European Society of ColoProctology (ESCP) Guideline for Haemorrhoidal Disease

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1. Recommendations

1.1 Evaluation: symptoms, diagnosis and classification

- Healthcare providers should make a provisional diagnosis of haemorrhoidal disease based on the clinical history whilst also thinking about the presence of other diseases like colorectal cancer and IBD (*expert opinion, upgraded by guideline development group*).
- Inspection and physical examination of the anorectal region should be performed to exclude other anorectal pathology (*expert opinion, upgraded by guideline development group*).
- Physical examination should be performed in a position that facilitates reliable diagnosis and comfort for the patient; i.e. the left lateral position. Lithotomy and knee-chest position may be alternatives (*expert opinion, upgraded by guideline development group*).
- If a provisional diagnosis of haemorrhoidal disease has been made, basic treatment (i.e. toilet training, laxatives, local anaesthetics and phlebotonics) can be started. Patients with refractory symptoms should be referred (*expert opinion, upgraded by guideline development group*).

Above bullet points are applicable for both primary care doctors and consultants.

- For documentation and classification, the Goligher classification has been used most widely and could be used in order to help healthcare providers choose the best therapeutic option for each patient (*expert opinion, upgraded by guideline development group*).
- A procedure (e.g. rigid anoscope, proctoscope or rectoscope) to visualize the entire anal canal must be performed in order to diagnose and to classify the severity of haemorrhoidal disease and to exclude other anal pathology (*expert opinion, upgraded by guideline development group*).
- If there are any indications found during history taking or physical examination of colorectal cancer or IBD, the relevant (inter)national guidelines for these conditions should be applied (*expert opinion, upgraded by guideline development group*).

1.2 Basic treatment

- Healthy life style measures, like sufficient water intake, a healthy diet and physical activity should be encouraged (*expert opinion, upgraded by guideline development group*).
- Toilet training, including adopting the correct body position during defecation should be advised. Straining and prolonged defecation sessions should be avoided (*expert opinion, upgraded by guideline development group*).
- The use of laxatives could be considered for symptom relief and to reduce bleeding (*low level of evidence*).
- Phlebotonics could contribute to symptom reduction (*low level of evidence*).

- NSAIDs and non-opioids analgesics could be prescribed for pain (*expert opinion*).

1.3 Outpatient procedures

- Choice of the outpatient procedure (i.e. rubber band ligation, injection sclerotherapy and infrared coagulation) should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for further procedures [*expert opinion, upgraded by guideline development group*].
- Rubber band ligation should be performed in grade I-III haemorrhoidal disease. Repeat banding may be necessary [*moderate level of evidence*].
- Infrared coagulation could be used as the first option in bleeding grade I haemorrhoids [*low level of evidence*].
- Injection sclerotherapy could be used in patients with grade I-II haemorrhoidal disease [*low level of evidence*].

1.4 Surgical interventions

- Choice of surgical treatment should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for surgical procedures (*expert opinion, upgraded by guideline development group*).
- Doppler - guided haemorrhoidal artery ligation +/- mucopexy could be used in patients with grade II-III haemorrhoids and/or in patients who are refractory to outpatient procedures (*low level of evidence*). However, because the effectiveness of using a Doppler is currently questioned, mucopexy alone could be considered (*very low level of evidence, upgraded by the guideline development group*).
- Stapled haemorrhoidopexy could be used in patients with grade II-III haemorrhoids and/or in patients who are refractory to outpatient procedures (*low level of evidence*).
- Haemorrhoidectomy could be used in patients with grade II-III haemorrhoids and/or should be used in patients who are refractory to outpatient procedures (*moderate level of evidence*).
- Haemorrhoidectomy should be used for grade IV haemorrhoids (*moderate level of evidence*).

1.5 Special situations

Thrombosed patients

- In patients with thrombosed haemorrhoids, treatment should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for further procedures (*expert opinion, upgraded by guideline development group*).
- Primarily, basic treatment (i.e. toilet training, laxatives, NSAIDS and non-opioid analgesics) can be considered in patients with thrombosed

haemorrhoids (*expert opinion*). Phlebotonics could be considered in patients with thrombosed haemorrhoids (*low level of evidence*). In selected cases, surgical options may be discussed with the patient (*very low level of evidence*).

- Surgical procedures (i.e. stapled haemorrhoidopexy and haemorrhoidectomy) can be considered in patients with thrombosed haemorrhoids (*very low level of evidence*).

Immunocompromised patients

- Outpatient procedures in immunocompromised patients can be considered if they are fit for the procedure (*very low level of evidence*).

Inflammatory Bowel Disease

- In patients with Inflammatory Bowel Disease (IBD), outpatient procedures and/or surgical procedures can only be considered when there is no sign of active disease (*expert opinion*).

Irradiated patients

- Outpatient/ and or surgical procedures in patients who have undergone pelvic radiotherapy can generally not be considered (*expert opinion*).

Anticoagulant patients

- If an outpatient procedure and/or surgical procedure is scheduled, appropriate cessation of anticoagulant therapy should be followed according to national guidance (*very low level of evidence, upgraded by guideline development group*).

Pregnant and post-partal women

- In pregnant and post-partal women basic treatment (i.e. laxatives, topical treatments, phlebotonics and analgesics) should be used (*expert opinion, upgraded by the guideline development group*).
- In pregnant and post-partal women with thrombosed haemorrhoids unresponsive to basic treatment, surgical procedures to treat thrombosis can be considered (*expert opinion*).

1.6 Other surgical techniques

- Both the closed and open haemorrhoidectomy (not using energy devices) could be used (*low level of evidence*). The closed haemorrhoidectomy is associated with less pain and bleeding (*low level of evidence*).
- Surgical energy devices (Ligasure^{R} and Harmonic scalpel^{R}) could be used for haemorrhoidectomy (*low level of evidence*).
- Alternative procedures (Laser and Radiofrequency ablation procedures) could be used/can be considered (*low level of evidence)*

- Rectal resection using a stapler device (including STARR^{R}) should not be used to treat haemorrhoids (*low level of evidence, downgraded by the experts*).

2. Introduction

The goal of this project, initiated by the European Society of ColoProctology (ESCP), was to establish an International European guideline for the treatment of grade I-IV haemorrhoidal disease, using the best available evidence.

The aim is to provide guidance on the most effective (surgical) treatment and management of patients with haemorrhoidal disease. By providing this guidance, the ESCP hopes to improve patient outcomes including recurrence of disease, complications, symptoms and quality of life.

The guideline will address both the diagnostic and therapeutic modalities for use in the management of haemorrhoidal disease and will include the following sections: diagnosis, basic treatment, outpatient procedures, surgical interventions, special situations (i.e. thrombosed haemorrhoids, coagulation defect, immunodeficiency and pregnant women) and other surgical procedures. The guideline will be applicable to patients with haemorrhoidal disease of all stages in whom (surgical) interventions are considered.

The guideline is intended for use by all healthcare providers treating patients with haemorrhoidal disease (e.g. general practitioners, surgeons, gastroenterologists, proctologists and dermatologists), healthcare workers and patients who desire information about the treatment and management of haemorrhoidal disease.

The guideline was supported by a grant from the ESCP enabling the Guideline Development Group (GDG) to meet and the surgical resident to work with the methodologist. The GDG had full control on the wording of the guideline without any influence from the funding body.

3. Methodology

The guideline was prepared by a Guideline Development Group (GDG) which included members from six European countries (i.e. Denmark, Italy, France, Germany, the Netherlands and Scotland). The GDG consisted of five colorectal surgeons (SB, DA, JJ, NQ, AW), one gastroenterologist and proctologist (TH), one general practitioner (JM) specializing in the treatment of haemorrhoidal disease, one surgical resident (RT) and one methodologist (JK) with extensive experience in guideline development. One dermatologist (CH) commented on the guideline drafts, but was not a member of the GDG (**table 1**).

Name	Profession	Institution	Country
Angus Watson	Colorectal surgeon	Raigmore Hospital	Scotland
Johannes Jongen	Colorectal surgeon	Park Klinik Kiel	Germany
Donato Altomare	Colorectal surgeon	University Aldo Moro of Bari	Italy
Niels Qvist	Colorectal surgeon	Odense University Hospital	Denmark
Stephanie Breukink	Colorectal surgeon	Maastricht University Medical Center (MUMC+)	The Netherlands
Thierry Higuero	Gastroenterologist/proctologist	Clinique a Beausoleil	France
Jean Muris	General practitioner	Maastricht University Medical Center (MUMC+)	The Netherlands
Jos Kleijnen	Methodologist	KSR Ltd & Maastricht University Medical Center (MUMC+) - CAPHRI	UK & The Netherlands
Robin van Tol	Surgical resident	Maastricht University Medical Center (MUMC+)	The Netherlands

Table 1: Guideline Development Group (GDG).

The GDG members were assisted by a team of methodologists (staff at Kleijnen Systematic Reviews) whose work covered input from information specialists, quality assurance, and evidence review and support.

At their first meeting, the GDG defined a hierarchy of important outcomes and formulated the research questions for the guideline.

A literature search was performed of MEDLINE, PubMed, EMBASE, and the Cochrane Database of Systematic Reviews in August 2017. Key word combinations included haemorrhoid, haemorrhoidal disease, interventions, techniques (rubber band ligation, h(a)emorrhoidopexy, h(a)emorrhoidectomy, Procedure for Prolapse and Haemorrhoids (PPH), Milligan-Morgan, Ferguson, Doppler guided, and stapled haemorrhoidopexy). There were no restrictions concerning publication format or language. The search strategy was designed and implemented by the surgical resident (RT) with help from an information specialist. The full search is available in **appendix X**.

Titles and abstracts were screened for inclusion by the surgical resident (RT). All GDG members contributed to the inclusion of studies from their own collections of

relevant papers. Data were extracted by the surgical resident (RT) and checked by the methodologist (JK) and the GDG members. Inclusion focused on available systematic reviews addressing each question, supplemented by further studies published after the time frame covered by the systematic reviews. We used a hierarchy of best available evidence for study selection, i.e. well performed systematic reviews, randomized trials, controlled observational studies, case series and expert opinion. If evidence of a higher level was available, no lower level of evidence was sought or included (**figure 1**).

Meta-analysis from the systematic reviews were updated by the surgical resident and the methodologist using ReviewManager version 5 software.

Grade evidence tables were prepared by the surgical resident and the methodologist and discussed and amended by the GDG members. Grade evidence tables, were used to describe the strength of the available evidence and informed the wording of the recommendations. We used “must”, or “must not” if the level of evidence was ++++ (according to GRADE). For level of evidence +++ we used “should” or “should not”, for the level of evidence ++ we used “could” and for the level of evidence + we used “can be considered”.

Figure 1: The pyramid of evidence.

In formulating the recommendations, the GDG members considered the evidence for all available outcomes important or critical for decision making as defined in the first meeting. The box also reflects the hierarchy of the outcomes by importance as judged by the GDG members.

Box 1: Outcomes important or critical for decision making

Outcomes

Symptoms (e.g. pain, blood loss etc)
Patient satisfaction
Recurrence
Complications
Quality of life
Re-operation
Time to return to normal
Costs of operation
Duration of operation
Duration of hospitalization

No Delphi process was conducted, GDG members reached consensus on all recommendations. Where there was minority dissent, we planned to explicitly report this, however, full consensus was reached on all recommendations.

The guideline was submitted to the ESCP who made it available on their website for all the members for one month. Each GDG member identified at least one patient in their country who could read English to comment on the draft guideline.

4. Evaluation: symptoms, diagnosis and classification

4.1 Definition and pathophysiology

In the sub-epithelial space of the anal canal haemorrhoid cushions are embedded in connective tissue and smooth muscle fibers. The connective tissue and smooth muscle fibers are supportive structures forming a fibro-elastic network. This network is also named the corpus cavernosum recti or plexus haemorrhoidalis and is supplied by a complex structure of blood vessels [1]. In the non-pathological state the cushions originate intraluminally proximal to the dentate line. The dentate line is the point at which the squamous anoderm meets the columnar mucosa (**image 1**). The haemorrhoids cushions contribute to 15-20% of the closing pressure of the anal canal [2]. With straining and increased abdominal pressure, the cushions fill with blood to prevent leakage of stool, fluid and/or gas.

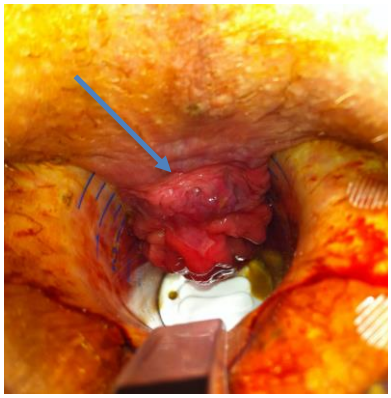
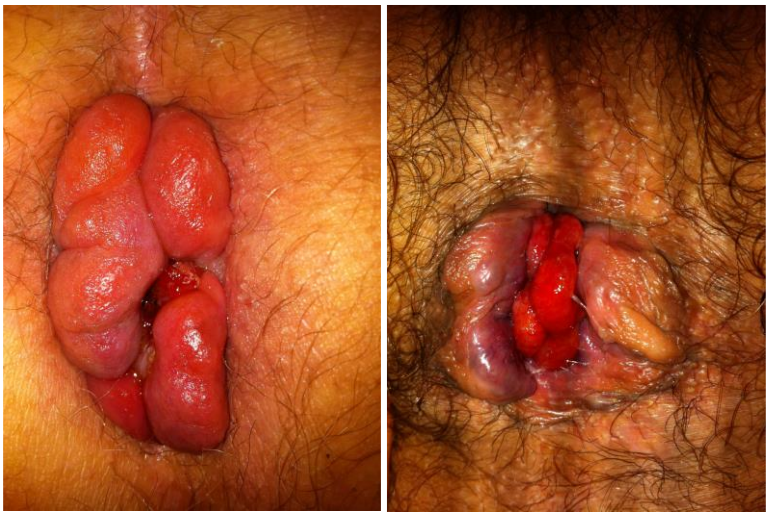


Image 1: dentate line

In a pathological state, abnormal swelling of the cushions, stretching of the suspensory muscles and dilatation of the submucosal arteriovenous plexus results in prolapsed haemorhoids which can descend below the dentate line. This prolapsed tissue is easily traumatized and may cause bleeding. In addition, deposition of mucus produced by the prolapsed tissue may cause itching of the perianal skin (**image 2**).



Images 2: (circular) prolapsed haemorrhoids

The most commonly used classification of haemorrhoids was described by Goligher. In the Goligher classification, Grade I describes haemorrhoidal prolapse through the proctoscope, grade II describes haemorrhoidal prolapse during straining which reduces spontaneously, grade III describes haemorrhoidal prolapse occuring during straining and requires manual reduction back into the anal canal and grade IV describes irreducible haemorrhoidal prolapse.

In the literature and daily practice, grade III and IV haemorrhoids are often called external haemorrhoids. However, the wording 'external haemorrhoids' is often used when 'thrombosis of perianal veins' or 'perianal thrombosis' has occured (image 3). However, thrombosis of perianal veins has a completely different etiology. In the anocutaneous junction there is a venous plexus, anatomically called 'plexus haemorrhoidalis externa', and here perianal thrombosis may develop, which can cause severe pain and swelling. Therefore, healthcare providers should be reluctant to use the term external haemorrhoids to avoid confusing with thrombosis of the perianal veins. Instead we advocate to use the Goligher classification to indicate severity of the haemorrhoids and to use thrombosis of perianal veins if we see **image 3**.

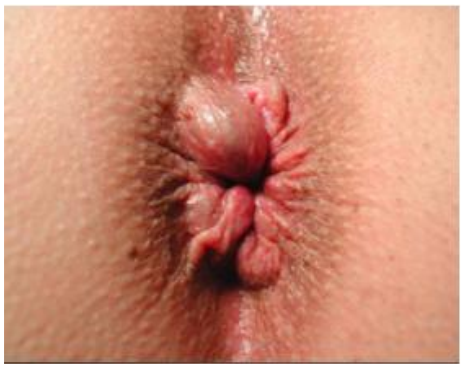


Image 3: Thrombosed perianal veins

4.2 Review questions

We considered the following questions for our evidence reviews of symptoms, diagnosis and classification:

1) Which factors should be assessed during history taking?
2) In which position should physical examination be performed? (knee-chest-, lithotomy- or left lateral position)
3) How should haemorrhoidal disease be classified?

4.3 Diagnosis

Diagnosis should start with a medical history to identify the symptoms suggestive of haemorrhoidal disease. Symptoms may include bleeding after passing a stool (the blood is usually bright red), changes in bowel habits, pain, prolapse (swelling), itching and soiling (stool and/or mucus discharge) [3, 4]. Further the healthcare providers should ask about risk factors: hard stools (constipation), the use of opioids or other medication causing constipation, increased intra-abdominal pressure (obesity, prolonged sitting on the toilet and pregnancy), low fiber diets and fluid intake [5-8]. In addition, a surgical history of previous anorectal procedures must be obtained.

A detailed physical examination must include external inspection of the anus and a digital rectal examination. Rectal examination could be performed in the knee-chest-, lithotomy or left lateral position [4]. The healthcare provider should consider positioning the patient to facilitate the most reliable anal diagnosis: left lateral or knee-chest position. The embarrassment of the patient must be addressed by a good preliminary explanation of the clinical examination. The rectal examination should include inspection, palpation for masses and tenderness and characterization of the anal sphincter tone. The initial examination should also include asking the patient to strain down. Haemorrhoids are generally not palpable on digital examination in the absence of thrombosis.

During history taking and physical examination the following diagnoses should be included in the differential diagnosis:

- Colon and/or rectal cancer (in more distal localization: blood mixed with faeces);
- Anal fissure: tearing pain with the passage of bowel movements. With regard to anal fissures, the passage of stool may be accompanied by a small amount of bright rectal bleeding usually limited to the toilet paper or on the surface of stool. Some patients complain of itching or perianal skin irritation;
- Inflammatory bowel diseases (i.e. Crohn's and Colitis): (bloody) diarrhoea, abdominal pain and/or general malaise;
- Sexually transmitted infections: intermittent rectal bleeding associated with the passage of mucus, mild diarrhoea with fewer than four small loose stools per day and/or urgency without defecation;
- Iatrogenic/traumatic causes, medication (e.g. anticoagulants, NSAIDs, opioids)

Great care should be taken to exclude colorectal cancer especially in patients aged >50 years, with first degree family members with colorectal cancer, changed

defecation pattern, blood mixed with defecation, weight loss, and perianal abnormalities [9, 10].

4.4 Classification

Haemorrhoids are classified by their location and severity this guides physicians in choosing the best therapeutic option for each patient. The most widely used classification is the Goligher classification: haemorrhoidal prolapse through the proctoscope (grade I), haemorrhoidal piles prolapse during straining but reducing spontaneously (grade II), haemorrhoidal prolapse during straining but requiring manual reduction (grade III) and irreducible haemorrhoidal prolapse (grade IV) [11]. Other recent developed classifications are the PATE, the Single Pile Classification (SPC) and the classification by Lunniss et al.[11-13]. These classifications might be interesting, but practically less usable than the Goligher classification. Altogether, we found no evidence favoring one classification over any of the others.

Noteworthy, classification is important for the therapy, however, one study, including 270 patients, showed that there is no correlation between the grade of haemorrhoid and the symptoms/complaints of the patient [14].

4.5 Conclusion

We found little useful evidence addressing these questions and the recommendations are predominantly based on expert opinion. The strongest wording used in the recommendations was “should”. In these cases, experts thought there would be broad consensus from their colleagues.

4.6 Recommendations for diagnostic assessment

- Healthcare providers should make a provisional diagnosis of haemorrhoidal disease based on the clinical history whilst also thinking about the presence of other diseases like colorectal cancer and IBD (*expert opinion, upgraded by guideline development group*).
- Inspection and physical examination of the anorectal region should be performed to exclude other anorectal pathology (*expert opinion, upgraded by guideline development group*).
- Physical examination should be performed in a position that facilitates reliable diagnosis and comfort for the patient; i.e. the left lateral position. Lithotomy and knee-chest position may be alternatives (*expert opinion, upgraded by guideline development group*).
- If a provisional diagnosis of haemorrhoidal disease has been made, basic treatment (i.e. toilet training, laxatives, local anaesthetics and phlebotonics) can be started. Patients with refractory symptoms should be referred (*expert opinion, upgraded by guideline development group*).

Above bullet points are applicable for both primary care doctors and consultants.

- For documentation and classification, the Goligher classification has been used most widely and could be used in order to help healthcare providers

choose the best therapeutic option for each patient (*expert opinion, upgraded by guideline development group*).

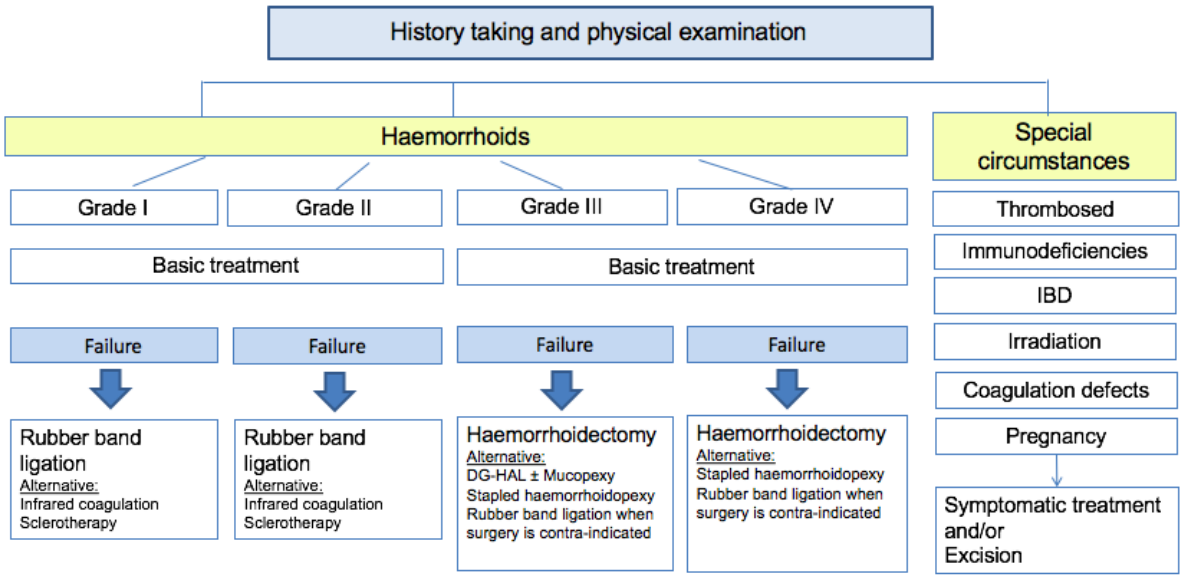
- A procedure (e.g. rigid anoscope, proctoscope or rectoscope) to visualize the entire anal canal must be performed in order to diagnose and to classify the severity of haemorrhoidal disease and to exclude other anal pathology (*expert opinion, upgraded by guideline development group*).
- If there are any indications found during history taking or physical examination of colorectal cancer or IBD, the relevant (inter)national guidelines for these conditions should be applied (*expert opinion, upgraded by guideline development group*).

5. Basic treatment for haemorrhoids

5.1 Introduction

When a patient visits the outpatient clinic with ano-rectal symptoms which may include bleeding, pain, prolapse, itching and/or soiling and the healthcare provider makes a diagnosis of haemorrhoidal disease, the first management step will consist of basic treatment. Basic treatments could be used for symptom relief and to prevent prolapse and includes toilet training, dietary changes (specifically high fiber diet), topical and pharmacological treatments (which may include phlebotonics such as flavonoids). In addition, it will be important to manage the patients' expectations about symptom control.

These interventions are given in addition to advice about adequate water intake, healthy diet and encouraging physical activity.



5.2 Review questions

We considered the following questions for our evidence reviews:

1) What are the effects of toilet training versus no toilet training on occurrence and symptoms in patients with haemorrhoidal disease?
2) What are the effects of laxatives versus no laxatives on occurrence and symptoms in patients with haemorrhoidal disease?
3) What are the effects of local treatments versus no local treatments on occurrence and symptoms in patients with haemorrhoidal disease?
4) What are the effects of phlebotonics versus no phlebotonics on occurrence and symptoms in patients with haemorrhoidal disease?

5.3 Interventions

5.3.1 Toilet training

No systematic reviews or (randomized) trials have been found regarding this subject.

5.3.2 Laxatives intake

Analysis of the literature reveals only one systematic review. In this systematic review, seven RCTs and a total of 378 patients were evaluated with regard to the impact of laxatives versus no laxatives on haemorrhoid symptoms. The types of laxatives included fiber administered orally (high fiber diet, bulking agents such as bran, ispaghula, psyllium), stimulant laxatives (senna and bisacodyl), faecal softeners (liquid paraffin, seed oils), and osmotic agents (lactulose, magnesium hydroxide, sorbitol and lactitol). Four studies reported bleeding as an individual outcome. The pooled analysis showed a 50% relative risk reduction in the laxatives group (RR 0.50, 95% CI 0.28 to 0.89). Three studies showed, in the pooled analysis, a non-significant difference between the laxatives group and the placebo group for persistent prolapse (RR 0.79, 95% CI 0.37 to 1.67) (Broader 1974, Moesgaard 1982, Webster 1978). Only one study looked at the number of recurrences in the long term in both groups (Jensen 1988). They reported less overall recurrence in the fiber group (15% versus 45%) at 18 months in patients with grade III haemorrhoids after rubber band ligation (RR 0.34, 95%CI 0.15, 0.77) [15].

5.3.3 Local anaesthetics

Local anaesthetics have been assessed in randomized trials and systematic reviews in post-surgery patients. There is no study proving the effectiveness of local anaesthetics for haemorrhoids as a basic treatment modality.

5.3.4 Phlebotonics

The analysis of literature reveals 2 systematic reviews [16, 17].

The first systematic review (Perera Nirmal 2012), including 24 RCTs with a total of 2,344 patients, investigated the efficacy of phlebotonics versus no phlebotonics in alleviating the signs, symptoms and severity of haemorrhoidal disease. In addition, they verified their effect post-haemorrhoidectomy. Phlebotonics demonstrated a statistically significant beneficial effect for the outcomes of pruritus (OR 0.23; 95% CI 0.07 to 0.79), bleeding (OR 0.12; 95% CI 0.04 to 0.37), bleeding post-haemorrhoidectomy (OR 0.18; 95% 0.06 to 0.58)(P=0.004), discharge and leakage (OR 0.12; 95% CI 0.04 to 0.42) and overall symptom improvement (OR 15.99 95% CI 5.97 to 42.84). The number of adverse events which took place as a result of taking phlebotonics were few and often consisted of mild gastro-intestinal side-effects. The systematic review demonstrated that there is no difference between the two groups (phlebotonics and control) with regards to adverse events (RD 0.00; 95% CI -0.04 to 0.04)(I2=0%) [16].

A systematic review (Alonso-Coello 2006), including 14 trials (of whom 4 trials not reported in the review of Perera Nirmal) with a total of 1,514 patients, evaluated the

impact of phlebotonics versus no phlebotonics in patients with symptomatic haemorrhoids after surgery. Similarly, in this review phlebotonics seemed to have a beneficial effect on symptoms, which included less bleeding, less pain, less itching and a lower recurrence rate. All but one study showed either a trend or a significant difference in favour of the phlebotonics group. The pooled analysis showed a significant 67% reduction in the RR of bleeding in the phlebotonics group (RR 0.33 (95% CI 0.19 to 0.57)). The pooled analysis, with seven trials comparing the number of patients still experiencing pain at the time of follow-up, showed a significant benefit in the phlebotonics group compared with placebo (RR 0.35 (95% CI 0.18 to 0.69)). Four studies, including a total of 450 patients evaluated recurrences in the short to midterm (2–6 months' follow-up) and showed a pooled estimate of 47% RR reduction in favour of the phlebotonics group (RR 0.53 (95% CI 0.41 to 0.69)) [17].

Unfortunately, all reported studies found no gradient of effect across doses and in addition, there is no study proving the effectiveness of phlebotonics in the long-term.

5.3.5 Other

There are no scientific data evaluating NSAIDs, cortisone and its derivates for the treatment of haemorrhoids.

5.4 GRADE

Comparison: Laxatives compared to no laxatives in patients with symptomatic haemorrhoids

Included studies: Broader 1974, Foster 1979, Hunt 1981, Jensen 1988, Moesgaard 1982, Perez-Miranda 1996 and Webster 1979.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laxatives	no laxatives	Relative (95% CI)	Absolute (95% CI)		
Remaining symptoms (overall assessment: (better, same or worse))												
4	randomised trials	serious [a,b]	not serious [c]	not serious [d]	not serious	publication bias strongly suspected [e]	0/0		**RR 0.47** (0.32 to 0.68)	**0 fewer per --** (from 0 fewer to 1 fewer)	⨁⨁◯◯ LOW	CRITICAL
Remaining symptoms (bleeding)												
4	randomised trials	serious [a,b]	not serious [f]	not serious [d]	not serious	publication bias strongly suspected [e]	0/0		**RR 0.50** (0.28 to 0.89)	**1 fewer per 1,000** (from 0 fewer to 1 fewer)	⨁⨁◯◯ LOW	CRITICAL
Recurrence												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Laxatives	no laxatives	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a,b]	not serious	not serious	not serious	publication bias strongly suspected [e]	0/0		**RR 0.34** (0.15 to 0.77)	**0 fewer per 1,000** (from 0 fewer to 1 fewer)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Moderate study quality with very little detail provided concerning key validity methodologies. By asking the authors they provided additional information concerning the methodological criteria. None of the studies used validated questionnaires to assess the study outcomes.

b. Forrest plots of meta-analyses were not downloadable, therefore numbers of patients per group were not available.

c. Significant heterogeneity was not observed for the overall assessment and I2 ranged from 1.1% to 45.6%.

d. Most trials assessed the degree of improvement of individual (bleeding, pain, itching and prolapse) or overall symptoms by patient.

e. Publication bias is suggested because of the small number and size of the trials.

f. No statistically significant heterogeneity was present but I2 was moderate.

Comparison: Phlebotonics compared to no phlebotonics in patients with symptomatic haemorrhoids

Included studies: A ba-bai-ke-re 2011, Annoni 1986, Basile 2001, Basile 2002, Belcaro 2010, Chauvenet 1994, Colak 2003, Cospite 1992, Cospite 1994, Debien 1996, Dimitroulopoulos 2005, Godeberge 1994, Ho 1995, Ho 2000, Jiang 2006, La Torre 2004, Mentes 2001, Misra 2000, Mlakar 2005, Panpimanmas 2010, Sarabia 2001, Squadrito 2000, Thanapongsathorn 1992, Wijayanegara 1992

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	phlebotonics	no phlebotonics	Relative (95% CI)	Absolute (95% CI)		
Remaining symptoms (bleeding)												
2	randomised trials	not serious [a]	serious [b]	not serious	not serious	publication bias strongly suspected [c]	4/99 (4.0%)	23/91 (25.3%)	**RR 0.15** (0.05 to 0.44)	**215 fewer per 1,000** (from 142 fewer to 240 fewer)	⨁⨁◯◯ LOW	CRITICAL
Remaining symptoms (overall symptom improvement)												
5	randomised trials	not serious [d]	serious [e]	not serious	not serious	publication bias strongly suspected [c]	181/193 (93.8%)	99/175 (56.6%)	**RR 1.69** (1.57 to 1.74)	**390 more per 1,000** (from 322 more to 419 more)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	phlebotonics	no phlebotonics	Relative (95% CI)	Absolute (95% CI)		
Remaining symptoms (pain assessed with: dosis analgesics)												
2	randomised trials	not serious [f]	serious [b]	not serious	not serious	publication bias strongly suspected [c]	11/99 (11.1%)	48/91 (52.7%)	**RR 0.21** (0.02 to 1.05)	**417 fewer per 1,000** (from 26 more to 517 fewer)	⊕⊕◯◯ LOW	CRITICAL
Complications												
7	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected [c]	10/246 (4.1%)	10/265 (3.8%)	**RR 0.00** (-0.04 to 0.04)	**-- per 1,000** (from 36 fewer to 39 fewer)	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. No serious study limitations. Adequate blinding, however methods of sequence generation or allocation concealment unclear for Misra 2000 or Ho 1995 .

b. Serious inconsistency; high statistical heterogenity (I2>75%). Perhaps due to differences in formulations.

c. The funnel plot indicates that there is some publication bias present.

d. No serious limitations. Adequate methods of blinding, however allocation concealment or sequence generation unclear for Cospite 1994, Mentes 2001, Thanapongsathorn 1992 and Wijayanegara 1992.

e. Serious inconsistency; high statistical heterogeneity (I2>75%). Heterogeneity may most likely be due to differences in formulations, doses and regimes of phlebotonics.

f. No serious limitations. Adequate methods of blinding, however allocation concealment unclear for Basile 2001, Basile 2002 and Colak 2003.

5.5 Recommendations for basic treatment

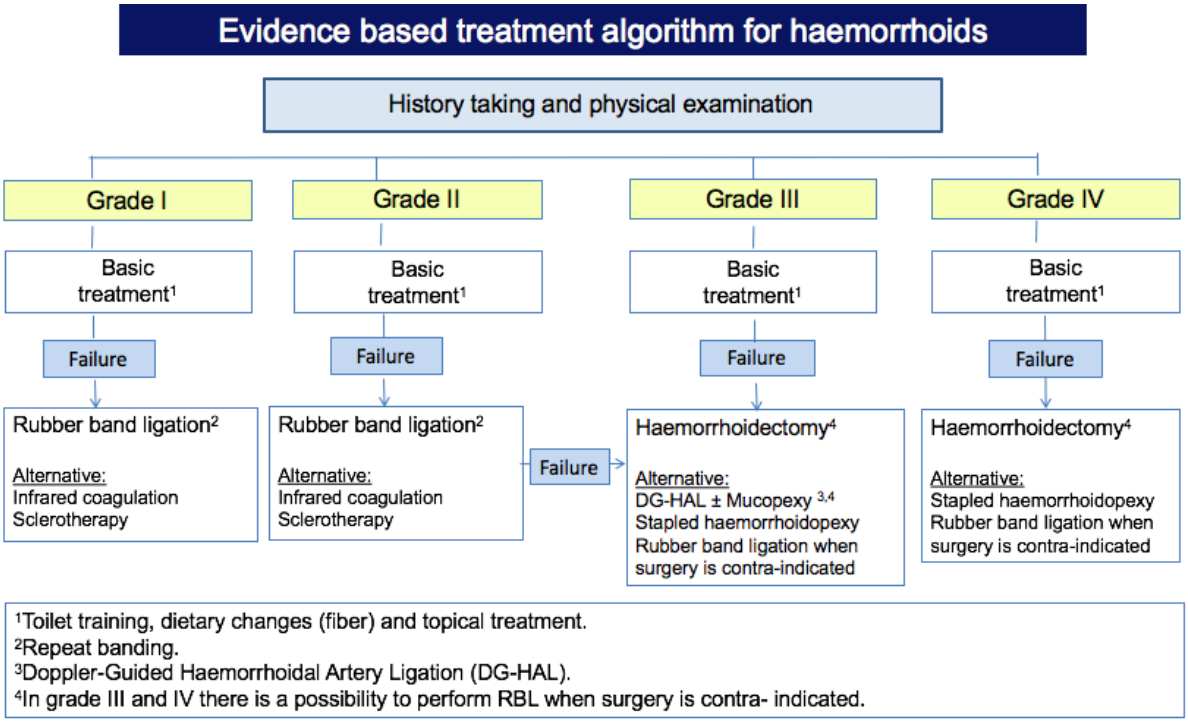
- Healthy life style measures, like sufficient water intake, a healthy diet and physical activity should be encouraged (*expert opinion, upgraded by guideline development group*).
- Toilet training, including adopting the correct body position during defecation should be advised. Straining and prolonged defecation sessions should be avoided (*expert opinion, upgraded by guideline development group*).
- The use of laxatives could be considered for symptom relief and to reduce bleeding (*low level of evidence*).
- Phlebotonics could contribute to symptom reduction (*low level of evidence*).
- NSAIDs and non-opioids analgesics could be prescribed for pain (*expert opinion*).

6 Outpatient procedures

6.1 Introduction

In patients where basic treatment has not resulted in acceptable symptom reduction, further procedures should be considered. As some treatments are less invasive, have fewer and/or less serious reported complications and are quicker and cheaper than others, we propose that clinicians first consider outpatient procedures (i.e. Rubber Band Ligation (RBL), Infrared Coagulation (IRC) or Sclerotherapy (SCL)). Nevertheless, patients with circular prolapsing grade III and especially grade IV haemorrhoidal disease (HD) could be better treated with primary surgical interventions like mucopexy + Doppler Guided-Haemorrhoidal Artery Ligation (DG-HAL), Stapled Haemorrhoidopexy (SH) or Haemorrhoidectomy. However, outpatient procedures could be performed in patients with grade III and IV HD when primary surgery is contra-indicated or the patient refuses primary surgery. This is represented in the figure below.

The guideline development group (GDG) acknowledges that this not a rigid system. The treatment algorithm is guided by the grade of the haemorrhoidal disease and doctors and patients' preferences.



6.2 Review questions

We considered the following questions for our evidence reviews:

- What are the effects of Rubber Band Ligation (RBL) versus Sclerotherapy (SCL) versus Infrared Coagulation (IRC) on symptoms, recurrence and complications in patients with haemorrhoids?
    - What are the effects of RBL versus IRC on symptoms, recurrence and complications in patients with haemorrhoids?
    - What are the effects of RBL versus SCL on symptoms, recurrence and complications in patients with haemorrhoids?
- What are the effects of RBL versus Doppler-Guided Haemorrhoidal Artery Ligation (DG-HAL) versus Stapled Haemorrhoidopexy (SH) versus Haemorrhoidectomy on symptoms, recurrence and complications in patients with haemorrhoids?

6.3 Techniques

6.3.1 Rubber band ligation (RBL)

A device applies a rubber band to the base of each haemorrhoidal cushion by using an anoscope. This band constricts the blood supply of the haemorrhoidal cushion causing ischaemia. The ischaemic haemorrhoidal cushion will shrink and scar tissue is formed with subsequent repositioning of the prolapsing part of the cushion higher up in the anal canal.

6.3.2 Infrared coagulation (IRC)

With IRC, the tissue is coagulated through infrared light. The infrared photo coagulator produces infrared light that penetrates the tissue and converts to heat, promoting coagulation of vessels that will result in local ischaemia and the formation of scar tissue which causes repositioning of the prolapsing part of the cushion higher up in the anal canal. The amount of tissue destruction depends on the intensity and duration of the application. The infrared probe is applied for 0.9 to 1.5 seconds to the apex of each internal cushion, and this could be repeated three times on each haemorrhoidal cushion.

6.3.3 Injection sclerotherapy (SCL)

With SCL, an agent (i.e. polidocanol or aluminium potassium sulfate) is injected into the haemorrhoidal cushions (upper, deep middle, shallow middle, and lower parts). Local infiltration leads to inflammation of the haemorrhoidal tissue and scar tissue is formed with subsequent fixation of mucosa to the submucosa [18].

6.4 Evidence in the literature

6.4.1 Rubber Band Ligation (RBL) versus Infrared Coagulation (IRC)versus Sclerotherapy (SCL)

The analysis of the literature reveals one meta-analysis that meet the search criteria [19].

In a meta-analysis (McRae 1995), including 18 RCTs and observational studies and patients with grade I-III HD, the following comparisons were made: RBL versus surgical haemorrhoidectomy (3 trials), Lord-procedure (e.g. manual dilatation) versus surgical haemorrhoidectomy (6 trials), sclerotherapy versus infrared coagulation (2 trials), sclerotherapy versus RBL (4 trials) and RBL versus infrared coagulation (3 trials). They showed that RBL resulted in a better treatment response in patients with grade I, II and III compared to SCL. No significant difference was seen regarding the complication rates between the two techniques. In addition, patients treated with RBL were significantly less likely to require further therapy than those treated with either SCL or IRC. However, pain was significantly more likely to occur after RBL than SCL and IRC. No difference was found between SCL and IRC regarding pain. IRC was not evaluated for grade III haemorrhoids in any of the studies. However, in view of the finding that patients who undergo IRC are more likely to require further therapy than those who have RBL for early haemorrhoids, it seems reasonable to assume that RBL would be more effective in treating more advanced disease [19].

RBL versus IRC

The analysis of literature reveals five RCTs that meets the search criteria [20-24].

A RCT (Ricci 2008), including 48 patients with grade I, II and III haemorrhoidal disease, compared RBL (n=23) or IRC (n=25). After RBL, significantly more patients (60,8%) required medication for pain relief versus just one patient (4,0%) after IRC. RBL relieved bleeding and prolapse in 90,0% and 82,4% respectively. IRC treated bleeding and prolapse in 93,7% and 87,5% respectively. Those differences were not significant [20].

Another RCT (Marques 2006), including 94 patients, compared RBL with IRC and showed that there was no significant difference in pain scores between the two procedures immediately and 24 hours after the procedures. After 72 hours and one week, the pain scores for RBL and IRC were similar. There were significantly higher incidences of bleeding immediately, 6 hours, and 24 hours after RBL compared to IRC (immediate: 32.4% vs. 4.3%; 6 hours: 13.4% vs. 3.6%, 24 hours: 26.8% vs. 10.2%, respectively). However, there were no significant differences noted regarding the incidence of bleeding between the two groups at 72 hours. Complications were more likely after RBL than IRC, however this difference was not significant [21].

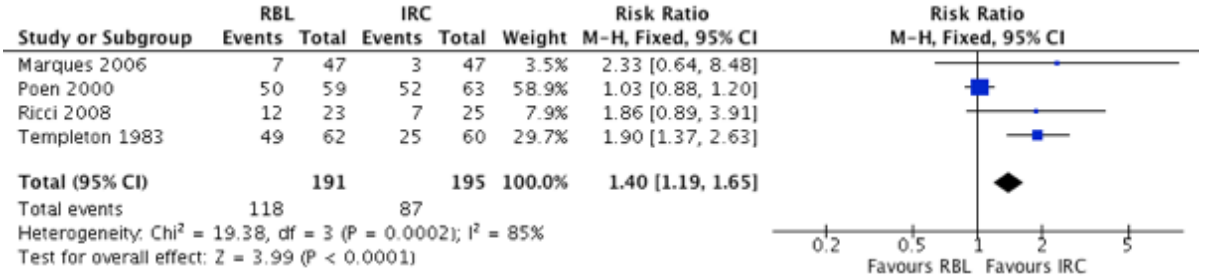
In the RCT of Poen et al. (2000) a total of 133 patients with haemorrhoids (grade not specified) were randomized to RBL (n= 65) or IRC (n = 68). They showed that in the RBL group 58 patients (97%), and in the IRC group 59 patients (92%) were symptom-free or had satisfactorily improved. Pain following treatment was significantly more common and more severe after RBL (VAS 5.5 +/- 3.7) than after IRC (VAS 3.3 +/- 3.3) [22].

A RCT (Templeton 1983), including 137 patients with grade I and II haemorrhoids, compared IRC (n=66) and RBL (n=71). They showed that both methods were equally effective in grade I and II haemorrhoids. The number of treatments necessary to cure symptoms did not differ significantly between the two methods. IRC was performed significantly faster than RBL. The incidence of side effects, particularly discomfort, during and after treatment was significantly higher in those treated by RBL [23].

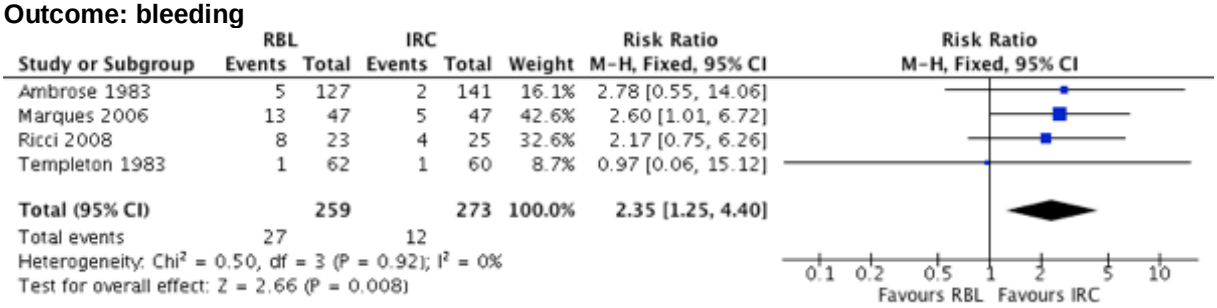
A RCT (Ambrose 1983), including 268 patients with grade I and II haemorrhoids, compared IRC (n=141) with RBL (n=127). At four months, patients with grade I haemorrhoids appeared to fare better if treated by photo- coagulation (excellent:10 of 25 in IRC vs four of 16 in the RBL group) but more patients with grade II haemorrhoids were classified as excellent after RBL. At 12 months, there was no significant difference in the symptomatic response to treatment between the two treatment groups. Side effects of treatment (bleeding or severe pain) were significantly more common after rubber band ligation (n=11) than after IRC (n=2) [24].

Meta-analysis of above mentioned studies

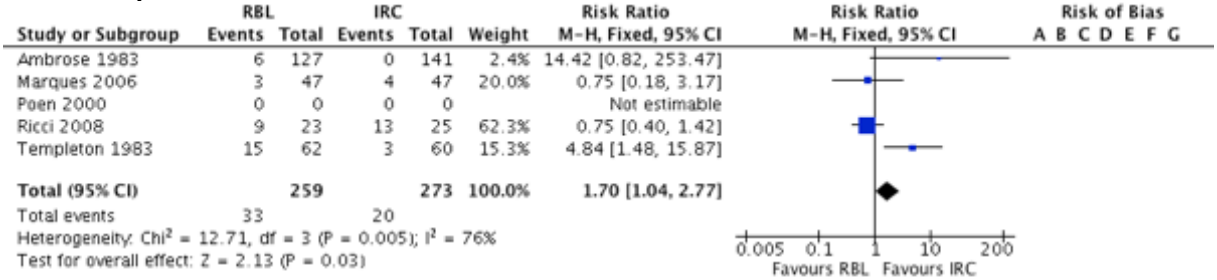
Outcome: complications



Outcome: bleeding

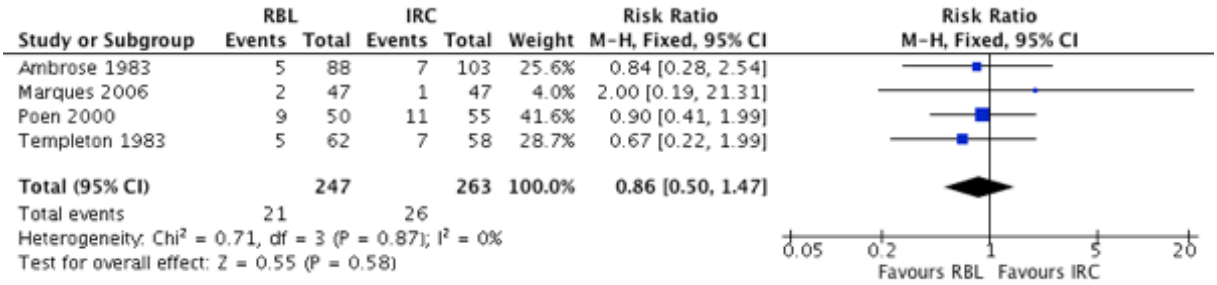


Outcome: pain

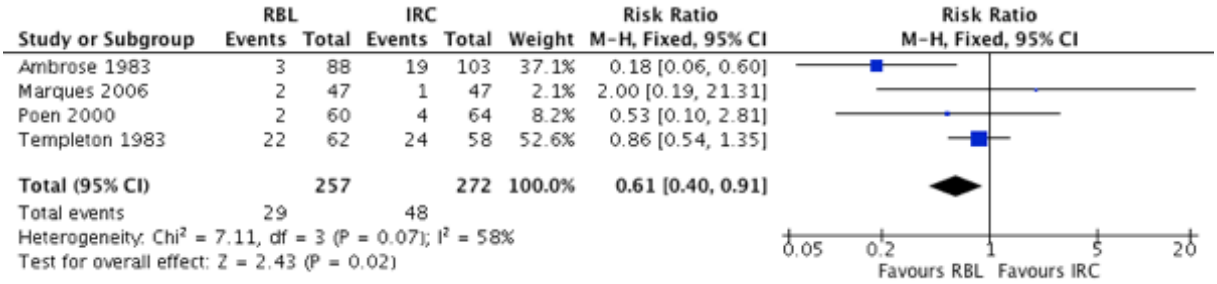


Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Outcome: recurrence



Outcome: re-intervention



RBL versus SCL

The analysis of the literature reveals three RCTs that meet the search criteria [25-27].

A RCT (Kanellos 2003), including 255 patients with grade II haemorrhoids, compared three groups of patients: either patient received SCL, RBL or a combination of SCL and RBL. Twenty-four patients (30%) of the SCL group, and 14 patients (17%) of the RBL group required additional sessions 6–24 months after the initial therapy, due to symptom recurrence. Significantly more patients of the SCL group required additional sessions compared to the RBL group. Comparing SCL versus RBL, SCL alone resulted in significantly fewer complications after treatment compared to RBL [25].

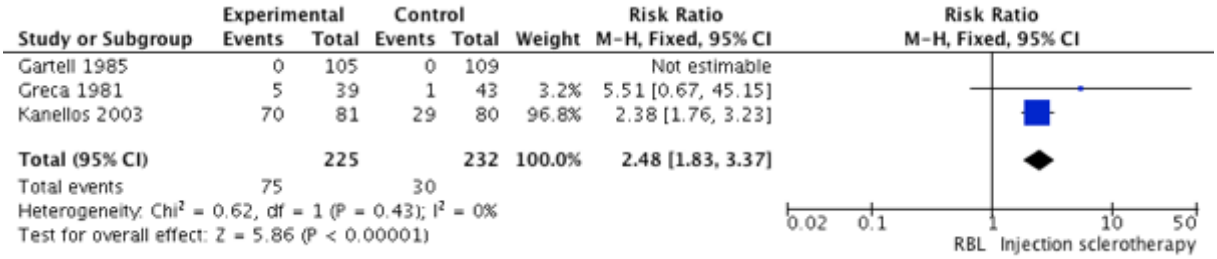
A RCT (Gartell 1985), including 269 patients with symptomatic haemorrhoids (patients with grade III and IV haemorrhoids were also included in the trial if either they refused surgery, or were considered medically unsuitable for operation), compared RBL (only ligating one haemorrhoid) (n=135) versus SCL (n=134). There was no difference in the severity of pain experienced by the patient following either treatment. A significantly higher successful outcome was achieved in 89% of those receiving RBL compared with 70% for SCL. All symptoms tended to respond more favourably with RBL, the results achieving statistical significance in patients complaining of bleeding and prolapse. Similarly, all grades tended to have a better response to treatment with RBL, although only in those patients with grade II haemorrhoids was this difference significant [26].

A RCT (Greca 1981), including 82 patients with grade I-III haemorrhoids, compared SCL (n=43) with RBL (n=39). The symptomatic results in all patients 12 months after treatment were indistinguishable, 64% being improved after SCL compared with 70% after RBL. Repeated treatment was significantly more necessary in 13 patients after SCL versus only 4 patients in the RBL group. Complications were recorded in 5

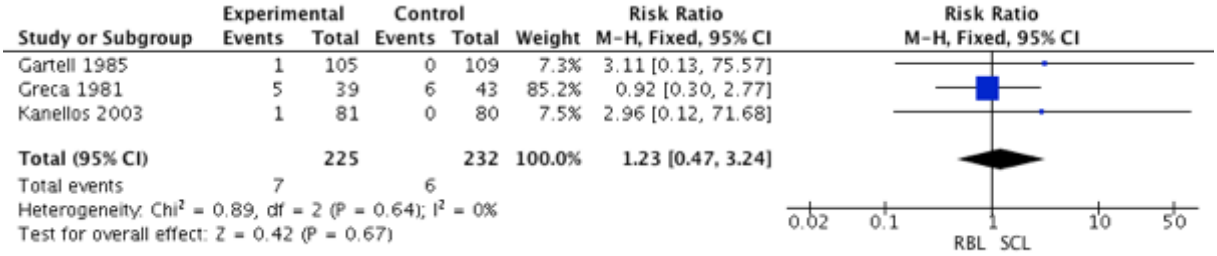
patients after RBL (severe pain and bleeding) and in only one patient who underwent SCL (transient incontinence) [27].

Meta-analysis of above mentioned studies

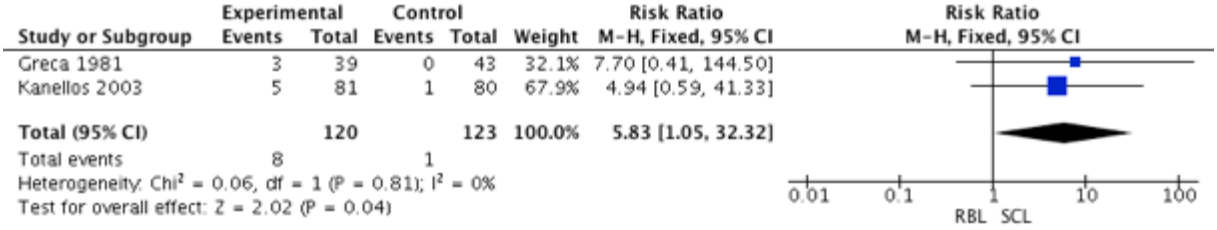
Outcome: complications



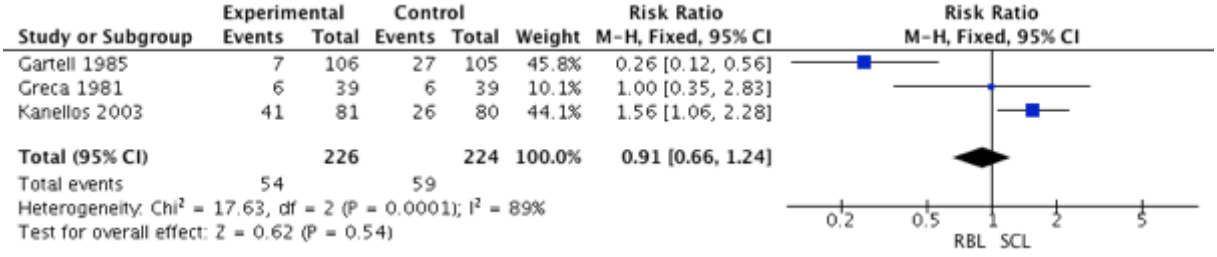
Outcome: postoperative bleeding



Outcome: postoperative pain



Outcome: re-intervention



6.4.2 RBL versus DG-HAL versus SH versus Haemorrhoidectomy

The analysis of literature reveals one meta-analysis and three RCTs [28-31].

RBL versus Haemorrhoidectomy

The meta-analysis (Shanmugam 2005), including three trials (Murie 1980, Cheng 1981 and Lewis 1983) and 216 patients, compared RBL with the haemorrhoidectomy. The overall cure rate in patients with grade II haemorrhoids (60 patients) was similar for the two treatments (RR 1.16, 95% CI 0.98 to 1.38). The overall cure rate in a mixed population with grade II and III haemorrhoids (88 patients) was better in the group who had a Haemorrhoidectomy (RR 1.43, 95% CI 1.18 to 1.75). The overall cure rate in the population with grade III haemorrhoids (54 patients) was much better in the group after haemorrhoidectomy (RR 5.56, 95% CI 2.24 to 14.28). The fixed-effect model demonstrated that significantly more patients undergoing haemorrhoidectomy experienced postoperative pain (RR 1.94, 95% CI, 1.62 to 2.33). The random-effect model even demonstrated a RR of 3.11 (95% CI, 0.26 to 37.90), however with more uncertainty. Haemorrhoidectomy was associated with an overall greater individual complication rate compared to RBL, however this difference did not reach statistical significance [28].

RBL versus DG-HAL

A RCT (Brown 2016), including 372 patients with grade II and III haemorrhoidal disease, compared RBL with DG-HAL. They showed that 87 of 167 patients (49%) in the RBL group and 48 of the 161 patients (30%) in the DG-HAL group had haemorrhoid recurrence (OR 2.23, 95% CI 1.42 to 3.51) after one year. This odds ratio corresponds to a relative risk of approximately 1.63. The main reason for the difference was the number of extra procedures required to achieve improvement. If a single DG-HAL was compared with multiple RBLs then only 37.5% recurred in the RBL arm (OR 1.35, 95% CI 0.85 to 2.15). In the RBL group 2 of the 178 patients (1%) had a serious event including pain requiring hospital admission and vasovagal upset. In the DG-HAL group 12 of the 162 patients (7%) had a serious event including excessive bleeding (2%), urinary retention (1%), sepsis (<1%), pain requiring hospital admission and vasovagal upset (<1%). Additional, a subgroup analysis was carried out. In the RBL group recurrence was higher for grade III haemorrhoids (57%) compared with grade II haemorrhoids (42%). The recurrence rates in the DG-HAL group were 27% in grade III and 33% in grade II HD. However, this difference was not significant. Unfortunately, the study did not report the number of ligatures [29].

RBL versus SH

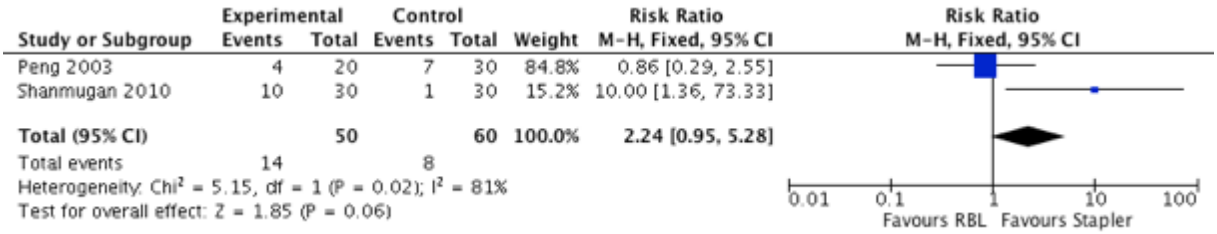
A RCT (Shanmugam 2010), including 60 patients with grade II haemorrhoids, compared RBL with the SH. They showed a lower of recurrence rate in the SH group compared with the RBL group at one year (OR 0.18, 95% CI 0.03 to 0.86). However, patients took longer to become pain free after the SH procedure [7 days (n = 30) vs 3 days (n = 28) compared to the RBL group. Among the patients treated with RBL, one patient developed a severe postoperative anal fissure. This did not resolve with medical treatment and required internal sphincterotomy. In the SH group 2 patients developed urinary retention, 1 patient faecal impaction and 1 patient anal stenosis which was managed conservatively [30].

A RCT (Peng 2003), including 55 patients with grade III and IV haemorrhoids, compared RBL (n=25) with the SH (n=30). Slightly more patients in the SH group had

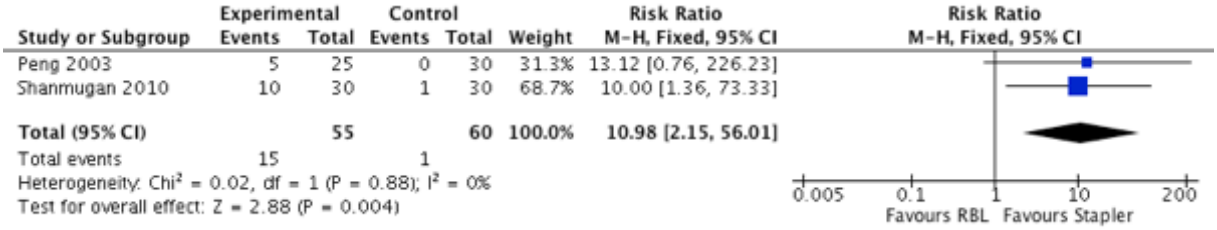
small grade IV piles when compared to the RBL group (7/30 SH vs. 3/25 RBL), but this failed to reach statistical significance. They showed that the SH was significantly associated with increased pain and analgesia. This difference had reduced to a non-significant level by two months' follow-up. RBL was associated with significant higher bleeding than the SH. There was no difference in the incidence of bleeding at two months. No significance was seen regarding the complication rate. Also, there was no difference between the two groups regarding continence scores, patient satisfaction and quality of life [31].

Meta-analysis of above mentioned studies

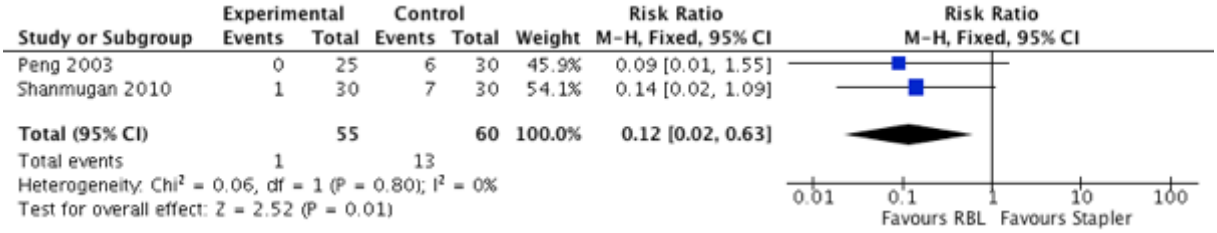
Outcome: recurrence



Outcome: re-intervention



Outcome: complications



6.5 Complications

6.5.1 Rubber Band Ligation (RBL)

It seems that complications are more common after RBL when compared with the other outpatient procedures (SCL and IRC). However, RBL is also more commonly performed than the other procedures. Minor complications include: moderate pain, minimal rectal bleeding, thrombosis and prolapse [32, 33]. RBL is also associated with a majority of reported septic complications [34, 35]. Other major complications are endocarditis [36] and liver abscess [37]. Further, the patient should be informed that severe bleeding may occur after 8-10 days after the banding. Immediate intense

pain after RBL could be caused by a too low placed band and requires removal of the band.

6.5.2 Infrared Coagulation (IRC)

Fewer complications are reported for IRC. Minor complications include pain, bleeding [32, 38]. Severe bleeding may occur after 8-10 days after IRC.

6.5.3 Sclerotherapy (SCL)

SCL is associated with major but rare complications including necrotizing fasciitis [39, 40] and abdominal compartment syndrome [40]. Further prostatic abscess, epididymitis, chronic cystitis, seminal vesicle abscess and urinary– perineal fistula have all been reported [41].

6.6 Relative effectiveness and ranking of the three options

The best symptom improvement for RBL, IRC and SCL was seen in patients with grade I and II haemorrhoidal disease.

RBL, which often necessitates repeated procedures, is effective in grade I-II HD. RBL can even be considered in selected cases of grade III haemorrhoids. Repeated RBL seems equally effective regarding recurrence rate compared to DG-HAL+ mucopexy. Additional, a subgroup analysis showed that in the RBL group recurrence was higher for grade III haemorrhoids compared with grade II haemorrhoids. However, this difference was not significant [29]. In comparison with SH, RBL showed a higher recurrence rate. Furthermore, RBL was associated with significant higher bleeding direct post-operatively (<2 months) than SH [30]. In comparison with haemorrhoidectomy, RBL showed a lower overall cure rate than the patients who underwent haemorrhoidectomy. Nevertheless, RBL procedure is associated with less post-operative pain and higher non-significant complication rates compared to haemorrhoidectomy [28].

IRC is considered to be effective in grade I-II haemorrhoids. A RCT showed that at four months, patients with grade I haemorrhoids appeared to fare better if treated by IRC than RBL. However, more patients with grade II haemorrhoids were classified as excellent after RBL. At 12 months, there was no significant difference in the symptomatic response to treatment between the two treatment groups [24]. One RCT showed that IRC treats bleeding and prolapse better compared to RBL. This difference was not significant [20]. In addition, one RCT showed that IRC was performed significantly faster than RBL [23].

SCL which often necessitates repeated procedures, is considered to be effective in grade I-II haemorrhoids. Three RCTs showed that significantly more patients who underwent SCL required additional sessions compared to the RBL [25-27]. One RCT showed that all grades of haemorrhoids tended to have a better response to

treatment with RBL compared to SCL, although only in those patients with grade II haemorrhoids this difference was significant [26].

6.7 Conclusions

For grade I and II haemorrhoids, RBL appears to be the treatment of choice, because patients who undergo RBL showed a significantly better response to therapy than did those treated with SCL and a significantly decreased need for further therapy than patients having either SCL or IRC. IRC may be the first option in bleeding grade I haemorrhoids because it causes less pain and complications [24]. Complication rates were similar between these three outpatient procedures [42-44].

It seems justifiable to use repeat RBL for grade III prolapsing haemorrhoids, recognizing that surgical procedures will be necessary for patients whose symptoms are not relieved with RBL and with circular prolapse.

6.8 GRADE

Comparison: Rubber Band Ligation compared to Infrared Coagulation in patients with symptomatic haemorrhoids

Included studies: Ricci 2008, Marques 2006, Poen 2000, Templeton 1983 and Ambrose 1983.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**rubber band ligation**	**infrared coagulation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Remaining symptoms (pain)												
4	randomised trials	not serious [a]	serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	33/259 (12.7%)	20/273 (7.3%)	**RR 1.70** (1.04 to 2.77)	**51 more per 1,000** (from 3 more to 130 more)	⨁◯◯◯ VERY LOW	CRITICAL
Re-intervention												
4	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected [d]	29/257 (11.3%)	48/272 (17.6%)	**RR 0.61** (0.40 to 0.91)	**69 fewer per 1,000** (from 16 fewer to 106 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT
Complications												
4	randomised trials	not serious [a]	not serious	not serious	not serious	publication bias strongly suspected [d]	118/191 (61.8%)	87/195 (44.6%)	**RR 1.40** (1.19 to 1.65)	**178 more per 1,000** (from 85 more to 290 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Recurrence												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rubber band ligation	infrared coagulation	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	not serious [a]	serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	21/247 (8.5%)	26/263 (9.9%)	**RR 0.86** (0.50 to 1.47)	**14 fewer per 1,000** (from 46 more to 49 fewer)	⨁◯◯◯ VERY LOW	IMPORTANT
Remaining symptoms (bleeding)												
4	randomised trials	not serious	serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	27/259 (10.4%)	12/273 (4.4%)	**RR 2.35** (1.25 to 4.40)	**59 more per 1,000** (from 11 more to 149 more)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations
a. Quality not considered.
b. Serious inconsistency, perhaps due to different formulations.
c. Wide 95% CI.
d. Publication bias is suggested based on the small number and size of the studies.

Comparison: Rubber Band Ligation compared to Sclerotherapy in patients with symptomatic haemorrhoids.

Included study: Kanellos 2003, Gartell 1985, Greca 1981.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rubber band ligation	sclerotherapy	Relative (95% CI)	Absolute (95% CI)		
Postoperative bleeding												
3	randomised trials	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [c]	7/225 (3.1%)	6/232 (2.6%)	not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Postoperative pain												
2	randomised trials	serious [a]	not serious	not serious	very serious [b]	publication bias strongly suspected [c]	8/120 (6.7%)	1/123 (0.8%)	not estimable		⨁◯◯◯ VERY LOW	CRITICAL
Re-intervention												
3	randomised trials	serious [a]	serious [d]	not serious	not serious	publication bias strongly suspected [c]	54/226 (23.9%)	59/224 (26.3%)	not estimable		⨁◯◯◯ VERY LOW	IMPORTANT
Complications												
3	randomised trials	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [c]	75/225 (33.3%)	30/232 (12.9%)	not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

Explanations
a. Moderate study quality with very little detail provided concerning the key validity methodologies.

b. Wide 95% CI.
c. Publication bias is suggested based on the small number and size of the studies.
d. Serious inconsistency due to different formulations.

Comparison: Rubber Band Ligation compared to Doppler-Guided Haemorrhoidal Artery Ligation in patients with symptomatic haemorrhoids

Included study: Brown 2016.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**rubber band ligation**	**Doppler-guided haemorrhoidal artery ligation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Pain (requiring hospital admission) (follow up: 21 days)												
1	randomised trials	not serious	not serious	not serious	not serious	none	1/178 (0.6%)	5/162 (3.1%)	not estimable		⨁⨁⨁⨁ HIGH	CRITICAL
Persistent symptoms												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	44/150 (29.3%)	13/143 (9.1%)	**OR 4.35** (2.19 to 8.65)	**212 more per 1,000** (from 89 more to 373 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Recurrence												
1	randomised trials	not serious	not serious	not serious	serious [a]	none	87/176 (49.4%)	48/161 (29.8%)	**OR 2.23** (1.42 to 3.51)	**188 more per 1,000** (from 78 more to 300 more)	⨁⨁⨁◯ MODERATE	IMPORTANT
Re-intervention												
1	randomised trials	not serious	not serious	not serious	not serious	none	57/176 (32.4%)	23/161 (14.3%)	not estimable		⨁⨁⨁⨁ HIGH	IMPORTANT
Complications												
1	randomised trials	not serious	not serious	not serious	not serious	none	2/178 (1.1%)	12/162 (7.4%)	not estimable		⨁⨁⨁⨁ HIGH	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations
a. Wide 95% CI.

Comparison: Rubber Band Ligation compared to Stapled Haemorrhoidopexy in patients with symptomatic haemorrhoids

Included studies: Shanmugam 2010, Peng 2003.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rubber band ligation	stapled haemorrhoidopexy	Relative (95% CI)	Absolute (95% CI)		
Recurrence												
2	randomised trials	not serious [a]	very serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	14/50 (28.0%)	8/60 (13.3%)	**RR 2.24** (0.95 to 5.28)	**165 more per 1,000** (from 7 fewer to 571 more)	⨁◯◯◯ VERY LOW	IMPORTANT
Re-intervention												
2	randomised trials	not serious	very serious [b]	not serious	serious [c]	publication bias strongly suspected [d]	15/55 (27.3%)	1/60 (1.7%)	**RR 10.98** (2.15 to 56.01)	**166 more per 1,000** (from 19 more to 917 more)	⨁◯◯◯ VERY LOW	NOT IMPORTANT
Complications												
2	randomised trials	not serious	not serious	not serious	not serious	publication bias strongly suspected [d]	1/55 (1.8%)	13/60 (21.7%)	**RR 0.12** (0.02 to 0.63)	**191 fewer per 1,000** (from 80 fewer to 212 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations
a. Quality not assessed for these two studies.
b. Very serious inconsistency. High statistical heterogeneity, perhaps due to different formulations.
c. Wide 95% CI.
d. Small number and size of the studies.

Comparison: Rubber Band Ligation compared to Haemorrhoidectomy in patients with symptomatic haemorrhoids

Included studies: Murie 1980, Cheng 1981 and Lewis 1983.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rubber band ligation	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Remaining symptoms: bleeding												
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	62/80 (77.5%)	61/80 (76.3%)	**RR 1.12** (0.97 to 1.29)	**92 more per 1,000** (from 23 fewer to 221 more)	⨁⨁◯◯ LOW	CRITICAL
Remaining: prolapse												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	rubber band ligation	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected	53/60 (88.3%)	56/60 (93.3%)	**RR 1.05** (0.98 to 1.12)	**47 more per 1,000** (from 19 fewer to 112 more)	⨁⨁◯◯ LOW	CRITICAL
Overall cure rate												
3	randomised trials	serious [a]	serious [c]	not serious	serious [d]	publication bias strongly suspected	59/101 (58.4%)	95/101 (94.1%)	**RR 1.68** (1.00 to 2.83)	**640 more per 1,000** (from 0 fewer to 1,000 more)	⨁◯◯◯ VERY LOW	CRITICAL
Re-intervention												
3	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected	42/101 (41.6%)	6/101 (5.9%)	**RR 0.20** (0.09 to 0.40)	**48 fewer per 1,000** (from 36 fewer to 54 fewer)	⨁⨁◯◯ LOW	NOT IMPORTANT
Complications												
3	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected	5/110 (4.5%)	18/106 (17.0%)	**RR 3.70** (0.62 to 22.08)	**458 more per 1,000** (from 65 fewer to 1,000 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations

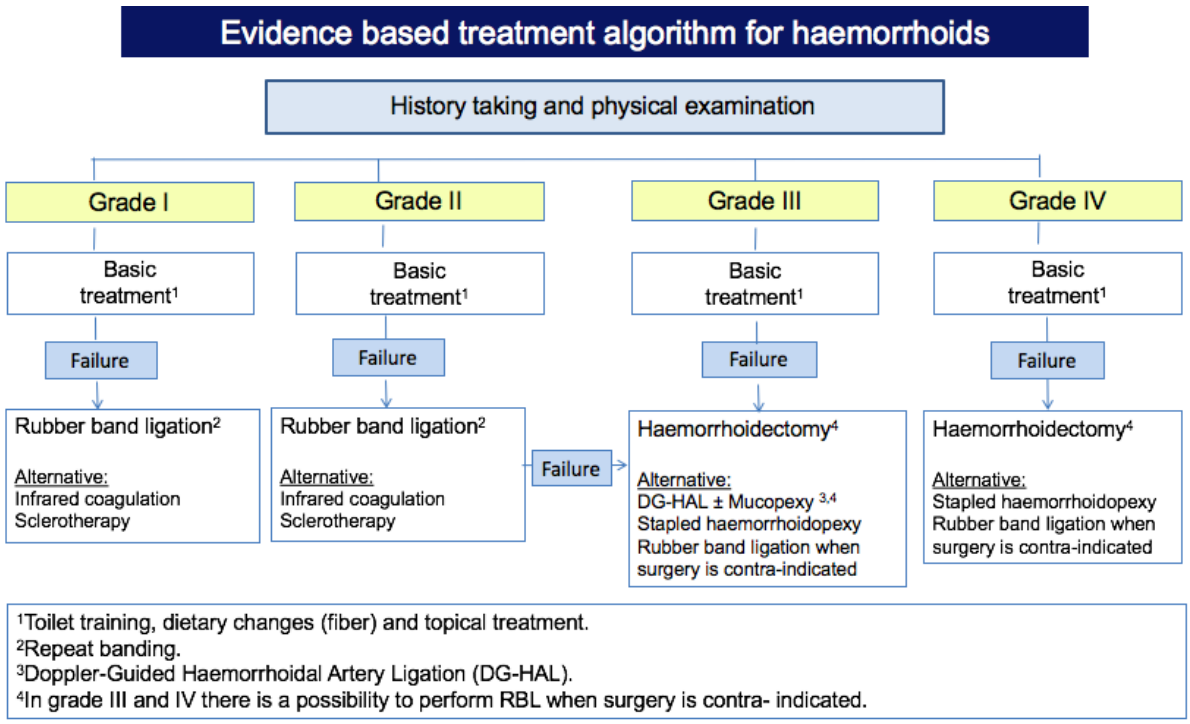
a. Moderate study quality with very little detail provided concerning the key validity methodologies. Investigators of the included studies were contacted if data were incomplete or missing.
b. publication bias is suggested based on the small number and size of the trials.
c. Serious inconsistency. High statistical heterogeneity. Perhaps due to different formulations.
d. Wide 95% CI.

6.9 Recommendations for outpatient procedures

- Choice of the outpatient procedure (i.e. rubber band ligation, injection sclerotherapy and infrared coagulation) should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for further procedures [*expert opinion, upgraded by guideline development group*].
- Rubber band ligation should be performed in grade I-III haemorrhoidal disease. Repeat banding may be necessary [*moderate level of evidence*].
- Infrared coagulation could be used as the first option in bleeding grade I haemorrhoids [*low level of evidence*].
- Injection sclerotherapy could be used in patients with grade I-II haemorrhoidal disease [*low level of evidence*].

7 Surgical interventions

In patients where basic treatment and/or outpatient procedures have not resulted in acceptable outcomes or in grade III and IV haemorrhoidal disease, surgical procedures could be considered. These include mucopexy with or without Doppler-Guided Haemorrhoidal Artery ligation (DG-HAL), Stapled Haemorrhoidopexy (SH) and Haemorrhoidectomy.



7.1 Review questions

We considered the following questions for our evidence reviews:

- What are the effects of DG-HAL + mucopexy versus mucopexy alone on symptoms, recurrence and complications in patients with haemorrhoidal disease?
- What are the effects of DG-HAL + mucopexy versus Stapled Haemorrhoidopexy on symptoms, recurrence and complications in patients with haemorrhoidal disease?
- What are the effects of DG-HAL + mucopexy versus Haemorrhoidectomy on symptoms, recurrence and complications in patients with haemorrhoidal disease?
- What are the effects of Stapled Haemorrhoidopexy versus Haemorrhoidectomy on symptoms, recurrence and complications in patients with haemorrhoidal disease?

7.2 Techniques

7.2.1 Doppler Guided Haemorrhoidal Artery Ligation (DG-HAL) plus mucopexy

During a DG-HAL procedure the internal haemorrhoidal plexus will be de-arterialized by ligation of the terminal branches of the superior rectal artery using an ultrasound system. DG-HAL is often combined with modifications of suture ligations which serve to lift and then secure the protruding haemorrhoid cushions in place. Many descriptive terms are used, such as ‘recto anal repair’ (RAR)’ [45-47], ‘transanal haemorrhoid mucopexy’ [48] and ‘anal lifting’ [49]. In this guideline, we use the term ‘mucopexy’.

7.2.2 Stapled Haemorrhoidopexy (SH)

Stapled haemorrhoidopexy (SH) is also known as circumferential mucosectomy or ‘procedure for prolapse and haemorrhoids’ (PPH). With SH a transanal circular stapler is used to excise a complete circular strip of rectal mucosa approximately four cm proximal to the dentate line removing the redundant mucosa (including a part of the muscular layer of the lower rectum) and stapling off the end of the branches of the superior haemorrhoidal artery. In this way, the prolapsed haemorrhoidal tissue is lifted proximal to the dentate line.

7.2.3 Haemorrhoidectomy

Haemorrhoidectomy involves excision of the haemorrhoidal tissue. There are technical variants depending on the treatment of the bridges and/or the addition of a posterior mucosal anoplasty. In Europe, the open (Milligan-Morgan) method is most commonly in use. In an open Haemorrhoidectomy (Milligan-Morgan), a Y-shaped incision is made at the mucocutaneous junction and the vascular pedicle is ligated. Afterwards the wound is not closed. The Closed Haemorrhoidectomy (Ferguson) consists of excision of three vascular pedicles with complete wound closure using absorbable sutures. This technique is often used in the United States.

7.3 Evidence in literature

7.3.1 DG-HAL+ mucopexy versus mucopexy alone

The analysis of literature reveals two RCTs that meets the search criteria [50, 51].

DG-HAL + mucopexy versus mucopexy alone

A recent RCT (Aigner 2016) included 40 patients with grade III haemorrhoids. Twenty patients underwent DG-HAL with mucopexy and the other 20 patients underwent mucopexy alone. At 12-month follow-up, two (10%) patients in the DG-HAL+mucopexy group and one (5%) in the mucopexy alone group showed recurrent and symptomatic grade III haemorrhoids. One month after the operation zero patients in the DG-HAL+mucopexy group had mucous discharge versus twenty percent of the patients who underwent a mucopexy alone. This was a significant difference between the two groups [50].

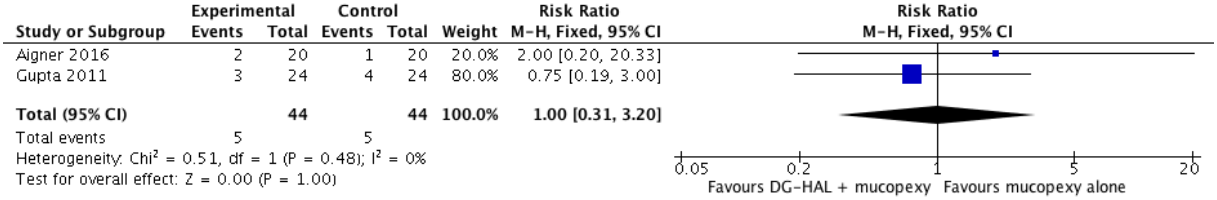
DG-HAL versus mucopexy alone

A RCT (Gupta 2011), including 48 patients with grade III haemorrhoids, compared DG-HAL (n=24) versus mucopexy alone (n=24). They showed that the operative time in the DG-HAL group was significantly longer (31 vs 9 min). The postoperative pain

score was significantly higher in the DG-HAL group (4.4 vs 2.2 VAS). At 1-year follow-up, the recurrence of haemorrhoids was similar in both groups (3 in the DG-HAL group vs 4 in the mucopexy group). Complications were similar in both groups. This study showed the lack of superiority to use the Doppler probe [51].

Meta-analysis of above mentioned studies

Outcome: recurrence



7.3.2 DG-HAL + mucopexy versus SH

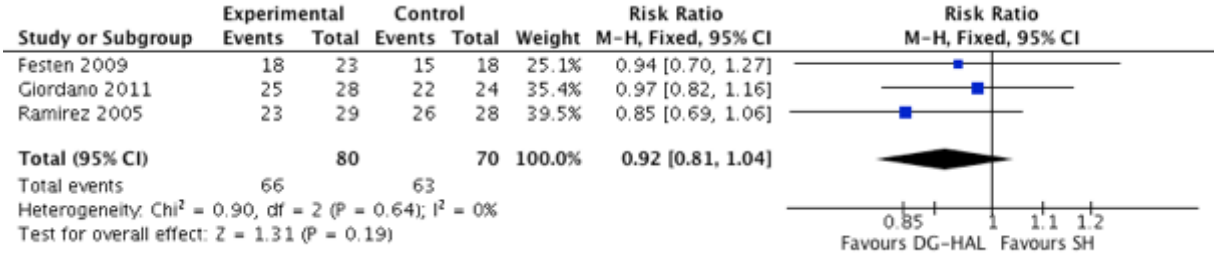
Two systematic reviews and one RCT were found in literature [52-54].

The first systematic review (Pucher 2013), including 28 trials involving 2904 patients (6 trials were RCTs) with grade II-IV HD, compared the DG-HAL+mucopexy versus SH. No significant difference in recurrence rates or postoperative complications was found in all trials. Giordano et al. described a significant reduction in the time taken to return to normal activity by almost half for DG-HAL vs SH (3.2 vs 6.3 days) in patients with grade II/III haemorrhoids [55]. Infantino et al. found no difference between DG-HAL + mucopexy and SH for pain, postoperative complications and recurrence rates at median follow-up of 17 months in patients with grade III HD. However, they did report significantly higher rates of late postoperative complications such as pain persisting over 30 days and abscess formation after SH [56]. They also considered a shorter length of stay and lower equipment costs for DG-HAL + mucopexy group. These results were for the combined grade II, III and IV patients, but unfortunately results for grade II, III and IV patients separately were not reported [52].

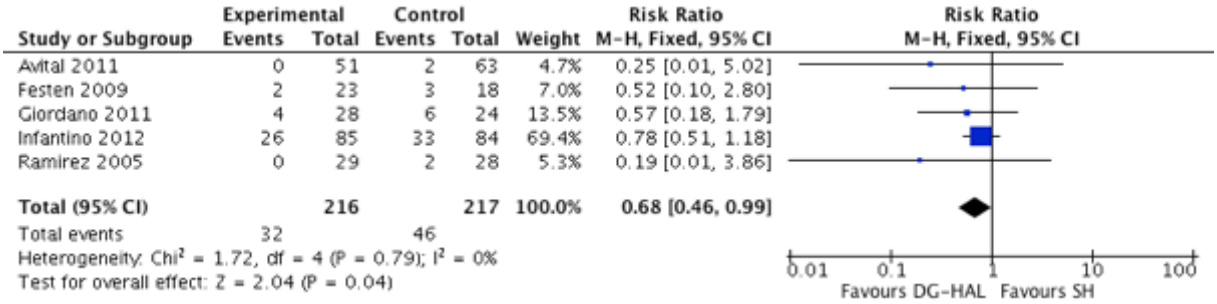
Another systematic review (Sajid 2012), including three randomised trials (two of these were also reported in the review mentioned above) and 150 patients with grade II-IV, showed that the treatment success rate following DG-HAL+mucopexy (n=80) compared to SH (=70) was not statistically significant (RR, 0.92; 95% CI, 0.81 to 1.04). All three trials showed no significant difference regarding recurrence rate between DG-HAL and SH (RR, 1.33; 95% CI, 0.62 to 2.84). Further, DG-HAL was associated with significantly less postoperative pain (MD, -2.00; 95% CI, -2.06 to -1.49,) compared with SH. Three trials showed a non-significant reduction of 52% in postoperative complications for DG-HAL compared with SH (RR, 0.48; 95% CI, 0.20 to 1.18). Again these results were combined for grade II, III and IV patients, but unfortunately the results for grade II, III and IV patients separately were not reported [53].

Meta-analysis of above mentioned studies

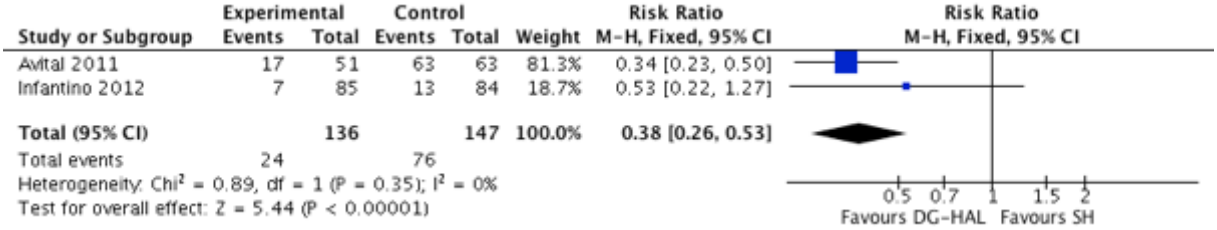
Outcome: treatment success



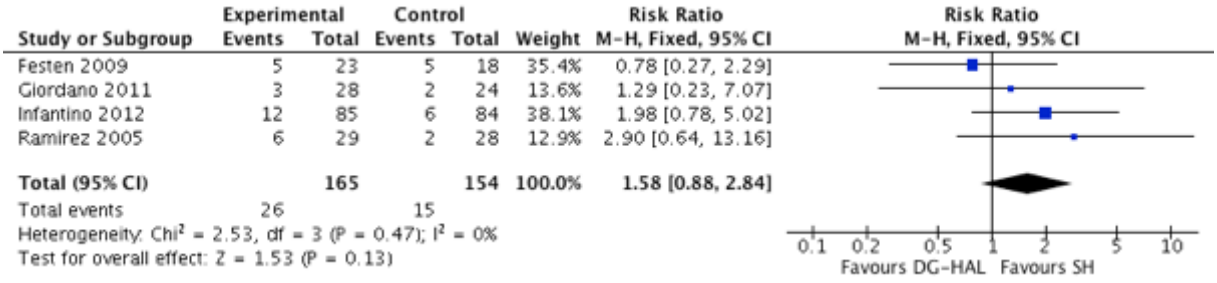
Outcome: complications



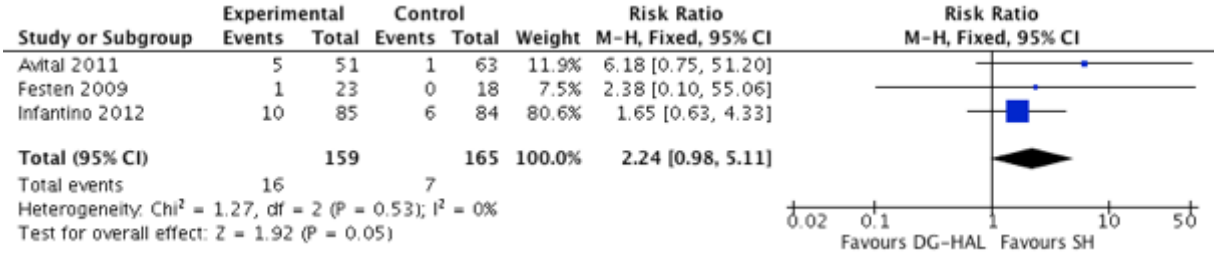
Outcome: postoperative pain



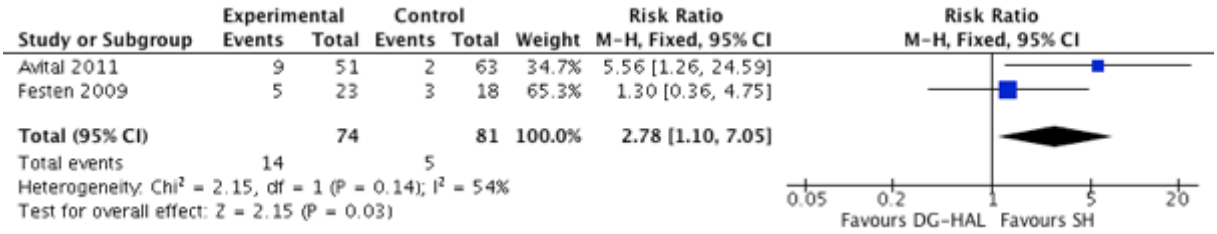
Outcome: recurrence



Outcome: re-intervention



Outcome: remaining symptoms



7.3.3 DG-HAL + mucopexy versus Haemorrhoidectomy

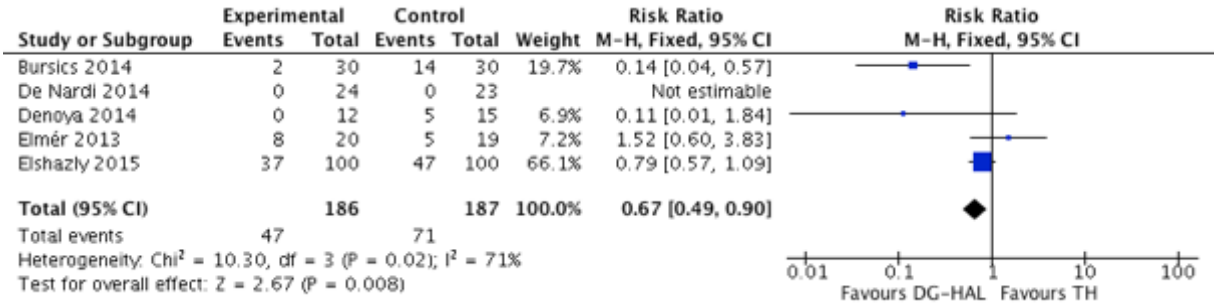
One meta-analysis and one RCT were identified. Among these studies, one older trial did not include mucopexy [57] and another did not involve the use of Doppler in the search for rectal arteries [58]. One study has a haemorrhoidectomy of only two pedicles in almost half of cases [59]. One study is a historical comparison of two cohorts [60]. Finally, one study shows the same patients who entered a previous study [61, 62]. Certain biases are noteworthy in these studies, which may limit their value or interpretation.

The meta-analysis (Xu 2016), including four RCTs and 316 patients with grade II-IV haemorrhoids, showed there was no significant difference in the recurrence rate between both groups (OR 2.17, 95% CI 0.72 to 6.56). These data were based on very small numbers of events (10 recurrences in the DG-HAL + mucopexy group and 5 in the Haemorrhoidectomy group). In addition, three trials showed that there was no significant difference between DG-HAL+mucopexy and Haemorrhoidectomy regarding postoperative pain 7 days after surgery. There was a lower total complication rate in the DG-HAL+mucopexy group compared to the Haemorrhoidectomy group (OR 0.69, 95% CI 0.42 to 1.13). This difference was not statistically significant. Further, there was no significant difference regarding bleeding rate (OR 0.41, 95% CI 0.16 to 1.05, favours DG-HAL) and recurrent prolapse rate (OR 3.15, 95% CI 0.91 to 10.82, favours Haemorrhoidectomy) between the two groups. These results were for the combined grade II, III and IV patients, but unfortunately results for grade II, III and IV patients separately were not reported [63].

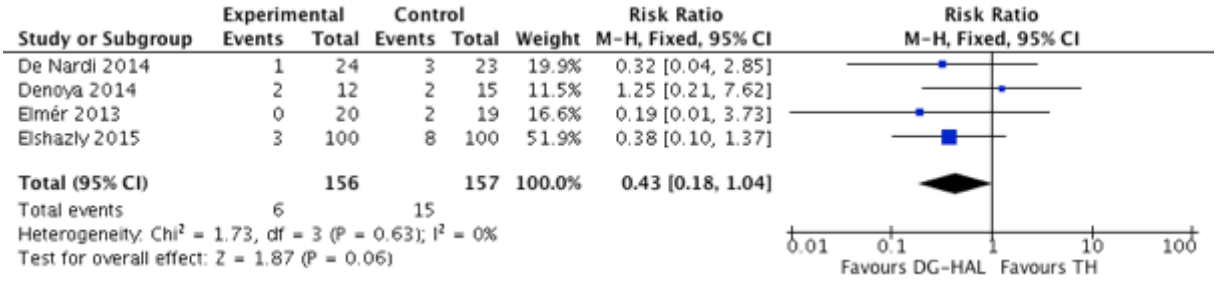
A RCT (Bursics 2004), including 60 patients with grade I-IV haemorrhoids, which was not included in the meta-analysis mentioned above, found similar results. Return to normal daily activities was 24.5±24.9 days in the Haemorrhoidectomy group and 3.0±5.5 days in the DG-HAL+mucopexy group. Neither the disappearance (25 vs. 26 patients) nor the recurrence of preoperative symptoms (6 vs. 5 patients) differed significantly between the two groups. Again these results were for the combined grade I, II, III and IV patients, but unfortunately results for grade I, II, III and IV patients separately were not reported [57].

Meta-analysis of above mentioned studies

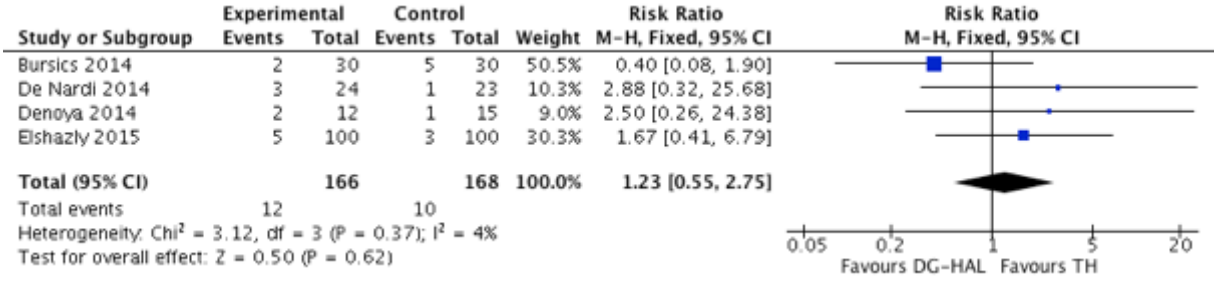
Outcome: complications



Outcome: postoperative bleeding



Outcome: recurrence



7.3.4 SH versus Haemorrhoidectomy

Three meta-analyses, four systematic reviews and one RCT were found [64-71].

The systematic review of Nisar et al. (2004) included fifteen trials with in total 1077 patients with grade III and IV haemorrhoids. They showed that SH is less painful, has a significant shorter inpatient stay (WMD=1.02 days; 95% CI, –1.47 to –0.57), operative time (WMD, –12.82 minutes; 95% CI, –22.61 to –3.04), and return to normal activity (SMD, – 4.03 days; 95% CI, –6.95 to –1.10) compared to haemorrhoidectomy. Nevertheless, SH is associated with a significant higher recurrence rate (OR= 3.64; 95 % CI, 1.40–9.47) at a minimum follow- up of six months [64].

In the systematic review of Jayaraman et al. (2006) twelve RCTs were included. They also showed that haemorrhoidectomy had a significantly lower recurrence rate (7 RCTs, 537 patients, OR= 3.85, 95% CI 1.47 to 10.07). Further, haemorrhoidectomy was superior in preventing prolapse (OR=2.96, 95% CI 1.33 to 6.58) [66].

In the systematic review by Tjandra et al. (2007) a total of 25 RCTs were reviewed. Again, SH was associated with significant less operating time (WMD= -11.35 minutes), earlier return of bowel function (WMD= -9.91 hours), and shorter hospital stay (WMD= -1.07 days). In addition, there was an increase in the recurrence of haemorrhoids at one year or more after SH (5.7 vs. 1%; OR= 3.48). The overall incidence of recurrence was similar between both groups [67].

The systematic review by Burch et al. (2009) included 27 RCTs (n = 2279 with grade II-IV haemorrhoids). In the early postoperative period 95% of trials reported less pain following SH; by day 21 the pain reported following both techniques were minimal, with little difference between the two techniques. Again, SH resulted in shorter operating times, hospital stay, time to first bowel movement and return to normal activity compared to the haemorrhoidectomy group. In the short term (between 6 weeks and a year) prolapse was more common after SH (OR 4.68, 95% CI 1.11 to 19.71, six RCTs) [68].

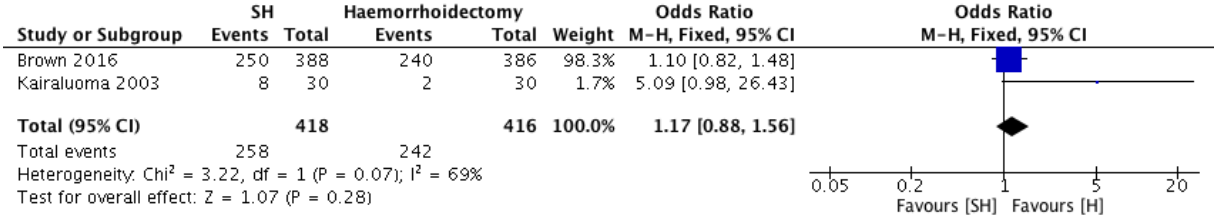
A meta-analysis of Yang et al. (2013) includes 5 trials with 397 patients with grade III and IV haemorrhoids. Pooled analysis of four trials on reporting operating time showed that the operating time was significantly longer in the SH group compared to the haemorrhoidectomy group (WMD = -6.39, 95%CI: -7.68 to -5.10). Data showed that the incidence of recurrence was significantly lower in the haemorrhoidectomy group than in the SH group [2/173 (1.2%) vs 13/174 (7.5%); OR = 0.21, 95%CI: 0.07 to 0.59] [70].

Another recent meta-analysis (Lee 2013) included the same studies as in the meta-analysis mentioned above. They showed a statistically higher rate of recurrence associated with the SH (OR 5.529, 95% CI 1.383 to 22.189) [71].

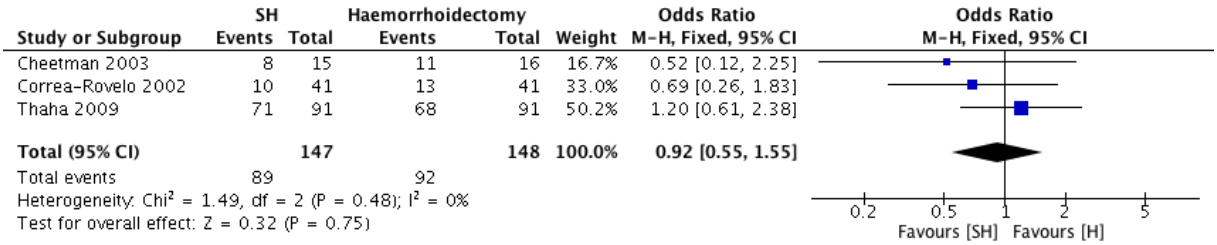
A recent RCT included 777 patients with grade II-IV haemorrhoids (389 underwent a SH and 388 a haemorrhoidectomy). They found a higher EQ-5D-3L area under the curve (AUC) over 24 months in the haemorrhoidectomy group (MD −0.073 (95% CI −0.140 to −0.006). The AUC at 12 months' follow-up showed no difference between the two interventions. In the SH group, 94 of 295 participants (32%) reported that their symptoms had returned compared with 39 of 278 in the haemorrhoidectomy group (14%) (OR 2.96; 95% CI 2.02 to 4.32). This difference was maintained till 24 months. Analgesia use at three weeks was lower in the SH group than in the haemorroidectomy group (OR 0.58, 95% CI 0.45 to 0.75), but no difference was reported at 1 and 6 weeks. [72].

<u>Meta-analysis of above mentioned studies (last 15 years)</u>

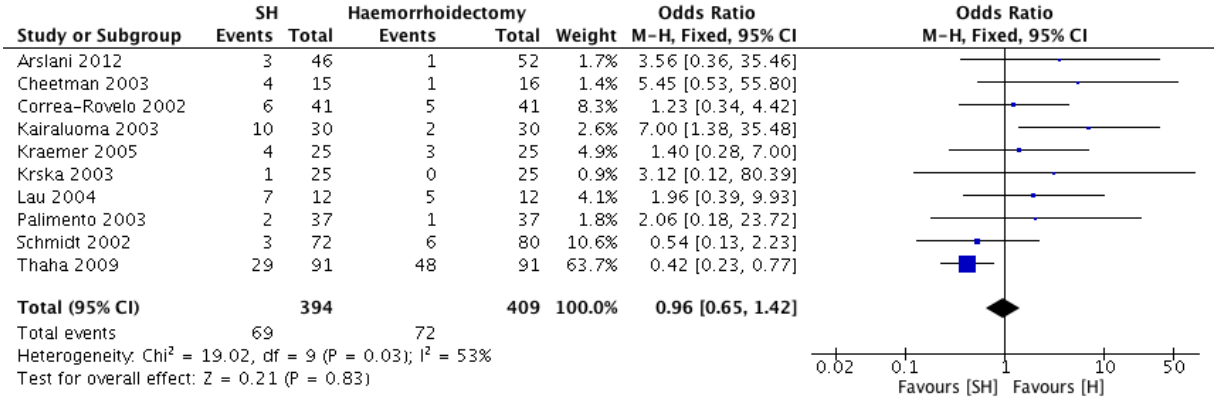
Outcome: symptom score (1 year)



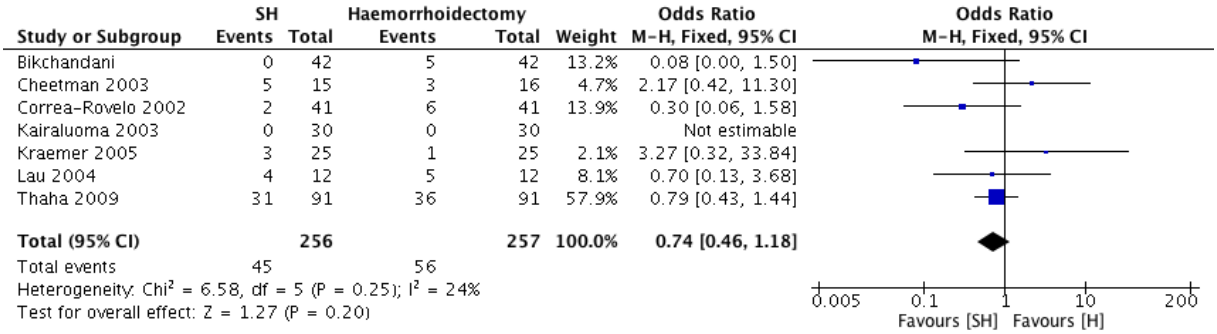
Outcome: symptoms (2 months)



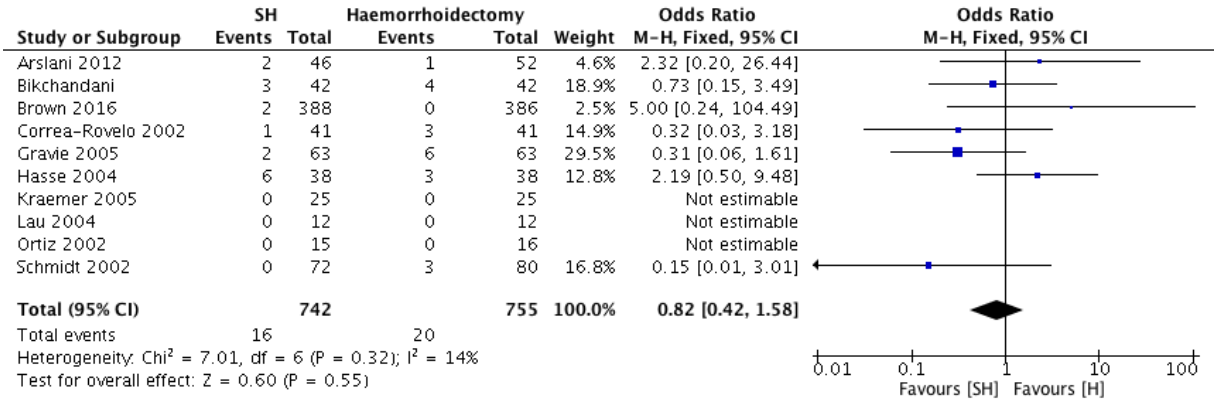
Outcome: postoperative blood loss (2 months)



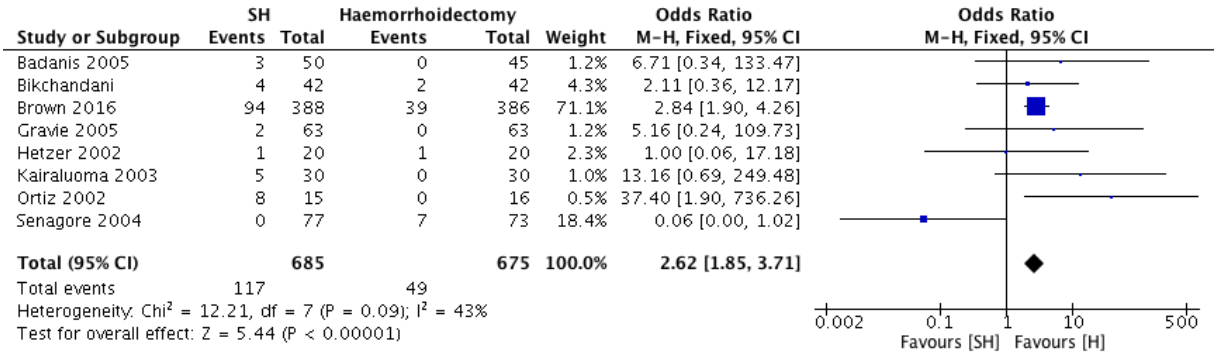
Outcome: postoperative pain (<2 months)



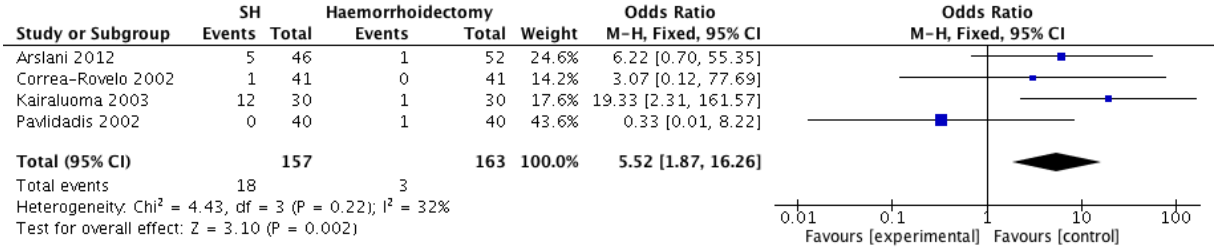
Outcome: fecal incontinence (1 year)



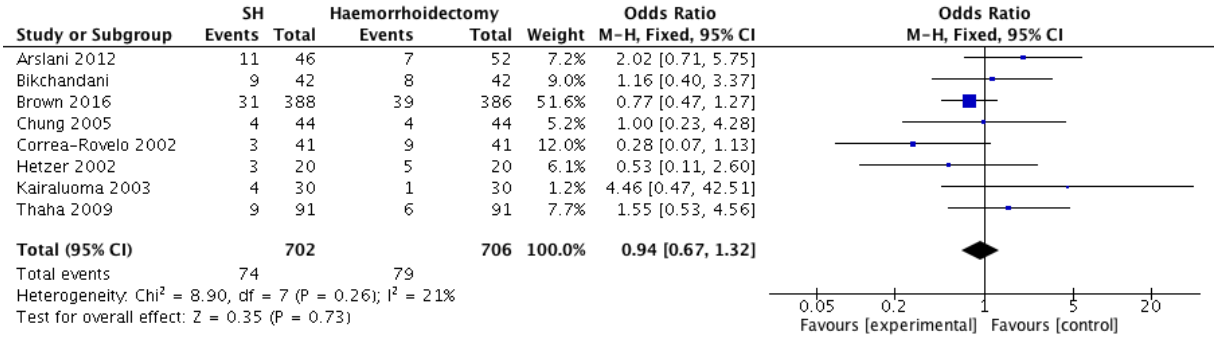
Outcome: recurrence (1 year)



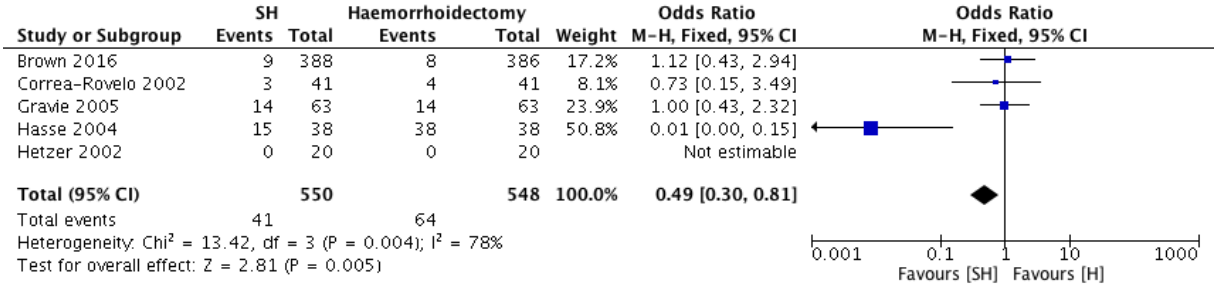
Outcome: recurrence (2 months)



Outcome: early complications



Outcome: late complications



7.4 Complications

7.4.1 DG-HAL

The most reported complications after DG-HAL are bleeding and pain. Less reported complications are thrombosis and anal fissure formation [52]. There were no reported cases of anal stenosis, faecal incontinence, or chronic pain [73].

7.4.2 SH and Haemorrhoidectomy

Similar minor complications after the SH and haemorrhoidectomy are pain, bleeding [74], urinary retention and thrombosis [69, 75]. Major complications are sepsis [76-78], necrotising fasciitis [79-81], retro rectal haematoma [75], pelvic cellulitis [82-84] and rectal perforation with peritonitis [85, 86].

Currently there is a lot of debate in literature regarding the rare but severe of complications of patients who underwent SH [85].

A recent RCT, comparing the SH and the Haemorrhoidectomy in 777 patients, showed that 11 participants required catheterisation for urinary retention; seven had received Haemorrhoidectomy and four SH. Ten participants remained in hospital or were readmitted with pain in the Haemorrhoidectomy group compared with six in the SH group. A few participants had a combination of pain, constipation, and bleeding, but bleeding on its own was more common in the SH group than in the Haemorrhoidectomy group. Two participants in each group reported pain caused by an anal fissure. No episodes of pelvic sepsis or rectal perforation were recorded in this trial [87].

In a study of Naldini et al. 23 centres were asked by questionnaire to return reports of serious complications following SH and how they were treated. Forty-six reports were received. Twenty-seven serious complications were reported. All patients developed significant continuous anal pelvic pain. Several patients developed progressive haematoma (n=10), a complete dehiscence of the anterior staple line because of stapler malfunction (n=6) and even perianal sepsis (n=3) [88].

A network meta-analysis of the studies revealed that the Closed Haemorrhoidectomy group had significantly more complications than the Open, SH and DG-HAL groups. There were fewer episodes of postoperative bleeding after DG-HAL than after open, SH [89].

Patients should be informed about the possibility of (severe) complications.

7.5 Relative effectiveness and ranking of the three options

The DG-HAL + mucopexy, is considered to be effective in patients with grade II-III HD. Two RCTs assessed the efficacy of the Doppler transducer, the addition of a mucopexy and ligation under visual control followed by a mucopexy. One RCT showed that significantly more complications and unscheduled postoperative events were reported in the Doppler with mucopexy group than the mucopexy alone group [90]. Another RCT showed at 12 months' follow-up that the recurrence rate of haemorrhoids was similar in both groups (3 in the DG-HAL group vs 4 in the

Mucopexy group) [51]. Most studies showed that there was no significant difference regarding the recurrence rate or postoperative complications between the DG-HAL+ mucopexy and SH [52, 53]. Further, one study showed that DG-HAL plus Mucopexy was associated with significantly less postoperative pain compared to SH [53]. In comparison with the haemorrhoidectomy, studies showed that there was no significant difference in the recurrence rate between DG-HAL and the haemorrhoidectomy. Besides, DG-HAL was associated with a faster return to normal activity compared to the haemorrhoidectomy [57].

SH and Haemorrhoidectomy are considered to be effective in patients with grade II, III and IV haemorrhoids. Almost all meta-analysis and systematic reviews showed that SH is associated with a higher recurrence rate, but is a less painful procedure, has a significant shorter operative time and inpatient stay, and faster return to normal activity compared to the haemorrhoidectomy. Only Yang et al. showed that SH was associated with a longer operative time than the haemorrhoidectomy [70]. Nevertheless, a recent conducted RCT which included 777 patients, demonstrated that SH was associated with less pain, equal inpatient stay and operative time and a significant higher recurrence rate than the haemorrhoidectomy. In an additional subgroup analysis (unpublished results), patients with grade II, III and IV prolapse were isolated. In all grades the efficacy of SH remains generally lower than that of haemorrhoidectomy. In patients with grade IV the recurrence rate after SH is so high compared with the haemorrhoidectomy that this intervention is not recommended in these cases [72].

7.6 Conclusions

The DG-HAL + mucopexy, is considered to be effective in patients with grade II-III HD. The Doppler is currently being questioned since studies showed that significantly more complications and unscheduled postoperative events were reported in the Doppler + mucopexy group than the mucopexy alone group [90]. Nevertheless, the DG-HAL + mucopexy is associated with a faster return to normal activity compared to the haemorrhoidectomy [57]. SH and Haemorrhoidectomy are considered to be effective in patients with grade II- IV haemorrhoids. Comparing SH and Haemorrhoidectomy, the efficacy of SH remains generally lower than that of the haemorrhoidectomy [72], especially in grade IV haemorrhoidal disease [72].

7.7 GRADE

Comparison: Doppler-guided haemorrhoidal artery ligation + mucopexy compared to mucopexy alone in patients with symptomatic haemorrhoids

Included studies: Aigner 2016 and Gupta 2011.

Certainty assessment	№ of patients	Effect	Certainty	Importance

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Doppler-guided haemorrhoidal artery ligation + mucopexy	mucopexy alone	Relative (95% CI)	Absolute (95% CI)		
Recurrence (follow up: 1 years)												
2	randomised trials	serious [a]	not serious	not serious	serious [b]	publication bias strongly suspected [c]	4/42 (9.5%)	5/43 (11.6%)	not estimable		⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval

Explanations
a. The limitations of this study are that both the surgical procedures were performed by a single surgeon and that it shows results of medium-term follow-up.
b. Wide 95% CI.
c. Publication bias suggested based on the small numbers and size of the studies.

Comparison: DG-HAL + mucopexy compared to Stapled Haemorrhoidopexy in patients with symptomatic haemorrhoids

Included studies: Festen 2009, Giordano 2011 and Ramirez 2005, Avital 2011 and Infantino 2012.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DG-HAL + mucopexy	Stapled haemorrhoidopexy	Relative (95% CI)	Absolute (95% CI)		
Pain (postoperative)												
3	randomised trials	serious [a]	not serious [b]	not serious	not serious	publication bias strongly suspected [c]			**MD -2.00** (-2.06 to -1.94)	**-- per 1.000** (from -- to --)	⨁⨁◯◯ LOW	CRITICAL
Recurrence (follow up: mean 2 years)												
4	randomised trials	serious [a]	not serious	not serious	not serious [d]	publication bias strongly suspected	14/80 (17.5%)	9/70 (12.9%)	**RR 1.33** (0.62 to 2.84)	**42 more per 1.000** (from 49 fewer to 237 more)	⨁⨁◯◯ LOW	IMPORTANT
Complications (follow up: mean 2 years)												
5	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected	6/80 (7.5%)	11/70 (15.7%)	**RR 0.48** (0.20 to 1.18)	**82 fewer per 1.000** (from 28 more to 126 fewer)	⨁⨁◯◯ LOW	CRITICAL
Treatment success (follow up: mean 2 years)												
3	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected	66/80 (82.5%)	63/70 (90.0%)	**RR 0.92** (0.81 to 1.04)	**72 fewer per 1.000** (from 36 more to 171 fewer)	⨁⨁◯◯ LOW	CRITICAL

Comparison: DG-HAL + mucopexy compared to the Haemorrhoidectomy in patients with symptomatic haemorrhoids

Included studies: Xu 2016, Bursics 2014, De Nardi 2014, Denoya 2014, Elmér 2013 and Elshazly 2015.

Certainty assessment	№ of patients	Effect	Certaint	Importanc

№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DG-HAL + mucopexy	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)	y	e
Complications												
5	randomised trials	serious [a]	not serious [b]	not serious	not serious	publication bias strongly suspected [c]	47/186 (25.3%)	71/187 (38.0%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Bleeding												
4	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	6/156 (3.8%)	15/157 (9.6%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Recurrence												
4	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	12/166 (7.2%)	10/168 (6.0%)	not estimable		⊕⊕◯◯ LOW	IMPORTANT

CI: Confidence interval

Explanations
a. There was a wide variation in the included studies regarding determining outcome measures.
b. There was no significant heterogeneity.
c. Only five RCTs were included with a low number of patients which implies that the quantitative analysis was not very powerful.

Comparison: SH compared to the Haemorrhoidectomy in patients with symptomatic haemorrhoids

Included studies: Basdanis 2005, Bikchandani 2005, Cheetman 2003, Chung 2005, Correa-Rovelo, Gravie 2005, Hasse 2004, Hetzer 2002, Kairaluoma 2003, Kraemer 2005, Krska 2003, Lau 2004, Ortiz 2002, Palimento 2003, Pavlidadis 2002, Schmidt 2002, Senagore 2004, Thaha 2004, Au-Yong 2004, Picchio 2006, Racalbuto 2004, Arslani 2012, and Brown 2016

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapled haemorrhoidopexy	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Symptom score (follow up: 1 years)												
2	randomised trials	not serious	serious [a]	not serious	not serious	publication bias strongly suspected [b]	258/418 (61.7%)	242/416 (58.2%)	**OR 1.17** (0.88 to 1.56)	**38 more per 1.000** (from 31 fewer to 103 more)	⊕⊕◯◯ LOW	CRITICAL
Symptoms (follow up: 2 months)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapled haemorrhoidopexy	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	not serious [c]	not serious	not serious	not serious	publication bias strongly suspected [d]	89/147 (60.5%)	92/148 (62.2%)	**OR 0.92** (0.55 to 1.55)	**20 fewer per 1.000** (from 96 more to 147 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Blood loss (follow up: 2 months)												
10	randomised trials	serious [e]	serious [f]	not serious	not serious	publication bias strongly suspected [d]	69/394 (17.5%)	72/409 (17.6%)	**OR 0.96** (0.65 to 1.42)	**6 fewer per 1.000** (from 54 fewer to 57 more)	⨁◯◯◯ VERY LOW	CRITICAL
Pain (follow up: 2 months)												
7	randomised trials	serious [g]	not serious	not serious	not serious	publication bias strongly suspected [d]	45/256 (17.6%)	56/257 (21.8%)	**OR 0.74** (0.46 to 1.18)	**47 fewer per 1.000** (from 30 more to 104 fewer)	⨁⨁◯◯ LOW	CRITICAL
Incontinence (follow up: 1 years)												
10	randomised trials	serious [h]	not serious	not serious	not serious	none	16/742 (2.2%)	20/755 (2.6%)	**OR 0.82** (0.42 to 1.58)	**5 fewer per 1.000** (from 15 fewer to 15 more)	⨁⨁⨁◯ MODERATE	CRITICAL
Recurrence (follow up: 1 years)												
8	randomised trials	serious [h]	serious [i]	not serious	not serious	none	117/685 (17.1%)	49/675 (7.3%)	**OR 2.62** (1.85 to 3.71)	**98 more per 1.000** (from 54 more to 152 more)	⨁⨁◯◯ LOW	IMPORTANT
Recurrence (follow up: 2 months)												
4	randomised trials	not serious [j]	serious [k]	not serious	not serious	publication bias strongly suspected [d]	18/157 (11.5%)	3/163 (1.8%)	**OR 5.52** (1.87 to 16.26)	**75 more per 1.000** (from 15 more to 215 more)	⨁⨁◯◯ LOW	IMPORTANT

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapled haemorrhoidopexy	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Early complications												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapled haemorrhoidopexy	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
8	randomised trials	serious [a]	not serious	not serious	not serious	none	74/702 (10.5%)	79/706 (11.2%)	**OR 0.94** (0.67 to 1.32)	**6 fewer per 1.000** (from 31 more to 34 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
Late complications												
5	randomised trials	serious [a]	serious [b]	not serious	not serious	none	41/550 (7.5%)	64/548 (11.7%)	**OR 0.49** (0.30 to 0.81)	**56 fewer per 1.000** (from 20 fewer to 79 fewer)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. I2= 69%

b. In both studies no selective outcome reporting. However, publication bias is suspected in the study of Kairaluoma et al. due to a small number patients.

c. Patients were blinded. However, caregivers, those recording outcomes, those adjudicating outcomes and data analysts are aware of the arm to which patients are allocated.

d. Published evidence is limited to a small number of small trials.

e. Only two studies (Correa-Rovelo, Thaha) reported 'blinding' of patients. In two studies (Schmidt and Krska) patients were not randomized to a study arm.

f. I2=53%

g. The following studies reported blinding (of patients): Correa-rovelo, Thaha, Bikchandani. Lau reported no randomization process.

h. Several studies did not report blinding (of patients). Further, not all patients were randomized to one treatment arm.

i. I2= 43%

j. Two studies blinded the patients. And patients were randomized in all studies to one treatment option.

k. I2=32%

7.8 Recommendations of surgical treatment

- Choice of surgical treatment should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for surgical procedures (*expert opinion, upgraded by guideline development group*).
- Doppler - guided haemorrhoidal artery ligation +/- mucopexy could be used in patients with grade II-III haemorrhoids and/or in patients who are refractory to

outpatient procedures (*low level of evidence*). However, because the effectiveness of using a Doppler is currently questioned, mucopexy alone could be considered (*very low level of evidence, upgraded by the guideline development group*).

- Stapled haemorrhoidopexy could be used in patients with grade II-III haemorrhoids and/or in patients who are refractory to outpatient procedures (*low level of evidence*).
- Haemorrhoidectomy could be used in patients with grade II-III haemorrhoids and/or should be used in patients who are refractory to outpatient procedures (*moderate level of evidence*).
- Haemorrhoidectomy should be used for grade IV haemorrhoids (*moderate level of evidence*).

8 Special situations

8.1 Review questions

- How could we define and treat *thrombosed haemorrhoids* in a primary care setting?
    - What are the effects and side effects of basic treatment (i.e. analgesics, flavonoids, heparin and nifedipine) versus surgical treatment (i.e. stapler and traditional haemorrhoidectomy)?
- How should haemorrhoids be treated in patients with *immune deficiencies*?
    - What are the effects and side effects of an outpatient procedure (i.e. RBL) in patients with immune deficiencies compared to patients who underwent an outpatient procedure with no immune deficiencies?
- How should haemorrhoids be treated in patients with *inflammatory bowel disease (IBD)*?
    - What are the effects and side effects of an outpatient procedure (i.e. RBL) in patients with IBD compared to patients who underwent an outpatient procedure without IBD?
    - What are the effects and side effects of a surgical intervention (i.e. Haemorrhoidectomy) in patients with IBD compared to patients who underwent a surgical intervention without IBD?
- How should haemorrhoids be treated in patients who have undergone pelvic radiotherapy?
    - What are the effects and side effects of an outpatient procedure (i.e. RBL) in patients who have undergone pelvic radiotherapy compared to patients who did not have radiotherapy?
- How should we treat haemorrhoids in patients with *coagulation defects*?
    - What are the effects and side effects of an outpatient procedure (i.e. RBL and sclerotherapy) in patients with coagulation defects compared to patients who underwent an outpatient procedure without coagulation defect?
    - What are the effects and side effects of a surgical intervention (i.e. stapled haemorrhoidopexy or Haemorrhoidectomy) in patients with coagulation defects compared to patients who underwent a surgical intervention without coagulation defect?
- How should we treat *pregnant women* with haemorrhoids?
    - What are the effects and side effects of basic treatment (i.e. sith bath and flavonoids) versus surgical treatment?

8.2 Thrombosed haemorrhoids

In the anocutaneous junction there is a venous plexus (anatomically called “plexus haemorrhoidalis externa”) and here perianal thromboses or perianal haematomata develop, which can cause severe pain and swelling. We suggest this phenomenon is called “perianal thrombosis” to make it distinguishable from thrombosed haemorrhoids since it is also possible for haemorrhoids to become incarcerated/ thrombosed (that may happen with haemorrhoids grade II, III and IV). In this guideline, we focus on thrombosed haemorrhoids.

This thrombosis is often slowly absorbed by the body and the haemorrhoid will resolve over the course of several weeks. However, surgical treatment could result in more rapid resolution.

8.2.1 Basic treatment

No systematic reviews have been found regarding this subject.

Analgesics

There are no scientific data evaluating NSAIDs for the treatment of thrombosed haemorrhoids. However, analgesics could be prescribed for pain.

Flavonoids versus placebo

A recent randomized controlled trial (Giannini 2015), including 134 patients, assessed the efficacy of the oral intake of flavonoids versus placebo in patients with acute 'haemorrhoidal crisis'. They showed a statistically significant difference between the two groups after day 12: 58/66 in the flavonoids group and 38/68 in the placebo group experienced pain reduction during treatment. The ANOVA models showed a significant reduction in VAS scores over time in both groups. Bleeding decreased over time in 42/66 in the flavonoids group and 29/68 in the placebo group. Again, the ANOVA models showed a significant reduction in bleeding over time in both groups. No significant differences were noted regarding the occurrence of haemorrhoidal prolapse between the two groups (Chi-square=2.78) [91].

Topical use of heparin

A case controlled study, including 89 patients with thrombosed haemorrhoids, compared heparin ointment (ten tablets of trypsin and chymotrypsin powdered and mixed with 30 grams of heparin) with a group treated conservatively with bed rest in the Trendelenburg or jack-knife position, administration of liquid diet, stool softeners, antibiotics, and anti-inflammatory drugs along with warm Sitz baths and local application of glycerin and magnesium sulphate paste. In the patients receiving the application of the enzyme paste, local pain was reduced to a great extent, defecation was comfortable, there was negligible local pruritus and the routine body movements of the patient were painless. Local signs observed in the form of the size of the piles, perianal edema, and tenderness, were also found to be significantly reduced [92].

Nifedipine

A cohort study, including 98 patients with acute thrombosed haemorrhoids, compared oral nifedipine (n = 50) versus 1.5% lidocaine ointment every 12 hours for two weeks. They showed a statistically significant complete relief of pain in 43 patients (86%) of the nifedipine-treated group versus 24 patients (50%) of the control group after 7 days of therapy. Resolution of thrombosed haemorrhoids was achieved significantly after 14 days of therapy in 46 patients (92%) of the nifedipine-treated group, compared to 22 patients (45.8%) in the control group [93].

8.2.2 Surgical treatment

Some drugs that act by reducing internal anal sphincter tone have proved effective in the treatment of thrombosed haemorrhoids. A RCT trial (Perrotti 2017), including 30 patients with thrombosed haemorrhoids, evaluated the effect of an intrasphincteric injection of botulinum toxin for pain relief in patients versus a control group. There was no difference between the groups in pain intensity before treatment (pain score 5.9(1.8) in botulinum group versus 6.2(1.7) in placebo group [94].

Some patients with thrombosed haemorrhoids may benefit from surgical excision. A cohort study, including 231 patients with thrombosed haemorrhoids, compared basic and surgical treatment. Patients were managed conservatively with dietary modifications, stool softeners, Sitz baths, localized hygiene, and oral and topical analgesics. Surgical management included either excision or, rarely, incision of the thrombus-containing vessel. Of these patients, 119 (51.5 percent) were initially treated conservatively and 112 (48.5 percent) were treated surgically. Time to symptom resolution was 24 days for conservatively managed patients vs. 3.9 days for surgical patients ($P < 0.0001$). Moreover, surgically managed patients had more than a threefold longer time interval to recurrence than conservatively treated patients (25 months vs. 7.1 months; $P < 0.0001$) [95].

SH versus Haemorrhoidectomy

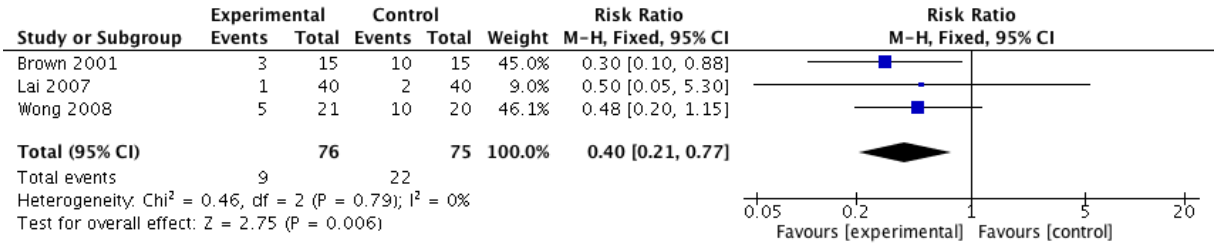
A RCT (Lai 2007), including 80 patients, compared stapled haemorrhoidectomy with an open haemorrhoidectomy in patients with thrombosed haemorrhoids. SH did not significantly increase the risk of complications (early and late) compared with haemorrhoidectomy, according to multivariate analyses (OR, 1.09; 95% CI, 0.38–3.16; $P = 0.88$). The postoperative pain scores were significantly lower in patients who had undergone SH [96].

Another RCT (Brown 2001) compared Haemorrhoidectomy with SH in 35 patients with acute thrombosed haemorrhoids (prolapsed piles). They reported that patients in the SH group had more postoperative pain than the Haemorrhoidectomy group. Two weeks postoperatively three patients (20%) in the stapled group and 10 patients (67%) in the Haemorrhoidectomy group complained of persistent bleeding. Pain was significantly less in the SH group. Six weeks after the operation no patients in the SH group versus 5 patients (33%) in the Haemorrhoidectomy group reported pain and bleeding [97].

Another RCT (Wong 2008) including 41 patients compared the SH with the Haemorrhoidectomy in patients with acute thrombosed haemorrhoids (e.g. thrombosis of the anal cushions). They showed that both groups had similar pain scores. However, patients in the SH group had a significantly lower pain score the first postoperative week and wound healing was significantly speedier. After one year follow-up, 5 patients in the Haemorrhoidectomy group complained of recurrent symptoms, whereas not a single patient in the SH group reported symptoms [98].

Meta-analysis of above mentioned studies

Outcome: postoperative bleeding



8.2.3 Conclusion

Haemorrhoidectomy could be proposed in patients with thrombosed haemorrhoids. However, basic treatment is associated with shorter inpatient stay. Comparing the SH with the Haemorrhoidectomy, SH is superior regarding post procedure pain.

8.2.4 Grade

Comparison: Flavonoids vs placebo in patients with thrombosed haemorrhoids

Studies: Giannini 2015

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	flavenoids	placebo	Relative (95% CI)	Absolute (95% CI)		
Main symptoms: pain												
1	randomised trials	serious [a]	not serious	not serious [b]	not serious	publication bias strongly suspected [c]	58/66 (87.9%)	38/68 (55.9%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Main symptoms: bleeding												
1	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	42/66 (63.6%)	29/68 (42.6%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Main symptoms: itching												
1	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	37/66 (56.1%)	22/68 (32.4%)	not estimable		⨁⨁◯◯ LOW	CRITICAL
Prolapse (follow up: 42 days)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	flavenoids	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	20/66 (30.3%)	23/68 (33.8%)	not estimable		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval

Explanations
a. Blinding not reported.
b. Evidence consists of research that directly compares the interventions which we are interested in, delivered to the populations in which we are interested, and measures the outcomes important to patients.
c. Publication bias is suggested based on the small number and size of the studies.

Comparison: Stapled Haemorrhoidopexy versus Haemorrhoidectomy for thrombosed haemorrhoidal disease

Studies: Wong 2008, Lai 2007 and Brown 2001

Certainty assessment							Aantal patiënten		Effect		Certainty	Importantie
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapled haemorrhoidopexy	haemorrhoidectomy	Relative (95% CI)	Absoluute (95% CI)		
Bleeding (follow up: mediaan 7)												
3	Randomised studies	Not serious	serious [a]	Not serious	serious [b]	publication bias strongly suspected	9/76 (11.8%)	22/75 (29.3%)	not estimable		⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

Explanations
a. Quality not considered.
b. Serious inconsistency, perhaps due to different formulations.
c. Wide 95% CI.
d. Publication bias is suggested based on the small number and size of the studies.

8.2.5 Recommendations

- In patients with thrombosed haemorrhoids, treatment should be informed by shared-decision making, taking into account patient preferences, availability of procedures and fitness for further procedures (*expert opinion, upgraded by guideline development group*).

- Primarily, basic treatment (i.e. toilet training, laxatives, NSAIDS and non-opioid analgesics) can be considered in patients with thrombosed haemorrhoids (*expert opinion*). Phlebotonics could be considered in patients with thrombosed haemorrhoids (*low level of evidence*). In selected cases, surgical options may be discussed with the patient (*very low level of evidence*).
- Surgical procedures (i.e. stapled haemorrhoidopexy and haemorrhoidectomy) can be considered in patients with thrombosed haemorrhoids (*very low level of evidence*).

8.3 Immunodeficiency

Immunocompromised patients have an increased risk of anorectal sepsis and poor tissue healing after any intervention. Therefore an operation should be avoided, or performed only after careful consideration [99]. Also, antibiotic prophylaxis should be given before performing any intervention.

Two studies assessed if Sclerotherapy (SCL) can be safely performed in patients with acquired immunodeficiency syndrome (HIV).
One observational study included 22 patients with HIV who underwent SCL for bleeding grade II-IV haemorrhoids according to standard outpatient clinic routines. SCL was successful in all patients. Nineteen patients improved after their first injection, whereas 3 patients required two to six weeks repeated SCL to improve. Four subjects with the longer follow-up (4 years) showed an improvement lasting 12 to 18 months and then required one to two treatments per year to stop recurrent bleeding (Scaglia 2001).

Another observational study, including a total of 76 patients with haemorrhoids (36 positive HIV and 40 negative HIV), showed similar recurrence rates between the HIV positive group and negative group postoperative 6 months of 22.2% (8/36) and 22.5% (9/40) and postoperative 1 year of 30.6% (11/36) and 30.0% (12/40) without significant differences. Morbidity of postoperative complication was also not significantly different between two groups [100].

One observational study assessed if rubber band ligation (RBL) can be safely performed in select HIV-positive patients. This study comprised 11 HIV-positive patients who underwent RBL for symptomatic haemorrhoids. There were no deaths or complications in any study group patient. Eight patients (73%) had excellent results, with complete resolution of symptoms. Two patients (18%) had initial improvement but subsequently had haemorrhoidectomy because of recurrent symptoms. Only one patient (9%) had no benefit from RBL and underwent haemorrhoidectomy [101].

8.3.1 GRADE

Question: Sclerotherapy (SCL) in patients with acquired immunodeficiency syndrome (HIV)

Study: Scaglia 2001

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SCL	no SCL	Relative (95% CI)	Absolute (95% CI)		
Recurrence (1 year)												
1	observational studies	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	11/36 (30.6%)	-	-	-	⊕◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval

Explanations
a. No allocation concealment. No blinding reported.
b. Selective outcome reporting. Further we suspect publication bias since published evidence is limited to a small number of small trials.

8.3.2 Recommendation:

Outpatient procedures (including rubber band ligation and sclerotherapy) in immunocompromised patients seems to be safe, but very limited data are available (*very low level of evidence*).

8.4 Inflammatory Bowel Disease (IBD)

Haemorrhoids are relatively uncommon in Inflammatory Bowel Disease (IBD) patients, who usually report few symptoms [102]. However, this anal problem could be underestimated, because of a bias due to the higher attention paid to the other clinical features of IBD.

One of the first retrospective studies of Jeffrey et al. (1977), included 42 patients with ulcerative colitis and 20 patients with Crohn's disease. They showed that the patients with ulcerative colitis had low complication-rates (4 complications after 58 courses of treatment). In Crohn's disease, the complication-rate was high (11 complications after 26 courses of treatment). One of the 42 patients with ulcerative colitis and six of the 20 with Crohn's disease required rectal excision for complications apparently dating from the treatment of haemorrhoids. These results suggest that treatment of symptomatic haemorrhoids is usually safe in patients with ulcerative colitis but is contraindicated in those with Crohn's disease [103].

On the contrary, more recent studies reported that, when the intestinal disease is quiescent and after failure of conservative treatments, a surgical option may be offered in selected cases [104]. A prospective study (D'Ugo 2013) included 86 patients with Crohn's disease. Fourty-five patients were treated for haemorrhoids. Conservative approach was initially adopted for all patients; in case of medical treatment failure, the presence of stable intestinal disease made them eligible for surgery. Fifteen patients underwent haemorrhoidectomy (open 11; closed 3; stapled

1), and two rubber band ligation. A high complication rate of 41.2% was observed. The most common complication was postoperative bleeding, observed in 3 (17.6%) out 17 patients, during the first four days postoperatively. One bleeding was self-limiting, while the other two required Emergency Room visits. The bleeding was stopped with local compression with hemostatic gauze. Further, two (11.8%) postoperative anal fissures, effectively treated with topic glycerin trinitrate (GTN) 0.4% were observed. In two cases (11.8%) perianal sepsis was detected one month and fourty days after surgery, in the form of abscess and intersphinteric fistula close to one site of haemorrhoid excision. These patients were then successfully treated by drainage and fistulotomy [105].

In a study of Cracco et al. (2014), eleven retrospective studies including 135 patients with IBD were identified. They showed that among the 99 patients with Crohn's Disease who had a haemorrhoidectomy, 17 (17.1%) patients had a complication. Of these, 10 were due to sepsis and in six of these a proctectomy was required. There were two patients who developed faecal incontinence resulting in a colostomy in one and a proctectomy in the other. Four developed stenosis and one an anal fissure/ulcer, both requiring a proctectomy. In conclusion, of the 99 patients, nine (10%) required a proctectomy and one other a colostomy. Of the 36 patients with ulcerative colitis (UC), two (5.5%) had a complication, including anorectal stenosis in one and a proctectomy in the other. The complications occurred more frequently in patients with unknown IBD than in those with a proven diagnosis of Crohn's Disease (50% vs 9.8%) or Ulcerative Colitis (9.1% vs 4%) [106].

8.4.1 Conclusion

An outpatient procedure (i.e. RBL) or surgery (i.e. haemorrhoidectomy), may have a role after failure of medical treatments. However, more data are needed to confirm these outcomes and to correlate them with complications and disease activity.

8.4.2 Grade

Question: Haemorrhoidectomy for haemorrhoidal disease in patients with IBD

Study: Cracco 2014

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	haemorrhoidectomy	no treatment	Relative (95% CI)	Absolute (95% CI)		
New outcome												
11	observational studies	serious [a]	not serious	not serious	not serious	[a,b]	19/135 (14.1%)	-	-	-	-	CRITICAL

CI: Confidence interval

Explanations

a. Few authors have reported the duration of the interval from haemorrhoidectomy to complications leading to major surgery. Unfortunately, the severity of the disease and the medical therapy at the time

of haemorrhoidectomy were not given although as with other authors the operation was apparently performed during remission of CD, e.g. a Crohn's Disease Activity Index score of < 150.
b. We suspect publication bias since published evidence is limited to a small number of small trials.

8.4.3 Recommendation

In patients with Inflammatory Bowel Disease (IBD), outpatient procedures and/or surgical procedures can only be considered when there is no sign of active disease (*expert opinion, upgraded by the guideline development group*).

8.5 Irradiation

In the literature, there is no evidence regarding the outcome of haemorrhoidal treatment in irradiated patients. However, there are some papers indicating that treatment in patients who have undergone pelvic radiotherapy can have catastrophic sequelae.

Radiation therapy has a major role in the treatment of a number of malignancies arising in the pelvis (i.e. carcinoma of the prostate, bladder, rectum and gynecological malignancies). The study of Hayne et al. showed that more than three-quarters of patients receiving pelvic radiotherapy, experience acute anorectal symptoms and up to one-fifht suffer from late phase radiation proctitis [107].

In a study of Theodorescu et al. seven hundred sixty-five patients received outpatient brachytherapy (BT) using a computed tomography (CT)-guided or transrectal ultrasound (TRUS)-guided technique. They showed that seven prostatourethralrectal fistula (PRF) were developed among 754 patients (1%) between 9 months and 12 months after treatment. Six out of these seven patients developed a rectourethral fistula after a biopsy of the distal rectum [108].

In a prospective study of Shakespeare et al. 1455 patients, treated with prostate brachytherapy (BT), were followed at least 2 years. They showed that in three patients a recto-urethral fistula occurred at 19–27 months following BT. All three patients developed a recto-urethral fistula after biopsy of the distal rectum [109].

In both studies the authors discourage rectal biopsies of the anterior rectum in patients who have had BT unless there is a very high clinical suspicion of malignancy.

8.5.1 Recommendation

Outpatient/ and or surgical procedures in patients who have undergone pelvic radiotherapy can generally not be considered (expert opinion)

8.6 Coagulation disorder

Conservative measures are the mainstay of treatment for patients with a coagulation disorder.

A retrospective review, who identified 364 patients undergoing RBL while on antithrombotic therapy (AT), showed 23 complications involving bleeding not statistically different from those not taking antithrombotic therapy. Patients on clopidogrel experienced 50% of the significant bleeding episodes and 18% of the insignificant bleeding episodes [110].

A controlled study, including 37 patients, compared patients undergoing SCL while on AT versus patients with haemorrhoids with non-AT. The efficacy in patients with bleeding did not differ between the two groups. The efficacy in patients with prolapse was significantly lower in the AT group than in the non-AT group. Six patients in the AT group underwent a second round of ALTA therapy, compared with no patients in the non-AT group [111].

A retrospective cohort study compared AT patients (n=36) versus non-AT patients (n=70) with symptomatic haemorrhoids who underwent DG-HAL. The postoperative morbidity between the two groups was similar, and specifically there was no statistical difference in the rate of postoperative hemorrhage (19.4 vs. 15.7 %; odds ratio 1.295, 95 % CI 0.455–3.688) AT patients who underwent DG-HAL were significantly less likely to have recurrent haemorrhoidal disease during the study's 6-month (3–24 months) medium follow-up period (2.8 vs. 7.1 %) compared to non-AT patients [112].

8.6.1GRADE

Comparison: Rubber Band ligation (RBL) in patients with antithrombotic therapy (AT)

Study: Nelson 2009

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	antithrombotic therapy	non-antithrombotic therapy	Relative (95% CI)	Absolute (95% CI)		
Bleeding												
1	observational studies	serious [a]	not serious	very serious [b]	not serious	publication bias strongly suspected [c]	23/364 (6.3%)	0.0%	not estimable		⊕◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval

Explanations
a. Lack of allocation concealment. No blinding. Incomplete accounting of patients and outcome events. Selective outcome reporting.
b. No direct evidence regarding the non-AT patient group.

c. Selective outcome reporting. Further we suspect publication bias since published evidence is limited to a small number of small trials.

8.6.2Recommendation

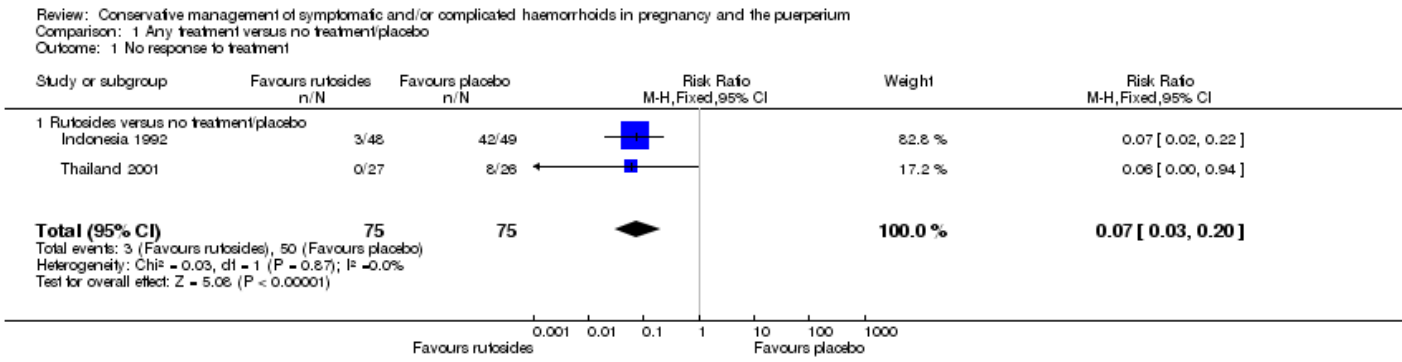
- If an outpatient procedure and/or surgical procedure is scheduled, appropriate cessation of anticoagulant therapy should be followed according to national guidance (*very low level of evidence, upgraded by guideline development group*).

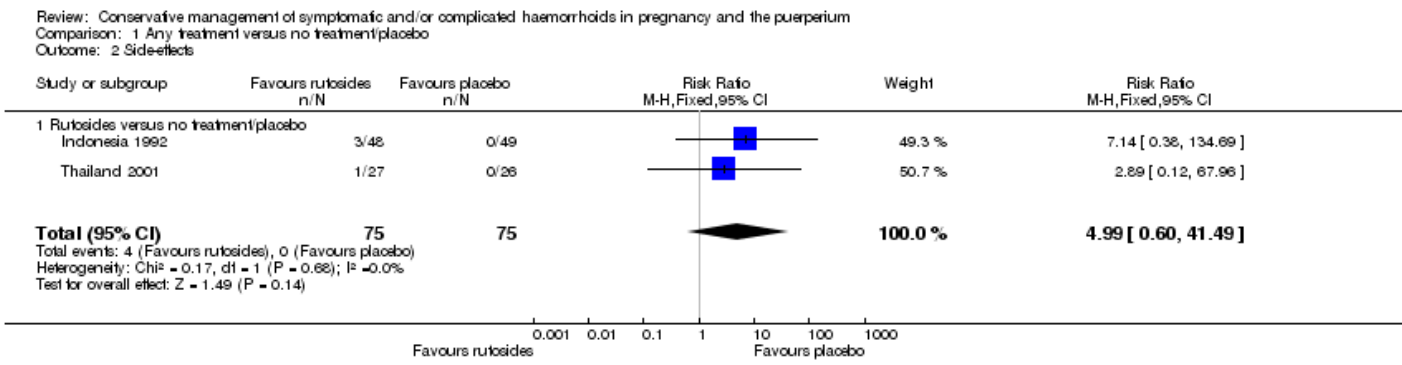
8.7 Pregnant women

(Thrombosed) haemorrhoids are a common condition in pregnant women due to an increased endopelvic pressure. The exact prevalence is unknown. One study evaluated the incidence of anal fissure in the postpartum period, which was reported to be 9% [113]. Another study reported that external haemorrhoid thrombosis affects 8% of women during last trimester pregnancy and 20% of women immediately after delivery [114, 115]. A survey including 165 obstetricians showed that only 42% of obstetricians refer these females to the specialist for HD [116]. For many women, symptoms will resolve spontaneously soon after birth, and so the primary goal of treatment is to relief acute symptoms mostly by means of dietary and lifestyle modification (Abramowitz 2011).

One review, including 2 trials and 150 pregnant females, compared oral hydroxyl ethilrutosides, a flavonoid drug given to improve the microcirculation in venous insufficiency, with placebo. The drug was effective in reducing the clinical signs of haemorrhoidal disease, as non-response after four weeks of treatment was significantly lower in the treatment arm (two trials, 150 women: RR 0.07, 95% CI, 0.03 to 0.20) [117].

Meta-analysis of above mentioned studies





Two studies evaluated the effectiveness of Proctofoam-HC, a combination of corticosteroid and a local anaesthetic in a total of 292 pregnant females. All haemorrhoidal symptoms, including pain, pruritus, swelling, itching, decreased significantly ($P < 0.001$) and overall well-being improved. The improvement was clinically very significant after correction for potential placebo effect [118, 119].

A recent prospective observational study including 495 pregnant females compared three times per day salty warm Sitz bath (using 20 gram of commercial salt) (n=284) with topical cream (containing corticoid and anaesthetic) twice daily. The females also received supportive treatments of 2 gram glycerin suppositories per rectum 20 minutes before defecation as lubricant and Metamucil bulk-forming fiber (a mix of one dose (sachet) within 240 ml (8 oz) of cold liquid) once daily after breakfast for constipation. Complete healing was achieved in all patients 284 (100%) in the Sitz bath group, compared to 179 (84.8%) in the cream group. Sitz bath was found to represent a statistically significant difference in achieving complete healing for haemorrhoids in pregnant females compared to an anorectal cream [120].

When medical therapy fails to relieve pain, operative intervention may be necessary.

One cohort study, including 25 pregnant women with haemorrhoids who underwent a traditional haemorrhoidectomy, showed that the traditional haemorrhoidectomy is not associated with surgical-related fetal complications [121].

8.7.1GRADE

Comparison: Conservative treatment compared to no treatment for pregnant women with symptomatic haemorrhoids

Studies: Wijayanegara 1992, Titapant 2001

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	conservative treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
No response to treatment												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	conservative treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	3/75 (4.0%)	50/75 (66.7%)	**RR 0.07** (0.03 to 0.20)	**620 fewer per 1.000** (from 533 fewer to 647 fewer)	⊕⊕◯◯ LOW	NOT IMPORTANT
Side effects												
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	4/75 (5.3%)	0/75 (0.0%)	**RR 4.99** (0.60 to 41.49)	**0 fewer per 1.000** (from 0 fewer to 0 fewer)	⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval; **RR:** Risk ratio

Explanations
a. Lack of allocation concealment. Incomplete accounting of outcome events.
b. In general, methodological quality was poor. Both trials were scored as 'B' when considered attempts to conceal the allocation sequence. Although they reported the use of placebo, it was not described enough (neither in its characteristics nor in the preparation of the treatment sequence) to assure the unpredictability of the following assignment. The same criteria apply for assessment of outcomes. Random generation was not described, as well as the sample sizes and power calculations. Although authors did look at the safety of the drug and possible effects on the baby, the trials were too small to demonstrate any difference in any of these outcomes. The study from Indonesia withdrew three women (3%) from analysis, while seven women (12%) were excluded from the study conducted in Thailand. Informed consent was mentioned in both trials.

8.7.2Recommendation

- In pregnant and post-partal women basic treatment (i.e. laxatives, topical treatments, phlebotonics and analgesics) should be used (*expert opinion, upgraded by the guideline development group*).
- In pregnant and post-partal women with thrombosed haemorrhoids unresponsive to basic treatment, surgical procedures to treat thrombosis can be considered (*expert opinion*).

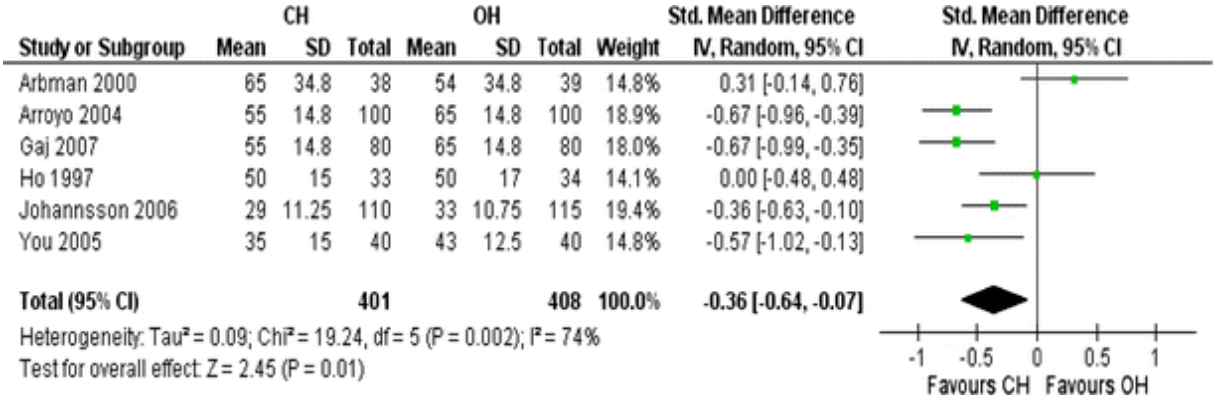
9 Other surgical techniques

9.1 Open haemorrhoidectomy versus the closed haemorrhoidectomy

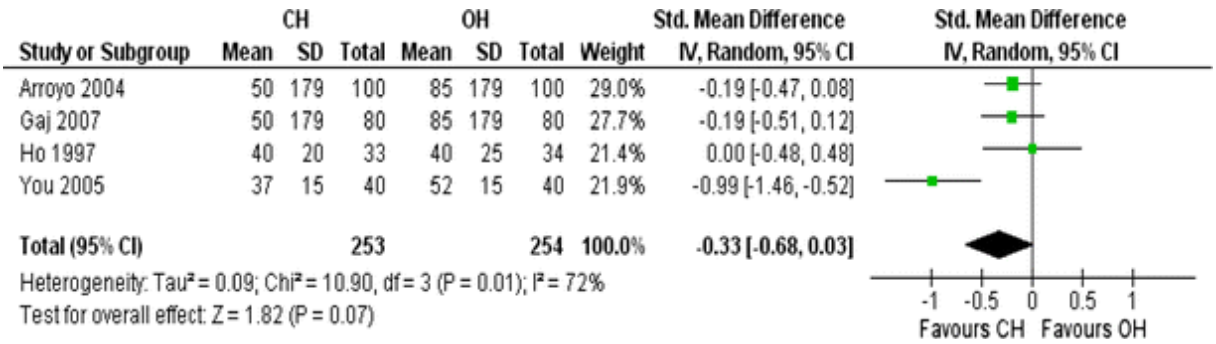
A meta-analysis (Bhatti 2016) including 11 RCTs and 1326 patients with grade II-IV haemorrhoids compared open haemorrhoidectomy with closed haemorrhoidectomy. Eleven RCTs presented data looking at recurrence and showed no significant difference between the open haemorrhoidectomy and the closed haemorrhoidectomy (OR=0.91, 95% CI 0.56 to 1.48). Six RCTs showed that the closed haemorrhoidectomy was associated with reduced post-operative pain (SMD= -0.36, 95% CI, -0.64 to -0.07). Eleven RCTs showed that the closed haemorrhoidectomy resulted in less post-operative bleeding than the open haemorrhoidectomy (OR=0.50, 95%CI 0.27 to 0.91). Seven RCTs showed that the closed haemorrhoidectomy is associated with a longer duration of the operation (SMD=6.10, 95% CI, -0.86 to 0.03). Eleven RCTs presented data regarding post-operative complications showing no significant difference between CH and OH was found (OR= 0.81, 95% CI, 0.44 to 1.48). In conclusion, the closed haemorrhoidectomy has clinically measurable advantages over the open haemorrhoidectomy with regards to less pain, less bleeding and faster wound healing [122].

Meta-analysis of the above mentioned studies:

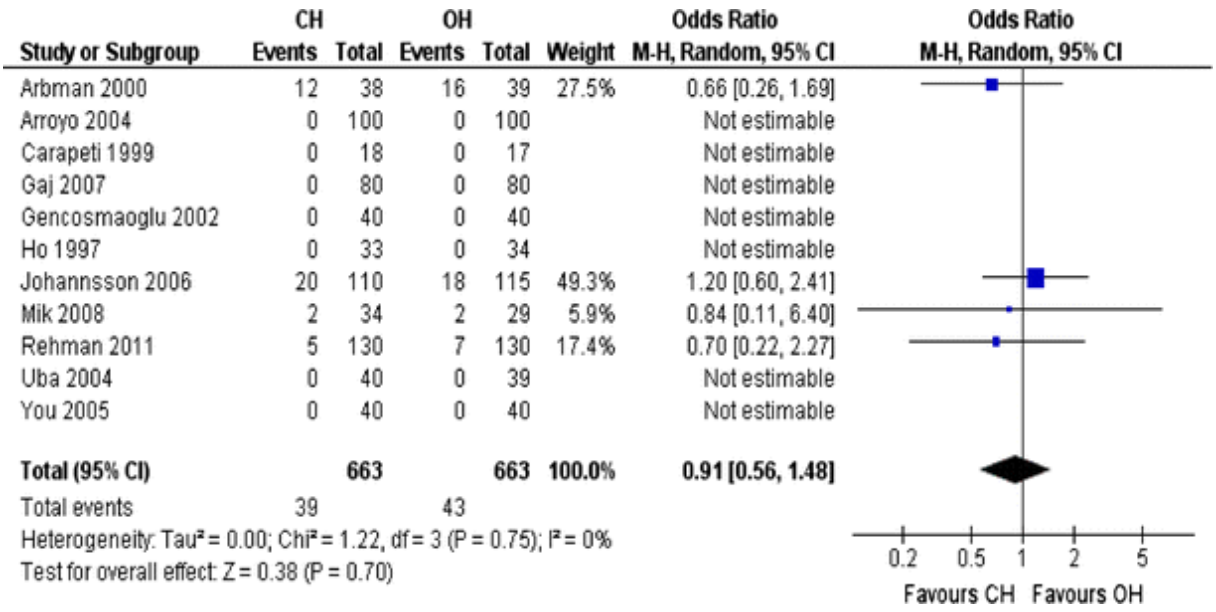
Outcome: postoperative pain



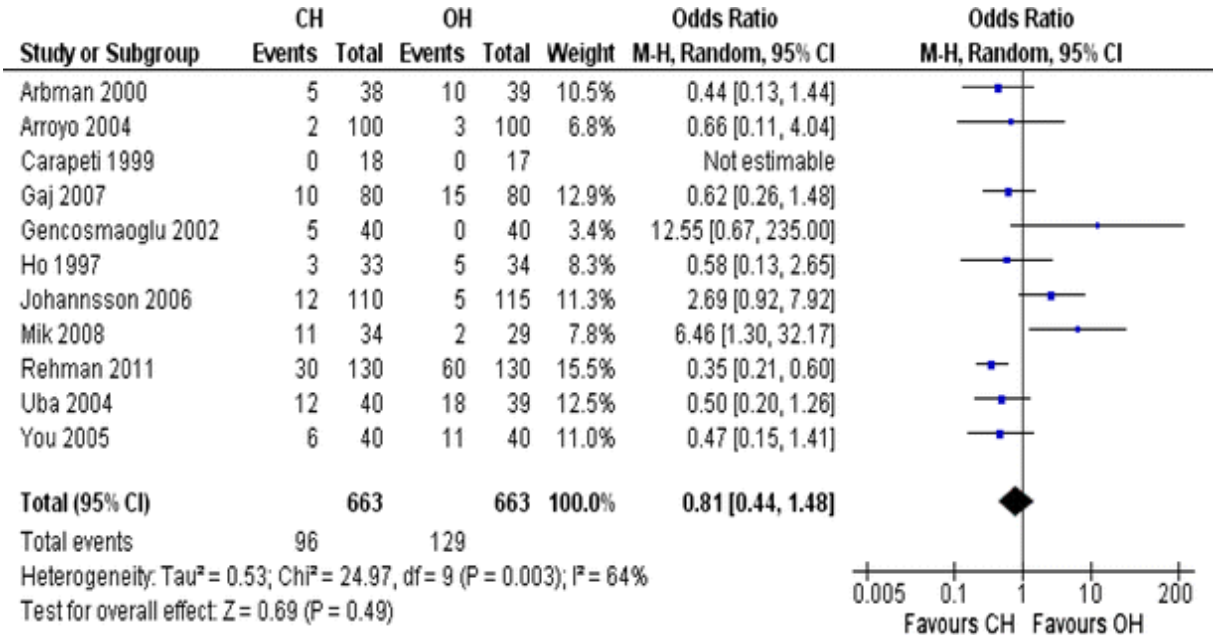
Outcome: pain of defecation



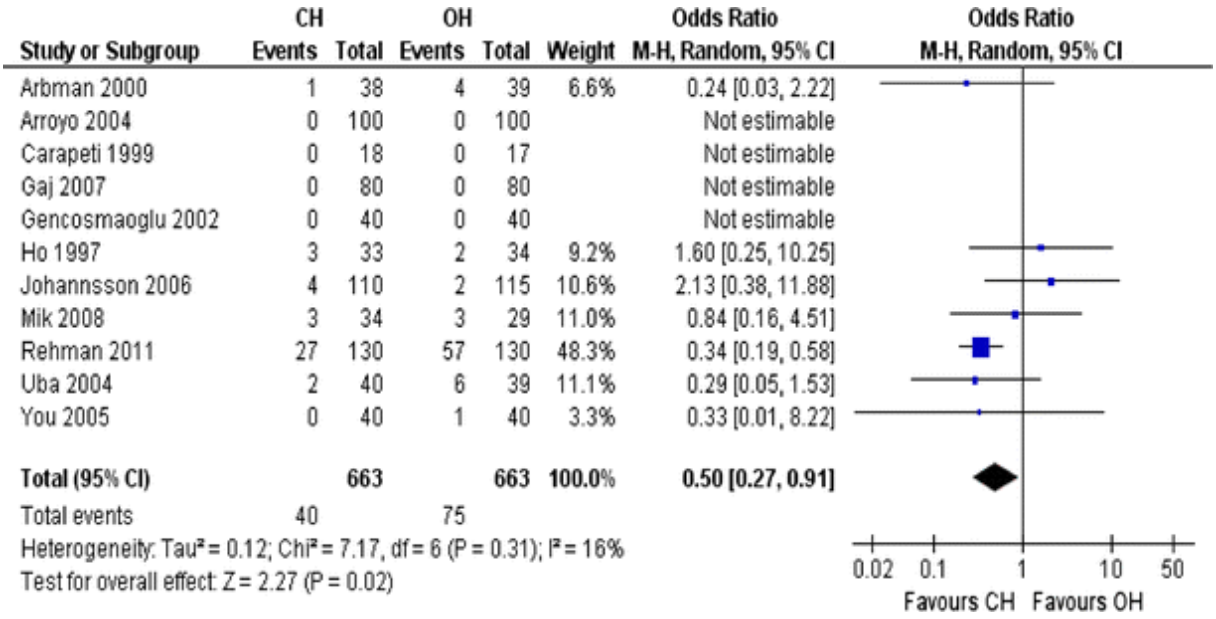
Outcome: recurrence



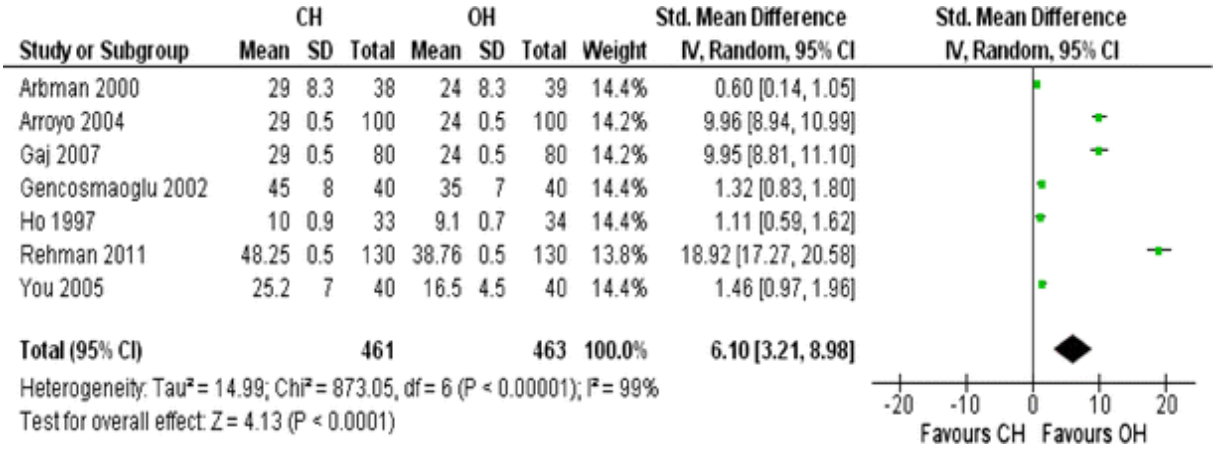
Outcome: postoperative complications



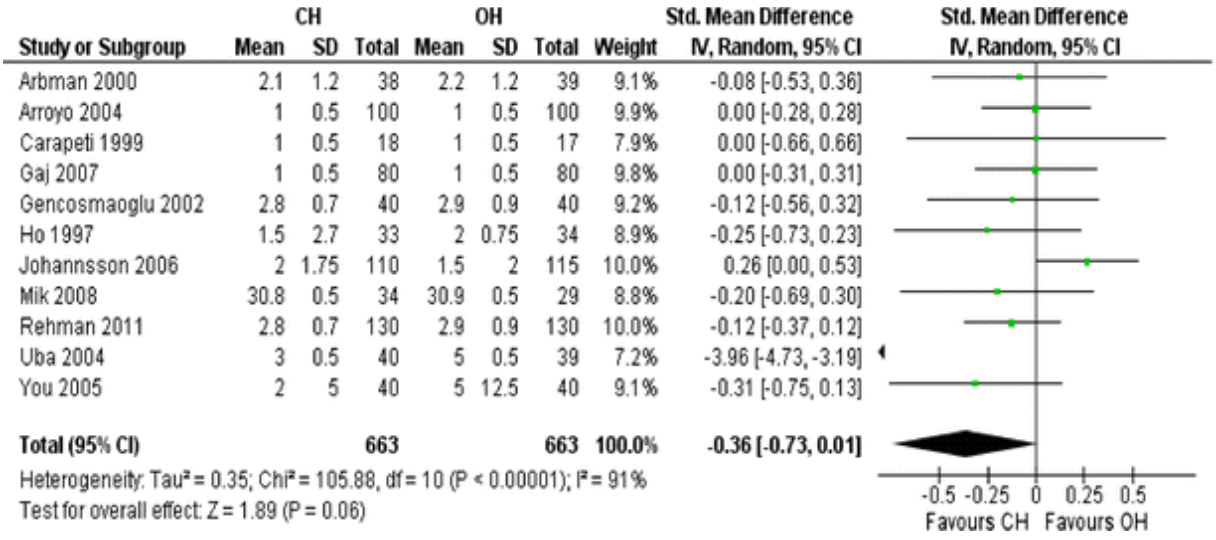
Outcome: postoperative bleeding



Outcome: duration of operation



Outcome: length of hospital stay



9.4.1 Grade

Comparison: Open haemorrhoidectomy compared to closed haemorrhoidectomy in patients with symptomatic haemorrhoids

Included studies: Arbman 2000, Arroyo 2004, Carapeti 1999, Gaj 2007, Gencosmaoglu 2002, Ho 1997, Johansson 2006, Mik 2008, Rehman 2011, Uba 2004, You 2005

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	open haemorrhoidectomy	closed haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Pain												
6	randomised trials	not serious [a]	serious [b]	serious [c]	not serious	publication bias strongly suspected [d]	408/663 (61.5%)	401/663 (60.5%)	**SDM -0.36** (-0.46 to -0.07)	**-- per 1.000** (from -- to --)	⨁◯◯◯ VERY LOW	CRITICAL
Postoperative complications												
11	randomised trials	not serious	serious [b]	not serious	not serious	publication bias strongly suspected [d]	129/663 (19.5%)	96/663 (14.5%)	**OR 0.81** (0.44 to 1.48)	**24 fewer per 1.000** (from 56 more to 75 fewer)	⨁⨁◯◯ LOW	CRITICAL
Postoperative bleeding												
11	randomised trials	serious [e]	not serious [f]	not serious	not serious	publication bias strongly suspected [d]	75/663 (11.3%)	40/663 (6.0%)	**OR 0.50** (0.27 to 0.91)	**29 fewer per 1.000** (from 5 fewer to 43 fewer)	⨁⨁◯◯ LOW	CRITICAL
Recurrence												
11	randomised trials	serious [e]	not serious	not serious	not serious	publication bias strongly suspected [d]	43/663 (6.5%)	39/663 (5.9%)	**OR 0.91** (0.56 to 1.48)	**5 fewer per 1.000** (from 25 fewer to 26 more)	⨁⨁◯◯ LOW	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. No serious study limitations. Adequate blinding, however methods of sequence generation or allocation concealment unclear for Gaj 2007 . Remaining trials were considered of good quality due to adequate methodology following analysis of reported quality variables.

b. Serious inconsistency; high statistical heterogenity (I2>74%). Perhaps due to differences in formulations.
c. Operator dependent pain score differences were not reported adequately.
d. Studies included in this review that recruited a small number of patients may not have had sufficient power to reveal small differences in outcomes. Due to fewer numbers of patients and fewer trials on this subject, it is still unwise to generalize the results of this study to all groups of patients undergoing HD surgery. Six included studies were of poor methodological quality. No funnel plot is included.
e. Gaj 2007, Gencomanoglu 2002, Mik 2008, Rehman 2011 and Uba 2004 were of poor quality due to lack of adequate randomization technique, absence of blinding, lack of power calculations and in-adequate methods of concealment.
f. I2 16%

9.2 Harmonic^{R} scalpel versus haemorrhoidectomy

A Haemorrhoidectomy can be performed using advanced instruments, such as the harmonic scalpel. The Harmonic device uses high-speed vibration instead of electric current to make incisions. This may result in less damage to the tissue, which is important in the overall recovery after surgery. The difference with Laser is that the harmonic scalpel uses temperatures lower than those of Lasers [123].

A meta-analysis (Mushaya 2014), including 8 studies and 468 patients with grade III and IV haemorrhoids, compared the Harmonic scalpel haemorrhoidectomy with the traditional haemorrhoidectomy. Four RCTs showed that patients were able to return to work faster in the Harmonic scalpel group (RR 2.4, 95% CI 1.4 to 4). Six RCTs showed that the Harmonic scalpel haemorrhoidectomy was associated with less postoperative pain (SMD -0.70, 95% CI 01.06 to -0.34). There was no significant difference between the groups as regards to operating time or length of hospital stay. These results were for the combined grade III and IV patients, but unfortunately results for grade III and IV patients separately were not reported [124].

9.2.1GRADE

Comparison: Harmonic scalpel compared to (traditional) haemorrhoidectomy for patients with symptomatic haemorrhoids

Included studies: Tan 2001, Khan 2001, Armstrong 2001, Chung 2002, Ramadan 2002, Abo-hashem 2010, Ozer 2008, Ivanov 2007

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Harmonic scalpel	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Postoperative pain score (assessed with: Visual analog scale)												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Harmonic scalpel	traditional haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
8	randomised trials	serious [a]	very serious [b]	not serious	not serious	publication bias strongly suspected [c]			**Mean difference -0.98** (-1.42 to -0.53)	**-- per 1.000** (from -- to --)	⨁◯◯◯ VERY LOW	CRITICAL
Complications												
8	randomised trials	serious [a]	very serious [d]	not serious	not serious	publication bias strongly suspected [c]	33/233 (14.2%)	83/265 (31.3%)	**RR 0.45** (0.28 to 0.72)	**172 fewer per 1.000** (from 88 fewer to 226 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Time to return to work												
4	randomised trials	serious [a]	very serious [e]	not serious	not serious	publication bias strongly suspected [c]	48/115 (41.7%)	25/139 (18.0%)	**RR 2.4** (1.4 to 4.0)	**252 more per 1.000** (from 72 more to 540 more)	⨁◯◯◯ VERY LOW	NOT IMPORTANT

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. The studies by Tan and Seow-Choen and Khan et al. were identified as being of lower design quality, as neither had blinded outcome assessment, the question of representativeness of the participants was not addressed, and use and reporting of statistical procedures may have been inadequate. In addition, the study by Ozer et al. was probably not strictly randomized as patients were consecutively allocated into one of the four groups. Overall, only three studies reported potentially confounding characteristics at baseline. Abo-hashem et al. reported that participants were blinded, and only Chung et al. reported that participants and researchers were blinded. Agreement between the two assessors about the quality of the eight studies was initially only moderate.

b. Statistical heterogeneity was unacceptably large in this analysis, driven by two studies with rather large effect sizes. When these two studies were excluded, heterogeneity was still significant but at an appreciably lower level ($Q = 11.6$; $p = 0.040$), while the effect measure remained significant: −0.70; 95 % CI = (−1.06, −0.34); $p < 0.001$.

c. Published evidence is limited to a small number of small trials. No funnel plot included.

d. The study only provided tables showing the standard mean difference or risk ratio.

e. Statistical heterogeneity was unacceptably large in this analysis, driven by two studies with rather large effect sizes.

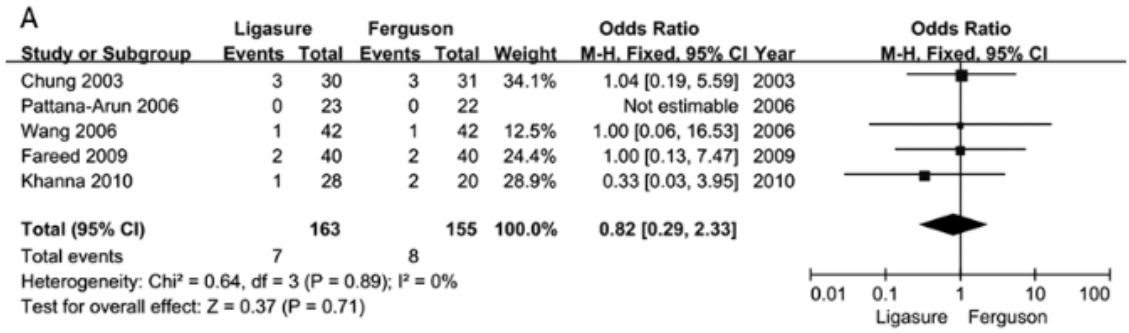
9.3 Ligasure[R] with the Ferguson (closed) haemorrhoidectomy

The ligasure is a 'vessel-sealing system'. This system delivers electro-diathermy energy across its jaws, similar as a bipolar diathermy device.

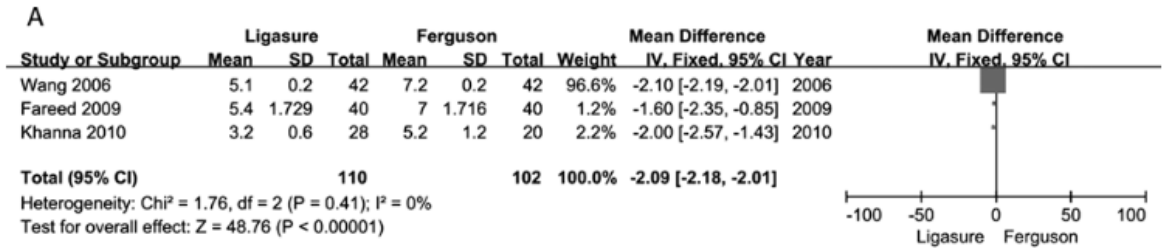
A meta-analysis (Xu 2015), including 5 RCTs and 318 patients, compared the Ligasure with the Ferguson (closed) haemorrhoidectomy. Three RCTs showed that the Ligasure is associated with significant less bleeding than the closed haemorrhoidectomy (OR 018.52, 95% CI -26.13 to -10.90). Three RCTs presented data regarding early postoperative pain scores, showing less pain in the Ligasure group (MD -2.09, 95% CI -2.18 to -2.01). Five RCTs reported data regarding urinary retention and showed less urinary retention in the Ligasure group (OR 0.32, 95% CI 0.13 to 0.79). In conclusion, Ligasure is an effective device with regards to blood loss, postoperative pain and complications compared to the open haemorrhoidectomy [125].

Meta-analysis of the above mentioned studies

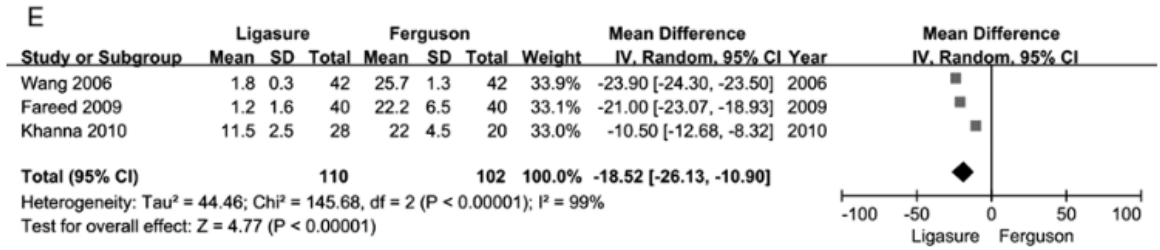
Outcome: (complications) postoperative bleeding



Outcome: early postoperative pain



Outcome: blood loss



9.3.1GRADE

Comparison: Ligasure compared to Ferguson (closed haemorrhoidectomy) for in patients with symptomatic haemorrhoids

Included studies: Wang 2006, Fareed 2009, Khanna 2010, Chung 2003, Pattana-Arun 2006

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ligasure	Ferguson (closed haemorrhoidectomy)	Relative (95% CI)	Absolute (95% CI)		
Postoperative bleeding (complications)												
5	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	7/163 (4.3%)	8/155 (5.2%)	**OR 0.82** (0.29 to 2.33)	**9 fewer per 1.000** (from 36 fewer to 61 more)	⨁⨁◯◯ LOW	CRITICAL
Postoperative pain scores												
3	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [c]	-/110	-/102	**Mean difference -2.09** (-2.18 to -2.01)	**-- per 1.000** (from -- to --)	⨁⨁◯◯ LOW	CRITICAL
Postoperative blood loss												
3	randomised trials	serious [c]	very serious [d]	not serious	not serious	publication bias strongly suspected [b]	-/110	-/102	**Mean difference -18.52** (-26.13 to -10.90)	**-- per 1.000** (from -- to --)	⨁◯◯◯ VERY LOW	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. There was great variation in included studies in surgical protocol, postoperative care regiment, and the methods of outcome measures. This trial only reported the short term outcomes.

b. Evidence is limited to a small number of small trials. However, they included a funnel plot.

c. Standardized outcome measures, especially for postoperative pain and bleeding, and recurrence with a long-term follow-up are required.
d. There was significant heterogeneity among trials (I2=145.68)

9.4 Laser

The Laser is an outpatient procedure reserved mostly for grade I and II and some grade III haemorrhoids. Laser therapy may be used alone or in combination with other modalities. The haemorrhoid is vaporized or excised using carbon dioxide. This technique is supposed to cause a decrease in haemorrhoidal arterial flow.

The Haemorrhoid Laser Procedure (HeLP) consists of Doppler-guided laser dearterialization of the terminal branches of the superior haemorrhoidal arteries, without the need for sutures.

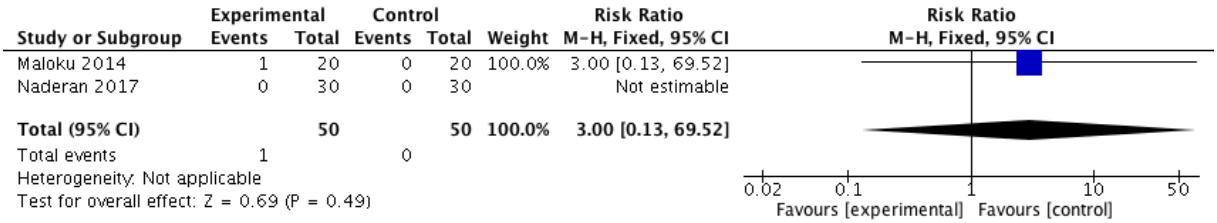
A RCT (Naderan 2017), including 60 patients with grade II or III HD, compared the outcomes of intra-haemorrhoidal coagulation with 980-nanometer (nm) diode laser with open Milligan–Morgan (MM) surgical haemorrhoidectomy. Postoperative pain scores (at 12, 18, and 24 hr after surgery) were significantly lower in the laser group compared with the MM group. Laser was associated with a significant shorter operative time and less intra-operative blood loss were than MM. Two patients in the laser group were presented with thrombosis of external haemorrhoid 7-10 days after the procedure, which was resolved with medical treatment. No patients in the MM group developed haemorrhoidal thrombosis. One-year follow-up showed comparable results in terms of the resolution of symptoms and sustainable cure [126].

A RCT (Maloku 2014), including 40 patients with grade III and IV patients, compared haemorrhoid laser procedure (n=20) versus open haemorrhoidectomy (n=20). They showed that the laser procedure was associated with a significant reduced length of operative time and less early postoperative pain. The procedure time for Laser was 15.94 min vs. 26.76 min for open surgery. No major adverse effects or complications were reported in both techniques [127].

A RCT (Giamundo 2011), including 60 patients with grade II and III HD, compared the haemorrhoid laser procedure with RBL. The laser procedure was associated with significant less pain (pain score 1.1 (range, 0 –2) for haemorrhoid laser procedure vs. 2.9 (range, 1–5) with RBL). At 6 months, a significant better resolution of symptoms was observed with haemorrhoid laser procedure (90%) vs ligation (53%). Further, a significantly higher quality of life was seen in the haemorrhoid laser procedure group [128].

<u>Meta-analyses of above mentioned studies</u>

Outcome: postoperative bleeding



9.4.1GRADE

Comparison: laser compared to open Milligan–Morgan (MM) surgical haemorrhoidectomy in patients with symptomatic haemorrhoids

Included studies: Naderan 2017 and Maloku 2014

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	laser	haemorrhoidectomy	Relative (95% CI)	Absolute (95% CI)		
Postoperative bleeding												
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	1/50 (2.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval

Explanations
a. There was great variation in included studies in surgical protocol, postoperative care regiment, and the methods of outcome measures. The study of Maloku only reported the short term outcomes.
b. Evidence is limited to a small number of small trials.

9.5 Stapled Trans Anal Rectal Resection (STARR^{R})

The STARR procedure consists of a double transanal rectal resection and is aimed at correcting the anatomical disorder of the rectum in patients with rectocele and rectal intussusception causing obstructed defecation.

A RCT (Corsale 2014), including 285 patiens with grade II (n=8), III (n=158) and IV (n=2) HD, compared stapled haemorrhoidopexy (SH) (n=237) with the STARR procedure (n=48). The average operation time resulted to be overlapping for the SH group and STARR group: 25 vs. 35 min. Seven patients of the SH group and two of the STARR group (3 vs. 5 %) have reported relevant or persistent rectum bleeding. Recurrence was reported in a similar percentage of patients (5 %) in the two groups, but with a statistically significant difference for the STARR group in relation to the occurrence of the asymptomatic residual of disease (24 vs. 10 %) [129].

A RCT (Zanella 2014), including 320 patients with grade III (n=218) and IV (n=102), compared SH (n=281) with the STARR (n=39). The rate of postoperative bleeding (53.8% vs. 74.4%, p<0.01) was significantly reduced in patients who underwent STARR procedure. However, the STARR procedure required a significant longer (45 ± 22 vs. 26 ± 11 min in the SH group) operative time. Further, patients treated with the STARR procedure had a non-significant lower recurrence rate of haemorrhoids and a non-significant lower incidence of prolapse, both at one year (none vs. 1.4%, and 2.6% vs. 5.3%, respectively) and at two years (none vs. 6.8%, and none vs. 13.2%, respectively) [130].

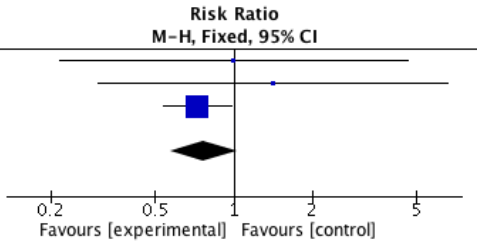
A RCT (Boccasanta 2006), including sixty-eight patients with grade II (n=53) and III HD, compared the SH (n=34) versus STARR operation (n=34). The mean VAS-score in the first postoperative week was remarkably low (VAS 1.7-3.4), without a significant difference among the two groups. At a mean follow-up period of 8 months the incidence of residual prolapse was significantly higher in the SH group (29.4% vs 5.9% in the STARR group), while the incidence of residual skin tags was significantly lower after STARR operation (58.8% vs 23.5 in the SH group). No significant difference was seen between SH and the STARR regarding the early complications (i.e. thrombosis, bleeding and urinary retention) [131] .

Meta-analyses of above mentioned studies

Outcome: bleeding

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccasanta 2006	3	34	3	34	5.3%	1.00 [0.22, 4.61]
Corsale 2014	2	48	7	237	4.2%	1.41 [0.30, 6.58]
Zanella 2014	21	39	209	281	90.5%	0.72 [0.54, 0.98]
Total (95% CI)		**121**		**552**	**100.0%**	**0.77 [0.57, 1.03]**
Total events	26		219			

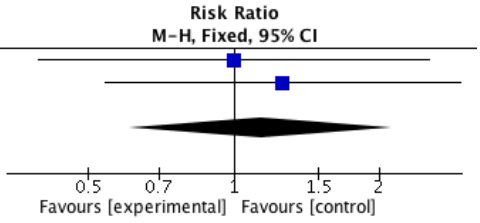
Heterogeneity: Chi² = 0.86, df = 2 (P = 0.65); I² = 0%
Test for overall effect: Z = 1.78 (P = 0.08)



Outcome: complications

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Boccasanta 2006	7	34	7	34	47.2%	1.00 [0.39, 2.54]
Corsale 2014	6	48	22	222	52.8%	1.26 [0.54, 2.94]
Total (95% CI)		**82**		**256**	**100.0%**	**1.14 [0.61, 2.13]**
Total events	13		29			

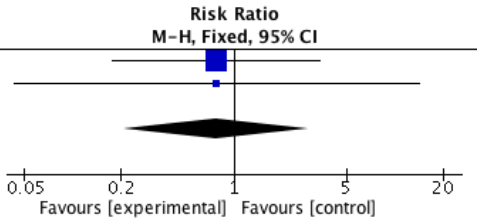
Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%
Test for overall effect: Z = 0.40 (P = 0.69)



Outcome: recurrence

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Corsale 2014	2	40	9	140	78.2%	0.78 [0.18, 3.46]
Zanella 2014	0	39	4	281	21.8%	0.78 [0.04, 14.28]
Total (95% CI)		**79**		**421**	**100.0%**	**0.78 [0.21, 2.94]**
Total events	2		13			

Heterogeneity: Chi² = 0.00, df = 1 (P = 1.00); I² = 0%
Test for overall effect: Z = 0.37 (P = 0.71)



A RCT (Renzi 2011), including 425 patients (grade HD not specified), was conducted to compare the clinical and functional results of STARR performed with 2 staplers (PPH-01 vs. PPH-03). Eligible patients were assigned to undergo STARR with 2 PPH-01 or STARR with 2 PPH-03 staplers. The incidence of bleeding at the stapled line was significantly lower in the PPH-03 group than in the PPH-01 group (58/207 [28.0%] vs. 145/201 [72.1%]; P < .0001); the mean number of haemostatic stitches was significantly higher in the PPH-01 than in the PPH-03 group (3.2 ± 0.1 vs. 1.8 ± 0.8; P < .0001). The mean operative time was 25.1 ± 11.5 minutes in the PPH-03 group and 38.1 ± 15.7 minutes in the PPH-01 group (P < .0001). No major complications occurred in either of the groups. At 12-month follow-up, the success rate in the 2 groups was 94.5% in the PPH01 group and 94.2% in the PPH03 group [132].

9.5.1Complications

Common complications are rectal bleeding, pain and fecal incontinence after the STARR procedure. Postoperative rectal bleeding occurred in 11% of the cases in a multicentre study [133] but was lower (4.4%) in the European STARR Registry [134]. De novo anorectal and pelvic pain developed in 9.5% of patients in a prospective multicentre study involving more than 1000 patients [134]. Rates of de novo incontinence to flatus in prospective series range from 3% to 19% [135, 136].

Uncommon complications are rectal perforation, rectovaginal fistula and retro pneumoperitoneum. Further the risk of dehiscence of the staple line is lower after STARR procedure [137].

Enterocele and anismus are contraindications to perform a STARR and this operation should be used with caution in patients with weak sphincters.

9.5.2Conclusion

The STARR procedure required a significant longer operative time. No significant difference was seen between SH and the STARR regarding the early complications (i.e. thrombosis, bleeding and urinary retention).

9.5.3GRADE

Comparison: SH compared to the STARR procedure in patients with symptomatic haemorrhoids

Included studies: Zanella 2014, Corsale 2014, Boccasante 2006

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapler	STARR	Relative (95% CI)	Absolute (95% CI)		
Bleeding												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	stapler	STARR	Relative (95% CI)	Absolute (95% CI)		
3	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	219/552 (39.7%)	26/121 (21.5%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Complications												
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	29/256 (11.3%)	13/82 (15.9%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Recurrence												
2	randomised trials	serious [a]	not serious	not serious	not serious	publication bias strongly suspected [b]	13/421 (3.1%)	2/79 (2.5%)	not estimable		⊕⊕◯◯ LOW	CRITICAL

CI: Confidence interval

Explanations
a. Lack of allocation concealment. No blinding. Incomplete accounting of patients and outcome events. Selective outcome reporting.
b. Publication bias is suggested based on the small number and size of the studies.

9.6 Recommendations

- Both the closed and open haemorrhoidectomy (not using energy devices) could be used (*low level of evidence*). The closed haemorrhoidectomy is associated with less pain and bleeding (*low level of evidence*).
- Surgical energy devices (Ligasure^{R} and Harmonic scalpel^{R}) could be used for haemorrhoidectomy (*low level of evidence*).
- Alternative procedures (Laser and Radiofrequency ablation procedures) could be used/can be considered (*low level of evidence)*
- Rectal resection using a stapler device (including STARR^{R}) should not be used to treat haemorrhoids (*low level of evidence, downgraded by the experts*).

10 Economic evidence

10.1 Published evidence

Author	Country	Question	Outcome	Results
Kilonzo MM[138]	UK	Cost Effectiveness of Stapled Haemorrhoidopexy and Traditional Excisional Surgery for the Treatment of Haemorrhoidal Disease.	The primary economic outcome was incremental cost measured in pounds (£), year 2016 values, relative to the incremental benefit, which was estimated using quality-adjusted life-years (QALYs)	Total costs were higher for the SH group: mean difference £337 (95% CI 251–423). Total QALYs were lower in the SH group: mean difference −0.074 (95% CI −0.070 to −0.011).
Alshreef A[139]	England	Cost-Effectiveness of Haemorrhoidal Artery Ligation versus Rubber Band Ligation for the Treatment of Grade II-III Haemorrhoids: Analysis Using Evidence from the HubBLe Trial.	Main outcomes included healthcare costs, quality-adjusted life-years (QALYs) and recurrence.	In the primary base-case within-trial analysis, the incremental total mean cost per patient for HAL compared with RBL was £1027 (95% confidence interval [CI] £782-£1272, p < 0.001). The incremental QALYs were 0.01 QALYs (95% CI -0.02 to 0.04, p = 0.49). This generated an incremental cost-effectiveness ratio (ICER) of £104,427 per QALY.
Brown S[140]	England	The HubBLe Trial: haemorrhoidal artery ligation (HAL) versus rubber band ligation (RBL) for symptomatic second- and third-degree haemorrhoids: a multicentre randomised controlled trial and health-economic evaluation.	Secondary outcome cost-effectiveness	In the base-case analysis, the difference in mean total costs was £1027 higher for HAL. Quality-adjusted life-years (QALYs) were higher for HAL; however, the difference was very small (0.01) resulting in an incremental cost-effectiveness ratio of £104,427 per additional QALY.
Ribaric G[141]	UK	Stapled haemorrhoidopexy, an innovative surgical procedure for haemorrhoidal prolapse: cost-utility analysis.	Main outcome measures were the cost per procedure at the hospital level, total direct costs from the health care system perspective, quality adjusted life years (QALY) gained and incremental cost per QALY gained.	A decrease in operating theater time and hospital stay associated with PPH led to a cost saving compared to CH of GBP 27 (US $43.11, €30.50) per procedure at the hospital level and to an incremental cost of GBP 33 (US $52.68, €37.29) after one year from the societal perspective. Calculation of QALYs induced an incremental QALY of 0.0076 and showed an incremental cost-effective ratio (ICER) of GBP 4316 (US $6890.47, €4878.37).
McKenzie L[142]	England	Economic evaluation of the treatment of grade II haemorrhoids: a comparison of stapled haemorrhoidopexy and rubber band ligation.	Primary outcomes measured at 52 weeks were cumulative costs to the NHS, clinical diagnosis of recurrence and quality adjusted life years (QALYs).	The mean cost per patient treated using SH was significantly higher than that for RBL (£1757 compared to £273).
Burch J[143]	UK	Stapled haemorrhoidectomy (haemorrhoidopexy) for the treatment of haemorrhoids: a systematic review and economic evaluation.	Economic evaluation.	On average, the difference in costs between the procedures was 19 pounds and the difference in QALY was -0.001, favouring CH, over 3 years. The probabilistic sensitivity analysis showed that, at a threshold incremental cost-effectiveness ratio of 20,000-30,000 pounds per QALY, SH had a 45% probability of being cost-effective.
Watson AJ[87]	UK	A pragmatic multicentre randomised controlled trial comparing stapled haemorrhoidopexy with	The primary economic outcome was the incremental cost-effectiveness ratio.	The average participant costs were £31.48 (95% CI £5.00 to £57.00) higher for SH (£69.83, SD 229.33) than for TH

		traditional excisional surgery for haemorrhoidal disease: the eTHoS study. To compare the clinical effectiveness and cost-effectiveness of SH with that of TH.		(£38.35, SD 72.80). On average, SH cost £287.87 (95% CI £190.17 to £385.56) more than TH and had – 0.060 (95% CI – 0.113 to – 0.007) fewer QALYs than TH.
Lehur PA[54]	France	Cost-effectiveness of New Surgical Treatments for Haemorrhoidal Disease: A Multicentre Randomized Controlled Trial Comparing Transanal Doppler-guided Haemorrhoidal Artery Ligation With Mucopexy and Circular Stapled Haemorrhoidopexy.	Total cost, cost-effectiveness, and clinical outcome were assessed at 1 year.	Total cost at 1 year was greater for DGHAL [&OV0556;2806 (&OV0556;2670; 2967) vs &OV0556;2538 (&OV0556;2386; 2737)]. The D.90, incremental cost-effectiveness ratio (ICER) was &OV0556;7192 per averted complication.

11 Patient information

Adapted from: https://www.nhs.uk/conditions/piles-haemorrhoids/. Translated in French, Italian, German and Dutch. See appendix XX.

12 Implementation

We invite you to provide any feedback you wish to make. Especially about barriers to implementation of any of our recommendations. In addition, we welcome feedback on any aspect of the guideline that may not be applicable, feasible or correct in your particular setting.

Please clearly describe which country and which setting your concern applied to. Guideline email address: Haemorrhoidsescpguideline@hotmail.com

13 Updating

We plan to update the guideline on an annual basis. This will involve update searches and assessment of any relevant research found in relation to the current recommendations and consideration whether recommendations need to be adapted or changed. GDG members plan to reconvene at the annual ESCP conferences to discuss an updated version of the guideline.

14 Conflict of interest

Jos Kleijnen (Kleijnen Systematic Reviews Ltd) has cooperated in the development and is co-author of the ROBIS, PRISMA, QUADAS, STARD and PROBAST tools.

15 Reviewers' comments

From: Tomas Poškus

Thank you very much for your effort and excellent work in compiling these important guidelines for such a common problem. However, I would like to point out, that guidelines serve not only as a systematic review of the topic, but also as our society's endorsement of one or another technique.

Current version of the guideline says that "Stapled haemorrhoidopexy could be used in patients with grade II-III haemorrhoids and/or in patients who are refractory to outpatient procedures (low level of evidence)".

However, there are well documented instances of severe and life-threatening complications, associated with stapled hemorrhoidopexy (they are mentioned withtin the guideline). Tenesmus, described in significant number of patients after stapled procedure is well reported in several trials and meta-analyses, and, once occurs, is persistent and difficult to treat. Up to 38 percent of patients 12 years after stapled hemorrhoidoplexy procedure are reporting tenesmus [1]. Fecal incontinence in the same population is reported to be 39%.

I would urge guidelines committee to add a cautionary note to the use and especially to new introduction of stapled hemorrhoidopexy to colorectal practices, that are currently not using it based on immediate and long-term patient safety concerns.

- *We thank the reviewer for this comment and we agree with the reviewer. The complications of stapled haemorrhoidopexy (SH) are well known. The guideline developing group choose to mention the specific complications of each intervention in a separate chapter. For the SH the complications are extensively described at page 48. In our flow diagram the SH is indicated as third option for grade III haemorrhoids and as second option for grade IV haemorrhoids. Based on literature the guideline developing group did not change the recommendations of using SH but we added a sentence in the complication part of SH.*

From: Steven Brown

Can I congratulate the guidelines committee on the recent guidelines. They are very extensive and well worked through. I have just a couple of comments.

There is no obvious discussion of the generic drawbacks of the published data. The lack of validated scoring systems and the huge variability in outcome measures as illustrated by Van Tol. This really distracts from the meaningful data that can be extrapolated from these guidelines. A section on how this could be improved for the future ie future areas for research would be welcome and it is pertinent guidance if the quality of guidance is to be improved in future updates. You have the expertise to do this on your committee.

- *We thank the reviewer for this comment. We choose to add this section in the discussion of the paper which will be a short version of the guideline. This manuscript will be published separately in Colorectal Disease.*

The economic data is mentioned but there is minimal discussion or guidance. This also is important I think, with more and more innovation clouding what is actually cost effective for society. It influences what we can offer, certainly in the UK, and there is good data out there as you have shown.

- *We thank the reviewer for this comment. Unfortunately, the financial reimbursement for HD is different for each country. Therefore, it is difficult to indicate what the best option is per country. The guideline development group choose to give an overview of the published economic data. We will address this topic in the discussion section of the paper which will be published in Colorectal Disease.*

These points perhaps link into the justification for this guidance and make it exceptional when you consider there have been 4 other international guidelines produced in the last 10 years. What makes the escp's so different?

- *We thank the reviewer for this comment. Only several national guidelines have been published recently, including the American Society of Colon and Rectal Surgeons guideline [144], the French HD guideline [145] and the Italian HD guideline [146]. The overall methodology quality of these guidelines for HD is not always optimal. I.e. in most guidelines, the review questions and methods for formulating their recommendations are not reported. The ESCP guideline for treatment of HD is the first international high quality guideline in which the AGREE II checklist is rigorously followed and can be used in the European setting.*

From: Neil Smart

Overall the guidelines are good and there is little I disagree with, except the stapled haemorrhoidectomy aspect, which I think needs to be contextualised in terms of patient safety. I'd also recommend PPI involvement at GDG level in future, their views would be most illuminating.

- *We thank the reviewer for this comment. We addressed this topic by adding a sentence in the guideline which indicates that there is a current debate regarding the safety of SH (see also discussion above).*
- *We agree that patient involvement is very important in developing guidelines. For the coming update which is planned within 3 years a patient will be member of the guideline development group. Meanwhile we have asked, Dutch, British, German, Italian and French patients to read the guideline in its final concept and asked them for feedback. In general, they did not have substantial comments to change the guideline. A separate patient information*

chapter describing the different techniques, including pictures, will be added to the current guideline.

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