Cochrane Library

Cochrane Database of Systematic Reviews

Endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids (Protocol)

Khan K, Lakshminarayan R, Yiasemidou M, Long J, Sayeed S, Smith GE, Hunter I, Chetter I

Khan K, Lakshminarayan R, Yiasemidou M, Long J, Sayeed S, Smith GE, Hunter I, Chetter I.
Endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids (Protocol).
Cochrane Database of Systematic Reviews 2024, Issue 5. Art. No.: CD014829.
DOI: 10.1002/14651858.CD014829.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Protocol]

Endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids

Khalid Khan[1,2], Raghuram Lakshminarayan[3], Marina Yiasemidou[4], Judith Long[5], Saira Sayeed[6], George E Smith[7], Iain Hunter[8], Ian Chetter[7]

[1]Department of Colorectal Surgery, Hull University Teaching Hospitals NHS Trust, Hull, UK. [2]Department of Colorectal Surgery, Sherwood Forest Hospitals NHS Foundation Trust, Sutton in Ashfield, Nottinghamshire, UK. [3]Department of Interventional Radiology, Hull University Teaching Hospitals NHS Trust, Hull, UK. [4]University of Hull, Hull, UK. [5]Department of Vascular Surgery, University of Hull, Hull, UK. [6]Radiology, Hull University Teaching Hospitals NHS Trust, Hull, UK. [7]Academic Vascular Surgical Unit, Hull York Medical School, Hull University Teaching Hospitals NHS Trust, Hull, UK. [8]Colorectal Surgery, Hull University Teaching Hospital, Hull, UK

Contact: Marina Yiasemidou, marinayiasemidou@gmail.com.

Editorial group: Cochrane Vascular Group, Cochrane Colorectal Group.
Publication status and date: New, published in Issue 5, 2024.

Citation: Khan K, Lakshminarayan R, Yiasemidou M, Long J, Sayeed S, Smith GE, Hunter I, Chetter I. Endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids (Protocol). *Cochrane Database of Systematic Reviews* 2024, Issue 5. Art. No.: CD014829. DOI: 10.1002/14651858.CD014829.

ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the safety and clinical effectiveness of endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids.

BACKGROUND

Description of the condition

Haemorrhoids is a common anorectal condition with reported prevalences ranging from 4.4% to 39% (Ganz 2013; Riss 2012). However, the true prevalence of the disease is unclear, as people often self-medicate instead of seeking medical attention. The highest incidence of haemorrhoids is observed in people between 45 and 65 years old (Sun 2016). According to one review published in 2016, haemorrhoidal disease is the fourth leading gastrointestinal diagnosis in outpatient clinics in the USA, accounting for around 3.3 million visits (Sun 2016).

Population-based studies report a significant variation in prevalence, from 4% in the USA (Johanson 1990), to 13% in Spain (Violan 2013), to 17% in Japan (Asakura 2018). Prevalence in specific population groups is higher, with reported rates varying from 12% to 41% among women during pregnancy and the postpartum period (Mao 2016; Poskus 2014).

Haemorrhoids are enlarged blood-filled pads of tissue in the anal canal (Sun 2016). These pads, in their normal state, are smaller and help to prevent leakage of flatus and liquid faeces when compressed by the surrounding muscles. They provide 15% to 20% of the mechanism that prevents such leakage (Ganz 2013; Lester 1989). When enlarged, these anal cushions lead to symptoms such as bleeding, discomfort, swelling, mucous discharge, and itching (Sun 2016). The diagnosis of haemorrhoids is based on clinical examination and proctoscopic examination of the anal canal (Lohsiriwat 2012).

The pathophysiology of haemorrhoids has been linked to several contributing factors. The most common and well-recognised trigger is increased pressure in the haemorrhoidal venous plexus. Hence, haemorrhoidal disease is seen more frequently in conditions that lead to chronically increased intra-abdominal pressures such as pregnancy, portal hypertension, pelvic floor dysfunction, obesity, constipation, and straining during defecation (Jacobs 2014). This chronic increase in abdominal pressure leads to vascular dilation and stretching of submucosal connective tissues. Distension and weakening of the fibroelastic tissues coupled with dilated venous plexus lead to symptomatic haemorrhoids (Kopljar 2011).

Haemorrhoids can be internal (originating from the internal haemorrhoidal plexus above the dentate line) or external (originating from the external haemorrhoidal plexus below the dentate line; Johanson 1990; Kann 2004). Internal haemorrhoids are further divided into four grades as per the Goligher classification (see Table 1; Goligher 1984; Rubbini 2019; Thomson 1992).

Description of the intervention

Treatment for grade I and II haemorrhoids is largely conservative and involves lifestyle modification (avoiding prolonged straining), dietary measures (e.g. increased dietary fibre and fluid intake to avoid constipation), and topical applications such as local anaesthetics and corticosteroid creams (Alonso-Coello 2005; Mounsey 2011). Intervention is reserved for cases of grade I and II haemorrhoids that have not responded to conservative treatment, or for symptomatic grade III and IV haemorrhoids (Brisinda 2000).

Interventional modalities available for treating symptomatic haemorrhoids can be classified into minimally invasive bedside treatments, surgical interventions, and endovascular interventions.

Minimally invasive bedside treatments

Rubber band ligation (RBL) is an outpatient procedure that requires no anaesthesia. During proctoscopy, a banding device is used to apply tight rubber bands to the tissue at the base of each of the internal haemorrhoids. This leads to ischaemic necrosis of the banded haemorrhoids, which will eventually slough off (Ohning 2009).

Injection sclerotherapy for haemorrhoids is an outpatient procedure. During proctoscopy, a sclerosant is injected submucosally at the base of each of the internal haemorrhoids (Mishra 2020). The sclerosant causes thrombosis of blood vessels and scarring, which causes the haemorrhoids to shrink (Madroff 2004). The most commonly used sclerosant is 5% phenol in almond oil.

Surgical interventions

Common surgical modalities include infrared or bipolar coagulation, cryotherapy, radiofrequency ablation, laser therapy, Doppler-guided haemorrhoidal de-arterialisation, stapling, and surgical excision (McRae 1995).

Direct surgical ablation techniques include electrocoagulation, infrared coagulation, cryotherapy, laser therapy, and radiofrequency therapies. All these procedures are performed via a transanal approach, and each therapy is delivered using specific equipment in direct contact with haemorrhoids (ASGE Technology Committee 2014).

In bipolar diathermy, an electrocoagulation machine delivers 20 watts of heat energy directly onto the internal haemorrhoid. This causes coagulation of the haemorrhoidal plexus. Over the next few days, the area ulcerates and scars. This results in shrinkage of the internal haemorrhoid (Piskun 2012).

In stapled haemorrhoidectomy, a circular stapling device is used to excise the redundant rectal mucosa, just above internal haemorrhoids, under general anaesthesia. The device excises a ring of tissue and concurrently staples the remaining rectal wall defect closed. The aim of treatment is to interrupt the blood supply to the haemorrhoids and excise redundant rectal mucosa.

Two types of excisional haemorrhoidectomy have been described; both procedures are carried out under general anaesthesia and involve surgical excision of the haemorrhoids. In Milligan-Morgan haemorrhoidectomy, the resulting defect can be left open; while in Ferguson haemorrhoidectomy, the defect is closed.

Both excisional and stapled haemorrhoidopexy are employed for sizeable haemorrhoids or when RBL has not produced the desired result. The eTHoS trial compared the clinical effectiveness and cost-effectiveness of these two techniques (Watson 2016). The results suggested that both techniques were safe, but that excisional haemorrhoidectomy was more cost-effective and resulted in better quality of life, fewer postoperative symptoms, and lower recurrence.

A newer, less invasive surgical technique is called haemorrhoidal artery ligation (HAL). Under general anaesthesia, haemorrhoidal arteries are identified using a Doppler probe. Following identification, the vessel is ligated with a suture to stop the arterial blood flow into the haemorrhoid. Each blood vessel is treated separately. In cases of large prolapsing haemorrhoids, the operator can deal with excessive haemorrhoidal tissue after vessel ligation using adjunct mucopexy (continued suturing to hitch up excessive haemorrhoidal tissue; Brown 2016).

The HubBLe study compared RBL with HAL. Recurrence after HAL was significantly lower than after a single RBL; however, recurrence was similar in people who had HAL and those who had repeated RBL. The study authors concluded that people may prefer a repeated course of RBL to the more invasive and painful HAL (Brown 2016).

Endovascular interventions

In rectal artery embolisation (RAE), the rectal vessel is approached through a peripheral artery entry (femoral) and embolised to interrupt the blood supply to the haemorrhoids. This process alleviates venous congestion in the haemorrhoids, thereby reducing venous pressure. Minimally invasive procedures similarly impact the blood supply, albeit to a smaller portion of the haemorrhoids. Lower venous pressure facilitates the restoration of connective tissue within the haemorrhoid, leading to tissue contraction and alleviation of symptoms.

Superior RAE was first described in 1991 (Vidal 2014). Later, Sun and colleagues described superior and inferior RAE for symptomatic haemorrhoids (Sun 2017). RAE aims to permanently occlude the blood supply to the haemorrhoids, resulting in atrophy. The procedure stops common symptoms such as bleeding and prevents progression to grade IV, prolapsed, or thrombosed painful haemorrhoids (Hollingshead 2015; Tradi 2018). RAE is most frequently performed in interventional radiology departments under local anaesthesia. Endovascular arterial access is achieved via the femoral artery. First, an introducer sheath is inserted to allow placement of an arterial microcatheter into the terminal branches of the rectal arteries, through the inferior mesenteric artery approach. Small coils are then deployed into its most distal branches to occlude the vascular supply to the haemorrhoids (Tradi 2018).

How the intervention might work

Endovascular RAE and most surgical interventions aim to interrupt the arterial supply to the haemorrhoids. This reduces haemorrhoidal venous congestion and decreases venous tension. The minimally invasive techniques also affect the blood supply, but to a smaller segment of the haemorrhoids. Reduced venous tension enables regeneration of connective tissue within the haemorrhoid, shrinking the tissue and reducing symptoms.

Why it is important to do this review

People with haemorrhoids often experience bleeding and pain, which can have a significant impact on their quality of life. The associated conditions of thrombosis or fissure may lead to emergency presentations with considerable pain (Talaie 2022). Rørvik and colleagues found that people with haemorrhoids experienced a high symptom load, as demonstrated by decreased physical health scores compared to healthy subjects, and that haemorrhoids impaired quality of life in men, women aged under 50 years, and people with higher education (Rørvik 2023).

Invasive treatment and readmission after conservative treatment may be associated with a financial burden (McKenzie 2010). Around 25,000 interventions for haemorrhoids are performed in the UK every year (Ross 2012; Watson 2017). One-year recurrence after RBL incurred a cost of GBP 4945 per patient in 2010 (McKenzie 2010). The estimated cost today would be GBP 7819.03. Mean per-patient costs in 2016 were GBP 723 for RBL and GBP 1750 for HAL, according to the HubBLe trial (Brown 2016). Yang and colleagues investigated the burden and cost of outpatient assessment and management of haemorrhoids in an employer-insured population in the USA in 2014. They reported that 1.4 million individuals sought care for haemorrhoids, incurring a cost of USD 770 million (Yang 2014).

Traditionally, surgical treatment for haemorrhoids includes excisional or stapled haemorrhoidectomy (Brown 2016). According to the landmark eTHOS trial, both techniques are safe, but traditional excisional surgery offers better results in terms of quality of life, symptoms, and haemorrhoid recurrence. Furthermore, the excisional technique is considered more cost-effective (Watson 2016). Both procedures require general anaesthetic and are associated with significant postoperative discomfort, at times leading to prolonged recovery and repeated visits to hospital or primary care centres (Brown 2016). Other reported risks associated with these procedures are bleeding, infection, urinary retention, recurrence, scarring, anal stenosis, and damage to sphincters (Similis 2015; Trompetto 2015).

The landmark HubBLe trial compared HAL to RBL. After one year, HAL and repeated RBL led to comparable recurrence rates. There were no significant differences between the procedures in terms of symptom scores, complications, quality of life, and continence scores, but participants who had HAL experienced more pain during the early postoperative period. In addition, HAL is more expensive and is unlikely to be cost-effective in terms of incremental cost per quality-adjusted life year (Brown 2016).

RAE is a highly promising technique that does not require a transanal approach or general anaesthesia. These differences compared with surgical techniques are expected to reduce the length of hospital stay, the time needed to return to normal activities, postoperative pain and discomfort, and morbidity related to perianal approaches (scarring and sphincter damage). A review by the National Institute for Health and Care Excellence (NICE) identified four case series (99 patients in total) and indicated that the evidence regarding the safety and efficacy of superior RAE for haemorrhoids is inadequate in quality and quantity (NICE 2018). NICE recommended further research into superior RAE and highlighted the importance of reporting details of participant selection, follow-up, efficacy (including symptom relief), need for subsequent treatments, quality of life, and safety outcomes for at least one year (NICE 2018). We aim to present the current evidence on the effectiveness and safety of RAE compared with other treatments for haemorrhoidal disease to aid decision-making for patients and healthcare professionals.

OBJECTIVES

To assess the safety and clinical effectiveness of endovascular rectal artery embolisation (RAE) for symptomatic haemorrhoids.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) investigating endovascular RAE for symptomatic haemorrhoids.

Types of participants

We will include participants aged 16 years and older diagnosed with symptomatic haemorrhoids (grades II and III according to the Goligher Classification; Goligher 1984). Symptoms can include pain, bleeding, painful lump in the anus (i.e. prolapse), mucus discharge, painful defecation, and faecal leakage. We will exclude people diagnosed with grade I symptomatic haemorrhoids, as treatment is usually conservative. We will exclude people diagnosed with grade IV haemorrhoids, as treatment is usually excisional haemorrhoidectomy. When studies involve a mixture of grades I to IV, we will include studies only if it is possible to separate the data of interest, or if most participants have grade II or III. We will not include people with combined externo-internal haemorrhoids.

Types of interventions

We will include studies that compare endovascular RAE with any treatment (conservative or surgical intervention) for symptomatic haemorrhoids. Endovascular RAE includes superior or inferior RAE.

The following comparisons will be eligible.

- RAE versus minimally invasive bedside treatment
  - RBL
  - Injection sclerotherapy
- RAE versus any transanal surgical procedure (elective or emergency)
  - Direct surgical ablation techniques (electrocoagulation, infrared coagulation, cryotherapy, laser therapy, radiofrequency ablation)
  - Bipolar electrocoagulation (diathermy)
  - Stapled haemorrhoidopexy
  - HAL
  - Excisional haemorrhoidectomy

Types of outcome measures

Primary outcomes

- Symptom recurrence (participant-reported or clinical recurrence, up to one year)
- Early complications (within three months after the procedure), including but not limited to bleeding. Bleeding refers to a secondary or delayed haemorrhoidal bleed, which starts between seven and 14 days after the procedure (Chen 2002; Kishik 1993; Lee 2018)
- Late complications (over three months from date of procedure), including but not limited to sphincter damage. Sphincter damage refers to any sign of incontinence, as defined clinically through the Wexner score or other validated scores, or as documented after the complication of or functional or anatomical abnormalities of the sphincter complex as reported in anophysiology studies following excisional haemorrhoidectomy (Lawes 2004).

Secondary outcomes

- Postoperative pain scores, measured using validated scales such as a visual analogue scale (VAS; Brown 2016)
- Postoperative faecal incontinence scores, measured using validated scales such as the Vaizey faecal incontinence score (Brown 2016) or Cleveland Clinic Incontinence Score (Jayne 2021)
- Length of hospital stay (days)
- Need for reintervention (any procedure performed for recurring symptoms of haemorrhoids, either the same as the index procedure or another procedure)
- Technical success (occlusion of terminal arterial branches to haemorrhoidal plexus) at time of procedure
- Additional complications (early and late), including ischaemia of anorectum, pseudoaneurysm, infection, urinary retention, death, anal stenosis, and long-term health effects of radiation (e.g. cancer)

Search methods for identification of studies

Electronic searches

We will aim to identify all relevant RCTs regardless of language or publication status (published, unpublished, in press, or in progress).

The Information Specialist will search the following databases for relevant trials.

- Cochrane Vascular Specialised Register via the Cochrane Register of Studies (CRS-Web)
- Cochrane Central Register of Controlled Trials (CENTRAL) via the Cochrane Register of Studies Online (CRSO)
- MEDLINE (Ovid MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE Daily and Ovid MEDLINE; from 1946)
- Embase Ovid (from 1974)
- CINAHL EBSCO (from 1982)

The Information Specialist has devised a draft search strategy for MEDLINE (Appendix 1). The search strategies for the other databases will be based on the MEDLINE strategy.

The Information Specialist will search the following trials registries.

- World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP; trialsearch.who.int)
- U.S. National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov)

Searching other resources

We will also search the following databases of ongoing trials.

- ISRCTN registry
- EU Clinical Trials register (www.clinicaltrialsregister.eu)

We will check the reference lists of included studies for any relevant research that could be included in this review. Furthermore, if any review authors are aware of a centre conducting relevant research, they will contact the investigators directly to request any published or unpublished data.

Data collection and analysis

Selection of studies

Two of three review authors (KK, MY, JL) will independently review the abstract or title (or both) of all records identified from searches and exclude all records that are clearly ineligible. We will retrieve the full-text articles of all potentially eligible records, and two of three review authors (KK, MY, JL) will independently assess them against our inclusion and exclusion criteria. We will resolve any discrepancies by discussion or by involving a third review author (GES, ICC, or RL). We will identify and remove duplicates and collate multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We will illustrate the study selection process in a PRISMA diagram (Liberati 2009). If we exclude any studies that readers could reasonably assume meet our eligibility criteria, we will list them in a 'Characteristics of excluded studies' table, providing a reason for their exclusion.

Data extraction and management

Two of three review authors (KK, MY, JL) will independently extract data from included trials, resolving any disagreements by discussion with a third author (GES, ICC, or RL). We will create a bespoke data collection tool (spreadsheet), which will include the following information.

- Names of the data extractors and the date of data extraction
- Bibliographic information of papers
- Setting: study duration, country/countries, and number of centres
- Methods: number of recruiting centres, recruitment methodology, study design, randomisation process, concealment, enrolment period, and length of follow-up
- Participant characteristics: total number of participants and their demographics, diagnosis, grade of haemorrhoids, indication for procedure, elective or emergency
- Inclusion and exclusion criteria
- Details of intervention: type of intervention, endovascular embolisation technique, names and number of arteries embolised, surgical intervention information, type of anaesthesia
- Outcomes: symptom recurrence, complications, technical success of endovascular embolisation of rectal artery, rates of successful reduction in symptoms, postoperative pain scores, postoperative faecal incontinence scores, length of hospital stay, need for reintervention
- Results: sample size, number of participants allocated to each group, and missing participants
- Funding: any reported source(s) of funding or other material support for the included studies
- Declarations of interest of the study authors

We will contact study authors for additional information where necessary.

Assessment of risk of bias in included studies

Two review authors (KK, MY) will independently assess the risk of bias for each included study using Cochrane's risk of bias tool (RoB 1), as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2017). We will resolve any disagreements by discussion or by involving a third review author (GES, ICC, or RL). RoB 1 covers the following domains.

- Random sequence generation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome data
- Selective outcome reporting
- Other bias

We will grade each study at high, low, or unclear risk of bias for each domain, providing a statement to justify our judgement in the 'Characteristics of included studies' table. We will summarise the risk of bias judgements across different studies for each of the domains.

Measures of treatment effect

We will express dichotomous data as odds ratios (ORs) with 95% confidence intervals (CIs). We will express continuous data as mean differences (MDs) with 95% CIs. If different studies report the same continuous outcome using different scales, we will calculate the standardised mean difference (SMD) with its 95% CI.

Unit of analysis issues

Preliminary knowledge of the literature indicates we are unlikely to encounter study designs that could give rise to a unit-of-analysis error (e.g. cross-over trials, cluster-randomised trials, or studies with multiple intervention groups where more than two groups are included in the same meta-analysis). However, if we do, we will address them using methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2023).

Dealing with missing data

We will contact study authors to obtain missing study characteristics or outcome data when necessary. If this is not possible, and we consider the missing data may introduce bias (i.e. if they are imbalanced between study arms or may be related to the intervention), we will perform a sensitivity analysis to explore the impact of including such studies.

Assessment of heterogeneity

We will interpret the level of statistical heterogeneity using the following thresholds of the I^2 statistic (Higgins 2023).

- 0% to 40% might not be important.
- 30% to 60% may represent moderate heterogeneity.
- 50% to 90% may represent substantial heterogeneity.
- 75% to 100% represents considerable heterogeneity.

Assessment of reporting biases

Where we include 10 or more studies in a meta-analysis, we will create a funnel plot to assess publication bias, bearing in mind that asymmetric funnel plots are not necessarily caused by publication bias (and that publication bias does not necessarily cause asymmetry in funnel plots).

Data synthesis

When appropriate, we will synthesise data using Review Manager Web (RevMan Web 2020). We will use a random-effects model to account for the possible heterogeneity of the participant demographics and the different surgical/treatment techniques between studies.

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses.

- Treatment of acute haemorrhoidal bleeding as an emergency versus elective procedure (considerable bleeding will be treated as an emergency, compared to usual bleeding treated by elective procedures in clinics)
- Participants with multiple comorbidities (American Society of Anesthesiology (ASA) score greater than 2) versus those without comorbidities (ASA score of 2 or lower)
- Participants aged over 70 years versus those aged 70 years and under

Sensitivity analysis

We plan to perform the following sensitivity analyses to evaluate the robustness of our results.

- Removal of studies at high risk of bias in any domain
- Removal of studies that include people with grade I or grade IV haemorrhoids
- Removal of studies with imbalanced missing data between study arms

Summary of findings and assessment of the certainty of the evidence

We will create summary of findings tables using GRADEpro software and following methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (GRADEpro GDT 2015; Higgins 2023). We will create a separate table for each comparison of interest and present the following outcomes in each table.

- Symptom recurrence
- Early complications (within three months)
- Late complications (after three months)
- Postoperative pain scores
- Postoperative faecal incontinence scores
- Length of hospital stay
- Need for reintervention

Three review authors (KK, MY, JL) will independently rate the certainty of the evidence for each outcome as high, moderate, low, or very low based on the five GRADE considerations: risk of bias, inconsistency, indirectness, imprecision, and publication bias (Atkins 2004). We will resolve any disagreements by consensus or discussion with a senior author (RL). We will justify all decisions to downgrade the evidence using footnotes and will make comments to aid the reader's understanding of the review where necessary. Table 2 presents an example summary of findings table.

ACKNOWLEDGEMENTS

The authors and the Cochrane Vascular Editorial base are grateful to the following peer reviewers for their time and comments: Dr Steve Brown, Department of Surgery, Sheffield Teaching Hospitals, UK; Prof Varut Lohsiriwat MD, PhD, Colorectal Surgery Unit, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. We are also grateful to the reviewer who wished to remain anonymous.

The following people conducted the editorial process (post peer review) for this article:

• Sign-off Editor (final editorial decision): Professor Jacob Rosenberg, Department of Surgery, Centre for Perioperative Optimization, University of Copenhagen, Herlev Hospital, Denmark

• Managing Editor (provided editorial guidance to authors, assisted the process to publication): Anupa Shah, Cochrane Central Editorial Service

• Copy Editor (copy editing and production): Julia Turner, Cochrane Central Production Service

REFERENCES

Additional references

Alonso-Coello 2005

Alonso-Coello P, Guyatt G, Heels-Ansdell D, et al. Laxatives for the treatment of hemorrhoids. *Cochrane Database of Systematic Reviews* 2005, Issue 4. Art. No: CD004649. [DOI: 10.1002/14651858.CD004649.pub2]

Asakura 2018

Asakura K, Nakano M, Omae K. Relationship between bidet toilet use and haemorrhoids and urogenital infections: a 3-year follow-up web survey. *Epidemiology and Infection* 2018;**146**:763-70.

ASGE Technology Committee 2014

ASGE Technology Committee, Siddiqui UD, Barth BA, Banerjee S, Bhat YM, Chauhan SS, Gottlieb KT, et al. Devices for the endoscopic treatment of hemorrhoids. *Gastrointestinal Endoscopy* 2014;**79**:8-14.

Atkins 2004

Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. *BMJ* 2004;**328**(7454):1490-4.

Brisinda 2000

Brisinda G. How to treat haemorrhoids. Prevention is best: haemorrhoidectomy needs skilled operators. *BMJ* 2000;**321**(7262):582-3.

Brown 2016

Brown SR, Tiernan JP, Watson AJ, Biggs K, Shephard N, Wailoo AJ, et al. Haemorrhoidal artery ligation versus rubber band ligation for the management of symptomatic second-degree and third-degree haemorrhoids (HubBLe): a multicentre, open-label, randomised controlled trial. *Lancet* 2016;**388**(10042):356-64.

Chen 2002

Chen HH, Wang JY, Changchien CR, Yeh CY, Tsai WS, Tang R. Effective management of posthemorrhoidectomy secondary hemorrhage using rectal irrigation. *Diseases of the Colon & Rectum* 2002;**45**:234-8. [DOI: 10.1007/s10350-004-6154-8]

Ganz 2013

Ganz RA. The evaluation and treatment of hemorrhoids: a guide for the gastroenterologist. *Clinical Gastroenterology and Hepatology* 2013;**11**:593-603.

Goligher 1984

Goligher J, Duthie H, Nixon H. Surgery of the anus, rectum and colon. 5th edition. London: Balliere Tindal, 1984.

GRADEpro GDT 2015 [Computer program]

GRADEpro GDT. Hamilton (ON): McMaster University, 2015 (developed by Evidence Prime), 2015. Available from gradepro.org.

Higgins 2017

Higgins JP, Altman DG, Sterne JA, editor(s). Chapter 8: Assessing risk of bias in included studies. In: Higgins JP, Churchill R, Chandler J, Cumpston MS, editor(s), Cochrane Handbook for Systematic Reviews of Interventions Version 5.2.0 (updated June 2017). Cochrane, 2017. Available from www.training.cochrane.org/handbook/archive/v5.2.

Higgins 2023

Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 6.4 (updated August 2023). Cochrane, 2023. Available from training.cochrane.org/handbook.

Hollingshead 2015

Hollingshead JR, Phillips RK. Haemorrhoids: modern diagnosis and treatment. *Postgraduate Medical Journal* 2015;**92**:4-8. [PMID: 10.1136/postgradmedj-2015-133328]

Jacobs 2014

Jacobs D. Clinical practice. Hemorrhoids. *New England Journal of Medicine* 2014;**371**(10):944-51.

Jayne 2021

Jayne DG, Williams AE, Corrigan N, Croft J, Pullan A, Napp V, et al. Sacral nerve stimulation versus the magnetic sphincter augmentation device for adult faecal incontinence: the SaFaRI RCT. *Health Technology Assessment* 2021;**25**(18):1-96. [DOI: 10.3310/hta25180]

Johanson 1990

Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. *Gastroenterology* 1990;**98**(2):380-6.

Kann 2004

Kann BR, Whitlow CB. Hemorrhoids: diagnosis and management. *Techniques in Gastrointestinal Endoscopy* 2004;**6**(1):6-11.

Kishik 1993

Kishik K. Secondary hemorrhage after hemorrhoidectomy. *Journal of the Korean Society of Coloproctology* 1993;**13**:461-66.

Kopljar 2011

Kopljar M, Balduzzi S, Patrlj L, Mihanovic J, Markulin H, Bakota B, et al. Topical treatment for hemorrhoids. *Cochrane Database of Systematic Reviews* 2011, Issue 11. Art. No: CD009443. [DOI: 10.1002/14651858.CD009443]

Lawes 2004

Lawes DA, Palazzo FF, Francis DL, Clifton MA. One year follow up of a randomized trial comparing Ligasure™ with open haemorrhoidectomy. *Colorectal Disease* 2004;**6**:233-5.

Lee 2018

Lee KC, Liu CC, Hu WH, Lu CC, Lin SE, Chen HH. Risk of delayed bleeding after hemorrhoidectomy. *International*

Journal of Colorectal Disease 2018;**34**:247-53. [DOI: 10.1007/s00384-018-3176-6]

Lester 1989

Lestar B, Penninckx F, Kerremans R. The composition of anal basal pressure. An in vivo and in vitro study in man. *International Journal of Colorectal Disease* 1989;**4**:118-22.

Liberati 2009

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Medicine* 2009;**6**:e1000100.

Lohsiriwat 2012

Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. *World Journal of Gastroenterology* 2012;**18**:2009-17.

Madroff 2004

Madoff RD, Fleshman JW, Clinical Practice Committee, American Gastroenterological Association. American Gastroenterological Association technical review on the diagnosis and treatment of hemorrhoids. *Gastroenterology* 2004;**126**:1463-73.

Mao 2016

Mao L, Ma L, Liu N, et al. Self-reported health problems related to traditional dietary practices in postpartum women from urban, suburban and rural areas of Hubei province, China: the 'zuo yuezi'. *Asia Pacific Journal of Clinical Nutrition* 2016;**25**(1):158-64.

McKenzie 2010

McKenzie L, de Verteuil R, Cook J, Shanmugam V, Loudon M, Watson AJ, Vale L. Economic evaluation of the treatment of grade II haemorrhoids: a comparison of stapled haemorrhoidopexy and rubber band ligation. *Colorectal Disease* 2010;**12**:587-93.

McRae 1995

MacRae HM, McLeod RS. Comparison of hemorrhoidal treatment modalities. A meta-analysis. *Diseases of the Colon and Rectum* 1995;**38**:687-94.

Mishra 2020

Mishra S, Sahoo AK, Elamurugan TP, Jagdish S. Polidocanol versus phenol in oil injection sclerotherapy in treatment of internal hemorrhoids: a randomized controlled trial. *Turkish Journal of Gastroenterology* 2020;**31**(5):378-83.

Mounsey 2011

Mounsey AL, Halladay J, Sadiq TS. Hemorrhoids. *American Family Physician* 2011;**84**(2):204-10.

NICE 2018

National Institute for Health and Care Excellence. Superior rectal artery embolisation for haemorrhoids: clinical guideline IPG627. nice.org.uk/guidance/ipg627 (Accessed 15 August 2020).

Ohning 2009

Ohning GV, Machicado GA, Jensen DM. Definitive therapy for internal hemorrhoids - new opportunities and options. *Reviews in Gastroenterological Disorders* 2009;**9**:16-26.

Piskun 2012

Piskun G, Tucker R. New bipolar tissue ligator combines constant tissue compression and temperature guidance: histologic study and implications for treatment of hemorrhoids. *Medical Devices (Auckland)* 2012;**5**:89-96.

Poskus 2014

Poskus T, Buzinskiene D, Drasutiene G et al. Haemorrhoids and anal fissures during pregnancy and after childbirth: a prospective cohort study. *BJOG* 2014;**121**:1666-71.

RevMan Web 2020 [Computer program]

Review Manager Web (RevMan Web). Version 1.22.0. The Cochrane Collaboration, 2020. Available at revman.cochrane.org.

Riss 2012

Riss S, Weiser FA, Schwameis K, Riss T, Mittlböck M, Steiner G, et al. The prevalence of hemorrhoids in adults. *International Journal of Colorectal Disease* 2012;**27**:215-20.

Ross 2012

Ross NP, Hildebrand DR, Tiernan JP, Brown SR, Watson AJ. Haemorrhoids: 21st-century management. *Colorectal Disease* 2012;**14**(8):917-9.

Rubbini 2019

Rubbini M, Ascanelli S. Classification and guidelines of hemorrhoidal disease: present and future. *World Journal of Gastrointestinal Surgery* 2019;**11**:117-21.

Rørvik 2023

Rørvik HD, Davidsen M, Gierløff MC, Brandstrup B, Olaison G. Quality of life in patients with hemorrhoidal disease. *Surgery Open Science* 2023;**12**:22-8.

Similis 2015

Simillis C, Thoukididou SN, Slesser AA, Rasheed S, Tan E, Tekkis PP. Systematic review and network meta-analysis comparing clinical outcomes and effectiveness of surgical treatments for haemorrhoids. *BJS* 2015;**102**(13):1603-18.

Sun 2016

Sun Z, Migaly J. Review of hemorrhoid disease: presentation and management. *Clinics in Colon and Rectal Surgery* 2016;**29**:22-9. [DOI: 10.1055/s-0035-1568144]

Sun 2017

Sun X, Bai X, Cheng L, Gu X, Yuan Q, Jing J, et al. Embolization of the superior and inferior rectal artery for chronic bleeding caused by hemorrhoidal disease: a case report. *Journal of Vascular and Interventional Radiology* 2017;**28**(12):1753-6. [DOI: 10.1016/j.jvir.2017.07.031]

Talaie 2022

Talaie R, Torkian P, Moghadam AD, Tradi F, Vidal V, Sapoval M, et al. Hemorrhoid embolization: a review of current evidences. *Diagnostic and Interventional Imaging* 2022;**103**:3-11.

Thomson 1992

Thomson JP, Leicester RJ, Smith LE. Haemorrhoids. In: Henry MM, Swash M, editors(s). Coloproctology and the pelvic floor. 2nd edition. London: Butterworth-Heinemann, 1992:373-93.

Tradi 2018

Tradi F, Louis G, Giorgi R, Mege D, Bartoli JM, Sielezneff I, et al. Embolization of the superior rectal arteries for hemorrhoidal disease: prospective results in 25 patients. *Journal of Vascular and Interventional Radiology* 2018;**29**:884-92.

Trompetto 2015

Trompetto M, Clerico G, Cocorullo GF, et al. Evaluation and management of hemorrhoids: Italian society of colorectal surgery (SICCR) consensus statement. *Techniques in Coloproctology* 2015;**19**:576-75.

Vidal 2014

Vidal V, Louis G, Bartoli JM, Sielezneff I. Embolization of the hemorrhoidal arteries (the emborrhoid technique): a new concept and challenge for interventional radiology. *Diagnostic and Interventional Imaging* 2014;**95**:307-15.

Violan 2013

Violán C, Foguet-Boreu Q, Hermosilla-Pérez E, Valderas JM, Bolíbar B, Fàbregas-Escurriola M, et al. Comparison of the information provided by electronic health records data and a population health survey to estimate prevalence of selected health conditions and multimorbidity. *BMC Public Health* 2013;**13**:251. [DOI: 10.1186/1471-2458-13-251]

Watson 2016

Watson AJ, Hudson J, Wood J, Kilonzo M, Brown SR, McDonald A, et al, eTHoS study group. Comparison of stapled haemorrhoidopexy with traditional excisional surgery for haemorrhoidal disease (eTHoS): a pragmatic, multicentre, randomised controlled trial. *Lancet* 2016;**388**:2375-85.

Watson 2017

Watson AJ, Cook J, Hudson J, Kilonzo M, Wood J, Bruhn H, et al. A pragmatic multicentre randomised controlled trial comparing stapled haemorrhoidopexy with traditional excisional surgery for haemorrhoidal disease: the eTHoS study. *Health Technology Assessment* 2017;**21**(70):1-224.

Yang 2014

Yang JY, Peery AF, Lund JL, Pate V, Sandler RS. Burden and cost of outpatient hemorrhoids in the United States employer-insured population, 2014. *American Journal of Gastroenterology* 2019;**5**:798-803.

ADDITIONAL TABLES

Table 1. Grades of haemorrhoids (Goligher classification)

Grade of haemorrhoids	Features
Grade I	Haemorrhoids that bleed but do not prolapse
Grade II	Haemorrhoids that prolapse but spontaneously reduce
Grade III	Haemorrhoids that prolapse and have to be manually reduced
Grade IV	Haemorrhoids that prolapse and cannot be reduced

Goligher classification (Goligher 1984).

Table 2. Example summary of findings table: endovascular embolisation of rectal arteries for symptomatic haemorrhoids

Rectal artery endovascular embolisation compared with any surgical intervention or conservative treatment for symptomatic haemorrhoids
Patient or population: symptomatic grade II and III haemorrhoids
Settings: hospital
Intervention: RAE
Comparison: any surgical intervention or conservative treatment[a]

Table 2. Example summary of findings table: endovascular embolisation of rectal arteries for symptomatic haemorrhoids *(Continued)*

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with surgical intervention or conservative treatment	Risk with RAE				
Symptom recurrence (to follow-up)	**Study population**		**RR [value]** ([value] to [value])	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**	
	[value] per 1000	**[value] per 1000** ([value] to [value])				
Early complications: bleeding (up to 3 months)	**Study population**		**RR [value]** ([value] to [value])	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**	
	[value] per 1000	**[value] per 1000** ([value] to [value])				
Late complications: sphincter damage (after 3 months)	**Study population**		**RR [value]** ([value] to [value])	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**	
	[value] per 1000	**[value] per 1000** ([value] to [value])				
Postoperative pain scores (VAS, to follow-up)	The mean [outcome] ranged across control groups from [value][measure]	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]		[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low**	

Table 2. Example summary of findings table: endovascular embolisation of rectal arteries for symptomatic haemorrhoids *(Continued)*

					⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**
Postoperative faecal incontinence scores (range of scale or scale description, to follow-up)	The mean [outcome] ranged across control groups from **[value][measure]**	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]		[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**
Length of hospital stay (days)	The mean [outcome] ranged across control groups from **[value][measure]**	The mean [outcome] in the intervention groups was **[value] [lower/higher]** [(value to value lower/higher)]		[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**
Need for reintervention (to follow-up)	**Study population** **[value] per 1000**	**[value] per 1000** ([value] to [value])	**RR [value]** ([value] to [value])	[value] ([value])	[Delete as appropriate] ⊕⊖⊖⊖ **Very low** ⊕⊕⊖⊖ **Low** ⊕⊕⊕⊖ **Moderate** ⊕⊕⊕⊕ **High**

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **RAE**: endovascular rectal artery embolisation; **RR:** risk ratio; **VAS:** visual analogue scale.

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Table 2. Example summary of findings table: endovascular embolisation of rectal arteries for symptomatic haemorrhoids *(Continued)*

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

[a] Surgical intervention may include rubber band ligation, injection sclerotherapy, transanal surgical procedure including direct surgical ablation, haemorrhoidal artery ligation operation, stapled haemorrhoidopexy, or excisional haemorrhoidectomy. Conservative treatment may include lifestyle modifications (avoiding prolonged straining); dietary measures, such as increased dietary fibre and fluid intake to avoid constipation; and topical applications such as local anaesthetics and corticosteroid creams.

APPENDICES

Appendix 1. MEDLINE search strategy

1 exp Hemorrhoids/

2 haemorhoid*.ti,ab.

3 haemorrhoid*.ti,ab.

4 haemorroid*.ti,ab.

5 hemorhoid*.ti,ab.

6 hemorrhoid*.ti,ab.

7 hemorroid*.ti,ab.

8 rectal arter*.ti,ab.

9 rectal bleed*.ti,ab.

10 or/1-9

11 exp Embolization, Therapeutic/

12 RAE.ti,ab.

13 embolization.ti,ab.

14 embolisation.ti,ab.

15 or/11-14

16 10 and 15

CONTRIBUTIONS OF AUTHORS

KK: drafted the protocol. For the full review, they will acquire trial reports; select trials; assess the risk of bias; extract, analyse and interpret the data; draft the review and future review updates, and act as a guarantor of the review.
RL: drafted the protocol. For the full review, they will arbitrate any disagreement in trial selection and risk of bias judgements; analyse and interpret data; and draft the review and future review updates.
MY: drafted the protocol. For the full review, they will acquire trial reports; select trials; assess the risk of bias; extract, analyse and interpret the data; and draft the review and future review updates.
JL: drafted the protocol. For the full review, they will acquire trial reports; select trials; extract, analyse and interpret the data; and draft the review and future review updates.
GES: drafted the protocol. For the full review, they will arbitrate any disagreement in trial selection and risk of bias judgements; analyse and interpret data; and draft the review and future review updates.
IH: drafted the protocol. For the full review, they will analyse and interpret data; and draft the review and future review updates.
ICC: drafted the protocol. For the full review, they will arbitrate any disagreement in trial selection and risk of bias judgements; analyse and interpret data; and draft the review and future review updates.

DECLARATIONS OF INTEREST

KK: none known.
RL: RL has declared that they have received payment as Proctor (Lombard Medical Limited, Terumo Cardiovascular Systems Corporation), speaking commitments (Penumbra, Inc. and ShockWave Medical), speaking engagement (W. L. Gore & Associates). RL has also declared that they work as a health professional (Consultant Vascular Radiologist, Hull University Teaching Hospitals NHS Trust, UK).
MY: none known. MY has declared they work as a health professional (NIHR Academic Clinical Lecturer in General Surgery, UK).
JL: none known.
SS: none known.
GES: GES has declared that they have received payment for lecturing (BSN Medical, Inc), and their institution received payment that they have access to or control of, for lecturing and writing evidence reviews (Essity).
IH: none known. IH has declared that they work as a health professional (consultant colorectal surgeon, Hull University Teaching Hospitals NHS Trust, UK).
ICC: none known. ICC has declared that they work as a health professional (Prof of Surgery, University of Hull, UK).

SOURCES OF SUPPORT

Internal sources

- No sources of support provided

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK

  The Cochrane Vascular editorial base is supported by the Chief Scientist Office.
- National Institute of Health and Research, UK

  Miss Yiasemidou is an NIHR Academic Clinical Lecturer in general surgery

NOTES

Parts of the methods section of this protocol are based on a standard template established by Cochrane Vascular.