



Review Article

Ligation of the intersphincteric fistula tract procedure and its modifications

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ABSTRACT

Purpose: Treatment of anal fistulae is regarded as a challenge due to the diverse nature of this disease and its countless complications. Ligation of the intersphincteric fistula tract procedure and its modifications have been popularized among many surgeons worldwide due to their simplicity and promising outcomes. The main purpose of this article was to conduct a comprehensive review of the published literature on ligation of the intersphincteric fistula tract procedure and its modifications.

Method: PubMed, the Cochrane database and Ovid were searched from January 2007 to June 2017. Fully published peer-reviewed studies which applied ligation of the intersphincteric fistula tract procedure and its modifications for the treatment of anal fistulae of cryptogenic origin with follow-up of median 12 months were eligible. Uncompleted studies, case reports, reviews, abstracts, letters, short communication, comments, and studies which did not fulfill inclusion criteria were excluded. The primary outcome was to measure primary healing, overall healing, failure, and recurrence of ligation of the intersphincteric fistula tract procedure and its modifications.

Results: Twenty-two studies were identified with only ten studies meeting criteria of inclusion. Original ligation of the intersphincteric fistula tract was performed in five studies with a population of 199 patients while the remaining five studies showed four different modifications of the ligation of the intersphincteric fistula tract with a total number of 147 patients. Both original LIFT and its modifications have promising as well as potentially similar outcomes; primary healing in the original ligation of the intersphincteric fistula tract (73.95%) (95% CI 60.3–85.6) performed less than the modifications (82.3%) (95% CI 64.8–94.7). Overall healing in the original ligation of the intersphincteric fistula tract (78.9%) (95% CI 58.5–93.7) performed relatively less than in the modifications (93.6%) (95% CI 81.4–99.6). Failure in the original ligation of the intersphincteric fistula tract (17.9%) (95% CI 4.9–36.5) performed almost the same as the modifications (17.7%) (95% CI 5.3–35.2). Recurrence in the original ligation of the intersphincteric fistula tract was 9.7% (95% CI 1.7–23.2). However, there was no recurrence in the modifications.

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Conclusion: Ligation of the intersphincteric fistula tract and its modifications are effective and simple procedures in treating simple anal fistulae, especially high transsphincteric ones. However, more trials should be performed to evaluate its effectiveness regarding complex fistulae.

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Procedimento de ligadura de trato de fístula interesfincteriana e suas modificações

R E S U M O

Palavras-chave:

Ligação do trato da fístula interesfincteriana
Fístula
Fístula no ânus
Fístula anal
Revisão

Objetivo: O tratamento de fístulas anais é considerado um desafio devido à natureza diversa dessa doença e suas incontáveis complicações. O procedimento de ligadura do trato da fístula interesfincteriana e suas modificações foi popularizado entre cirurgiões em todo o mundo devido a sua simplicidade e desfechos promissores. O principal objetivo deste artigo foi conduzir uma revisão abrangente da literatura publicada sobre o procedimento de ligadura do trato da fístula interesfincteriana e suas modificações.

Método: as bases de dados PubMed, Cochrane e Ovid foram pesquisadas de janeiro de 2007 a junho de 2017. Estudos publicados com revisão por pares que aplicaram o procedimento de ligadura do trato da fístula interesfincteriana e suas modificações para o tratamento de fístulas anais de origem criptogênica com acompanhamento de mediana de 12 meses foram elegíveis. Estudos incompletos, relatos de casos, revisões, resumos, cartas, comunicação breve, comentários e estudos que não preenchiam os critérios de inclusão foram excluídos. O desfecho primário foi medir a cicatrização primária, a cicatrização geral, falhas e recorrência do procedimento de ligadura do trato da fístula interesfincteriana e suas modificações.

Resultados: Vinte e dois estudos foram identificados com apenas dez estudos atendendo aos critérios de inclusão. A ligadura original do trato da fístula interesfincteriana foi realizada em cinco estudos com uma população de 199 pacientes, enquanto os cinco estudos restantes apresentaram quatro modificações diferentes da ligadura do trato da fístula interesfincteriana com um total de 147 pacientes. Tanto o LIFT original quanto suas modificações têm resultados promissores e desfechos potencialmente semelhantes; cicatrização primária na ligadura original do trato da fístula interesfincteriana de 73,95% (IC 95% 60,3-85,6) menos realizada que as modificações de 82,3% (IC 95% 64,8-94,7). Cicatrização geral na ligadura original do trato da fístula interesfincteriana de 78,9% (IC 95% 58,5-93,7) realizada relativamente menos do que as modificações (93,6%, IC 95% 81,4-99,6). A falha na ligadura original do trato da fístula interesfincteriana (17,9%; IC 95% 4,9-36,5) realizada quase tanto quanto as modificações (17,7%; IC 95% 5,3-35,2). Recidiva na ligadura original do trato da fístula interesfincteriana em 9,7% (IC 95% 1,7-23,2). No entanto, não houve recorrência nas modificações.

Conclusão: A ligadura do trato da fístula interesfincteriana e suas modificações são procedimentos eficazes e simples no tratamento de fístulas anais simples, especialmente as transesfincterianas altas. No entanto, mais estudos devem ser realizados para avaliar sua eficácia em relação às fístulas complexas.

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Introduction

Anal fistula, fistula-in-ano, or perianal fistula is a hollow tract lined with granulation tissue, connecting a primary opening inside the anal canal or rectum to a secondary opening in the perianal skin.¹

Over the centuries, the probing of the fistula tract has been the procedure of choice for final identification of its anatomy

and planning the treatment. Laying open a fistulous tract (fistulotomy) is the treatment of choice.² However, this treatment can become challenging when a larger portion of the sphincter muscle is involved. Use of Seton is a traditionally favored method for treating high fistulae to minimize the incontinence problem. More surgical procedures in the form of fibrin glue, Anal Fistula Plug (AFP), Anorectal Advancement Flap (ARAF), and Ligation of the Intersphincteric Tract (LIFT) have been introduced and have met a wide recognition.²

In 2007, Rojanasakul, a Thai colorectal surgeon, and his coworkers presented a new novel approach called “ligation of Intersphincteric Fistula Tract” or LIFT procedure. The procedure included identification and exposure of the intersphincteric tract; then, the tract was ligated and divided. The main idea of LIFT is that ligation and excision of the intersphincteric tract could block the entrance for fecal particles into the tract, therefore, eliminating the intersphincteric sepsis.³

Although its simplicity and high success rates in its initial results, many recent studies had recorded lower healing rates and higher recurrences; this was mainly due to nonstandardized operative techniques and nonstandardized inclusive criteria of patients.

Many researchers tried to add modification to the LIFT technique targeting better results, insertion of a bioprosthetic in the intersphincteric plane to reinforce the closure of the fistula tract BioLIFT,⁴ and adding a transanal advancement flap to evaluate the effect of an additional ligation of the fistula tract on the outcome of transanal advancement flap repair.⁵ LIFT with partial coreout fistulectomy (LIFT plus)⁶ and insertion of bioprosthetic plug (LIFT Plug).⁷

The main aim of this review is to outline healing rates, primary and overall of the original LIFT procedure and compare them with the healing rates of LIFT modification described in literatures. Failure, recurrence rates, incontinence status, and other main complications were also outlined. Complications included wound dehiscence, hematoma, secondary bleed, and purulent discharge at the intersphincteric wound.

Methods

This study was a systematic review and meta-analysis of ligation of intersphincteric fistula track or LIFT procedure as a management of perianal fistula. This review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁸

Search strategy

Two independent reviewers searched PubMed (from January 2007 to June 2017), the Cochrane database and Ovid (January 2007 to June 2017). The keywords used were “fistula, fistulas, fistula-in-ano, perianal fistula, anal fistula, ligation of intersphincteric fistula tract, LIFT procedure and LIFT”. Searches were limited to English articles.

The abstracts of all potentially relevant studies were examined to identify suitable studies for inclusion. The full texts of all eligible articles were obtained. Additional searching of the cited references of selected studies for unidentified articles was also done.

Inclusion criteria

All randomized/non-randomized, controlled/non-controlled clinical trials, retrospective and prospective studies involving the procedure, and its modification were eligible. Full original peer-reviewed studies and fully published in English were

eligible. The trials had to have a minimal median follow-up of one year.

Exclusion criteria

Case reports, reviews, abstracts, letters, short communication, and comments were excluded. Incomplete studies or studies with primary results were excluded. Studies with median follow-up less than 12 months were excluded. Studies which include fistulas of noncryptogenic origin were excluded. Studies which did not have a clear view of not including fistulas in HIV patients, tuberculosis, inflammatory bowel diseases, and recto-vaginal origin were excluded. Studies with unclear results or results favoring the procedure were excluded to eliminate the fall in the trap of authors' bias.

Study selection and study quality

Two independent reviewers identified the relevant studies. All of the abstracts were initially reviewed for potential inclusion; selected articles were then reviewed, categorized as meeting or not meeting the inclusion criteria, and scored according to the level of evidence using the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence system.⁹

Data extraction

Data were extracted from the included articles by an independent reviewer. Data included; authors, period of study, year of publication, study design, operative technique, patient criteria and number, types and complexity of fistula, and all data related to the defined in the outcomes.

Data analysis

Meta-analysis was done using the open source software “OpenMetaAnalyst”.¹⁰ The outcome studies are proportions of primary healing, overall healing, failure and recurrence in both original LIFT and modified LIFT. The last group included more than one modification of the operation. The program output included the pooled estimate with the 95% confidence interval for both the fixed effect and random effect models. A test of homogeneity of the outcomes was performed and when proved statistically significant the random effect model estimates should be used, otherwise the fixed effect model is satisfactory.

Search outcome

The literature search identified 208 results for further reviewing. After careful reviewing of articles, a total of 10 studies were included, according to the review criteria for analysis (Fig. 1).

Results

After reviewing of operative details of the selected 10 studies (Table 1), we concluded original LIFT in 5 studies and 4 modifications in the remaining 5 studies; two studies included LIFT with partial coreout fistulectomy, and the remaining 3

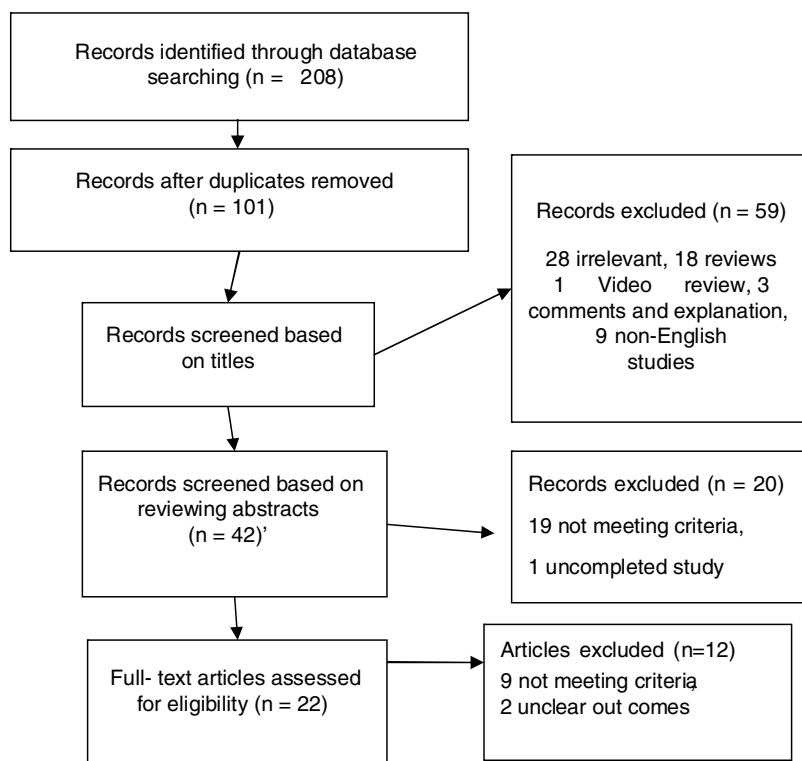


Fig. 1 – Flow diagram of the search strategy.

Table 1 – Original LIFT data by author, type of study, procedure, type of fistula, etc.

| Author | Period of study | Year published | Type of study | Procedure (n) | Type of fistula (%) | 1ry healing (%) | Follow-up, months (n) | Continence evaluation | OC-EBM level ^a |
|------------------------|-----------------------------|----------------|---------------|----------------------------------|---------------------------------------|-----------------|-----------------------|-----------------------|---------------------------|
| Tan ¹¹ | April 2006–July 2011 | 2012 | R | Original LIFT (24) vs. ERAF (31) | Transsphincteric (100%) | 62.5% | 13.0 | Clinical | 4 |
| Mushaya ¹² | December 2007–February 2011 | 2012 | RCT | Original LIFT (25) vs. ARAF (14) | Transsphincteric (100%) | 68.0% | 19.2 | CCF-FI | 2 |
| Madbouly ¹³ | July 2011–February 2013 | 2014 | P | Original LIFT (33) vs. MAF (35) | Transsphincteric (100%) | 94.2% | 12 | WIS | 3 |
| Wallin ¹⁴ | March 2007–September 2011 | 2012 | R | Original LIFT (93) | Transsphincteric (77%), complex (16%) | 66% | 19 | CCF-FI | 4 |
| Dalbem ¹⁵ | May 2012–September 2013 | 2014 | P | Original LIFT (22) | Transsphincteric (100%) | 77% | 14 | Clinical | 4 |

R, retrospective; RCT, randomized controlled; P, prospective; LIFT, ligation of intersphincteric tract; ERAF, endorectal advancement flap; ARAF, anorectal advancement flap; MAF, mucosal advancement flap; CCF-FI, Cleveland Clinic Florida Fecal Incontinence score; NR, not reported; WIS, Wexner Incontinence Score; OCEBM, Oxford Centre for Evidence-based.

studies included LIFT with partial coreout with intraoperative Seton, LIFT with partial coreout with advancement flap, and the LIFT-plug.

Original LIFT outcomes

Regarding original LIFT, a total of 5 studies were included with a population of 199 patients (Fig. 2 and Table 1),¹¹⁻¹⁵ all of cryptoglandular origin and mostly transsphincteric.

The pooled data of primary healing were 73.95% (95% CI 60.3–85.6) (Table 2), median healing time was 3.8 to 4 weeks when reported, and median follow-up period varied from 12 months to 19.2 months.

On the other hand, overall healing rates of the pooled data were 78.9% (95% CI 58.5–93.7) (Table 3). Overall healing rates increased in 2 studies: 92% (95% CI 73.969–99.016) and 100% (95% CI 84.56–100.0).^{13,15} However, overall healing rates decreased in only 2 studies: 56% (95% CI 45.238–66.20)

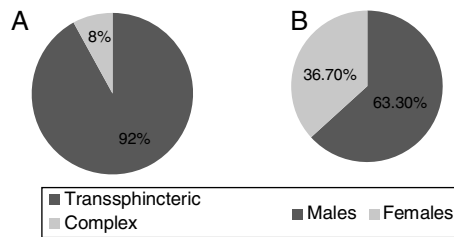


Fig. 2 – Population of original LIFT: (A) type of fistula; (B) gender.

and 74.3% (95% CI 56.744–87.511).^{14,15} Rates did not have any change in one study regarding overall healing (62.5%) (95% CI 40.594–81.201).¹¹

Failure rates from the pooled data were 17.9% (95% CI 4.9–36.5) (Table 4). Causes and management of failure were only mentioned in 3 studies^{11,13,15} (Table 6). However, it is noticeable that 2 studies^{14,15} with 37 failures showed that 14 failed transsphincteric fistulas were converted into intersphincteric fistulas and were treated successfully by simple

fistulectomy and one of these studies mentioned that all its failure and management were of similar pattern.¹⁵ Recurrences data from the pooled studies were 9.7% (95% CI 1.7–23.2). Recurrences occurred in only 3 studies with 8% (95% CI 0.984–26.031),¹² 20% (95% CI 8.441–36.938),¹³ and 25.8% (95% CI 17.287–35.923)¹⁴ with median time to recurrence of 3.5, 4, and 7 months respectively (Table 5).

Other notable complications when mentioned were, secondary bleeding in 1 patient,¹¹ one patient had hematoma in a study with 93 patient,¹³ and finally wound dehiscence and infection in intersphincteric wound of 7 patients in 2 studies with 47 patient.^{12,15}

In all five studies, there was no change in continence function, except in one study which reported that 1 patient had incontinence for liquid and gas, and 4 patients reported incontinence for gas.¹⁵

Three of those 5 trials compared LIFT with other procedures.^{11–13} One retrospective study by Tan¹¹ compared ligation of the intersphincteric fistula tract with endorectal advancement flap with healing rates of 62.5% and 93.5% respectively. Failure rates of the former (37.5%) were almost five times higher than the latter (6.5%).

Table 2 – Meta-analysis: proportion of primary healing in original lift.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|------------------------|-------------|----------------|---------------|------------|--------------|
| | | | | Fixed | Random |
| Tan et al. (2012) | 24 | 62.5 | 40.594–81.201 | 12.25 | 18.46 |
| Mushaya et al. (2012) | 25 | 68 | 46.500–85.050 | 12.75 | 18.7 |
| Wallin et al. (2012) | 93 | 65.591 | 55.021–75.139 | 46.08 | 24.37 |
| Dalbem et al. (2014) | 22 | 77.273 | 54.630–92.179 | 11.27 | 17.94 |
| Madbouly et al. (2014) | 35 | 94.286 | 80.843–99.300 | 17.65 | 20.53 |
| Total (fixed effects) | 199 | 72.414 | 65.739–78.426 | 100 | 100 |
| Total (random effects) | 199 | 73.95 | 60.255–85.605 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 15.7797 |
| DF | | | | | 4 |
| Significance level | | | | | $p = 0.0033$ |
| I^2 (inconsistency) | | | | | 74.65% |
| 95% CI for I^2 | | | | | 37.33–89.75 |

Table 3 – Meta-analysis: proportion of overall healing in original LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|------------------------|-------------|----------------|----------------|------------|--------------|
| | | | | Fixed | Random |
| Tan et al. (2012) | 24 | 62.5 | 40.594–81.201 | 12.25 | 19.36 |
| Mushaya et al. (2012) | 25 | 92 | 73.969–99.016 | 12.75 | 19.47 |
| Wallin et al. (2012) | 93 | 55.914 | 45.238–66.203 | 46.08 | 21.76 |
| Dalbem et al. (2014) | 22 | 100 | 84.563–100.000 | 11.27 | 19.11 |
| Madbouly et al. (2014) | 35 | 74.286 | 56.744–87.511 | 17.65 | 20.29 |
| Total (fixed effects) | 199 | 71.489 | 64.766–77.575 | 100 | 100 |
| Total (random effects) | 199 | 78.893 | 58.498–93.652 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 36.9388 |
| DF | | | | | 4 |
| Significance level | | | | | $p = 0.0001$ |
| I^2 (inconsistency) | | | | | 89.17% |
| 95% CI for I^2 | | | | | 77.48–94.79 |

Table 4 – Meta-analysis: proportion of failure in original LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|--------------------------------|-------------|----------------|---------------|------------|-------------|
| | | | | Fixed | Random |
| Tan et al. (2012) | 24 | 37.5 | 18.799–59.406 | 12.25 | 19.29 |
| Mushaya et al. (2012) | 25 | 0 | 0.000–13.719 | 12.75 | 19.42 |
| Wallin et al. (2012) | 93 | 34.409 | 24.861–44.979 | 46.08 | 21.95 |
| Dalbem et al. (2014) | 22 | 22.727 | 7.821–45.370 | 11.27 | 19.02 |
| Madbouly et al. (2014) | 35 | 5.714 | 0.700–19.157 | 17.65 | 20.32 |
| Total (fixed effects) | 199 | 21.983 | 16.500–28.299 | 100 | 100 |
| Total (random effects) | 199 | 17.858 | 4.943–36.472 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 33.4762 |
| DF | | | | | 4 |
| Significance level | | | | | p < 0.0001 |
| I ² (inconsistency) | | | | | 88.05% |
| 95% CI for I ² | | | | | 74.65–94.37 |

Table 5 – Meta-analysis: proportion of recurrence in original LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|--------------------------------|-------------|----------------|---------------|------------|-------------|
| | | | | Fixed | Random |
| Tan et al. (2012) | 24 | 0 | 0.000–14.247 | 12.25 | 19.06 |
| Mushaya et al. (2012) | 25 | 8 | 0.984–26.031 | 12.75 | 19.22 |
| Wallin et al. (2012) | 93 | 25.806 | 17.287–35.923 | 46.08 | 22.61 |
| Dalbem et al. (2014) | 22 | 0 | 0.000–15.437 | 11.27 | 18.72 |
| Madbouly et al. (2014) | 35 | 20 | 8.441–36.938 | 17.65 | 20.39 |
| Total (fixed effects) | 199 | 14.784 | 10.213–20.410 | 100 | 100 |
| Total (random effects) | 199 | 9.711 | 1.723–23.165 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 25.429 |
| DF | | | | | 4 |
| Significance level | | | | | p < 0.0001 |
| I ² (inconsistency) | | | | | 84.27% |
| 95% CI for I ² | | | | | 64.71–92.99 |

Table 6 – Showing anatomy of failure recurrence of original LIFT.

| Author | Time to recurrence | Failure n (%) | Recurrence n (%) | Treatment of failure |
|------------------------|--------------------|---------------|------------------|---|
| Tan ¹¹ | NA | 9 (37.5%) | 0 | Incision and drainage1 Fistulectomy 4 Seton 4 ERAF 2 LIFT 1 |
| Mushaya ¹² | 4 months | 0 | 2 (8%) | NA |
| Madbouly ¹³ | 3.5 months | 2 (5.7%) | 7 (20%) | NA |
| Wallin ¹⁴ | 7.0 months | 32 (34.4%) | 24 (25.8%) | 9 intersphincteric by fistulectomy 2 transsphincteric by fistulectomy 20 by Seton 13 by LIFT 2 by PLUG 1 by advancement flap |
| Dalbem ¹⁵ | NA | 5 (23%) | 0 | 9 by drainage 5 intersphincteric by fistulectomy |

A prospective study by Madbouly comparing LIFT with Mucosal Advancement Flap (MAF) showed that primary healing was 94.2% in LIFT vs. 91.4% in MAF,¹³ with median healing time in first group (26.6 days) significantly less than the second group (38.1 days). Failure rates were 5.8% in LIFT group and 8.5% in MAF group. After complete healing, 7 out of 35

(21.2%) patients showed recurrence after LIFT while 9 out of 35 (28.1%) patients after MAF. Overall, all healing were higher in LIFT (74.3%) in comparison to MAF (65.7%).

A notable part of this trial was the satisfactory scaling of patient stating that LIFT has the advantage of less postoperative pain. In addition, there was no change of continence levels

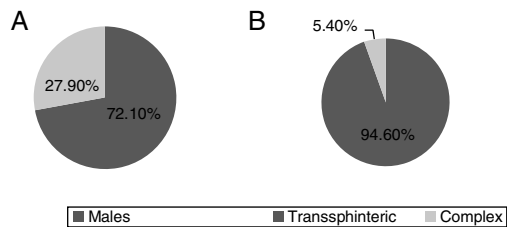


Fig. 3 – Population of LIFT modification group: (A) gender; (B) type of fistula.

after 16 weeks in patients who underwent lift, but 2 patients who underwent MAF showed insentience to (1) gas and (1) liquid.

A controlled randomized study by Mushaya¹² comparing LIFT with Anorectal Advancement Flap (ARAF) concluded that the major findings were that the LIFT technique can be performed more rapidly with less pain, a better satisfaction score, and faster resumption of normal activities than the ARAF technique. Although the overall recurrence rate was low in both procedures (7% and 8% respectively), there was no difference in recurrence rate between the 2 procedures. However, one patient in the ARAF group reported a slight incontinence (a CCF-FI score of 4) which had resolved in a few weeks.¹²

LIFT modifications results

Regarding LIFT modifications, 5 trials were included in this review, with population of 147 patients with demographic values according to Fig. 3. Four modifications were identified (Table 3).

First modification of original LIFT procedure included coring out of fistula tract from the external opening of the fistula tract to the lateral border of the external sphincter. It was described by Sirikurnpiboon “LIFT PLUS” in 2013.⁷ Two studies, included in this review, applied this technique, one prospective¹⁶ and another retrospective,¹⁷ with total numbers of 61 patients with 22 low transsphincteric fistulas and 39 with transsphincteric fistula respectively (Table 7).

Primary healing rates of this variation were reported as 81.8% (95% CI 59.715–94.813) and 87.17% (95% CI 72.570–95.703). Overall, all healing rates reached 100% (95% CI 84.563–100.000) in both studies. Median follow-ups were 19.5 and 15 months. There were no changes in continence levels in both studies.

There was no recurrence; however, an interesting fact was that both studies reported 9 failures only in the form of intersphincteric fistulas rather than the original transsphincteric and they were treated successfully with simple fistulectomy.

Other complications also were wound dehiscence (6 out of 39 patients) mentioned in one study.¹⁷

A second modification included in this review was LIFT with partial coring out fistulectomy and an additional transanal advancement flap. Only one study was included in this review with primary healing rates of 51.2% (95% CI 35.134–67.122) in 41 patients with 73.1% (95% CI 57.056–85.779) overall healing rates.⁶

There was no recurrence after median follow-up of 15 months. 20 patients had failure of procedure; however, in 8 (40%) patients, transsphincteric fistulas were converted into intersphincteric treated with simple fistulectomy.

There was no change in continence levels. Other complications also were purulent discharge at the intersphincteric wound resolved spontaneously in 4 patients.

LIFT Plug, a third alternation, which involve insertion of a plug in the external portion of the track. One prospective study was included, and primary healing rates were 95.2% (95% CI 76.184–99.880) in total of 21 patients, with failure in one patient and no recurrence. Only 1 (5%) patient reported rare incontinence for gas postoperatively.⁴

A final modification was included in this review which was left with partial coring out fistulectomy and insertion of Seton during operation. Only one study was included with 20 patients, and 12 of them were with low transsphincteric fistulas and 8 were complex transsphincteric. Healing rates were 95% (95% CI 75.127–99.873). With no recurrence and one reported failure, however, there was no explanation of the failure. No change in the continence levels was observed. Additionally, other complications included were 1 patient with wound dehiscence.¹⁸

Overall, pooled data from LIFT modifications included primary healing rates of 82.3% (95% CI 64.8–94.7) (Table 8), overall healing rates of 93.6% (95% CI 81.4–99.6) (Table 9), failure rates of 17.7% (95% CI 5.3–35.2) (Table 10), and 0 recurrences.

In conclusion, when comparing the original LIFT and its modification, it can be seen that primary healing rates in the original LIFT were 73.95% (95% CI 60.3–85.6), which performed less than that in the modified LIFT with 82.3% (95% CI 64.8–94.7). Overall healing rates in the original LIFT were 78.9% (95% CI 58.5–93.7), which performed less than that in the modified LIFT with 93.6% (95% CI 81.4–99.6). Failure rates in the original LIFT were 17.9% (95% CI 4.9–36.5), which performed almost the same as the modified LIFT with 17.7% (95% CI 5.3–35.2). Recurrence rates in the original LIFT were 9.7% (95% CI 1.7–23.2), which performed less than the modified LIFT with zero recurrence.

Funnel plots for all estimates of original LIFT showed equal balanced distribution of the estimates of different studies around the pooled estimate. However, Funnel plots of the modified LIFT showed some bias toward higher values around the estimates (Figs. 4–17).

Discussion

This review had concluded that LIFT procedure and its modification have an effective healing in over two-third of the population included. It showed that this procedure had minimal or no changes in continence levels. Failed cases usually transformed transsphincteric fistulae into intersphincteric ones which were treated simply by fistulectomy (Tables 6 and 11). Recurrence rates were low and even absent in most of the studies. Other complications were mainly limited to the intersphincteric wound either with hematoma or mostly wound dehiscence which resolved spontaneously without any surgical intervention. LIFT procedure was introduced in 2007 to find a better outcome in anal surgery

Table 7 – LIFT modifications data by author, type of study, procedure, type of fistula, etc.

| Author | Period of study | Year published | Type of study | Procedure (n) | Type of fistula (%) | 1ry healing (%) | Follow-up, months (n) | Continence evaluation | OCEBM level |
|-----------------------|--------------------------|----------------|---------------|---|--|-----------------|-----------------------|----------------------------|-------------|
| Onkelen ¹⁶ | June 2009–March 2012 | 2012 | P | LIFT with partial coreout fistulectomy (22) | Low transsphincteric fistula | 82% | 19.5 | RFISI | 4 |
| Feng Ye ¹⁷ | June 2012–March 2013 | 2014 | R | LIFT with partial coreout fistulectomy (39) | High transsphincteric fistula | 87.2% | 15 | WIS | 4 |
| Onkelen ⁶ | June 2009–December 2010 | 2012 | p | LIFT with partial coreout fistulectomy and TAFR (41) | High transsphincteric fistula | 51.0% | 15 | RFISI | 4 |
| Han ⁴ | December 2010–March 2011 | 2012 | P | LIFT-plug (21) | Transsphincteric | 95.0% | 14 | WIS | 4 |
| Tsunoda ¹⁸ | March 2010–August 2012 | 2012 | p | LIFT with partial coreout fistulectomy and Seton (20) | Low transsphincteric (60%), complex (40%). | 95.0% | 18.0 | Manometry, RFISI, clinical | 4 |

R, retrospective; P, prospective; LIFT, ligation of intersphincteric tract; TARA, transanal advancement flap; RFISI, Rockwood Fecal Incontinence Severity Index; WIS, Wexner Incontinence Score; OCEBM, Oxford Centre for Evidence-Based.

Table 8 – Meta-analysis: proportion of primary healing in Modifications of LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|------------------------|-------------|----------------|---------------|------------|--------------|
| | | | | Fixed | Random |
| Onkelen et al. (2012) | 22 | 81.818 | 59.715–94.813 | 15.54 | 19.36 |
| Onkelen et al. (2012) | 41 | 51.22 | 35.134–67.122 | 28.38 | 21.29 |
| Han et al. (2012) | 21 | 95.238 | 76.184–99.880 | 14.86 | 19.19 |
| Tsunoda et al. (2012) | 20 | 95 | 75.127–99.873 | 14.19 | 19 |
| Feng Ye et al. (2014) | 39 | 87.179 | 72.570–95.703 | 27.03 | 21.16 |
| Total (fixed effects) | 143 | 79.506 | 72.100–85.693 | 100 | 100 |
| Total (random effects) | 143 | 82.297 | 64.764–94.668 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 24.1237 |
| DF | | | | | 4 |
| Significance level | | | | | $p = 0.0001$ |
| I^2 (inconsistency) | | | | | 83.42% |
| 95% CI for I^2 | | | | | 62.39–92.69 |

Table 9 – Meta-analysis: proportion of overall healing in modifications of LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|------------------------|-------------|----------------|----------------|------------|--------------|
| | | | | Fixed | Random |
| Onkelen et al. (2012) | 22 | 100 | 84.563–100.000 | 15.54 | 19.28 |
| Onkelen et al. (2012) | 41 | 73.171 | 57.056–85.779 | 28.38 | 21.44 |
| Han et al. (2012) | 21 | 95.238 | 76.184–99.880 | 14.86 | 19.09 |
| Tsunoda et al. (2012) | 20 | 95 | 75.127–99.873 | 14.19 | 18.88 |
| Feng Ye et al. (2014) | 39 | 100 | 90.975–100.000 | 27.03 | 21.3 |
| Total (fixed effects) | 143 | 92.853 | 87.442–96.436 | 100 | 100 |
| Total (random effects) | 143 | 93.62 | 81.420–99.577 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 21.5523 |
| DF | | | | | 4 |
| Significance level | | | | | $p = 0.0002$ |
| I^2 (inconsistency) | | | | | 81.44% |
| 95% CI for I^2 | | | | | 56.92–92.01 |

Table 10 – Meta-analysis: proportion of failure in modifications of LIFT.

| Study | Sample size | Proportion (%) | 95% CI | Weight (%) | |
|------------------------|-------------|----------------|---------------|------------|--------------|
| | | | | Fixed | Random |
| Onkelen et al. (2012) | 22 | 18.182 | 5.187–40.285 | 15.54 | 19.36 |
| Onkelen et al. (2012) | 41 | 48.78 | 32.878–64.866 | 28.38 | 21.29 |
| Han et al. (2012) | 21 | 4.762 | 0.120–23.816 | 14.86 | 19.19 |
| Tsunoda et al. (2012) | 20 | 5 | 0.127–24.873 | 14.19 | 19 |
| Feng Ye et al. (2014) | 39 | 12.821 | 4.297–27.430 | 27.03 | 21.16 |
| Total (fixed effects) | 143 | 20.494 | 14.307–27.900 | 100 | 100 |
| Total (random effects) | 143 | 17.703 | 5.332–35.236 | 100 | 100 |
| Test for heterogeneity | | | | | |
| Q | | | | | 24.1237 |
| DF | | | | | 4 |
| Significance level | | | | | $p = 0.0001$ |
| I^2 (inconsistency) | | | | | 83.42% |
| 95% CI for I^2 | | | | | 62.39–92.69 |

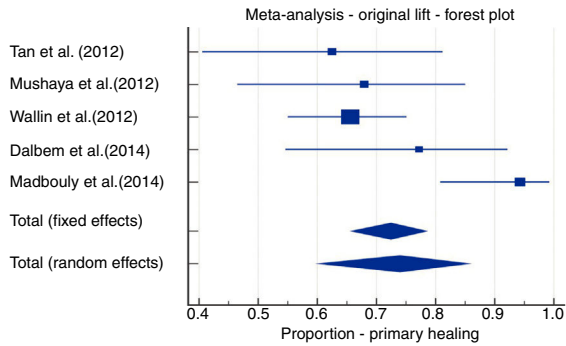


Fig. 4 – Meta-analysis; original LIFT, primary healing forest plot.

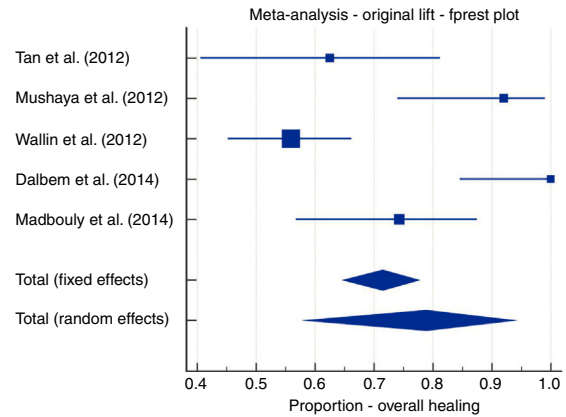


Fig. 6 – Meta-analysis; original LIFT, overall healing forest plot.

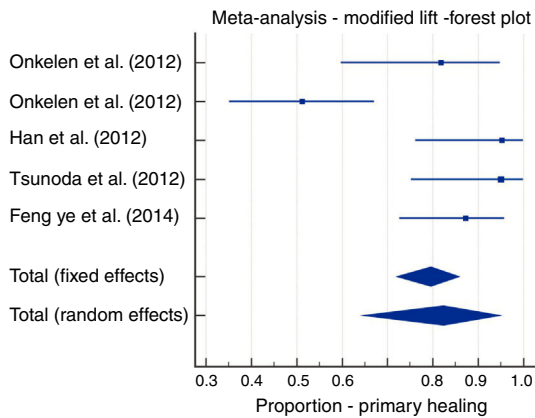


Fig. 5 – Meta-analysis; LIFT modifications, primary healing forest plot.

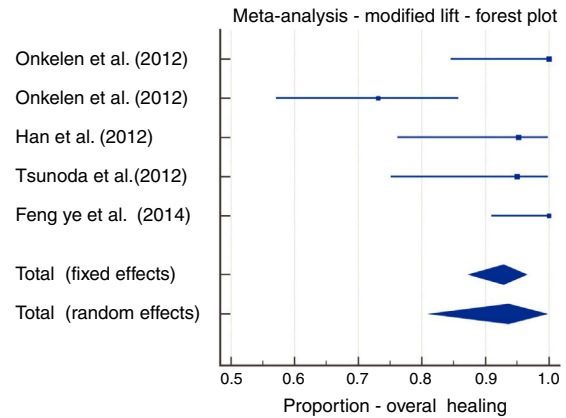


Fig. 7 – Meta-analysis; original LIFT, overall healing forest plot.

regarding saving sphincters unlike other procedure, also to provide better healing and lower recurrence rate. And since then it has been popularized among many surgeons' worldwide, thanks to its simplicity and its promising outcomes, comparing its result to other procedures.

The original LIFT procedure appeared most frequently in the literature. Rojanasakul initially reported 94% healing rates, and healing rates from pooled data were 73.95% (95% CI 60.3–85.6) for primary healing and 78.9% (95% CI 58.5–93.7) for overall healing in original LIFT in this review. Other reviews reported healing rates in 759 patients that ranged from 51% to 94%.¹⁹ Another review showed success rates from 40% to 95%, in 352 of 495 patients.²⁰

Additionally, healing rates from the pooled data of LIFT modification were 82.3% (95% CI 64.8–94.7) for primary healing and 93.6% (95% CI 81.4–99.6) for overall healing. Overall, healing rates of LIFT and its modifications showed better results than other sphincter-preserving procedures, for example, 10–67% for fibrin glue,²¹ <50% for fistula plug²² and 25–95% for advancement flap.²² All of the studies in our review included a standard definition of healing whether primary healing or overall healing.^{11,14} However, a clear definition of failure or recurrence has not been universally described yet.

What is interesting is that time to heal after surgery in given studies ranged from 2 weeks¹⁷ to 7 weeks,¹⁸ however, time for healed fistulae to reoccur were around 3 to 7 months in

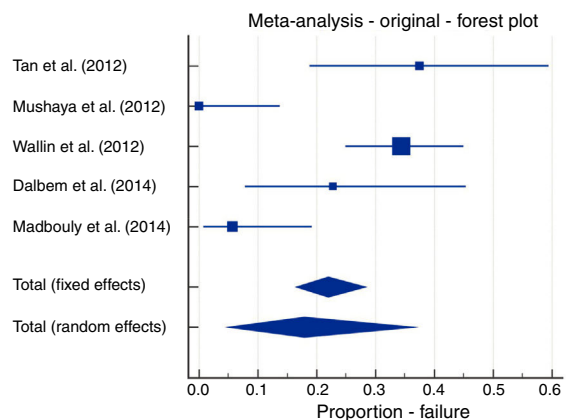


Fig. 8 – Meta-analysis; original LIFT, failure forest plot.

reported studies.¹²⁻¹⁴ This means that long follow up is essential to determine the overall success of this procedure and its modifications. Nevertheless, all reviews which discussed this types of anal surgery did not put consideration on follow up period, and what makes this review more reliable is that it only included studies with follow up more than or equal to 12

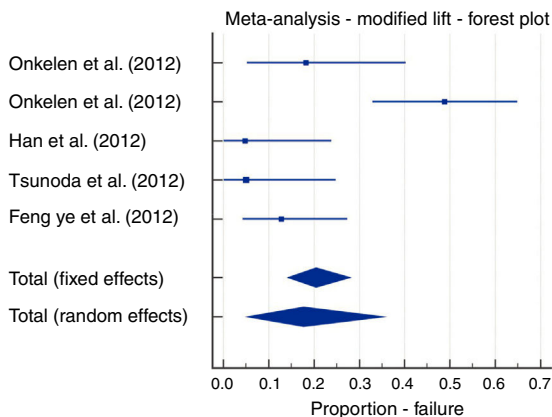


Fig. 9 – Meta-analysis; LIFT modification, failure forest plot.

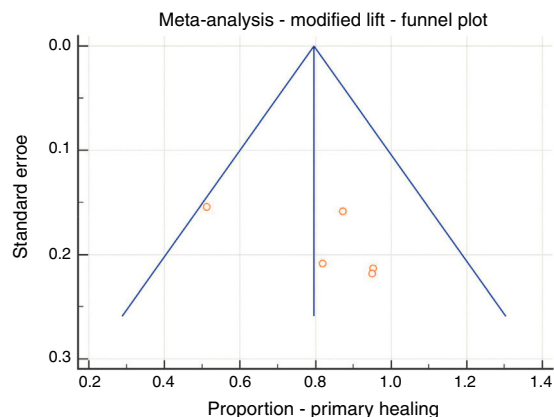


Fig. 12 – Meta-analysis; LIFT modification, primary healing, funnel plot.

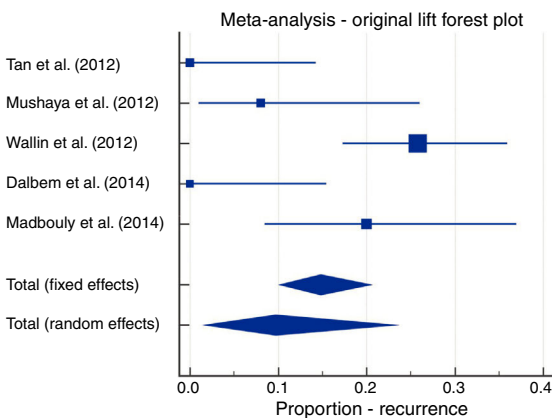


Fig. 10 – Meta-analysis; original LIFT, recurrence forest plot.

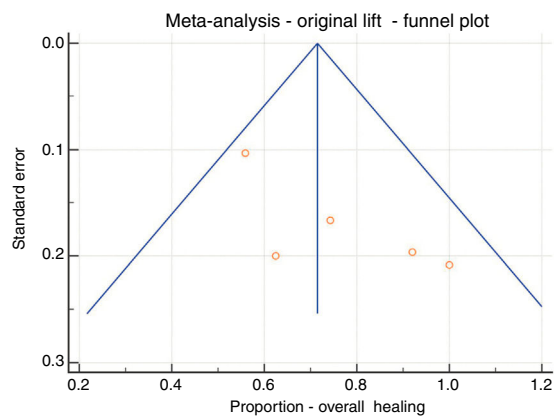


Fig. 13 – Meta-analysis; original LIFT, overall healing, funnel plot.

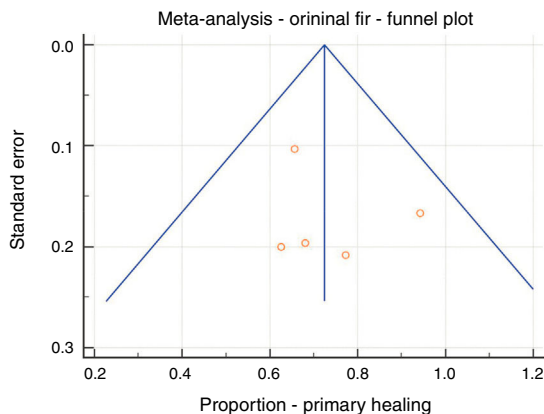


Fig. 11 – Meta-analysis; original LIFT, primary healing, funnel plot.

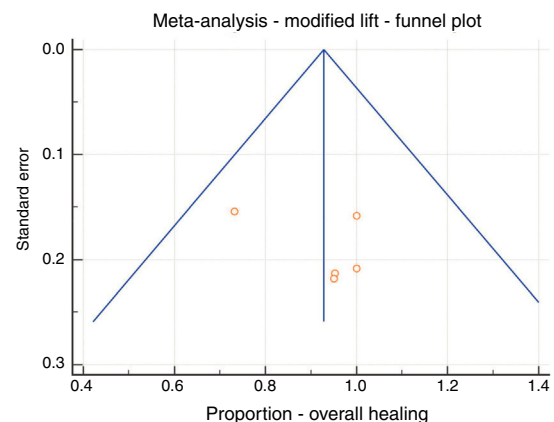


Fig. 14 – Meta-analysis; LIFT modification, overall healing, funnel plot.

months. Also, most of the reviews regarding this procedure did not compare original results with LIFT modifications results. However, more studies are needed to compare the techniques to fulfill better understanding of a superior approach.

Systemic risk factors did not play any major role in studies. In addition, preservation of continence levels play a key in favoring LIFT and its modulations over other sphincter

preserving procedure and other anal procedures like fistulectomy; as seen is this review, continence was rarely damaged in all patients (1 patient mild incontinence to liquid and 5 to gas in total of 340 patients).

Table 11 – Anatomy of failure and recurrence in LIFT modifications.

| Author | Time to recurrence | Failure | Recurrence | Treatment of failure |
|-----------------------|--------------------|---------------|------------------|---|
| Onkelen ¹⁶ | NA | 4 (18%) | No recurrence | 4 intersphincteric by fistulectomy |
| Feng Ye ¹⁷ | NA | 5 (1.2%) | No recurrence | 5 intersphincteric fistula and fistulectomy |
| Onkelen ⁶ | NA | 49% 20 pts | No recurrence | 8 intersphincteric fistula by fistulectomy 4 by TARF 8 by Seton |
| Han ⁴ | NA | 1(5%) | No recurrence | NA |
| Tsunoda ¹⁸ | NA | 1 (5%) | No recurrence | NA |

NA, not given.

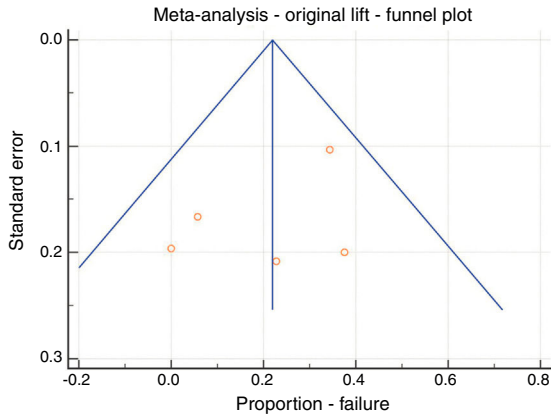


Fig. 15 – Meta-analysis; original LIFT, failure, funnel plot.

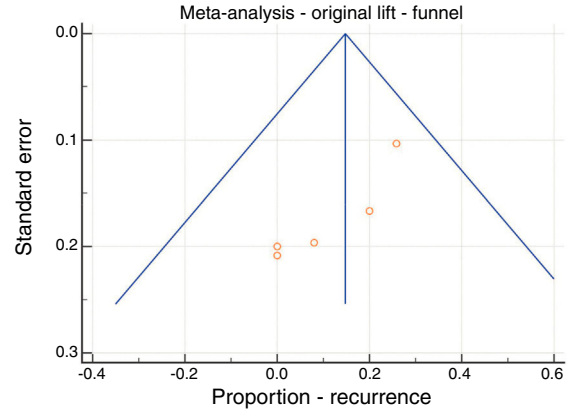


Fig. 17 – Meta-analysis; original LIFT, recurrence, funnel plot.

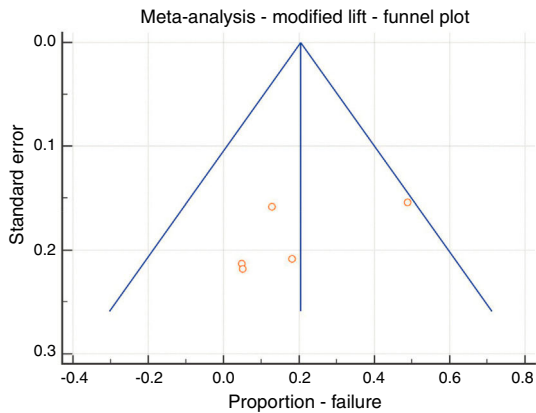


Fig. 16 – Meta-analysis; LIFT modification, failure, funnel plot.

On the other hand, other sphincter-preserving procedures turned out to have greater impact on it. For example, various studies of advancement flap repairs have reported rates of incontinence ranging from 0% to 35%.²² The impact on continence appears to be minimal; also, most of studies included had a formal assessment of incontinence (8 out of 10 studies)^{4,6,12-14,16-18} (Tables 1 and 7). Therefore, we may conclude complete results of the rates and nature of continence changes after this procedure from this review.

This review also highlighted other minor complications following surgery, the main and most notable one

is wound dehiscence and surgical site infection or discharge in intersphincteric incision, 18 patients of 340; however, all patients resolved spontaneously with proper dressing, wound care and sometime antibiotics, with no further intervention.^{6,4,12,15,17}

Regarding preoperative Seton insertion in original and modified LIFT, its result was irrelevant and did not promote better healing. Nevertheless, one study included preoperative Seton to enforce or enhance fibrosis in the tracts to make them well defined.¹⁵ Therefore, further future studies should elaborate the factor of preoperative Seton insertion and its outcomes on healing and recurrence. Similarly, preoperative imaging, with endoanal ultrasound or MRI, in included studies did not play a major role in pre-evaluating the fistula and most surgeons relied heavily on intraoperative examination to outline the anatomy of the fistula. Results from studies which used MRI and endoanal ultrasound were similar to those that discarded imaging. Therefore, there is no need for routine preoperative Seton placement and imaging if not needed, because it could provide patients and the health system with significant cost and time reduction to achieve the targeted outcomes. Regarding fistula complexity, most of the studies on LIFT and its modifications were performed on high transsphincteric fistulae with limited numbers on complex branching ones which could limit the use of these procedures on straight forward fistulae, and therefore more trials should be conducted to access their effectiveness on various types of fistulae.

Conclusion

Ligation of the intersphincteric fistula tract is a feasible, minimally invasive, cheap, and relatively easy procedure, which is safe and effective at the same time. LIFT and its modifications can be ideal for treating straightforward high anal fistulas in patient with no previous intervention. Additionally, more studies should be conducted to compare results regarding different approaches of this procedure with longer follow-up and randomization of patients. Finally, a universal explanation of failure and recurrence should be applied with a proposition that failure should be explained as an unsuccessful achievement of primary healing and recurrence as a failure after successful primary healing.

Conflicts of interest

The authors declare no conflicts of interest.

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