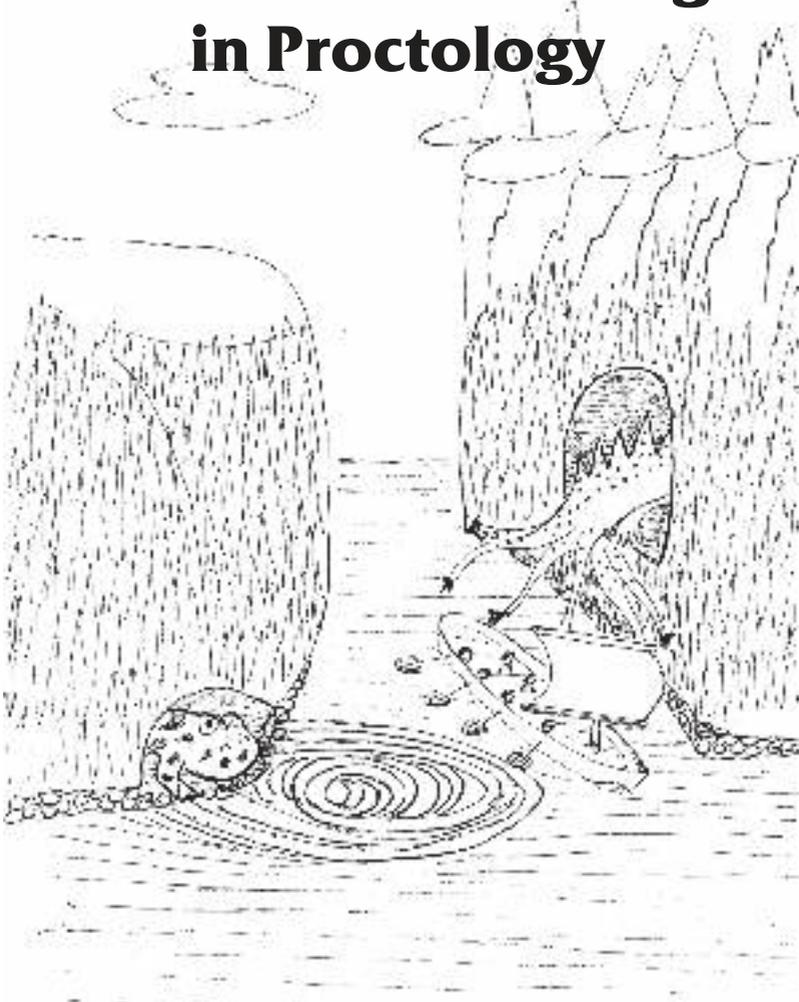


Evidence Based Strategies in Proctology



*Zo voeren wij de beide kapen langs,
Links Scylla, rechts de afschuwelijke Charybdis*

Homerus Odysee XII v. 260-261

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Evidence Based Strategies in Proctology

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Aan mijn vader

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Eviden ce as a strat egy for proc essing topology

General introduction

General introduction

Pelvic floor and proctologic disorders are commonly encountered in surgical practice. Although regarded as routine pathology by many, choosing the right treatment at the right time can pose a real challenge to the treating surgeon, and often involves choosing between two evils. Radical treatment leads to good symptom control but is likely to result in functional deterioration, whereas less invasive treatment is safe but often leads to insufficient results. This has been the core problem in the treatment of pelvic floor and proctologic disorders for centuries. The close interaction between the anatomy and physiology of the rectum and anus is responsible for this compromise the surgeon often has to make. Historically functionality was of secondary importance to healing of the disorder, but nowadays it is considered unacceptable to cause permanent disability for a benign disorder. Many classic surgical therapies such as anal stretching and lateral internal sphincterotomy for anal fissure, haemorrhoidectomy and (extensive) lay-open procedures for anal fistula have been re-evaluated over the past decades with special respect to postoperative functionality. Reports of high rates of impaired continence, severe postoperative pain and high rates of recurrence have boosted the incentive to introduce new techniques in the field of proctology.

Anatomical considerations

The rectum constitutes the last 12-15 cm of the large bowel and starts at the level of the promontory. It is situated within the pelvic cavity. Part of it is extraperitoneal, depending on the depth of the Douglas pouch, which is generally considered to be deeper in woman. The female pelvic cavity can be divided into three compartments: the anterior compartment consisting of the bladder and the urethra, the middle pelvic compartment formed by the vagina and uterus, and the rectum representing the posterior pelvic compartment¹.

The anal canal is the last part of the rectum, starting at the anorectal junction where the rectum passes through the levator muscle, ending at the anal verge (figure 1). The length of the functional anal canal is about 4 cm, whereas the anatomical anal canal, extending from anal verge to dentate line is only 2 cm in length². The anal canal is lined with squamous epithelium below the dentate line, and columnar epithelium above. The dentate line is also marked by the lower end of the columns of Morgagni, where the ducts of the anal glands terminate. A substantial number of these glands branch out into the intersphincteric plain. Between the upper border

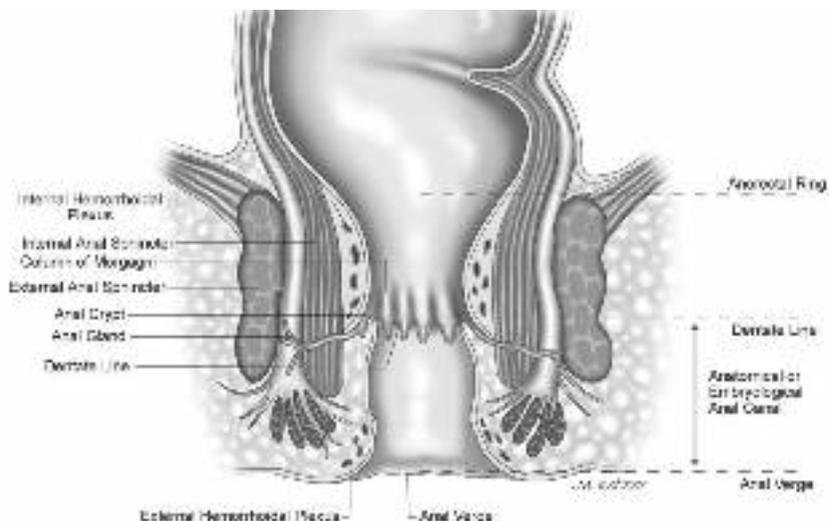


Figure 1 Anatomy of the anal canal (reprinted with permission from Springer⁶)

of the anal canal and the dentate line lie three vascularised cushions. These cushions of thickened submucosa, or haemorrhoidal tissue, contribute to the anal resting pressure and thus to faecal continence³⁻⁵. The most important contributor to faecal continence is the anal sphincter, which consists of an internal and external part. The internal sphincter is the thickened continuation of the smooth muscle wall of the rectum, while the external sphincter constitutes an elliptical cylinder of skeletal muscle, formed by the conjunction of multiple pelvic floor muscles.

Anal Fistula

A perianal fistula is an abnormal connection between the anal canal and the perianal skin or perineum, lined with epithelium. A perianal fistula develops in approximately one-third to a half of all patients after drainage of an anorectal abscess^{7,8}. The origin of these fistulas is cryptoglandular in 90% of patients. Fistulas are classified based on their relation to the anal sphincter complex according to Parks; submucosal, intersphincteric, trans-sphincteric, suprasphincteric and extrasphincteric⁹.

The treatment of anal fistula is dictated by its aetiology and by the amount of sphincter complex that is encompassed by its tract¹⁰. Treatment of cryptoglandular fistulas can grossly be divided in procedures that aim to close off the fistula tract and its internal opening, and the more traditional approach of laying open or excising

the fistula tract (fistulotomy and fistulectomy). By preserving at least the puborectal muscle during these latter procedures, it was believed that continence could be preserved⁹. However, reports on continence impairment, even after lay open procedure of intersphincteric fistulas¹¹⁻¹³ generated interest in new procedures that preserve sphincter muscle.

Fibrin glue was introduced as a minimal invasive tool to obliterate the fistula tracts, without the trade-off of impairment of continence^{14,15}. It is a soluble consisting of a fibrinogen and a thrombin component, that, after injection into the fistula tract, seals it by the formation of a fibrin clot (figure 2). It was first described for fistulas after proctectomy by Hjörtrup and co-workers resulting in a success rate of 74%¹⁶. However, in following studies that evaluated fibrin glue for cryptoglandular perianal fistulas, success rates varied considerably, ranging from 10%¹⁷ to 80%¹⁸.

Anal Fissure

Anal fissure is an ulcer or split located in the squamous epithelium of the anus between the dentate line and the anal verge. It is predominantly seen in the posterior midline²⁰. Spasm of the Internal Anal Sphincter (IAS) is likely to play an important role in the pathophysiology^{21,22}. An acute fissure should be distinguished from a chronic fissure. Acute fissures can usually be treated with conservative measures²³, whereas chronic fissures are more difficult to treat. An acute fissure is likely to become chronic if healing has not occurred within 4 weeks.

Not much has changed in our concepts and treatment of anal fissures since the 19th century. In a report by Cripps in the British Medical Journal of 1895, laxatives and ointment are stated to be the first line of treatment, while in chronic fissures a sphincterotomy through the fissure is advised²⁴. The mainstay of current therapy for chronic fissures is directed towards lowering the resting pressure of the IAS. This can be achieved surgically by a Lateral Internal Sphincterotomy (LIS), or by manually stretching the sphincter muscle, also known as the Lord procedure²⁵. These techniques show excellent healing rates, but at the cost of jeopardizing faecal continence²⁶⁻²⁸. Although there is a considerable variation in these incontinence rates between publications, therapy has nonetheless shifted towards pharmacological treatment. Topical Isosorbide Dinitrate (ISDN) has been for long the pharmacological treatment of choice in the Netherlands. It acts as a nitric oxide (NO) donor, lowering the IAS pressure and inducing vasodilatation in the anoderm²⁹. Another NO donor

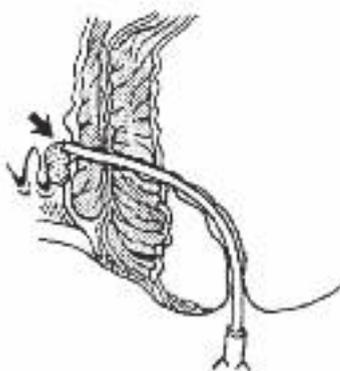
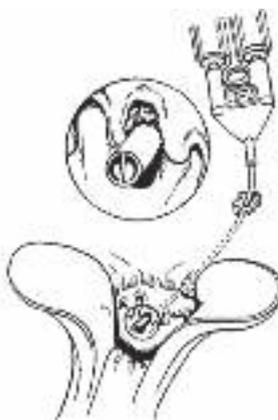
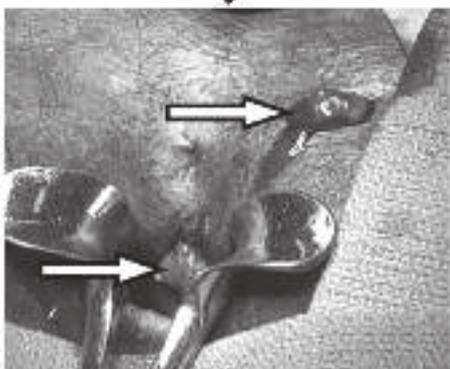


Figure 2 Injection of fistula tract with fibrin glue (reprinted with permission from Elsevier¹⁹)

that is being used in numerous reports is Glyceryl Trinitrate (GTN)³⁰⁻³². Initial success rates of 68% seemed promising, but subsequent studies failed to confirm these figures as was shown in a recent Cochrane review³³.

Moderate healing rates combined with a high incidence of headache associated with NO donors, and impairment of continence after sphincter-tone lowering surgery, have led to an interest in other treatment modalities³⁴⁻³⁹. Calcium channel blockers such as diltiazem and nifedipine show healing rates that are equivalent to NO donors but with fewer side effects^{30,34,35}. Treatment of anal fissures with Botulin Toxin (BT) was first described in 1993 by Jost et al.⁴⁰ BT injected into the anal sphincter blocks acetylcholine release, thereby stopping neural transmission, causing transient relaxation of the sphincter⁴¹. Since the publication by Maria and co-workers reported on excellent healing rates with BT, found in a randomized controlled trial between BT and nitro-glycerine topical⁴², BT has become increasingly popular, resulting in numerous papers comparing BT with other treatment modalities⁴⁰.

Haemorrhoids

Haemorrhoids are highly vascular tissue in the submucosal space in the anal canal, and are separated into internal and external haemorrhoids based on location above or below the dentate line. The word haemorrhoid is derived from the Greek *haema* (blood) and *rhoos* (flow). It was Hippocrates (460 BC) who was the first to use the word haemorrhoid in its current context. These vascular cushions contribute to faecal continence by accounting for approximately 15-20% of the anal resting pressure⁴³ and by physically acting as a 'plug'⁴. Haemorrhoidal tissue gives rise to symptoms, such as bleeding, prolapse or pruritus, when it slides downward⁴. Etiologic factors are multifactorial and include prolonged straining, irregular bowel habits and heredity. Internal haemorrhoids are classified according to their severity into four degrees (table 1).

Table 1 Grading of haemorrhoids according to Goligher

	Grade 1	Grade 2	Grade 3	Grade 4
<i>Examination</i>	Bulge into lumen anal canal	Prolapse at time of defecation	Spontaneous prolapse which requires manual reposition	Permanently prolapsed and irreducible
<i>Symptoms</i>	<ul style="list-style-type: none"> ● Painless bleeding 	<ul style="list-style-type: none"> ● Painless bleeding ● Anal mass with defecation 	<ul style="list-style-type: none"> ● Painless bleeding ● Anal mass with defecation ● Soiling 	<ul style="list-style-type: none"> ● Pain ● Bleeding ● Soiling

Hippocrates was probably also the first to describe surgical treatment of haemorrhoids: *"And haemorrhoids in like manner you may treat by transfixing them with a needle an tying them with very thick and woollen thread"*. He also described the technique of haemorrhoidal excision⁴⁴. Currently, when conservative measures like dietary- and defecation habit advice fail, the treatment of choice in most clinics is rubber band ligation (RBL) followed by haemorrhoidectomy. So surprisingly not much has changed in haemorrhoidal treatment in two and a half thousand years.

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RBL, as first described by Baron, lifts the prolapsed haemorrhoids by banding redundant mucosa just above the apex of the haemorrhoidal complex. This procedure is reported to be successful in 65-85% of the patients⁴⁵. The setback however is that treatment often needs to be repeated in order to be successful and that recurrence of symptoms is very common⁴⁶.

Classic open or closed haemorrhoidectomy is a very effective procedure for resolving haemorrhoidal symptoms with low recurrence rates. However, postoperative pain can persist for weeks. Moreover, by excising the functional important haemorrhoidal tissue, anal resting pressure and maximal squeeze pressure are significantly lowered⁴⁷. Particularly in patients with an already compromised sphincter, this can give rise to incontinence³. Therefore, other operative techniques have been developed to treat patients that do not react to conservative treatment or rubber band ligation.

The Procedure for Prolapse and Haemorrhoids (PPH) and the Transanal Haemorrhoidal Dearterialisation (THD) are the two most utilised new techniques. PPH or stapled anopexy is a technique that was first described by Longo⁴⁸, and was based on the stapled transanal mucosectomy, first proposed by Pescatori et.al.⁴⁹ With a circular stapler device a circumferential doughnut of mucosa and submucosa above the haemorrhoids is resected, hereby creating a haemorrhoidopexy (figure 3). PPH is reported to be an effective and safe alternative for surgical haemorrhoidectomy with less postoperative pain, shorter hospital stay, and greater patient satisfaction⁵⁰⁻⁵⁴. Long-term success rates have been reported to be around 70 – 90 %^{50,55,56}. Its introduction however, has not been without controversy. There have been case reports of serious postoperative complications, including recto-vaginal fistula, anal stenosis and perforation leading to pelvic sepsis⁵⁷⁻⁶⁰. Recurrence of prolapse is

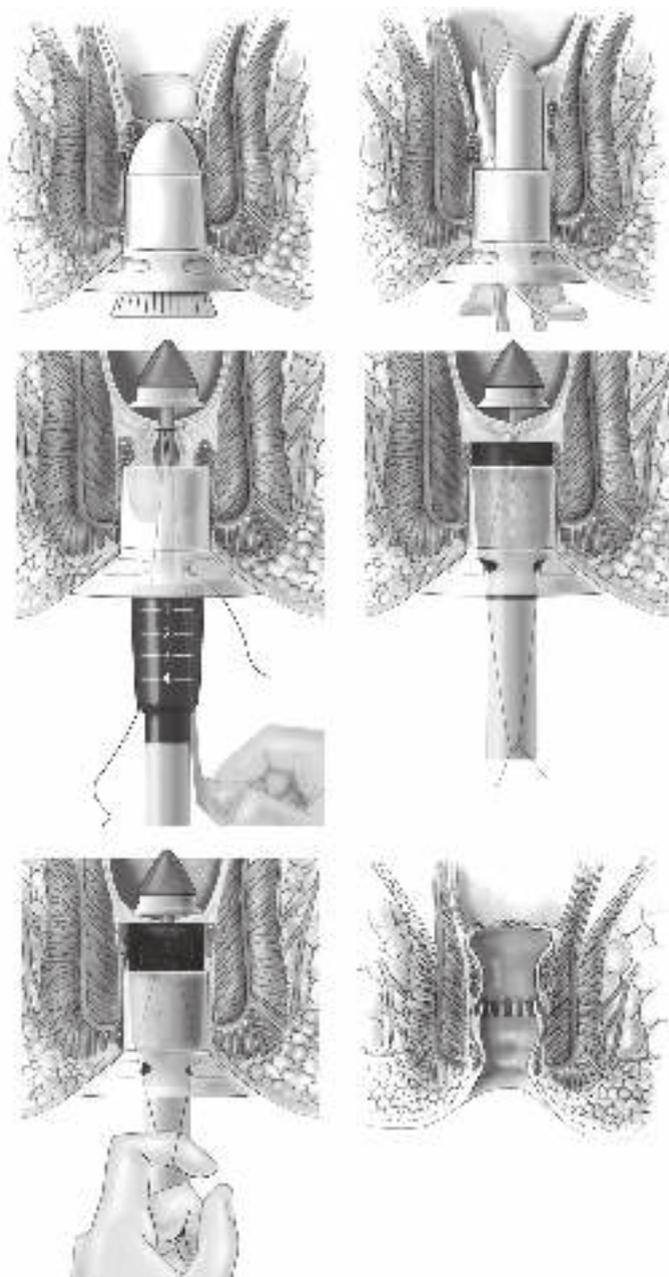


Figure 3 PPH procedure (reprinted with permission from Elsevier)

reported more frequently after PPH compared to haemorrhoidectomy⁶¹. Combined with reports of chronic postoperative pain and faecal urgency after PPH^{56,62}, this has made some surgeons reluctant to implement this form of treatment into their practices.

Transanal Haemorrhoidal Dearterialisation (THD) uses a specially developed proctoscope combined with a Doppler transducer to identify the haemorrhoidal arteries (originating from the superior rectal artery) and to ligate them selectively⁶³ (figure 4). It is based on the theory that haemorrhoids occur when there is an imbalance in the blood flow of the haemorrhoidal plexus, either caused by increased inflow or decreased venous outflow. By arterial ligation the inflow is reduced, causing the plexus to diminish and the haemorrhoids to shrink. Reports on this procedure showed low complication rates, minimal postoperative pain and overall good results⁶⁴⁻⁶⁷.

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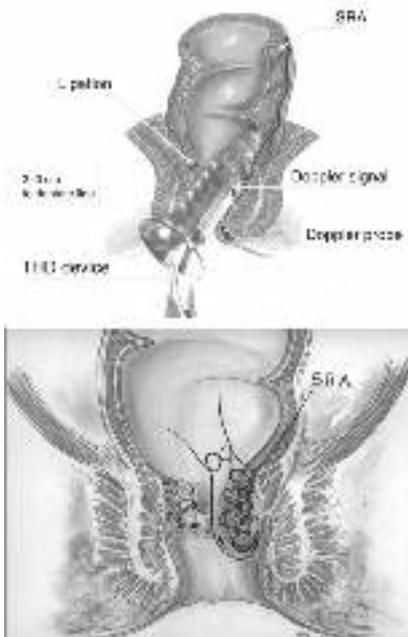


Figure 4 THD (reprinted with permission from Springer⁶⁴)



Figure 5 LVR (reprinted with permission from Springer⁷⁴)

Internal Rectal Prolapse

Internal Rectal Prolapse (IRP) is a full thickness intussusception of the rectum during defecation. It can be graded from low-grade (recto-rectal intussusception) to high-grade (recto-anal intussusception) prolapse⁶⁸. This prolapse may lead to an outlet obstruction and/or to faecal incontinence.

Debate has been going on for decades about the clinical significance of IRP. Initial studies failed to show consequent progression of IRP into External Rectal Prolapse (ERP)^{69,70}. Consequently, IRP was regarded a non-surgical disorder to be treated conservatively. However, biofeedback physiotherapy has been shown to improve symptoms in only 33% of patients^{71,72}. There appears to be a renewed interest in the clinical relevance and surgical treatment of IRP. The long disputed progression into ERP has been made more plausible by recent published data on the natural history of IRP⁷³. Moreover, traditionally used surgical techniques to correct IRP and ERP, including posterior rectopexy and Delorme's procedure, have been replaced by new techniques with better functional outcomes and lower recurrence rates.

Surgical correction of an internal rectal prolapse is possible via a trans-abdominal or trans-anal approach. Currently the most common procedures are laparoscopic



Figure 6 Transtar® procedure (reprinted with permission from Wiley⁷⁷)

ventral rectopexy (LVR) (figure 5) and stapled trans-anal rectal resection (STARR) (figure 6)⁷⁴⁻⁷⁶. LVR corrects the intussusceptions of the rectum and reinforces the rectovaginal septum by the use of a mesh, which suspends the rectum and vaginal vault to the sacral promontory, whereas in the STARR procedure a stapled resection of the redundant rectal wall is performed.

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Outline of the thesis

Outline of the thesis

The aim of this thesis is to evaluate new treatment strategies in several proctologic conditions. In **part one**, treatment of anal fistulas with fibrin glue is studied. **Part two** examines the efficacy of botulinum toxin in the treatment of anal fissure. In **part three** several aspects of haemorrhoidal treatment with PPH are evaluated and in **part four** the treatment of internal rectal prolapse is reviewed.

Part I

In **chapter one**, a consecutive cohort of patients with a primary or recurrent perianal fistula was prospectively enrolled into a pilot study and subsequently treated with fibrin glue. The aim of this study was to assess healing of the fistula in relation to side effects and complications.

Part II

Chapter two describes the first study to compare botulinum toxin with isosorbide dinitrate in a double blind randomised controlled trial. Primary outcome measure is macroscopic healing, while secondary outcome parameters are fissure related pain, side effects, recurrence and costs.

Part III

In **chapter three** the procedure for prolapse and haemorrhoids and transanal haemorrhoidal dearterialisation in the treatment of haemorrhoids grade 3 and 4 are compared in a randomised controlled pilot study. Control of symptoms and postoperative pain are assessed six weeks postoperatively. In **chapter four** the results of a multivariate analysis on predictors of persistence and recurrence of prolapse after PPH, in a series of 159 consecutive patients treated for haemorrhoids grade two to four, are presented. In **chapter five** the feasibility of a redo-PPH in case of recurrent symptoms after a primary PPH for grade 2 to 4 haemorrhoids is assessed. Treatment success and postoperative complications are described. **Chapter six** evaluates the treatment of haemorrhoids among Dutch surgeons in general, and the incorporation of PPH as a treatment modality in specific, by conducting a nation wide survey.

Part IV

In **chapter seven**, treatment strategies in patients with internal rectal prolapse are reviewed. Theoretical differences between the Stapled Anorectal Resection (STARR) and the Laparoscopic Ventral Rectopexy (LVR) are discussed and literature based outcomes are compared.

Part I

Perianal Fistulas

chapter

1

Treatment of Fistulas in Ano With Fibrin Glue

Gisbertz SS, Sosef MN, Festen S, Gerhards MF

Digestive Surgery. 2005;22(1-2):91-4

Abstract

Background: Recent publications show promising results using fibrin glue in the treatment of anal fistulas. The technique is simple, repeatable, with minor surgical trauma so that sphincter function is preserved and further treatment options are not compromised. The aim of this pilot study was to analyse if we could reproduce the results reported in the literature, using this simple technique.

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Methods: Patients with a primary or recurrent anal fistula were included in this trial. Patients with a complex fistula were excluded. Under general or spinal anaesthesia, the fistulas were curetted and injected with fibrin glue. Follow-up visits were scheduled for 1 week, 6 weeks and 6 months.

Results: Twenty-seven patients were included. The overall success rate was 33% after a mean follow-up of 27 weeks. Patients with a recurrent fistula had a poorer outcome (success rate 14%). None of the patients suffered from postoperative continence problems, and no other complications were recorded.

Conclusion: This study confirms the safety of fibrin glue in the treatment of anal fistulas. However, a high success rate could not be reproduced.

Introduction

Conventional surgical therapy for anal fistulas can be frustrating considering its recurrent nature and, when the sphincter muscle is divided, disturbance of anal continence¹⁻⁶. Accordingly, alternative, less invalidating treatment options are frequently sought for. One such new technique is the use of fibrin glue, which consists of a fibrinogen and a thrombin component. By forming a fibrin clot, which seals the fistula tract, it enhances wound healing and supports haemostasis and angiogenesis. Furthermore the fibrin network serves as a matrix for fibroblast ingrowth and formation of a collagen network, without production of an extensive inflammatory reaction^{7,8}. Many advantages have been described using fibrin glue in the treatment of anal fistulas⁹⁻²⁰. It is simple, repeatable, with minor surgical trauma so sphincter function is preserved and further surgical treatment is not compromised. Recent publications show promising results using this technique. Success rates of 85% have been reported^{13,18}, and even a 100% cure rate for low output enterocutaneous fistulas has been shown²¹. However, other studies show less fortunate results as Aitola et al.¹⁴ had a 100% failure rate in 10 patients. The follow-up of these trials varied from 6 to 22 months. Reported results are not univocal in their treatment protocols. A great variety of techniques have been described, such as placement of a draining seton before fibrin glue closure and the use of fibrin glue-antibiotic mixtures¹⁶⁻¹⁸. Also there is a great variation in success rates of different fistula types. Some studies show excellent results treating complex fistulas, whereas others show better results treating simple ones^{12,13,19}. The aim of this pilot study was to assess the use of fibrin glue in the treatment of primary and recurrent anal fistulas, and to analyse if we could reproduce the promising results reported in the literature.

Patients and Methods

Consecutive patients, aged 18 years or older, presenting with a primary or recurrent anal fistula were included. Patients with complex (extrasphincteric, suprasphincteric and high transsphincteric) or Crohn's anal fistulas were excluded to simplify the objective of our study. When during physical examination suspicion was raised upon a complex fistula, an MRI scan using an endo-anal coil was obtained to confirm this diagnosis.

Procedure

Two days prior to surgery, patients were placed on a liquid diet. The procedure took place in Day Care Surgery under general or spinal anaesthesia with the patient placed in the lithotomy position. The fistula was probed to identify the internal opening. When this failed, methylene blue was used. Classification of the fistula was based on sphincter involvement detected during probing. Subsequently the fistula tract was curetted using a blunt curette. When identified, the internal opening was closed with a single suture or a mucosal advancement flap. Fibrin glue from a commercial kit (Tissucol®, Baxter, Vienna, Austria) consisting of two deep-frozen solutions in prefilled syringes was retrieved from storage and thawed. One contained the fibrinogen component, the other thrombin. Both solutions were injected simultaneously into the fistula tract through a designed catheter. To prevent the fibrin glue from leaking, the external opening was closed with a purse-string suture. A laxative was prescribed for 4 weeks after surgery.

Follow-Up

Follow-up visits were scheduled for 2 days, 1 week, 6 weeks and 6 months. After 2 days, the purse-string suture was removed. In case of recurrence patients were scheduled for conventional treatment, which usually consists of placement of a loose draining seton for 3–6 months for extrasphincteric, suprasphincteric and high transsphincteric fistulas and fistulotomy for intersphincteric and low transsphincteric fistulas.

Statistical Analysis

All data were analysed using SPSS 11.5 for Windows XP. A Student t-test or chi square test was used as indicated, to compare the healed and unhealed fistulas. Differences were considered statistically significant at $p < 0.05$.

Results

Twenty-seven patients (23 male) were included. The median age was 43 years, ranging from 19 to 80 years. The median duration of symptoms before treatment was 18 months, ranging from 5 to 60 months.

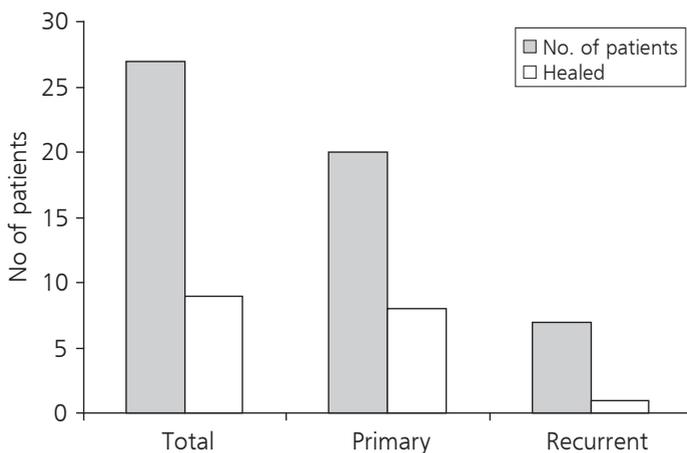
Nineteen patients were classified as having an intersphincteric fistula whereas 8 were considered as having a transsphincteric fistula. As shown in table 1 it regarded 20 primary fistulas and 7 recurrent ones.

Table 1 type of fistula in treated patients

	Primary fistula	Recurrent fistula	total
intersphincteric	15	4	19
transsphincteric	5	3	8
total	20	7	27

Table 2 number of healed patients after fibrin glue treatment

	Primary fistula	Recurrent fistula	total
intersphincteric	7	1	8
transsphincteric	1	0	1
total	8	1	9

Figure 1. Fistula healing. The results of fibrin glue instillation delineated by recurrence.

In 16 cases, the internal opening was identified. Fourteen times it was closed using a single suture, in 2 cases a mucosal advancement flap was created. The mean operation time was 20 min. The follow-up ranged from 3 to 96 weeks, with a median of 27 weeks. None of the patients suffered from continence problems after the procedure, and no other complications were encountered. Pre-existent symptoms of soiling, described in 2 patients, did not increase after treatment.

Our results are listed in table 2. Nine (33%) of 27 fistulas healed with fibrin glue treatment (8 male), regarding 8 intersphincteric fistulas and 1 transsphincteric fistula. Of these fistulas, 8 were primary (success rate 40%) versus 1 recurrence (success rate 14%; fig. 1). Whether the internal opening could be identified and closed did not significantly improve results (38 vs. 27%, $p = 0.66$). One of the 2 patients who were treated with a mucosal advancement flap healed. Eighteen patients suffered from a recurrence in a median period of 9 weeks (range 1–32 weeks) after instillation. Eventually, 13 were treated with conventional surgery (lay-open or fistulectomy), with an overall success rate of 77%. Five patients were treated expectantly (median follow-up of 30 weeks), since they had very mild symptoms only, despite incomplete healing.

Discussion

This study describes the use of fibrin glue in the treatment of primary and recurrent anal fistulas. Although fibrin glue closure is a safe procedure, without complications such as incontinence, our results show a higher recurrence rate than expected compared with the recent literature.

A possible explanation could be the use of different treatment protocols. Mizrahi et al.⁴ and Zmora et al.²⁰ had success rates of 54% with fibrin glue sealing in combination with an endorectal advancement flap versus 33% in patients who had fibrin glue sealant as their principal treatment, although they had even better results without fibrin glue in a different series. In our series, only 2 patients were treated with a mucosal advancement flap.

Sentovich^{17,18} described a two-stage technique: at the first operation, a loose draining seton was placed in the tract, and 6–8 weeks later, when all inflammation around the tract had healed, fibrin glue was instilled. After a mean follow-up of 22 months, a success rate of 69% was shown after 1 or 2 attempts.

Hjortrup et al.⁹ mechanically cleaned the fistulas with saline and decontaminated them with antibiotics for 3 consecutive days prior to surgery. Their success rate was 74% after 1–3 instillations. Patrlj et al.¹⁶ used the same principle of decontaminating the fistulas with antibiotics, and furthermore they used a fibrin glue-antibiotic mixture in their definite treatment. Success rates of 74% were reported. A number of trials described the standard use of prophylactic parenteral antibiotics perioperatively, with success rates of 60%^{10,11}. Others however state similar success rates without

the use of antibiotics^{12,13,15}. Neither systemically nor locally administered antibiotics were used in our trial.

Different forms of bowel preparation were used in different trials. There were no noticeable differences between the trials using extensive mechanical bowel preparation versus preparation using enemas or liquid diet^{10-12,15-18,20}. In our study, patients were placed on a liquid diet 2 days prior to surgery.

Differences could also be explained by different patient selection. Treatment of recurrent fistulas with fibrin glue seems to be less successful than that of primary ones^{12,13,15,17}. This is confirmed in our study in which only 14% of recurrent fistulas healed, lowering the overall success rate. However, in the study performed by Venkatesh and Ramanujam¹¹ recurrences were treated successfully in 60%.

The type of fistula treated best with fibrin glue varies greatly among different trials. A recently performed randomized, controlled trial by Lindsey et al.¹⁹ showed that complex fistulas gave fewer recurrences after fibrin glue treatment than simple ones whereas complex fistulas in our series were excluded. Others do not confirm this however^{12,13}. Also, there is no consensus about fistula length and width and success of fibrin glue treatment. Patrj et al.¹⁶ had the best results with long and narrow fistulas whereas Sentovich^{17,18} had the opposite outcome.

In conclusion, we were not able to reproduce high success rates, although we confirmed the safety of the procedure. However, randomized data will be needed to support these considerations. Also anal continence should be objectified with anorectal manometry and standardized questionnaires.

In further studies, the use of combined techniques such as fibrin glue treatment in combination with mucosal advancement flap needs to be addressed, as well as selection of fistulas that will benefit most from fibrin glue treatment.

Conclusion

An advantage for fibrin glue in the treatment of anal fistulas has not been shown in our small series. Yet, since it is not associated with complications such as incontinence, it can be considered in patients with complex anal fistulas.

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Part II

Anal Fissure

chapter **2**

Blinded Randomized Clinical Trial of Botulinum Toxin versus Isosorbide Dinitrate Ointment for Treatment of Anal Fissure

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Abstract

Background: Nitric oxide donors such as isosorbide dinitrate (ISDN) are considered the first choice of treatment for anal fissure. After reports of the successful treatment of such fissures with botulinum toxin, this randomized blinded trial compared botulinum toxin with ISDN in the treatment of chronic anal fissure.

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Methods: Patients were randomized to receive an injection of botulinum in the internal anal sphincter and a placebo ointment, or a placebo injection and ISDN ointment. The primary endpoint was macroscopic fissure healing after 4 months.

Results: After 4 months macroscopic healing of the fissures was noted in 14 of 37 patients in the botulinum group and 21 of 36 in the ISDN group. Pain scores were lower among patients who received ISDN, although the difference was not significant. Side-effects were similar in the two groups.

Conclusion: In contrast with previous reports on botulinum toxin as a therapeutic agent for anal fissure, this study found no advantage over treatment with a nitric oxide donor as regards fissure healing and fissure-related pain.

Introduction

An anal fissure is an ulcer or split located in the squamous epithelium of the anus. It predominantly occurs in the posterior midline^{1,2}. The aetiology is debated, but spasm of the internal anal sphincter (IAS) is likely to play an essential role in the pathophysiology^{3,4}. Pain, during and after defaecation, is the main symptom and can be disabling. Anal bleeding may occur intermittently. Successful treatment results in an improved quality of life⁵.

The mainstay of current therapy is directed at lowering the resting pressure of the IAS. Historically this was achieved surgically, but therapy has shifted towards pharmacological treatment owing to the high incidence of incontinence-related complications⁶. Topical isosorbide dinitrate (ISDN) has long been the pharmacological treatment of choice in the Netherlands. It acts as a nitric oxide donor, lowering IAS pressure and producing vasodilatation in the anoderm⁷. Another commonly used nitric oxide donor is glyceryl trinitrate (GTN)⁸⁻¹⁰. In a recent review of both nitrate oxide donors, the mean healing rate was approximately 65 per cent⁶.

Treatment of anal fissures with botulinum toxin was first described in 1993 by Jost and Schimrigk¹¹. Injection of botulinum toxin into the anal sphincter blocks acetylcholine release, thereby stopping neural transmission, causing transient hypotonia of the sphincter¹². Since the randomized controlled trial of botulinum toxin versus topical nitroglycerine¹³, botulinum toxin has become increasingly popular and has been compared with other treatment modalities⁶. This double-blind randomized trial compared botulinum toxin with ISDN in the treatment of chronic anal fissure.

Patient and Methods

All consecutive patients over the age of 18 years presenting to a surgical outpatient clinic with a chronic anal fissure between June 2002 and March 2006 were eligible for inclusion in the study. The fissure was considered chronic if symptoms had been present for at least 4 weeks, and physical examination showed typical signs such as visible fibres of the IAS and a sentinel pile. Exclusion criteria were pregnancy, previous anal surgery, Crohn's disease and systemic causes of anal fissure. Patients who had already been prescribed ISDN by a general practitioner were included only once they had stopped taking it for a minimum of 2 months.

Patients were included after confirmation of the diagnosis by physical examination and/or proctoscopy, and after giving informed consent. They were assigned randomly

to one of two treatment groups and given an appointment to receive treatment. Randomization was done by a pharmacist using a block-design, computer-generated list. Both the surgeon and the patient were blinded to the treatment received.

Patients in the first group received an injection of 10 units botulinum toxin (Botox®; Allergan, Irvine, California, USA) in the IAS on each side of the anterior midline¹⁴. In addition, they were given a placebo ointment to apply to the anoderm six times daily. Injection of the IAS was accomplished by palpating the intersphincteric groove, after which the needle was guided into the IAS, under guidance of the index finger in the anal canal. Patients in the second group received a placebo injection and ISDN 1 per cent ointment.

Complaints related to the anal fissure were evaluated by means of a questionnaire completed before treatment, and at 1, 2, 4, 6 and 12 months after treatment. Pain was scored on a visual analogue scale ranging from 0 to 10. Proctoscopy was carried out at 2, 4 and 6 months. If the fissure was still present at the 2-month follow-up or pain scores did not improve, the treatment was repeated in accordance with the initial randomization. If symptoms persisted after 4 months, the surgeon was free to choose any other treatment modality. The protocol was reviewed and approved by the medical ethics committee. The primary endpoint of the study was macroscopic healing of the fissure at 4 months. Secondary endpoints were fissure-related pain, treatment-induced complications, fissure recurrence and costs.

Statistical Analysis

A power calculation was made, based on healing rates for ISDN (65 per cent) and botulinum toxin (90 per cent) from published data. At 80 per cent power and a significance level of $P < 0.050$, it was calculated that 43 patients were required in each arm of the study. Statistical analysis was undertaken using χ^2 test for clinical outcomes, and Student's paired t-test for comparison of pain scores before and after treatment. Patients were analysed according to the intention-to-treat principle.

Results

Of 73 patients enrolled in the study, 37 were randomly assigned to injection with botulinum toxin and placebo ointment, and 36 to receive a placebo injection and ISDN ointment (Fig. 1).

Patient characteristics were similar in the two groups (Table 1). The intersphincteric groove was palpated easily in all patients followed by injection into the IAS. Pain experienced as a result of the injection scored a mean(s.d.) of 5.8(2.6) on a scale

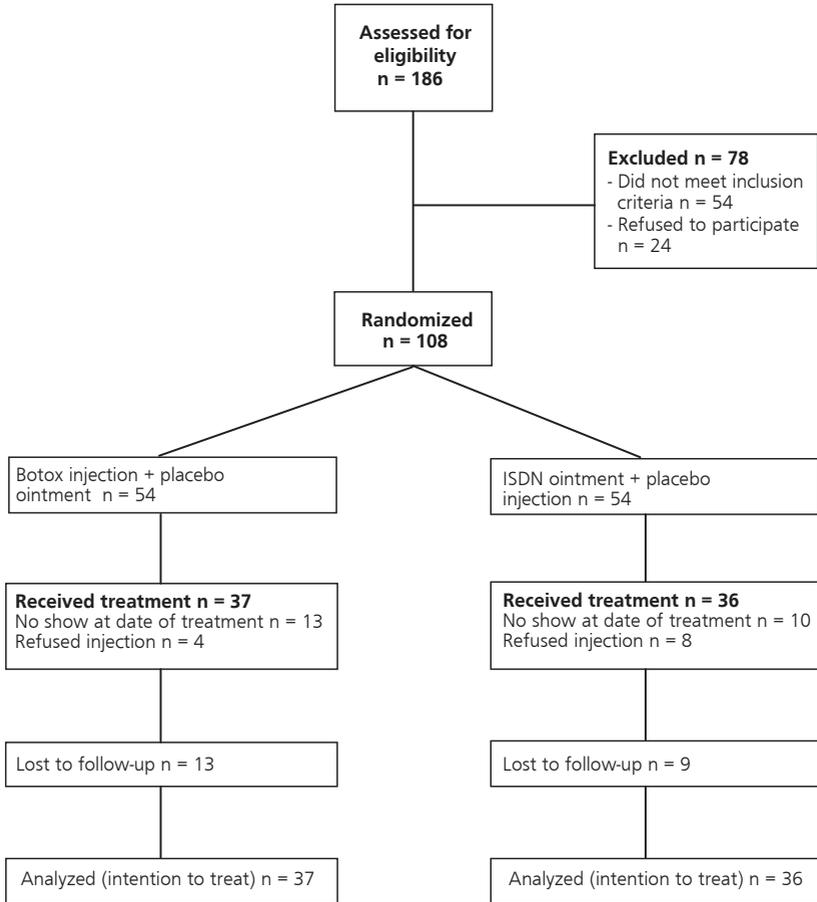


Figure 1 CONSORT diagram

of 0–10. Compliance with the prescribed application frequency of the ointment (six times daily) is shown in Table 2.

Figure 2 shows the clinical course in the two groups with time. One patient who showed no improvement 2 months after botulinum toxin injection chose not to undergo a repeat treatment but instead had a lateral internal sphincterotomy. Another two patients in the botulinum group did the same after 4 months. One patient in the ISDN group had a fissurectomy after 2 months.

Table 1 Patient characteristics

Characteristic	Group I (N = 37)	Group II (N = 36)	P
Age (yr)	40 (\pm 11 SD)	40 (\pm 11 SD)	0.762
Sex (M/F)	20/17	18/18	0.601
Duration of symptoms (mo)	3.4 (\pm 2.7 SD)	3.4 (\pm 2.5 SD)	0.742
History of ISDN usage	17	21	0.290
Painscore (mean)	6.7 (\pm 1.6 SD)	6.4 (\pm 1.0 SD)	0.629
Site of fissure:			
Posterior	30	29	0.955
Anterior	4	5	0.689
Other	3	2	0.317
Bleeding from fissure	24	27	0.345
Sentinel Pile	17	21	0.290
Increased sphincter tonus†	29	28	0.951
Visible IAS	17	16	0.897

† on physical examination

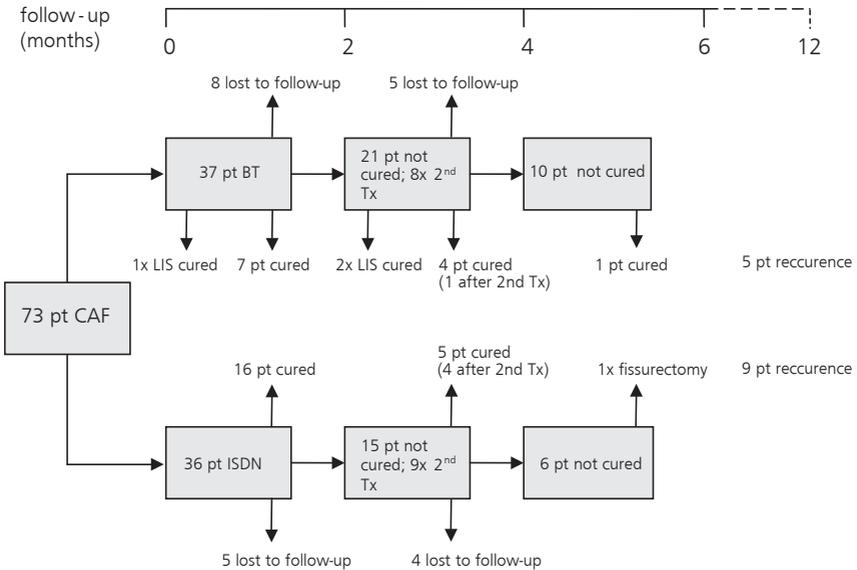
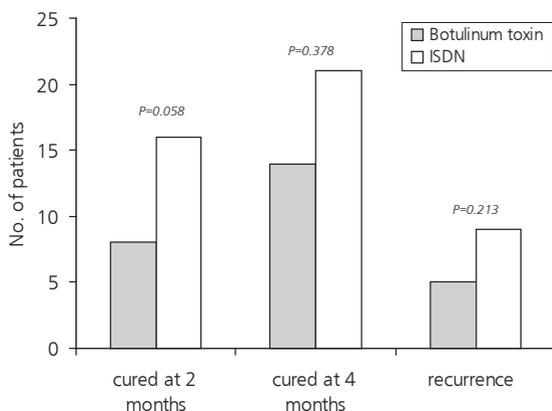


Figure 2 Flow chart showing course of treatment. LIS, lateral internal sphincterotomy; ISDN, isosorbide dinitrate; CAF, chronic anal fissure

Table 2 Number of applications of ointment daily

	1st month	2nd month
BT group	4.29 (95% CI 3.59 to 4.99)	4.91 (95% CI 4.48 to 5.34)
ISDN group	4.87 (95% CI 4.22 to 5.52)	4.62 (95% CI 4.04 to 5.20)
difference	-0.58 (95% CI -1.54 to 0.37) $p = 0.229$	2.92 (95% CI -0.47 to 1.06) $p = 0.445$

**Figure 3.** Number of patients cured and with recurrence after treatment with botulinum toxin or isosorbide dinitrate (ISDN).

After 4 months, the fissure was healed in 21 of 36 patients in the ISDN group compared with 14 of 37 in the botulinum toxin group (odds ratio 1.69 (95 per cent confidence interval (c.i.) 0.53 to 5.43)) (Fig. 3). After a median follow-up of 6.7 months, five of 37 patients in the botulinum toxin group and nine of 36 in the ISDN group had recurrence of the fissure (odds ratio 1.35 (95 per cent c.i. 0.36 to 5.44)). A substantial number of patients were lost to follow-up.

Thirteen patients in the botulinum toxin group and nine in the ISDN group did not attend the 4-month follow-up appointment. Mean pain scores in both groups during follow-up are shown in figure 4. A repeated-measures analysis showed no difference between the groups. The proportions of patients with an improved pain score at 1, 2 and 4 months' follow-up compared with baseline was similar in the two groups (Fig. 5). The reduction in mean pain scores from baseline values was also comparable (Table 3). There were no significant differences between the two groups in the incidence of the most important side-effects (Table 4).

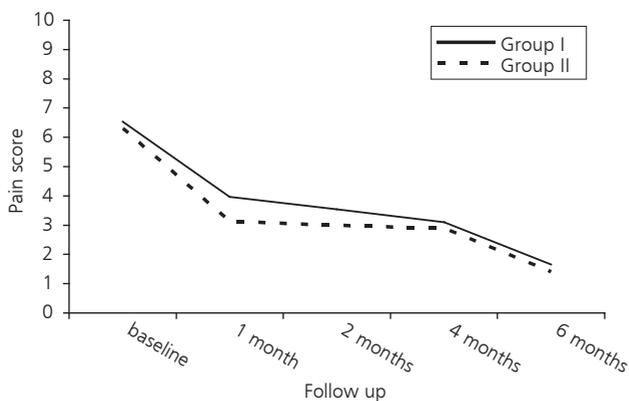


Figure 4. Mean pain scores at baseline and follow-up after treatment with botulinum toxin or isosorbide dinitrate (ISDN)

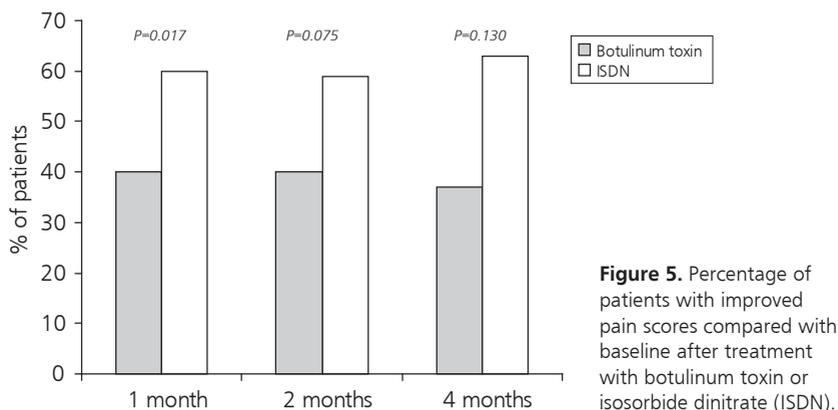


Figure 5. Percentage of patients with improved pain scores compared with baseline after treatment with botulinum toxin or isosorbide dinitrate (ISDN).

Table 3 Reduction in mean pain scores compared with baseline

	Reduction in mean pain score between baseline and 1 month	Reduction in mean pain score between baseline and 2 months	Reduction in mean pain score between baseline and 4 months
Botox + placebo	2.32 (95% CI 1.324 to 3.316)	2.64 (95% CI 1.346 to 3.934)	2.90 (95% CI 1.364 to 4.436)
ISDN + placebo	2.94 (95% CI 2.128 to 3.752)	3.29 (95% CI 2.370 to 4.21)	3.44 (95% CI 2.340 to 4.540)
Difference in mean	-0.615 (95% CI -1.897 to 0.667)	-0.647 (95% CI -2.213 to 0.918)	-0.540 (95% CI -2.393 to 1.313)
P value	0.314	0.411	0.561

Table 4 side effects

	Group I (N = 37)	Group II (N = 36)	P
Headache			
1 month	9 of 31	6 of 32	0.473
2 months	7 of 28	6 of 31	0.667
4 months	7 of 21	7 of 27	0.290
Incontinence for flatulence			
1 month	5 of 31	2 of 32	0.176
2 months	2 of 28	1 of 31	0.468
4 months	1 of 21	0 of 27	0.175

The price of preparing one treatment with botulinum toxin was 271.00 euro, compared with 10.07 euro for one tube of ISDN ointment, which lasted for approximately 1 month.

Discussion

This study found no statistically significant advantage of botulinum toxin over ISDN in the treatment of chronic anal fissure, in terms of healing and recurrence rates, fissure-related pain and side-effects.

Treatment of anal fissure, which affects about 10 per cent of patients in a colorectal practice¹⁵, remains difficult. A Cochrane review published in 2006 stated that medical therapy for chronic anal fissure, acute fissure and fissure in children has a chance of cure that is marginally but significantly better than that of placebo¹⁶. Moreover, because patient satisfaction with the current topical treatment is low owing to frequent side-effects and the tedious application routine, a better alternative is needed. Botulinum toxin was first described as an agent for anal fissure in 1993¹¹ and early results seemed promising, although variable results have been reported since^{6,13}. This study is the first double-blind randomized trial to compare botulinum toxin with a nitric oxide donor. Double-blinding was of crucial importance, especially in analysing the pain scores, to avoid bias related to use of injections.

The primary endpoint of macroscopic healing after 4 months was achieved in a higher proportion of patients in the ISDN group, but the healing rate was not statistically significant from that in the botulinum group. More patients treated with ISDN showed improvement in pain scores and the absolute improvement was

greater than seen with botulinum toxin, although these differences were again not statistically significant. This trend towards better healing in favour of ISDN must be interpreted with caution because the study was not powered to prove an advantage of ISDN over botulinum toxin. One explanation for the lack of statistically significant findings could be that the study was underpowered. The goal of 43 patients in each group was not reached because the trial was ended prematurely owing to stagnating inclusion. It is also possible that the power calculation was based on incorrect assumptions about expected healing rates with botulinum toxin. The present study was initiated after Brisinda and colleagues¹³ published a randomized trial showing a significantly higher healing rate with botulinum toxin in comparison to GTN ointment; an almost 100 per cent healing rate was achieved with botulinum toxin. The figures used in the power calculation in the present study were based partly on data from this trial, but also took into account the modest healing rates achieved with botulinum toxin reported in the more recent literature. In a Cochrane review, success rates with botulinum toxin were equal to those of GTN, a nitric oxide donor¹⁶. The review identified heterogeneity of the botulinum toxin results, which disappeared after excluding Brisinda and co-workers' data¹³. Owing to the shortcomings of the present study, a better success rate for botulinum toxin over ISDN cannot be excluded, but seems unlikely.

There has been some debate about the optimal dose of botulinum toxin to be used in the treatment of anal fissure. One randomized trial showed better results with a total of 30 units instead of the 20 units used in the present study¹⁷. In contrast, other papers have reported equally poor results with higher doses of botulinum toxin^{18,19}. The near 100 per cent success rate reported by Brisinda and colleagues¹³ was achieved with 20 units.

A significant number of patients did not attend follow-up appointments during the course of this trial. It is not known whether their fissures healed or they were dissatisfied with the treatment result. Calculations were carried out with all patients lost to follow-up considered to have either a healed or an unhealed fissure. In both scenarios, there was no advantage of one treatment over the other. One reason for the low attendance could be poor compliance with the routine of ISDN application six times daily, necessary owing to its short pharmacological activity of approximately 3 hours.

The need for multiple daily applications is a clear disadvantage of ISDN. The single injection of botulinum toxin may turn out to be a more important factor in favour of this agent as a primary treatment over ISDN than the questionably better healing

rates. In this respect, topical GTN or diltiazem, a calcium channel blocker, could also be considered as first-line treatment as these have to be applied only twice daily and have comparable results to ISDN ointment²⁰. Moreover, diltiazem cream has fewer side-effects than nitric oxide donors²¹. In a recent meta-analysis comparing botulinum toxin with GTN for chronic anal fissure, botulinum toxin was found to be as effective as GTN, but with a lower complication rate, especially headache²². In contrast, adverse effects in both groups were similar in the present study. The reason for this is unclear as headache is not a commonly reported side-effect of botulinum toxin.

In conclusion, the healing rates of botulinum toxin compared with ISDN, in combination with the difference in costs, do not support the use of botulinum toxin as a primary agent in the treatment of anal fissure. Moreover, in contrast to those who have advocated botulinum toxin as 'rescue' treatment²³⁻²⁵, the present authors believe that this agent will offer no real benefit after other treatment modalities. However, it may prove beneficial in combination with other treatments such as fissurectomy^{26,27}. Finally, botulinum toxin may be considered as an alternative treatment for patients who suffer headache with nitric oxide donors or those unable to comply with the application regimen.

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Part III

Haemorrhoidal Disease

Evidence3 chapter

Treatment of Grade III and IV Haemorrhoidal Disease with PPH or THD. A Randomized Trial on Postoperative Complications and Short-Term Results

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Abstract

Purpose: Haemorrhoidal disease is a frequently occurring entity in the western world. The Procedure for Prolapse and Haemorrhoids (PPH) and Transanal Haemorrhoidal Dearterialisation (THD) are the most important surgical treatments that respect normal anal anatomy. This is the first randomized trial that compares both techniques in the treatment of grade III and IV haemorrhoids.

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Methods: Patients with grade III or IV haemorrhoids were randomized between PPH and THD. Patients were seen after one day, three weeks and six weeks postoperatively. Primary endpoint was resolved symptoms six weeks postoperatively. Secondary endpoints were pain, measured with a visual analogue scale (VAS) after one day, one week and three weeks, and complications.

Results: Eighteen patients were allocated to PPH versus twenty-three to THD. Success rates after six weeks were 83% in the PPH group versus 78% in the THD group. VAS scores were significantly lower after one day and one week in the THD group, but equalled out after three weeks. Twelve per cent of the patients after PPH and 4% after THD needed an urgent readmission to treat an acute bleeding. Overall complication rates did not differ significantly.

Conclusion: Both PPH and THD are safe treatments for grade III and IV haemorrhoids with acceptable complication rates and good short-term results. THD might be the preferred treatment because it carries the similar complication rate and short-term results, but results in less postoperative pain when compared with PPH. Moreover, it is a less invasive, more easily learned and less costly procedure.

Introduction

Haemorrhoidal disease is a frequently occurring entity in the western world and constitutes the most common proctologic disorder. Prevalence ranges from 4 – 10%¹. Haemorrhoids are highly vascular tissue in the submucosal space in the anal canal. They contribute to anal continence in providing complete closure of the anus². When haemorrhoidal tissue gives rise to symptoms, such as bleeding, prolapse or pruritus, one can speak of haemorrhoidal disease. Etiologic factors are multifactorial and include prolonged straining, irregular bowel habits and heredity. Prolapsing internal haemorrhoids are classified according to their severity into four degrees.

When conservative treatment like dietary- and defecation habit advises fails, the primary treatment of choice in most clinics is rubber band ligation (RBL). This procedure is reported to be successful in 65-85% of the patients³. The setback is however that treatment often needs to be repeated in order to be successful and that grade 3 to 4 haemorrhoids seem to be less suitable for banding. This leaves a substantial group of patients, which are not treated sufficiently.

Classic haemorrhoidectomy is still an effective procedure for resolving haemorrhoidal symptoms but also further affects the already altered anal anatomy. Therefore, other techniques have been developed to treat patients that have not reacted to conservative treatment or rubber band ligation. The Procedure for Prolapse and Haemorrhoids (PPH) is a technique that was first described by Longo⁴, and was based on the stapled transanal mucosectomy, first proposed by Pescatori et al.⁵ With a circular stapler device (Ethicon Endo-Surgery) a circumferential resection of mucosa and submucosa above the haemorrhoids is performed, hereby creating a haemorrhoidopexy. PPH is reported to be an effective and safe alternative for surgical haemorrhoidectomy with less postoperative pain, shorter hospital stay, and greater patient satisfaction⁶⁻¹⁰. However, reports on long-term outcome are still scarce¹¹⁻¹⁵. Moreover, incidental but serious complications have been described¹⁶⁻²³. Doppler-Guided Haemorrhoidal Artery Ligation (DGHAL) or Transanal Haemorrhoidal Dearterialisation (THD) uses a specially developed proctoscope combined with a Doppler transducer to identify the haemorrhoidal arteries (originating from the superior rectal artery) and to ligate them selectively²⁴. It is based on the theory that haemorrhoids occur when there is an imbalance in the blood flow of the haemorrhoidal plexus, either caused by increased inflow or decreased venous outflow. By arterial ligation the inflow is reduced, causing the plexus to diminish and

the haemorrhoids to shrink. Reports on this procedure showed low complication rates, minimal postoperative pain and overall good results²⁵⁻²⁸.

Patients and Methods

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We conducted a pilot study in a randomized fashion. All consecutive patients with persistent grade III-IV haemorrhoids after former RBL treatment were eligible for inclusion. Exclusion criteria were age below 18 years, unavailability for follow-up (language, residence), inflammatory bowel disease and a history of haemorrhoidal or anal surgery.

After having obtained informed consent, patients were randomized between PPH and THD by means of opaque envelopes. Both procedures were performed in day care treatment. Before treatment patients had bowel preparation with a sodium phosphate solution (Fosforal/Fleet™). Patients were treated under general or spinal anaesthesia in supine position.

The PPH-procedure was performed according the protocol as described before by Longo (PPH-03 stapler, Ethicon Endo-Surgery™). The stapled mucosectomy was placed approximately 2 cm above the haemorrhoidal complex. During the THD-procedure all feeding arteries were ligated with a braided suture, using the Doppler proctoscope (Endomed™). The prolapse was treated by additional reefing of the mucosa with the same suture used for ligating the vessel.

On discharge, patients were given three tablets of diclofenac 50 mg for the first postoperative day and were advised to take 4000 mg of paracetamol daily for one week. All patients were asked to score postoperative pain on a Visual Analogue Scale (VAS) on the first day, after 1 week and after 3 weeks. All complications and side effects were registered. Six weeks postoperatively patients were asked to evaluate the result of their treatment.

All procedures were performed by two dedicated surgeons with sufficient experience in both procedures. Primary endpoint of the study was the success rate, defined as resolved preoperative symptoms with no need for further treatment. Secondary endpoints were postoperative pain and complications.

Statistical Analysis

Statistical analysis was undertaken with Fisher's exact test for clinical outcomes and Student's paired t-test for comparison of pain scores after treatment. Patients were analysed according to the intention to treat principle. The software used was SPSS version 16.1 for Windows (SPSS Inc., Chicago, IL).

Results

From December 2006 till November 2007, forty-one patients with grade three or four haemorrhoids were included. Patient characteristics were comparable in both groups and are depicted in table 1.

Table 1: patient characteristics

variable	PPH	THD	P-value
sex (male:female)	2.4 : 1	2.3 : 1	0.640
Mean age (yr)	35	39	0.549
Grade haemorrhoids			
Grade 3	94%	84%	
Grade 4	6%	16%	0.361
Median number of RBL sessions	3.2	2.1	0.153
Median number of rubber bands	9.3	6.3	0.156
Mean operation time (min)	23	34	0.000

All patients had a history of rubber band ligations. The average age was 50 years (range 32-79). Male to female ratio was 3:1. Eighteen patients were randomized to PPH treatment versus twenty-three to THD. Postoperative VAS scores are shown in table 2.

There was a significant difference in the postoperative VAS score on day one and after one week in favour of THD. The VAS scores after three weeks did not significantly differ between the two groups. After six weeks preoperative symptoms were resolved in 15 patients (83%) in the PPH group versus 18 patients (78.3%) in the THD group ($p=0.648$). Of the three patients in the PPH group with persisting symptoms, one patient had persistent anal blood loss, which was eventually treated by haemorrhoidectomy. Two others had persistent symptomatic prolapse (11%). Five patients (22%) in the THD group complained of persistent prolapse.

Table 2: Postoperative VAS score

VAS score	PPH (range)	THD (range)	Difference (95% CI)	P-value
Day 1	5.1 (2 – 10)	3.1 (1 – 6)	1.98 (1.02 to 2.94)	0.00
Day 7	3.2 (1 – 8)	1.6 (0 – 5)	1.66 (0.70 to 2.62)	0.00
Day 21	1 (0-7)	0.2 (0 – 2)	0.78 (-0.18 to 1.74)	0.06

The postoperative course was complicated by bleeding in two patients in the PPH group (11%). They were both admitted to the hospital and successfully treated by the intra anal application of an in lidocaine and adrenaline soaked gauze. One other patient from this group had mild postoperative bladder dysfunction, which resolved spontaneously within six weeks. In the THD group, one patient was re-operated upon for persistent rectal blood loss. At operation a haemostatic stitch was placed to control the bleeding. Another patient was successfully put on fibre supplements to treat complaints of soiling. No cases of mortality were encountered in both groups.

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Discussion

For patients with haemorrhoidal disease that is unresponsive to RBL treatment, there are a wide variety of surgical options. The standard surgical treatment has for long been the haemorrhoidectomy. It is still considered standard surgical treatment in many surgical practices today. However, for those who believe in maintaining the functional anal anatomy, the most common surgical options in current practice are PPH and DGHAL. On both techniques various reports have been published, but never has there been a direct comparison between the two techniques.

Although most systematic review show that haemorrhoidectomy is superior to PPH with respect to recurrence, but seems to do worse when it comes to postoperative complications^{7,9,29}, a recently published meta-analysis, pooling data from 25 randomized trials, showed the same recurrence rates for both procedures¹⁰. Moreover, it showed that PPH was associated with less operative time, faster recovery, less postoperative pain and greater patient satisfaction compared to haemorrhoidectomy. Recurrent prolapse after PPH is reported between 4 and 23%. In this study, of the 16% of patients with recurrence or persistence of symptoms after PPH, 11% complained of prolapse. The reason for this early recurrence or persistence of prolapse was not studied in particular, although positioning of the stapler line too high above the haemorrhoidal apex is in our experience the most common cause.

The PPH has been subject to some controversy. There have been publications reporting serious complications after this procedure ranging from anal stenosis to perforation and sepsis¹⁶⁻²³. Faecal urge incontinence after PPH also has gained some attention, initially affecting about 10% of the patients, but this seems to be a self limiting condition³⁰. We believe that the PPH technique possesses technical pitfalls and therefore has a long learning curve. The serious complications that have been

reported in the literature may have been caused by a lack of experience in those performing this procedure. Prior to starting this study, we had performed over 90 PPH procedures. In this trial we did not encounter any serious complications. Even though we routinely check the stapler line for bleeding at the end of the procedure, still 11% of our patients had to be treated for postoperative bleeding. Possibly the postoperatively prescribed non-steroidal anti-inflammatory drugs (NSAID) played a role in its relatively frequent occurrence. Pain seemed to affect the patients more after PPH than after THD, although this was self-limiting. No patients with persistent complaints of pain were encountered.

In contrast, Doppler-Guided Haemorrhoidal Artery Ligation is an easy to learn technique. It has been reported under different names in various publications. In these reports, grade two to four haemorrhoids are being treated with more or less comparable results. Although success is defined in various ways (patient satisfaction, resolves symptoms, disappearance of haemorrhoids), the short-term success is reported around 90%. The long term success rate, as reported in numerous studies with follow up varying between 6 months and 46 months, is between 70% and 96%. In the publication by Dal Monte et al., with the longest reported follow of 46 months, the success rate, defined as completely resolved symptoms, was 92%. In the present study, 22% of the patients in the THD group complained of persistent prolapse after six weeks, which is remarkably higher when compared to some of the papers in the literature. However, in the paper by Wilkerson et al, a comparable 69% prolapse reduction was seen after six weeks. Although it remains speculation due to the small number of patients, the relatively advanced grade of haemorrhoids treated in this study could have been responsible for the high recurrence. Another explanation could be that the atrophy induced by ligating the vessels takes more time to reduce the prolapse.

In this study, no significant difference in the primary endpoint between PPH and THD was found. Success rates were similar in both groups and comparable to those reported in the literature. Based on these results, THD might be the preferred treatment because it carries the similar complication rate and short-term results, but results in less postoperative pain when compared with PPH. Moreover, it is a less invasive, more easily learned and less costly procedure. However, further randomized studies with larger number of patients and longer follow-up are needed to confirm these preliminary data. Although not an end-point of this study, prolapse reduction seemed to occur more rapidly in the patients treated with PPH. This may be due to the fact that prolapse reduction after THD is caused by a combination

of sutured pexy and gradual atrophy of the haemorrhoidal plexus, resulting in postponed reduction of prolapse. This is of importance in the decision algorithm on the treatment of haemorrhoidal disease. When blood loss or mild prolapse is the predominant symptom, THD could be the treatment of choice. When however, severe prolapse is the main complaint, PPH could be preferred because of immediate prolapse reduction.

In conclusion, PPH and THD are both safe treatment options with good short results in the treatment of persistent grade III and IV haemorrhoidal disease. We believe that both procedures can be performed side by side in a specialized centre. Patient selection can be the key in the definitive success rate and patient satisfaction.

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chapter 4

Predictors of Recurrence of Prolapse After Procedure for Prolapse and Haemorrhoids

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In press (Colorectal Disease)

Abstract

Aim: The Procedure for Prolapse and Haemorrhoids (PPH) is an effective surgical therapy for symptomatic haemorrhoids. Compared to haemorrhoidectomy, meta-analysis has shown PPH to be less painful, with higher patient satisfaction and quicker return to work, but at the cost of higher prolapse recurrence rates. This is the first report describe predictors of recurrence of prolapse after PPH.

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Methods: A cohort of patients with symptomatic haemorrhoids, treated with PPH in our hospital between 2002 and 2009 was retrospectively analysed. Multivariate analysis was performed to identify patient-related and peri-operative predictors responsible for persisting prolapse and recurrence of prolapse.

Results: In total, 159 consecutively enrolled patients were analysed. Persistence and recurrence of prolapse was observed in 16% of the patients. Increased surgical experience showed a trend towards lower recurrence rates. Multivariate analysis identified female sex, long duration of PPH surgery, and the absence of muscle tissue in the resected specimen as independent predictors of postoperative persistence of prolapse of haemorrhoids. The absence of prior treatment with rubber band ligation (RBL) as well as increased PPH experience at the hospital showed a trend towards a higher rate of recurrence of prolapse.

Conclusions: In order to reduce recurrence of prolapse, PPH should be performed by a surgeon with adequate PPH experience, patients should be treated with RBL prior to PPH, and a resection of mucosa with underlying muscle fibres should be strived for.

Introduction

Haemorrhoidal prolapse is a very common entity in the western world¹. Change in life-style and diet have increased its prevalence over the last decades. Insight in the physiology of the haemorrhoidal complex and its role in continence have shifted treatment from excision to preservation. The Procedure for Prolapse and Haemorrhoids (PPH), or stapled anopexy, has gained popularity over the last decade and has developed into an important alternative to haemorrhoidectomy. Its introduction however, has not been without controversy. There have been case reports of serious complications after PPH, including recto-vaginal fistula, perforation with pelvic sepsis and anal stenosis²⁻⁶. Combined with reports of chronic postoperative pain and faecal urgency after PPH^{7,8}, it has made surgeons weary to implement this form of treatment into their practices. Multiple systematic reviews and one meta-analysis have however shown PPH to be superior to haemorrhoidectomy in terms of patient satisfaction, postoperative pain and return to work, but most of them show a higher recurrence rate of prolapse after PPH⁹⁻¹². Since postoperative pain and faecal urgency have shown to be self-limiting in most patients¹³, prevention of recurrence is most likely to increase the acceptance of PPH as a valuable alternative to haemorrhoidectomy. This report aims to identify predictors of recurrence of prolapse in a large, single centre, series of patients treated for haemorrhoidal disease with PPH.

Patients and Methods

Consecutively treated patients with Goligher grade 2 to 4 haemorrhoidal disease, that received PPH at the Onze Lieve Vrouwe Gasthuis hospital (OLVG) between May 2002 and September 2009, were included for review, no patients were excluded from review. The OLVG is a large teaching hospital in the centre of Amsterdam and was an early adopter of the PPH in the Netherlands. Preoperative status of the patient, including previous treatment with RBL, was well documented. All patients underwent proctoscopy at the time of the first visit to confirm the diagnosis, and haemorrhoids were graded according to Goligher's classification. Most patients were treated because of persisting symptoms after one or more sessions of RBL, whereas some patients were directly scheduled for stapled anopexy. Patients presenting with grade 4 haemorrhoids were only treated if strangulation was absent. Stapled anopexy was performed with the patient in lithotomy position, using the PPH-01

stapler (Ethicon Endo-Surgery™, Cincinnati, USA) in the first few patients and after its introduction in 2003 the PPH-03 stapler (Ethicon Endo-Surgery™, Cincinnati, USA), Surgery was performed under general or spinal anaesthesia in day care setting. All procedures were done by, or under supervision of one of two dedicated gastro-intestinal surgeons. The stapled mucosectomy was placed approximately 2 cm above the apex of the haemorrhoidal complex. After stapling, the stapler line was injected with a Marcaine®/ adrenaline solution to prevent postoperative pain and bleeding. The operating time was documented. The procedure was considered technically successful if a circular resection was obtained, if the stapler line was situated above the anoderm and if the prolapse was adequately reduced. If there were any deviations from this operative protocol (fragmentation of the resection doughnut, stapler line on the anoderm, incomplete reduction of prolapse requiring additional measures), this was documented as such. The excised doughnut shaped specimen was sent to pathology to determine the depth of the resection. Patients were seen for follow-up two weeks after surgery, and thereafter only if this was indicated. Complications and postoperative symptoms were documented. Postoperative outcome was classified as persistence of prolapse or recurrence of prolapse. This was established on physical examination and where necessary using proctoscopy. Patients with persisting prolapse were diagnosed as such at the first follow up visit. Recurrence was defined as all patients returning to our outpatient clinic with haemorrhoidal prolapse after being discharged from follow up.

Data Management and Analysis:

The data were analysed using Intercooled Stata version 11 (StataCorp, College Station, TX, USA). To describe the study population, Chi-square (categorical variables) or Mann-Whitney U test (comparing medians of continuous data) were used to compare characteristics of male and female patients having undergone PPH surgery. The distribution of socio-demographic, haemorrhoid treatment history, and PPH factors (type of surgeon, duration of surgery, deviations from standard operative protocol and the presence of muscle tissue in the resected doughnut) was assessed, and continuous variables categorized.

A priori confounding variables (age) and potential confounders were tested for an association with early and long-term adverse PPH outcomes. Potential confounding factors associated with both the outcome and the exposure ($P < 0.10$) as well as age (*a priori*) were included in the multivariate logistic regression models identifying

independent predictors of adverse PPH treatment outcome. Using a stepwise forward logistic regression, potential confounders were included in the model beginning with the covariate with the lowest P value. Variables that did not markedly alter the model fit (< 10% change in odds ratio) were removed from the model. Where biologically plausible, variables were evaluated for effect modification using a likelihood ratio test. Adjusted odds ratios were presented based on the final models.

Results

Between May 2002 and June 2009, 159 consecutive patients were treated for haemorrhoids with PPH (figure 1). Socio-demographic, treatment history and PPH surgery characteristics of these patients are summarized in table 1.

The main indication to perform PPH was persisting symptoms of haemorrhoids despite previous treatment with RBL, done at the OLVG after enrolment or before enrolment at another hospital (79%). After enrolment 113 patients were treated

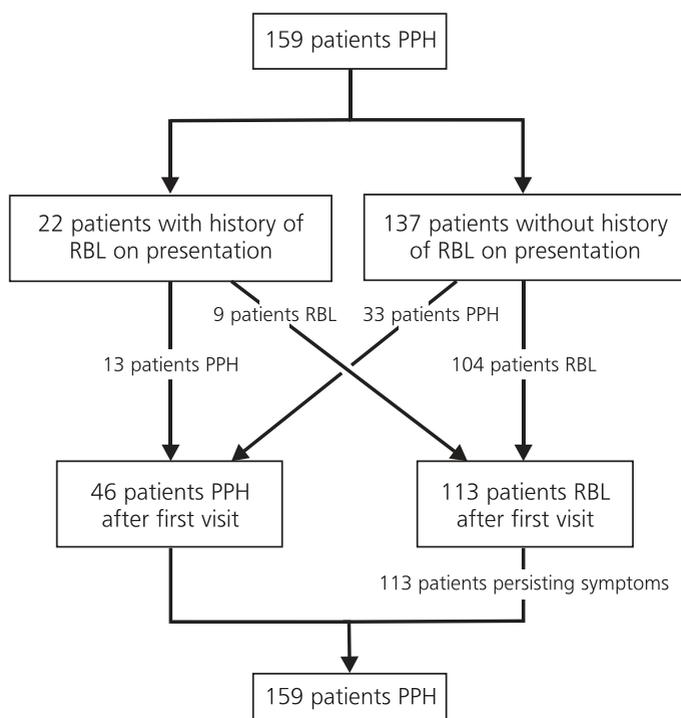


Figure 1

Table 1

	Characteristics	All patients (N=159)	Female patients (n=51)	Male patients (n=108)	P value*
Age	Age, median years (IQR)	46 (38-55)	50 (42-55)	45 (37.5-55)	0.11 [‡]
	Age, n/N (%)				
	≤ 50 years	98/159 (61.6%)	27/51	71/108	
	≥ 51 years	61/159 (38.4%)	24/51	37/108	0.12
Disease stage and treatment history	Pre-treatment rectal blood loss, n/N (%)				
	Yes	139/159 (87.4%)	43/51	96/108	
	No	20/159 (12.6%)	8/51	12/108	0.42
	Haemorrhoid stage, n/N (%)				
	Grade 2	13/159 (8.2%)	5/51	8/108	
	Grade 3	106/159 (66.7%)	31/51	75/108	
	Grade 4	40/159 (25.2%)	15/51	25/108	0.56
	Previous treatment with RBL, n/N (%)				
	No	33/159 (20.8%)	14/51	19/108	
	Yes, at peripheral health facility	22/159 (13.8%)	8/51	14/108	
	Yes, at research hospital (OLVG)	104/159 (65.4%)	29/51	75/108	0.17
	Number of previous RBL treatments at research hospital, n/N (%)				
	None at research hospital	46/159 (28.9%)	17/51	29/108	
	1 to 3 RBLs	74/159 (46.5%)	28/51	48/108	
4 or more RBLs	39/159 (24.5%)	8/51	33/108	0.13	
PPH characteristics	Qualifications PPH surgeon, n/N (%)				
	Surgeon	92/159 (57.9%)	33/51	59/108	
	Surgeon in training	67/159 (42.1%)	18/51	49/108	0.23
	Duration of PPH surgery, n/N (%)				
	≤ 24 minutes	99/158 (62.7%)	31/51	68/107	
	≥ 25 minutes	59/158 (37.3%)	20/51	39/107	0.74
	Per protocol PPH operation, n/N (%)				
	No	48/159 (30.2%)	8/51	40/108	
	Yes	111/159 (69.8%)	43/51	68/108	0.006
	PPH doughnut circular?				
Yes	132/159 (83.0%)	46/51	86/108		
No	27/159 (17.0%)	5/51	22/108	0.098	
Muscle tissue in histology sample?					
Yes	31/121 (25.6%)	14/41	17/80		
No	90/121 (74.4%)	27/41	63/80	0.12	

Table 2

Variable	Early post-PPH haemorrhoids persistence				
	n/N (%)	Crude OR (95%CI)	P-value	Adjusted OR (95%CI)	P-value
Sex					
female	12/51 (23.5)	2.25 (0.93-5.43)		3.24 (1.12-9.35)	
male	13/108 (12.0)	1.0	0.064	1.0	0.029
Age					
≤ 50 years	18/98 (18.4)	1.0			
≥ 51 years	7/61 (11.5)	0.58 (0.22-1.48)	0.25		
Pre-treatment rectal blood loss					
Yes	20/139 (14.4)	1.0			
No	5/20 (25.0)	1.98 (0.64-6.12)	0.22		
Haemorrhoid stage					
Grade 2 or 3	16/119 (13.5)	1.0			
Grade 4	9/40 (22.5)	1.87 (0.75-4.68)	0.17		
Previous treatment with RBL, n/N (%)					
No	6/33 (18.2)	1.25 (0.45-3.45)			
Yes	19/126 (15.1)	1.0	0.66		
Number of previous treatments with RBL at research hospital, n/N (%)					
None	8/46 (17.3)	1.39 (0.51-3.81)			
1 to 3 RBLs	11/74 (14.8)	1.0			
4 or more RBLs	6/39 (15.3)	1.01 (0.34-2.99)	0.58		
Health facility experience with PPH over time					
First 81 PPH operations	13/81 (16.1)	1.0			
Subsequent 78 operations	12/78 (15.4)	0.95 (0.40-2.24)	0.91		
Qualifications PPH surgeon					
Surgeon	12/92 (13.0)	1.0			
Surgeon in training	13/67 (19.4)	1.6 (0.68-3.80)	0.28		
Duration of PPH surgery					
≤ 24 minutes	11/99 (11.1)	1.0		1.0	
≥ 25 minutes	14/59 (23.7)	2.49 (1.03-6.02)	0.036	2.91 (0.98-8.65)	0.055
Per protocol PPH operation					
Yes	20/111 (18.0)	1.89 (0.66-5.42)			
No	5/48 (10.4)	1.0	0.23		

Variable	Early post-PPH haemorrhoids persistence				
	n/N (%)	Crude OR (95%CI)	P-value	Adjusted OR (95%CI)	P-value
PPH doughnut circular					
Yes	22/132 (16.7)	1.0			
No	3/27 (11.1)	0.63 (0.17-2.27)	0.47		
Muscle tissue in histology sample					
Yes	2/31 (6.5)	1.0		1.0	
No	18/90 (20.0)	3.6 (0.77-17.07)	0.081	6.49 (1.26-33.25)	0.025
Postoperative pain?					
Yes	15/81 (18.5)	1.52 (0.63-3.65)			
No	10/77 (13.0)	1.0	0.34		
Postoperative faecal urgency?					
Yes	5/22 (22.7)	1.71 (0.56-5.18)			
No	20/136 (14.7)	1.0	0.34		
Postoperative rectal blood loss?					
Yes	10/49 (20.4)	1.62 (0.67-3.95)			
No	15/110 (13.6)	1.0	0.28		
Any postoperative complication?					
Yes	18/102 (17.7)	1.53 (0.59-3.94)			
No	7/57 (12.3)	1.0	0.37		

primarily with RBL (71%) whereas a PPH was done as the first procedure in 29% of the patients, either because of severe symptoms or because the patient refused treatment with RBL. There were no significant differences between men and woman, except for deviation from the standard PPH protocol, which was observed significantly more frequent in male patients (37 vs. 16%). The mean follow up time was 48 months (range: 9 – 95 months). Table 2 shows the factors that were studied in a univariate and multivariate model on their association with postoperative persistence of prolapse. Persistence of prolapse was noted in 25 patients (16%). Six of these patients chose not to be treated again, 5 were treated with a redo-PPH, 2 underwent a haemorrhoidectomy, 2 a transanal haemorrhoidal de-arterialisation (THD) and in 10 patients the residual prolapse was treated with RBL. In the univariate model there was a non-significant trend towards a higher rate of persistence in the female population (24 vs. 12%), after prolonged operation time (24 vs. 11%)

Table 3

Variable	Recurrence of prolapse after PPH surgery				
	n/N (%)	Crude OR (95%CI)	P-value	Adjusted OR (95%CI)	P-value
Sex					
female	8/51 (15.7)	0.93 (0.37-2.31)			
male	18/108 (16.7)	1.0	0.88		
Age					
≤ 50 years	19/98 (19.4)	1.0			
≥ 51 years	7/61 (11.5)	0.54 (0.21-1.38)	0.19		
Pre-treatment rectal blood loss					
Yes	23/139 (16.6)	1.0			
No	3/20 (15.0)	0.89 (0.24-3.30)	0.86		
Haemorrhoid stage					
Grade 2 or 3	20/119 (16.8)	1.0			
Grade 4	6/40 (15.0)	0.87 (0.32-2.36)	0.79		
Previous treatment with RBL, n/N (%)					
No	9/33 (27.3)	1.0		1.0	
Yes	17/126 (13.5)	0.42 (0.16-1.06)	0.058	0.42 (0.17-1.03)	0.058
Health facility experience with PPH over time					
First 81 PPH operations	18/81 (22.2)	1.0		1.0	
Subsequent 78 operations	8/78 (10.3)	0.40 (0.16-1.00)	0.042	0.42 (0.16-1.10)	0.078
Qualifications PPH surgeon					
Surgeon	17/92 (18.5)	1.0			
Surgeon in training	9/67 (13.4)	0.68 (0.28-1.65)	0.40		
Duration of PPH surgery					
≤ 24 minutes	16/99 (16.2)	1.0			
≥ 25 minutes	9/59 (15.3)	0.93 (0.38-2.28)	0.88		
Per protocol PPH operation					
Yes	16/111 (14.4)	1.0			
No	10/48 (20.8)	1.56 (0.65-3.77)	0.32		
PPH doughnut circular					
Yes	19/132 (14.4)	1.0			
No	7/27 (25.9)	2.08 (0.77-5.65)	0.14		

Variable	Recurrence of prolapse after PPH surgery				
	n/N (%)	Crude OR (95%CI)	P-value	Adjusted OR (95%CI)	P-value
Muscle tissue in histology sample					
Yes	8/31 (25.8)	1.0			
No	13/90 (14.4)	0.49 (0.18-1.33)	0.15		
Postoperative pain					
Yes	14/81 (17.3)	1.13 (0.49-2.64)			
No	12/77 (15.6)	1.0	0.77		
Postoperative faecal urgency					
Yes	5/22 (22.7)	1.61 (0.53-4.87)			
No	21/136 (15.4)	1.0	0.39		
Postoperative rectal blood loss					
Yes	7/49 (14.3)	0.80 (0.31-2.05)			
No	19/110 (17.3)	1.0	0.64		
Any postoperative complication					
Yes	16/102 (15.7)	0.87 (0.37-2.09)			
No	10/57 (17.5)	1.0	0.76		

and with the presence of muscle tissue in the resected doughnut (20% vs. 7%). In the multivariate model, female sex and the absence of muscle tissue were both independent predictors of persistence of prolapse. Shorter operation time showed a trend towards less persistence of prolapse. Factors potentially associated with recurrence of prolapse are depicted in table 3. Recurrence was seen in 26 patients (16%). Seven of these chose conservative measures over re-intervention, 7 were re-treated with PPH, in 4 a haemorrhoidectomy was done, in 2 a THD and in 6 patients RBL. In the univariate analysis, experience of our institution with the procedure was the only factor significantly associated with recurrence, but did not prove to be an independent factor in the multivariate analysis. In the multivariate analysis patients that were not treated with RBL prior to PPH, showed a trend towards being more at risk of developing recurrent prolapse. The number of preceding RBL treatments did not prove to be predictive in the multivariate analysis.

Discussion

If non-operative treatment of haemorrhoids fails, usually surgery is the next step. The main choice the surgeon has is between excisional therapy, and treatment that aims to restore the anatomy. Numerous meta-analyses have shown PPH to be superior to haemorrhoidectomy with respect to patient satisfaction and postoperative pain. However, higher recurrence rates of prolapse seem to be the major drawback after stapled anopexy. Apart from one systematic review¹², most papers confirm the higher rate of recurrence^{9,11,14,15}. These recurrence rates range between 1% after 6 years¹⁶ follow up to 79% residual symptoms at 1-year follow up¹⁷. Although the true rate of recurrence is difficult to determine due to a great variance in definition, it is clear that it constitutes a significant problem. One potential pitfall in comparing these papers with the current study is that a considerable number of patients treated with the PPH-01 went into these analyses, while most patients in our study were treated with the PPH-03 stapler. The main theoretical advantage for the PPH-03 stapler is however haemostasis due to reduced stapler height. No difference in prolapse reduction or recurrence has been shown¹⁸. To our knowledge, the study presented is the first identify independent predictors of persistence and recurrence of prolapse after PPH.

Surgery duration of 25 minutes or more and the absence of muscle tissue in the doughnut shaped specimen are independently associated with persistence of prolapse after PPH. Duration of surgery might reflect a more complex surgical situation and in itself lead to worse outcomes, although deviations from our standard surgical protocol were weighed separately in the multivariate analysis. Of more interest is the strong predictive value of absence of muscle tissue in the resected specimen with persistent prolapse. The resection of some muscle tissue along with mucosa, instead of only mucosa, constitutes a more extensive resection, possibly resulting in a better and firmer pexy. This deeper than mucosa resection is something we deliberately aim for during the placement of the purse-string suture. This theory however, is in conflict with the paper by Ohana et al.¹⁹ They observed no influence on the recurrence rate with respect to the pathology of the resected specimen.

One possible important factor of early failure was not investigated in this study. The height of the stapler line in relation to an anatomic marker like the anal verge or dentate line was not measured during our procedures. We strongly believe that if

the positioning of the stapler line is too high above the apex of the haemorrhoidal complex, it will not lift the haemorrhoidal complex enough. On the other hand, placing the stapler line too close to the anoderm will result in postoperative pain and possibly more faecal urgency. In a report by Plocek et al.¹⁹ it was shown that positioning of the stapler line 2.2 cm or higher above the dentate line was correlated with an earlier return to work. They did not however, show a correlation between the height of the stapler line and recurrence of prolapse.

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Although it is not reflected by the results of our multivariate analysis, we feel that persistence of prolapse is related to failure of surgical technique. This might be due to the fact that some factors are difficult to measure, but probably play an important role. When looking at results in respect to the height of the stapler line, what should be the reference point in measuring this distance? The distance between the dentate line and the apex of the haemorrhoidal complex is in our opinion variable. But also the severity of prolapse is difficult to quantify. Goligher's classification doesn't truly capture the amount of prolapsed haemorrhoidal tissue. Some patients with grade three haemorrhoids have a more severe prolapse than others and may need to be treated with a 'double PPH' instead of the standard technique in order to reach an adequate prolapse reduction²⁰.

Recurrence of prolapse was in our multivariate model independently predicted by no previous treatment with RBL, though did not reach statistical significance. Interestingly enough, patients after previous treatment with RBL seem to do better than the patients that underwent a primary PPH. Where we increasingly felt that patient with considerable prolapse should be spared the multiple RBL treatments prior to PPH, it now seems that these treatments do serve a purpose, even if they don't completely solve the prolapse. Possibly, stage migration of haemorrhoidal prolapse after RBL might play a role here, although one would have expected the initial grade of prolapse to show up as an independent factor for recurrence in our analysis.

Although it did not reach statistical significance, the recurrence rate of 22 % in the first half of our study population was considerably higher than the 10 % in the second half. Is it because patients operated upon during the first period had more time to develop a recurrent prolapse, or is it the surgeon's experience that plays an important role in the outcome of these patients? PPH is not to be considered

a simple procedure and possesses many technical pitfalls. Over time and with increasing experience, we have made small adjustments to the procedure that have increasingly improved safety and treatment outcome.

In conclusion, anatomy-restoring procedures like PPH remain in our opinion the preferred method of treating symptomatic haemorrhoids, despite considerable recurrence rates. To prevent persistence or recurrence of prolapse, the surgeon should be sufficiently experienced in performing the technique, preferably all patients should undergo RBL as initial treatment, and when performing PPH, a resection containing muscle fibres should be strived for. Finally, all patient in general should be properly informed about the possibility of recurrent prolapse after PPH.

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Evidence-based chapter 5

Redo Procedure for Prolapse and Haemorrhoids (PPH) for Persistent and Recurrent Prolapse after PPH

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Abstract

Background/Aims: Procedures for haemorrhoidal prolapse that maintain functional haemorrhoidal anatomy are progressively used. The Procedure for Prolapse and Haemorrhoids (PPH) has advantages over conventional haemorrhoidectomy, but is associated with a higher recurrence rate. The feasibility and efficiency of a second PPH instead of haemorrhoidectomy in case of recurrent symptoms were studied.

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Methods: a retrospective chart review was conducted of all patients that were treated with PPH for haemorrhoidal prolapse in our hospital between May 2002 and November 2008. All patients in need for a second PPH because of persistent or recurrent symptoms of prolapse were identified and analysed.

Results: Out of 137 patients who underwent a PPH, 22 patients (16%) were in need of a reoperation for symptoms of prolapse. Of these, 12 (55%) were treated with a second PPH. Successful prolapse reduction was achieved in 11 out of 12 patients. No postoperative complications were encountered during a median follow up of 35 months.

Conclusion: Redo PPH, in case of persisting or recurrent symptoms of haemorrhoidal prolapse after PPH, is feasible and is a good alternative for excisional haemorrhoidectomy. It possesses the same advantages over haemorrhoidectomy as the initial PPH and does not lead to more morbidity.

Introduction

Haemorrhoidal disease is a frequently occurring entity in the western world¹. Haemorrhoidectomy used to be the standard treatment for patients with grade 3 en 4 disease, and is still being practiced around the world today. However, in the recent years treatment seems to have turned towards preserving instead of excising the haemorrhoidal complex. The Procedure for Prolapse and Haemorrhoids (PPH), or the stapled anopexy (SA), has gained widespread popularity as a relatively new technique. PPH offers a shorter hospital stay, faster functional recovery, less postoperative pain with similar symptomatic control^{2,3}. Long-term success rates have been reported to be around 70 – 90 % depending on the definition of success⁴⁻⁷. Recurrence of prolapse after PPH is claimed to be higher in comparison to the excisional haemorrhoidectomy^{3,8,9}. In case of a persistent or recurrent prolapse after PPH, a new intervention is sometimes required and frequently a haemorrhoidectomy is the treatment of choice^{4,10,11}. We believe however that a second PPH is feasible with good results in most of these patients. In this study, we describe our experience with the repeated PPH.

Patients and Methods

All patients treated for prolapsed (grade III and IV) haemorrhoids with PPH in our institution, were included for review. Patient charts and office notes were reviewed. All patients underwent proctoscopy prior to PPH and prior to the second PPH. The initial and the second PPH was done with the PPH 03 stapler (Ethicon Endo-Surgery™), under general or spinal anaesthesia in day care setting. In the beginning of the series, the purse-string suture (Prolene 2-0, polypropylene; Ethicon, Inc., Somerville. New Jersey) and subsequently the stapler line, was placed four centimetres above the dentate line as dictated by the company. With experience this position changed to approximately 2 cm above the apex of the haemorrhoidal complex. The second PPH was done in the same fashion as the initial one. During operation it was determined, depending on the location of the original stapler line, whether the new anopexy was placed above or below it. After stapling, the stapler line was injected with a marcaine®/ adrenaline solution to prevent postoperative pain and bleeding. After discharge at the day of operation, patients were scheduled for follow up appointment after a month. Additional follow up was planned if necessary.

Results

Between May 2002 and November 2008, one hundred thirty-seven patients were treated for haemorrhoids by PPH in our hospital. All procedures were carried out by senior surgeons experienced in colorectal surgery. The patient characteristics are depicted in table 1.

Table 1

PPH (n = 137)

Median age (years)	46 (range 21 – 86)
Male : Female	2:1
Grade Hemorrhoids:	
Grade 2	10 (7%)
Grade 3	91 (66%)
Grade 4	36 (26%)
Median number of RBL treatments	2 (range 0 – 10)
Median number of rubber bands	7 (range 0 – 29)
Median follow up period (months)	40 (range 3 – 81)

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Because of persisting or recurrent haemorrhoidal symptoms, 22 patients (16%) required a reoperation at a median time of seventeen months (range 2–65) after PPH. Of these patients, 12 underwent a second PPH. The characteristics of these patients are shown in table 2. During the first PPH, the resected donut of mucosa was circular in 9 patients. In one patient the donut was not circular and during the same operation a haemorrhoidectomy was performed on one side. In another, there was an inadequate prolapse reduction due to a very thin donut and a sutured pexy was done. In the third patient, the donut was asymmetrical being thinner on one side. In half of the patients there was muscular tissue seen in the resected specimen during pathologic review.

All the redo procedures were done by the same surgeon, who had sufficient experience in performing the PPH procedure. During the redo operation the new anopexy was placed approximately two centimetres above the haemorrhoidal apex. Depending on the position of the original stapler line, this was proximal in four patients, and distal in eight patients. The median operation time was 20 minutes (range 12–31 minutes). After the redo PPH, in 11 out of 12 patients, symptoms resolved completely. After discharge, none of the patients required analgesia in

Table 2

Redo PPH (n = 12)	
Median age (years)	44 (range 30 – 58)
Male : Female	3:1
Medical history	Previous RBL in 4 patients
Grade of hemorrhoids:	
Grade 3	9
Grade 4	3
Median number of RBL treatments	2 (range 0 – 5)
Median number of elastic bands placed	5 (range 0 – 13)
Median operation time first PPH (min)	27 (range 15 – 45)
Indication redo PPH:	
Persisting prolapse	5
Recurrent prolapse	7
Median time between 1 st and redo PPH (months)	20 (range 4 – 65)
Median follow up period (months)	51 (range 15 – 81)

the postoperative period. The median follow-up time was 35 months (range 5 – 75 months). One patient had persisting complaints of prolapse and underwent treatment with rubber band ligation 10 months after the redo PPH that was unsuccessful. After this, a transanal haemorrhoidal dearterialisation (THD) was planned, but the patient did not show up at the day of the operation and was lost to follow up. One patient had a recurrence of haemorrhoidal prolapse 6 years after the redo PPH and was successfully treated with rubber band ligation. There were no major complications in the postoperative period. One patient had complaints of soiling, but this resolved spontaneously. An anal fissure developed after the redo PPH in one patient and was successfully treated with isosorbide dinitrate ointment.

Discussion

Despite its advantages over excisional haemorrhoidectomy in terms of hospital stay, postoperative pain, functional recovery and patient satisfaction, the stapled anopexy is known to be associated with a higher recurrence of prolapse^{3,8,9}. Recurrence or persistence of prolapse after PPH is well reported in the literature and is encountered between three and twenty-four per cent of patients^{4-6,11-13}. When bleeding is the recurrent or persistent complaint, patients can usually be adequately treated with

rubber band ligation or THD. Four patients who experienced recurrent blood loss after PPH were treated with THD in our series with good result. In case of prolapsing haemorrhoids, our experience is that people do not want to go back to treatment with RBL. When we just started doing the PPH treatment, most patients had multiple sessions of RBL prior to PPH, whereas nowadays we tend to perform a primary PPH in case of grade three or four haemorrhoids. Due to the initial failing of RBL these patients usually wanted an operative solution for their complaints. Reoperation rates after PPH have been reported between seven and fourteen per cent^{2,7,11,14}. Although most authors prefer to perform a haemorrhoidectomy in case of a failed PPH^{4,10,13}, redo-PPH has been reported^{7,10}. We performed a haemorrhoidectomy in six out of the 22 patients. These were mainly done in the beginning of our series. With more experience, we switched to doing redo PPH for symptoms of prolapse after the first PPH. Raahave et al described 31 patients with residual prolapse, in a cohort of 258 patients, who required a second PPH with good results. They observed the pain to be significantly higher after the second PPH in comparison with pain after the first PPH. However, we found no severe complaints of pain resulting in the need for oral analgesia in any of our patients after the second PPH. The authors relate this to the lower position of the stapler line. However, the position of the second stapler line in respect to the first one is not mentioned. In most of our patients who received a second PPH, the new stapler line was situated below the first one. This finding suggests that the first PPH was placed too high above the apex of the haemorrhoidal complex leading to inadequate prolapse reduction. This correlates with a change in technique we have adopted over the years. In the beginning of our series our reference point for the purse-string suture was the dentate line. Now we believe that the apex of the haemorrhoidal complex is a more useful anatomic marker. The dentate line is difficult to visualize during the procedure and we believe the distance between the apex of the haemorrhoidal complex and the dentate line is variable. In four patients there was not enough space below the first stapler line, and therefore the new stapler line was placed proximal to it. Besides the possible too high positioning of the stapler line, we were not able to identify other factors that were associated with the need for a second PPH. There was no relation with the severity of preoperative mucosal prolapse, age, gender, or the integrity of the resected mucosal donut. In the four patients in whom the first PPH was not placed too high, we have to speculate about the cause of the recurrence. It could be that the height of the resected mucosa ring was insufficient in these patients. The study by Raahave et al. found that the risk for the need of a reintervention is greatest in

the first year after PPH⁷. This suggests that an inadequate initial PPH is the main risk factor for a repeat intervention instead of recurrent prolapse. In our experience, sixty per cent of the patients who underwent a redo PPH had their recurrence of prolapse after a mean of 25 months.

In conclusion we believe that a second PPH, in case of persistent or recurrent prolapse, after PPH is a feasible and efficient intervention. It has a high success rate with the same benefits the PPH has over the excisional haemorrhoidectomy, without resulting in more morbidity when compared to that after the initial PPH.

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chapter 6

Adaptation of PPH as Treatment Modality for Haemorrhoids in the Netherlands; A Nationwide Survey

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Submitted

Abstract

Introduction: New techniques in the treatment of haemorrhoidal disease have been introduced in the past two decades. The most significant are the Procedure for Prolapse and Haemorrhoids (PPH) and the Transanal Haemorrhoidal Dearterialisation (THD).

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Methods: An email based, twenty-seven-question survey was sent to all Dutch surgeons concerning the daily practice of haemorrhoidal treatment in general and the position of PPH in particular.

Results: 215 of the 969 surgeons electronically returned their questionnaire (response rate 22%). 35 % of these were gastro-intestinal (GI) surgeons. General surgeons were more likely to perform haemorrhoidectomy in case of grade 3 and 4 disease whereas GI surgeons were 6 times more likely to have PPH incorporated into their practice. 42% of the surgeons reported to have PPH experience. Of these only 25% had experience with 30 or more procedures. Perforation to the peritoneal cavity, anal stenosis and pre-sacral abscess were reported by 11%, 18% and 12%.

Conclusion: Haemorrhoidal treatment with PPH has earned a substantial role in current treatment strategies in the Netherlands, especially in grade 3 and 4 haemorrhoids, although experience is still limited. Serious complications are reported by a substantial part of PPH experienced surgeons. Haemorrhoidectomy remains a popular treatment modality, especially among general surgeons.

Introduction

New techniques in the treatment of haemorrhoidal disease have been introduced in the past two decades. The most significant and widespread used are unarguably the stapled anopexy or Procedure for prolapse and Haemorrhoids (PPH)¹ and the Transanal Haemorrhoidal Dearterialisation (THD)². Excessive pain after haemorrhoidectomy and the growing awareness about the functional importance of haemorrhoidal tissue³ has boosted the popularity of these techniques. Particularly PPH is competing with haemorrhoidectomy as the procedure of choice for grade 3 and 4 haemorrhoids, especially on the European mainland. Several systematic reviews and meta-analyses have shown its superiority in patient satisfaction, occurrence of postoperative pain and ability to return to work⁴⁻⁸. However, serious adverse events have been reported⁹⁻¹¹. Higher rates of recurrence¹², combined with reports on postoperative pain and faecal urgency^{13,14}, have made surgeons reluctant to implement this technique into their practice. A 2002 survey about haemorrhoidal management in Great Britain among general and colorectal surgeons was performed when PPH had not yet gained widespread acceptance¹⁵. Now, a decade later, a nationwide survey among Dutch surgeons was conducted to determine the position of PPH in the daily practice of haemorrhoidal treatment. In addition, technical aspects of PPH and occurrence of serious complications were addressed in this survey.

Methods

Study Population

The address database of the Dutch society of surgeons was used to collect e-mail addresses of all surgeons in the Netherlands. Retired surgeons and paediatric surgeons were excluded from the survey. Since treatment of haemorrhoids in the Netherlands is not the exclusive territory of gastro-intestinal (GI) surgeons, the survey was also sent to vascular and trauma surgeons, from here on referred to as general surgeons.

Data Collection

In February 2010, a twenty-seven-question survey was emailed to 969 surgeons. The questionnaires were identical and were returned anonymously. Questions 1-12 were designed to identify the type of surgeon and its type of practice. Surgeons were asked about general concepts regarding haemorrhoids and about treatment preferences for the different grades of haemorrhoids. Questions 13-26 were directed

towards those with experience with stapled anopexy. Indication for PPH, treatment strategy in case of recurrence and PPH related morbidity was addressed.

Results

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Two hundred and fifteen surgeons electronically returned their questionnaire (22%). One hundred and thirteen surgeons (53%) spend more than 25% of their time in treating colorectal disorders, whereas 97 surgeons (46%) spent less than 25% of their time. Thirty-five per cent of the responding surgeons were GI surgeons. Fifty-one per cent of the respondents work in a non-academic training hospital, 33% in a peripheral hospital, 15% in an academic hospital and 3% in a private clinic. Fifty per cent had more than 10 years of experience as a surgeon.

In almost all hospitals of the responding surgeons, rubber band ligation (RBL) was performed (93%), whereas sclerotherapy was done in only 9%. PPH was done in 45% and THD in 31% of the hospitals. The statement that restoring anatomy by lifting the haemorrhoidal complex instead of resecting haemorrhoidal tissue was agreed upon by 43% of the respondents. Twenty-four per cent disagreed and 34% gave no opinion. In case of grade I haemorrhoids, most surgeons choose conservative measures (51%) over RBL (38%). Grade II haemorrhoids were most treated by RBL (78%). This was also the case in grade III haemorrhoids (35%), followed by haemorrhoidectomy (20%), PPH (19%) and THD (11%). In case of grade IV haemorrhoids, PPH was most often performed (24%), followed by (initial) conservative treatment (21%), RBL (20%) and THD (10%). Treatment of grade 1 and

Table 1 difference in treatment preferences between GI and general surgeons

Preferred treatment	GI surgeons (%)	General surgeons (%)	P value	Odds ratio	95% CI
Conservative grade 3	0 (0)	3 (2)	0.202	1.022	0.997-1.047
RBL grade 3	36 (48)	39 (28)	0.003	2.391	1,322-4,289
Haemorrhoidectomy grade 3	4 (5)	38 (27)	0.000	6.623	2.257-19.231
PPH grade 3	16 (21)	24 (17)	0.452	1.311	0.647-2,655
THD grade 3	13 (17)	11 (8)	0.035	2.459	1.042-5.800
Conservative grade 4	22 (29)	23 (16)	0.027	2.112	1.082-4.120
RBL grade 4	10 (13)	33 (24)	0.074	2.004	0.927-4.329
Haemorrhoidectomy grade 4	2 (3)	15 (10)	0.037	4.386	0.974-19.608
PPH grade 4	23 (31)	28 (20)	0.080	1.769	0.931- 3.363
THD grade 4	8 (11)	14 (10)	0.878	1.075	0.429-2.691

2 haemorrhoids did not differ between GI surgeons and general surgeons. However, when treating grade 3 haemorrhoids, GI surgeons were twice as likely to perform RBL compared to general surgeons who in turn were six times more likely to perform a haemorrhoidectomy. Moreover, GI surgeons were 2.5 times more likely to perform THD in case of grade 3 haemorrhoids. Initial conservative treatment was favoured by GI surgeons in grade 4 haemorrhoids compared to general surgeons, who were four times more likely to perform a haemorrhoidectomy (table 1). Eighty per cent of the respondents thought that placement of the rubber bands should be just above the apex of the haemorrhoids, whereas 13% stated that it should be placed on the haemorrhoidal tissue. Forty-five per cent thought one should proceed with a form of surgery (Haemorrhoidectomy, PPH or THD), after a maximum of three treatments sessions with RBL.

Ninety surgeons indicated to have experience with PPH (42%). The most important reasons for surgeons not to perform PPH were satisfaction with other forms of treatment (26%) and the fear of complications associated with PPH (10%). GI surgeons were five times more likely to have experience with PPH than general surgeons ($p = 0.000$ 95% CI 2.960 – 10.030). Forty per cent of the surgeons with PPH experience had performed less than 10 procedures, whereas 26% had done more than 30. To the question “ after how many PPH procedures is a surgeon qualified to perform the procedure independently” the majority (63%) answered “between 10 en 20 procedures”. Fifty-four per cent thought a stapled anapexy should exclusively be performed by gastro-intestinal surgeons.

Participants were questioned about complications after PPH. Eleven per cent reported to have experienced a perforation to the peritoneal cavity. Anal stenosis was reported in 18% and 12% of the surgeons with PPH experience reported to have experienced a pre-sacral abscess after PPH. Nineteen per cent of the respondents reported faecal urgency and 36% reported tenesmus.

Recurrence of prolapse was attributed by 34% of the respondents to the grade of prolapse. An equal percentage thought incorrect positioning of the stapler line was the most important factor while 16% believed an incomplete mucosal donut was the main cause of recurrence. In case of recurrence, most respondents would perform a redo PPH (34%), followed by a haemorrhoidectomy (31%). When performing a redo-PPH, 41% would chose the new stapler line height depending on the position of the previous placed stapler line. Twenty-nine per cent would position it above the old stapler line while only 3% would choose a position below the old one. When

opting for a redo-PPH, 47% advised to wait for 3 – 6 months after the first PPH, while 47% would wait for 6 months or more.

Discussion

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This survey was undertaken to analyse the implementation of new concepts and techniques in the treatment of symptomatic haemorrhoids in the Netherlands in general, and PPH in particular. Since treatment paradigm is increasingly shifting from resection of haemorrhoidal tissue to restoring anatomy, it was interesting to see if these new developments would get a foothold in daily practices around the country. It was therefore a deliberate decision to include all surgeons in this survey, instead of GI surgeons only. This however explains why the response rate was that low. Trauma, vascular and academic surgeons less likely deal with treatment of haemorrhoids. Mostly, the colorectal orientated GI surgeons in non-academic units are involved in treatment of this disease. It could therefore well approximate the actual percentage of Dutch surgeons involved in the treatment of haemorrhoids. It was interesting to see whether GI surgeons would be more willing to implement new techniques into their practices compared to general surgeons. For grade 1 and 2 haemorrhoidal prolapse, there was no difference in treatment strategy between GI and general surgeons. In addition, there was very limited space for new techniques (grade 2: PPH 0.5% and THD 3%) in both groups. When treating grade 3 haemorrhoids, general surgeons were more likely to proceed to excisional therapy versus a more restorative approach (RBL, THD and PPH) preferred by GI surgeons. In grade 4 haemorrhoids, there was a non-significant trend towards more use of PPH among GI surgeons. Interestingly, again haemorrhoidectomy seemed to be more popular with general surgeons. With only 5 and 3% of GI surgeons opting for haemorrhoidectomy in case of grade 3 and 4 haemorrhoids, one can conclude that this form of treatment is being considered out-dated by most Dutch GI surgeons. The reluctance of the general surgeons to use the novel technique is probably caused by lack of awareness, lack of training and lack of knowledge of up to date innovations. This is in strong contrast with the 2001 survey done in the United Kingdom, where 72% of GI surgeons favoured a form of excisional therapy and 11% only performed stapled anopexy¹⁵. Does this reflect a 10-year difference in accepting new techniques or is it a matter of cultural difference?

Although results from a survey should be interpreted with caution, this survey provides insight into the occurrence of serious complications after PPH. Literature on this topic up till now has been merely of anecdotal nature. There has been a survey among American colorectal surgeons on 'post-PPH syndrome'¹⁶. This survey focused mainly on postoperative symptoms. However, anal stenosis was reported by 16% of the respondents in this survey, which is in concordance with the 18% in our survey. Surprisingly, 11% and 12% of the surgeons in our survey reported to have experienced a perforation to the peritoneal cavity or the formation of a pre-sacral abscess. Of course these figures do not reflect the true incidence, but it does suggest that the occurrence of dehiscence of the stapler line is perhaps more than anecdotal. However, large single-centre series on PPH did not show these complications to occur on a frequent basis¹⁷⁻¹⁹. Possibly, since our survey comprised a very heterogeneous group of surgeons, relative inexperience with the technique (only 25% performed 30 or more procedures) might have played a role.

Relative new techniques in haemorrhoidal treatment like PPH and THD have earned a substantial role in current treatment strategies, especially in grade 3 and 4 haemorrhoids among Dutch surgeons. However, haemorrhoidectomy remains a popular treatment modality, especially among general surgeons. This can probably be attributed to a high rate of symptom resolution combined with its relatively low technical procedural complexity. Lowering recurrence after PPH by identifying risk factors and reducing complications by better surgical training of the technique might increase its popularity even further. Knowing when to select a specific technique, combined with a thorough knowledge of its technical pitfalls to avoid procedure related complications, is essential in the successful management of haemorrhoids.

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Part IV

Internal Rectal Prolapse

Evidence-based chapter **7**

Controversy in the Treatment of Symptomatic Internal Rectal Prolapse – Suspension or resection?

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Surgical Endoscopy. 2010 Dec 8

Introduction

Internal Rectal Prolapse (IRP) is a full thickness intussusception of the rectum during defecation. Radiologically, different grades have been proposed: From low-grade (recto-rectal intussusception) to high-grade (recto-anal intussusception) prolapse. This prolapse may lead to an outlet obstruction and/or to faecal incontinence. IRP plays an important role in the pathophysiology of obstructed defecation (OD), which is the inability to satisfactorily empty the rectum during defecation and is more specifically defined in the Rome III criteria.

There has been debate for decades about the clinical significance of IRP. However, there appears to be a renewed interest in the clinical relevance and treatment of IRP. The long disputed progression into ERP has been made more plausible by recent data published by Wijffels et al¹. on the natural history of IRP. Moreover, various recent publications on new surgical techniques show improved functional outcome after prolapse correction in comparison to historical surgical series. Patient selection however remains critical.²⁻⁴

Surgical correction for internal rectal prolapse is possible via a trans-abdominal or trans-anal approach. Currently the most common procedures are laparoscopic ventral rectopexy (LVR) and stapled trans-anal rectal resection (STARR). LVR corrects the intussusceptions of the rectum and reinforces the rectovaginal septum by the use of a mesh, which suspends the rectum and vaginal vault to the sacral promontory, whereas in the STARR procedure a stapled resection of the redundant rectal wall is performed. Most of the recent publications on IRP and OD are divided between proponents of these two techniques. There are, however, no comparative studies, making it difficult to select the optimal treatment for each individual patient. Therefore, our aim is to give an overview of the existing data and controversies on these techniques.

Treatment

Laparoscopic ventral (mesh) rectopexy (LVR), was first described by D'Hoore et al. in 2004 and has gained widespread acceptance⁵⁻⁷. The technique is based upon correcting the descent of the posterior and middle pelvic compartments combined with reinforcement of the recto-vaginal septum. In contrast with previous described posterior rectopexy techniques, where induction of constipation proved to be a major deterrent, this procedure limits the chance of damaging the autonomous

nerves by avoiding posterolateral rectal dissection. The initial papers reported favourable functional results in treating patients with an ERP². These good results in treating ERP by LVR have been confirmed by others^{8,9}. Recently data have become available on the results of this procedure in patients with symptomatic high-grade IRP. Reports by Collinson et al. and Slawik et al have shown similar functional improvement in the short and medium term, with improvement in constipation in about 80% of patients with almost no new onset constipation^{4,6} and acceptably low recurrence rates (about 5%). A recent meta-analysis on ventral rectopexy, with or without posterior dissection, for IRP and ERP, concluded that there is a greater reduction in postoperative constipation if no posterior dissection is performed¹⁰.

Instead of correcting the descent of the pelvic compartments, the stapled trans-anal rectal resection (STARR) resects redundant tissue. Moreover, reduced rectal sensitivity is improved as shown on postoperative manometry¹¹. The original technique was derived from the Procedure for Prolapse and Haemorrhoids (PPH), using the same stapling device (PPH01, Ethicon Endo-Surgery; Cincinnati). Recently this technique has been refined with the development of the Contour® Transtar™ stapler (Ethicon Endo-Surgery; Cincinnati), resulting in a further controlled full-thickness resection of even more tissue.

The rate of improvement after both techniques ranges from 56-95% at short and medium term follow up¹¹⁻¹³, with more recent studies claiming a fairly consistent success rate of around 80%^{3,14,15}. Although there are reports of serious complications after STARR¹⁶, most large series show a low and acceptable morbidity rate.

Discussion

When comparing the trans-abdominal and trans-anal route of surgery, it is clear that both techniques hinge on a different theoretical basis. One could argue that LVR corrects the leading cause (the rectal intussusceptions) of the symptoms, whereas STARR only treats its consequences. In addition, LVR makes correction of co-existing prolapse of the middle pelvic compartment, an enterocoele or vaginal descent, possible. On the other hand, STARR has been shown to improve the rectal sensitivity, as has been confirmed objectively by anal manometry. In one report this increased sensitivity was significantly correlated with higher patient satisfaction¹⁷. STARR certainly reduces the rectal capacity and possibly hereby the rectal sensitivity, but the final consequences on faecal continence are still unknown. Transient urgency and urgency incontinence has been described to occur in about 15-47% of patients

after STARR^{3,11,17,18}, and this can persist for up to 12 months in about 10%¹⁸. In most patients however, urgency is reported to be a self-limiting symptom¹⁸. It is difficult to determine the role of rectal sensitivity after LVR, since almost no studies have reported on volumetry and manometry values before and after LVR. One study, however, has reported on rectal manometry after LVR for complex rectoceles, showing no significant decrease of rectal capacity or compliance¹⁹.

Although short and medium term success rates of both techniques have proved to be comparable, long-term results have still to be awaited. It can be hypothesised that IRP is a precursor stage of ERP. In ERP, resectional therapy has been shown to have high recurrence rates in contrast to rectopexy²⁰⁻²³. If we extrapolate this to the results after LVR and STARR in the treatment of IRP, it is perhaps reasonable to expect a better long-term outcome after LVR. However, since these data are not yet available, other factors have to be taken into account when choosing one surgical technique over the other.

Another reason to choose one technique over another is the risk of morbidity. Constipation after LVR may constitute the counterpart of faecal urgency after STARR. Although D'Hoore et al found no worsening or new onset of constipation in their patients⁵, there are some papers that report its occurrence to be between 15 and even up to 50%¹⁰. On the contrary, while constipation is not reported after STARR, it may induce faecal incontinence (FI). Stretching of the anal sphincter muscle during the procedure and postoperative faecal urgency (reduction of rectal compliance properties), threatening marginal sphincters, are two potential causative factors. Therefore, some authors advise avoidance of STARR in patients with already impaired sphincter function. Moreover, symptoms of OD may mask co-existing FI that only becomes apparent after successful treatment of OD. In contrast, it is believed that STARR in itself can relieve symptoms of incontinence by correction of recto-anal intussusception, eliminating the sphincter impairing obstruction of the anal canal. Even though not all studies report on postoperative incontinence rates after STARR, the papers that do, report a low incidence and spontaneous resolution on the long-term^{17,18}.

Apart from the above-mentioned functional complications, both techniques have procedure-specific complications. Various reports describe stapler line dehiscence, rectal necrosis and even recto-vaginal fistula after STARR¹³. STARR proponents claim these complications to be anecdotal, although the true incidence is not known. Some authors attribute these complications to a steep learning curve, the reason why surgeons are now only allowed to perform STARR after a company

initiated training and proctorship. On the contrary, LVR carries a relative low risk of laparoscopy related complications like port site hernia, port site hematoma and inadvertent bowel perforation and procedure specific, mesh related complications, which have been reported rarely but can have serious consequences⁷. Moreover, to be able to perform LVR, the surgeon must have substantial experience in laparoscopic colorectal surgery, but even then there appears to be a continuing learning curve concerning operation time^{5,7}. Although not reported, the learning curve might influence the functional outcome after LVR.

One important difficulty in comparing data of both treatment modalities is the variability of used parameters and lack of clarity in patient selection. Not all potentially relevant factors are analysed pre- and postoperatively in most studies. For instance, almost none of the LVR papers report on the coexistence of a rectocele in their patients with IRP, whereas in the group of patients treated with a stapling technique, almost all patients had a rectocele. Is this a matter of patient selection, or are rectoceles just not documented in the LVR studies? Probably it is mentioned in STARR procedures because in this treatment a rectocele is considered to be redundant rectal tissue, whereas it is considered physiological or the sequelae of prolapse by those who perform LVR. The use of a universal, validated disease specific symptom based scoring system, such as the one proposed by Altomare²⁴, is mandatory in comparing functional treatment outcomes.

Is it possible with the available evidence⁵ to design a treatment algorithm for patients with OD and IRP? A decision-making algorithm for the STARR procedure is already developed²⁵, but would it not be better to have a disease-based algorithm, irrespective of the treatment modality? In our opinion symptomatic IRP and FI needs to be distinguished from IRP associated with OD. A high-grade prolapse giving rise to sphincter dysfunction and faecal incontinence should be considered a close precursor of ERP, and therefore be treated, probably with LVR, to prevent further sphincter deterioration.

When IRP is associated with OD however, choosing treatment becomes more difficult. Until long-term follow-up data on function and recurrence are available, it is up to the surgeon to choose between a trans-anal stapled procedure and LVR in an uncomplicated patient with IRP with (or, in the unusual case, without) a rectocele. However, in the complicated patient with a fixed enterocele or sigmoidocele, a STARR is contraindicated. In addition, one can correct these coexisting conditions that may contribute to the OD during the same procedure when doing a LVR. Also in the patient with a concomitant prolapse of the vagina a LVR is preferred, since

a correction of the descent of the middle pelvic compartment is feasible. Finally, in a patient with compromised anal sphincter function we believe it is better to avoid trans-anal procedures to prevent worsening of these symptoms. On the other hand, if a patient has sustained severe pelvic inflammation in the past, has undergone several abdominal surgical procedures, or has substantial co-morbidity contraindicating a laparoscopy, it may be better to perform a stapled trans-anal procedure.

Conclusion

Surgical decision-making for OD remains difficult and complex. Even more important than surgical technical skills is the surgeon's experience is the understanding of pelvic anatomy and pathophysiology. Preoperative functional investigation and the use of an objective scoring system should improve selection of patients that would benefit from surgery. Furthermore, assessment of the functional outcome (and new onset functional sequelae) is more important than the evaluation of the anatomic result. The success of surgery is not dictated only by choosing between a trans-abdominal and a trans-anal route. To be able to offer these patients a tailored approach, a colorectal surgeon who is specialized in pelvic floor pathology, should be able to perform both techniques.

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Summary and Conclusions

Summary and Conclusions

The aim of the present thesis was to evaluate new treatment strategies in several proctologic conditions, weighing treatment success against the loss of function, the occurrence of side effects and complications and the chance of recurrence.

Part I

Surgical treatment of anal fistulas often involves dividing sphincter muscle to some extent, thereby risking impairment of faecal continence. Less invasive treatment options have been developed, including closing off the fistula canal with fibrin glue. In **chapter one**, feasibility, safety and treatment success of fibrin glue for anal fistulas was studied in a prospective trial. Twenty-seven consecutive patients with an anal fistula were enrolled. Patients with a suspected complex fistula (extrasphincteric, suprasphincteric and high transsphincteric) were analysed preoperatively by MRI and subsequently excluded from inclusion. Definitive classification of the fistula was based on sphincter involvement detected during probing. Fibrin glue from a commercial kit (Tissucol®, Baxter, Vienna, Austria) consisting of two deep-frozen solutions in pre-filled syringes was injected after curetting the fistula tract. The external opening was closed with a purse-string suture. The follow-up ranged from 3 to 96 weeks, with a median of 27 weeks.

None of the patients suffered from continence problems after the procedure, and no other complications were encountered. Nine (33%) of 27 fistulas healed with fibrin glue treatment, including 8 intersphincteric fistulas and 1 low transsphincteric fistula. Of these fistulas, 8 were primary (success rate 40%) versus 1 recurrence (success rate 14%).

This study confirms the feasibility and safety of the use of fibrin glue in the treatment of anal fistulas. Primary and intersphincteric fistulas seem to respond better to this therapy than recurrent or transsphincteric fistulas.

Part II

Chronic anal fissures are notoriously resistant to therapy. Surgical treatment yields excellent success rates, but at the risk of compromising faecal incontinence. Less invasive ways of lowering the resting pressure of the IAS have been developed. In **chapter two** the results of a double-blinded randomised controlled trial between isosorbide dinitrate (ISDN) and botulinum toxin (BT) are presented. Primary endpoint

was macroscopic fissure healing after 4 months. Secondary endpoints were fissure related pain, treatment induced complications, fissure recurrence and costs.

Between 2002 and 2006 73 patients were enrolled in this trial. Thirty-seven were randomly assigned to injection with 10U of BT in the IAS on each side of the anterior midline and placebo ointment (group I), and 36 were assigned to receive a placebo injection and ISDN ointment (group II).

After 4 months, the fissure was healed in 58% of the patients in the ISDN group versus 38% in the BT. Pain scores, as measured on a visual analogue scale, did not differ between the two groups at the different follow up times. After a median follow up of 6.7 months, 43% in the BT group had recurrence of the fissure versus 36% in the ISDN group. The price of preparing one treatment with BT was 271 euro compared to 10 euro for treatment with ISDN ointment.

The healing rates of BT compared to ISDN in combination with the difference in costs as presented here in this trial, do not support BT as a primary agent in the treatment of chronic anal fissure

Part III

Surgery for haemorrhoidal disease is indicated when conservative measures and in-office procedures have failed. Procedures that offer good symptomatic control with minimal postoperative morbidity are sought for as an alternative to haemorrhoidectomy. The Procedure for Prolapse and Haemorrhoids (PPH) and Transanal Haemorrhoidal Dearterialisation (THD) are the most utilised new surgical treatments.

Chapter three describes the results of the first randomized trial comparing these techniques in the treatment of grade 3 and 4 haemorrhoids. Patients were randomized between PPH and THD, and operated in day-care treatment. Postoperatively, patients were seen after one day, three weeks and at six weeks. Primary endpoint was resolved symptoms six weeks postoperatively. Secondary endpoints were postoperative complications and procedure-induced pain, measured using a visual analogue scale (VAS) at day one, after one week and three weeks. Eighteen patients were allocated to PPH versus 23 to THD. Success rates after six weeks were 83% in the PPH group versus 78% in the THD group. VAS scores were significantly lower after one day and one week in the THD group, but equalled out after three weeks. Twelve per cent of the patients after PPH and 4% after THD

needed an urgent readmission to treat an acute bleeding. Overall complication rates did not differ significantly.

Both PPH and THD are safe treatments for grade 3 and 4 haemorrhoids with acceptable complication rates and good short-term results. THD might be the preferred treatment because it is a less invasive, more easily learned and less costly procedure compared to PPH.

Stapled anopexy or PPH has shown to be advantageous over conventional haemorrhoidectomy, resulting in less postoperative pain, earlier return to work and higher overall patient satisfaction, but has frequently been associated with a higher recurrence rate.

Chapter four describes the first report to identify predictors of recurrence of prolapse after PPH. A retrospective cohort of patient with symptomatic haemorrhoids, treated with PPH between 2002 and 2009, was studied. A multivariate analysis was performed to identify patient-related and perioperative factors responsible for persisting prolapse and recurrence of prolapse.

159 consecutive patients were analysed. Persistence and recurrence of prolapse were both observed in 16% of the patients. Multivariate analysis identified female sex, long duration of PPH surgery and the absence of muscle tissue in the resected specimen as independent predictors of persistence of prolapse. The absence of prior treatment with rubber band ligation (RBL), as well as increased PPH experience at the hospital, showed a trend towards a higher rate of recurrence of prolapse.

In order to reduce recurrence of prolapse, PPH should be performed by a surgeon with adequate PPH experience, patients should be treated with RBL prior to PPH, and a resection of mucosa with underlying muscle fibres should be strived for.

The feasibility and efficacy of a second PPH instead of haemorrhoidectomy, in case of recurrent symptoms after PPH, were studied in **chapter five**. A retrospective chart review was conducted for all patients that were treated with PPH for haemorrhoidal prolapse between May 2002 and November 2008.

Out of 137 patients who underwent a PPH, 22 patients (16%) were in need of a reoperation for symptoms of prolapse. Of these, 12 (9%) were treated with a second PPH. Successful prolapse reduction was achieved in 11 out of 12 patients. No postoperative complications were encountered during a median follow up of 35 months.

Redo PPH, in case of persisting or recurrent symptoms of haemorrhoidal prolapse after PPH, is feasible and is a good alternative for haemorrhoidectomy. It possesses the same advantages over haemorrhoidectomy as the initial PPH and does not lead to increased morbidity.

In **chapter six** the results of a nationwide survey on haemorrhoidal treatment in general and stapled anopexy in specific is described.

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A twenty-seven-question survey was emailed to 969 surgeons. Two hundred and fifteen surgeons returned the questionnaire (22%). Treatment of grade 1 and 2 haemorrhoids did not differ between gastrointestinal (GI) surgeons and general surgeons. However, when treating grade 3 haemorrhoids, GI surgeons were twice as likely to perform RBL compared to general surgeons, who in turn were six times more likely to perform a haemorrhoidectomy. Ninety surgeons indicated to have experience with PPH (42%). Forty per cent had performed less than 10 procedures, whereas 26% had done more than 30. GI surgeons were five times more likely to have experience with PPH than general surgeons. Eleven per cent of the surgeons with PPH experience reported to have experienced a perforation to the peritoneal cavity, anal stenosis was reported in 18% and 12% had experienced a pre-sacral abscess after PPH. Nineteen per cent of the respondents reported faecal urgency and 36% reported tenesmus.

Haemorrhoidal treatment with PPH has earned a substantial role in current treatment strategies in the Netherlands, especially in grade 3 and 4 haemorrhoids, although experience is still limited. Serious complications are reported by a substantial part of PPH experienced surgeons. Haemorrhoidectomy remains a popular treatment modality, especially among general surgeons.

Part IV

Internal Rectal Prolapse (IRP) is a full thickness intussusception of the rectum during defecation. Debate has been going on for decades about its clinical significance and the role of surgical correction. Surgery is possible through a trans-abdominal or a trans-anal approach. Traditional techniques suffered from high recurrence rates and induction of constipation. Currently the most common procedures are laparoscopic ventral rectopexy (LVR) and stapled trans-anal rectal resection (STARR).

Chapter 7 reviews the theoretical differences between these two techniques and compares literature-based outcomes. The LVR technique is based upon correcting

the descent of the posterior and middle pelvic compartments combined with reinforcement of the recto-vaginal septum by the use of a mesh, which suspends the rectum and vaginal vault to the sacral promontory. Instead of correcting the descent of the pelvic compartments, the stapled trans-anal rectal resection (STARR) resects redundant tissue. The rate of improvement after both techniques ranges from 56-95% at short and medium term follow up, with more recent studies claiming a fairly consistent success rate of around 80%. Although short and medium term success rates of both techniques have proved to be comparable, long-term results have still to be awaited.

Surgical decision-making for IRP remains difficult and complex. The success of surgery is not dictated only by choosing between a trans-abdominal and a trans-anal route. To be able to offer these patients a tailored approach, a colorectal surgeon who is specialized in pelvic floor pathology, should be able to perform both techniques.

Conclusions of this thesis:

- Treatment of perianal fistulas with fibrin glue is safe, although it results in healing of the fistula in only one-third of the patients. Primary, intersphincteric fistulas seem to respond best to this therapy.
- The healing rates of BT compared to ISDN ointment in combination with the difference in costs as presented here in this trial, do not support BT as a primary agent in the treatment of anal fissure.
- Both PPH and THD are safe treatments modalities for grade 3 and 4 haemorrhoids with acceptable complication rates and good short-term results.
- In order to reduce recurrence of prolapse, PPH should be performed by a surgeon with adequate PPH experience, patients should be treated with RBL prior to PPH, and a resection of mucosa with underlying muscle fibres should be strived for.
- Redo PPH, in case of persisting or recurrent symptoms of haemorrhoidal prolapse after PPH, is feasible and is a good alternative for excisional haemorrhoidectomy. It possesses the same advantages over haemorrhoidectomy as the initial PPH and does not lead to increased morbidity.
- Haemorrhoidal treatment with PPH has earned a substantial role in current treatment strategies in the Netherlands, especially in grade 3 and 4 haemorrhoids, although experience is still limited. Haemorrhoidectomy remains a popular treatment modality, especially among general surgeons.

- The success of surgery for internal rectal prolapse is not dictated only by choosing between a trans-abdominal and a trans-anal route. To be able to offer these patients a tailored approach, a colorectal surgeon who is specialized in pelvic floor pathology, should be able to perform both techniques.

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Samenvatting en Conclusies

Samenvatting en Conclusies

Het doel van dit proefschrift was het evalueren van nieuwe therapeutische strategieën in de behandeling van proctologische aandoeningen. De kans op succes werd afgezet tegen postoperatief functieverlies, het optreden van bijwerkingen en complicaties en het voorkomen van recidieven.

Deel I

Chirurgische behandeling van een perianale fistel noodzaakt nogal eens het klieven van een deel van de anale sfincter, waardoor er een kans bestaat op verminderde fecale continentie. Minder invasieve behandel methodes zijn ontwikkeld, zoals het sluiten van het fistelkanaal en de inwendige opening met fibrine lijm.

In **Hoofdstuk 1** werd de veiligheid, haalbaarheid en het behandelingsucces van de behandeling van perianale fistels met fibrine lijm onderzocht in een prospectieve pilot studie. Zeven-en-twintig achtereenvolgende patiënten met een perianale fistel werden geïncludeerd. Bij verdenking op een complexe fistel (hoog-transsfincterisch, extrasfincterisch en suprasfincterisch) werd er preoperatief een MRI vervaardigd, waarna bij bevestiging deze patiënten werden geëxcludeerd. Definitieve classificatie van de fistel gebeurde met behulp van een knop-sonde op de operatiekamer. Een commercieel preparaat fibrine lijm (Tissucol®, Baxter, Vienna, Austria), bestaande uit 2 spuitjes met een bevroren vloeistof, werd na het uitkrabben van het kanaal met een scherpe lepel, in het fistelkanaal geïnjecteerd. Hierna werd de uitwendige opening gesloten met een tabakzaknaad. De gemiddelde follow-up bedroeg 27 weken (range 3-96 weken).

Bij geen van de patiënten ontstond er postoperatief een verminderde continentie. Er deden zich geen complicaties voor. Negen van de 27 fistels (33%), bestaande uit 8 intersfincterische en 1 laag-transsfincterische fistels, genazen met fibrine lijm. Van deze 9 fistels waren er 8 primaire fistels en 1 recidief fistel.

Deze studie laat zien dat behandeling van een perianale fistel met fibrine lijm veilig is. Primaire fistels en intersfincterische fistels lijken het beter te doen dan recidief of transsfincterische fistels.

Deel II

Chronische fissura ani zijn notoir resistent voor behandeling. Chirurgische behandeling geeft over het algemeen goede resultaten met betrekking tot genezing, maar met

een risico op verminderde fecale continentie. Minder invasieve behandelingen om de rustdruk van de interne anale sfincter te verlagen winnen in toenemende mate aan populariteit. In **hoofdstuk 2** worden de resultaten van een dubbel blind, gerandomiseerd onderzoek tussen botuline toxine (BT) en isosorbidedinitraat crème (ISDN) gepresenteerd. Primair eindpunt was de macroscopische genezing van de fissuur, terwijl fissuur gerelateerde pijn, complicaties van de behandeling, het optreden van recidieven en de kosten secundaire eindpunten waren.

Tussen 2002 en 2006 werden 73 patiënten geïncludeerd. Zeven-en-dertig patiënten lootten voor een injectie met 10U BT aan weerszijde van de anterieure commissuur, in de interne anale sfincter, gecombineerd met placebo crème. Zes-en-dertig patiënten kregen een placebo injectie in combinatie met ISDN crème. De prijs van een behandeling met BT en ISDN was respectievelijk 271 euro en 10 euro.

Het percentage genezen patiënten in de BT groep, vergeleken met de ISDN groep, gecombineerd met het verschil in kosten, ondersteunt BT niet als eerstelijns behandeling bij patiënten met een chronische anale fissuur.

Deel III

Chirurgie voor hemorroiden is aangewezen indien conservatieve maatregelen en poliklinische behandeling gefaald heeft. Tegenwoordig geeft men steeds meer de voorkeur aan procedures die een goede symptoom verlichting bieden, maar zonder de morbiditeit van de hemorroïdectomie. De Procedure for Prolapse and Haemorrhoids (PPH) en de Transanal Haemorrhoidal Dearterialisation (THD) zijn de meest gebruikte nieuwe technieken.

Hoofdstuk 3 geeft de resultaten weer van de eerste gerandomiseerde studie tussen PPH en THD voor graad 3 en 4 hemorroiden. Patiënten werden na randomisatie in dagbehandeling geopereerd. Na 1 dag, 3 weken en 6 weken werden de patiënten ter controle gezien. Primair eindpunt was het verdwijnen van symptomen na 6 weken. Secundaire eindpunten waren postoperatieve complicaties en procedure gerelateerde pijn, gemeten op een Visuele Analoge Schaal (VAS), op dag 1, na 3 en 6 weken.

Achttien patiënten ondergingen een PPH, terwijl 23 een THD ondergingen. Symptomen waren succesvol bestreden bij 83% van de patiënten in de PPH groep versus 78% in de THD groep. De VAS scores waren significant lager op dag 1 en na 1 week in de THD groep. Dit verschil verdween na 3 weken. In de PPH groep moest 12% van de patiënten heropgenomen worden in verband met een nabloeding

versus 4% in de THD groep. Het totaal aantal complicaties was niet verschillend in beide groepen.

Zowel PPH als THD zijn veilige behandelingen voor graad 3 en 4 hemorroiden met een goed succespercentage op de korte termijn tegen een acceptabel complicatiepercentage. THD verdient wellicht de voorkeur gezien het feit dat het een minder invasieve behandeling is die bovendien gemakkelijk te leren is en minder kostbaar is.

PPH heeft aangetoonde voordelen boven hemorroïdectomie, zoals minder postoperatieve pijn, een snellere werkhervatting en grotere patiënt tevredenheid, maar is tevens geassocieerd met een hoger recidiefpercentage.

In **hoofdstuk 4** zijn de resultaten weergegeven van een retrospectieve cohort studie naar voorspellende factoren voor persisterende prolaps en prolapsrecidief, bij patiënten die een PPH onderging tussen 2002 en 2009. In een multivariaat model werden patiëntgebonden en perioperatieve factoren geanalyseerd op causaliteit.

Honderd-negen-en-vijftig patiënten werden geanalyseerd. Persisterende en recidief prolaps werden gezien bij 16% van de patiënten. In het multivariaat model kwamen het vrouwelijk geslacht, de duur van de operatie en de afwezigheid van spierweefsel in het resectiepreparaat naar voren als voorspellers van persisterende prolaps. Een voorgeschiedenis van rubber band ligatie en de ervaring van de instelling met PPH bleken voorspellende factoren voor recidief prolaps.

Om de kans op persisterende prolaps en prolapsrecidief te verkleinen, zouden patiënten met een indicatie voor PPH eerst moeten worden behandeld met rubberband ligatie. Verder moet er worden gestreefd naar een resectie die dieper gaat dan mucosa alleen, en speelt de ervaring van het behandelend team een rol.

De veiligheid en haalbaarheid van een herhaalde PPH, in plaats van een hemorroïdectomie, in het geval van persisterende prolaps of prolapsrecidief na primaire behandeling met PPH, worden beschreven in **hoofdstuk 5**. Alle patiënten die tussen 2002 en 2008 een PPH ondergingen werden geïncludeerd voor retrospectieve analyse.

Van 137 patiënten, was er bij 22 patiënten (16%) een indicatie voor re-interventie, waarvan 12 patiënten (9%) een 2^e PPH ondergingen. Deze behandeling was succesvol bij 11 van de 12 patiënten. Er deden zich geen ernstige complicaties voor gedurende een mediane follow-up periode van 35 maanden.

In het geval van persisterende of recidief prolaps na een PPH, is een 'redo-PPH' een goed alternatief voor hemorroïdectomie. 'Redo-PPH' lijkt dezelfde voordelen te bieden boven hemorroïdectomie vergeleken met een primaire PPH.

In **hoofdstuk 6** worden de resultaten van een landelijke enquête onder alle Nederlandse chirurgen naar de behandeling van hemorroiden in het algemeen, en naar de implementatie van PPH in de chirurgische praktijk in het bijzonder, beschreven.

130 Een lijst met 27 vragen werd naar 969 chirurgen via e-mail gestuurd. Tweehonderdvijftien chirurgen stuurden de ingevulde enquête terug (22%). De behandeling van graad 1 en 2 hemorroiden was niet verschillend tussen gastro-intestinale (GI) chirurgen en algemeen chirurgen. In het geval van graad 3 hemorroiden kozen GI chirurgen twee keer zo vaak voor rubberband ligatie vergeleken met algemeen chirurgen, die 6 keer zo vaak een hemorroïdectomie de voorkeur gaven. Negentig chirurgen (42%) gaven aan ervaring met PPH te hebben, waarvan maar 26% meer dan 30 procedures gedaan had. Vijf keer zo veel GI chirurgen hadden ervaring met PPH vergeleken met algemeen chirurgen. Van de chirurgen die ervaring hadden met PPH, gaf 11% aan ooit een perforatie naar de vrije buikholte te hebben meegemaakt, 18% zag ooit een anale stenose en 12% een pre-sacraal abces na PPH. Tenesmus en fecale urgency werden in respectievelijk 36% en 19% gerapporteerd.

PPH heeft een belangrijke rol opgeëist in de behandeling van hemorroiden in Nederland, met name in het geval van graad 3 en 4 hemorroiden. Ernstige complicaties worden nog steeds door een aanzienlijk aantal chirurgen gemeld. Hemorroïdectomie blijft een populaire behandeling, met name onder algemeen chirurgen.

Deel IV

Interne Rectale Prolaps (IRP) is een intussusceptie van de wand van het rectum gedurende defecatie. Over de klinische relevantie, en de rol van chirurgische behandeling, wordt al sinds tientallen jaren gediscussieerd. Chirurgische correctie is mogelijk via een trans-abdominale en een trans-ale route. Traditionele chirurgische technieken zoals de posterieure rectopexie en de Delorme procedure hebben verergering van obstipatie en een grote kans op recidief als belangrijk nadeel. Tegenwoordig zijn de Laparoscopische Ventrle Rectopexie (LVR) en de Stapled TransAnal Rectal Resection (STARR) de meest gebruikte technieken.

In **hoofdstuk 7** worden de belangrijkste theoretische verschillen en behandelresultaten uit de medische literatuur tegen elkaar uiteengezet. De LVR is gebaseerd op het corrigeren van de verzakking van de posterieure en middelste compartimenten van het bekken, in combinatie met de versterking van het rectovaginale septum met behulp van een matje, terwijl de STARR de overtollige rectumwand reseceert. Symptoomverbetering op korte en middellange termijn is vergelijkbaar na beide technieken en wordt tegenwoordig in ongeveer 80% van de patiënten gezien. Over lange termijn resultaten is nog onvoldoende bekend.

De keuze voor een chirurgische behandeling van IRP is complex. Het succes van de behandeling wordt niet alleen bepaald door de gekozen chirurgische route. Patiënten met een IRP zijn gebaat bij een op maat gemaakte behandeling door een gespecialiseerde chirurg, die beide technieken beheerst.

Conclusies van dit proefschrift:

- Behandeling van een perianale fistel met fibrine lijm is veilig, maar resulteert maar bij een derde van de patiënten in genezing. Primaire, intersfincterische fistels lijken het beter te doen dan recidief of transsfincterische fistels.
- Het percentage genezen patiënten na behandeling met botuline toxine, vergeleken met ISDN, gecombineerd met het verschil in kosten, ondersteunt botuline toxine niet als eerstelijns behandeling bij patiënten met een chronische anale fissuur.
- Zowel PPH als THD zijn veilige behandelingen voor graad 3 en 4 hemorroiden met een goed succespercentage op de korte termijn tegen een acceptabel complicatiepercentage.
- Om de kans op persisterende prolaps en prolapsrecidief te verkleinen, zouden patiënten met een indicatie voor PPH eerst moeten worden behandeld met rubberband ligatie. Verder moet er worden gestreefd naar een resectie die dieper gaat dan mucosa alleen, en speelt de ervaring van het behandelend team een rol.
- In het geval van persisterende of recidief prolaps na een PPH, is een 'redo-PPH' een goed alternatief voor hemorroïdectomie. 'Redo-PPH' lijkt dezelfde voordelen te bieden boven hemorroïdectomie vergeleken met een primaire PPH.
- PPH heeft een belangrijke rol opgeëist in de behandeling van hemorroiden in Nederland, met name in het geval van graad 3 en 4 hemorroiden. Ernstige complicaties worden nog steeds door een aanzienlijk aantal chirurgen gemeld.

Hemorroïdectomie blijft een populaire behandeling, met name onder algemeen chirurgen.

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Curriculum vitae

Sebastiaan Festen (Nijmegen, 31 januari 1972) behaalde in 1991 zijn eindexamen VWO aan de Nijmeegse Scholen Gemeenschap. In dat zelfde jaar begon hij de studie geneeskunde aan de UvA te Amsterdam, om in 1999 zijn doctoraalexamen te halen. In januari 2001 startte Sebastiaan de opleiding algemene chirurgie, bestaande uit 4 jaar OLVG (opleider dr. N.J.M. Out), en 2 jaar AMC (opleider prof. dr. D.J. Gouma). In het zesde jaar van zijn opleiding koos hij voor de differentiatierichting gastro-intestinale chirurgie in het OLVG. Hierna begon Sebastiaan aan de chirurgische vervolg opleiding (CHIVO) kinderchirurgie in het Sophia kindziekenhuis te Rotterdam (opleider prof. dr. N.M.A. Bax), echter na 1 jaar verwisselde hij deze voor een CHIVO gastro-intestinale chirurgie in het OLVG te Amsterdam (opleider dr. M.F. Gerhards). Gedurende deze periode legde hij de basis voor het huidige promotieonderzoek. Sinds oktober 2009 werkt Sebastiaan als gastro-intestinaal chirurg in het Reinier de Graaf ziekenhuis in Delft. Binnenkort treed hij in dienst als gastro-intestinaal chirurg in het OLVG.

