

Porcine dermal collagen matrix injection may enhance flap repair surgery for complex anal fistula

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Abstract

Introduction The use of biomaterials to treat anal fistula has drawn great interest. More recently, a porcine dermal matrix injection has been proposed as infill biomaterial to treat fistulas.

Methods We propose a novel approach consisting in non-cutting seton positioning followed by flap repair associated with dermal matrix injection into the fistula tracts after several weeks.

Results We report our experience with this two-staged procedure on 11 consecutive patients with recurrent high trans-sphincteric fistulas with a minimum follow-up of 6 months.

Conclusions In our experience, this two-stage approach seems to be safe and effective.

Keywords Permacol · Complex anal fistula · Flap repair

Introduction

The management of fistula-in-ano aims minimizing recurrences while maintaining continence. Low fistulas, where the tract is submucosal, intersphincteric, or located in the lower third of the external anal sphincter are usually treated by fistulotomy with low recurrence rates and relatively little

impact on incontinence [1, 2]. On the other hand, surgical treatments for high and complex fistulas may result in variable degree of anal sphincter apparatus impairment. Various alternative surgical options have been proposed such as flap repair, fibrin glue injection, seton drainage and fistula track plug insertion with variable success rates [3–9]. Currently, the transanal rectal advancement flap represents the most effective treatment for complex anal fistulas allowing the closure of the internal opening with successful rates, in some series, above 90%. However commonly, recurrence rate is approximately 30%, a rate that leaves much room for improvement.

Over the last two decades, the use of biomaterials to treat anal fistula has drawn great interest. Among these, fibrin glue injection has been proposed to obliterate the fistula tract/s, but initial enthusiasms have been tempered by high rates of recurrences [4–6, 10, 11]. Several authors have tried a combination of fibrin glue and flap repair in order to enhance its success rates [7, 12]. Results have been disappointing, showing worse outcomes after the combination of the two compared to flap repair alone [5]. Reasons why fibrin glue addition is ineffective or even worse are unclear. A possible explanation can be that the closure of the fistula tract with the glue leads to a situation where insufficient drainage from the primary and eventual secondary fistula tract occurs [7]. More recently, a porcine dermal matrix injection, named Permacol injection (Covidien plc, Dublin, Ireland) has been proposed as infill biomaterial to treat fistulas [13, 14] but data on its use on anal fistula treatment is scant. We propose a novel approach consisting in non-cutting seton positioning followed by flap repair associated with Permacol injection into the fistula tracts after. We also report our experience with this two-staged procedure on 11 consecutive patients with recurrent complex anal fistulas.

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Methods

Between July 2009 and April 2010, 11 consecutive patients underwent mucosal advancement flap repair and Permacol injection for complex anal fistula in our institution. Inclusion criteria for this study were age between 18 and 75 years and the presence of a complex anal fistula, defined as Crohn's, rectovaginal, and high trans-sphincteric fistulas. Patients' characteristics are resumed in Table 1.

All patients underwent outpatient clinic evaluation and preoperative MRI and/or endoscopic ultrasound. Fecal incontinence before and after surgery was evaluated using the Fecal Incontinence Severe Index (FISI) score. Patients with a score >6 underwent anal manometry before surgery. All procedures consisted in two-stage approach.

Surgical technique, stage I On the day of the surgery, an enema was administered to the patient. All patients underwent surgery under general anesthesia in lithotomy position and broad-spectrum antibiotics given at induction. The internal orifice was found using oxygen peroxide injection through the external opening and gently probed. At this point a non-cutting seton (Silicone Surgical Vessel Loop, Dev-o-Loop, Mini-red, Covidien) was placed for a period of at least 8 weeks aiming adequate drainage of the sepsis and followed up routinely as outpatient.

Surgical technique, stage II Surgery was performed in a day surgery setting, under general anesthesia in the lithotomy position. Initial step was the identification and creation of an elliptical excision below the internal opening encompassing 20–30% of the circumference of the anus. The rectal flap, fashioned with mucosa, submucosa, and a small amount of internal sphincter fibers, was adequately mobilized to overlap and cover the internal opening. Particular care on hemostasis was given to prevent hematomas (Fig. 1).



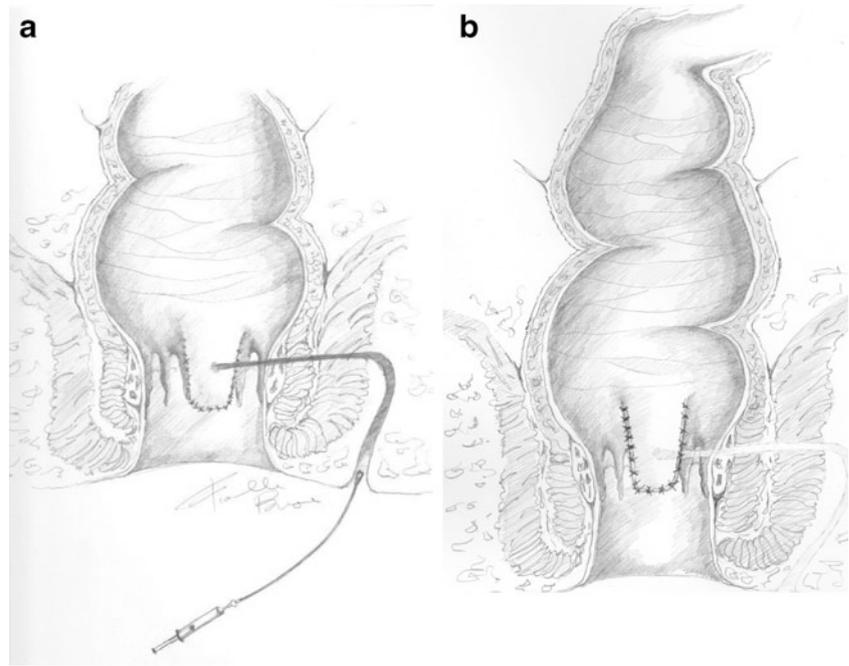
Fig. 1 Flap preparation (mucosa, submucosa, and a small amount of internal sphincter fibers) after >6 weeks drainage seton insertion which aimed draining the fistula tract thus abolishing collateral tracts while transforming it in a more straight one

The flap base was performed large enough to avoid its ischemia and mobilization to avoid tension. The fistula tract was probed, curetted, and irrigated with saline. The internal opening underneath the mobilized flap was not closed before suturing. The flap was sutured distally using full-thickness-interrupted vicryl 2-0 sutures (Fig. 2a). At this point, liquid dermal porcine matrix (Permacol Injection, Covidien plc, Dublin, Ireland) was gently injected in the retrograde manner through the external orifice to fill the entire tract. The entire procedure was performed under

Table 1 Patients' characteristics and follow-up

Patient gender/age (years)	Previous surgery	IBD	Findings at stage I	Follow-up
Female/31	Y (×1)	N	3 tracts, abscess,	Healed at 15 months
Male/22	Y (×1)	Crohn's	1 tract	Healed at 12 months
Male/31	Y (×1)	N	1 tract	Healed at 11 months
Female/32	Y (×4)	Crohn's	5 tracts, abscess	Recurrence at 9 weeks
Female/44	Y (×3)	RCU	2 tracts, abscess	Healed at 9 months
Female/28	Y (×2)	Crohn's	2 tracts, abscess	Healed at 8 months
Female/34	Y (×3)	Crohn's	1 tract, abscess	Healed at 7 months
Female/71	Y (×3 and stoma)	Crohn's	Rectovaginal	Healed at 7 months
Male/67	Y (×2)	N	1 tract	Healed at 7 months
Female/54	Y (×1)	N	2 tracts, abscess	Healed at 6 months
Female/38	Y (×1)	N	1 tract	Healed at 6 months

Fig. 2 a and b The flap (mucosa, submucosa and a small amount of muscular fibers) was sutured using interrupted 00 absorbable sutures. Subsequently the fistula tract was filled with the preparation under direct visual control. The external orifice was then closed with a 00 silk suture to prevent early extrusion. The infill preparation was also injected all around the fistula tract nearby the external orifice



direct vision of the flap in order to prevent anterograde extrusion and flap tension (Fig. 2b). In order to prevent early extrusion of the matrix injection, at this point, additional injection was performed next to the fistula tract at 360° through a 20-gauge needle and the external orifice was closed using a purse-string or figure of eight suture with silk 00. This suture was then removed at the first outpatient visit.

After the discharge, patients were followed-up 1, 2, 4 weeks after surgery and then routinely every 4 months. Data was collected prospectively including demographics, previous treatments, details of surgery, and follow-up results.

Results

Overall, 11 patients who had complex anal fistula of cryptoglandular origin (five patients) and inflammatory bowel disease (IBD) related (six patients) were treated. Results are summarized in Table 1. The median age was 41 years (range 22–71 years).

One patient had previous rectovaginal fistula surgery which failed and required fecal diversion. All first-stage procedures were performed as planned day surgery cases. Eight out of 11 second-stage procedures were carried in a day surgery setting, while three required overnight admission because of age (one patient) and postoperative pain (two patients). No postoperative complications were observed as part of a fungi infection sustained by *Candida albicans*, which was successfully treated with a 7-days cycle of

fluconazole (per os 200 mg/day). Mean follow-up after surgery was 9 months and we observed a single failure after 6 weeks secondary to partial displacement. This failure was observed in a Crohn's disease patient who experienced a severe recurrence of intraluminal disease with frequent bowel motions (>10/day). No difference in terms of preoperative and postoperative FISI scores was observed in all but one patient who experienced transitory gas incontinence for 3 months after surgery.

Discussion

Nowadays, flap repair remains the “gold standard” approach for the treatment of high trans-sphincteric perianal or complex fistulas. The flap repair, closing the internal anorectal opening, eliminates the source of persisting anal fistula where fecal material is forced through. Healing rates are reported to range between 37% and 98% [5, 7, 15]. Lower recurrence rates have been observed after non-cutting seton insertion prior flap repair [16, 17].

Over the last two decades the use of biomaterials to treat anal fistula has drawn great interest. Advantages of this approach include simple and repeatable applications, preservation of sphincter integrity, minimal patient's discomfort, and the ability for subsequent surgical options if needed. Among these, fibrin glue injection has been proposed to obliterate the fistula tract/s, but initial enthusiasms have been tempered by disappointing high rates of recurrences [4–6, 10, 11]. Failures are attributable to the displacement of the glue from the fistula tracts early after

surgery secondary to increased pressure from coughing or straining [18]. Other reasons suggested for the persistence of fistula tracts have included chronic infection, residual granulation tissue or islands of epithelium being left behind in the tract. As a matter of fact most of the authors point out the need of the tract curettage before sealant injection [19].

Several authors have tried a combination of fibrin glue and flap repair in order to enhance its success rates [5, 7, 20]. Results have been disappointing, showing worse outcomes after the combination of the two compared to flap repair alone [5]. Reasons why fibrin glue addition is ineffective or even worse are unclear. A possible explanation can be that the closure of the fistula tract with the glue leads to a situation where insufficient drainage from the primary and eventual secondary fistula tract occurs [7]. Furthermore, other authors have mentioned incomplete filling of the fistula tract because of cavitory fistula tracts or the presence of side branches. Lindsey et al. reported the efficacy of endorectal ultrasound to identify fistula anatomy, thus, the use of this approach preoperatively to improve results [20]. A two-staged technique, using non-cutting seton followed by a period of healing before glue injection may also improve results.

Recently, a porcine dermal matrix injection (Permacol Injection-Covidien plc, Dublin, Ireland) has been used as infill biomaterial to treat fistulas [13, 14]. Permacol is a commercially available porcine dermal collagen developed as sheet or liquid injection. It is non-allergenic, non-antigenic, and entirely biocompatible. It has been used successfully in many different ways, including abdominal wall hernia repairs including incisional and parastomal hernia as well as for pelvic floor surgery [14]. The injectable form is a 50% per by volume collagen particles in saline and presently the most evident limit to fill in a fistula track is its extremely liquid consistency. It has been used in cases of anal and urinary incontinence and for plastic surgery. At the present time, literature data experience on its use to treat anal fistulas is scant. Himpson et al., in a experimental porcine model of fistula-in-ano, concluded that when the fistula track is completely removed and durable infill material used, it is possible to treat fistulas successfully even in presence of infection or contamination [13]. The same authors suggested that it is likely that because of the cross-linked nature of Permacol, it provides tissue repair regeneration with stability and facilitates controlled and ordered wound healing. However in their experience, the “too liquid” injectable preparation was modified by centrifugation to produce a thicker paste to prevent extrusion from the tract. Initial clinical use is even less documented. In this study, we report our experience with a novel approach consisting in non-cutting seton positioning followed by flap repair associated with Permacol injection into the fistula tracts after. We believe

that this combined approach offers several potential advantages compared to fibrin glue injection alone or after flap repair. The earlier non-cutting seton insertion allows a good drainage of the sepsis, fistula cavities, and, when present, the obliteration of all (either known or unrecognized) secondary fistula tracts. At the second-stage surgery, the injection would cover a single, possibly straight-line fistula tract.

The flap repair (mucosal, submucosal, and some muscle fibers), covering the internal source of the fistula, would prevent extrusion of the Permacol injection as already shown by several studies using fibrin glue. In our opinion, the reported failures using the combination of the two techniques can be explained with the need of correct fistula anatomy identification and previous drainage of the sepsis obtained with the use of loose seton drainage as bridge to flap repair surgery. The injected matrix offers a scaffold for scar formation and tissue regeneration. However some limits are still evident. At the present time, this injectable preparation is too liquid and this may lead to an immediate extrusion after injection. Despite that it has been successfully used for this purpose in outpatient setting as single injection through the external orifice and around it [14], our experience with its use in outpatient setting for anal fistula (after previous seton placement) or sinus resulted unfavorable and all patients (5 patients, data not published) eventually required surgery. The sudden extrusion of the infill material might be responsible for this result. The early extrusion is also observed after flap advancement surgery, thus in order to prevent extrusion we perform a purse-string suture around the external orifice to avoid leaks during the first three postoperative days and thereafter we remove the suture to prevent potential suppurations.

In conclusion, Permacol injection with advancement flap repair seems to be safe and effective. A previous seton insertion is mandatory to “clean” the fistula cavities and tracts and to “ameliorate” fistula anatomy. The current preparation does not allow the use as infill material in outpatient care even if fistula tract has been previously drained with seton. Obviously a longer follow-up and large series are needed to confirm our findings.

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