

Cost-effectiveness of New Surgical Treatments for Hemorrhoidal Disease

A Multicentre Randomized Controlled Trial Comparing Transanal Doppler-guided Hemorrhoidal Artery Ligation With Mucopexy and Circular Stapled Hemorrhoidopexy

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Objective: To compare Doppler-guided hemorrhoidal artery ligation (DGHAL) with circular stapled hemorrhoidopexy (SH) in the treatment of grade II/III hemorrhoidal disease (HD).

Background: DGHAL is a treatment option for symptomatic HD; existing studies report limited risk and satisfactory outcomes. DGHAL has never before been compared with SH in a large-scale multi-institutional randomized clinical trial.

Methods: Three hundred ninety-three grade II/III HD patients recruited in 22 centers from 2010 to 2013 were randomized to DGHAL (n = 197) or SH (n = 196). The primary endpoint was operative-related morbidity at 3 months (D.90) based on the Clavien-Dindo surgical complications grading. Total cost, cost-effectiveness, and clinical outcome were assessed at 1 year.

Results: At D.90, operative-related adverse events occurred after DGHAL and SH, respectively, in 47 (24%) and 50 (26%) patients (P = 0.70). DGHAL resulted in longer mean operating time (44±16 vs 30±14 min; P < 0.001), less

pain (postoperative and at 2 wks visual analogic scale: 2.2 vs 2.8; 1.3 vs 1.9; P = 0.03; P = 0.013) and shorter sick leave (12.3 vs 14.8 d; P = 0.045). At 1 year, DGHAL led to more residual grade III HD (15% vs 5%) and a higher reoperation rate (8% vs 4%). Patient satisfaction was >90% for both procedures. Total cost at 1 year was greater for DGHAL [€2806 (€2670; 2967) vs €2538 (€2386; 2737)]. The D.90, incremental cost-effectiveness ratio (ICER) was €7192 per averted complication. At 1 year DGHAL strategy was dominated.

Conclusions: DGHAL and SH are viable options in grade II/III HD with no significant difference in operative-related risk. Although resulting in less postoperative pain and shorter sick leave, DGHAL was more expensive, took longer, and provided a possible inferior anatomical correction suggesting an increased risk of recurrence.

Keywords: circular stapled hemorrhoidopexy, cost-effectiveness, Doppler-guided artery ligation, hemorrhoidal disease, morbidity, multicenter randomized trial, outcome, patient satisfaction, risk assessment, surgical treatment

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Hemorrhoidal disease (HD) is a common reason to see a colorectal specialist. The decision for surgery is often guided by the grade of hemorrhoidal prolapse.¹ Patients with HD have several surgical options available to them, particularly with grade (G)II and GIII hemorrhoids; recent less invasive procedures include the following: stapled hemorrhoidopexy (SH) and subsequently Doppler-guided hemorrhoidal artery ligation (DGHAL).^{2–6}

Stapled hemorrhoidopexy is widely performed in France with a tariff since 2007. SH is a standard treatment for GIII and selected GII HD despite rare adverse events (AEs).^{7,8} As an alternative, DGHAL could be considered as less invasive, although not yet on the French tariff.⁵ Current literature contains only small randomized clinical trials (RCTs) between SH and DGHAL, and most studies are case studies.^{9–11}

The cost of these techniques has yet to be compared, although HD surgery has significant implications for health service resources: the French database recorded 27,606 surgical procedures for HD in 2013; similar figures have been recorded in comparable countries.^{12–14}

We report hereby the results of a multicenter RCT identified as “LigaLongo” and conducted under the auspices of the French Ministry of Health. The trial postulated the hypothesis that “DGHAL with less postoperative risk and a lower risk of sequelae is more cost-effective in comparison to SH.”

METHODS

Patient Selection

Adult patients with bleeding and/or prolapsing HD classified as GII (spontaneously reduced after defecation) or GIII (requiring digital reduction) hemorrhoids were given information about the trial.¹ Those who accepted trial entry were randomly assigned treatment by either DGHAL or SH. Common exclusion criteria were applied (see SDC1, Text 1, <http://links.lww.com/SLA/B20>).

Baseline and follow-up assessment included a past medical history, clinical examination, and HD grading, symptom and quality-of-life (QoL) [The Short Form (36) Health Survey (SF36)] questionnaires, pain level, and work activity.^{1,7,15}

Procedures

Randomization was carried out online and stratified according to HD grade (see SDC2, Text 2, <http://links.lww.com/SLA/B20>). Investigators did not vary from their normal practice for patient care. Both procedures have already been described.^{5–7} DGHAL was carried out using THD (THD, Correggio, Italy; 106 patients) and AMI HAL-RAR (A.M.I.GmbH, Feldkirch, Austria) devices (96 patients; unrecorded: 1). After anal dilation and proctoscopy, a series of Doppler-guided absorbable sutures were placed to interrupt hemorrhoidal artery blood flow. Vertical mucopexy was carried out on hemorrhoidal prolapses upon request. SH was carried out using a PPH-03 (Ethicon Endo-Surgery, Cincinnati, OH; 106 patients) and a HEM stapler (Covidien, Inc.; 79 patients, unrecorded: 5).

Endpoints

Patient data were collected over 13 months. Patients were evaluated 1 month before surgery and were reviewed at Day 15 (D.15), 3 months (D.90), Month 6 (M.6), and Month 12 (M.12). Unscheduled visits were also recorded. The reporting of AE was done using the Clavien-Dindo grading system adapted to HD surgery.^{16,17} Pain levels, analgesics consumption, hospital stay, and sick leave were all recorded.¹⁵

Primary Endpoint

The trial primary endpoint was defined as the morbidity rate at D.90 postoperatively for both procedures, and computed as “the percentage of patients suffering 1 or more AE according to the

procedure-related complication score,” whatever the grade of complication.¹⁶

Secondary Endpoints

Cost-effectiveness

The prospective economic evaluation was concurrent to the RCT as per the Consolidated Health Economic Evaluation Reporting Standards recommendations.¹⁸ The analysis was conducted from a healthcare perspective to determine the cost per averted AE, with DGHAL compared with SH over a 90-day and a 1-year period. Both hospital and nonhospital resources were considered and valued using actual costs (hospital resources), or tariffs and compensation (days off work). Health outcomes for the economic evaluation were measured by the primary clinical endpoint at D.90 and M.12. Costs are expressed as 2015 Euro (€) and not discounted.

Clinical Endpoints

The comparison between the procedures was made for the number/type of intraoperative AEs, number/severity of postoperative AEs at D.90 after surgery, and the success rate in the reduction of HD at M.12. Persisting or recurrent symptoms were recorded. In cases of multiple AEs, the most serious was recorded.

Sample Size Calculation

The superiority of DGHAL compared with SH was expected with respect to the primary endpoint. We foresaw a possible switch to a noninferiority study, should the superiority of DGHAL not be proven. Therefore, the trial was planned to demonstrate the noninferiority of DGHAL, defined as a complication rate lesser or equal to the complication rate of SH (equal to 15% from a literature search) proportionally increased by 20% (ie, $15\% \times 20\% = 3\%$ for the planning step). This increase is considered clinically insignificant. Power and type I error were defined, respectively, at 80% and 5%, the required sample size was computed at 438 and 420 patients, respectively, for a superiority or a noninferiority analysis.

Statistical Analysis

Continuous and qualitative variables were, respectively, described as a mean \pm standard deviation (SD) and percentages. Intergroup comparisons of complications and costs were performed using statistical tests adapted to group sizes (Student, chi-square, Mann-Whitney, and Fisher exact tests).

Primary Endpoint

To switch to a noninferiority analysis, we used the superior limit of the unilateral 95% confidence interval (CI) of the complication rate in the DGHAL group. The demonstration of DGHAL noninferiority in terms of complications is defined by a limit inferior to that of the SH group, proportionally increased by 20% (noninferiority margin).¹⁹

Economic Evaluation

Univariate sensitivity cost-analyses were performed and represented on tornado diagrams. A joint comparison of costs and effects was performed by bootstrapping with 1000 resamples, and the result of the bootstrap replications presented on cost-effectiveness planes.

The significance threshold was <0.05 .

Ethical Committee Approval

The study protocol was approved by the “Ouest-1” Ethical Committee (Tours, France; Ref: 2010-R26) for all investigating

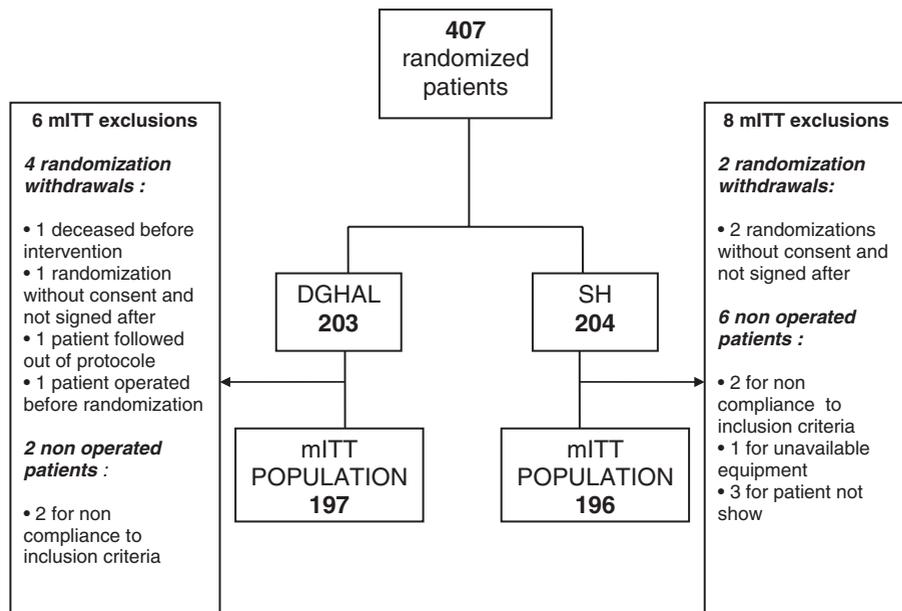


FIGURE 1. Flow chart—“LigaLongo” RCT. Note: 14 patients excluded in the modified intention-to-treat (mITT) population.

centers. Informed consent was obtained from each patient (except for 3 patients subsequently excluded from the analysis). A detailed information leaflet was provided to patients and they were informed of the assigned procedure when entering the hospital for surgery.

RESULTS

Baseline

Twenty-two French public institutions with expertise in the management of HD registered as investigators. Over a period of 29 months (September 2010–January 2013), ending with the last follow-up visit on February 28, 2014, 407 patients (DGHAL n = 203; SH n = 204) were recruited (Fig. 1).

At baseline, the 2 groups were well matched (Table 1). Respectively, 91(23%) and 302 (77%) patients had GII and GIII HD, which was circumferential in 27%. No difference was found at baseline with respect to pain levels, symptoms, disease severity

TABLE 1. Patient Characteristics

| Variable Category | Frequencies, % | |
|--------------------------|--------------------|--------------------|
| | DGHAL (n = 197) | SH (n = 196) |
| Male patients | 121 (61%) | 126 (64%) |
| Age, yrs* | 50.0±11.7 | 50.5±12.6 |
| Body mass index* | 24.6±3.6 | 24.7±4.4 |
| Work activity | 133 (67%) | 120 (61%) |
| Grade II/III [1]† | 45 (23%)/152 (77%) | 46 (23%)/150 (77%) |
| Anticoagulant medication | 15 (8%) | 12 (6%) |
| Previous treatments | | |
| Medical | 151 (76%) | 136 (69%) |
| Instrumental | 60 (31%) | 60 (31%) |

Center recruitment amongst the 22 French public investing centers. Patient range: 1–75; mean: 17.9; median: 9.5 (a sensitivity analysis excluding low-volume centers did not change the primary outcome).

*Mean ± SD.

†No difference in terms of ease of anal examination/proctoscopy (difficult to assess clinically, n = 10 vs n = 11 patients), presence of external hemorrhoids (n = 65 vs n = 71), and/or tags (n = 78 vs n = 91) or anal tone.

score, QoL, or stool consistency (see SDC3, Table 1, <http://links.lww.com/SLA/B20>).

Surgery

The procedure was performed under general anesthesia in 94% of cases within half a Ropivacaine pudendal nerve block. The procedure was completed in a time of 37±16 minutes (range 9–94). The duration of the procedure and operating room (OR) occupation was significantly longer with DGHAL (see SDC4, Fig. 1, <http://links.lww.com/SLA/B20>). The number of arterial ligations and mucopexies was, respectively, 7.3±2.4 and 3.6±1.9. In the SH group, the staple line was 2.5±2.0 cm above the dentate line. Doughnut width was 2.8±1.2 cm. HD external components were excised in 11% of cases with DGHAL and 9% with SH.

The assigned procedure was not performed for 12 patients (see SDC5, Text 3, <http://links.lww.com/SLA/B20>). Intraoperative device dysfunctions were reported in 12 DGHAL (nonfunctioning Doppler probe) and 2 SH (purse string fracture, empty staple cartridge) procedures.

Hospital Stay

Mean hospital stay was 1.2±1.2 days in each group. Out-patient surgery was more often performed for DGHAL (n = 64, 35% vs n = 52, 25%; P = 0.20). Visual analogic scale pain score on discharge was significantly less for DGHAL (2.2±1.9 vs 2.8±2.2; P = 0.003). In-hospital operative-related AEs were reported for 23 patients (6%) (DGHAL: 10; SH: 13; NS), and the most frequent complication was urinary retention (DGHAL: 6; SH: 4).

Follow-up to D.90

Primary Endpoint at D.90

Ninety-seven patients (25%; DGHAL: 47, SH: 50) experienced 1 or more procedure-related postoperative AEs before D.90, including those recorded during hospitalization (Table 2). One hundred fourteen AEs occurring in 63 patients were deemed not procedure-related. No statistical difference was found between the 2 groups with respect to the trial hypothesis, and as foreseen in the

TABLE 2. Adverse Events (AEs) Classified According to Clavien-Dindo* Grading System at D.90 (primary endpoint), and From D.90 to M.12, With Repartition and Details (Secondary Clinical Endpoints)

| Grade* | Patients Suffering At Least 1 AE† N AE and Details§ | Frequencies (% of the All Group) | | P |
|--------------------------|--|-----------------------------------|-----------------------------------|-------|
| | | DGHAL (n = 197) | SH (n = 196) | |
| At D.90 | | | | |
| Total† | n = 97 (25%) AE = 132 | 47 (24%) AE = 64 | 50 (26%) AE = 68 | 0.70 |
| 1 | n = 52 AE = 80 | 27 (14%) AE = 40 | 25 (13%) AE = 40 | 0.78 |
| | Urinary retention | 11 | 10 | |
| | Symptomatic anal complication (thrombosis, fissure, etc) | 18 | 6 | |
| | Impaction | 5 | 9 | |
| | Local infection | 2 | 2 | |
| | Incontinence or urgency impairing normal recovery | 4 | 13 | |
| 2 | n = 33 AE = 38 | 17 (9%) AE = 21 | 16 (8%) AE = 17 | 0.87 |
| | Bleeding either exteriorized or retroperitoneal | 12 | 8 | |
| | Severe septic complications | 1 | 2 | |
| | Severe pain requiring prolonged hospital stay or rehospitalisation | 8 | 7 | |
| 3 | n = 12 AE = 14 | 3 (2%) AE = 3 | 9 (5%) AE = 11 | 0.087 |
| | Surgical reoperation whatever the indication¶ | 3 | 11 | |
| From D.90 to M.12 | | | | |
| Total† | n = 47 (12%) AE = 55 | 28 (14%) AE = 34 | 19 (10%) AE = 21 | 0.17 |
| 1 | n = 20 AE = 24 | 10 (5%) AE = 12 | 10 (5%) AE = 12 | 0.99 |
| | Symptomatic anal complication/recurrence | 10 | 2 | |
| | Impaction | 2 | 1 | |
| | Local infection | 0 | 2 | |
| | Incontinence or urgency | 0 | 7 | |
| 2 | n = 4 AE = 6 | 2 (1%) AE = 4 | 2 (1%) AE = 2 | 0.65 |
| | Persisting bleeding | 4 | 2 | |
| | Severe septic complications | 0 | 0 | |
| | Severe pain | 0 | 0 | |
| 3 | n = 23 AE = 25 | 16 (8%) AE = 18 | 7 (4%) AE = 7 | 0.055 |
| | Surgical reoperation whatever the indication | 18 | 7 | |

*Adapted from the postoperative therapy-oriented complication score [14]—no grade 4 (severe organ failure/intensive care required) or 5 (death) declared in the trial series.

†In the all series, respectively, grades 1, 2, and 3 represent 61%, 29%, and 9% of the observed AEs.

‡According to the protocol in case of more than 1 AE for a patient the highest grade has been recorded.

§Respectively, in groups DGHAL and SH, 34 and 40 patients, 12 and 12, and 2 and 1 suffered 1, 2, or 3 and more AEs.

¶Grade 3 (need reoperation) AEs: 14 before D.90: DGHAL: fissure, thrombosis, prolapse (1 each); SH: bleeding (6), pain (1), stenosis (1), fissure (2), prolapse (1).

||No significant difference in any endpoints.

protocol, a switch to a noninferiority analysis was performed. Since the CI entirety (0%; 28.9%) is above the obtained value (30.6%), the noninferiority of DGHAL versus SH in terms of rate of complications at D.90 with a 5% type I error was demonstrated and confirmed in the per-protocol analysis [the 95% unilateral CI (0%; 30.5%) does not include the 33.5% threshold].

Secondary Clinical Endpoints at D.90

There was a statistical difference in pain levels (1.3 ± 1.9 vs 1.9 ± 2.1 ; $P = 0.013$) during the second postoperative week, but not in analgesic requirements (37% vs 44%; $P = 0.17$). At D.90, pain levels (1.1 ± 1.9 vs 1.2 ± 1.8 ; $P = 0.57$) and analgesic requirements (5 vs 10; $P = 0.18$) were similar. One hundred sixty-six out of 253 working patients (62.1%) had an initial sick leave of 13.6 ± 7.8 days (DGHAL: 12.4 ± 8.2 vs SH: 14.8 ± 7.3 ; $P = 0.045$) and 21 (DGHAL: 7 vs SH: 14; $P = 0.11$) delayed returning to work (DGHAL: 17.6 ± 22.0 vs SH: 24.9 ± 23.0 d; $P = 0.37$).

Seventeen patients were readmitted up to D.15 (DGHAL: 9; SH: 8). Reasons included bleeding (DGHAL: 3; SH: 4), urinary

retention (DGHAL: 3; SH: 2), thrombosis/abscess (DGHAL: 3; SH: 2). From D.15 to D.90, only 1 SH patient was readmitted (painful chronic fissure; Table 2).

Follow-up From D.90 to 1 Year

At M.6 and M.12, 338 (86%) and 329 (84%) patients were reassessed (DGHAL: 170, 167; SH: 168, 162; Table 2).

At M.6, proctologic examination was considered difficult in 4 and 7 patients ($P = 0.54$). Hypertrophic external hemorrhoids (35.2% vs 17.1%; $P = 0.006$) and hemorrhoidal prolapse (25.1% vs 13.8%; $P = 0.049$) were significantly more common after DGHAL. GIII hemorrhoids were seen in 9% and 4% of the patients ($P = 0.27$).

At M.12, data on anal examinations were similar to that at M.6, with more GIII HD after DGHAL (15% vs 5%; $P = 0.007$). There was no difference in pain levels (DGHAL 1.0 ± 1.9 vs SH 0.9 ± 1.6 ; $P = 0.47$), analgesics (5 vs 2; $P = 0.28$), QoL, and satisfaction score (82.8 ± 25.6 vs 83.1 ± 25.1 ; $P = 0.94$)⁷ (see SDC3, Table 1, <http://links.lww.com/SLA/B20>). Both groups

TABLE 3. Comparison of Direct and Total Costs—“Ligalongo” RCT

| | Costs Mean [95% CI] | DGHAL (n = 197) | SH (n = 196) | P |
|------|---------------------|---------------------|---------------------|---------|
| D.90 | Direct* | €2406 [€2317; 2524] | €2123 [€2016; 2250] | <0.0001 |
| | Total† | €2619 [€2514; 2755] | €2421 [€2286; 2575] | 0.0002 |
| M.12 | Direct* | €2579 [€2462; 2722] | €2234 [€2111; 2397] | <0.0001 |
| | Total† | €2806 [€2670; 2967] | €2538 [€2386; 2737] | <0.0001 |

Procedure costs were obtained with a bottom-up microcosting approach identifying all relevant cost components of the procedure and valued each component for all individual patients using procedure duration, staff, devices, and type of OR as variables. Cost of medical devices were the manufacturers’ retail price (including a mean €400 for the probe in DGHAL), staff costs for the surgical procedure were estimated from gross salaries and OR costs from the hospital’s accounting systems (pathology examination of the doughnut in SH group cost a mean €26). Out-of-hospital costs were based on tariffs.

Costs were compared using nonparametric tests. 95% confidence intervals were generated using bootstrap replications.

*Direct costs (in €2014) relates to in-hospital and out-of-hospital management during the follow-up period.

†Total costs include the compensated days-off work fees.

(DGHAL 93%, SH 94%; $P = 0.67$) would recommend their operation (see SDC3, Table 1, <http://links.lww.com/SLA/B20>).

From D.90 to M.12, 47 patients (25%) experienced HD problems. Sixteen (8%) DGHAL and 7 (4%) SH ($P = 0.055$) required further surgery and sick leave (7 vs 4 cases). No unusual complications were reported.

Health Economics

Cost comparison for the index admission procedure and the contribution of each cost item to uncertainty at D.90 and M.12 are presented (Table 3; see SDC6, Tornado diagram 1, <http://links.lww.com/SLA/B20>).

At D.90 and M.12, mean direct and indirect total cost was higher for DGHAL than for SH, respectively, by €198 ($P < 0.001$) and €268 ($P < 0.001$). At D.90, there was a 67% chance that DGHAL would be more effective but also more costly than SH, with an ICER of €7192 (direct and indirect costs) or €12,007 (direct costs only) per averted complication, whereas at M.12, DGHAL was less effective and more costly (ie, dominated; Fig. 2).

DISCUSSION

Hemorrhoidal disease can be successfully treated using less aggressive surgery.² SH is associated with less pain and a faster

recovery when compared with standard excisional hemorrhoidectomy. Despite the outlay on the disposable device, it can be cost-effective.^{14,20} DGHAL based on a different concept is even less invasive, appropriate for outpatient surgery with low postoperative pain and reduced sick leave, as recently reported.²⁰ To date, there has been no significant study comparing the 2 procedures.

The present study also aimed to fill a gap between ongoing trials on HD management.^{21–23} The “LigaLongo” trial was conducted within the day-to-day practice of 22 public centers, and should be interpreted in the context of the French healthcare system.

The primary endpoint differs from recent HD studies; we focused on safety by looking at AEs according to the Clavien-Dindo grading system.^{17,24} The hypothesis that DGHAL is less risky compared with SH has not been confirmed in this trial. However, switching to a noninferiority study, we can conclude that DGHAL does not produce a significantly higher risk than SH. In fact, our AE data are similar to previous studies.²⁴ DGHAL is, however, not without complications; significant postoperative pain and/or urinary retention were, respectively, reported in 13.0% and 8.6% of cases in a large series, with an overall morbidity of 18%.²¹ In a smaller series, 24% of patients suffered complications after DGHAL with severe pain (16%), bleeding (7%), constipation (7%), local sepsis (6%), anal fissure (5%), and temporary incontinence (2%).¹³ In another small

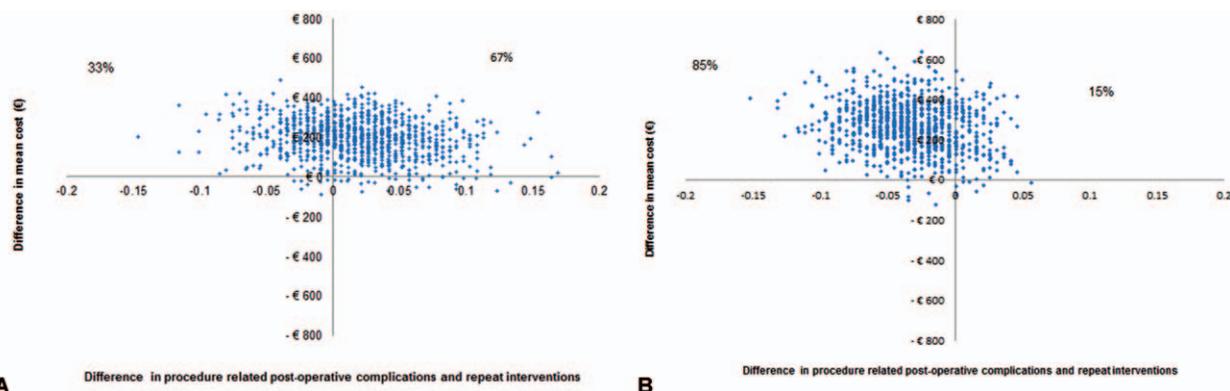


FIGURE 2. Uncertainty associated with cost-effectiveness as scatter plot of mean cost and mean effectiveness differences. Note: D.90 and M.12 cost and effectiveness of DGHAL versus SH. Costs (in €2015) include direct healthcare cost and compensated days-off work. Effectiveness is measured by the rate of patients with at least 1 postoperative complication or repeat intervention during the initial admission and follow-up period. At D.90, 67% of replications are located in the upper right quadrant, indicating that DGHAL is more expensive and more efficient than SH. At M.12, 85% of replications are located in the upper left quadrant, indicating that DGHAL is still more expensive, but less efficient (ie, dominated) than SH.

RCT comparing DGHAL with open hemorrhoidectomy, whereas postoperative peak pain was significantly lower in DGHAL during the first week, there was no overall difference in pain.²⁶ However, DGHAL patients expressed earlier normal well-being, took less analgesics, and resumed professional activities earlier, as in the present trial. In this study, patients undergoing DGHAL had less postoperative pain and a faster return to work. Similarly, SH also seems to be a safe procedure without major complications and only a limited number of expected AEs.

In follow-up, both procedures showed equivalent results in terms of symptom reduction, QoL, and overall satisfaction. Long-term pain was not an issue in either group. Some SH patients experienced minor incontinence or urgency, not seen in the DGHAL group, but these symptoms did not persist. The excellent satisfaction rates after DGHAL in this study confirm other studies.^{5,6,13,23,25} Residual or recurrent HD has been a concern after DGHAL, especially when performed for higher grades of HD, estimated at 8.7% at 12 months in a recent study. Other studies report between 0% and 20%.^{10,12,21} Our findings of a higher number of GIII HD at 1 year after DGHAL, with the need for albeit minor procedures, are concerning, although long-term results with DGHAL are not yet available in current literature. Are the initial benefits offset by an increased risk of late failure as reported for SH?² Perhaps, careful patient selection, dietary advice, and hygienic behavior may improve long-term results.

This study is the first to perform a robust economic comparison between DGHAL and SH with careful collection of cost data.²⁷ It also provides solid data for resource allocation in the management of HD. We observed during the trial that DGHAL resulted in a modest but significant increase in healthcare costs, partly compensated by a decrease in sick leave. At 12 months, DGHAL seemed finally dominated. The resource utilization and costs of SH in our study were comparable with those previously reported.^{14,28,29} A cost-utility analysis was not performed in the absence of a significant difference of SF36.¹⁴ In this study, the duration of DGHAL and the OR occupation times were about 10 minutes longer than previously reported.^{21,25} Although DGHAL was more frequently performed with outpatients than SH, the mean hospital length of stay was actually >1 day for DGHAL patients, longer than in other series. Reducing OR time and the length of stay for DGHAL could make the procedure cost-effective compared with SH. Indeed, is Doppler arterial guidance really necessary? Systematically positioning ligations and mucopexies around the anal canal may be sufficient as reported in a single-center RCT, potentially cutting time and equipment costs.³⁰

Several limitations in our study need to be taken into account when interpreting the results. Firstly, we failed to reach the required sample size, although a reasonable cohort size for comparison was studied and a majority of patients were followed up at 1 year. The sample size allows the conclusion that DGHAL is certainly no worse when compared with SH in terms of complications. Secondly, we were unable to set up an independent postoperative assessment. However, independently filled questionnaires and records of any re-do surgery are solid data. Although investigators underwent training and had to perform 10 DGHAL before entering patients into the trial, they were probably less familiar with DGHAL.^{13,26} Finally, the disparity in center recruitment could have affected the results (Table 1), although no significant center effect was identified.

CONCLUSIONS

In this RCT, we report that both DGHAL and SH are viable, safe, and effective treatments for GII to GIII HD, confirming results of other studies.²⁵ Postoperative outcomes slightly favor

DGHAL. However, a superior anatomical correction associated with only a marginal increase in pain and no additional morbidity make SH a suitable surgical treatment option for GIII symptomatic hemorrhoids. Conversely, the DGHAL shorter postoperative recovery and lower pain would be appealing for patients especially GII HD informed of the potential risk of incomplete success and recurrence.

Cost analysis showed SH to be cheaper than DGHAL. To be cost-effective compared with SH, DGHAL has to take less than 35 minutes and be performed with outpatients, an achievable goal according to literature.

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DISCUSSANTS

D. Winter (Dublin, Ireland):

Thank you for the opportunity to read this manuscript detailing a multicenter trial in which patients with grade II/III hemorrhoids were randomly assigned to stapled hemorrhoidectomy or Doppler-guided hemorrhoidal artery ligation. Congratulations on achieving an enrolment of 393 patients across 22 centers with 3 month of follow-up of morbidity (the primary outcome) and 1 year analysis of efficacy and cost (secondary outcome). There was no difference in primary outcome with adverse events recorded in a quarter of patients.

Do the authors accept this to be a real result rather than a type II error given that the sample size was not achieved (for either

superiority or noninferiority) according to the power calculation? Were the authors surprised by a higher morbidity in the stapled hemorrhoidectomy group than the expected 15% and do they have any suggestions how to lower it?

Doppler-guided hemorrhoidal artery ligation took 50% longer to perform and was more costly. Do subtle differences in pain (0.6 on a visual scale) and recuperation (barely significant) make up for these deficiencies?

The fact that Doppler-guided ligation led to a 3-fold higher residual/recurrent prolapsing haemorrhoid tissue requiring reoperation in twice as many patients is deeply concerning. Do the authors have any tips on how this could be reduced (? routine mucopexy) or should Doppler-guided ligation be abandoned as an operation?

Thank you for performing a very useful, informative, and practice-changing trial.

Response From P.-A. Lehur (Nantes, France):

Thank you for your comments and questions.

We have a large enough cohort (nearly 200 patients in each arm). Most certainly we can rule out a type II error with the RCT. For both groups, there were no major adverse events. Our study gives also precise information on cost. We stopped the study after 3 years because it was not easy to proceed further.

Regarding a higher morbidity than expected, this probably relates to a careful and longer postoperative assessment in this RCT. More information to prevent adverse events will come from subgroups analysis presently underway (comparison between devices or according to HD grades).

The study results did not confirm our trial hypothesis, which is frequently the case when doing a trial. Within the limitation of this trial, there are no major benefits to use DGHAL to treat grades II and III HD. The role of Doppler guidance is presently debated and could perhaps be abandoned reducing cost without clinical difference in outcome. For sure patients have to be fully instructed of the “pro and cons” of both techniques to select accordingly their procedure.

S. Biondo (Barcelona, Spain):

I would like to congratulate Prof Lehur et al for their interesting work. Could you comment on the surgical training of the involved surgeons? Were they all colorectal surgeons? Was there a minimum number of operations before studying the inclusion patients? In your opinion, what do you think about THD in grade IV hemorrhoids since in the literature good results have been reported?

Response From P.-A. Lehur (Nantes, France):

Thank you for asking on these clarifications. I am also in favor of DGHAL in selected patients. When starting the trial to introduce DGHAI in France, which is not yet reimbursed the investigators were probably not as much of an expert as you are in doing that procedure. However, it is of interest to observe that the SH provided safe and satisfactory outcome at 1-year follow-up. Our trial was a “real-life” study (22 centers - confirmed colorectal surgeons and proctologists in all centers well knowing HD management). It provided an excellent survey of the French practice at the time of the trial in the treatment of hemorrhoids. Regarding grade 4 HD, we are not presently recommending DGHAI in that situation and wait for convincing evidence.