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Efficacy of Platelet-Rich Plasma on Perianal Wound Healing after Anal Fistula Operations: A Randomized Controlled Clinical Trial

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ABSTRACT

Background: Boosting of healing for anal wounds following operations for anal fistulae may contribute to a more rapid recovery and resumption of work activities.

Objectives: To evaluate the impact of platelet-rich plasma (PRP) injection on the postoperative outcome of perianal wound after anal fistula surgeries in terms of healing time, reduction in wound size, pain score, and therefore quality of patients' life.

Patients and Methods: This was a prospective study conducted on subjects who were randomly assigned to either PRP injections in addition to standard surgical procedures (group A), or the standard surgery only (group B). The primary outcome measured the number of weeks required for complete healing of the anal wound in both groups, whereas, secondary outcomes included the incidence of complications, pain levels, and quality of life (QoL) assessments.

Results: Group A demonstrated complete healing in a notably shorter time frame compared to group B (P=0.003). The average postoperative pain (POP) scores were consistently lower in group A at all measured intervals compared to group B. Group A was associated with a significant improvement in QoL compared to group B (34.75 versus 21.8) (P<0.001). Both groups exhibited identical rates of complications.

Conclusion: Platelet-rich plasma is considered a safe treatment option that is associated with reduced healing time and diminished POP. While it does not enhance the overall healing rate, it is linked to a notable improvement in short-term quality of life.

Keywords: Anal fistula; PRP injection; Healing time; Pain score.

INTRODUCTION

Fistula-in-ano is an inflammatory tract lined with epithelial tissue that connects anal canal with perianal skin [(1)].

The proper management of anal fistulae is primarily to drain any infection, eliminate the fistulous tract, and prevent ongoing or recurring disease, all while maintaining the integrity of anal sphincter function[(2)].

Essentially, POP and delayed wound healing are the primary adverse events following anal surgery accompanied by poor QoL [(3)]. The treatment of anal fistula through surgical intervention is generally adequate in the majority of instances. However, postoperative healing typically requires duration of eight to twelve weeks**,** necessitating consistent dressing changes and care for the anal wound. This process may lead to some discomfort for the patient and could potentially postpone their ability to return to work and engage in daily activities. The literature has documented various efforts to enhance recovery following anal surgery [(4)].

Platelet-rich plasma (PRP) application has been observed in facilitating healing across various tissues, particularly in the field of plastic surgery, with some documented cases involving fistula-in-ano [(5)]. It serves as a significant reservoir of growth factors (GFs) that play an essential function in tissue repair process [(6)].

This study aimed to evaluate the impact of platelet-rich plasma (PRP) injection on the postoperative outcome of perianal wound after anal fistula surgeries in terms of healing time, reduction in wound size, pain score, and therefore quality of patients' life.

PATIENTS AND METHODS

Trial Design:

This trial was designed as a prospective, randomised, single-blind controlled study. Patients were recruited from General Surgery Department, Mansoura University Hospital between July 2023 to September 2024.

Inclusion criteria:

Patients of both genders between the ages of 18 and 65 who had a simple anal fistula (inter-sphincteric, or low trans-sphincteric affecting less than twenty five percent of external anal sphincter fibers). The included patients had no abscess cavities, no collection, no supralevator extension and with only one external opening (in order to achieve nearly the same depth of wound in all the patients).

Exclusion criteria:

Patients with accompanying anorectal pathologies which include anal fissure, hemorrhoids, rectal prolapse, tumours, solitary rectal ulcer, Crohn's disease and ulcerative colitis. Also, those on long-acting corticosteroids or immunosuppressive medications, or having connective tissue diseases were excluded.

Random sequence generation and blinding:

Patients were randomly divided into two equal groups; group A (treatment group) was injected with PRP in addition to the usual surgery, whereas, group B (control group) was treated with the usual surgery only

Randomization was undertaken by online randomization software (www.randomizer.at).

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Preoperative Assessment:

History Taking:

A comprehensive history was obtained from the patients concerning their current complaints, including the duration, nature of perianal discharge, presence of pruritus, rectal bleeding, and anal pain. Additionally, patients were inquired about any concurrent medical conditions.

A local anorectal examination was conducted with the patient positioned in the left lateral recumbent posture. Direct visualization of the anus and perineum was performed to recognize the location and number of external openings, as well as to rule out the existence of skin tags or prolapsed hemorrhoids. A digital rectal examination was also conducted to locate the internal opening, evaluate the status of the anal sphincter muscles, and exclude any concurrent anorectal pathologies.

Investigation:

Routine laboratory investigations including complete blood count, liver and kidney function tests, bleeding profile, and random blood glucose level was conducted. Fistulography was done to confirm the diagnosis of anal fistula and exclude anal sinus. Intracavitary rectal ultrasound (EAUS) or MRI was performed for patients suspected to have complex anal fistula (CAF).

Platelet-rich plasma (PRP) preparation:

Preparation of PRP was conducted by utilizing the approach formerly defined by **Sarvajnamurthy *et al.*** [(7)]. Under complete aseptic conditions, twenty mL of venous blood was withdrawn from the patient 24 hours before the approach and was added to a test tube comprising acid citrate dextrose (ACD) in a ratio of nine: one (blood: ACD), centrifuged at rpm > 3000 for ten min to separate the erythrocytes from the platelets and plasma using an advanced rapid point-of-care technology, centrifuge system. After that, the PRP tubes were put in the refrigerator.

Surgical procedure:

Patients underwent mechanical bowel preparation before the approach, which involved a single enema administered the evening before the operation and a restriction of oral intake to clear fluids for 12 hours leading up to the procedure. The anal operations for both groups were performed by the same surgical team, all of whom have equivalent levels of expertise in anal fistula surgery. All patients received spinal anaesthesia and then, positioned in the lithotomy position. Identification of internal opening of fistulous track was done by injection of povidone iodine from external opening. A metallic probe was subsequently inserted through the external orifice until it reached the internal one. Lay open of the track was undertaken followed by curettage of the granulation tissue inside the track, or coring-out fistulectomy of the track and cutting seton placement. Cauterization of internal opening and coring of external opening were done in all patients.

Proper hemostasis was asserted and wound measurements (length and width) were evaluated. Regarding the wounds, they were elliptical in shape, the surface area was measured using the linear equation [length x width x 0.7854] defined by **Thomas and Wysocki**[(8)]. After that, the platelet-rich plasma solution was drawn into an insulin syringe and subsequently injected into the edges of the external wound in group A patients (Figure 1). Finally, a pressure dressing was placed on the anal verge for 8 hours. All patients were instructed to follow a strict perineal hygiene and to have a warm sitz bath.

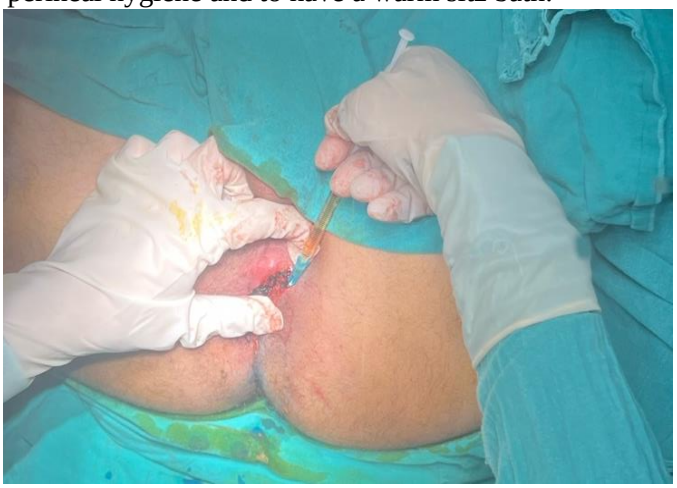

Figure (1): Intraoperative injection of PRP.

Follow-Up:

Patients were followed at one week, two weeks, and then every two weeks until three months postoperatively. Wound healing was assessed at every visit and recorded. Pain score was assessed at 6, 12, 24 hours, one week and up to one month, after the intervention using visual analogue score. Continence was evaluated using Wexner continence score at one and 3 months postoperatively. Quality of life was assessed in terms of time taken to return to work due difficult filling of the SF-12 form by the patients. As our included patients had neither preoperative perineal collections nor abscess, the observed discharge was serous either due to local reaction to seton or from the healing of wound. The cutting seton was either fallen spontaneously as stated by the patient, or following the granulation tissue growing adjacent to the seton area and the area becoming fibrosed, patients were admitted for seton removal under anesthesia.

Outcome measures:

Primary endpoint was the duration in weeks needed to achieve complete healing of the anal wound in both groups on postoperative follow-up. Secondary endpoints were pain score, complications and quality of life.

Sample size:

Sample size was calculated by the STATA software (Stata Corp, 2021, Version 17), and published study by **Boztug *et al.*** [(9)]. Considering moderate effect size (f) of 0.25, number of measurements were 3 among 2 groups, using repeated measures one way ANOVA test for measuring sample

size. The required minimal sample size was 28 patients, equally divided into two groups (14 per group), needed to achieve a study power of 80% with αset at 5%. For possible attrition, sample size was increased to 40 patients (20 per group).

Ethical approval:

This study has been approved by the Mansoura Faculty of Medicine's Ethics Committee. Patients provided informed consent to participate in the trial. Each patient was properly informed about the procedures, as well as the possible advantages and hazards associated. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

The collected data were reviewed, coded, and tabulated using SPSS Version 25.0. Mean±SD, median, and range were used for numerical data, whereas, frequency and percentage were used for non-numerical data. To evaluate the relationship between two qualitative variables, the X^2-test or Fisher exact test was employed. The significance of the difference between two groups in a non-parametric variable was assessed using the U test. To assess the significance of the parametric variable difference between the means of the two research groups, the Student-T Test was employed. A p value is considered significant if <0.05 at CI 95%.

RESULTS

The analysis shows that regarding sex and age, there was no significant difference between the two groups (Table 1).

Table (1): Comparison of treatment group and the control group regarding demographic data

	Treatment n = 20		Control n = 20		Test	p
	No.	%	No.	%		
Sex						
Male	13	65.0	14	70.0	χ^2= 0.114	0.736
Female	7	35.0	6	30.0		
Age (years)						
Mean ± SD.	40.25 ± 11.42		41.40 ± 8.36		U= 225.5	0.495
Median	37.50		41.50			
Min. – Max.	25.0 – 59.0		28.0 – 56.0			

U: Mann Whitney test. χ^2: Chi Square test.

Only 10.0% of the treatment group and 15.0% of the control group were smokers, indicating a relatively low prevalence of smoking in both groups, without significant difference between the 2 groups. The majority of individuals in both groups were free from comorbidities. Specifically, none of the individuals in the treatment group had DM or hypertension, while some participants in the control group had these conditions. The differences in comorbidities between the groups weren't statistically significant (Table 2).

Table (2): Comparison of treatment group and the control group regarding risk factors

	Treatment n = 20		Control n = 20		Test	p
	No.	%	No.	%		
Smoking						
No	18	90.0	17	85.0	χ^2= 0.229	FE 1.000
Yes	2	10.0	3	15.0		
Comorbidities						
Free	19	95.0	17	85.0	χ^2= 1.111	FE 0.605
Positive	1	5.0	3	15.0		
DM	0	0.0	2	10.0	2.105	FE 0.487
HTN	0	0.0	1	5.0	1.026	FE 1.000
Hyperthyroidism	1	5.0	0	0.0	1.026	FE 1.000

χ^2: Chi Square test, FE: Fisher Exact test

The type of intervention didn't significantly differ between the two groups (Table 3).

Table (3): Comparison of treatment group and the control group regarding type of intervention

	Treatment n = 20		Control n = 20		Test	p
	No.	%	No.	%		
Type of intervention						
Lay open fistulotomy	14	70.0	12	60.0	χ^2= 0.440	0.507
Fistulectomy and seton	6	30.0	8	40.0		

χ^2: Chi Square test.

The mean time of wound healing was significantly shorter in the treatment group compared to the control group. Additionally, the mean wound decrease in size was significantly greater in the treatment group compared to the control group (Table 4).

Table (4): Comparison of treatment group and the control group regarding time of wound healing and wound decrease in size.

	Treatment n = 20	Control n = 20	Test	p
Time of wound healing (weeks)				
Mean ± SD.	4.30 ± 1.03	5.50 ± 1.15	U= 307.5*	0.003*
Median	4.0	5.50		
Min. – Max.	3.0 – 6.0	4.0 – 7.0		
Wound decrease in size (cm)				
Mean ± SD.	1.72 ± 0.35	1.33 ± 0.17	t= 4.516*	<0.001*
Median	1.70	1.30		
Min. – Max.	1.30 – 2.50	1.0 – 1.70		

*: Significant, t: Student t test, U: Mann Whitney test.

The mean pain scores in the treatment group were consistently but insignificantly lower than those in the control group across all time points. This trend continues across 6 hours, 12 hours, 24 hours, 1 week, and 1 month, with decreasing mean pain scores in the treatment group compared to the control group, indicating a potential benefit of the treatment in managing pain levels over time (Table 5).

Table (5): Comparison of treatment group and the control group regarding pain score

Pain score	Treatment n = 20	Control n = 20	Test	p
After 6 hours				
Mean ± SD.	7.0 ± 2.20	8.0 ± 0.86	U= 262.0	0.096
Median	8.0	8.0		
Min. – Max.	0.0 – 10.0	6.0 – 9.0		
After 12 hours				
Mean ± SD.	6.15 ± 1.23	7.05 ± 1.70	U= 264.5	0.081
Median	6.0	7.0		
Min. – Max.	3.0 – 8.0	3.0 – 10.0		
After 24 hours				
Mean ± SD.	4.65 ± 1.23	5.10 ± 2.59	U= 255.0	0.142
Median	5.0	5.50		
Min. – Max.	2.0 – 7.0	0.0 – 8.0		
After 1 week				
Mean ± SD.	3.65 ± 0.93	4.10 ± 2.27	U= 246.0	0.221
Median	4.0	4.50		
Min. – Max.	2.0 – 5.0	0.0 – 7.0		
After 1 month				
Mean ± SD.	2.85 ± 0.81	3.0 ± 1.08	U= 214.5	0.698
Median	3.0	3.0		
Min. – Max.	2.0 – 4.0	1.0 – 5.0		

U: Mann Whitney test.

The mean QOL was significantly higher in the treatment group compared to the control group (Table 6 and figure 2). This indicates that individuals in the treatment group had better QOL, suggesting potential differences in postoperative outcomes impacting their ability to resume work duties compared to the control group.

Table (6): Comparison of treatment group and the control group regarding QOL

	Treatment n = 20	Control n = 20	Test	p
QOL				
Mean ± SD.	34.75 ± 4.72	21.80 ± 6.87	U= 22.50*	<0.001*
Median	35.0	22.50		
Min. – Max.	30.0 – 40.0	7.0 – 30.0		

*: Significant, U: Mann Whitney test

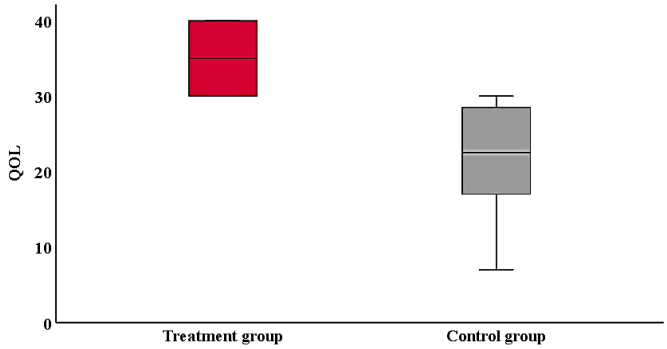

Figure (2): Boxplot chart for comparison of treatment group and the control group regarding QOL: return to work.

In terms of recurrence, no patients in either group reported a recurrence of anal fistula throughout the follow-up period.

In addition, both groups had equal percentages of patients who were incontinent to flatus, with 25% in each group experiencing incontinence, indicating that this aspect may not have been influenced by the PRP treatment, with incontinence rates remaining consistent across both groups (Table 7). There was no other form of incontinence observed in both groups and no other form of postoperative complications occurred as infection and bleeding.

Table (7): Comparison of treatment group and the control group regarding incontinent to flatus.

	Treatment n = 20		Control n = 20		Test	p
	No.	%	No.	%		
Incontinent to flatus						
No	15	75.0	15	75.0	χ^2= 0.0	1.000
Yes	5	25.0	5	25.0		

χ^2: Chi Square test.

DISCUSSION

The treatment of anal fistula through surgical intervention is generally adequate in the majority of instances. However, due to prolonged postoperative healing, which might have deleterious effects on quality of patients' life, the literature has documented various efforts to enhance recovery following anal surgery [3]. For instance, in 2019, **Omar *et al.*** [10] examined the impact of use of an external anal sphincter–sparing seton on the duration of wound healing in the management of CAF. Whereas, **El-Said *et al.*** [11] assess the effect of modified Park's technique on QoL in cases with CAF.

One of the agents utilized to enhance the process of wound healing is PRP. Given its physiological function in the process of wound healing, PRP is increasingly utilized across various clinical applications, and it has gained popularity as a

standard component of routine wound management [12].

In this prospective randomized trial we included 40 patients presented with anal fistula. Approximately 70% of the participants were males, in an agreement with the male predominance observed by **Elfeki *et al.*** [13], **Giarratano *et al.*** [14] and **Emile *et al.*** [15].

The mean age of the randomly selected patients in the current study was 41 years, which aligns closely with the average age documented in existing literature. This finding is consistent with the results recorded by **Emile *et al.*** [16], in which the average age of patients presenting with anal fistula was found to be 41.7 years.

Patients were randomly assigned to either PRP injections in addition to standard surgical procedures (group A), or the standard surgery only (group B).

In terms of wound healing, our results suggest that the average duration for wound healing was shorter in the treatment group (4.30 ± 1.03 weeks) compared to the control group (5.50 ± 1.15 weeks). These findings also match with **Madbouly *et al.*** [17], who found that in the PRP group, the mean postsurgical recovery time was significantly reduced (15.7±4 days) compared with the group without PRP (21.6±5.4 days). The observed results are attributable to the production of GFs by the platelets, which have an essential role in initiating the wound healing process.

Also, **Boztug *et al.*** [9] have investigated the role of PRP application on wound healing after pilonidal sinus disease. They found that the time taken for complete wound healing was shorter after PRP application (37.1 ± 16.6 vs 54.4 ± 24.3).

Additionally, the mean wound decrease in size was greater in the treatment group (1.72 ± 0.35 cm) compared to the control group (1.33 ± 0.17 cm). Comparable results were noticed by **Shehab *et al.*** [18] as they found that PRP application as adjunct to compression for venous ulcer wounds caused significant reduction in ulcer area compared with conventional compression alone. The area of ulcer decreased by 74% in PRP group compared to 40% in compression therapy group.

Regarding pain score after one day, our results show that the mean pain score in group A was 4.65±1.23, whereas that of group B was 5.10±2.59. These results were likewise in agreement with those of **Madbouly *et al.*** [17] who investigated the role of PRP on the treatment of trans-sphincteric fistula. Patients were divided into two groups; LIFT plus PRP injection group and LIFT group. They found that LIFT-PRP group had significantly ($p<0.05$) lower pain scores on day one than the other group.

In relation to pain experienced after the first week, our findings indicate that the treatment group reported a pain score of 3.65±0.93, while the control group had a score of 4.10±2.27. This suggests a tendency towards reduced pain levels in the treatment group. These results are in accordance with the study conducted by **De la Portilla *et al.*** [19] who compared the efficiency of autologous PRP (APRP) and fibrin glue in anal fistula treated. Their research revealed a reduction in median pain scores among cases managed with PRP compared to those treated with fibrin glue during the initial follow-up visit, which was one-week postoperatively (zero, range zero–4 vs. 3, range 1.75–5.25).

In the current study, the PRP-treated group displayed a significant reduction in mean pain scores over time, from 7.0 ± 2.20 after 6 hours to 2.85 ± 0.81 after 1 month ($p<0.001$). In the same line, in the control group, there was a substantial reduction in mean pain scores from 8.0 ± 0.86 after 6 hours to 3.0 ± 1.08 after 1 month ($p < 0.001$). This was compatible with the study done by **De la Portilla *et al.*** [19], which showed that the remainder of the visits displayed a significant reduction in pain scores for PRP treated patients over fibrin glue -treated group.

Another important element is quality of life (QOL). It was markedly greater in the treatment group (34.75 ± 4.72) than in the control group (21.80 ± 6.87), ($P< 0.001$). This finding suggests that participants in the treatment group experienced an improved QOL, which may reflect variations in postoperative results that influence their capacity to return to work responsibilities in contrast to the control group. This was compatible with the findings observed in **Madbouly *et al.*** [17], in which the QOL and level of happiness were significantly higher in the group injected with PRP compared with non-injected group (9.0±0.6, 9.2±0.4 vs 8.1±0.4,8.2±0.3). Our results, also, match with **Moreno-Serrano *et al.*** [20] who used APRP for the treatment of CAF in 23 patients. They found that concerning QoL, 19 patients (80%) recorded improvements following operation.

Regarding the postoperative complications, our study shows that both groups exhibited identical percentages of patients experiencing incontinence to flatus, with 25% in each group affected and no other form of incontinence were observed. Statistically, there was no significant difference between the groups ($p = 1.000$) concerning flatus incontinence, suggesting that this factor was likely unaffected by the PRP treatment. **Sheikh *et al.*** [21] concluded that the total incidence of incontinence after surgical intervention for anal fistula can reach up to 73.7%, whereas, after the fistulectomy procedure, the rates of incontinence may vary between 11.5% and 20%.

These findings suggest that the PRP treatment could have a positive effect on pain score, wound healing time and wound size reduction, potentially indicating better postoperative outcomes in terms of wound recovery. Similar outcomes were recorded in other studies as mentioned before.

Limitations of the present trial include being a single-center trial with a small sample size. The short

follow-up period of patients is another limitation; as a result, longer follow-up is required to prove or disprove the positive preliminary results of the trial.

CONCLUSIONS

The current study comes to conclude that PRP promotes wound healing, relieves postoperative pain, and accelerates patients' recovery after surgical procedures for anal fistula.

RECOMMENDATION

Further larger trials evaluating topical application of PRP versus PRP injection versus both are recommended to ascertain the results of the present trial.

Fund: Nil.
Conflict of Interest: Nil.

REFERENCES

1. **Gafar A (2013):** Fistulotomy versus fistulectomy as a treatment for low anal fistula in infants: a comparative study. Ann Pediatr Surg., 9(3):103–107.
2. **Alabiso M, Iasiello F, Pellino G *et al.* (2016):** 3D-EAUS and MRI in the activity of anal fistulas in Crohn's disease. Gastroenterol Res Pract., 16: 1895694. doi: 10.1155/2016/1895694
3. **Alvandipour M, Ala S, Tavakoli H *et al.* (2016):** Efficacy of 10% sucralfate ointment after anal fistulotomy: A prospective, double-blind, randomized, placebo-controlled trial. Int J Surg., 36(Pt A): 13-17.
4. **Xu Y, Liang S, Tang W (2016):** Meta-analysis of randomized clinical trials comparing fistulectomy versus fistulotomy for low anal fistula. Springerplus, 5(1):1722. doi: 10.1186/s40064-016-3406-8
5. **Zhang W, Guo Y, Kuss M *et al.* (2019):** Platelet-rich plasma for the treatment of tissue infection: preparation and clinical evaluation. Tissue Eng Part B Rev., 25(3): 225–236.
6. **Chandanwale K, Mahakalkar C, Kothule A *et al.* (2020):** Management of wounds of peripheral arterial disease using platelet rich plasma. J Evol Med Dent Sci., 9: 2239–2245.
7. **Sarvajnamurthy S, Suryanarayan S, Hurkudli D (2013):** Autologous platelet rich plasma in chronic venous ulcers: study of 17 cases. J Cutan Aesthet Surg., 6:97–99.
8. **Thomas A, Wysocki A (1990):** The healing wound: a comparison of three clinically useful methods of measurement. Decubitus, 3(1): 18–25.
9. **Boztug C, Karaagac Akyol T, Benlice C *et al.* (2021):** Platelet-rich plasma treatment improves postoperative recovery in patients with pilonidal sinus disease: a randomized controlled clinical trial. BMC Surg., 21(1): 373. doi: 10.1186/s12893-021-01370-5.
10. **Omar W, Alqasaby A, Abdelnaby M *et al.* (2019):** Drainage seton versus external anal sphincter– sparing seton after rerouting of the fistula tract in the treatment of complex anal fistula: A randomized controlled trial. Dis Colon Rectum, 62: 980–987.
11. **El-Said M, Emile S, Shalaby M *et al.* (2019):** Outcome of modified Park's technique for treatment of complex anal fistula. Journal of Surgical Research, 235: 536-542.
12. **Chicharro-Alcantara D, Rubio-Zaragoza M, Damiá-Giménez E *et al.* (2018):** Platelet rich plasma: new insights for cutaneous wound healing management. J Funct Biomater., 9(1): 10. doi: 10.3390/jfb9010010.
13. **Elfeki H, Shalaby M, Emile S *et al.* (2020):** A systematic review and meta-analysis of the safety and efficacy of fistula laser closure. Techniques in Coloproctology, 24:265–274.
14. **Giarratano G, Shalaby M, Toscana C *et al.* (2020):** Video-assisted anal fistula treatment for complex anal fistula: a long-term follow-up study. Colorectal Dis., 8:939-944.
15. **Emile S, Khafagy W, Elbaz S (2022):** Impact of number of previous surgeries on the continence state and healing after repeat surgery for recurrent anal fistula. Journal of Visceral Surgery, 159: 206-211.
16. **Emile S, Elgendy H, Sakr A *et al.* (2018):** Gender-based analysis of the characteristics and outcomes of surgery for anal fistula: analysis of more than 560 cases. Journal of Coloproctology, 38(3):199–206.
17. **Madbouly K, Emile S, Issa Y *et al.* (2021).** Ligation of intersphincteric fistula tract (LIFT) with or without injection of platelet-rich plasma (PRP) in management of high trans-sphincteric fistula-in-ano: Short-term outcomes of a prospective, randomized trial. Surgery, 170(1): 61-66.
18. **Shehab A, Eleshra A, Fouda E *et al.* (2023):** Randomized prospective comparative study of platelet-rich plasma versus conventional compression in treatment of post-phlebitic venous ulcer. Vascular, 31(6): 1222-1229.
19. **De la Portilla F, Muñoz-Cruzado M, Maestre M *et al.* (2019):** Platelet-rich plasma (PRP) versus fibrin glue in cryptogenic fistula-in-ano: a phase III single-center, randomized, double-blind trial. International Journal of Colorectal Disease, 34: 1113–1119.
20. **Moreno-Serrano A, Garcia-Diaz J, Ferrer-Marquez M *et al.* (2016):** Using autologous platelet-rich plasma for the treatment of complex fistulas. Rev Esp Enferm Dig., 108:123-128.
21. **Sheikh P, Baakza A (2014):** Management of fistula-in-ano-The current evidence. Indian J Surg., 76: 482–486.