A pragmatic multicentre randomised controlled trial comparing stapled haemorrhoidopexy with traditional excisional surgery for haemorrhoidal disease: the eTHoS study

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Scientific summary

The eTHoS RCT

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Scientific summary

Background

Haemorrhoids are swellings in the veins underlying the lining of the bowel at the top of the anal canal. Symptoms from haemorrhoids include bleeding, pain, prolapse and perianal itch, all of which are common within the general population.

The initial management of haemorrhoids is community-based. Persistent symptoms merit referral for investigation and treatment. Outpatient treatment principally involves rubber band ligation (RBL) for lower-grade haemorrhoids, whereas surgical interventions are used for higher-grade haemorrhoids when banding has been unsuccessful. The Goligher system for grading haemorrhoids is used widely and was adopted for this study.

Given the prevalence of the condition, the management of haemorrhoidal disease continues to have considerable workload and cost implications for the NHS, with approximately 25,000 haemorrhoidal procedures being performed as hospital day-case or inpatient admissions in England over the period of 2006–7.

Over the last two decades (1997–2017), there has been an improved understanding of the anatomy of haemorrhoids, leading to the introduction of new surgical technologies into clinical practice. These technologies include stapled haemorrhoidopexy (SH) and haemorrhoidal artery ligation (HAL). The purported advantages of the new treatments, when compared with an existing surgical technique [excisional (or traditional) haemorrhoidectomy (TH)], were less postoperative pain and equal efficacy of symptom control.

Despite numerous small-scale randomised controlled trials (RCTs), significant doubts remain about the utility, efficiency and cost-effectiveness of SH and HAL. Evidence synthesised in systematic reviews and health technology assessments has highlighted the lack of good-quality data on which to base management choices.

Objectives

The aim of the eTHoS (either Traditional Haemorrhoidectomy or Stapled haemorrhoidopexy for haemorrhoidal disease) study was to answer the question ‘is SH more clinically effective and cost-effective than TH in the treatment of II–IV-grade haemorrhoids?’ The primary objective was to compare health-related quality of life between the two treatment arms derived over 24 months.

Methods

The eTHoS study was a large, multicentre UK pragmatic two-arm parallel-group RCT to establish whether or not SH surgical treatment improves clinical effectiveness and cost-effectiveness compared with TH. A discrete choice experiment (DCE) was conducted to estimate willingness to pay (WTP).

Study design and participants

Thirty-two UK NHS hospitals were involved in the study. Patients aged ≥ 18 years, with haemorrhoids of grades II–IV and from whom written informed consent could be obtained, were eligible to take part. Participants referred to hospital with haemorrhoids were included in the study if their symptoms did not resolve with RBL or HAL, or if their haemorrhoids were thought to be too large for these treatments to be successful. Patients who had received other haemorrhoid surgery were excluded.

Randomisation

Participants were randomised using minimisation to one of the two study groups on a 1 : 1 basis, using an automated system with telephone and web-based interfaces run from the study office.

Procedures

Participants were recruited by surgeons and research nurses in the outpatient department, who were also responsible for initiating randomisation. Study outcomes were collected at baseline, 1 week, 3 weeks, 6 weeks, 12 months and 24 months. Other data collected at baseline included, height, weight, grade of haemorrhoid, anticoagulant medication prescriptions, previous treatments for haemorrhoids and participant's treatment preference.

On the day of surgery, the grade of surgeon and anaesthetist was recorded, as well as the type of anaesthesia and the surgical technique performed. In addition, the length of time the procedure took and any intraoperative complications were recorded. Data on postoperative complications prior to discharge, which included postoperative bleeding, pelvic sepsis, the need for blood transfusion and urinary retention, were collected.

Follow-up consisted of a single clinical visit at the hospital and postal questionnaires over 24 months. At the 6-week clinic appointment, data on postoperative complications, including haemorrhage, requirement for blood transfusion, anal stenosis, anal fissure, urinary retention (which required catheterisation), residual anal skin tags, difficult defaecation, wound discharge, pelvic sepsis and pruritus, were collected. Further haemorrhoid-related interventions since discharge were recorded, as well as the need for further planned medical or surgical interventions for haemorrhoids or complications associated with treatment.

EuroQol-5 Dimensions, three-level version (EQ-5D-3L) and visual analogue scale (VAS) pain data were collected by postal questionnaire at 1 and 3 weeks following surgery. The EQ-5D-3L and the Short Form questionnaire-36 items (SF-36), Haemorrhoid Symptom Score (HSS), Cleveland Incontinence Score (CIS) and VAS data were collected by postal questionnaire at 6 weeks following surgery. In addition, questionnaires distributed at 12 and 24 months after randomisation also collected data on patient-reported haemorrhoid recurrence and further operations. The main outcome assessment was planned at the 24-month (from the date of randomisation) follow-up.

Consent was sought from all participants to be flagged for notification of haemorrhoidal recurrence and, to evaluate long-term safety, the participants were investigated for further haemorrhoidal surgery through Hospital Episode Statistics (HES) in England, the Patient Episode Database Wales (PEDW) in Wales and Information Services Division (ISD) data in Scotland, when all participants had reached 12 months post randomisation.

Outcomes

The primary outcome was the area under the curve (AUC) over 24 months measured by the EQ-5D-3L at baseline, 1 week, 3 weeks, 6 weeks (post operative), 12 months and 24 months (post randomisation). The AUC is expressed in years and can be interpreted as quality-adjusted life-years (QALYs).

Patient-reported secondary outcomes were generic health profile as measured by the SF-36 and the EQ-5D-3L, VAS pain score, CIS, HSS, postoperative analgesia consumption, recurrence of haemorrhoids and tenesmus. The clinical secondary outcomes were further interventions, intra- and postoperative complications, including haemorrhage, requirement for blood transfusion, anal stenosis, anal fissure, urinary retention (which required catheterisation), residual anal skin tags, difficult defaecation, wound discharge, pelvic sepsis and pruritus. The primary study economic outcome was incremental cost per QALYs gained with QALYs based on the responses to the EQ-5D-3L over 24 months.

Results

In total, 1127 patients were screened between January 2011 and August 2014, with 777 randomised to receive either SH or TH (389 to SH and 388 to TH). There were 774 participants included in the analysis as a result of one postrandomisation exclusion in the SH arm and two in the TH arm. There were 721 participants who received surgery; of these, 37 participants randomised to SH received TH and 29 randomised to TH received SH. The remainder of participants (18 in the SH arm and 11 in the TH arm) received a non-randomised intervention, and two in the SH arm were unknown. The duration of the operation (0.4 hours) and length of hospital stay (0.4 days) was the same in each group and the median time of follow-up was 731 days [interquartile range (IQR) 377–736 days] for the SH arm and 731 days (IQR 514–738 days) for the TH arm.

The primary outcome, EQ-5D-3L AUC over 24 months, favoured TH [–0.073, 95% confidence interval (CI) –0.140 to –0.006; $p = 0.034$]. The secondary analysis over 24 months post randomisation showed no evidence of a difference between treatment arms, but favoured SH over 6 weeks post surgery. For the secondary outcomes, both the physical and mental component scores (SF-36) at 12 months post randomisation showed evidence of a difference in favour of TH [physical summary: –1.79, 95% CI –3.06 to –0.51, $p = 0.006$; and mental summary: –1.71, 05% CI –3.34 to –0.08, $p = 0.040$]. At 12 months post randomisation, more participants reported that their haemorrhoids had come back in the SH arm ($n = 94$, 31.9%) than in the TH arm (39, 14.0%) (odds ratio 2.96 95% CI 2.02 to 4.32; $p < 0.001$). This also occurred at 24 months, with more participants reporting reoccurrence in the SH arm ($n = 134$, 42.3%) than in the TH arm ($n = 76$, 25.3%). There was no clear sign of a participant treatment-preference effect.

The number of serious adverse events (SAEs) reported was 24 out of 337 (7.1%) for participants who received SH and 33 out of 352 (9.4%) for those who received TH. There were two deaths in the SH arm, both unrelated to the eTHoS study.

The mean cost per patient for SH was £941 [standard deviation (SD) £415], and £602 (SD £507) for TH. The adjusted analysis mean difference in total costs was £337 (95% CI £251 to £423) higher for SH than for TH. The QALY results for SH were 1.62 (0.43), and 1.69 (0.38) for TH. The adjusted analysis mean difference in QALYs was –0.070 (95% CI –0.127 to –0.011). Therefore, on average, SH costs were higher than those for TH, and SH had lower QALYs than TH, so it was dominated by TH. The cost–utility analysis indicated that SH had zero probability of being cost-effective at both £20,000 and £30,000 thresholds. The DCE results indicated that WTP was highest for TH, but the values were not statistically significantly different. Although total WTP estimates were positive for both treatments (£1277 for SH and £1367 for TH), the net benefit was higher for TH than that for SH (£765 vs. £330).

Conclusions

The eTHoS study showed better generic quality-of-life scores over the 24-month follow-up period for TH over SH. Short-term post-surgery quality-of-life scores favoured SH, reflecting the lower rates of pain in the immediate postoperative period. SH was less painful, but this difference disappeared by 6 weeks. At 12 months, the EQ-5D-3L quality-of-life scores were similar; however, the physical and mental health domains of the SF-36 favoured TH. At 24 months the primary outcome favoured TH. In addition, there were also fewer residual haemorrhoid symptoms, recurrences and re-interventions.

Both treatments showed similar operating times, length of stay and return to normal activity at 6 weeks. This refutes the common argument that a shorter operating time and length of stay after SH offsets the cost of a stapler.

Clinical recurrence of haemorrhoids was measured using the HSS, a patient-reported dichotomous outcome measure, and recurrence data were collected from national registry databases (HES, ISD and PEDW). We chose to assess recurrence over 24 months, expecting to capture a proportion of patients who report symptom relapse after 12 months.

Continence was an important outcome measure for this study. As expected, in the immediate postoperative period, the scores were relatively impaired when compared to the baseline. Thereafter, continence scores were significantly better in the TH arm up to 24 months after randomisation.

The economic analysis convincingly demonstrated that TH dominates SH, as it costs £337 less than SH and is 0.07 QALYs more clinically effective than SH. SH has a $< 1\%$ probability of being considered cost-effective at the £30,000 threshold. The results of the economic analysis differ from work previously published that reported that TH and SH had similar costs and QALYs, but the costs of a staple gun were offset by savings in length of hospital stay. In our study, the length of inpatient stay was similar across both groups, so there were no cost-savings in that area, and our QALY results, based on a 2-year follow-up period, indicated that SH had fewer QALYs than TH.

The main limitations of this study are twofold; final recruitment to eTHoS was just short (97%) of the target number and, furthermore, there were substantial and greater than expected missing data at the 24-month follow-up, despite multiple strategies to mitigate this. This perhaps reflected the population (working age), the condition (chronic and considered by some to be a sensitive subject) and the nature of the follow-up. Nevertheless, the study still had sufficient statistical precision to detect differences between treatment groups. There was also a noticeable level of non-compliance with allocation (some not receiving surgery, and some receiving a different operation), reflecting, perhaps, a mixture of clinical reality and some surgeon and patient preferences regarding treatment. Such non-compliance tends to dilute a genuine effect. Despite this, the primary analysis still supported a difference in favour of TH, and the per-protocol analysis of only those who complied with allocation was consistent with this finding. Participant treatment preferences also did not seem to affect the findings. More generally, it is worth noting that the delivery of the interventions reflected routine clinical practice across a range of centres in terms of the surgeons participating (their experience) and how the interventions were delivered (specific technique and centre practices). Taken together, we believe the findings are robust and generalisable.

Despite some published postoperative complications having been severe, particularly with regard to pelvic sepsis, rectal perforation and rectovaginal fistula formation, in the introduction of a new surgical treatment there were no reports of these complications within this study. SAEs were equally distributed through both arms of the eTHoS study. All the events were expected and largely consisted of pain, bleeding, constipation and urinary retention.

This study is among the largest RCTs for haemorrhoids ever carried out. No prescriptive entry criteria were set for hospital inclusion and we are therefore confident that the results are generalisable. A 24-month follow-up period was used to capture symptom recurrence and further interventions; therefore, a median follow-up of 731 days is a further strength of this study. A pragmatic approach to surgeon's credentials was adopted. At the inception of the study, both SH and traditional excisional surgery were established in common surgical practice and surgeons were required to have undergone appropriate recognised training for both procedures. The effect of surgical experience on outcomes can partially be mitigated by the high level of consultant involvement in performing the surgery (71.5% in the SH arm and 62.0% in the TH arm) and the low incidence of adverse events.

Traditional haemorrhoidectomy is both more clinically effective and less costly than SH; it is more painful in the short term. Return to normal activity rates were equal. In addition to superior quality-of-life measures, HSS, continence and tenesmus rates and the need for further surgery were all lower in TH. TH is, therefore, a superior surgical treatment for the management of grades II–IV haemorrhoids than SH.

Future work should include an updated network meta-analysis that encompasses the results from this trial and other large contemporary trials on haemorrhoids.

Trial registration

This trial is registered as ISRCTN80061723.

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