



Can Perianal Fistula Be Treated Non-surgically with Platelet-Rich Fibrin Sealant?

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Abstract

Introduction In the last 20 years, various procedures have been suggested for the treatment of anal fistula whilst minimising anal sphincter injury and preserving optimal function. Since 2011, patients at our hospital have been treated for anal fistula by means of platelet-rich fibrin plugs. To do so, three different application techniques have been used, the most recent of which is a non-surgical approach. In this paper, we compare and contrast the results obtained by each of these three techniques.

Material and Method This study compares three procedures in which the anal fistula was sealed using platelet-rich fibrin: for the patients in group A, the plug was surgically inserted, under anaesthesia, and traditional methods were used to curette the fistula tract and close the internal orifice; for those in group B, the plug was surgically inserted, under anaesthesia, after curettage of the fistula tract using a graduated set of cylindrical curettes, and the internal orifice was closed as before; and for those in group C, the plug was inserted during outpatient consultation, without anaesthesia, without curettage and without closure of the internal orifice.

Results The patients in the three groups were homogeneous in terms of sex, age, ASA classification, location of the fistula and previous insertion of the seton. There were no significant differences in morbidity or postoperative continence. However, there was a statistically significant difference in the outcomes achieved, in favour of group B, while groups A and C obtained similar results.

Conclusions Outpatient treatment of perianal fistula is totally innocuous. It is a very low cost procedure and the results obtained are highly acceptable (similar to those of the surgical insertion of a plug, with traditional curettage). Therefore, we believe this approach should be considered a valid initial treatment for perianal fistula, reserving surgical treatment (curettage and sealing using a cylindrical-curette kit) for cases in which this initial method is unsuccessful. This would avoid many complications and achieve considerable financial savings for the health system.

Keywords Anal fistula · Non-surgical treatment

Introduction

A fistula is an anomalous passage connecting two epithelialised surfaces; an anal fistula connects the anorectal region with the skin. The internal orifice of such a fistula is mainly located in

the anal canal, and the external orifice is in the perianal skin, which often provokes a chronic suppurative condition.^{1,2}

Ideally, surgical treatment for anal fistula will eradicate sepsis, promote healing of the tract, leave the sphincters intact and preserve the mechanism of continence.

A variety of approaches have been proposed for the treatment of complex perianal fistulas, which reflects the fact that no method has yet proven complete satisfactory.

Conventional surgery for anal fistula often provokes continence disorders, and so much consideration has been given to new procedures aimed at achieving significant preservation of the sphincter apparatus. Although to date insufficient evidence has been obtained from high-quality randomised prospective studies, an obvious advantage of some new techniques is that

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they do not affect continence, and so if this treatment outcome is unsuccessful, other procedures can be applied without detriment to the final result.³

Our hospital has adopted such a new approach. Since 2011, we have been treating patients with anal fistula, when not suitable for fistulotomy, by means of a technique based on sealing the fistula with platelet-rich fibrin (PRF). This PRF application method has been modified over the years, and so the aim of the present study is to compare and contrast the three variant techniques (the most recent of which is performed without surgical intervention) employed during this evolutionary process.

Material and method

This retrospective study was approved by the Research and Ethics Committee, and is based on the analysis of 102 patients treated at our hospital for perianal fistula during the period November 2011–November 2017.

The patients included had been diagnosed (by magnetic resonance imaging) with single-tract transsphincteric and suprasphincteric anal fistulas. We also included patients who presented intersphincteric fistulas with sphincter dysfunction (diagnosed by means of patient history, anal examination, endoanal ultrasound and manometry).

We excluded all patients with Crohn's disease, acute inflammatory processes, complex anal fistulas with multiple tracts and cavities.

The PRF technique for fistula sealing was applied to all patients. The first step in this procedure is to extract blood for processing. Once the PRF has been obtained, it is divided into four parts. One is applied in the initial treatment and the other three are frozen and stored for possible future use.

Three treatment groups were formed, according to the PRF application technique employed, as follows.

Group A was composed of patients operated on, under spinal anaesthesia. The surgical technique applied is quite simple, and involves the following steps:

1. Channel the tract with a grooved probe.
2. Resect the fibrous areas of the internal and external orifices.
3. Curette the tract (traditional method), to create a raw surface.
4. Wash with hydrogen peroxide, since active bleeding impedes the action of growth factors.
5. Seal the tract, using an applicator unit, which is fitted with a monitor showing the amount of product remaining.
6. Close the internal orifice.

For the patients in group B, the PRF application was performed using the same technique as for those in group A,

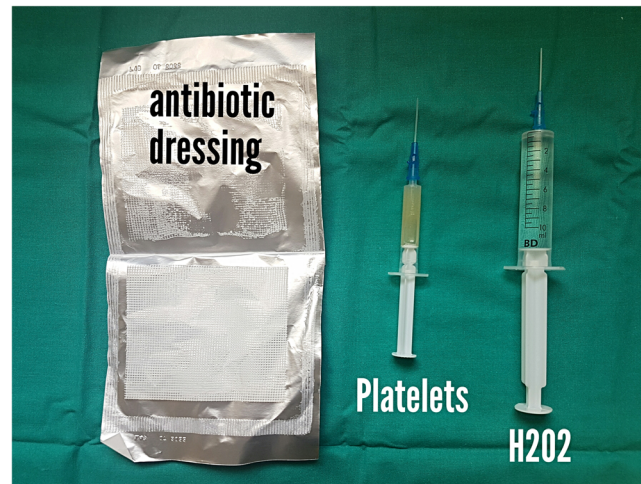


Fig. 1 Sealing in outpatient consultation: materials and devices needed

except that the curettage was not carried out by the traditional method, but using a graduated set of purpose-built cylindrical curettes.

Finally, group C was composed of patients in whom the PRF was applied in outpatient consultation (Fig. 1), with no type of anaesthesia and with no other technical manoeuvre. The following procedure was employed. At a scheduled outpatient consultation (prior fasting not required), the patient is asked to lie on the treatment table in a foetal position (Fig. 2). The tract is washed with hydrogen peroxide (Fig. 3A) and the PRF preparation is injected through the external orifice (Fig. 3B), sealing the tract. Finally, an antibiotic dressing is applied to the external orifice (Fig. 3C) and the patient can go home immediately. No observation period is required, as no type of anaesthesia was used.

Subsequently, all patients were reviewed in outpatient consultations, at 3, 6, 9, 12 and 24 months after the intervention. The three groups were compared in terms of the results obtained, taking into account the following variables: sex, age, ASA classification, location of fistula, seton placement prior to treatment, fistula closure (defined as complete resolution), Wexner test score pre- and post-surgery and follow-up time.



Fig. 2 Sealing in outpatient consultation: foetal position in lateral decubitus

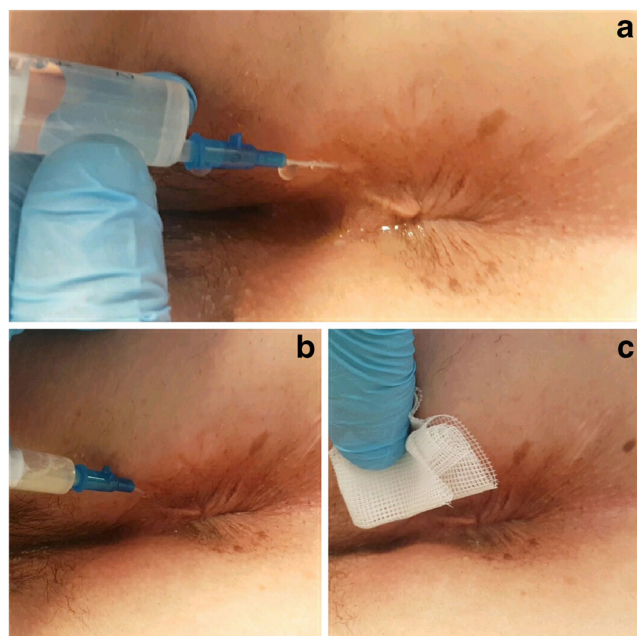


Fig. 3 Sealing in outpatient consultation: (a) flushing with hydrogen peroxide via external orifice; (b) sealing with platelets via external orifice; c) application of antimicrobial dressing

Statistical Analysis

In the statistical analysis, qualitative variables are expressed in absolute and relative frequencies, and quantitative ones as the mean and the standard deviation. The chi-square test was applied to determine the association between qualitative

variables, and if more than 20% of the expected values were less than five, Fisher's test was also applied. The normality of distribution was verified by the Shapiro-Wilk test. Parametric quantitative variables were compared by ANOVA, and non-parametric ones by the Kruskal-Wallis test.

Results

The three groups were homogeneous by sex ($p = 0.61$), age ($p = 0.56$), ASA classification ($p = 0.39$), location of the fistula ($p = 0.43$), previous placement of the seton ($p = 0.82$) and follow-up time ($p = 0.48$).

As shown in Tables 1, 2 and 3, there were no significant differences in terms of morbidity (one case of abscess in group A, one mild infection in group B and one mild infection in group C) or post-operative continence (difference between pre- and post-surgery Wexner test scores: 1/20 and 3/20 for two patients in group B and zero for all patients in groups A and C) ($p = 0.09$).

For the variable "fistula healing", Group B presented the highest rate of healing (80.7% $p = 0.03$), while the statistical test (chi-square) revealed no statistically significant differences between groups A and C (52.9% vs. 54%).

Discussion

Fistulous disease is one of the most common anorectal disorders. It has a prevalence of 8.6 to 10 per 100,000 persons per

Table 1 Baseline characteristics of the three groups

		Group A		Group B		Group C		Total		p value
		n	%	n	%	n	%	n	%	
Sex	M	23	67.7	24	77.4	25	67.6	72	70.6	0.61 (a)
	F	11	32.4	7	22.6	12	32.4	30	29.4	
ASA	All	34	100.0	31	100.0	37	100.0	102	100.0	0.39 (b)
	1	20	58.8	15	48.4	26	70.3	61	59.8	
	2	12	35.3	13	41.9	8	21.6	33	32.4	
	3	2	5.9	3	9.7	3	8.1	8	7.8	
Seton	All	34	100.0	31	100.0	37	100.0	102	100.0	0.82 (a)
	No	26	76.5	22	71.0	26	70.3	74	72.5	
	Yes	8	23.5	9	29.0	11	29.7	28	27.4	
Fistula	All	34	100.0	31	100.0	37	100.0	102	100.0	0.43 (b)
	Suprasphincteric	0	0	0	0	1	2.7	1	0.98	
	Intersphincteric	3	8.8	4	12.9	10	27.0	17	16.7	
	High transsphincteric	5	14.7	5	16.1	4	10.8	14	13.7	
	Low transsphincteric	7	20.6	3	9.7	4	10.8	14	13.7	
	Medium transsphincteric	19	55.9	19	61.3	18	48.6	56	54.9	
All	34	100	31	100	37	100	102	100		

(a) Chi-square test

(b) Fisher test

Table 2 Baseline characteristics of the three groups

	Group A	Group B	Group C	<i>p</i> value
Age (years)	47.20 (± 13.72)	50.48 (± 14.99)	47.59 (± 11.03)	0.557 (a)
Follow-up (months)	27.08 (± 8.87)	24.90 (± 13.17)	23.75 (± 24.14)	0.489 (b)

(a) ANOVA test

(b) Kruskal-Wallis test

year, and affects men and women in a ratio of 8:14, respectively. Most fistulas are of cryptoglandular origin, and are thought to be provoked by an infection in the intersphincteric space, although there is no unequivocal confirmation of this theory.⁴

Much controversy surrounds the surgical treatment of anorectal fistula of cryptoglandular origin, since case histories are heterogeneous, various definitions of complex fistula have been proposed, diverse techniques (each with variants) have been applied, a variety of criteria have been used to evaluate the results obtained, and follow-up periods are often short. In consequence, no definitive conclusions have yet been drawn.³

For simple and more distal fistulas, conventional surgical options such as fistulectomy appear to be relatively safe, and so are well accepted in clinical practice. However, for more complex fistulas affecting a significant proportion of the anal sphincter, there remains great concern about possible damage to the sphincter and subsequent poor functional outcome. Indeed, this is believed to be almost inevitable after conventional surgical treatment.

Functional studies of patients before and after fistulotomy show that any section of the anal sphincter will affect maximum and minimum contraction values and is associated with impaired continence in 50% of patients.⁵ Subsequent rates of incontinence vary widely (reported levels vary from 0 to 82%^{6,7}), while success rates range from 79 to 100%.^{6–12}

For these reasons, new procedures have been considered in recent years, seeking enhanced outcomes regarding sphincter preservation and postoperative continence. Novel approaches in this respect include biological sealants (fibrin glue was the first biological material to be used in fistula repair¹³), bioprosthetic plugs,¹⁴ stem cells¹⁵ and nitinol clips,¹⁶ with their respective variants and combinations.³ However, the results obtained have been uneven.

PRF preserves the growth factors present in the fibrin network and enables their sustained long-term release, which can accelerate healing.

Many reports have described the clinical use of PRF, initially in the field of maxillofacial surgery for the repair of defects caused by tumour resection, and later in areas such as thoracic surgery,¹⁷ cardiovascular medicine,¹⁸ plastic surgery,¹⁹ traumatology²⁰ and nephrology.²¹

In 2009, our hospital began to use PRF for the treatment of vascular ulcers of the lower limbs. This produced very good results, and so in 2011 we considered the possibility of using this substance to seal perianal fistulas (in the view that a fundamental treatment goal is to accelerate and enhance healing within the fistulous tract). Accordingly, a multicentre study was launched, the results of which were published in 2015.²²

This study was conducted according to the following protocol: the sample of PRF was divided into four parts, one of which was used in the operating room, with the remaining

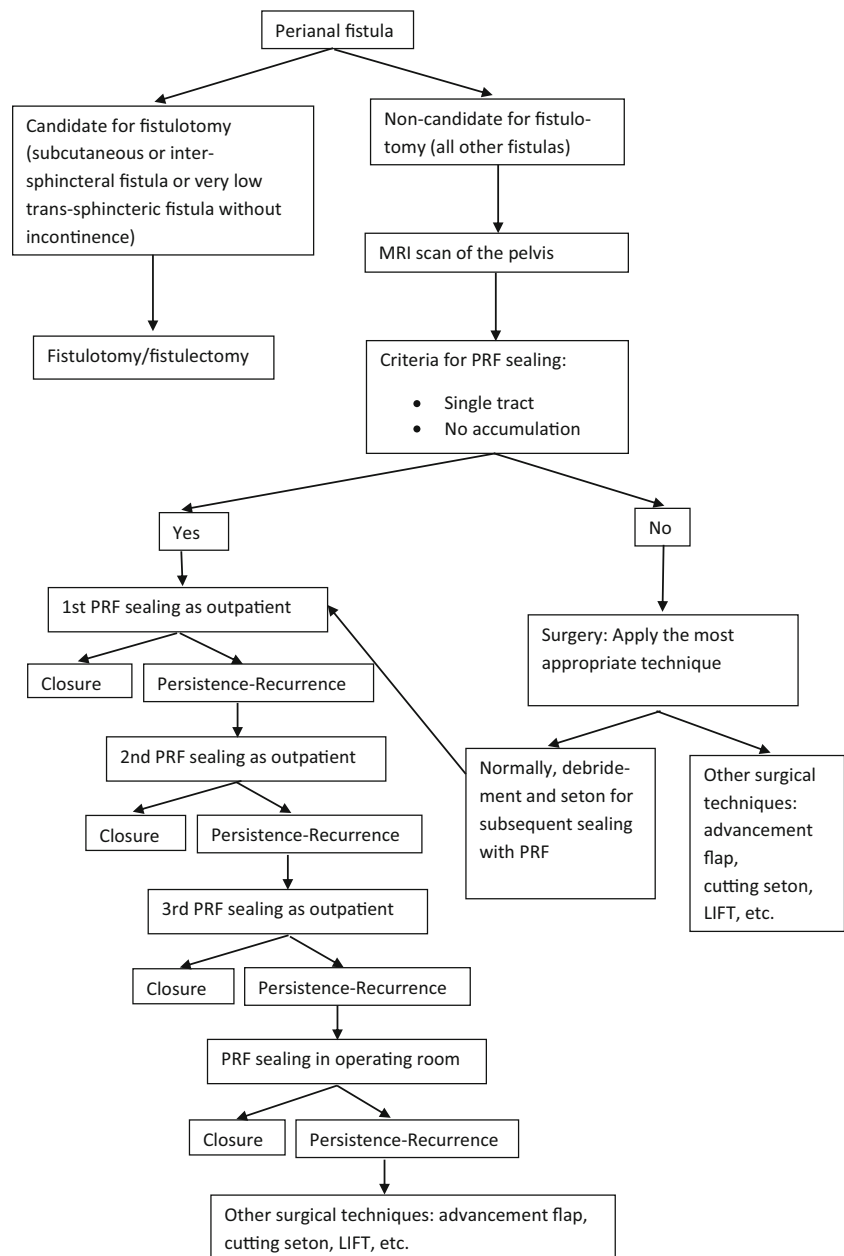
Table 3 Results obtained for the three groups

		Group A		Group B		Group C		Total		<i>p</i> value
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Morbidity	Infection	1	0.0	1	3.2	1	2.7	3	1.9	0.99 (a)
	No mobility	33	100.0	30	96.8	36	97.3	99	98.1	
	All	34	100.0	31	100.0	37	100.0	102	100.0	
Fistula healing	No	16	47.1	6	19.4	17	46.0	39	38.2	0.03 (a)
	Yes	18	52.9	25	80.7	20	54.0	63	61.8	
	All	34	100.0	31	100.0	37	100.0	102	100.0	
Difference Wexner pre postoperative	0 point	34	100.0	29	93.5	37	100.0	100	98.0	0.09 (b)
	1 point	0	0.0	1	3.2	0	0.0	1	1.0	
	3 points	0	0.0	1	3.2	0	0.0	1	1.0	
	All	34	100.0	31	100.0	37	100.0	102	100.0	

(a) Chi-square test

(b) Fisher test

Fig. 4 Action protocol based on the approach currently taken in our hospital



three being frozen for possible future use. Thus, if follow-up showed that closure of the fistulous orifice had not been obtained, successive applications could be performed in outpatient consultation without the need for anaesthesia or surgery.

Analysis of the results obtained with this protocol revealed a surprisingly high rate of successful healing. Therefore, we decided to reverse the process; i.e. of the four parts of PRF obtained, the first sealing was performed in the outpatient consultation (and if necessary a second and even a third attempt was made), reserving the fourth batch for treatment by the corresponding surgical procedure only for patients in whom this initial outpatient consultation had failed. The patients for whom this approach was adopted composed group C in our study.

From experimental models in pigs, it has been suggested that curettage prior to the application of fibrin glue can improve the results obtained.²³ Methods that have been used to debride the fistula tract include the injection of hydrogen peroxide, the application of saline solution, and curettage with a brush or curette. However, none were found to remove all of the granulation tissue from the tract.

In view of these considerations, and with the experience obtained from our multicentre study, we concluded that outcomes might be improved if a complete curettage of the fistula tract could be achieved. Therefore, we examined 50 pelvic MRI scans of patients with perianal fistula and measured the diameter of fibrous tissue surrounding the tract. In 95% of cases, this was less than 5 mm, and so we created sets of

curettes of increasing thickness, up to 5 mm. We calculated that the successive passage of these curettes, from smallest to greatest thickness, through the tract would resect all the fibrous tissue in at least 95% of the cases.^{24, 25} The patients who received this surgical technique composed group B of the present study.

We emphasise that the procedure used for the patients in group C provides up to three opportunities to achieve closure of the fistula without having to resort to surgical techniques, thus reducing financial costs for the hospital and avoiding physical discomfort for the patient. In view of the surprisingly good results obtained with these patients, we believe that referral to the waiting list for surgery can be avoided for 54% of patients with perianal fistula.

In financial terms, the following implications can be deduced. If we ignore the cost of the platelets (which is the same for the outpatient procedure and for use in the operating room), the cost per patient treated surgically for perianal fistula is €1212 versus €20 for outpatient treatment. Therefore, taking into account the rates of treatment success obtained by each procedure, we estimate that each outpatient session (a total of eight patients) produced a saving of €6329 with respect to group B and €9899 with respect to group A.

Furthermore, patients who are treated in outpatient consultation have no need of anaesthesia (whether general or spinal), with its corresponding risks, or of a surgical intervention (which can provoke sphincter injuries and future anal incontinence). Accordingly, patient safety may be significantly improved.

Another important finding of the present study is that it confirms the indications of prior experimental models regarding the curettage of the tract.²⁵ The use of our purpose-designed curettes in conjunction with the standard technique raised the success rate of the surgical procedure from 52.9 to 80.7% ($p = 0.03$).

Following the experience acquired over the last 7 years in the treatment of perianal fistula with PRF, and with the results obtained in the present study, we propose an action protocol based on the approach currently taken in our hospital (Fig. 4). According to this protocol, the initial sealing of the perianal fistula is performed in outpatient consultation; if this is ineffective, we proceed to a second and even a third attempt. Finally, if the fistula nevertheless persists, the surgical curettage procedure is employed, using the set of cylindrical curettes plus sealing (which has proven to be more effective than traditional curettage). By this means, with four possibilities of achieving closure, very satisfactory healing rates can be obtained.

In conclusion, the data we present highlight the efficacy of curettage using our set of cylindrical curettes (the possibility of fistula closure is increased by 27.8%; $p = 0.03$). Moreover, sealing the fistula with PRF in outpatient consultation (without surgery) is an innocuous method, avoiding the risks of

anaesthesia and sphincter manipulation. In addition, it has no side effects, is less intrusive for the patient and produces very acceptable results. In short, the method described may constitute the best approach in the initial treatment of perianal fistula.

Authors Contributions FJ Pérez Lara made a substantial contribution to the concept and design, drafted the article or revised it critically for important intellectual content, and approved the version to be published. JM Hernández Gonzalez approved the version to be published. A Ferrer Berges approved the version to be published. I. Navarro Gallego approved the version to be published. H Oehling de los Reyes approved the version to be published. H Oliva Muñoz approved the version to be published.

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