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OTSC® Proctology vs. fistulectomy and primary sphincter reconstruction as a treatment for low trans-sphincteric anal fistula in a randomized controlled pilot trial.

Short title: OTSC® Proctology.

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ABSTRACT

Background – To compare OTSC® Proctology and fistulectomy with primary sphincter reconstruction results as treatment strategies for anorectal low trans-sphincteric fistula.

Methods – Between February 2012 and March 2013, patients affected by trans-sphincteric anal fistula were consecutively enrolled in the trial. Patients were randomized to receive fistulectomy with primary sphincter reconstruction or OTSC® Proctology. Demographic characteristics, comorbidities, previous anorectal treatments, and recurrent fistula data were acquired. Postoperative therapy data and pain and Wexner scores (30 and 60 dd) were acquired during follow-up. Furthermore, patients were contacted by telephone after six months, and were visited both one year and three years after surgery.

Results – 30 consecutive patients were included in the study. 15 patients underwent the OTSC® Proctology procedure and 15 underwent the standard fistulectomy. The success rate was 93.3% in the OTSC group. The mean postoperative stay was 1.3 days in the OTSC® patients and 3.6 days in the fistulectomy group patients. The mean medications required for complete healing was 3.2 in the OTSC group and 8.9 in the FIPS group.

Conclusions – Our results suggest that OTSC® Proctology is an effective and safe treatment in achieving permanent closure of the internal fistula opening in selected patients, with excellent results in terms of pain, postoperative incontinence, healing time, and days of hospitalization.

KEYWORDS: anal fistula; fistulectomy; clip; fecal incontinence; anal pain; sphincteroplasty.

INTRODUCTION

Anal fistulas are a prevalent worldwide condition with an incidence of 5.6 per 100 000 in women and 12.3 per 100 000 in men¹. The main goal of anal fistula treatment is the complete eradication of the disease, combined with anal sphincter preservation and a low surgical recurrence rate. The fistulectomy is one effective surgical treatment procedure used in removing low trans-sphincteric fistulas. However, as it requires the partial sectioning of the anal sphincter muscle, the fistulectomy exposes patients to a higher risk of postoperative complications, such as fecal incontinence (6-40%)².

Although regarded with skepticism, fistulectomy and primary sphincter reconstruction (FIPS) seems to be effective in reducing the postoperative deterioration of continence with a success rate of about 90%³⁻⁴.

Recently, the percentage of sphincter-saving treatments has begun to increase (flap, ligation of the intersphincteric fistula track (LIFT), video-assisted anal fistula treatment (VAAFT), fibrin glue and plug)⁵⁻⁸.

Nevertheless, contention concerning the side-effects, such as fecal postoperative incontinence and pain, healing time and long-term result issues, still abound in the scientific community^{9,10}. Several mini-invasive procedures have been adopted in order to minimize these complications. However, there are still insufficient data to assess the effectiveness of these procedures¹¹. An Over the Scope Clip (OTSC®) system has been adopted worldwide to decrease the morbidity and mortality associated with the complications secondary to both diagnostic and therapeutic endoscopy¹². The Nitinol material it is made of ensures constant compression and produces strong and atraumatic tissue approximation.

The special characteristics of this material allowed the development of endoscopic-derived clips, devoted to the proctologic pathology: OTSC® Proctology. This system has previously demonstrated appropriate effectiveness¹³⁻¹⁵. The aim of our randomized, two-arm controlled pilot

trial was to evaluate the efficacy and safety of OTSC® Proctology as a first-line treatment for trans-sphincteric anal fistula, compared to FIPS.

MATERIALS and METHODS

Previously informed patients affected by low trans-sphincteric anal fistula as classified by Parks¹⁶, between February 2012 and March 2013, were consecutively enrolled in our prospective randomized controlled trial. The study was designed and conducted according to the guidelines of the Helsinki Declaration. Demographic characteristics, comorbidities, previous anorectal treatments and recurrent fistula data were acquired. All patients with inflammatory bowel disease (IBD), HIV positive results, more than one internal and external fistula opening, and previous proctological surgery were excluded. Patients were 1:1 consecutively randomized to receive FIPS or OTSC® Proctology treatment. All patients underwent a clinical evaluation and rectal examination to confirm the anal fistula diagnosis. Fistulas were evaluated preoperatively by endoanal ultrasound imaging and Magnetic Resonance Imaging (MRI). Only patients with low trans-sphincteric anal fistula were enrolled. A colonoscopy was performed to exclude IBD or colon comorbidities.

FIPS surgical procedure

Anorectal preparation was performed preoperatively by a small volume enema. With the patient in lithotomy position, after the introduction of the Eisenhammer retractor, the fistula tract and its relation with sphincters were verified (Fig 1A-B). A probe was positioned into the internal opening to confirm the fistula tract direction. The sphincters were identified by a stitch or a clamp to achieve a dissection that respected the muscles as much as possible. Afterwards, a total resection of the fistula tract from the external orifice up to the internal orifice was completed (Fig. 1C). Curettage of the residual cavity, and irrigation with betadine and saline solution, were performed. Subsequently, an approximating sphincteroplasty with interrupted absorbable stitches (Vicryl 2-0) was completed in two phases. First, the internal sphincteroplasty with external-internal side crossing advancing

stitches was performed, and then the external sphincteroplasty (Fig. 1D). The mucosal and submucosal layers were reconstructed, avoiding the mucosal eversion, to obtain a physiologic stool transit without wound contamination. The anoplasty was extended distally to the anal margin. A partial reduction of the residual cavity was obtained by interrupted 3-0 vicryl stitches.

The postoperative analgesic protocol in the FIPS group was: morphine 10 mg IV in continuous infusion for 24 hours, then oxycodone 10 mg orally daily for three days, and lastly paracetamol 1000 mg orally as needed.

OTSC® Proctology surgical procedure

Anorectal preparation was performed preoperatively by a small volume enema. After the introduction of an Eisenhammer retractor, an examination of the anal canal and the distal rectum was performed to find the internal opening of the fistula track, and its relationship with the anal sphincters and the external orifice and, possibly, other secondary extensions. To create a false track through the perineal tissue, a cystic forcep (or a Lockhart – Mummery probe) was introduced into the internal opening, together with another probe through the external orifice.

Debridement and curettage by alternative movements of the OTSC® fistula brush to remove all the granulation tissue were done (Fig. 2). Excision of a circular area of anoderm of about 2 cm around the internal opening to expose the sphincteric muscle was completed.

Application of one resorbable Z-shaped stitch through the sphincter muscle, using a resorbable thread of a minimal length of 90 cm to enable the passage through the device, centering of the internal opening of the fistula, and an allowing of the internal sphincter muscle as a stable area of anchorage, was applied (Fig. 3). The suture was knotted at its distal end and pulled through the working channel of the clip applicator using the thread retriever. The applicator was aligned parallel to the axis of the anal canal to achieve an anatomical orientation of the bent clip. After deactivation of the safety-lock, the clip was released (Fig. 4). The applied clip closed the internal opening of the fistula (Fig. 5). An iodoform gauze swab was placed in the residual cavity.

The protocol for the management of postoperative pain in the OTSC® group was: paracetamol 1000 mg IV thrice daily during the first 24 hours, and then paracetamol 1000 mg orally as needed. In both groups, postoperative therapies, pain and Wexner scores¹⁷ (30 and 60 dd) were acquired during follow-up to evaluate: technique effectiveness, postoperative pain and fecal incontinence. An effective treatment was defined as the absence of any discharge or abscess at the time of the last follow-up.

All patients were followed up after postoperative discharge to exclude recurrence at 2, 4 and 12 weeks and verify the internal and external wound conditions by digital rectal exam and anoscopy. The patient's clinical continence status was also ascertained. Furthermore, patients were contacted by telephone after six months and visited one year and three years after surgery.

Statistical analysis

The sample size calculations were based on the following assumptions:

- mean (SD) postoperative stay in OTSC® group: 1 day (0.49);
- mean (SD) postoperative stay in the FIPS group: 3 days (0.91).

The alpha and beta-error were fixed at 0.05 and 0.20, respectively. The sample size calculated for both groups, using EpiCalco2000, was 15 patients. Differences for the two groups for quantitative and qualitative variables were tested using Mann-Whitney and Chi-square tests, respectively. The statistical analysis was carried out using SPSS, release 21. The p-value was set at $p < 0.05$.

RESULTS

30 consecutive patients, 19 males (mean age 45.5 years, age range 20–78 years) and 11 females (mean age 42 years, age range 34–59 years) were included in the study. 15 patients underwent the OTSC® Proctology procedure (OTSC® group) and 15 underwent FIPS (FIPS group). Table 1 summarizes their characteristics. The two groups were homogeneous in age/gender distribution.

A three years follow-up was completed in all enrolled patients. The success rate was 93.3% in the OTSC group. One patient in the OTSC® group needed a repeated surgical treatment. No recurrence was reported in the FIPS group. There were no short-term complications, excluding one patient in the OTSC® group, who need clip removal by the OTSC® Proctology Clip Cutter for pain in the seventh postoperative day. The mean postoperative stay was 1.3 days in the OTSC® patients (range 1-2 days) and 3.6 days in the FIPS group (range 2-6 days).

The patients in the FIPS group usually stay in hospital for more than one day because we prefer to evaluate and manage the surgical wound as an inpatient in the first 48 hours. Patients who experienced intense postoperative pain required a longer hospital stay.

Among the OTSC® group, 3 patients (20%) needed an additional Ketorolac, due to immediate postoperative pain. On the other hand, among the FIPS group, 4 patients (26.7%) needed additional analgesic treatment by an extra Ketorolac dose. In 14 patients (OTSC group), the clip fell autonomously within 24 days (mean 19 days, range 15-24 days).

The mean medications required for complete healing were 3.2 in the OTSC® group (range 2-5) and 8.9 in the FIPS group (range 7-12).

The only one recurrence in the OTSC® group patients, diagnosed about thirty days after surgery, was successfully treated by fistulectomy in association with sphincteroplasty.

The follow-up interviews and proctological examinations were performed one month, two months, six months, one year and three years after surgery on all the thirty patients in both groups.

After one month, the Wexner score in the OTSC® group was 0 (range 0-0), and in the FIPS group was 3 (range 0-6). The Wexner score was realigned to 60 days follow-up, showing no postoperative incontinence in both groups.

After six months, an MRI was performed. MRI findings showed complete healing in all patients.

After three years, no patients reported any pain after defecation. No cases of gas or fecal incontinence were reported. No recurrence was reported.

DISCUSSION

Current surgical techniques for treating anal fistulas are based on three main principles: identification of the tract and the internal opening, excision of the fistula tract, and preservation of anal sphincter function.

The main objective of anal fistula surgery is to eradicate the fistula tract while maintaining anal continence. A simple laying open procedure is effective for low or simple fistulas. However, treatment of complex anal fistulas is challenging, because internal and external sphincters are involved in the fistulous track, and fecal continence can be impaired after surgery. Seton placement has been the standard approach to complex anal fistulas, and has been recommended to reduce postoperative incontinence.

FIPS has not yet a clear consensus, although some studies have demonstrated its high success rate and low risk of postoperative incontinence against the simple fistulectomy¹⁸⁻²¹. FIPS is also effective in low trans-sphincteric fistulas with risk factors for postoperative incontinence²¹.

Recently, the percentage of sphincter-saving treatments is increasing (mucosal advancement flaps, LIFT, VAAFT, fibrin glue and plug).

Mucosal advancement flaps are technically challenging and are associated with recurrence rates that vary from 2 to 54%⁸. These failure rates may result from some mobilization of structures or a tendency for the flap to retract or dehiscence. Moreover, advancement flaps are often associated with postoperative incontinence, and the incidence of this complication has reached 35% in some series. Fibrin glue injection is a technically easy, low-risk technique, but results have been disappointing, showing a long-term recurrence rate as high as 37%²². Similarly, the use of the anal fistula plug is a simple, sphincter-sparing technique, but very expensive, and with reported success rates ranging between 29% and 87%. The latest conservative technique reported in the literature is the LIFT procedure. This approach consists of ligation of the tract in the intersphincteric space, curettage of the tract, and closure of the external anal sphincter defect. This technique, like VAAFT, is based on

the principle of a secure closure of the tract near the internal opening, and makes healing rates possible between 57 to 94.4%⁷.

Several mini-invasive procedures were adopted in order to minimize these complications; however, there are still insufficient data to assess the effectiveness of these procedures. The OTSC® Proctology system has been adopted worldwide to decrease the morbidity and mortality associated with the complications secondary to both diagnostic and therapeutic endoscopy. Its Nitinol characteristics have allowed the development of endoscopic-derived clips devoted to the proctologic pathology: OTSC® Proctology. This clip permanently adapts to the thickness of the tissue and maintains a consistent compression on the internal fistula opening. Thus, the super elastic Nitinol characteristics and the design of the clip guarantee a permanent closure of the fistula opening during its healing process.

Our OTSC® Proctology rating success was comparable to the results reported by Prosst et al¹⁵. The evaluation of the incontinence by Wexner score at 30 days was statistically significant compared to the FIPS group patients, showing the advantages of the mini-invasive approach in short-term follow-up. The Wexner score was realigned to 60 days follow-up, showing no postoperative incontinence in both groups. After the three years follow-up, recurrence was not reported in either group. Of course, we have to properly consider the low sample size, and we need to complete randomized multicenter studies to have a more realistic idea of the effectiveness of the device.

CONCLUSIONS

The main advantages of the minimally invasive approach by OTSC® Proctology are the reduced number of hospitalization days and medications after treatment. Our results suggest that OTSC® Proctology, as well as FIPS, is an effective and safe treatment in selected patients. Even considering the small sample size, our results encourage further randomized multicenter studies, especially by proposing the OTSC® Proctology as a first-line treatment for low trans-sphincteric anal fistula.

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Figure Legend

Figure 1. A) Fistula tract and its relation with sphincter identification; B) Preparation of the sphincter muscle; C) Fistulectomy; D) Sphincter repair.

Figure 2. Curettage by alternative movements of the OTSC® fistula brush in order to remove all the granulation tissue through the fistula tract.

Figure 3. Using resorbable Z-shaped stitch to obtain a stable area of anchorage for the OTSC® Proctology device.

Figure 4. Clip releasing on the internal orifice.

Figure 5. Clip closure and final stationing.

Table 1. Population characteristics, pre-operative data and statistical evaluation.

Variables	FIPS (median, range, number, %)	OTSC (median, range, number, %)	P-value
Age	40.5 (25-69)	47.9 (20-78)	0.148
Gender			
Females	6 (40)	5 (33.3)	0.144
Males	9 (60)	10 (66.7)	
Medications	8.9 (7-12)	3.2 (2-5)	<0.001
Final outcome			
Recurrence	0 (0)	1 (6.7)	1.034
Post-surgery pain			
No	11 (73.3)	12 (80)	0.186
Yes	4 (26.7)	3 (20)	
Days of post-op stay	3.6 (2-6)	1.3 (1-2)	<0.001
Wexner 30 days	3 (0-7)	0 (0-0)	<0.001