Patient-centred haemorrhoidal disease management

Summary

Background

The main research question of this thesis was *'How can we optimize the management of haemorrhoidal disease (HD)?'*.

The first part – *Introduction to the field of proctology and haemorrhoidal disease* – gives an introduction into the field of proctology, with a focus on HD. Furthermore, this part elaborates on the pathophysiology of HD.

The second part – *Effective treatment for haemorrhoidal disease* – elaborates on successful interventions for the treatment of HD.

The third part – *Patient-reported outcomes in haemorrhoidal disease* – explores the role of PROMs in the management of HD and, consequently, the development and validation of an (inter) national PROM for HD (PROM-HISS).

Introduction to the field of proctology and haemorrhoidal disease

The prevalence of anal symptoms ranges from 11 to 15% in the adult population[1,2]. Despite the high prevalence and noteworthy negative impact of proctologic illnesses on quality of life, the level of evidence on effective and cost-effective treatments in this field remains very low. In **chapter 2** we emphasized the need to prioritize proctology on research agendas of different (inter)national forums to conduct more qualitative studies on proctologic ailments and to raise the level of robust evidence in this field. Haemorrhoids are one of the most common proctologic illnesses with an incidence of 8.3/1000 patients per year in the Netherlands and a prevalence of up to 39% in the general population[3,4]. **Chapter 3** aimed to highlight several dynamically evolving domains in current HD research, ranging from historical viewpoints to technical solutions and patient involvement.

The full picture of the aetiology of HD has not yet been grasped. Over the years, more and more studies investigating the correlation between connective tissue stability and the development of haemorrhoids have been published, but evidence is inconclusive. To contribute to this discussion, we compared the quantity and quality of anal collagen and vessel morphometrics in patients with symptomatic HD compared to normal controls. Quality of collagen was divided in young (immature) and old (mature) collagen, with old collagen being more cross-linked.

The study group consisted of twenty-two samples of grade III and grade IV HD tissue from patients who underwent a haemorrhoidectomy. The control group comprised of fifteen persons without symptomatic HD who donated their body to science and died a natural death. In **chapter 4** we described the results of this study, showing that patients with HD had an increased percentage of total collagen (62.1 ± 13.8 vs. 18.7 ± 14.5%; $p = 0.0001$), a decreased percentage of young collagen (0.00009 ± 0.00008 vs. 0.0008 ± 0.0008%; $p = 0.001$), and a smaller surface area of the anal vessels (795.1 ± 1215.9 micrometre^2 vs. 1219.0 ± 1976.1; $p = 0.003$) compared with normal controls. These outcomes suggest that alterations in anal collagen composition may play a role in the formation of haemorrhoids.

Effective treatment for haemorrhoidal disease

Prolapse of haemorrhoids is usually classified according to the Goligher grading; in which grade I defines a haemorrhoid that does not prolapse; grade II prolapses but reduces spontaneously; grade III is a prolapsing haemorrhoid that needs manual reduction; and grade IV is a prolapsing haemorrhoid that cannot be manually reduced [5]. Most common symptoms of HD include 'pain', 'prolapse', 'itching', 'soiling' and 'blood loss'[6]. The various available treatments focus on diminishing these symptoms and range from conservative to surgical procedures. The first treatment step is usually offered by the general practitioner and consists of laxatives and a high fibre diet[7]. If conservative treatment is not successful, the next treatment modality is often rubber band ligation (RBL), which can be repeated multiple times. RBL is an easy, relatively cheap, and outpatient-based procedure[8]. However, 30% of the patients develop recurrent symptoms after basic treatment and repeat RBL[9]. If symptoms reoccur after multiple bandings, no consensus exists regarding the best treatment option: continuing RBL or a surgical procedure. One of the first operations for HD is the haemorrhoidectomy[10]. However, this procedure can be painful and is costly compared to RBL. A relatively novel, but regularly performed surgical alternative is the sutured haemorrhoidopexy[11]. The costs of sutured haemorrhoidopexy are similar to the haemorrhoidectomy, but the procedure is less painful. High-level evidence on the most (cost-) effective treatment is lacking and thus the treatment of recurrent grade II and III HD currently depends on the preference of the surgeon and the patient.

Therefore, **chapter 5** entails the study protocol to conduct a multicentre randomized controlled trial comparing the effectiveness and cost-effectiveness of RBL versus sutured haemorrhoidopexy versus haemorrhoidectomy (*Napoleon Trial*). Over a timespan of two years, the *Napoleon Trial* was implemented in 20 medical centres across the Netherlands. Patients with recurrent HD grade II and III, ≥18 years of age and who had at least two RBL treatments in the last three years were eligible for inclusion. Exclusion criteria included previous rectal or anal surgery, rectal radiation, pre-existing sphincter injury or otherwise active pathologies of the colon and rectum, pregnancy, presence of hypercoagulability disorders, and/or medically unfit for surgery (ASA>III). The anticipated sample-size was 558 patients with a 1:1:1 randomization to either RBL, sutured haemorrhoidopexy, or haemorrhoidectomy. The primary outcomes were recurrence after 52 weeks and patient-reported symptoms measured by the PROM-Haemorrhoidal Impact and Satisfaction Score (PROM-HISS), which is described in the next part – *Patient-reported outcomes in haemorrhoidal disease* –. Secondary outcomes were impact on daily life, treatment satisfaction, early and late complication rates, health-related quality of life, costs and cost-effectiveness, and budget impact.

One of the interventions assessed in the *Napoleon Trial* is the sutured haemorrhoidopexy. The technique of the sutured haemorrhoidopexy comprises of the resection of a small rectal mucosa flap (mucosectomy) followed by a suture, stitching the anal mucosa to the rectal wall. This prevents the prolapsing component of the haemorrhoidal tissue protruding through the anus, while preserving as much anal mucosal tissue as possible. **Chapter 6** assessed the long-term safety and efficacy of the sutured haemorrhoidopexy in the Maastricht University Medical Centre+ (MUMC+). Between January 2009 and December 2021, 145 patients of which 70 women (48.3%), with a mean age of 61 years (±12.8) who underwent a sutured haemorrhoidopexy in the last twelve years were included.

Perioperative and postoperative data were collected via the electronic patient file and the PROM-HISS was probed via telephone calls to get an in-depth understanding of the current HD status. Perioperative complications occurred in 4 cases (2.8%). The cumulative efficacy in terms of freedom of recurrence was 88.3% (95% CI, 83.1-93.5) at six months, 80.0% (95% CI, 73.5-86.5) at one year and 67.7% (95% CI, 59.7-75.7) at five years. A subgroup of 50 patients (34.5%) was interviewed via telephone according to the PROM-HISS. More than half of the patients still experienced some feeling of a prolapse from the anus (56.0%), ranging from 'very little' to 'a lot'. Both blood loss and pain were reported in 19 cases (38.0%). About one-quarter of the patients still experienced 'itching' or 'fluid loss', with 'itching' being reported in 13 cases (26.0%) and fluid loss in 12 cases (24.0%).

Patient-reported outcomes in haemorrhoidal disease

Literature research and patient interviews indicate that the most common symptoms of HD are blood loss, prolapse, pain, itching and soiling. These symptoms can have a noteworthy negative impact on quality of life[6,12,13]. The burden of these symptoms for a patient can be captured by a Patient-Reported Outcome Measure (PROM). A PROM is a tool which grasps a deeper understanding of a disease-burden for a patient, without the interference of a caregiver. The European Society of ColoProctology (ESCP) acknowledges the importance of symptoms and their impact on daily life as crucial outcomes of effectiveness in the Core Outcome Set (COS) for HD, by identifying patient-reported symptoms as the primary outcome for clinical HD studies[14]. A COS is a consensus-based agreed minimum set of outcomes that should be measured and reported in all clinical studies of a specific disease[15]. As no established PROM for HD was available, our objective was to develop a disease-specific PROM for HD, according to standardized guidelines and with the active involvement of patients[16].

In **chapter 7** we discussed the added value of a PROM in both clinical research as clinical practice, allowing the physician to obtain information directly from the patient about their experiences with the ailment. In the field of HD, there are two validated PROMs that followed specific guidelines. One of them is the PROM-HISS, developed by our research team.

Following the COSMIN-guideline for designing and evaluating the measurement properties of a PROM, the PROM-HISS was tested on several psychometric aspects. First, the face and content validity were evaluated by conducting individual cognitive interviews with ten patients. Second, structural properties, reliability and construct validity were measured in a cross-sectional HD population consisting of 102 patients (65% male) with a mean age of 58 years (23-81 years). Results reported in **chapter 8** indicate that the PROM-HISS is a valid and reliable tool to assess symptoms of HD, impact on daily activities and satisfaction with HD treatment.

Besides the reliability and validity of the PROM-HISS, a PROM should also be tested on the aspect 'responsiveness', i.e. the ability to assess improvement or deterioration of health or symptoms. **Chapter 9** shows that the PROM-HISS is a responsive instrument that can detect change in the patient's symptom burden over time. The clinically important difference was found to be 0.3 points on the symptom score of the PROM-HISS. This cut-off point can be used to give insight in whether a meaningful change in HD symptoms has occurred as a result of HD treatment from a patient's perspective.

To promote adoption of the COS and use of the PROM-HISS internationally, the PROM-HISS was translated to English, followed by cross-cultural validation. First, a forward translation of the PROM-HISS from Dutch to English was performed, followed by a backward translation from English to Dutch. Thereafter, ten patients from the United Kingdom completed the preliminary translated PROM-HISS and were subsequently interviewed to probe the comprehensives and comprehensibility of the questionnaire. Patients indicated that they understood the questions posed and that they could adequately reflect their disease experience in the PROM-HISS. As discussed in **chapter 10**, the translated PROM-HISS shows that it is a reliable and valid instrument in English to be used for research purposes. We propose the use of the PROM-HISS in clinical practice, but an implementation study needs to be performed to adequately put this tool into practice.

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