 50% vermindering van incontinentie episodes optrad tijdens de ambulante proefstimulatiefase. De standaard preoperatieve work-up werd gedaan. De follow-up bezoeken de permanent geïmplanteerde patiënten werden gepland op 1, 3, 6, 12 maanden en daarna jaarlijks. De stoelgangsdagboeken en anale manometrie werden herhaald tijdens de follow-up bezoeken.
Een totaal van 134 patiënten werden geïncludeerd en ondergingen sub chronische teststimulatie. Honderd patiënten (74,6%) hadden positieve test stimulatie en kwamen in aanmerking voor een definitieve SNM implantatie. Deze groep bestond uit 89 mannen en 11 vrouwen.
De gemiddelde leeftijd was 55 jaar (26-75). De gemiddelde follow-up was 25,5 maanden (2,5-63,2). Het gemiddelde aantal incontinentie episodes daalde significant tijdens de test stimulatie (baseline, 31,3; test: 4.4, $p<0,0001$) en bij follow-up (36 maanden na de operatie: 4.8, $p<0,0001$). Er was geen significante verandering in de gemiddelde anale rustdruk. De knijpkracht was significant hoger na 6 maanden (109,8 mmHg, $p=0,03$), 12 maanden (114,1 mmHg, $p=0,02$) en 24 maanden postoperatief

(113,5 mmHg, p=0.007). De eerste sensatie, drang en de maximaal toelaatbare volume was niet significant veranderd. Eenentwintig patiënten werden beoordeeld als laat-falers en ontvingen verdere behandeling. Dit was toentertijd de grootste single-center studie gepubliceerd over fecale incontinentie behandeld met SNM. Vergelijkbare resultaten zijn in grote series gepubliceerd door andere onderzoeks-groepen.[2-4]

In hoofdstuk vijf werden twee groepen patiënten retrospectief geanalyseerd om te bepalen of SNM is even effectief bij patiënten met fecale incontinentie geassocieerd met een anale sfincter defect als bij patiënten met een morfologisch intacte anale sluitspier na anal repair (AR). Patiënten in groep A hadden een AR in de voor-geschiedenis resulterend in een intacte anale sluitspier. Groep B omvatte patiënten met een sluitspier defect, dat niet werd hersteld alvorens aan de behandeling met neurostimulatie te beginnen. Alle patiënten ondergingen een percutane zenuw evaluatie (PNE), gevolgd door een teststimulatie gedurende 3 weken. Als de PNE succesvol was, werd een permanente SNM elektrode geïmplanteerd. Follow-up bezoeken voor de permanent geïmplanteerde patiënten werden gepland op 1, 3, 6, 12 maanden en daarna jaarlijks.
Groep A bestond uit 20 (19 vrouwen) patiënten. Achttien (90%) hadden een positieve sub chronische teststimulatie. Twaalf patiënten hadden een succesvolle permanent SNM implantatie tijden de follow-up. Groep B bestond uit 20 vrouwen. De grootte van het defect in de anale sfincter varieerde tussen 17% en 33% van de anale omtrek. Veertien (70%) patiënten hadden een positieve sub chronische teststimulatie. Twaalf patiënten hadden een succesvolle permanent SNM implantatie tijden de follow-up. In beide groepen daalde het gemiddelde aantal incontinentie episodes aanzienlijk na permanente SNM implantatie (test vs baseline: p=0.0001). Er was geen significant verschil in rust en knijpkracht tijdens chronische stimulatie in groep A, maar in groep B was de knijpkracht bij de follow-up na 24 maanden aanzienlijk gestegen. Vergelijking tussen de baseline kenmerken van de patiënten en de resultaten tussen de groepen A en B liet geen statistische verschillen zien. Aangezien deze studie geen gerandomiseerde gecontroleerde trial was, is het moeilijk om significante conclusies te trekken. Bijna alle AR's van patiënten in groep A werden uitgevoerd in andere ziekenhuizen. Het is mogelijk dat de oorspronkelijke grootte van de anale sluitspier defecten anders was dan bij de patiënten uit groep B. Echter, de behandelings-strategie in ons ziekenhuis voor patiënten met fecale incontinentie en een anaal sfincter defect is veranderd als gevolg van de huidige studie. We beginnen nu met een PNE en sub chronische teststimulatie ongeacht de morfologische toestand van het anale sluitspier complex. Als de test positief is, gaan we verder met de implantatie van een permanent systeem. De huidige gegevens tonen aan dat een intact anaal sluitspier complex niet noodzakelijk is voor succes. Anderen studies tonen identieke bevindingen.[7,8]

Uit een recente systematische review bleek dat de kwaliteit van het bewijs ter ondersteuning van sacrale zenuwstimulatie voor fecale incontinentie geassocieerd met een anale sluitspier laesie slecht was. Zoals we in onze publicatie vermeldden, zou een gerandomiseerd onderzoek moeten worden uitgevoerd.[6]

Hoofdstuk zes behandelt een prospectieve studie van patiënten bij wie een conservatieve behandeling van constipatie mislukt is. Zij ondergingen op vijf Europese sites een teststimulatie gedurende 21 dagen. Patiënten met >50% verbetering van de symptomen ondergingen een permanente neurostimulator implantatie. Primaire eindpunten waren toegenomen defecatie frequentie, verminderd persen en een verminderd gevoel van onvolledige ontlasting.
Twee en zestig patiënten (55 vrouwen, gemiddelde leeftijd 40 jaar) werden geïncludeerd en ondergingen een teststimulatie. Hiervan zijn er 45 (73%) overgegaan tot chronische stimulatie, nadat ze aan een of meerde inclusie criteria voldeden. 39 (87%) van deze 45 patiënten bereikte succes van de behandeling door een of meerdere primaire eindpunten te bereiken. Na een mediane follow-up va 28 (bereik 1-55) maanden, werd de defecatiefrequentie verhoogd van 2,3 tot 6,6 evacuaties per week ($p<0,001$). Het aantal dagen per week met defecatie werd verhoogd van 2,3 tot 4,8 ($p<0,001$). De Cleveland Clinic constipatie score (0=geen constipatie tot 30=ernstige obstipatie) daalde 18 naar 10 ($p<0,001$). De visueel analoge schaal (VAS) score (0=ernstig tot 100=geen symptomen) steeg van 8 naar 66 ($p<0,001$). Zowel patiënten met een trage als een normale passage profiteerden van de behandeling. De kwaliteit van leven verbeterde aanzienlijk.
Een recente studie uitgevoerd door Govaert et al.[10] toonde aan dat, ondanks de verbetering van de Wexner scores, iets meer dan 50% van de patiënten, die begonnen met permanente stimulatie, diezelfde niet meer gebruikten op de middellange termijn follow-up. Helaas was deze studie beperkt door een gebrek aan consistente uitkomstmaten. Zij concludeerden dat er meer gegevens nodig waren om met zekerheid een rol voor SNM voor therapie resistente constipatie toe te kennen. Misschien zou een verandering in de stimulatie parameters een oplossing kunnen bieden op de lange termijn.[11,12]

Toekomstperspectieven

De klassieke chirurgische aanpak van functionele darmstoornissen is aan het veranderen. De frequentie van anal repair en sfincter vervangende procedures neemt af. Niet alleen nemen de resultaten af in de tijd, ook is de chirurgische morbiditeit aanzienlijk. Voortdurend onderzoek is daarom noodzakelijk om ervoor te zorgen dat de huidige standaard van zorg goed genoeg is. In Nederland heeft dit geleid tot een aantal actieve centra met enthousiaste artsen, die de behandeling van fecale

incontinentie hoog op hun agenda hebben staan. Je kunt dit beschouwen als centralisatie "avant la lettre".
Een van de belangrijkste veranderingen in de behandeling van functionele darmstoornissen is de introductie van sacrale zenuw modulatie door Matzel et al.[13] Door observatie, van een patiëntenpopulatie met urine-incontinentie, die behandeld waren met SNM, kwam hij erachter dat een aantal patiënten met functionele darmproblemen met ook met succes behandeld konden worden. Deze resultaten werden later bevestigd in andere studies.[14]
Het uitblijven van significante post operatieve sfincterdruk toename, leidde tot een aantal hypothesen over het werkingsmechanisme. Sceptici beweerden dat het slechts een placebo-effect behelsde, maar lange termijn analyse van de functie en dubbelblind onderzoek heeft anders[15-18] getoond. Nadat de werkzaamheid was vastgesteld, werd de kosten van de behandeling van SNM besproken. Een recente studie van de situatie in Nederland bevestigde een aantal andere studies. Hieruit blijkt dat het kosteneffectief is om fecale incontinentie te behandelen met sacrale zenuw modulatie.[19-24]
Wat overblijft is echter de "Heilige Graal" van de sacrale zenuw modulatie : het werkingsmechanisme. Zodra we begrijpen hoe het werkt, kan de selectie van patiënten gemakkelijker worden gemaakt.
Verschillende ideeën zijn reeds onderzocht (rectale sensatie, rectale bloedstroom, anaal knijpkracht, colon peristalsis, recto-anale hoek enz.). Veel van deze studies waren niet in staat om het werkingsmechanisme volledig verklaren. Misschien is het niveau van de actie is niet alleen perifere, maar meer centraal, in de hersenen zelf.
Blok et al.[25] toonde aan in urologische patiënten die behandeld waren met chronische sacrale zenuw modulatie dat bepaalde hersen gebieden beïnvloed worden, vermoedelijk via het ruggenmerg. Deze gebieden zijn betrokken bij detrusor hyperactiviteit, de sensatie van de blaasvulling, de drang om te urineren en de timing van de mictie. Bovendien beïnvloedt chronische SNM hersengebieden die betrokken zijn bij alertheid en bewustzijn. Echter, acute SNM beïnvloedt voornamelijk gebieden die betrokken zijn bij sensomotorische leren, deze zouden minder actief kunnen worden tijdens chronische SNM. Dit zou de verklaring kunnen zijn van laat-falen tijdens chronische stimulatie na de eerste succesvolle acute-en subacute stimulatie.
Duelund-Jakobsen et al.[15] hebben aangetoond dat bij patiënten met een verminderde werkzaamheid verbetering zouden kunnen optreden als alternatieve pacemaker instelling zouden worden getest.
We weten dat de hersenplasticiteit groot is en dat de hersenen direct kunnen aanpassen aan nieuwe situaties. De test met de prisma bril, waarbij initieel de wereld op zijn kop ervaren wordt is bekend. De hersenen corrigeren dat beeld na drie dagen.
Lange termijn gestimuleerde "breinen" met sacrale zenuw modulatie zijn nog niet onderzocht.

Een recente studie van Gaini et al.[26] liet zien dat de meting van P40 latency van somatosensorische evoked potentials bij aanvang en na een maand van de sacrale zenuw modulatie van 40 Hz kan helpen om de uitkomst van SNM te voorspellen. Tevens zou het de besluitvorming voor permanente implantatie bij patiënten met incontinentie en obstipatie beïnvloeden. Dit zou ook kunnen betekenen dat verschillende mensen verschillend reageren op sacrale zenuw modulatie. Functionele MRI en/of CT-PET onderzoeken zouden het antwoord kunnen geven waarom sommige patiënten falen. Deze onderzoeken kunnen ook inzicht in de hersenen responsiviteit geven tijdens de verschillende stimulatie parameterinstellingen. Het zal een grote hoeveelheid inspanning van de patiënten en onderzoekers kosten, maar ik kijk uit naar de resultaten van deze studies.

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Valorisation addendum

Valorisation addendum

Introduction

Faecal incontinence (FI) has gained a significant increase in treatability during the last 20 years. The introduction of the Dynamic Graciloplasty (DGP) by Baeten and simultaneously by Williams has made a huge impact on the whole colorectal community. Together with the Artificial Bowel Sphincter, these two surgical procedures offered patients dealing with faecal incontinence, an opportunity to augment their defective anal sphincter. Before this period of surgical innovations, the standard treatment of a defective sphincter was an anal repair, however the results of this procedure failed in time. Also conservative therapy, e.g. constipating medicine and (biofeedback) pelvic behavioural therapy wasn't providing the success that patients with severe faecal incontinence needed. These patients frequently ended with a definitive stoma. The introduction of Sacral Nerve Modulation (SNM) also known as Sacral Nerve Stimulation (SNS) provided a minimal invasive procedure with less morbidity to treat faecal incontinence. As a spinoff of this treatment modality it also seemed possible to treat idiopathic constipation by means of SNM. This thesis focused on the surgical treatment of faecal incontinence and the treatment of idiopathic constipation by means of SNM.

Epidemiology and etiology of faecal incontinence

Faecal incontinence is a common health care problem, affecting 5% to 10% of community-dwelling adults with 1% to 2% experiencing huge impact on daily activities. It aggravates with advancing age and disability. It is a disorder, which is particularly embarrassing and socially unacceptable, and many patients do not seek professional help. Therefore, a huge underestimation of the problem can be expected. The part of the population that seeks help is merely “the tip of the iceberg”. Faecal incontinence has a negative impact on physical and psychological health and lifestyle, with social activity restriction in many instances.
The aetiology of faecal incontinence is divers and multi-factorial. It is a combination of sphincter pressure, anorectal sensation and compliance, rectal storage function, faecal consistence and brain function. Trauma to the sphincter complex is one of the most frequent causes of FI. It can be due to birth trauma or iatrogenic trauma in anal surgery. Bols et at found that 3rd of 4th degree ruptures contribute significantly to postpartum faecal incontinence. The anorectal sensation and compliance can be altered due to inflammatory processes, as seen in Crohn’s disease and ulcerative colitis. Nerve damage post-partum can cause diminished sensation of rectal filling. Altered anorectal storage function, as seen after low anterior resection for rectum carcinoma, can contribute to faecal incontinence. Due to chronic inflammatory bowel diseases the liquidity of the faeces increases, which decreases the “grip” on the faecal

matter and can lead to incontinence. Neurologic diseases, e.g. spina bifida, multiple sclerosis, can cause FI. Disorders of brain function, e.g. after cerebrovacular events, can cause FI.
The above-mentioned multi-variability makes it challenging to solve the problem of FI. A holistic approach is necessary to solve every aspect of the problems encountered by FI. Preferably this should take place in specialised centres, where dedicated teams operate closely together. Such teams ideally consist of a colorectal surgeon, gynaecologist, urologist, gastro-enterologist, psychiatrist and physiotherapist.

Epidemiology of constipation

Based on a recent systematic review, the prevalence of constipation is very variable, ranging from 2.5% to as high as 79%. However, the variability in prevalence can be due to a lack of uniformity in the definition of constipation. When applying the Rome III criteria, the prevalence varies between 11% and 18%. It is present in all age groups and is most commonly seen in women and non-Caucasians. Other symptoms such as bloating and pain can be present. Different subtypes have been distinguished; colonic inertia, outlet obstruction, functional constipation. The outlet obstruction can be caused by pelvic floor dyssynergia, but also by anatomical obstructions such as a rectal prolapse, intussusception, enterocele and/or rectocele, but also by a rectum carcinoma. Thorough investigation is necessary since the treatment of the above-mentioned entities is very different.
Sacral nerve modulation has shown some promising results in the study that has been addressed in this manuscript. Is has still to earn its placed in the treatment algorithm. During a modified Delphi method this specialists from several European centres have stated that SNM for constipation is less effective than when used in FI and further research is needed.

Valorisation

For the addendum of valorisation five questions can be used a guideline:
- What is the socio-economic relevance off the research results (relevance)?
- For whom, outside the peer researchers, are the results relevant (target population)?
- Which concrete services/products can be obtained (products)?
- What is the innovation value of the results (innovation)?
- What are the marketing strategies that can be applied (planning and realisation)?

Socio-economic relevance

Functional bowel disorders are difficult entities to treat successfully. Usually patients are referred back and forth between different specialists thereby increasing costs and decreasing effectiveness. The MUMC has acknowledged this problem several years ago and a Pelvic care Unit was constructed to discuss these patients once a week in a systematic manner. Another important milestone was the construction of the Medpsych Unit, since functional bowel disorders and simultaneous psychological problems go hand in hand.
Years of investigation in the MUMC has made it possible to objectify the results of sacral neuromodulation. A line of consecutive researchers were able to seamlessly extract data from large cohort files. Van Wunnik et al were able to demonstrate that the introduction of SNM in the surgical management algorithm for faecal incontinence was both more effective and less costly than DGP or ABS without SNM. They concluded that it justified adequate funding for SNM for patients with faecal incontinence. The Dutch healthcare insurance companies were able to define a DOT and therefore made it possible to deliver sacral neuromodulation to a broader public. In the beginning it was only paid out of the academic budget of the MUMC.
The role for sacral neuromodulation in constipation has yet to be explored more thoroughly. Untill this date not much is known about the cost effectiveness. A research protocol has been made in the MUMC to address this problem. Is has been send for evaluation to the Zorg Instituut Nederland and ZonMw.

Target population

The results of this manuscript are relevant to patients with faecal incontinence and constipation. It can be used during information days for patient associations. Furthermore, it can be relevant for medical device corporations to develop less costly devices then the ones that are used today. This thesis showed that patients with faecal incontinence due to a sphincter defect can be treated successfully with sacral neuromodulation without restoring the anatomy first. This reduces the costs and burden for the patient since a sphincter repair is no longer a prerequisite for sacral neuromodulation.

Products

There are no new products that have been developed with the results of this thesis

Innovation and future

The past 30 years in the treatment of functional bowel disorders, especially for patients with faecal incontinence, have been very innovative. Were in the past a colostomy was the only treatment option, nowadays several treatment modalities are

available. We have learned that the artificial bowel sphincter can be successfully implemented in a surgical strategy to treat faecal incontinence. However we have also learned that the morbidity of this procedure is high. Other large colorectal centres have had the same experience, decreasing the initial enthusiasm. American Medical Systems, producer of the artificial bowel sphincter, is incorporated by Boston Scientific this year. This has led to the production stop of the neosphincter by the end of this year. Therefore it will be no longer possible to treat new patients or perform revisions of existing systems.

The dynamic graciloplasty has gained its role in the treatment of faecal incontinence. It was popular during the nineties of the previous century. A lot of patients have been treated with this procedure worldwide. It was the start of the era of electrical augmentation. Initial results were good, but results declined over time as shown in chapter two. To this date not much surgeons are able to perform the procedure. However with large anal sphincter defects and cloacal deformities, this procedure remains the only viable one. This can be said the same for faecal incontinent patient born with anal atresia and anal pull trough procedures. The only alternative for all of them is a colostomy.

The major advantage of sacral neuromodulation over the above mentioned surgical procedures, is the fact that it is less invasive for the patients with less morbidity and similar success rates. How ever it is not successful in all patients. The key lies in better patient selection and fully understanding the working mechanism of neuro-modulation. Several studies to address this issue are started in the nearby future in the MUMC. Chapter 7 discusses the future perspectives as well.

Dankwoord

Dankwoord

Mijn latijn leraar zei soms tegen mij, als het niet helemaal volgens plan verliep; lang verwacht, stil gezwegen, nooit gedacht, toch gekregen. Lang heb ik het inderdaad verwacht, tot zelfs aan het punt dat ik dacht dat het niet meer zou gaan gebeuren. Daarom zal ik niet zwijgen om dit “boekje” te verdedigen. Dit had ik natuurlijk niet kunnen doen, zonder hulp van anderen. Daarom zou ik graag een aantal mensen in het bijzonder te bedanken.

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List of publications

List of publications

1. Lansen-Koch SM, Govaert B, Oerlemans D, **Melenhorst J**, Vles H, Cornips E, Weil EH, van Heurn E, Baeten CG, van Gemert WG. Sacral nerve modulation for defaecation and micturition disorders in patients with spina bifida. Colorectal Dis. 2012;14:508-14.

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Curriculum vitae

Curriculum vitae

Jarno Melenhorst was born on the 30th of January 1978 in Zwolle. His parents are Hendrikus Wilhelmus Johannes Melenhorst and Berendje Melenhorst-Groothuis. He has one sister; Brenda Melenhorst. He attended primary School at the Basisschool De Driemaster in Hasselt. After graduating from the Carolus Clusius College in Zwolle, he started Medical School in 1996 at the Katholieke Universiteit Nijmgen, currently Radboud University. He fulfilled his last clinical internship in the Diakonessenhuis in Paramaribo in Surinam. An extra-curricular surgical internship was fulfilled in the Canisius Wilhelmina Ziekenhuis in Nijmegen. During his "wetenschap stage" he worked in the orthopedic laboratory collaborating with Stefan Bolder in writing his first article.

He obtained his medical degree in 2002. He immediately started to work as a surgical resident (ANIOS) in het Viecuri Medisch Centrum in Venlo (dr. H.M. Janzing). In 2004 he started working on this thesis under supervision of prof. dr. C.G.M.I. Baeten in the University Hospital Maastricht.

In July 2007 he started his surgical training in the same hospital (prof. dr. J.W.M. Greve, prof. dr. C.H.C. Dejong, prof. dr. L. Stassen). In July 2010 he continued his surgical training in Orbis Medical Centre in Sittard-Geleen (dr. T. Hoofwijk).

He finished his training in July 2013 and started a two-year gastro intestinal fellowship in the University Hospital Maastricht (MUMC, prof.dr. C.H.C. Dejong). He obtained a European Society of Colo Proctolgy (ESCP) fellowship and has visisted prof. dr. A. D'Hoore for three months in UZ Leuven. Currently he works as a staff colorectal surgeon in the MUMC.

Jarno Melenhorst lives together with his wife Anke Smeenk and is the proud father of four children; Tije (27-02-07), Sara (17-10-08), Finn (25-08-10) and Lieuwe (11-04-14).