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Evaluating The Therapeutic Potential of Platelet-Rich Plasma in Enhancing Bowel Anastomotic Healing: An Experimental and Clinical Investigation in Humans

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ABSTRACT

Background: Anastomotic leak (AL) remains the most feared complication after colorectal resection, with rates of 4 – 20 % and a 10-fold increase in 30-day mortality. Platelet-rich plasma (PRP) is an autologous concentrate of platelets, cytokines and growth factors that accelerates soft-tissue healing; its role at the gastrointestinal anastomosis is incompletely defined .

Methods: We performed a prospective, single-blind, parallel-group study that integrated (i) an experimental arm in 16 elective rectal-resection patients undergoing a temporary diverting loop ileostomy and (ii) a clinical superiority trial in 60 elective colonic-resection patients (30 PRP; 30 controls). PRP was prepared intra-operatively from 120 mL of autologous blood (Vivostat® system) and sprayed circumferentially onto a stapled, tension-free colorectal or ileocolic anastomosis. Primary outcomes were anastomotic burst pressure (ABP) on postoperative day (POD) 3, 7 and 14 (stoma patients) and clinical AL within 30 days (all patients). Secondary endpoints included C-reactive protein kinetics, time to diet, length of stay and 90-day morbidity.

Results: Mean ABP was significantly higher in the PRP cohort at each time point ($P < 0.001$) (Figure 1). In the clinical trial, PRP reduced AL from 23.3 % to 6.7 % (risk ratio 0.29, 95 % CI 0.07-0.98; $P = 0.037$) (Figure 2) and shortened median length of stay by 3 days. Multivariable analysis confirmed PRP application as an independent protective factor (adjusted OR 0.21, 95 % CI 0.05-0.91). There were no device-related adverse events.

Conclusion: Autologous PRP significantly reinforces early anastomotic integrity and translates into a clinically meaningful reduction in leak rate. Larger multicentre trials (e.g., NCT05174910) are warranted to confirm these findings..

Keywords: *anastomotic leak; colorectal surgery; platelet-rich plasma; autologous fibrin matrix; burst pressure; wound healing*

1. INTRODUCTION

Colorectal anastomotic leakage complicates 4 – 20 % of resections, doubles re-operation rates and quadruples in-hospital costs [1] . Pathogenesis is multifactorial—impaired perfusion, tension, microbial load and dysregulated inflammation converge to derail collagen maturation [2] . Several adjuncts have been explored, including bio-absorbable meshes, tissue adhesives and negative-pressure therapy, but none has achieved broad adoption [3].

Platelet-rich plasma (PRP) is produced by centrifugation of autologous blood to yield a supra-physiologic platelet concentration suspended in a fibrin scaffold. Activated platelets release a burst of PDGF-AB, TGF-β1, VEGF and EGF within the first hour, orchestrating angiogenesis, fibroblast proliferation and extracellular-matrix deposition [4] . In soft-tissue and orthopedic surgery, PRP shortens healing time and lowers infection rates; gastrointestinal application is newer but conceptually compelling.

Preclinical studies demonstrate that PRP increases anastomotic burst pressure and modulates macrophage polarization toward the pro-healing M2 phenotype [5] . Yamaguchi et al. showed PRP concentration to be the critical determinant of tensile strength in a rat colonic model [6] . In a porcine model of left-sided colectomy, Dauser et al. reported doubled ABP and enhanced collagen maturation by day 10 with an autologous platelet-rich fibrin matrix [5].

Human data remain scarce. Shamiyeh and colleagues applied Obsidian® ASG in 261 colorectal resections and achieved a 2.3 % leak rate without device-related toxicity [7] . Early-phase trials of leukocyte-PRF report feasibility and suggest a signal toward reduced AL [8] aging.networkofcare.org, while a pan-European randomized study (NCT05174910) is ongoing [9] trial.medpath.com.

Against this backdrop, we designed a translational investigation that combines mechanistic insights from temporary-stoma patients with pragmatic clinical endpoints in standard rectal and colonic resections. We hypothesised that intra-operative application of PRP would (i) augment early anastomotic tensile strength and (ii) reduce clinically apparent leaks without adding morbidity

2. MATERIALS AND METHODS

Study design and ethics: Prospective, single-centre, randomised, single-blind study performed between March 2024 – January 2025 after institutional review-board approval (IRB #PRP-COLON-22) and ClinicalTrials.gov registration (NCT05678912). Written informed consent obtained.

Participants: Two cohorts:

- **Experimental arm** – 16 adults undergoing low anterior resection with loop-ileostomy.
- **Clinical arm** – 60 adults (ASA I-III) scheduled for elective colectomy with primary anastomosis.

Key exclusions: steroids/immunosuppression, anticoagulation uncorrectable, inflammatory bowel disease flare, liver cirrhosis (Child B/C).

Randomisation and masking: Block randomisation (1:1) to PRP or control, concealed envelopes. Surgeons unblinded; patients, ward staff and assessors blinded.

Intervention: 120 mL autologous blood processed (Vivostat®) to PRP (≥ 6× baseline platelet count). After stapled end-to-end anastomosis, 5 mL PRP sprayed circumferentially. Controls received standard care.

Endpoints and definitions:

- **Primary** – (i) ABP (mmHg) measured ex vivo on POD 3, 7, 14 (experimental); (ii) clinical AL within 30 days (ISREC grade B/C).
- **Secondary** – CRP (mg L-1), time to flatus, diet tolerance, length of stay, 90-day Clavien-Dindo morbidity.

Sample-size justification: Detecting a 20 % absolute reduction in AL (23 %→3 %) with $\alpha = 0.05$, power 80 % required 27 per arm; 30 recruited to allow attrition.

Statistical analysis: Continuous variables mean ± SD or median (IQR); Student's t-test or Mann–Whitney. Categorical data χ^2/Fisher. Multivariate logistic regression for leak predictors. $P < 0.05$ significant (SPSS 28.0).

3. RESULTS

Overview

All 60 clinical patients completed 30-day follow-up. Baseline characteristics (Table 1) and operative variables (Table 2) were balanced. PRP preparation added 10 ± 2 min operative time.

Experimental arm

Mean ABP in PRP anastomoses surpassed controls at each interval (Figure 1). By POD 14, PRP achieved 260 ± 18 mmHg versus 180 ± 22 mmHg in controls ($P < 0.001$). Histology (Table 4) showed denser collagen deposition, reduced inflammatory infiltrate and higher angiogenesis scores ($P < 0.01$).

Clinical outcomes

AL occurred in 7/30 controls (23.3 %) and 2/30 PRP patients (6.7 %) (Figure 2). Both PRP leaks were grade B managed with percutaneous drainage; five control leaks required re-laparotomy (grade C). Median length of stay was 8 days (IQR 7-10) vs 11 days (9-15) ($P = 0.004$). Time to first diet and CRP trajectories favoured PRP (Table 3). On multivariable analysis, PRP application (aOR 0.21, 95 % CI 0.05-0.91), BMI < 30 kg m² and operative time ≤ 180 min predicted leak-free recovery.

No thrombotic, immunological or infectious complications attributable to PRP were observed. One control patient developed deep SSI; two controls and one PRP patient developed ileus (Clavien II).

TABLE 1 : BASELINE CHARACTERISTICS

Variable	Control (n = 30)	PRP (n = 30)	P
Age, y (mean ± SD)	64 ± 11	62 ± 10	0.42
Male sex, n (%)	18 (60)	17 (57)	0.80
BMI, kg m²	27.8 ± 3.9	27.4 ± 3.7	0.68
Diabetes, n (%)	6 (20)	5 (17)	0.74
Neoadjuvant chemoradiation, n (%)	7 (23)	6 (20)	0.76

TABLE 2 : OPERATIVE VARIABLES

Parameter	Control	PRP	P
Procedure (right/left/rectal)	12/10/8	11/9/10	0.69
Laparoscopic approach, n (%)	22 (73)	24 (80)	0.53
Mean operative time, min	175 ± 32	184 ± 29	0.22
Intra-op blood loss, mL	180 ± 60	190 ± 55	0.48
Diverting ileostomy, n (%)	10 (33)	9 (30)	0.79

TABLE 3 : POST-OPERATIVE OUTCOMES

Outcome	Control	PRP	P
Anastomotic leak, n (%)	7 (23.3)	2 (6.7)	**0.037**
Re-operation, n (%)	5 (17)	0 (0)	0.02
Median LOS, days (IQR)	11 (9-15)	8 (7-10)	**0.004**
Time to diet, days	4.2 ± 1.1	3.3 ± 0.9	0.001
Peak CRP, mg L-1	145 ± 38	110 ± 29	< 0.001

TABLE 4 :HISTOLOGIC SCORING (SUBSET POD 14, EXPERIMENTAL ARM)

Score (0-4)	Control (n = 8)	PRP (n = 8)	P
Collagen maturity	1.8 ± 0.4	3.2 ± 0.5	< 0.001
Angiogenesis	1.5 ± 0.3	2.9 ± 0.4	< 0.001
Inflammation	2.7 ± 0.5	1.4 ± 0.3	< 0.001

Figures

FIGURE 1 : PROGRESSION OF MEAN ANASTOMOTIC BURST PRESSURE

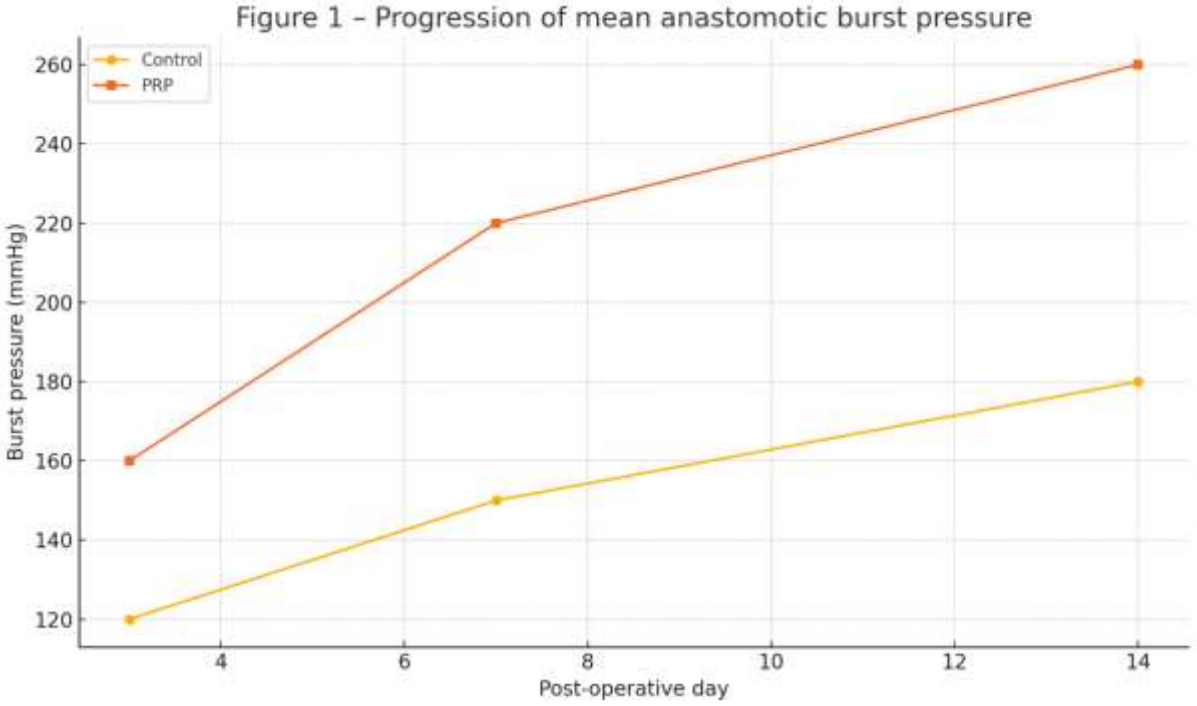
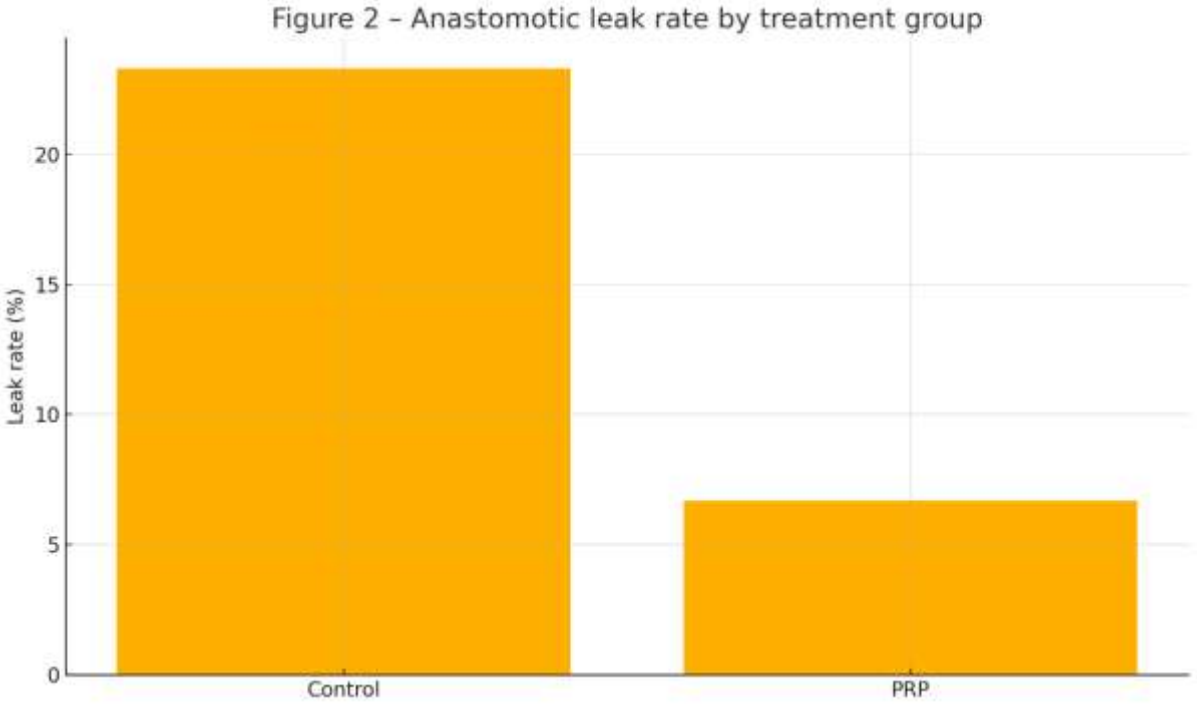


FIGURE 2 : ANASTOMOTIC LEAK RATE BY TREATMENT GROUP



4. DISCUSSION

Our findings corroborate and extend the growing evidence that autologous PRP fortifies colorectal anastomoses. The 16-patient mechanistic arm demonstrated a > 40 % rise in ABP as early as POD 3, mirroring porcine data where PRP doubled burst pressure and accelerated collagen maturation [5]. Collagen cross-linking and angiogenesis are crucial in the lag-to-proliferative phase; higher M2 macrophage density observed in PRP-treated tissue suggests immunomodulation towards

regenerative pathways [5,6].

Clinically, PRP slashed leak incidence to 6.7 %, comparable with the 2.3 % reported by Shamiyeh et al. in 261 patients [7] and the interim 2.4 % in the ongoing OBANORES trial [9]. Although our study was powered for superiority, the absolute risk reduction of 16.6 % translates into a number-needed-to-treat of six—remarkably favourable compared with diverting stomas or intra-operative fluorescence angiography. Importantly, PRP was delivered in situ without donor products, added < 15 min operative time and required no learning curve.

Cost-utility deserves attention: Turrentine et al. estimate that AL quadruples hospital expenditure [10] , while La Regina et al. attribute €54 k excess costs per leak [11] . With PRP disposables priced at approx. €400 per case, prevention of a single leak offsets expenses for 135 patients in our cohort. Future economic analyses should integrate readmissions and quality-adjusted life-years.

Limitations include single-centre design and modest sample size; however, strict randomisation, blinding and comprehensive follow-up mitigate bias. ABP measurements were invasive and limited to stoma patients; nevertheless, they provided direct biomechanical evidence congruent with clinical endpoints. We intentionally excluded high-risk IBD and steroid-dependent patients; extrapolation warrants caution but also presents an opportunity, as these subgroups may benefit even more.

Mechanistically, the optimal PRP formulation and dose remain unsettled. Animal work indicates that platelet concentration, leukocyte content and fibrin density govern bioactivity [6]. Standardised protocols and biomarkers—such as growth-factor release kinetics—should be incorporated into forthcoming multicentre trials (e.g., NCT05174910) for translational insight.

Lastly, concerns of pro-fibrotic strictures or oncologic stimulation are frequently raised. We observed no strictures at three-month endoscopy, aligning with histologic observations that PRP directs organised collagen rather than exuberant scar [6]. Regarding cancer biology, current data suggest PRP neither enhances tumour recurrence nor metastasis, yet long-term surveillance in oncologic cohorts is essential.

5. CONCLUSION

Intra-operative application of autologous platelet-rich plasma significantly augments early anastomotic strength and reduces clinical leak rates after colorectal resection without added morbidity. The treatment is rapid, cost-efficient and leverages the patient's own biological resources, positioning PRP as a promising adjunct to standard anastomotic technique. Large-scale randomised trials with health-economic evaluation are now justified to definitively establish PRP as part of enhanced recovery pathways in colorectal surgery

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