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Prospective Multicenter Study of a Synthetic Bioabsorbable Anal Fistula Plug to Treat Cryptoglandular Transsphincteric Anal Fistulas

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BACKGROUND: Although interest in sphincter-sparing treatments for anal fistulas is increasing, few large prospective studies of these approaches have been conducted.

OBJECTIVE: The study assessed outcomes after implantation of a synthetic bioabsorbable anal fistula plug.

DESIGN: A prospective, multicenter investigation was performed.

SETTING: The study was conducted at 11 colon and rectal centers.

PATIENTS: Ninety-three patients (71 men; mean age, 47 years) with complex cryptoglandular transsphincteric anal fistulas were enrolled. Exclusion criteria included Crohn's disease, an active infection, a multitract fistula, and an immunocompromised status.

INTERVENTION: Draining setons were used at the surgeon's discretion. Patients had follow-up evaluations at 1, 3, 6, and 12 months postoperatively.

MAIN OUTCOME MEASURES: The primary end point was healing of the fistula, defined as drainage cessation plus closure of the external opening, at 6 and 12 months. Secondary end points were fecal continence, duration of drainage from the fistula, pain, and adverse events during follow-up.

RESULTS: Thirteen patients were lost to follow-up and 21 were withdrawn, primarily to undergo an alternative treatment. The fistula healing rates at 6 and 12 months were 41%

(95% CI, 30%–52%; total n = 74) and 49% (95% CI, 38%–61%; total n = 73). Half the patients in whom a previous treatment failed had healing. By 6 months, the mean Wexner score had improved significantly (p = 0.0003). By 12 months, 93% of patients had no or minimal pain. Adverse events included 11 infections/abscesses, 2 new fistulas, and 8 total and 5 partial plug extrusions. The fistula healed in 3 patients with a partial extrusion.

LIMITATIONS: The study was nonrandomized and had relatively high rates of loss to follow-up.

CONCLUSION: Implantation of a synthetic bioabsorbable fistula plug is a reasonably efficacious treatment for complex transsphincteric anal fistulas, especially given the simplicity and low morbidity of the procedure.

Anal fistula disease is an old and common disorder, affecting approximately 2 of every 10,000 people,[1] but it remains difficult to treat. The goals of treatment are simple: eradication of infection, resolution of drainage with complete healing of the external opening, and preservation of fecal continence. Fistulotomy offers a high rate of success (74%–100%[1]) in achieving the first 2 goals, especially in patients with simple intersphincteric or low posterior fistulas, but even in those patients, fecal continence remains a concern. Although the average incontinence rate after fistulotomy has been found to be about 12%, rates as high as 50% have been reported.[2] Use of a cutting seton is one of the oldest therapies for anal fistulas, but it also does not reliably preserve continence.[1,3] Several factors may contribute to fecal incontinence after fistulotomy or cutting seton placement, but the most important appears to be damage to the sphincter.[2]

A fistula is considered complex when the tract involves more than 30% to 50% of the external sphincter muscle, it is located anteriorly in a woman, it is associated with Crohn's disease or radiation therapy, or it occurs in a patient with preexisting fecal incontinence, a recurrent fistula, or a clinical condition that may increase the risk of fecal incontinence.[4] High transsphincteric fistulas are especially challenging with respect to preservation of continence after treatment.

Concerns about fecal continence after traditional therapy for anal fistulas stimulated the development of several sphincter-sparing therapies. The approaches that have been studied most often are application of fibrin glue, advancement flap repair, ligation of the intersphincteric fistula tract (LIFT), and implantation of an anal fistula plug made of a biologic material. Unfortunately, fistula healing rates with approaches other than the advancement flap have been either disappointing or highly variable. Therefore, the optimal treatment for complex anal fistulas remains elusive.

A relatively new device for treating anal fistulas is a synthetic anal fistula plug composed of a copolymer (polyglycolic acid:trimethylene carbonate (PGA:TMC)) that is gradually absorbed by the body (GORE® BIO-A® Fistula Plug, W.L. Gore & Associates, Elkton, MD). No randomized controlled trials of this device have yet been reported, although 3 retrospective studies[5–7] and 2 small prospective investigations [8,9] have been published. We conducted a multicenter, prospective study of the use of the PGA:TMC plug in treating anal fistulas that included strict inclusion and exclusion criteria, a standardized plug-implantation method, and follow-up visits that involved not only clinical evaluations to determine whether fistula healing had occurred, but also the

administration of fecal continence and pain surveys.

METHODS

Patients

The study was approved by the institutional review board at each of the 11 centers, and all enrolled patients provided written informed consent to their participation. Patients presenting with a single-tract, transsphincteric anal fistula of probable cryptoglandular origin between March 2011 and September 2013 were considered for enrollment in the study. Exclusion criteria included the presence of Crohn's disease, an active local infection, a multitract fistula, a wound-healing or autoimmune disorder, a current condition or treatment producing immunocompromised or immunosuppression, a history of more than 2 previous failed fistula repairs, a superficial fistula, and a history of pelvic radiation therapy.

Anal Fistula Plug and Surgical Technique

The fistula plug used in the study consists of a PGA:TMC disk to which several PGA:TMC tubes are attached (Fig. 1). At the time of insertion, the surgeon can tailor the plug to fit and fill the specific fistula tract by removing one or more of the tubes. The material constituting the plug has a 3-dimensional matrix of interconnected pores that serves as a scaffold for tissue generation and healing. After implantation, PGA:TMC undergoes hydrolytic and enzymatic degradation, leaving no synthetic material behind. Studies in several species with this copolymer have indicated that the bioabsorption process is complete within 6 or 7 months.[10]

Draining setons were used preoperatively at the surgeon's discretion (n = 73 patients (78%)). Bowel preparation procedures were done in accordance with the standard of care at each institution. All plug implantations were performed in an outpatient setting. A single intravenous dose of an antibiotic agent was administered perioperatively.

Figure 1. Synthetic bioabsorbable anal fistula plug. The disk and tubes are both made of the copolymer polyglycolic acid:trimethylene carbonate. At implantation, the plug is tailored to fit and fill the specific fistula by removing one or more of the tubes. After the plug has been inserted into the fistula tract, the remaining tubes are trimmed flush with the skin.

The fistula tract was debrided by using a curette, gauze, or brush and irrigated with peroxide or saline. At plug insertion, as many tubes as necessary were cut off, although an effort was made to retain the maximum number possible to ensure that the fistula tract was snugly filled. The disk portion of the device was not trimmed. The disk was sutured to the anorectal wall by using at least 3 sutures (1 placed cranially and 1 placed on each side) of 2-0 Vicryl on a UR6 or SH needle (Ethicon, Somerville, NJ). Disks were neither covered with tissue nor buried in a tissue pocket. The ends of the retained tubes were trimmed flush with the skin. No sutures were placed in the external opening, which was left sufficiently open to allow drainage.

Pain medications were prescribed at the surgeon's discretion. Follow-up visits were scheduled for 1, 3, 6, and 12 months after surgery.

Data Collection and Study End Points

Demographic and clinical data collected at enrollment were age, sex, BMI, previous fistula treatment, and whether a draining seton was used. Data recorded at operation were fistula location (high or low), length of the fistula tract, and number of fistula plug tubes implanted.

At each postoperative visit, patients underwent a history and physical examination

by the primary surgeon to assess whether their fistula had closed, drainage had stopped, and the anal fistula plug remained in place. Patients were also asked to describe their perineal pain as either none, mild, moderate, or severe. Any fistula- or plug-related adverse events and their treatment were recorded. The Cleveland Clinic Florida (Wexner) fecal incontinence score questionnaire was administered to patients within a week before plug implantation and during their 6-month follow-up visit.

Healing of the fistula was defined as cessation of drainage and complete closure of the external opening. The primary end point of the study was the healing rate at 6 and 12 months after plug implantation. Secondary end points were changes in fecal continence (Wexner score) between the immediate preoperative period and 6 months after surgery, duration of drainage from the fistula, postoperative pain levels, and adverse events during follow-up.

Statistical Analysis

Results are reported as numbers, percentages, ranges, and rates with 95% CIs. The difference in mean Wexner score before and 6 months after plug implantation was assessed by using a paired t test. The possible effects on fistula healing of recurrent fistula (that is, first vs recurrent), seton use before plug implantation, the patient's sex, and the fistula type (high vs low) were evaluated by using the Fisher exact test. Logistic regression analysis was used to determine whether the number of tubes implanted, the length of the fistula tract, or the patient's sex was related to fistula healing. All statistical analyses used JMP software, version 10.0.2 (JMP/SAS Institute, Cary, NC). A p value of 0.05 was considered to represent a significant difference.

RESULTS

Ninety-three patients were initially enrolled in the study; Table 1 shows their demographic and preoperative characteristics. Fourteen percent of the patients were 65 years of age or older; 28% had previously undergone an unsuccessful treatment for their fistula. There were 11 sites registered and enrolling patients, with a median number of 7 patients per site and a range of 1 to 22. Six sites contributed at least 5 patients.

During the 1-year observation period in the study (Fig. 2), 13 patients were lost to follow-up and 21 patients were withdrawn. One patient was withdrawn by the investigators when that patient was found not to have met the inclusion criteria pertaining to type of fistula (multitract fistula). Another withdrew after she was given a diagnosis of endometrial cancer and scheduled to have a hysterectomy. Before the 12-month follow-up, 18 patients were considered to have a failure of healing with the fistula plug and underwent an alternative treatment. Of these patients, 6 subsequently had an advancement flap repair, 5 a LIFT operation, 3 a draining seton procedure, and 2 a fistulotomy. The alternative treatment for 2 of the 18 patients was not recorded.

Table 1. Demographic and operative characteristics in 93 patients with a cryptoglandular transsphincteric fistula who underwent implantation of a synthetic bioabsorbable anal fistula plug

Characteristic	Value[a]
Mean age, y (range)	47 (19–82)
Sex: male/female	71 (76)/22 (24)
Mean BMI, kg/m^2 (range)	29.4 (18.6–48.4)
Recurrent fistula	26 (27.9)
Previous fistula treatment	
Fistulotomy	7 (7.5)
Advancement flap	5 (5.4)
Cutting seton	4 (4.3)
Fistula plug	4 (4.3)
LIFT procedure	2 (2.2)
Fistulectomy	1 (1)
Fibrin glue	1 (1)
Unknown	2 (2.2)
Seton therapy before plug implantation	73 (78.4)
Mean duration of seton therapy, wk (range)	15 (3–50)
Fistula location: high/low[b]	34 (37)/58 (62)
Mean fistula tract length, cm (range)	4.2 (1.5–8)
Number of fistula plug tubes implanted	
1	5 (5)
2	20 (22)
3	21 (23)
4	27 (29)
5	4 (4)
6	16 (17)

LIFT = ligation of the intersphincteric tract.
[a]Values are n (%) unless otherwise specified.
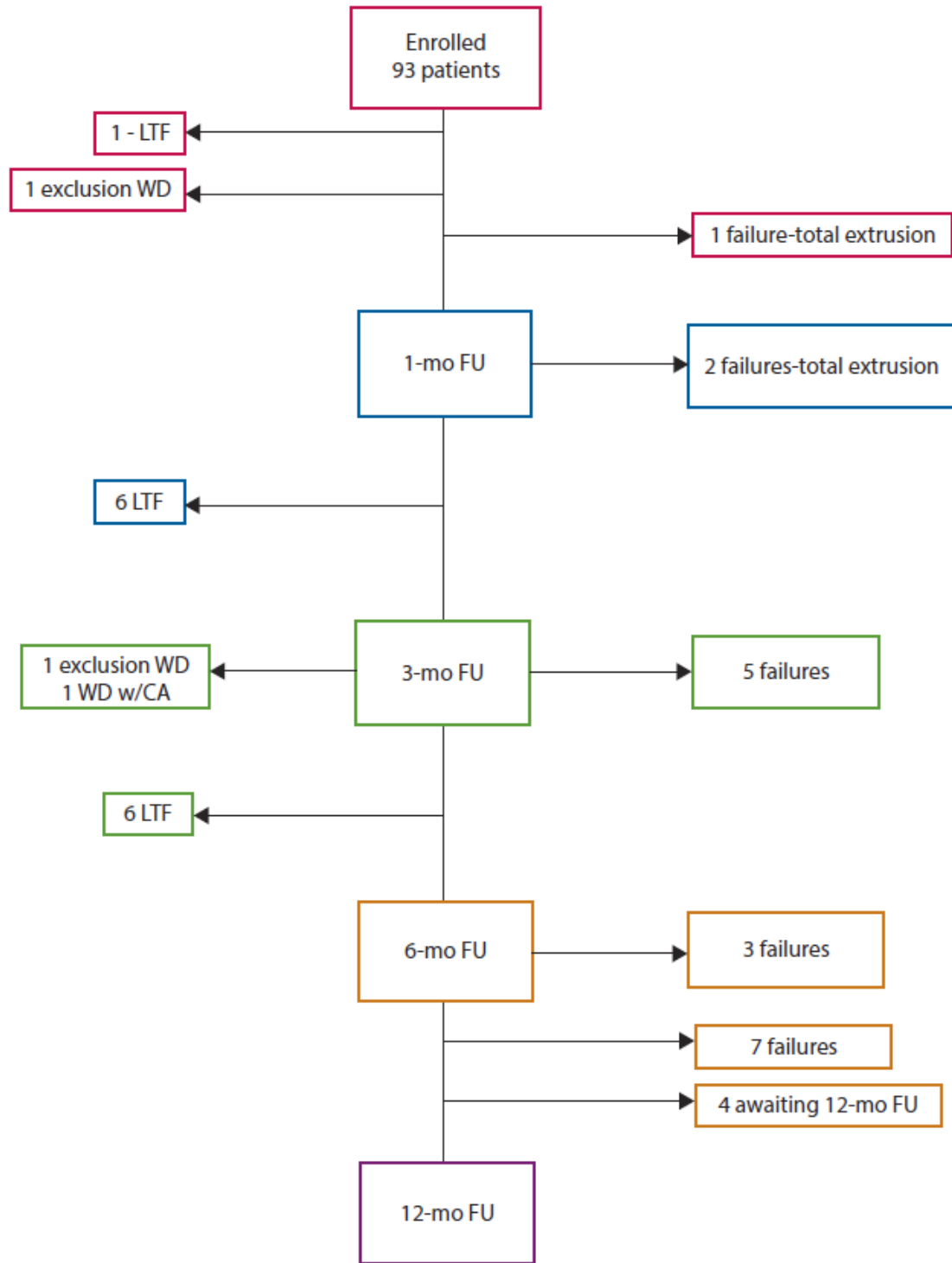[b]The location was not recorded for 1 patient.

Figure 2. Flow diagram showing the course of the study. LTF = lost to follow-up; exclusion WD = withdrawal by investigators after the patient was found not to have met the inclusion criteria; FU = follow-up; WD w/CA = withdrawal after receiving a diagnosis of endometrial cancer.

Of the 66 patients examined 6 months after plug implantation, 30 had a healed fistula. Plug implantation failed in 8 patients before that visit, and 4 patients did not complete a 6-month follow-up visit, but they did complete a 12-month follow-up. Of the 55 patients seen at 12 months, 36 had a healed fistula. In addition, plug implantation failed in 18 patients before the 12-month visit. The fistula healing rates at 6 and 12 months were 41% (95% CI, 30%–52%) and 49% (95% CI, 38%–61%). In 9 patients, the fistula healed between their 6- and 12-month follow-up visits. In 3 additional patients with 12 months of follow-up who were considered to have had a treatment failure, cessation of draining occurred between 6 and 12 months, but their fistula was not completely closed. Of the 26 patients in whom a previous treatment failed to heal their fistula, 13 had healing after implantation of the synthetic plug. The previous fistula therapies in these patients were fistulotomy (n = 4), cutting seton (n = 3), advancement flap (n = 2), fistula plug implantation (n = 1), fistulectomy (n = 1), and unknown (n = 2).

The mean score on the Wexner fecal continence assessment before fistula plug implantation was 5.3. At 6 months postoperatively (n = 64 patients), it was 2.6. The difference between the scores was significant (p = 0.0003), indicating an overall improvement in continence. However, 10 patients had a worsening of their Wexner score between the baseline and the 6-month assessment (mean increase, 4.4 points; range, 1–9) For 5 of these patients, the increase was 4 or fewer points. Six of the 10 patients with a worsened Wexner score did not have a healed fistula at 6 months, but they did have healing at 12 months. Two withdrew from the study to receive an alternative treatment.
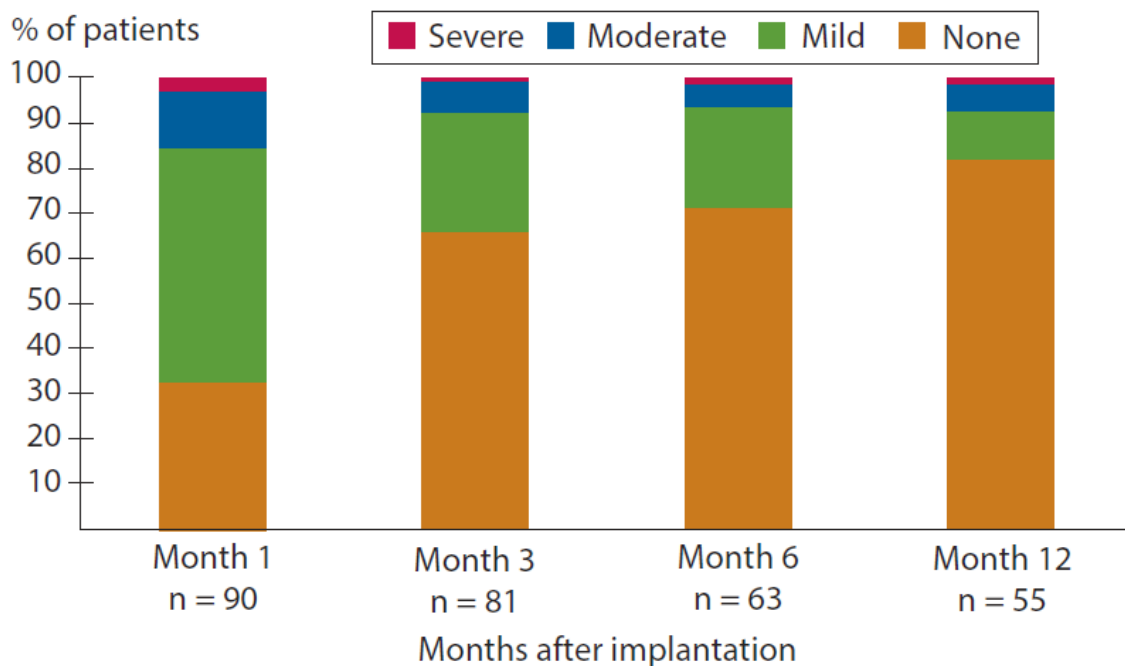

Figure 3. Bar graph showing percentage of assessed patients with no, mild, moderate, and severe perineal pain at 1, 3, 6, and 12 months after implantation of a synthetic bioabsorbable plug to treat cryptoglandular transsphincteric anal fistulas. The patient population at each assessment time included those with both healed and unhealed fistulas.

Figure 3 shows the results of the assessment of pain at the fistula site at 1, 3, 6, and 12 months after plug implantation. Most patients (52%; n = 47) had mild pain a month after surgery, although 32% (n = 29) had no pain and 3% (n = 3) had severe pain. By 3 and 6 months, most patients (65% (n = 53) and 71% (n = 45)) had no pain. At 12 months, 93% of patients (n = 51) had no or mild pain. Severe pain was reported by 3 patients at 1 month and by 1 patient at 3, 6, and 12 months. The same patient reported severe pain at 6 and 12 months; this patient had multiple clinical problems. Of the 18 patients with any pain at 6 months, 13 had an unhealed fistula. Of the 10 patients with pain at 12 months, 6 did not have healing.

Adverse events during the observation period are shown in Table 2. Nine of the 11 infections/abscesses were treated with antibiotics alone. Five of the infections resolved, but the fistula in 3 of the 5 patients did not heal. Two of the infections did not resolve during the observation period, and neither patient had fistula healing. The status of the other 2 infections treated with antibiotics is unknown because the patient withdrew (n = 1) or was lost to follow-up (n = 1) before the 1-month visit. One of the 11 patients with infection had incision and drainage of an abscess and seton placement; the patient's fistula did not heal. Another had spontaneous draining of an abscess that required packing of the wound. This patient was considered to have a failure of plug treatment of the fistula, and he underwent an advancement flap procedure 4 months after enrollment in the study.

The 2 new fistulas were reported at the 3- and 6-month follow-up visit, and both patients were considered to have had a fistula healing failure. Eight patients (8.6%) had total extrusion of the fistula plug. Two extrusions occurred within 2.5 weeks of surgery, 1 was noted at the 1-month follow-up visit, and 1 was noted at the 3-month visit. The other 5 were reported between 4 and 6 months after plug implantation. All patients with a total extrusion were considered to have treatment failures and were withdrawn from the study to receive alternative treatment. There were 5 partial extrusions of a plug, that is, the patient reported detachment of a small piece of a tube from the device. Three of the 5 patients with a partial extrusion had healing of their fistula; 2 had healing by 3 months and 1 had healing by 12 months after plug implantation.

The analyses of factors possibly related to fistula healing found that recurrent fistula compared with first fistula, sex, BMI, number of plug tubes implanted, and fistula tract length were not significantly associated with healing. Patients in whom a draining seton was not used before plug implantation had a significantly higher healing rate than those given a seton (73% (11 of 15 patients) vs 43% (24 of 56 patients); p = 0.045). The fistula healing rate was also significantly higher in patients with a high transsphincteric fistula compared with those who had a low transsphincteric fistula (66% (19 of 29 patients) vs 38% (16 of 42 patients); p = 0.03).

Table 2. Adverse events during 12 months of follow-up in patients who underwent implantation of a synthetic bioabsorbable anal fistula plug

Event	n
Infection/abscess	11
New fistula	2
Partial plug extrusion	5
Total plug extrusion	8
Treatment after total plug extrusion	
Advancement flap	4
Draining seton placement	3
Unknown	1

DISCUSSION

The original anal fistula plug, composed of lyophilized porcine small-intestine mucosa (Surgisis (now Biodesign) Fistula Plug, Cook Medical, Bloomington, IN), was first introduced in 2006. In a 2012 meta-analysis of 6 studies, Leng and Jin[11] concluded that implantation of a biologic plug has the same rate of success in healing fistulas as the advancement flap technique but a lower risk of complications because of its minimally invasive nature. They also observed that quality of life is better in patients treated with the plug compared with those who have undergone an advancement flap procedure, primarily because fecal continence is not affected.

Indeed, early results with the biologic fistula plug were especially promising, with some researchers reporting healing rates of higher than 80%.[12] However, in more recent studies, including randomized controlled trials,[13,14] large, multicenter investigations,[15] and the largest prospective studies,[16–19] success rates have ranged from 20% to 48%. The wide variation in results with the biologic plug may be due in part to differences in patient populations, study designs, surgical techniques, and follow-up times,[20] although these do not seem to explain the variation completely. As O'Riordan et al[20] noted in a systematic review, the divergent findings make it difficult for surgeons to quote an acceptable success rate during preoperative counseling of patients with anal fistulas considering treatment with the biologic plug. O'Riordan et al reviewed 20 studies and calculated that fistula closure is achieved in about 54% of patients treated with the biologic plug.

The synthetic bioabsorbable fistula plug used in our series was previously evaluated for use in complex fistulas in 5 published studies,[5–9] although our investigation enrolled more than twice as many patients as in the largest of the earlier trials.[6] Because of differences between study designs, comparing results in the 6 studies of the synthetic plug or summarizing the overall experience with the device is somewhat problematic. However, for 5 of the 6 investigations (including ours), the reported fistula healing

rate for the entire observation period ranged from 48% to 73%. The only outlier was the study in 19 patients by de la Portilla et al,[9] who had a fistula closure rate of 15.8% but noted a learning-curve effect and speculated that the low rate may have been due to the minimal preoperative use of setons in their series.

In a considerable number of patients in our study, fistula healing occurred more than 6 months after plug insertion. These patients had a decrease in their symptoms earlier, but complete symptom resolution and skin healing took longer. This finding was unanticipated and leads us to recommend continued observation, up to a year, in patients with evidence of improvement. In patients with cessation of drainage but not complete fistula closure at the external opening, further observation to allow complete healing to occur seems especially warranted. Other investigators have also reported delayed healing with the synthetic bioabsorbable fistula plug [1,8] and after LIFT procedures.[21]

None of the patients in the previous studies of the synthetic fistula plug reported a worsening in fecal incontinence. [5–9] In our study, the mean Wexner score decreased significantly (p = 0.0003) between baseline and 6 months after plug implantation, indicating an overall improvement in continence, but 10 patients had a higher score at 6 months. To our knowledge, this has not previously been observed or reported. It may reflect a problem with the use of the Wexner questionnaire in patients who have anal canal leakage that they have difficulty differentiating from leakage from a fistula. In addition, 3 of these 10 patients had a minimal change in their score, and variations in scores over time have previously been reported, as have issues with test-retest reliability.[22] Despite the challenges of assessing incontinence, the overall population of patients in our study had no worsening of incontinence after treatment with the synthetic fistula plug.

Our study and that of Heydari et al[6] were the only 2 investigations of the synthetic fistula plug to evaluate local pain after implantation of the device. Heydari et al used a 10-point visual analog scale (with 0 indicating no pain and 10 indicating the worst pain imaginable), whereas we asked patients to describe their pain as none, mild, moderate, or severe. In both series, pain evaluations were conducted 1, 3, 6, and 12 months after plug implantation; Heydari et al also performed a 1-week assessment. As expected, both studies showed that patients more commonly had pain and more severe pain in the early postoperative period (1-month evaluation). Moreover, in our study, most patients who continued to have pain at 6 and 12 months had an unhealed fistula. By 6 months after plug implantation, 93% of our patients and 100% of those of Heydari et al had no or minimal pain. These results indicate that the full course of treatment necessary for healing of fistulas after plug implantation is unlikely to be curtailed because of pain.

Plug extrusion or dislodgement was reported in 10 of the total of 221 patients (4.5%) in the 6 published studies, including ours, of the synthetic anal fistula plug. Thus, although our reported rate of total plug extrusion was 8.6% (n = 8), it appears that, overall, the ability of the plug to be tailored to the diameter of the individual fistula tract by removing 1 or more of its tubes may represent an advantage of the device. In our study, 5 of the 8 patients reported total extrusion after the 3-month follow-up visit. By that time, although there may be PGA:TMC material remaining in the tissue,10 it is likely not visible to the naked eye. Therefore, a report of plug extrusion more than 3 months after implantation should be interpreted with caution. In addition, because the plug bioabsorbs primarily by means of hydrolysis, partial extrusion of the distal segment of the

tubes may occur with the natural degradation process of the proximal or middle segment. In particular, partial plug extrusion did not predict treatment failure in our study: 3 of the 5 patients for whom this was reported had healing of their fistula.

Of the 11 infections/abscesses observed in our series, 5 resolved after antibiotic therapy, without removal of the fistula plug. This finding suggests that it is possible to successfully treat an infection in a patient who has a plug in place, thereby allowing fistula therapy to continue uninterrupted.

Our finding that the use of a draining seton before plug implantation was associated with a lower healing rate than nonuse of a seton should be interpreted with caution. Because seton use was not mandated by our study protocol (only encouraged), and active local infection was an exclusion criterion, a selection bias for using a seton in patients with higher-risk fistulas probably existed in the study. Although the results of previous, predominantly retrospective studies[5,9] indicated that fistula healing was improved by preoperative seton use, our findings suggest that this possible correlation requires additional evaluation. Perhaps more selective use of a draining seton is indicated. Our current data are insufficient for further analysis of this issue.

In our study, the healing rate was significantly higher for high fistulas compared with low fistulas ($p = 0.03$). If this finding were confirmed, it would suggest that the plug may be of particular benefit in patients with high fistulas.

The limitations of our study included its nonrandomized nature and the number of patients who were lost to follow-up or withdrawn.

CONCLUSIONS

Our findings indicate that implantation of the synthetic bioabsorbable fistula plug is a reasonably efficacious treatment for complex transsphincteric anal fistulas, especially given the simplicity and low morbidity of the procedure. The importance of long-term follow-up in patients treated with the plug is indicated by the occurrence of healing more than 6 months after plug implantation in about 10% of patients originally enrolled in the study (20% of those who healed). Our data should help surgeons obtain fully informed consent from patients considered good candidates for treatment with the synthetic plug.

REFERENCES

1. Ommer A, Herold A, Berg E, Fürst A, Sailer M, Schiedeck T; German Society for General and Visceral Surgery. Clinical practice guidelines: cryptoglandular anal fistulas. Dtsch Arztebl Int. 2011;108:707–713.

2. de Parades V, Zeitoun JD, Atienza P. Cryptoglandular anal fistula. J Visc Surg. 2010;147:e203–e215.

3. García-Aguilar J, Belmonte C, Wong DW, Goldberg SM, Madoff RD. Cutting seton versus two-stage seton fistulotomy in the surgical management of high anal fistula. Br J Surg. 1998;85:243–245.

4. Rizzo JA, Naig AL, Johnson EK. Anorectal abscess and fistulain-ano: evidence-based management. Surg Clin North Am. 2010;90:45–68.

5. Buchberg B, Masoomi H, Choi J, Bergman H, Mills S, Stamos MJ. A tale of two (anal fistula) plugs: is there a difference in short-term outcomes? Am Surg. 2010;76:1150–1153.

6. H eydari A, Attinà GM, Merolla E, Piccoli M, Fazlalizadeh R, Melotti G. Bioabsorbable synthetic plug in the treatment of anal fistulas. Dis Colon Rectum. 2013;56:774–779.

7. O mmer A, Herold A, Joos A, Schmidt C, Weyand G, Bussen D. Gore BioA fistula plug in the treatment of high anal fistulas: initial results from a German multicenter-study. Ger Med Sci. 2012;10:Doc13. doi: 10.3205/000164.

8. Ratto C, Litta F, Parello A, Donisi L, Zaccone G, De Simone V. Gore Bio-A® Fistula Plug: a new sphincter-sparing procedure for complex anal fistula. Colorectal Dis. 2012;14:e264–e269.

9. de la Portilla F, Rada R, Jiménez-Rodríguez R, Díaz-Pavón JM, Sánchez-Gil JM. Evaluation of a new synthetic plug in the treatment of anal fistulas: results of a pilot study. Dis Colon Rectum. 2011;54:1419–1422.

10. Katz AR, Mukherjee DP, Kaganov AL, Gordon S. A new synthetic monofilament absorbable suture made from polytrimethylene carbonate. Surg Gynecol Obstet. 1985;161:213–222.

11. L eng Q, Jin HY. Anal fistula plug vs mucosa advancement flap in complex fistula-in-ano: a meta-analysis. World J Gastrointest Surg. 2012;4:256–261.

12. Johnson EK, Gaw JU, Armstrong DN. Efficacy of anal fistula plug vs. fibrin glue in closure of anorectal fistulas. Dis Colon Rectum. 2006;49:371–376.

13. O rtiz H, Marzo J, Ciga MA, Oteiza F, Armendáriz P, de Miguel M. Randomized clinical trial of anal fistula plug versus endorectal advancement flap for the treatment of high cryptoglandular fistula in ano. Br J Surg. 2009;96:608–612.

14. van Koperen PJ, Bemelman WA, Gerhards MF, et al. The anal fistula plug treatment compared with the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: a double-blinded multicenter randomized trial. Dis Colon Rectum. 2011;54:387–393.

15. Blom J, Husberg-Sellberg B, Lindelius A, et al. Results of collagen plug occlusion of anal fistula: a multicentre study of 126 patients. Colorectal Dis. 2014;16:626–630.

16. A damina M, Ross T, Guenin MO, et al. Anal fistula plug: a prospective evaluation of success, continence, and quality of life in the treatment of complex fistulae (published online ahead of print February 13, 2014). Colorectal Dis. doi: 10.1111/codi.12594.

17. Chan S, McCullough J, Schizas A, et al. Initial experience of treating anal fistula with the Surgisis anal fistula plug. Tech Coloproctol. 2012;16:201–206.

18. Cintron JR, Abcarian H, Chaudhry V, et al. Treatment of fistulain-ano using a porcine small intestinal submucosa anal fistula plug. Tech Coloproctol. 2013;17:187–191.

19. M cGee MF, Champagne BJ, Stulberg JJ, Reynolds H, Marderstein E, Delaney CP. Tract length predicts successful closure with anal fistula plug in cryptoglandular fistulas. Dis Colon Rectum. 2010;53:1116–1120.

20. O 'Riordan JM, Datta I, Johnston C, Baxter NN. A systematic review of the anal fistula plug for patients with Crohn's and non-Crohn's related fistula-in-ano. Dis Colon Rectum. 2012;55:351–358.

21. L iu WY, Aboulian A, Kaji AH, Kumar RR. Long-term results of ligation of intersphincteric fistula tract (LIFT) for fistula-inano. Dis Colon Rectum. 2013;56:343–347.

22. S ansoni J, Hawthorne G, Fleming G, Marosszeky N. The revised faecal incontinence scale: a clinical validation of a new, short measure for assessment and outcomes evaluation. Dis Colon Rectum. 2013;56:652–659.

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