# Ligation of intersphincteric fistula tract (LIFT) for trans-sphincteric cryptoglandular anal fistula: long-term impact on faecal continence

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#### Abstract

**Background:** The ligation of intersphincteric fistula tract is a surgical technique designed to treat trans-sphincteric anal fistulas aiming to preserve sphincter integrity. Recent studies suggest its efficacy in short-term fistula healing with limited impact on continence. However, comprehensive prospective data on long-term outcomes, including recurrence and bowel continence, are limited. The present study aims to report on the long-term functional outcomes.

**Methods:** Patients who underwent the ligation of intersphincteric fistula tract procedure for trans-sphincteric cryptoglandular anal fistulas between July 2012 and October 2018 at two Dutch referral centres were retrospectively reviewed. The primary outcome of interest was the long-term bowel continence after the ligation of intersphincteric fistula tract procedure, using the faecal incontinence severity index. Short-term data (collected in 2018) and long-term data (collected in 2023) on bowel continence, healing rates and recurrences were obtained through electronic records and Rockwood questionnaires. Sankey diagrams were used to visually represent individual variations in continence status (preoperative versus follow-up).

**Results:** Among 110 patients included (50% female, median follow-up 92 months), 101 patients (92%) were treated with previous surgeries (median 2, range 0–6) and 80% had previous seton drainage. Preligation of intersphincteric fistula tract, 16% of the patients reported incontinence (mean(s.d.) faecal incontinence severity index: 2.4(7.5), increasing to 18% after ligation of intersphincteric fistula tract at short-term follow-up, including 11% newly induced cases. Long-term follow-up collected using Rockwood questionnaires (63% response rate) in 69 patients uncovered a 74% incontinency rate (mean(s.d.) faecal incontinence severity index: 9.22(9.5). In those patients without subsequent surgery 49% (17 of 35) reported incontinence at long-term follow-up. Primary fistula healing after ligation of intersphincteric fistula tract was 28%. Preoperative seton drainage significantly improved healing rates (33% versus 9%). Notably, 43% (34 of 79) of unhealed fistulas transitioned into intersphincteric tracts; in these patients, 19 were treated with subsequent fistulotomy achieving cure in 18 cases.

**Conclusions:** Ligation of intersphincteric fistula tract healing rates fell below recent literature standards. Although the immediate impact on postoperative continence appears minimal, long-term incontinence rates are concerning. In recognizing the deterioration of individual continence, we advocate for a patient-centered approach and urge fellow researchers and clinicians to collect comprehensive prospective continence data.

## Introduction

The management of trans-sphincteric anal fistulas remains challenging due to the involvement of the anal sphincter complex and the persistent nature of the condition. The primary treatment goal is to achieve healing without compromising continence, thereby minimizing the impact on quality of life.

Several sphincter-preserving techniques have emerged over the years<sup>1,2</sup>. Among them is the ligation of intersphincteric fistula tract (LIFT) procedure, introduced by Rojanasakul in 2007, which stands out for its positive outcomes and reduced morbidity rates<sup>2-4</sup>. A recent network meta-analysis highlighted LIFT's comparable success rates to other surgical techniques, with the added advantage of superior bowel continence preservation<sup>5</sup>. However, these findings come from limited trials, encompassing only a total of 172 patients and varied follow-up durations. The existing literature presents a diverse range of findings regarding LIFT for anal fistulas. Some studies demonstrate favourable outcomes in terms of success rates, while others report no significant differences when compared with alternative techniques<sup>6–10</sup>.

An apparent consistent advantage of LIFT is its minimal impact on faecal continence<sup>11</sup>. Nonetheless, there's a noticeable gap in the literature concerning the long-term efficacy of treatments,

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especially regarding continence preservation. Many studies lack comprehensive preoperative continence data and have limited follow-up durations<sup>12</sup>. For instance, a 2020 analysis reported a mid-term success rate of 76.5% but with a median follow-up of only 16.5 months (range 12–32)<sup>13</sup>. This underscores the need for extended follow-up studies that integrate preoperative data to draw more definitive conclusions.

Recognizing this gap, the present study focuses on the long-term outcomes of the LIFT procedure for trans-sphincteric cryptoglandular anal fistulas with particular respect to long-term continence preservation, treatment success, the influence of preoperative seton drainage and recurrence rates.

# Methods

## Study design and population

This is a retrospective observational cohort study using prospectively collected preoperative data from patients who underwent the LIFT procedure for anal fistula between July 2012 and October 2018. This data encompasses a combined cohort from two tertiary referral centres in The Netherlands: Proctos Clinic (PC) and Elisabeth-TweeSteden Hospital (ETZ). As part of the standard treatment protocol, preoperative continence data for all patients were systematically collected in a prospective manner. This information was extracted from electronic patient files and merged into a consolidated database. In May 2023, questionnaires were distributed to all patients to obtain long-term data on recurrences, additional fistula surgery and bowel continence. The study was approved by the Medical Ethical Committee (MEC nr 2022-33). The study was not preregistered in an independent, institutional registry, as it was a retrospective study design.

### Eligibility criteria

The study included consecutive patients with primary or recurrent cryptoglandular trans-sphincteric anal fistulas who underwent the LIFT procedure, irrespective of whether it was the initial treatment choice or subsequent to failed prior surgeries. The choice for the LIFT procedure was always based on consensus among surgeons and patient consent after considering alternative treatments.

Referral for LIFT encompassed various scenarios: simple fistula (intersphincteric or low trans-sphincteric), with tracts located too high (within the upper two-thirds of the external sphincter), and thus assessed at increased incontinence risk to perform a fistulotomy; patients with impaired continence: in these cases LIFT was offered after shared decision-making, particularly in low trans-sphincteric fistulas if technically feasible; women with anterior complex fistulas: for these patients, LIFT was considered the procedure of choice; and male patients with anterior fistulas: for these patients, LIFT was considered (if and when LIFT was deemed technically feasible) after shared decision-making with advancement flap repair (AFR) as the preferred alternative (as in all other patients with complex fistulas). Shared decision-making considered the substantial impact of AFR on functional impairment, as well as its increased morbidity rate, weighed against its higher healing rate and wider applicability.

At the time of LIFT, no septic criteria or abscess were present. Patients were excluded if under 18 years old, in case of Crohn's disease, malignancy, trauma or HIV, having a deviating stoma or having fistulas with rectovaginal, recto-urethral or non-trans-sphincteric anatomical courses; finally, patients treated using LIFT variants such as bio-LIFT (Permacol mesh) or Permacol paste (PMP) were also excluded.

## Diagnostics

All patients underwent a comprehensive physical examination. For preoperative determination of the fistula's anatomical course, three-dimensional endo-anal ultrasound (3D-EAUS) was used at PC, while magnetic resonance imaging (MRI) was performed in all patients at ETZ. Based on their anatomical course, fistulas were categorized into low, mid or high trans-sphincteric. The following definitions of trans-sphincteric fistula types were used: 'low' refers to the involvement of the lower third of the external sphincter; 'mid' refers to the middle third and 'high' relates to the upper third of the external sphincter respectively.

# Surgical procedure: LIFT technique

Both centres have used similar techniques. Patients were treated on a day-admission basis without preoperative bowel preparation. Preoperative seton drainage was not mandatory; however, if excessive inflammation existed, patients were treated by loose seton for 3–12 months first. Patients received a one-time only intravenous antibiotic prophylaxis consisting of cefazolin and metronidazole.

The LIFT procedure, performed under general or spinal anaesthesia with patients in the lithotomy position, followed the steps previously outlined<sup>9,10</sup>: incision at the intersphincteric groove, fistula tract identification and cleaning (curettage and irrigation), followed by ligation, removal and transfixing of both ends of the fistula (internal and external part). The external opening was left open for discharge, and tract closure was verified using either hydrogen peroxide or a sodium chloride (NaCl) 0.9% solution, based on the hospital's practice. In case of leakage, extra sutures were used to close the defect from within the intersphincteric plane. After surgery, patients received oral paracetamol and ibuprofen for pain relief and were instructed on wound self-care by cleansing with water.

## Data collection and questionnaires

Both centres prospectively collected continence data before the LIFT procedure. Specifically, ETZ provided comprehensive preoperative faecal incontinence severity index (FISI) scores for each patient, while PC recorded before surgery only the incontinence type without detailing frequency, leading to a partial acquisition of preoperative FISI scores for its patients. Continence changes were closely monitored, and long-term data were obtained from questionnaires. As part of routine clinical care, patients were scheduled for a postsurgery follow-up appointment at the outpatient clinic with their surgeon 2–6 weeks after the procedure. In cases where patients had ongoing complaints or if there were uncertainties during an endo-anal ultrasound, subsequent appointments were scheduled at 4–6-week intervals. All clinical data were extracted retrospectively from electronic patient records.

In May 2023, Rockwood questionnaires that included standardized FISI evaluations were distributed to obtain long-term data<sup>14</sup>. These questionnaires also explored fistula healing and additional treatments. Non-respondents were subsequently contacted via e-mail and/or phone.

### Outcomes of interest

The primary objective was to evaluate long-term bowel continence post-LIFT using the FISI<sup>14</sup>. Continence status from before the procedure was compared with short-/mid-term data (outpatient clinic visits in 2018) and long-term follow-up (2023

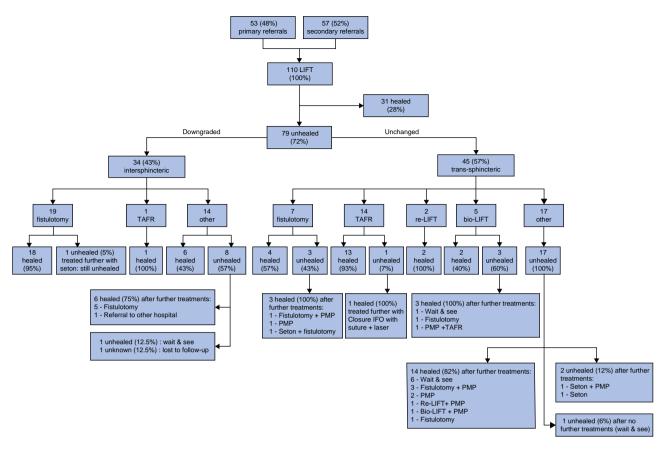


Fig. 1 Flow diagram showing outcome of patients with unhealed fistulas after LIFT procedure

LIFT, ligation of intersphincteric fistula tract; PMP, Permacol paste; TAFR, transanal advancement flap repair; IFO, internal fistula opening; 'other' category includes: Permacol paste, laser, bio-LIFT, seton and wait & see policy.

questionnaire responses), detailing incontinence types and frequencies<sup>9,10</sup>. Additionally, the FISI also provided insights into quality of life, related to the bowel<sup>15,16</sup>. Changes in continence were visualized using Sankey diagrams, see below<sup>17</sup>.

Secondary outcomes were focused on: fistula healing rate (defined as the complete closure of the external fistula opening without recurring symptoms during follow-up); fistulas were categorized as 'unhealed' if there was a reappearance of postinitial closure, a return of previous symptoms, or if the fistula persisted beyond 12 weeks<sup>18</sup>. All unhealed fistulas were confirmed radiologically through EAUS or MRI. For this outcome, the following variables were correlated with subgroups of healed and unhealed fistulas: internal opening of the fistula, previous surgeries, seton placement and surgical attempts of fistula closure. Particularly, the influence of preoperative seton drainage on the success rate of the LIFT procedure was evaluated, alongside complications and re-interventions in patients with post-LIFT unhealed fistulas, with a special focus on downstaging to an intersphincteric tract.

Finally, literature in this field was systematically reviewed using the PubMed database. Articles were assessed for the year of investigation, number of patients enrolled, nationality of the authors, study design, rate of complex fistula treated, clinical success rate, postoperative outcomes (incontinence) and mean follow-up time.

### Statistical analysis

Statistical analyses were performed using SPSS software (IBM, Armonk, NY, USA, SPSS Statistics 28). Continuous data were

presented by mean/median values, while categorical data were expressed as percentage proportions, employing descriptive statistics and crosstabs. For comparing differences between groups (or centres), the Fisher's exact test or Fisher-Freeman-Halton exact test was applied for categorical data, depending on distribution. Differences in continuous data were assessed with the t-test for parametric data or the Mann-Whitney U test for nonparametric data. Univariate and multivariate logistic regression analyses were employed to adjust for potential confounding factors. To evaluate changes in scores within individual patients over time, the Wilcoxon signed rank test was used. Sankey diagrams were computed, differentiating patients on the basis of preoperative bowel function (normal bowel continence versus minor incontinence—gas or mucus and versus major incontinence -liquid or solid stool) at different time points (short-mid versus long-term data). Kaplan-Meier survival analysis was done to estimate fistula-free survival after the LIFT procedure. Statistical significance was considered to be P < 0.05.

# Results

During the study interval, 129 patients underwent the LIFT procedure for trans-sphincteric anal fistulas across the two hospitals. Among them, 110 patients met the eligibility criteria and were included in the analysis (Fig. 1). Of these, 20 (18%) had simple fistulas, and 19 (17%) experienced impaired continence before surgery, with five (5%) categorized as having major issues (incontinence for liquid or solid stool). Additionally, 50 patients (45%) had anterior fistulas, with 30 (27%) being female.

#### Table 1 Patient demographic data stratified by centre

	Total <i>n</i> = 110 (100%)	PC n = 64 (58%)	ETZ n = 46 (42%)	Р
Sex				0.334
Male	55 (50)	29 (45)	26 (56)	
Female	55 (50)	35 (55)	20 (44)	
Age at time of LIFT (years), median (range)	44 (18–80)	44.5 (24-69)	44 (18-80)	0.596
Smoking	24 (22)	10 (16)	14 (30)	0.060
Secondary referral from another hospital	57 (52)	49 (77)	8 (17)	< 0.001
Previous fistula surgery		~ /	( )	
Number of previous surgeries, median (range)	2 (0–6)	2 (0-5)	2 (1)	0.214
Number of previous surgeries, mean(s.d.)	2.1(1.3)	2(1.4)	2.3(1.2)	
Total number of previous surgeries		( )	( )	n/a
0	9 (8)	9	0	
1	29 (26)	18	11	
2	36 (33)	14	22	
3	19 (7)	13	6	
4 or more	15 (9)	9	6	
Unknown number	2 (2)	1	1	
Only abscess or seton drainage	70 (69)	33 (52)	37 (80)	0.032
Previous attempts to close the fistula	31 (31)	22 (34)	9 (20)	0.090
Number of attempts to close fistula, median (range)	1 (1-4)	1 (1-4)	1 (1)	0.041
Number of attempts to close fistula, mean(s.d.)	1.45(0.8)	1.6(0.9)	1(0)	
Number of previous attempts to close the fistula			( )	n/a
1	22 (71)	13	9	
2	5 (16)	5	0	
3	3 (10)	3	0	
4	1 (3)	1	0	
Types of previous attempts to close the fistula				0.054
Laser	5 (16)	1	4	
Fistulotomy	10 (32)	8	2	
Fistulectomy	3 (10)	2	1	
TAFR	12 (39)	10	2	
Permacol paste	1 (3)	1	0	
Seton drainage before LIFT				<0.001
Yes	88 (80)	43 (67)	45 (98)	
No	22 (20)	21 (33)	1 (2)	
Duration of seton (weeks), median (range)	17 (4–136)	22 (7–136)	14 (4–67)	0.010

Values are n (%) unless otherwise stated. PC, Proctos Clinic; ETZ, Elisabeth-TweeSteden Hospital; TAFR, transanal advancement flap repair; n/a, not applicable; LIFT, ligation of intersphincteric fistula tract.

The median age was 44 years (range 18–80) and 50% of the cohort were females (*Table* 1). Data from short-/mid-term follow-up was available for 97% (107 of 110). Long-term follow-up data via questionnaires in 2023 was available for 63% (69 of 110). Median follow-up time was 92 months (range 57–129).

Fifty-two per cent (57 patients) were referrals from elsewhere due to persistent or recurrent disease after primary treatment failed. A significant 92% (101 patients) of the cohort had previous fistula surgeries, with a median of 2 (range 0–6) surgeries per patient. Within this group, 31% (31 patients) had earlier closure attempts. A wide range of surgical strategies were used during those attempts, which are detailed in *Table* 1. The vast majority (80%) underwent seton drainage before the LIFT procedure with a median duration of 17 weeks (range 4–136). At ETZ, only one patient did not undergo seton drainage before LIFT, in contrast to 21 patients at PC (P < 0.001). The duration of seton drainage before LIFT was longer at PC, with a median of 22 weeks (range 7–136), compared with 14 weeks (range 4–67) at ETZ (P = 0.010) (*Table* 1).

#### Bowel continence status

#### Preoperative bowel continence status

Data on preoperative continence status was available for all 110 included patients. Complete baseline FISI scores were only available for 25 patients. Before LIFT surgery, 18 patients (16%) reported incontinence: three patients for gas (3%), 11 patients

for mucus (10%), one patient for liquid stool (1%) and three patients for solid stool (3%) (*Table 2*). Before surgery, the mean(s.d.) FISI score was 2.4(7.5); available from 25 patients). Notably, only three of these 25 exhibited abnormal FISI scores, with individual scores of six, 24 and 30 respectively. The patient with a score of 30, indicating significant incontinence to solid stool, maintained a consistent score after surgery.

# Postoperative short-/mid-term bowel continence status (2018)

Data was available for 107 (97%) patients. Roughly the same proportion of patients, 20 in total (18%), reported postoperative bowel incontinence (*Table 2*). Among these, 12 patients (11%) experienced a change in their continence status, presenting new postoperative incontinence. However, the severity of incontinence in these cases was mild (gas/mucus).

# Long-term follow-up on bowel continence status via 2023 questionnaires

In 2023, Rockwood questionnaires were disseminated to the entire cohort for FISI score assessment. Of the 69 respondents (63% response rate), 50 (72%) reported some form of incontinence: 14 patients (21%) reported incontinence for gas, 25 patients (37%) for mucus, eight patients (12%) for liquid stool and three patients (4%) for solid stool (*Tables 2*, 3). After surgery, 39 respondents experienced incontinence despite being continent

#### Table 2 Continence status stratified by success of the LIFT procedure

	Total $n = 110$	Healed $n = 31$	Unhealed n = 79	Р
Preoperative continence status				0.954
Continent	92 (84)	28 (30)	64 (70)	
Incontinent	18 (16)	3 (19)	15 (81)	
Gas	3 (3)	0 (0)	3 (100)	
Mucus	11 (10)	2 (18)	9 (82)	
Liquid stool	1 (1)	0 (0)	1 (100)	
Solid stool	3 (3)	1 (33)	2 (67)	
Postoperative short-/mid-term continence status (2018)				0.821
Continent	89 (81)	25 (28)	64 (72)	
Incontinent	20 (18)	6 (30)	14 (70)	
Gas	4 (4)	2 (50)	2 (50)	
Mucus	11 (10)	3 (27)	8 (73)	
Liquid stool	2 (2)	0 (0)	2 (100)	
Solid stool	3 (3)	1 (33)	2 (67)	
Missing	1 (1)			
Change in postoperative continence status short-/mid-term (2018)				0.738
No	97 (88)	27 (28)	70 (72)	
Yes	12 (11)	4 (33)	8 (67)	
Missing	1 (1)			
Long-term (2023) continence status				0.075
Continent	19 (17)	4 (21)	15 (79)	
Incontinent	50 (46)	16 (32)	34 (68)	
Gas	14 (13)	6 (43)	8 (57)	
Mucus	25 (23)	7 (28)	18 (72)	
Liquid stool	8 (8)	2 (25)	6 (75)	
Solid stool	3 (3)	1 (33)	2 (67)	
Missing	41 (37)			
FISI score long term, median (range)	7 (0-45)	7 (0-45)	19 (12-24)	<0.009*
FISI score long term, mean(s.d.)	9.2(9.5)	9.6(10.5)	9.1(9.2)	
FU time (months), median (range)	92 (57–129)	94 (62–129)	80 (57–112)	0.921*

Values are n (%) unless otherwise stated. \*In unhealed group only 3 cases. FU, follow-up; s.d., standard deviation; FISI, faecal incontinence severity index; LIFT, ligation of intersphincteric fistula tract.

#### Table 3 Change in continence status per individual case; irrespective of additional surgical treatment after LIFT; exclusion of non-respondents in 2023

Respondents in 2023 N = 69

Preoperative continence status, n	Long	-term	continend	e status (	(2023), ı	1
	Continent	Gas	Mucus	Liquid	Solid	Total
Continent	19	12	15	8	1	55
Gas	0	1	2	0	0	3
Mucus	0	1	6	0	1	8
Liquid	0	0	1	0	0	1
Solid	0	0	1	0	1	2
Total	19	14	25	8	3	69

 $P\!=\!0.039.$  LIFT, ligation of intersphincteric fistula tract. Bold values highlight the number of patients with a worse continence status.

before surgery. The incontinence severity increased for two patients (*Table 3*). The overall median FISI score was 7 (range 0–45), as detailed in *Table 2*. A FISI score of >30 points (3 patients with a score of 32, 39 and 45) was present in three of the 69 respondents (4.2%).

While the above metrics provide median scores and proportions for the entire group, individual patient trajectories pre- and post-LIFT are best visualized using Sankey diagrams, as shown in Figs 2 and 3.

The cumulative impact of surgeries on bowel continence for all respondents is illustrated in a Sankey diagram and revealed significant individual long-term continence deterioration (Fig. 2). Of 55 patients with a preoperative normal continence

status, 19 reported no incontinence issues during long-term follow-up. However, 27 indicated minor, and 9 mentioned major incontinence. Interestingly, of the three patients with major incontinence complaints before surgery, two reported only minor issues in 2023.

Furthermore, a subset analysis of 45 respondents was conducted. These patients did not require subsequent surgeries after undergoing LIFT and reported no long-term incontinence issues if they did. Among this group, 18 patients reported normal bowel continence, while 27 patients experienced varying degrees of incontinence, including eight for gas, 15 for mucus, two for liquid stool and two for solid stool as detailed in *Table* 4. However, the Sankey diagram displayed in *Fig.* 3 illustrates that 17 patients who were initially continent before surgery reported some form of incontinence at long-term follow-up, including six for gas, nine for mucus and two for liquid stool. Notably, after surgery at the short-term follow-up, 31 of 35 patients maintained regular bowel continence, and this number dropped to 18 of 35 during the long-term follow-up interval.

Moreover, another subgroup analysis was conducted involving 11 patients who underwent fistulotomy for a downgraded intersphincteric tract after failed LIFT procedures. Among these patients, the majority (10 of 11) reported some level of incontinence, with four patients experiencing major issues (Fig. 4).

## Fistula healing rate

The initial healing rate post-LIFT in the cohort was 28% (*Table 5*). Radiologic confirmation of failure was detected after a median interval of 3.1 months (range 0.3–102.7). Healing rates for low, mid and high fistulas were 20%, 18% and 36% respectively

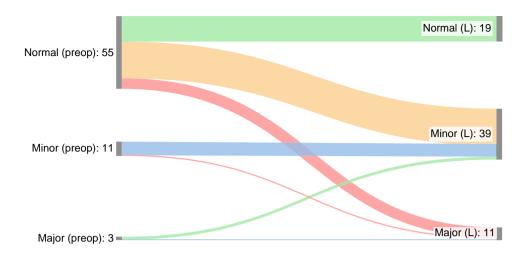


Fig. 2 Sankey diagram of long-term questionnaire respondents in 2023 (*n* = 69): change in continence status per individual case irrespective of additional surgical treatment after LIFT

LIFT, ligation of intersphincteric fistula tract; preop, preoperative bowel continence status; (L), long-term data from 2023 questionnaires; minor, incontinence for gas or mucus; major, incontinence for liquid or solid stool.

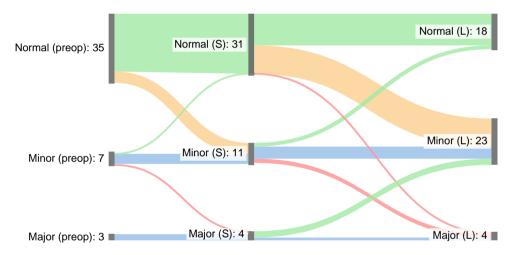


Fig. 3 Sankey diagram of continence status per individual case; exclusion of non-respondents in 2023, patients with additional surgical treatment after LIFT procedure and worsening of continence status (n = 45)

LIFT, ligation of intersphincteric fistula tract; preop, preoperative bowel continence status; (S), short-term (data from 2018); (L), long-term data from 2023 questionnaires; minor, incontinence for gas or mucus; major, incontinence for liquid or solid stool.

(P = 0.188). Among the 79 patients with persistent fistulas, 77 had an EAUS or MRI assessment, while the other two were prominent and easily diagnosed through physical examinations. The median recurrence-free survival time was 4.6 months (95% CI 3.23-5.97). A Kaplan-Meier curve of the healing rate during follow-up is shown in Fig. 5. The location of the internal fistula opening did not impact the success rate. Those healed post-LIFT had a higher prevalence of prior seton drainage, at 93.5%, compared with 74.7% in the unhealed group (P = 0.033). Multivariate regression analyses revealed that while seton drainage significantly influenced the LIFT procedure's success rate, its duration did not (Table 5). In the unhealed group of 79 patients, 89% had previous fistula surgeries, and 28% had prior fistula closure attempts. For the 31 patients in the healed group, this proportion was consistent at 29% (P = 1.000). The median count of two prior surgeries was similar across both groups. Similarly, there was no significant difference in the median number of past fistula closure attempts for both groups (Table 5).

However, of 79 unhealed fistulas, 34 (43%) were 'downgraded' to intersphincteric tracts after LIFT surgery (Table 6). The

median interval between LIFT and the subsequent surgical treatment was 6 months (range 1–30). The complete treatment trajectory during follow-up for these 79 unhealed patients is illustrated in Fig. 1. Among these patients, 53 individuals (67%) required a subsequent procedure, leading to fistula closure. For the 34 downgraded intersphincteric fistulas, 74% (25 cases) achieved closure after the secondary treatment. In contrast, only 62% (28 of 45) of the persistent trans-sphincteric fistulas closed after secondary treatment. The only observed complication was recurrent abscesses that required drainage. A mean(s.d.) of 1.3(1.2) subsequent surgeries were needed to achieve fistula healing following a failed LIFT procedure (Table 6). A breakdown shows 39% (43 patients) needed one additional surgery, 9% (10 patients) two, 5.5% (6 patients) three, and 4.5% (5 patients) four or more surgeries (Table 6).

#### Literature review

A comprehensive review of 50 studies investigating the success rate and postprocedural continence following the LIFT procedure for anal fistulas was conducted (*Supplementary*  *materials, Table S1*). These studies were published between 2007 and 2023 and predominantly comprised observational cohort studies. Additionally, 11 RCTs were included, with a notable concentration in the last decade. Success rates for the LIFT procedure varied from 21 to 94%, while reported rates of postprocedural incontinence ranged from 0 to 20%. The mean follow-up duration across all studies ranged from 1.5 to a maximum of 71 months.

## Discussion

In this retrospective cohort study from two tertiary referral centres in The Netherlands, the long-term outcomes of patients undergoing the LIFT procedure for trans-sphincteric cryptoglandular anal fistulas were evaluated using prospectively collected data.

Until this work, the most extensive prospective studies have only tracked patients for a median of 16.5 months<sup>13</sup>. Interestingly, only one author has reported 10-year results, demonstrating an 87.7% healing rate and zero incontinence after a median follow-up interval of 71 months<sup>18</sup>. It is noteworthy that that study lacked standardized questionnaires, reported subjective continence impairment and did not detail preoperative continence statuses.

In contrast, the findings of this study suggest a more significant long-term deterioration in bowel continence after

Table 4 Change in continence status per individual case; exclusion of non-respondents in 2023, patients with additional surgical treatment after LIFT procedure and worsening of continence status

Respondents in 2023, n = 45

Preoperative	Long-term continence status (2023), n						
continence status, n	Continent	Gas	Mucus	Liquid	Solid	Total	
Continent	18	6	9	2	0	35	
Gas	0	1	0	0	0	1	
Mucus	0	1	4	0	1	6	
Liquid	0	0	1	0	0	1	
Solid	0	0	1	0	1	2	
Total	18	8	15	2	2	45	

P = 0.008. LIFT, ligation of intersphincteric fistula tract. Bold values highlight the number of patients with a worse continence status.

LIFT than earlier short-term results and the prevailing literature suggest (as documented in *Supplementary materials*, *Table* S1). In the current cohort, (minor) incontinence rates rose from 18% in 2018 to 45.5% in 2023. With a median follow-up of 92 months, 74% of the respondents reported some degree of incontinence. Particularly alarming was the feedback from nine patients about liquid stool incontinence and three about solid stool incontinence. Such figures suggest a compromised quality of life, as is evidenced by the FISI score<sup>15,16</sup>. Yet, it's important to note that all patients aged during the study, and many underwent further anorectal surgeries post-LIFT due to persistent or recurrent disease.

The Sankey diagrams offer valuable insights, shedding light on the journeys of individual patients concerning continence status before and after LIFT. Among patients continent before LIFT, only one-third maintained this status. These diagrams are a visual representation emphasizing flow or transitions between states or over time, with arrow widths proportional to the flow rate<sup>19</sup>. They highlight major transfers or flows within a system and pinpoint significant contributors to a flow while demonstrating conserved quantities.

Notably, in the analysis excluding non-respondents and patients with additional surgeries post-LIFT (n = 45), varying impacts on continence status were evident. While the overall group showed consistent incontinence rates, individual continence profiles were significantly affected post-LIFT. Of particular interest was the subgroup analysis, revealing significant long-term continence deterioration in patients undergoing fistulotomy after a failed LIFT procedure, emphasizing the critical importance for surgeons to exercise caution when opting for a fistulotomy in cases of 'simple' fistulas within already scarred anuses.

The LIFT procedure yielded a primary healing rate of 28%. These data indicate a trend of higher healing rates for high fistulas compared with mid-low trans-sphincteric fistulas. This observation contrasts with prior research, which reported lower healing rates for high trans-sphincteric fistulas<sup>18</sup>. Contrary to expectations, the findings challenge the perceived technical complexity associated with the LIFT approach for higher fistulas. Additionally, although anal fistulas are more common in males, the present cohort had a higher representation of women (50%). This skewness can be traced back to our preference for LIFT over transanal advancement flap repair

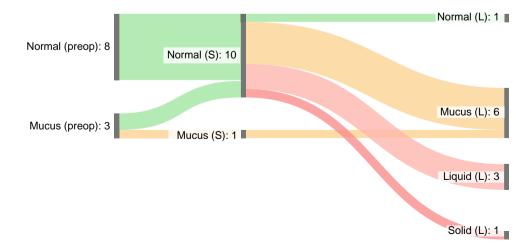


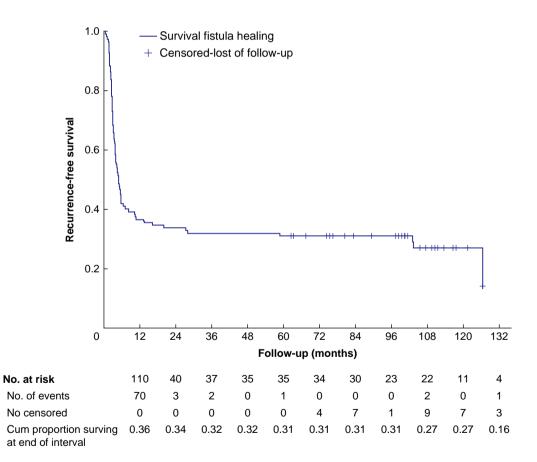
Fig. 4 Sankey diagram of continence status per individual case; subgroup of respondents who underwent fistulotomy for their intersphincteric tract after LIFT (n = 11)

LIFT, ligation of intersphincteric fistula tract; preop, preoperative bowel continence status, (S), short-term (data from 2018); (L), long-term data from 2023 questionnaires.

#### Table 5 Fistula classification stratified by success rate of the LIFT procedure

	Total n = 110 (100%)	Healed n = 31 (28%)	Unhealed n = 79 (72%)	Р
Preoperative classification tracts				0.188
Low trans-sphincteric	20 (18)	4 (20)	16 (80)	
Mid trans-sphincteric	28 (26)	5 (18)	23 (82)	
High trans-sphincteric	62 (56)	22 (35)	40 (65)	
Mid-low versus	48 (44)	9 (19)	39 (81)	0.058
High trans-sphincteric fistula	62 (56)	22 (35)	40 (65)	
Location IFO				0.934
Anterior	50 (45)	14 (28)	36 (72)	
Posterior	48 (44)	13 (27)	35 (73)	
Right lateral	8 (7)	3 (37)	5 (63)	
Left lateral	4 (4)	1 (25)	3 (75)	
Height IFO (mm), median (range)	15 (5–30)	13.5 (5-22)	16 (4–49)	0.142
Seton drainage before LIFT				0.033
Yes	88 (80)	29 (33)	59 (67)	
No	22 (20)	2 (9)	20 (91)	
Duration of seton before LIFT (weeks), median (range)	17 (4–136)	22 (5–136)	19 (4–49)	0.118
Number of previous surgeries, median (range)	2 (0–6)	2 (1–5)	2 (0–6)	0.680
Number of previous surgeries, mean(s.d.)	2.1(1.3)	2(1)	2.1(1.4)	
Number of previous attempts to close fistula, median (range)	0 (0-4)	0 (0-4)	0 (0–3)	0.838
Number of previous attempts to close fistula, mean(s.d.)	0.41(0.78)	0.52(1)	0.37(0.67)	

Values are n (%) unless otherwise stated. IFO, internal fistula opening; LIFT, ligation of intersphincteric fistula tract.



#### Fig. 5 Fistula healing rate following LIFT

LIFT, ligation of intersphincteric fistula tract.

(TAFR) for women with anterior fistulas. With 30 female patients presenting with anterior fistulas (comprising 27% of the cohort), this is in line with other recommendations, aiming for superior results in this particular patient group<sup>20</sup>. The exact influence of this strategy on this study's outcomes remains undefined but likely reflects prevalent clinical practice.

An interesting observation was that preoperative seton drainage appeared to enhance the healing rate. Thus, utilizing seton drainage before LIFT appears to significantly enhance the success rate; however, the duration of seton drainage appeared not to be a significant factor. This 'seton paradox', as previously described by this group concerning seton drainage in the preparation of TAFR,

#### Table 6 Characteristics of the LIFT procedure failures and their further treatment

	All unhealed fistulas post-LIFT $n = 79$		
Time until radiologic proof of failure (months), median (range)	3.1 (0.3–102.7)		
<b>Type of failure/recurrence</b> Downgraded to an intersphincteric tract Unaltered trans-sphincteric Time between LIFT and secondary treatment (months), median (range)	34 (43) 45 (57) 6 (1–30)		
Results of secondary treatment Healed Unhealed Referral other hospital	53 (67) 25 (32) 1 (1)		
Type of secondary treatment, $n = 79$	Treated	Healed	
Wait & see Seton drainage Fistulotomy TAFR Re-LIFT Bio-LIFT Collagen plug Permacol paste Laser Abscess drainage	$\begin{array}{c} 13 \ (16.5) \\ 11 \ (14) \\ 26 \ (33) \\ 15 \ (19) \\ 2 \ (2.5) \\ 5 \ (6) \\ 1 \ (1) \\ 3 \ (4) \\ 2 \ (2.5) \\ 1 \ (1) \end{array}$	11 (85) n/a 22 (85) 14 (93) 2 (100) 2 (40) 0 (0) 0 (0) 2 (100) 0 (0)	
Type of third treatment, $n = 24$	Treated	Healed	
Wait & see Seton drainage Fistulotomy Re-LIFT Permacol paste Closure IFO with suture Abscess drainage	4 (17) 3 (12.5) 6 (25) 1 (42) 6 (25) 1 (4) 3 (12.5)	2 (50) n/a 4 (67) 0 (0) 3 (50) 0 (0) 0 (0)	
Total number of surgeries required for healing after LIFT procedure Mean(s.d.) Median (range) 1 surgery 2 surgeries 3 surgeries 4 or more surgeries	$\begin{array}{c} 1.3(1.2) \\ 1 (0-5) \\ 42 (53) \\ 10 (13) \\ 6 (8) \\ 5 (6) \end{array}$		

Values are n (%) unless otherwise stated. n/a, not applicable; LIFT, ligation of intersphincteric fistula tract; TAFR, transanal advancement flap repair; IFO, internal fistula opening.

is an interesting phenomenon. It suggests that fistulas with pronounced inflammation (requiring seton drainage) tend to heal better post-LIFT than those without such inflammation<sup>21</sup>. Drawing definitive conclusions is challenging since many surgeons consistently use draining setons, and a substantial portion of the study's participants presented with a seton. Nevertheless, the influence of draining setons on LIFT outcomes and on inflammation more broadly remains a compelling research area.

During the short-term follow-up, 13 patients displayed unhealed fistulas after a median duration of 3.1 months; however, significant complaints were absent in this particular patient group. Consequently, after consulting these patients, a watchful waiting approach was adopted. Of these 13 patients, six had residual intersphincteric fistula tracts post-LIFT, while the original trans-sphincteric tracts persisted in the remaining seven. Remarkably, 11 of these 13 patients eventually exhibited fistula healing without additional surgical interventions. This pattern implies that after a LIFT procedure for trans-sphincteric fistulas, a prolonged observation interval might be advisable, as healing can manifest later. In the present cohort, 85% of those under watchful waiting exhibited this delayed healing. Current literature often associates MRI evidence with treatment failure. Some studies and guidelines nowadays even recommend routine MRI scans at the 3-month mark to identify postoperative

fistula failures<sup>22,23</sup>. Nonetheless, our findings indicate that waiting beyond this interval may be prudent, allowing potential healing to take its course.

On average, post-LIFT patients required a mean 1.3 additional operations, with 67% of the patients necessitating a re-intervention. Recurrent fistulas, particularly following previous surgeries, present significant challenges due to postoperative scarring, fibrosis and potential sphincter muscle damage. These complications not only make subsequent treatments more complex but also heighten the risk of incontinence. Current findings indicate that the success of the LIFT procedure diminishes with an increasing number of prior surgeries. A recent meta-analysis pinpointed the number of prior surgeries as a crucial factor affecting the outcomes of repeat fistula surgeries<sup>13</sup>. Despite the high number of prior fistula surgeries for some patients, the current data suggests that this should not dissuade surgeons from considering LIFT. The critical emphasis should remain on acquiring accurate preoperative imaging enabling proper patient selection.

This study has several limitations including the study's retrospective design and the moderate response rate to the questionnaire leading to incomplete data. The absence of systematic baseline questionnaires for the entire group may result in an underestimation of baseline incontinency. Also, the retrospective design inherently limited the ability to capture core

outcomes such as radiologic healing, fistula-related symptoms and post-treatment patient satisfaction. While early LIFT studies reported high success rates, more recent data, including this study, suggest a more nuanced picture. This discrepancy could be due to the learning curve or the limitations of retrospective studies, especially those with shorter follow-up intervals.

As in most studies related to perianal fistula surgery, clinical healing was determined by symptoms such as fistula discharge and pain, and confirmation of unhealed fistulas was obtained via EAUS or MRI within a median of 3 months postsurgery. Given that a fibrotic tract on MRI indicates long-term closure, it has been suggested that future studies should incorporate a 3-month postoperative MRI scan<sup>23</sup>. However, this statement can be debated in view of durability and cost-effectiveness. Aligning with the cryptoglandular Anal Fistula Core Outcome Set (AFCOS), which emphasizes radiologic healing and additional fistula development, this approach would ensure precise evaluations<sup>24</sup>. The retrospective nature of the present study, however, introduces certain limitations.

Given the variances in study populations across different studies, defined by differences in fistula complexity, recurrence status, type, and underlying causes, prioritizing specificity and consistency involves focusing solely on patients with transsphincteric cryptoglandular anal fistulas. It seems essential for future studies to align their methodologies with the AFCOS as closely as possible to ensure consistency.

The results of this study underscore the importance of considering individual patient experiences when evaluating treatments such as LIFT. While the findings suggest potential concerns regarding the impact on continence, the suitability of LIFT as a first-line therapy remains questionable, given the less-than-perfect outcomes observed. Notably, the impact on continence appears comparable to other more invasive techniques such as TAFR. The premature adoption of LIFT as a primary option for complex fistulas within the surgical community may stem from the lack of robust long-term functional outcome data<sup>25</sup>. We urge fellow researchers to collect comprehensive prospective continence data, ideally augmented with quality-of-life measurements, to provide a nuanced understanding of treatment outcomes. Until such data is available, caution should be exercised in the widespread adoption of LIFT as a primary option for complex fistulas.

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## Disclosure

The authors declare no conflict of interest.

# Supplementary material

Supplementary material is available at BJS Open online.

# Data availability

Study data are available on reasonable request.

# **Author contributions**

Justin van Oostendorp (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization,

Writing—original draft, Writing—review & editing), Carolien Verkade (Conceptualization, Data curation, Investigation, Methodology, Validation), Ingrid Han-Geurts (Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing review & editing), Grietje van der Mijnsbrugge (Data curation, Writing—review & editing), Dareczka Wasowicz-Kemps (Data curation, Writing—review & editing) and David Zimmerman (Conceptualization, Data curation, Investigation, Methodology, Supervision, Visualization, Writing—review & editing)

# Ethical approval

The study was approved by the Medical Ethical Committee Brabant, MEC nr 2022-33.

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