

Efficacy of Anal Fistula Plug *vs.* Fibrin Glue in Closure of Anorectal Fistulas

Eric K. Johnson, M.D., Janette U. Gaw, M.D., David N. Armstrong, M.D., F.R.C.S.

Georgia Colon & Rectal Surgical Clinic, Atlanta, Georgia

PURPOSE: Long-term closure rates of anorectal fistulas using fibrin glue have been disappointing, possibly because of the liquid consistency of the glue. A suturable bioprosthetic plug (Surgisis[®], Cook Surgical, Inc.) was fashioned to close the primary opening of fistula tracts. A prospective cohort study was performed to compare fibrin glue *vs.* the anal fistula plug. **METHODS:** Patients with high transphincteric fistulas, or deeper, were prospectively enrolled. Patients with Crohn's disease or superficial fistulas were excluded. Age, gender, number and type of fistula tracts, and previous fistula surgeries were compared between groups. Under general anesthesia and in prone jackknife position, the tract was irrigated with hydrogen peroxide. Fistula tracts were occluded by fibrin glue *vs.* closure of the primary opening using a Surgisis[®] anal fistula plug. **RESULTS:** Twenty-five patients were prospectively enrolled. Ten patients underwent fibrin glue closure, and 15 used a fistula plug. Patient's age, gender, fistula tract characteristics, and number of previous closure attempts was similar in both groups. In the fibrin glue group, six patients (60 percent) had persistence of one or more fistulas at three months, compared with two patients (13 percent) in the plug group ($P < 0.05$, Fisher exact test). **CONCLUSIONS:** Closure of the primary opening of a fistula tract using a suturable biologic anal fistula plug is an effective method of treating anorectal fistulas. The method seems to be more reliable than fibrin glue closure. The greater efficacy of the fistula plug may be the result of the ability to suture the plug in the primary opening, therefore, closing the primary opening more effectively. Further prospective, long-term studies are warranted. [Key words: Fistula-in-ano; Fibrin glue; Fistula recurrence; Fecal incontinence; Fistula; Surgical treatment; Biologics; Fistulotomy; Surgisis[®] AFP]

Recent studies have described disappointing results in long-term closure of anorectal fistulas using fibrin glue. Long-term closure rates as low as 16 percent have recently been described.¹ The liquid consistency of fibrin glue is not ideal for the purpose of closing anorectal fistulas, because the glue is easily extruded from the fistula tract during, for example, coughing and straining. To address these problems, a biologic anal fistula plug was developed, which could be securely sutured into the primary opening of the fistula tract. The plug was fashioned from Surgisis[®] (Cook Surgical, Inc., Bloomington, IN), a bioabsorbable xenograft, made of lyophilized porcine intestinal submucosa. The material has inherent resistance to infection, produces no foreign body or giant cell reaction, and becomes repopulated with host cell tissue during a period of three months. The material was fashioned into a conical plug and secured into the primary opening of the fistula tract. Insertion of a conical plug into the high-pressure area of the fistula also produces a mechanically stable system, whereby the higher pressures within the anal canal tend to maintain the plug in place, thus minimizing the potential for dislodgement of the plug. A prospective cohort study was conducted to compare the efficacy of fibrin glue *vs.* fistula plug in patients with high anorectal fistulas.

Dr. David Armstrong has a patent-licensing agreement with the manufacturers of Surgisis[®] (Cook Surgical, Bloomington, IN).

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Correspondence to: David N. Armstrong, M.D., F.R.C.S., Georgia Colon & Rectal Surgical Clinic, 5555 Peachtree Dunwoody Road, Atlanta, Georgia 30342, e-mail: GACRS@aol.com

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METHODS

Patients with high anorectal fistulas (high transphincteric or deeper) were prospectively enrolled

during a 12-month period. During the first six months, fistulas were closed by using fibrin glue, and during the second six months, the bioprosthetic plug was used. Patients with Crohn's disease or superficial fistulas (low transsphincteric or more superficial) were excluded. The institutional review board approved the use of both the fistula plug and fibrin glue, and informed consent was obtained in all patients.

Demographic data (age, gender) and fistula variables (type of fistula, number of fistulas, and number of previous fistula surgeries) were recorded for each patient. The number of primary and secondary openings was compared between groups. Significance was derived using chi-squared (gender), Mann-Whitney *U* test (age), or Wilcoxon's signed-rank test (number of fistulas, previous fistula surgeries, primary and secondary openings).

All patients underwent mechanical bowel preparation the day before surgery followed by 2 gm of Flagyl by mouth the same evening. A broad-spectrum parenteral antibiotic (Cefizox), 1 g, was given on induction of anesthesia. All procedures were performed under general anesthesia and in a prone jackknife position. All fistula tracts were identified and the primary opening located using conventional fistula probe, hydrogen peroxide installation, or fistuloscopy. All tracts were cleaned by irrigating with hydrogen peroxide.

Fibrin Glue

Five milliliters of fibrin glue (Tisseal[®] Baxter, Inc.) was reconstituted according to the manufacturer's directions. The glue was instilled into the secondary



Figure 1. A bioprosthetic anal fistula plug made of Surgisis[®] ES is rehydrated and rolled into a cone configuration, which is held in place with a chromic tie.



Figure 2. The fistula plug is pulled into the primary opening where it lodges snugly, therefore, occluding the high-pressure area of the fistula tract.

opening until all fistula tracts were filled. The primary and secondary openings of the fistula tracts were then securely closed using 0 chromic catgut sutures.

Bioprosthetic Plug

A conical bioprosthetic plug was fashioned from a 2-cm × 3-cm sheet of Surgisis[®] ES. The Surgisis[®] was rehydrated and rolled into a conical configuration, which was then held in place using a 0 chromic catgut tie, which was attached to the apex of the plug (Fig. 1). A fistula probe, hemostat, or fistuloscope was passed through the fistula tract from the secondary opening and exited *via* the primary opening. The chromic tie was grasped and the plug was pulled tip-first into the internal opening (Fig. 2),



Figure 3. The excess plug is trimmed at the level of the primary opening and is further secured into place using a figure-of-eight 0 chromic cat gut suture. The tip of the plug is additionally secured at the level of the secondary opening. Care is taken to avoid complete closure of the secondary opening, to allow free drainage of fluid and avoid a closed system.

Table 1.
Patient Demographics

	Fibrin Glue	Fistula Plug
Male/female ratio ^a	8/2	11/4
Age (yr ± SEM) ^b	46.5 ± 3.3	45.4 ± 2.4

SEM = standard error of the mean.

^a $P > 0.05$, chi-squared test.^b $P > 0.5$, Mann-Whitney U test.

where it was wedged snugly (Fig. 3). The excess plug material was trimmed flush with the mucosa, and the plug was buried into the primary opening using a figure-of-eight 0 chromic catgut suture, which was inserted deep to the internal sphincter muscle. The plug was further secured at the secondary opening by using a second chromic suture. Care was taken not to completely occlude the secondary opening to allow drainage of material and to avoid a closed system. Mechanical stability of the plug relies on firmly suturing the head of the plug to the primary opening, which is optimally covered by at least submucosa, and preferably internal sphincter. Although securing the tail of the plug to the secondary opening is important, it is equally important to avoid complete closure of the secondary opening, which may risk abscess formation. Leaving the secondary opening patent is more easily achieved using a suturable device, such as the plug, compared with fibrin glue, which tends to run out if both openings are not closed by some means.

In horseshoe fistulas, a single plug was inserted into one of the tracts, in an attempt to close the common primary opening, and close both tracts. In the event of multiple secondary openings along a single tract, the tract was accessed *via* the opening closest to the primary opening, the plug inserted *via* this opening and a counter-drain placed through the distal opening(s). In the event of an exceptionally long fistula tract, the primary opening may be accessed *via* a counter incision made along the fistula tract, but this was not necessary in this study.

Follow-Up

All patients were instructed to stay on a clear liquid diet for 48 hours, avoid any strenuous activity, take warm Sitz baths as needed, and apply topical 10 percent metronidazole *t.i.d.* (SLA Pharma[®], Watford, UK). The patients were followed-up at two weeks, four weeks, and then on an individual basis as clinically appropriate. In both groups, median time

Table 2.
Fistula Types

	Fibrin Glue	Fistula Plug
Horseshoe/hemi-horseshoe	7	9
Radial	3	6

 $P > 0.05$, Wilcoxon's signed-rank test.

to "failure" was calculated for failed closure attempts, and median follow-up in weeks was calculated for fistulas that were successfully closed. The status (open *vs.* closed) of the fistula was determined at final follow-up, which was similar in both groups. No patient was lost to follow-up. Success criteria were defined as closure of all secondary openings, an absence of fistula drainage, and an absence of abscess formation. In patients with multiple openings, the presence of one persistent tract was considered an overall failure, even if one or more tracts had been successfully closed.

The study was self-funded, and no financial support was requested or received. To facilitate and improve closure of fistulas using Surgisis[®], a custom-made plug Surgisis[®] Anal Fistula Plug[™] was designed and licensed to the manufacturer of Surgisis[®]. The senior author (DNA) receives royalties on sales of the product.

RESULTS

Twenty-five patients were prospectively studied. Ten patients were enrolled into fibrin glue followed by 15 patients enrolled in the fistula plug group. There was no significant difference in age or gender between groups (Table 1). Seven patients in the fibrin glue group had horseshoe or hemi-horseshoe fistulas compared with nine in the fistula plug group ($P > 0.05$, Wilcoxon's signed-rank test, Table 2). Six patients in each group had multiple fistula tracts (and therefore multiple secondary openings), two patients in the fibrin glue group and one in the plug group had more than one primary opening ($P > 0.05$,

Table 3.
Fistula Characteristics

	Fibrin Glue	Fistula Plug
Previous fistula closure attempts	8	12
Secondary openings	6	6
Primary openings	2	1

 $P > 0.05$, Wilcoxon's signed-rank test.

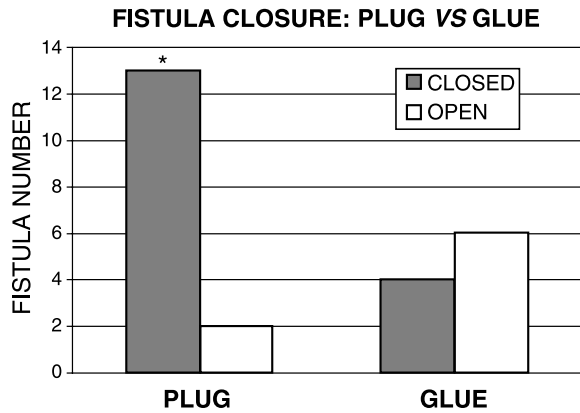


Figure 4. Open vs. closed fistulas in the anal fistula plug group vs. fibrin glue. Closure rates were significantly higher using the anal fistula plugs. * $P < 0.05$, Fisher's exact test.

Wilcoxon's signed-rank test). Eight patients in the fibrin glue group had undergone one or more attempted procedures to close the fistula tracts compared with 12 in the fistula plug group ($P > 0.05$, Wilcoxon's signed-rank test, Table 3).

Fistula Closure

Mean follow-up in the fibrin glue group was 13.6 ± 0.9 weeks vs. 13.8 ± 3.1 weeks in the plug group ($P > 0.05$, Mann-Whitney U test).

At final follow-up, six patients in the fibrin glue group (60 percent) had persistent drainage and a patent secondary opening. In the fistula plug group, two patients (13 percent) had persistent drainage and/or a patent secondary opening ($P < 0.05$, Fisher exact test; Fig. 4). Median time to failure was four weeks in both groups.

DISCUSSION

Closure of complex anorectal fistulas often is a difficult challenge. Surgical fistulotomy often is not an option because it will inevitably result in incontinence. Even when fistulotomy is considered safe, 30 percent of patient's complain of some degree of incontinence and 20 percent develop recurrent fistula/abscess.² The introduction of fibrin glue in the 1990s was a sound concept, to close fistula tracts using an occlusive material, and with minimal risk of incontinence. The current study was planned to prospectively evaluate the efficacy of fibrin glue at our institution, but the large number of early failures

led us to seek alternate means to close anorectal fistulas.

The current study was not randomized but compared two prospective cohort groups. Both groups were very similar in terms of demographics, fistula characteristics, and surgical management, and differed only in the material used to close the fistula tract. Fistulas were limited to high transsphincteric tracts, because these are the most difficult to close, and no simple effective surgery exists. More superficial intersphincteric and low transsphincteric tracts are best treated by fistulotomy, which is effective and carries little risk of incontinence. Crohn's fistulas and rectovaginal fistulas have been successfully closed using the same plug technique, but the current study is limited to a more homogenous group of high cryptoglandular fistulas.

Closure of the primary opening is the key to successful fistula surgery. Recent studies have attempted simple closure of the internal opening, without advancement flap. Although high success rates were claimed, multiple operations often were required, suture line dehiscence was frequently encountered, and the method has had little historic success.^{3,4} Closure of the internal opening also is the objective of endoanal or anocutaneous advancement flaps; however, these procedures often are technically challenging, associated with a 30 percent failure rate, and surprisingly high incontinence rate of 20 percent.⁵⁻⁸ Fibrin glue held great promise for closing anorectal fistulas with minimal impact on continence; however, reported success rates have dwindled from 80 percent in the early years to <50 percent in more recent reports.⁹⁻¹² A major drawback with fibrin glue is its liquid consistency, which tends to run out of the fistula tract, even when both primary and secondary openings are sutured closed. A further drawback is the inability of the glue to securely close the primary opening, which is the critical step.

A biologic anal fistula plug was developed to enable the primary opening to be securely and permanently closed, using a suturable material. Surgisis[®] was considered a suitable material because it is bioabsorbable, has an inherent resistance to infection, and can be safely implanted into infected surgical fields, in contrast with synthetic materials. The Surgisis[®] becomes repopulated with host cells and is remodeled into local tissues during the course of three to six months. The conical shape of the plug inserted in the high-pressure area of the primary

opening also adds an inherent mechanical stability, which avoids displacement or extrusion of the device. The higher pressures within the anal canal tend to maintain the plug-shaped device in place in the primary opening, thus minimizing risk of displacement.

The success rate of fibrin glue in the current study is consistent with previous reports, which average approximately 20 to 50 percent. Most of the failures of the fibrin glue patients occurred early in follow-up and was thought to represent extrusion of the fibrin glue shortly after surgery. Of the six "glue" failures, four occurred in patients with multiple fistula tracts, where one or more fistulas remained open at follow-up. Similarly, in the fistula plug group, both failures occurred in patients with horseshoe fistulas, where one of the original two tracts persisted in both patients. This failure to close both tracts may be the result of the use of a single plug to close both tracts of the horseshoe fistula. In both failed cases, the tract that contained the plug remained closed, and the "empty" tract remained open at final follow-up. This may be explained by proximal migration of the plug, potentially opening up the primary opening to the other fistula tract. This problem requires further evaluation.

One theoretic advantage of the fibrin glue is that unidentified fistula tracts may be filled with glue as it is injected into the fistula complex, provided the glue is allowed to extrude out through all primary openings. In practice, it is likely that failure of fibrin glue to permanently and adequately close the internal opening is the main reason for the observed high failure rates. Accurate location of all primary openings is an essential step when using the fistula plug, because persistence of one primary opening will almost inevitably result in a failed procedure. The greater success rate of the anal fistula plug compared with fibrin glue is likely a result of the ability to suture the plug firmly in the primary opening, which results in a more effective and secure closure. The mechanical stability of the plug shape and the ability to suture the plug in place avoids the problem of the material being dislodged, or extruded out of the tract.

No patient in the plug group developed anorectal abscess, despite inserting the plugs into obviously contaminated fields. Resistance to infection has been well described in previous studies of Surgisis[®] implanted into infected surgical fields, specifically abdominal hernia repairs with various degrees of

contamination. Two recent studies^{13,14} reported repair of abdominal hernias using Surgisis[®] in contaminated abdominal incisions, and neither study reported any instance of chronic implant infection. Of a combined 78 cases, 77 had successful integration of the material, despite significant contamination, and the graft material underwent degradation in only one patient, as a result of fasciitis. Resistance to infection is likely imparted from in-growth of host capillaries and immune-competent cells into the extracellular matrix, which is repopulated by native tissue during the course of the ensuing months. The extracellular matrix is eventually completely replaced by host tissues, thus avoiding the risks of chronic infection seen with implanted synthetic materials.

CONCLUSIONS

Closure of complex anorectal fistulas with biologic anal fistula plugs is a promising new technology. Although the current study is short-term, the method seems to be safe and effective, and offers an alternative to fibrin glue in "minimally invasive" management of anorectal fistulas. Longer-term follow-up is required and is currently in progress.

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