

Endosonography-confirmed long-term outcomes of ligation of the intersphincteric fistula tract procedure for complex perianal fistulas



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Endosonography-confirmed long-term outcomes of ligation of the intersphincteric fistula tract procedure for complex perianal fistulas

OBJECTIVE: *As the short-term outcomes may overestimate the true success rates of sphincter-sparing techniques, and follow-up protocols that were reported based on clinical criteria do not ideally reflect real world outcomes associated with complex perianal fistulas (CPF), this study aimed to reveal clinically and three dimensional endosonography confirmed long-term outcomes and analyze the factors associated with recurrences of ligation of intersphincteric fistula tract (LIFT) procedure.*

PATIENTS AND METHODS: *A retrospective cross-sectional review was conducted for patients who underwent the LIFT procedure for complex perianal fistulas between October 2015 and February 2017. Cox proportional regression model was used to estimate the mean failure free survival rates and log-rank test was used to compare the outcome distributions for patients who healed vs presented with failure.*

RESULTS: *A total of 42 patients with the majority of males (n=34, %81), who underwent LIFT procedure for CPF were analyzed. None of patients were lost at follow-up. Endosonography-confirmed fistula types were high transsphincteric (n=35), horseshoe fistula (n=5) and suprasphincteric (n=2). After a median follow-up of 25.1 (15-36) months, the overall healing rate was 57.1%, which subsequently increased to 85.7% with a simple secondary intervention. Based on Cox regression analysis, previous perianal intervention was found to be independent risk factor for failure (p=0.025). Having prior perianal surgery significantly increased the risk of recurrence 6.7 times (OR:6,7 95% CI:1,9-24,1 p=0,003). Outcomes were confirmed by endoanal ultrasound for all patients.*

CONCLUSIONS: *Endoanal ultrasound confirmed long-term assessment of the LIFT procedure provides an acceptable success rate, especially when combined with secondary simple interventions, without impairment on continence for the complex perianal fistulas.*

KEY WORDS: Complex perianal fistulas, Endoanal ultrasound, Ligation of intersphincteric fistula tract

Introduction

Due to the critical balance between treatment success and incontinence risk for complex perianal fistula (CPF),

there has been increasing interest in sphincter saving procedures among colorectal surgeons¹. While there is no clear agreement on which procedure is superior for CPF, surgical expertise and mapping of the fistula anatomy have been considered as main determinants of preferred surgery. Although a number of sphincter-sparing techniques including fibrin glue injection, advancement flaps for internal opening, radiofrequency ablation have been offered to heal CPF, these techniques carry their own incontinence and some degree of recurrence risk²⁻⁴. In addition to the decreasing success rates in long term, requirement of expensive equipment and/or high-technology has been limited their use.

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Ligation of intersphincteric fistula tract (LIFT) technique is now being broadly adopted with early satisfactory results, short healing time and no requirement of specialized or expensive materials to perform the procedure. As the short-term outcomes may overestimate the true success rates of the LIFT procedure long-term outcomes are needed. Additionally, follow-up protocols that were reported based on clinical criteria do not ideally reflect real world outcomes once considering recurrences in patients meeting clinical healing criteria ⁵. Therefore, this study aimed to reveal clinically and endosonography confirmed long-term outcomes and analyze the factors associated with recurrences of LIFT procedure.

Methodology

A retrospective cross-sectional review was conducted for patients who underwent the LIFT procedure for complex perianal fistulas between October-2015 and February-2017 at Çukurova University Department of Colorectal Surgery. After diagnosing the perianal fistula based on medical history and physical exam, fistula type was determined by three-dimensional ultrasound which is subsequently confirmed by concordance with the operative findings ⁶. With increasing experience, LIFT has become the primarily preferred procedure for patients with complex fistulas secondary to cryptoglandular disease at our department. A total of two European Society Coloproctology Board-certified (I.C.E and A.R) colorectal surgeons performed LIFT procedure during the study period. Both pre-and postoperative endoanal ultrasound are performed by the same team, who have particular interest and experience on the imaging technique and reporting. After approval by ethical committee patients were informed regarding the procedure and consented appropriately (approval number: CUM 2019-85/2). The diagram illustrating the excluded patients and fistula types of patients undergoing LIFT during the study

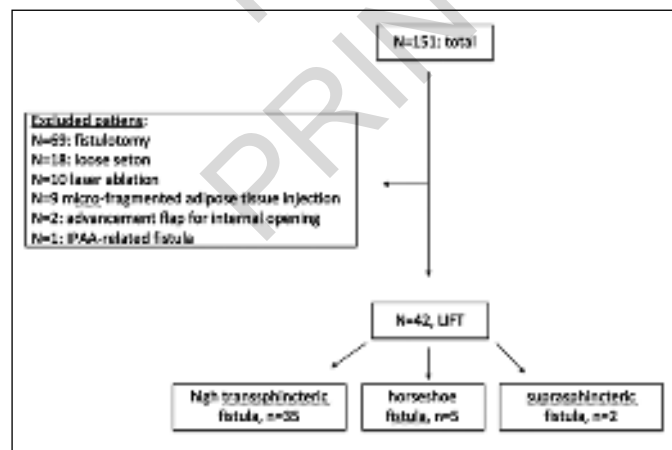


Fig. 1: The excluded patients and fistula types of patients undergoing LIFT during the study period.

period is shown (Fig. 1). Patients with intersphincteric fistulas that was considered amenable for fistulotomy, non-cryptoglandular etiology, rectovaginal and IPAA fistulas were excluded. Further management for patients who failed LIFT is reported as well. Anal incontinence was measured by Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scale.

The following parameters were evaluated to predict post-LIFT recurrence: age, sex, body mass index, tobacco use, previous perianal intervention, type of fistulous path. As described by Rojanasakul et al, paths of CPFs were also classified as straight or curved ⁷. All patients had an 3D Endoanal ultrasound examination (BK Focus 400, Denmark) combined with hydrogen-peroxide for classification and all cryptoglandular fistulas were classified by the use of the Parks classification ⁶. Contact gel was spread on outside cover in order to obtain sufficient acoustic contact during examination which was carried out in the left lateral position. All patients underwent endoanal ultrasound examination in the same fashion between postoperative 6 and 8 weeks to confirm healing or to determine the recurrence pattern to allow further management for patients who failed LIFT.

OPERATIVE TECHNIQUE

Patients were positioned based on localization of CPFs. While lithotomy position was preferred for anterior fistulas, prone jackknife position was preferred for posterior ones. Internal openings, which is determined by both endoanal ultrasound and by gentle digital exam, was attempted to probe. If cannulation of internal opening was not successful, the mixture of hydrogen peroxide-methylen blue solution was injected through the external opening. A curvilinear incision was made on the anal verge skin overlying the site of the fistula tract followed by meticulous fine dissection with electrocautery that was used to deepened. After facilitating the exposure of intersphincteric plane by the use of retractors, the intersphincteric tract was hooked and clamped at the border of the both sphincters with a right-angled clamp. With the help of scalpel, a small tract excised between the clamps and then both tracts were ligated close to the internal and external sphincters with polyglactin 3/0 sutures. The mixture of methylene blue-hydrogen peroxide was injected through the external opening to detect whether there was a leakage through the sutured area. If leakage was detected, additional sutures were used and then the intersphincteric plane was revised for hemostasis, and closed in 2 layers (muscle approximation and skin) using interrupted 3-0 vicryl (Fig. 2). The external orifice was left open to allow adequate drainage.

All patients were discharged with a 1-week course of oral antibiotics (ciprofloxacin and ornidazole). Subsequent follow-up was performed at 1- or 2-week intervals until complete healing. Our discharge criteria were the reso-

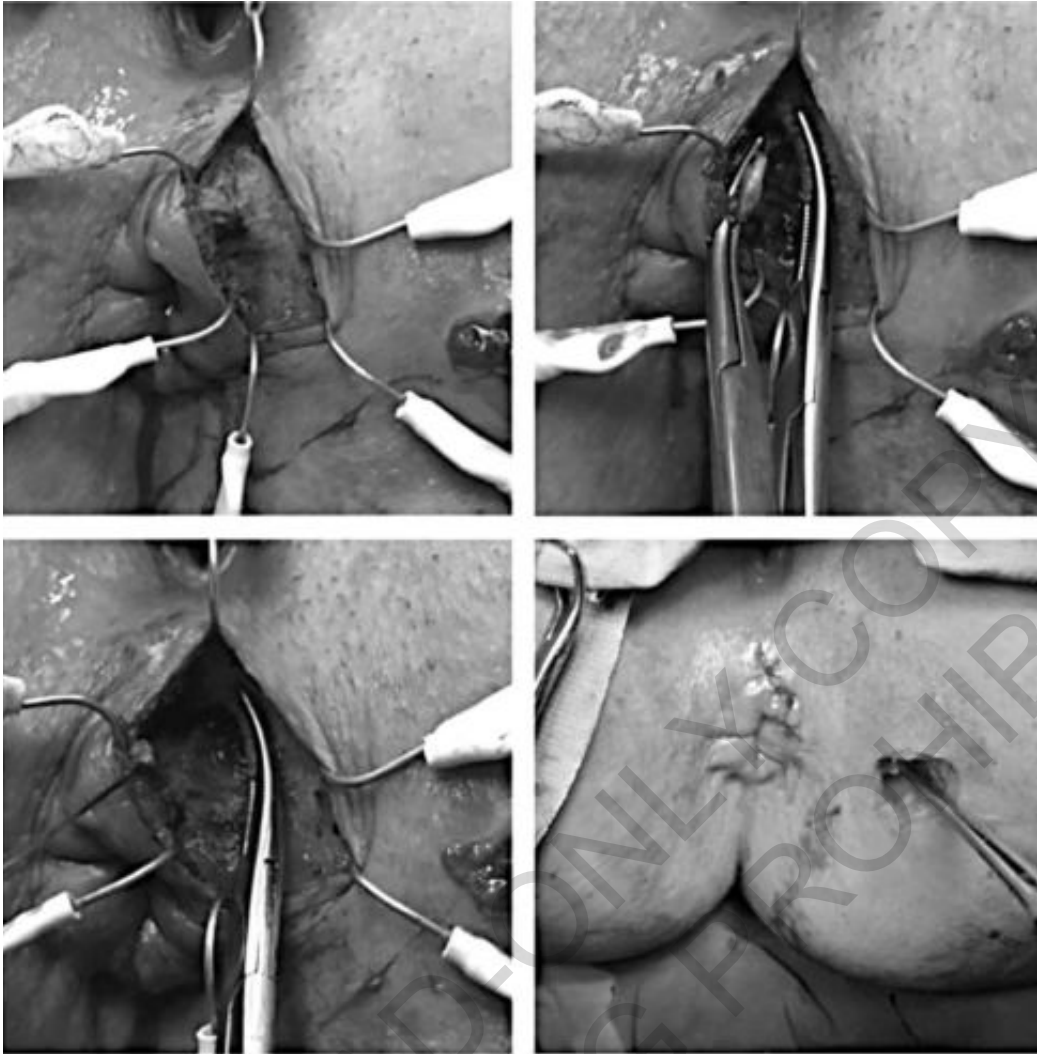


Fig. 2: The operative steps for ligation of intersphincteric fistula tract procedure.

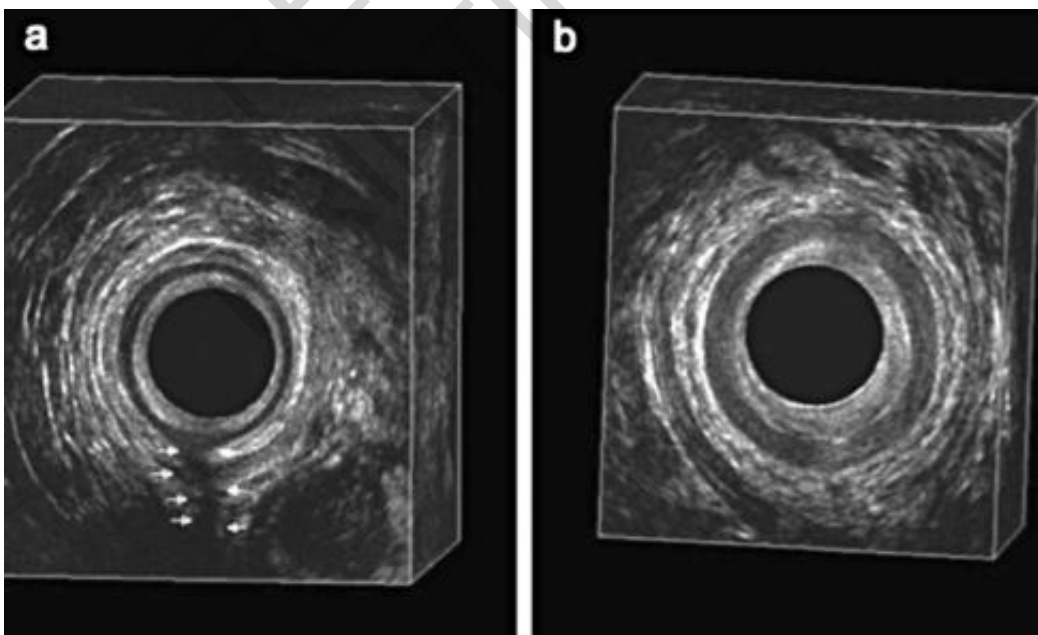


Fig. 3: A) 3-D endoanal ultrasonographic imaging of a transsphincteric fistula in a male patient; B) Postoperative imaging showing complete healing 8 weeks after the LIFT procedure at the same patient.

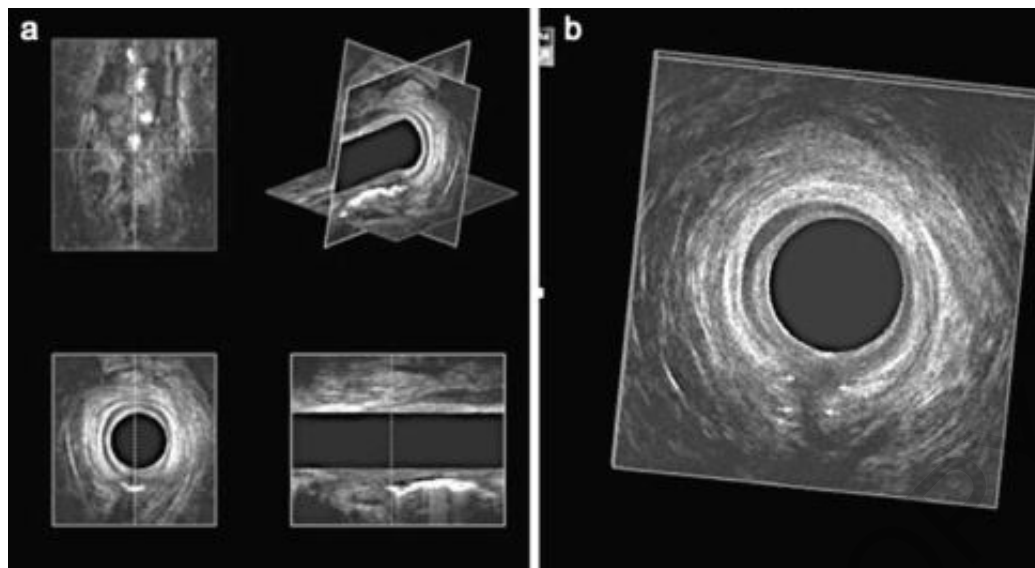


Fig. 4: A) type I failure after LIFT: intersphincteric fistula identified by hydrogen peroxide-enhanced EUS; B) Endosonographic imaging showing complete failure 8 weeks after LIFT procedure.

lution of symptoms and a healed wound. Patients with uneventful recovery were evaluated through 3D Endoanal ultrasound between 8-12 weeks and during the readmission for patients presenting with symptoms suggesting recurrence/failure. Patients meeting healing criteria were assessed within six months of primary LIFT procedure. The status of the patients was classified into 3 groups: healed, failed and recurrence. Healing was determined by both the complete healing of the intersphincteric incision, external opening along with the complete resolution of the symptoms and interruption of fistula tract at intersphincteric space demonstrated by 3D Endoanal ultrasound examination. Fig. III shows 3-D endoanal ultrasonographic imaging of a transphincteric fistula with postoperative normal postoperative anatomy 8 weeks after LIFT procedure. As described by Tan et al¹, failures were categorized into the following subtypes: type I (localized): discharge at the intersphincteric wound in the absence of an internal opening; type II (partial): tract from the internal opening to the intersphincteric wound; and type III (complete failure or recurrence): tract from the internal opening to the external opening with or without involvement of the intersphincteric wound. 3-D endoanal ultrasonographic images showing Type I and III failure patterns are demonstrated in Fig. IV.

STATISTICAL ANALYSES

Chi square test or Mann Whitney U test were used to compare the groups. Cox proportional regression model was used to estimate the mean-median failure free survival (FFS) rates, hazard ratios (HRs). Log-rank test was used to compare the outcome distributions between the groups. FFS was defined as the time from diagnosis to the time of any documented failure or recurrence. The

results were reported as mean \pm SD, median (range), number (n) and percent (%). A p value < 0.05 was considered as significant. Statistical analysis was performed using SPSS software (Version 20.0, SPSS Inc., Chicago, IL, USA).

Results

Between October-2015 and February-2017, 42 patients who underwent LIFT procedure for complex cryptoglandular perianal fistula were analyzed. None of patients were lost at follow-up. Majority of patients were male (n=34, %81) and the mean age of study population was 42.6. Fistula types were high transsphincteric (n=35), horseshoe fistula (n=5) and suprasphincteric (n=2) based on Park's classification. Curved type fistula tract was identified in % 45.2 (n=19) patients. None of patients were lost follow up and the overall healing rate was 57.1% after a median follow-up of 25.1 (15-36) months. The rate of failure free survival (FFS) was found to be 90% at 3rd month and 71% at 12th month. Failure pattern after LIFT procedure and further management are demonstrated in Fig. 5. While all patients with type I and II failures, which is confirmed with endosonographic examinations, were healed with simple curettage and fistulotomy, respectively, re-LIFT was performed for patients presenting with type III failure; 6 of whom were presented with re-recurrence. Type III failures were noted at a median follow-up of 3.7 months. The fistula healing rate was increased to 85.7% with a secondary intervention. Table II shows the outcomes associated with LIFT procedure, secondary interventions and incontinence scores.

The univariate analysis of baseline patient characteristics for patients who healed vs presented with failure is illustrated in Table III. Prior perianal fistula surgery was

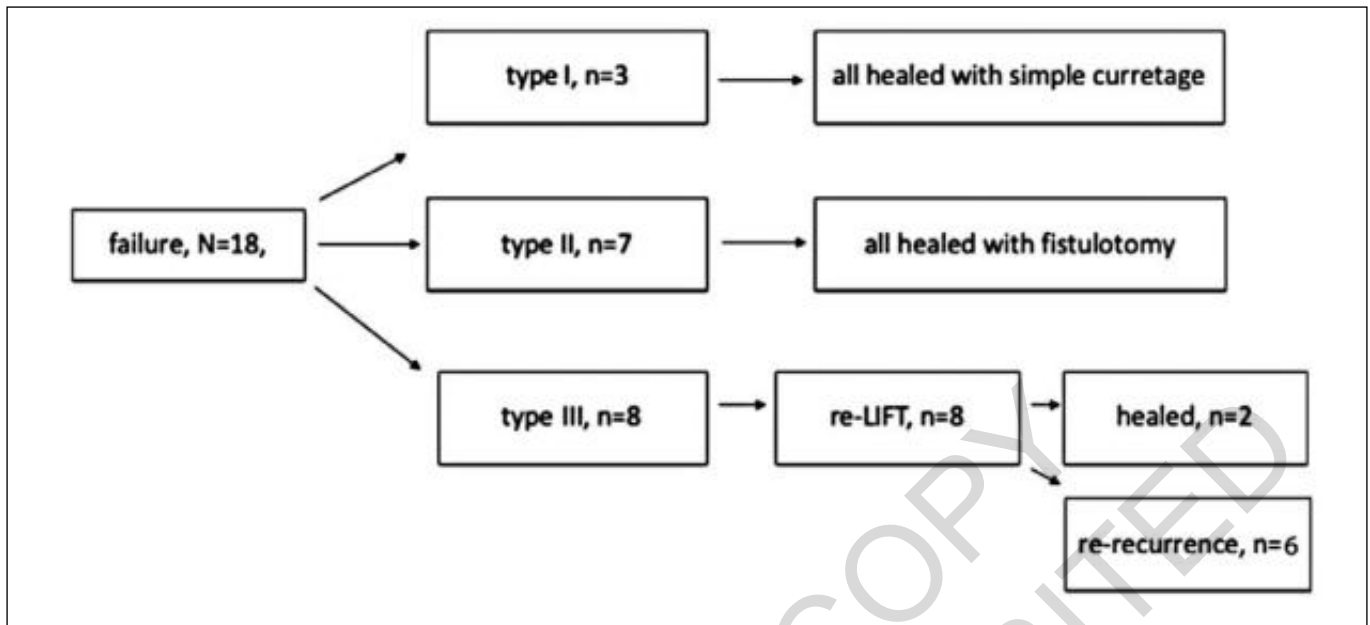


Fig. 5: Flow diagram showing outcomes of patients who failed after a primary LIFT procedure

TABLE I - Demographic data of patients undergoing LIFT procedure.

Variable	N.	%
Median age (range), years	42	40 (21-79)
Gender		
Female	8	19,0
Male	34	81,0
BMI	42	26,8 (18,4-35,9)
Type Of Fistula		
Htsf	35	83,3
Horse-Shoe	2	4,8
Supra	5	11,9
Type of Tract		
Curved	19	45,2
Straight	23	54,8
Previous intervention		
None	22	52,4
Var	20	47,6
Tobacco use		
None	16	38,1
Yes	26	61,9

TABLE II - Outcomes associated with LIFT procedure, secondary interventions and incontinence scores.

Outcomes	%
LIFT (primary)	
Healed	57,1
Type I-II failure	23,8
Type III failure	19,1
Secondary intervention	
Healed	85,7
Unhealed	14,3
CCF-FIS	
Preoperative (mean ±SD)	0,5 ±1,2
Postoperative (mean ±SD)	0,7 ±1,4

CCF-FIS: Cleveland Clinic Foundation Fecal Incontinence Score.

found to be associated with higher risk of failure (33.3%vs 66.7%, p=0,032). Similar to that finding, the mean FFS was significantly shorter in patients who have prior perianal surgery (mean FFS: 17,1 month) than the patients without prior perianal surgery (mean FFS: 28,0 month) (p=0,025). Despite statistically non-significant, the rates of curved type of fistula tract and tobacco use were higher in patients presenting with failure (p=0,073 and p=0,067, respectively). The FFS was significantly higher in patients with a straight vs curved fistula (26.5 months vs 18.4 months, p=0.021) (Fig. 6) Based on Cox

regression analysis, previous intervention was found to be independent risk factor for failure (p=0.025). Having prior perianal surgery significantly increased the risk of recurrence 6.7 times (OR:6.7, 95% CI:1.9-24.1, p=0.003).

Discussion

As a minimally invasive surgical technique for the complex perianal fistulas, this study revealed that long-term primary healing rate of 57.1% associated LIFT procedure. In a significant subset of patients who failed after their primary LIFT procedure, 'downstaging' of the external opening to a more medial location simplified further management resulted in a healing rate of 85.7%.

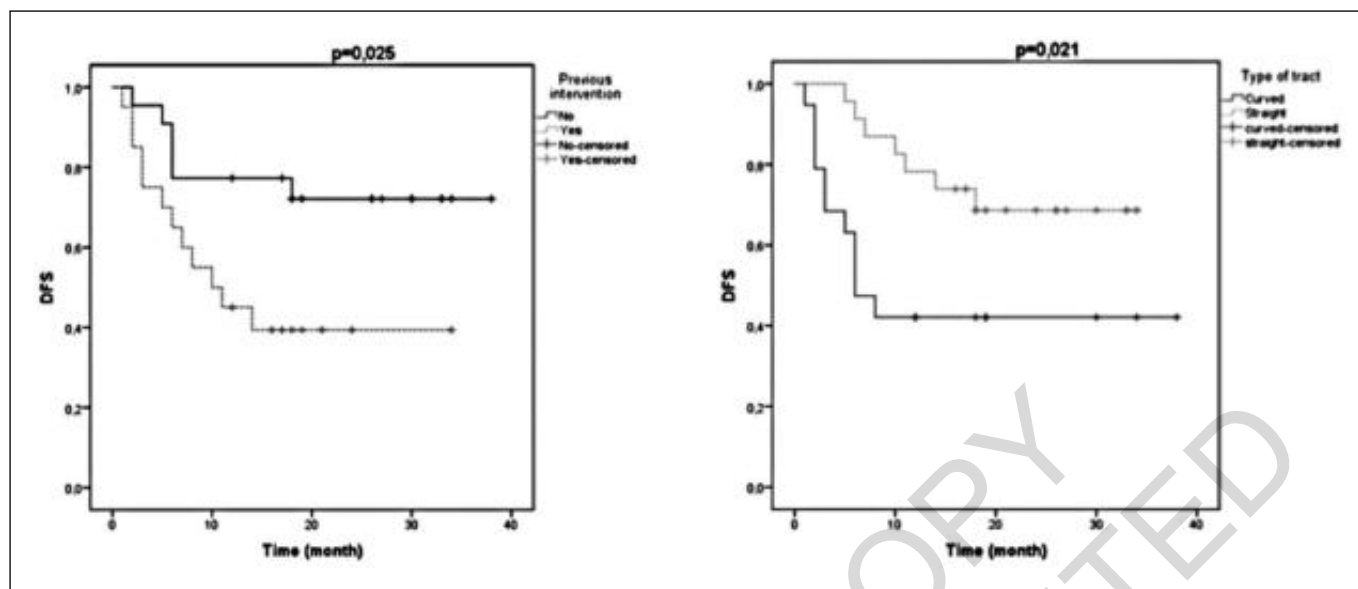


Fig. 6: Cox regression analysis revealing previous perianal surgery (A) and curved-type fistula pattern (B) as independent risk factors for failure for LIFT procedure.

TABLE III - The univariate analysis of baseline patient characteristics for patients who healed vs presented with failure.

	Healed (n=24) (%)	Failure(n=18) (%)	p
Median age (range)	42 (23-70)	39 (21-79)	0,798
Gender			0,734
Female	5 (20.8)	3 (16.7)	
Male	19 (79.2)	15 (83.3)	
Previous fistula surgery			0,032
Yes	8 (33.3)	12 (66.7)	
no	16 (66.7)	6 (33.3)	
Tobacco use			0,067
Yes	12 (50)	14 (77.8)	
No	12 (50)	4 (22.2)	
BMI			0,601
<25	5 (20.8)	5 (27.8)	
>25	19 (79.2)	13 (72.2)	
Type of tract			0,073
Curved	8 (33.3)	11 (61.1)	
Straight	16 (66.7)	7 (38.9)	

Our criticism on comparably lower success rate is mainly related to the patient selection. Rojanasakul et al reported healing rate of 87.65% reflecting ten-year experience of a large patient population with fistula in ano⁷. However, the success rates for high transsphincteric and horseshoe fistulas, which are considered main indications for LIFT in our series, were %60 and %40, respectively. In addition to that, we used strict definitions for unhealed patients by categorizing them into three groups based on Tan's classification. However, many publi-

shed series defined unhealed group as persistence of external opening, for which there is no clear data regarding the site^{1,4,5,7,8}. Nevertheless, eligibility for secondary interventions, which provided benefit for all patients with type I and II failures, can be considered as an advantage of the LIFT procedure.

Due to the data heterogeneity in summarized literature, there is no clear-cut conclusion for superiority of MRI vs endoanal ultrasound in terms of delineation of fistula anatomy. While there is no clear agreement in the literature for post-LIFT follow-up that is mostly reported based on clinical criteria, Liu et al introduced routine endoanal imaging ultrasound regardless of clinical situation⁵. The rationale behind routine endoanal imaging was long-term recurrences that were reported in patients meeting post-LIFT clinical healing criteria. Differently from commonly reported LIFT outcomes, we have routinely used endoanal ultrasound, as Sileri et al suggested⁹, to characterize the fistulas in preoperative setting instead of relying on intraoperative findings. Also, to confirm the correct ligation of 'true' fistula tract, which is characterized preoperatively, we supported our results with postoperative endoanal ultrasound imaging even in the absence of symptoms suggesting recurrence. Routine use of postoperative endoanal ultrasound imaging has led to both identification of missed and mostly deep-seated side tracts or persistence of primary fistula tract in failed patients and increase in patient satisfaction in healed group.

Two main advantages of the LIFT procedure should be underlined. Firstly, as a minimally invasive fistula surgery LIFT procedure is associated with lower complica-

tion rates including infection and hemorrhage, short healing time and preservation of sphincter complex. None of cases in this study experienced minor or major incontinence. Secondly, compared to other procedures necessitating infill, bioprosthetic, or plug materials, LIFT can be regarded as cost-effective^{9,10}.

The current study revealed that previous fistula surgery remarkably associated with increased risk of failure, as Abcarian et al reported¹¹. Healing rates in patients who underwent two or more previous perianal intervention was significantly higher than patients undergoing less perianal interventions. We believe that manipulation of operative field eventuating tissue devascularization followed by scarring is the main mechanism of the failure.

Whether the management of complex perianal fistulas with seton replacement before LIFT increases the healing rates remains highly debated. Reasoned benefits include eradication of septic foci, ease of tract maturation and minimization of tissue dissection during definitive procedure^{12,13}. Some authors have inversely advocated that seton replacement complicates tissue dissection causing sphincter damage through increased fibrosis and scarring^{1,14}. Additionally, Sileri et al has been reported higher failure rate in the group of patients who had previously a seton insertion¹⁰. They considered this finding as a result of creation a false way leading to increased risk of recurrence. Based on these concerns, we prescribed two weeks of antibiotics for patients presenting with purulent discharge, instead of seton replacement, and evaluated their eligibility for LIFT procedure until narrowing of fistula tract along with the minimal hypoechoic inflammatory changes are seen on endoanal ultrasound.

Small sample size and retrospective nature of study that predisposes to significant selection bias can be considered as limitations of this study. Nevertheless, incontinence assessment with baseline parameters and well-defined long-term follow-up protocol supported by endoanal ultrasound imaging, in conjunction with clinical examination, provide real world outcomes associated LIFT procedure.

In conclusion, endoanal ultrasound confirmed long-term assessment of the LIFT procedure provides an acceptable success rate, especially when combined with secondary simple interventions, without impairment on continence for the complex perianal fistulas. Randomized trials comparing this technique with others in larger sample size are needed.

Riassunto

Poiché i risultati a breve termine possono sovrastimare i reali tassi di successo delle tecniche di risparmio dello sfintere, e i protocolli di follow-up riportati in base a criteri clinici non riflettono idealmente i risultati nella loro realtà nel caso di fistole perianali complesse (CPF),

questo studio mirava a controllare i risultati a lungo termine confermati clinicamente e in modo tridimensionale con l'ecografia e ad analizzare i fattori associati alle recidive dopo la procedura della legatura del tratto di fistola intersfinctericca (LIFT).

Allo scopo è stata condotta una revisione retrospettiva trasversale sui pazienti sottoposti alla procedura LIFT per fistole perianali complesse tra ottobre-2015 e febbraio-2017. Il modello di regressione proporzionale di Cox è stato utilizzato per stimare i tassi medi di sopravvivenza libera da fallimento e il test log-rank è stato utilizzato per confrontare le distribuzioni degli esiti per i pazienti guariti rispetto a quelli con fallimento.

Sono stati analizzati un totale di 42 pazienti, di cui 34 (81%) di sesso maschile, sottoposti a procedura LIFT per CPF. Nessuno dei pazienti è stato perso al follow-up. Il tipo di fistola, come confermato all'endosonografia, era transsfinctericca alta (n= 35), a ferro di cavallo (n= 5) e soprasfinctericca (n= 2). Dopo un follow-up medio di 25,1 (15-36) mesi, il tasso di guarigione complessivo è stato del 57,1%, che successivamente è aumentato all'85,7% con un semplice intervento secondario. Sulla base dell'analisi di regressione di Cox, il precedente intervento perianale è risultato essere un rischio indipendente quale fattore di fallimento (p = 0,025). Avere un precedente intervento chirurgico perianale ha aumentato significativamente il rischio di recidiva 6,7 volte (OR: 6,7, IC 95%: 1,9-24,1, p = 0,003). I risultati sono stati confermati dall'ecografia endoanale per tutti i pazienti.

Possiamo concludere che per le fistole perianali complesse la valutazione a lungo termine con l'ecografia endoanale della procedura LIFT dimostra un tasso di successo accettabile, specialmente se combinato con semplici interventi secondari, senza compromissione della continenza.

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