Management of anal fistula by ligation of the intersphincteric fistula tract – a systematic review

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ABSTRACT
INTRODUCTION: Ligation of the intersphincteric fistula tract (LIFT) is a sphincter-preserving procedure for treatment of anal fistulas described in 2007 by Rojanasakul et al. Several studies have since then assessed the procedure with varied results. This review assesses the relevant literature on this topic.
METHODS: The primary endpoints were healing rates, length of follow-up, time to recurrence and post-operative complications. The secondary endpoints were details of the operative technique. A search was made in the PubMed and Embase electronic databases. Reports where LIFT was combined with other fistula treatment techniques were excluded. Only reports in English were included. Most reports were case studies with no control groups. One report could not be retrieved.
RESULTS: A total of 19 original reports were assessed. Details concerning preoperative assessment, antibiotic usage and tract ligation methods varied considerably. Primary healing was achieved in 432 out of 612 (70.6%) patients, and no sphincter function impairments were reported. However, ten out of 19 reports did not include an objective assessment of pre- and post-operative continence. No apparent correlation between length of follow-up and healing rate was found, and the longest time to recurrence was eight months.
CONCLUSION: LIFT is a safe procedure that provided a mean healing of 70.6% with no reports of impairment of the sphincter function. Future reports should include a follow-up length of a minimum of eight months. It remains uncertain whether the outcome may be improved by prior seton suture insertion.

An anal fistula is an abnormal communication between the anal canal and the perianal skin. It is most commonly due to infection originating from the anal glands leading to formation of abscess and/or fistula (crypto-glandular theory). Anal fistulas can be intersphincteric, trans-sphincteric, suprasphincteric and extrasphincteric according to the course of the fistula tract in relation to anal sphincters [1]. The optimal treatment of fistula in ano is one that provides healing, has a low recurrence rate and carries only minimal risk of incontinence. Different methods of treatment of transphincteric fistulas have shown varying recurrence and incontinence rates [2-6]. In 2007, Rojanasakul et al [7] described a novel procedure to treat anal fistulas that theoretically has a very low risk of anal incontinence. The authors reported a success rate of 94.4% in 18 patients. The procedure was named LIFT, the principles of which are identification and ligation of the fistula tract in the intersphincteric space. Several reports – with varying healing rates – have been published since the initial description of the ligation of the intersphincteric fistula tract (LIFT) procedure. We conducted a systematic review of the relevant literature on this topic.

METHODS
A search was made in PubMed and Embase on 28 March 2014 using the terms: (LIFT AND fistula) OR (Ligation AND Intersphincteric AND Fistula AND Tract). Only articles in English were included. The PRISMA guidelines were followed [8]. An additional filter in the form of exclusion of Medline journals was used in the Embase search. The search identified 43 articles. Only original papers describing the LIFT procedure as a separate procedure (i.e. not performed in combination with another surgical procedure for fistula) were included. All prospective and retrospective studies in English were included, regardless of the number of participants, patient demographics and length of follow-up. In case a report was not accessible, the corresponding author was contacted and asked if such a report could be provided. A total of 19 studies were selected for this review. See the PRISMA flow diagram (Figure 1). Five studies were excluded because the LIFT procedure was combined with other surgical techniques. These included perioperative seton insertion [9], bioprosthetic anal fistula plug [10, 11], bioprosthetic graft [12], and advancement flap repair [13]. The variables for which data were sought are summarised in Tables 1-3.

RESULTS
Indications for ligation of the intersphincteric fistula tract
The LIFT procedure is a simple surgical technique; and it has gained popularity since the original report by Rojanasakul et al [7] owing both to its simplicity and because of its sphincter-preserving nature. This is reflected in all studies in this review. Another indication made by au-
LIFT = ligation of the intersphincteric fistula tract.

FiguRe 1
Method of search and selection.

36 records identified through PubMed searching
7 of additional records identified through Embase
43 records screened
17 records excluded (non-original studies): 12 from PubMed 5 from Embase
26 full-text articles assessed for eligibility
19 studies included in qualitative synthesis
7 full-text articles excluded
LIFT in combination (n = 5)
Healing rate not described (n = 1)
Not accessible (n = 1)

LIFT = ligation of the intersphincteric fistula tract.

thors is their search for a procedure that can provide a higher healing rate than other fistula procedures. Rojanasakul et al [7] hypothesised that ligation of the fistula tract closes the entry point for faecal particles into the intersphincteric space, thus eradicating persistent sepsis. Thus, most studies describe LIFT mainly for transsphincteric fistulas. Some authors have included intersphincteric fistulas [14-17], and few studies included rectovaginal fistulas [14, 17-19].

Preoperative assessment
Some reports classified fistulas in accordance with Parks’ fistula classification [15, 18, 20-22]. Rojanasakul et al [7] defined low transsphincteric fistula as a track that passes between or just above the subcutaneous external anal sphincter. Ooi et al [16] classified complex fistulas as all intersphincteric, transsphincteric and suprasphincteric fistulas. In the report from Gentile et al [22], fistulas were reported as complex or high if more than 30% of the external sphincter was involved. Mushaya et al [23], added anterior fistula in a woman, multiple tracts, recurrent fistulas, or if there was pre-existing incontinence to their definition of complex fistulas. Silieri et al [18] extended this definition to include rectovaginal fistulas. Shanwani et al [21] added local irradiation and Crohn’s disease to indications for the LIFT procedure. Sirikurnpiboon et al [24] divided fistulas into simple (low transsphincteric and intersphincteric fistulas that cross less than 30% of the external sphincter) and complex (high transsphincteric fistulas with or without a high blind tract, suprasphincteric, extraspincteric, horse shoe, and those associated with inflammatory bowel disease (IBD), radiation, malignance, pre-existing continence or chronic diarrhoea). Tan et al [15] included a definition of a high fistula as one that encompasses more than one-third of the external sphincter complex.

In some studies, assessment was based solely on a clinical examination; whereas others added proctoscopy and/or magnetic resonance imaging (MRI) and/or endoanal ultrasonography (see Table 1).

The exclusion criteria varied much. In the original report on LIFT, Rojanasakul et al [7], only included patients with normal continence and normal hosts. Van Onkelen et al [25] and Wallin et al [26] excluded rectovaginal fistulas and those due to Crohn’s disease. Wallin et al [26] and Ooi et al [16] also excluded neoplastic fistulas, whereas Mushaya et al [23] added IBD. Tan et al [27] excluded patients with human immunodeficiency virus or IBD. Sirikurnpiboon et al [24] excluded patients with IBD and superficial fistulas. Gentile et al [22] excluded patients with IBD, high-grade haemorrhoids and patients with weakened continence. The report by Gingold et al [20] is, to date, the only study that solely included patients with Crohn’s disease. As shown in Table 1, most studies included patients who had previously undergone fistula surgery. This does not include the insertion of a seton, as all previous seton insertions are reported regardless of whether this was done only prior to LIFT or as a failed attempt to treat fistula. Seton insertion prior to LIFT was either routinely used in patients with clinical evidence of abscess [17, 18, 20, 23] or as a method to facilitate fibrosis around the fistula tract [22].

Operative details
Originally, LIFT procedure consisted of six steps: 1) identification of the internal and external opening, 2) Curvilinear incision of the intersphincteric plane, 3) identification of the intersphincteric tract, 4) ligation close to the internal sphincter, 5) division and removal of the intersphincteric tract and 6) curettage of the remaining tract and incision of the external opening to allow for drainage [7]. Some variations in the operative technique have been reported since the original description. These variations include ligation of each side of the intersphincteric tract [14, 15, 17, 18, 22, 24, 25, 27-29], suturing of the internal opening [22, 28, 30] and dissection of the external opening [16]. Nine studies in this review described some form of bowel preparation prior to LIFT procedure [7, 15, 17, 18, 20-27]. The more or less continence position of the patient also varied between studies. Patient position was not reported in two studies [19, 22], and one author in two publications included in this review [15, 18] reported that the procedure was performed in lithotomy position. The remaining authors primarily reported a prone jack knife position [10, 27]. Mushaya et al [23] reported both positions.

Studies varied in the description of antibiotic usage,
timing, type, duration and route of administration. The procedure was done either under general or regional anaesthesia (see Table 2). The median operative time varied from 10 to 67.5 minutes. The number of surgeons performing the procedure also varied among studies where this was reported; Bleier et al [14] reported that 11 different surgeons performed LIFT procedure in one department.
Post-operative outcomes

The reported endpoints concerning the definition of healing varied greatly among the studies. Rojanasakul et al [7] and Shanwani et al [21] defined healing as “complete epithelialisation of the wound”. Tan [15] and Sileri et al [30] specified healing definition to include both the external and internal wounds. Other authors used the combination of wound healing with resolution of symptoms [18, 19, 22-26]. Gingold et al [20] included “resolution of anal pain” in their definition.

In addition, the degree of wound healing was at times not equal to epithelialisation. Abcarian [29] and Wallin et al [26] used absence of drainage as an indicator of successful LIFT. Some authors did not define healing [14, 18, 23, 30, 31] or merely defined it as “cure of disease” [22].

Healing rate is defined as the rate of healing after the first LIFT procedure, excluding subsequent procedures as well as novel fistulas. In this review, 432 out of 612 patients had a successful outcome after the LIFT procedure, 12 were lost to follow-up. This gives an average healing rate of 70.6% (range: 40-94.4%) as shown in Table 3. Apart from two incidents of persistent anal pain [14], no major post-operative complications including de novo incontinence was reported, however baseline and post-operative continence was not systematically assessed.

Transsphincteric fistulas were converted to intersphincteric fistulas in some studies: [14, 20] where they were treated with subsequent fistulotomy [15, 17, 20, 22, 26, 28, 30] or seton insertion [16].

Follow-up details

The follow-up period varied among the series (average = 10.3 months, range: 4 weeks-26 months), and time to recurrence was reported to be between four weeks and 8 months (see Table 3).

There is no apparent correlation between the length of follow-up and the healing rate.

In the original study by Rojanasakul et al [7], patients were assessed 1 week after surgery and then every two weeks until healing. In the study by Abcarian...
et al [30], patients were clinically examined within the first two post-operative weeks and thereafter at intervals of 2-4 weeks. Patients were examined under general anaesthesia when failure was suspected. This procedure was also followed in the report by Liu et al if symptoms worsened or persisted 6 months after surgery with regular visits planned at 1, 2 and 6 weeks and at 3, 6 and 12 months after surgery [28]. In 2012 Tan et al [27] verified failures by endoanal ultrasound, preceded by reviews 1-2 weeks after surgery and at intervals of 2-4 weeks until healing. In the first report by Tan et al from 2011 [15], the first visit was scheduled for two weeks after surgery. Mushaya et al [23] assessed patients 2, 4 and 16 weeks after surgery and thereafter annually, and recurrences were proven by clinical examination and ultrasound. Sirikurnpiboon et al [24] conducted follow-up at 2, 4, 8 and 12 weeks after the intervention and at 4-weekly intervals thereafter. Follow-up in the series by Shanwani et al [21] was done at 2, 4, 8 and 16 weeks after surgery and every 12 weeks. In the report by Van Onkelen et al [25], visits were scheduled at 2, 8 and 26 weeks after LIFT. Aboulian et al [29] planned visits in the first, second and sixth post-operative week with a final follow-up after 6 months and as needed if swelling, pain and drainage occurred. Ooi et al [16] reviewed patients 2 weeks after the LIFT procedure, and for up to 1 year. Gingold et al [20] followed patients monthly. Gentile et al [22] planned three visits in their study: in the first week, the first month and finally 6 months after surgery. In the first report by Sileri et al [18] from 2011, reviews were scheduled at the first, second and fourth post-operative week and then every month for the first 6 months. In their report from 2013 [17], they assessed patients with endoscopic ultrasound or 3D 4 weeks after surgery as well as 1 and 2 weeks after surgery and every 6 months. They assessed continence by the Faecal Incontinence Severity Index (FISI) and manometry if the FISI score was over 6. Lehmann et al [19] conducted proctoscopy 16 weeks after surgery and 11 patients underwent further proctoscopy and anal 3D ultrasound. Some studies have not reported details on follow-up [14, 26, 31].
DISCUSSION

Due to the paucity of the literature on this relatively new operative technique, we have no reason to believe that significant study selection bias occurred. We do, however, have an incomplete retrieval of identified research leading to one potentially eligible report not being reviewed. This review is also limited by the quality of the included studies, which are patient series without randomisation or control groups, except for two studies where LIFT was compared with anorectal advancement flap [23, 27].

Selecting patients in the operative theatre as being eligible for LIFT carries a risk of selection as well as experience bias at least in one study [21]. The risk of experience bias is a limiting factor as the number of surgeons performing the procedure varied among studies. With few exceptions, few surgeons with long experience in proctology performed the procedures. This may have influenced the relatively high successful healing rates seen in some studies [7, 13]. The three studies with a larger number of operating surgeons showed healing rates between 40 and 74% [14, 26, 29]. On the other hand, Lehmann et al [19] also reported low healing rates in their study (47%), where a single surgeon performed the procedures. Seven out of 19 studies reported that a single surgeon performed the procedures [7, 13, 19, 20, 22, 28, 30], whereas the number of operating surgeons was not reported in eight studies [15-18, 21, 23, 24, 31]. It is logical, however, that this new technique is to be introduced with a few experienced proctologists performing it and with close auditing of the results. Reporting bias is another issue due to the retrospective nature of five studies [15, 26-28, 30].

Treatments of anal fistula by sphincter-preserving techniques like fistula plug and advancement flap have comparable results regarding recurrence and healing rates. These procedures are, however, technically demanding and operator-dependent [32]. The LIFT procedure was originally described specifically for the management of transsphincteric fistula [7]. The procedure is described for intersphincteric fistulas as well [14-17]. However, it is not evident from this review whether

<table>
<thead>
<tr>
<th>Reference</th>
<th>Healing rate, n/N (%)</th>
<th>Median follow-up</th>
<th>Time to recurrence</th>
<th>Post-operative complications</th>
<th>Assessment of continence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rojanasakul et al, 2007 [7]</td>
<td>17/18 (94.4)</td>
<td>4 wks</td>
<td>NR</td>
<td>0</td>
<td>Clinical continence grading</td>
</tr>
<tr>
<td>Bleier et al, 2010 [14]</td>
<td>20/35 (57)</td>
<td>20 wks</td>
<td>10 wks</td>
<td>1 anal fissure</td>
<td>Subjectively</td>
</tr>
<tr>
<td>Shanwani et al, 2010 [21]</td>
<td>37/45 (82.2)</td>
<td>9 mo.</td>
<td>3-8 mo.</td>
<td>0</td>
<td>Clinical</td>
</tr>
<tr>
<td>Sileri et al, 2011 [18]</td>
<td>15/18 (83)</td>
<td>6 mo.</td>
<td>NR</td>
<td>1 haemorrhoidal thrombosis</td>
<td>FISI, anal manometry if score &gt; 6</td>
</tr>
<tr>
<td>Mushaya et al, 2012 [23]</td>
<td>23/25 (92)</td>
<td>16.4 mo.</td>
<td>4 mo.</td>
<td>1 secondary bleed</td>
<td>Cleveland Clinic Florida Fecal Incontinence</td>
</tr>
<tr>
<td>Ooi et al, 2012 [16]</td>
<td>17/25 (68)</td>
<td>22 wks</td>
<td>7-20 wks</td>
<td>0</td>
<td>Wexner’s incontinence scale</td>
</tr>
<tr>
<td>Abcarian et al, 2012 [29]</td>
<td>29/39 (74)</td>
<td>18.3 wks</td>
<td>NR</td>
<td>NR</td>
<td>Subjectively</td>
</tr>
<tr>
<td>van Onkelen et al, 2013 [25]</td>
<td>18/22 (82)</td>
<td>19.5 mo.</td>
<td>None</td>
<td>NR</td>
<td>Rockwood Fecal Incontinence Severity Index</td>
</tr>
<tr>
<td>Tan et al, 2012 [27]</td>
<td>15/24 (62.5)</td>
<td>13 mo.</td>
<td>NR</td>
<td>NR</td>
<td>None</td>
</tr>
<tr>
<td>Wallin et al, 2012 [26]</td>
<td>37/93 (40)</td>
<td>19 mo.</td>
<td>7 mo.</td>
<td>NR</td>
<td>Cleveland Clinic Florida Fecal Incontinence</td>
</tr>
<tr>
<td>Lo et al, 2012 [31]</td>
<td>22/25 (88)</td>
<td>9.8 mo.</td>
<td>2 mo.</td>
<td>0</td>
<td>NR</td>
</tr>
<tr>
<td>Gingold et al, 2013 [20]</td>
<td>8/12 (67)d</td>
<td>11.2 mo.</td>
<td>4 wks</td>
<td>0</td>
<td>Wexner Perianal CD Activity Index</td>
</tr>
<tr>
<td>Sileri et al, 2014 [17]</td>
<td>19/36 (73)</td>
<td>16 mo.</td>
<td>4-8 wks</td>
<td>0</td>
<td>FISI, anal manometry if score &gt;6</td>
</tr>
<tr>
<td>Lehmann et al, 2013 [19]</td>
<td>7/15 (47)</td>
<td>13.5 mo.</td>
<td>NR</td>
<td>1 local haematoma</td>
<td>Clinical</td>
</tr>
<tr>
<td>Sirikurnpiboon et al, 2013 [24]</td>
<td>17/21 (81)</td>
<td>18 wks</td>
<td>10 wks</td>
<td>1 anal fissure</td>
<td>Wexner Incontinence score and clinical continence grading</td>
</tr>
<tr>
<td>Liu et al, 2013 [28]</td>
<td>23/38 (61)</td>
<td>26 mo.</td>
<td>4 mo.</td>
<td>2 vaginal fungal infection</td>
<td>Subjective</td>
</tr>
<tr>
<td>Gentile et al, 2013 [22]</td>
<td>11/15 (73.3)</td>
<td>6 mo.</td>
<td>5-25 wks</td>
<td>Persistent pain, n = 1</td>
<td>Wexner’s Incontinence Scale</td>
</tr>
</tbody>
</table>

FISI = Fecal Incontinence Severity Index; NR = not reported.

a) Minimum.
b) Mean.
c) Only for patients with successful fistula closure post-operative.
d) Including 3 patients with novel fistulas.
there is any benefit for this particular indication, where simple fistulotomy is probably a better option [33]. Several authors distinguish between high or low transphincteric fistulas. We believe, however, that this is a highly subjective assessment due to the lack of a standard method of preoperative evaluation. Perioperative use of transanal 3D ultrasound may increase the accuracy of fistula classification [34]. The variation in fistula classification is problematic and important in terms of indication for LIFT and ultimately for the healing rate. Consistency and standardisation is needed in order to achieve comparable healing rates. Park's classification [1] provides an easy and reproducible method of accurately defining the fistula, and this should be done intraoperatively in order to choose the optimal operative method. Fistulotomy is probably a safer procedure for the treatment of low transphincteric fistulas. However, anterior fistulas in women should be treated with caution as the risk of incontinence is very high [34].

The LIFT procedure is based on a sound principle of ligating a tract, and the best results are probably obtained in the absence of infection [24], on a “mature” tract [23] and without multiple secondary tracts. This raises the question of the benefits of inserting a seton suture prior to the LIFT procedure, which, theoretically at least, allows for drainage and maturation of the fistula tract and positively influences the outcome. However, seton insertion could increase the amount of fibrous tissue and impede healing. Mushaya et al [23] believe that a loose seton provides adequate drainage of the sepsis, which gives a more favourable tissue-healing environment and thus facilitates the LIFT procedure. They have a policy of revising the seton for persistent and recurrent infection a minimum of 6 months prior to surgery. Tan et al [27] hypothesised that the seton can result in scarring, which impedes localisation of the anal gland and its subsequent excision as well as the internal opening. The authors obtained a healing rate of 62.5%, although every patient had a seton inserted 14 weeks preoperatively. Gingold et al [21], who achieved a healing rate of 67%, reported that all their successful LIFT procedures had a seton placed preoperatively. Sileri et al [17] assume that the seton can create a via falsa, which predisposes to an increased risk of recurrence. In the study by Shanwani et al [21], none of the patients presented with sepsis and therefore none had a seton inserted prior to LIFT. Nevertheless, they achieved a healing rate of 82.2%. Future studies should investigate preoperative seton insertion as a means to increase the likelihood of successful treatment, preferably by randomisation.

There is no strong evidence from this review regarding the optimal way to perform LIFT when it comes to the perioperative details. Bowel preparation, antibiotic usage and patient position varied among the studies. The reason for choosing either the lithotomy or prone, jack-knife position is unclear, and is probably a matter of the surgeon’s personal preference. The level of evidence does not allow for solid conclusions regarding the optimal operative detail. Mushaya et al [23] conducted a randomised trial where patients underwent either LIFT or anorectal advancement flap repair (ARAF). Patients in the LIFT group experienced less pain, higher patient satisfaction and took shorter time to resume normal activities. In addition, the LIFT procedure took shorter time. The authors found no difference in recurrence rate or incontinence scores. Limitations include a 2:1 intervention versus control basis (25 in the LIFT group and 14 in the ARAF group).

Tan et al [27] performed a retrospective review of 31 patients who underwent the Endorectal Advancement Flap (ERAF) procedure; and they compared the results with the results in 24 patients who underwent a LIFT procedure. They found a higher success rate in the ERAF group (93.5% versus 62.5%). They postulated that while it is easy to address the internal opening, which is the key of the ERAF procedure, scarring could complicate the identification of the fistula tract and subsequent excision, which is an important step of the LIFT procedure. Sirikurnpiboon et al [24] compared 21 patients undergoing LIFT with 20 patients where LIFT was combined with partial core-out fistulectomy from the external opening to the external sphincter. They found no differences in results between the two groups. The study was limited by the risk of selection bias and lack of randomisation. There is, to date, no evidence for the benefit of fistulectomy of a tract extending from the ligated part to the external opening. We believe that the external opening should be enlarged and left open for drainage to ensure complete eradication of sepsis.

In our opinion, a successful outcome of LIFT should include complete healing and absence of drainage from the external opening and intersphincteric wound and resolution of symptoms.
Fistulas are classified into four different types: inter-, trans-, supra- and extraspincteric.

The preferred outcome is complete healing without compromising the sphincter function. Various sphincter-preserving techniques exist.

Ligation of the intersphincteric fistula tract is a promising new method which, theoretically, carries a low risk of incontinence.

Follow-up duration should at least be eight months as this is the latest report of recurrence to date. Future studies should include information on objectively assessed baseline and post-operative continence. The method of anaesthesia should be decided in accordance with the patient’s wishes.

The LIFT procedure can probably be done in either the lithotomy or the prone jack-knife position without any effect on healing rates.

In this review, the included studies have not used a standard definition of healing after LIFT. A healing rate of 70.6% is to be interpreted with caution.

CONCLUSION
LIFT is an inexpensive and safe procedure that provided primary healing of anal fistula in 432 patients out of 612 (70.6%) in this review with no reports of sphincter function impairment. However, ten out of 19 reports did not include an objective assessment of pre- and post-operative continence. It remains uncertain whether the outcome can be improved by prior insertion of a seton suture.

The procedure is easy to learn and has very few complications. The outcomes measured by healing rates vary considerably among the reported series. There is a need for well-conducted randomised studies that compare various modifications in the preoperative assessment and the operative details and compare LIFT with other sphincter-preserving techniques.

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LITERATURE