

Fibrin sealant versus autologous Platelet-Rich Plasma for prevention of seroma after breast cancer surgery: An exploratory randomized controlled trial

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ABSTRACT

Background: Seroma remains a frequent postoperative complication after breast cancer surgery, particularly following mastectomy and axillary lymph node dissection. Fibrin sealants may limit lymphatic leakage and dead space, whereas autologous platelet-rich plasma (PRP) may promote tissue repair. Direct randomized comparisons of these approaches are limited. **Patients and Methods:** This single-center, two-arm exploratory randomized controlled trial enrolled 50 women undergoing breast cancer surgery between December 2024 and December 2025. Participants were allocated 1:1 to topical fibrin sealant (n=25) or autologous PRP (n=25) applied to the operative bed before closure. The primary outcomes were clinically significant seroma incidence and postoperative fluid volume. Secondary outcomes included postoperative discomfort, therapeutic aspiration, time to functional recovery, and intervention-related adverse events. Analyses followed the intention-to-treat principle. **Results:** Clinically significant seroma occurred in 4/25 participants (16.0%) in the fibrin-sealant group and 5/25 (20.0%) in the PRP group (RR 0.80, 95% CI 0.24-2.64; Fisher exact P=1.000). Median postoperative fluid volume was lower with fibrin sealant (15.3 mL [IQR 13.8-16.8]) than with PRP (18.7 mL [IQR 16.7-20.7]; P<0.001).

Median discomfort scores were 2.1 versus 2.4 ($P < 0.001$), and median time to return to normal activities was 15 versus 16 days ($P < 0.001$), respectively; both differences were small in magnitude. Therapeutic aspiration was required in 4 versus 5 participants. No intervention-related adverse events were documented during the 2-month follow-up. Conclusions: Fibrin sealant and autologous PRP were associated with similar rates of clinically significant seroma. Fibrin sealant was associated with lower postoperative fluid accumulation and small differences in short-term recovery outcomes. Given the exploratory design, small sample size, absence of an a priori power calculation, and lack of prospective public trial registration, the findings should be considered hypothesis-generating rather than definitive evidence of superiority.

Keywords: Breast Cancer; Seroma; Fibrin Sealant, Platelet-Rich Plasma, Mastectomy, Axillary Lymph Node Dissection.

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1. INTRODUCTION

Seroma formation remains one of the most frequent postoperative complications following breast cancer surgery, particularly after mastectomy and axillary lymph node dissection [1, 2]. Several patient, disease, and procedure-related factors may influence the development of postoperative seroma, including the extent of breast and axillary surgery, disruption of lymphatic channels, the size of the residual dead space, and individual patient characteristics [1, 2]. Consequently, numerous preventive strategies have been investigated, including modification of drain management, mechanical obliteration of dead space using flap fixation or quilting sutures, tissue adhesives, and biological adjuncts [3–7]. Despite these efforts, no single intervention has been universally accepted as the optimal strategy for seroma prevention. Fibrin sealants have attracted considerable interest because of their ability to reproduce the final phase of the coagulation cascade through the interaction of fibrinogen and thrombin, resulting in the formation of a localized fibrin matrix [3–5]. More recent evidence has similarly suggested potential benefits of fibrin-based tissue adhesives, although the magnitude of effect appears to vary according to surgical technique, patient population, and outcome definition [6, 7]. Mechanical dead-space reduction techniques may also influence seroma formation. Contemporary meta-analyses have demonstrated that quilting sutures and flap fixation can reduce postoperative seroma following mastectomy, emphasizing the importance of eliminating dead space in addition to controlling lymphatic leakage [8,9]. Autologous platelet-rich plasma (PRP) represents a biologically distinct approach. PRP contains concentrated platelets, along with platelet-derived growth factors and bioactive mediators involved in tissue repair, angiogenesis, extracellular-matrix remodeling, and the modulation of the inflammatory response. Its use in breast surgery has been investigated for wound healing, reconstruction, and reduction of postoperative seroma [10–12]. The use of PRP in oncologic surgery also raises an additional consideration because platelet-derived growth factors are biologically active within the wound microenvironment. Although theoretical concerns have been raised regarding their potential interaction with residual malignant cells, currently available clinical evidence has not demonstrated a clear adverse oncologic signal. Nevertheless, long-term evidence remains limited, and continued evaluation of oncologic safety is warranted [13,14]. Despite the availability of studies evaluating fibrin sealants and PRP individually, direct randomized comparisons between these two biologically distinct interventions in breast cancer surgery remain limited. Fibrin sealant primarily acts through mechanical sealing and tissue adherence, whereas PRP is intended to promote biological tissue repair. Because no formal a priori sample-size calculation was performed, the study was designed to provide exploratory estimates of comparative treatment effects rather than definitive evidence of superiority.

2. PATIENTS AND METHODS

This was a single-center, two-arm, parallel group, exploratory randomized controlled trial conducted at Burjeel Hospital, a tertiary-care institution, between December 2024 and December 2025. Fifty eligible women undergoing breast cancer surgery were prospectively enrolled and randomly allocated in a 1:1 ratio to receive either topical fibrin sealant or autologous platelet-rich plasma (PRP) applied to the operative bed before wound closure.

Participants:

Women aged ≥ 18 years with histologically confirmed breast cancer who were scheduled for mastectomy or breast-conserving surgery with axillary lymph node dissection were eligible.

Exclusion criteria were pre-existing coagulopathy, active infection, current anticoagulant or antiplatelet therapy, thrombocytopenia, severe anemia, uncontrolled diabetes mellitus, systemic corticosteroid or immunosuppressive therapy, previous neoadjuvant treatment, recurrent breast cancer, and prior ipsilateral axillary surgery.

Eligible participants were randomly allocated in a 1:1 ratio to either the fibrin-sealant group or the platelet-rich plasma (PRP) group using simple randomization. The allocation sequence was generated before participant enrollment by the study statistician using a random-number method. No blocking was used; therefore, no block size was applicable. No stratification was documented. Allocation concealment was achieved using sequentially numbered, opaque, sealed envelopes prepared by operating-theatre nurses according to the randomization sequence generated by the statistician. The envelopes were maintained in numerical order and opened sequentially only after completion of the breast and axillary dissection, and immediately before application of the assigned study intervention. The operating surgeon remained unaware of the treatment allocation until the corresponding envelope was opened. After allocation, blinding of the surgeon was not feasible because fibrin sealant and PRP were visually and technically distinguishable. Patients, postoperative outcome assessors, ultrasonographers, and data analysts were not documented as blinded. Both groups nevertheless underwent the same surgical and postoperative management protocols, drain-management criteria, follow-up schedule, ultrasonographic surveillance, and criteria for therapeutic aspiration.

Surgical and perioperative standardization

Breast surgery consisted of mastectomy or breast-conserving surgery according to standard oncologic indications. Axillary lymph node dissection generally included levels I-II for clinically indicated cases. Surgical technique, hemostasis, drain placement, and postoperative management were standardized between the groups. The allocated adjunct was applied only after completion of oncologic dissection and satisfactory hemostasis. Residual blood and irrigation fluid were removed from the operative field before treatment application. A closed-suction drain was used in all participants. Drain output was recorded every 24 hours, and drains were removed when output was <30 mL during the preceding 24 hours, provided that no clinical indication for continued drainage was present. The same drain-management protocol was applied to both treatment groups.

Study interventions

Fibrin-sealant group:

Participants allocated to the fibrin-sealant group received VISTASEAL™ Fibrin Sealant (Human) (Instituto Grifols, S.A., Barcelona, Spain; application system distributed by Ethicon). The preparation consists of human fibrinogen (80 mg/mL) and thrombin (500 IU/mL), which combine during application to form a fibrin clot. After definitive hemostasis, a standardized volume of 10 mL was applied topically as a thin, uniform layer over the exposed operative surfaces. In patients undergoing mastectomy, the sealant was distributed over the mastectomy bed, pectoral surface, undersurface of the skin flaps, and axillary bed when applicable. In breast-conserving surgery, it was applied to the walls and base of the resection cavity and to the axillary bed when indicated. The operative field was left undisturbed for approximately 10 minutes to allow polymerization and tissue adherence. The drain was then positioned without deliberate disruption of the treated surfaces, and the wound was closed in layers.

Platelet-rich plasma group:

Autologous PRP was prepared from approximately 50 mL of peripheral venous blood collected under sterile conditions into sodium citrate-containing tubes. A standardized single-spin centrifugation protocol was used to separate the erythrocyte fraction from the platelet-containing plasma, yielding approximately 10 mL of PRP. Baseline peripheral platelet counts and final PRP platelet concentrations were assessed according to the institutional laboratory protocol. Immediately before application, PRP was activated using thrombin according to the predefined study protocol. Approximately 10 mL of activated PRP was then distributed uniformly over the raw operative surfaces after completion of surgery and achievement of hemostasis. The anatomical areas of application were equivalent to those treated in the fibrin-sealant group. Manipulation of the treated surfaces was minimized before drain placement and wound closure.

Primary outcomes:

The primary outcomes analyzed in this study were (1) the incidence of clinically significant postoperative seroma and (2) postoperative fluid volume. Seroma was defined as a postoperative fluid collection within the breast, mastectomy, or axillary operative bed detected clinically and/or by ultrasonography during follow-up. Small, asymptomatic collections detected only on ultrasonography and not requiring therapeutic intervention were recorded separately and were not classified as clinically significant seromas. A clinically significant seroma was defined as a postoperative fluid collection associated with clinically relevant swelling, discomfort, wound or skin-flap tension, functional limitation, or a requirement for therapeutic aspiration. Small asymptomatic ultrasonographic collections not requiring intervention were not classified as clinically significant seromas. Therapeutic aspiration was performed under sterile conditions when a postoperative collection was clinically significant according to the predefined clinical criteria. Postoperative fluid volume was defined as the maximum ultrasonographically estimated fluid-collection volume recorded during the 2-month follow-up period. When aspiration was performed at the same assessment, the measured aspirated volume was used. Seroma incidence was defined as the occurrence of at least one qualifying seroma during the 2-month postoperative observation period.

Secondary outcomes:

Secondary outcomes were postoperative discomfort, therapeutic seroma aspiration, the number of aspiration procedures,

time to functional recovery, and intervention-related adverse events. Postoperative discomfort was assessed using a 10-point Visual Analogue Scale (VAS), where 0 represented no discomfort and 10 represented the worst imaginable discomfort. VAS assessments were performed approximately 1 week, 2 weeks, and 1 month after surgery. The 1-week postoperative VAS score was used for the principal between-group comparison. Time to functional recovery was defined as the number of days from surgery until the patient resumed normal daily activities without substantial surgery-related limitations. Functional recovery was considered achieved when the participant was able to perform routine self-care, ambulate independently, resume usual household and social activities, and return to her customary occupational activities. The date on which functional recovery had first occurred was recorded. Time to functional recovery was calculated as the number of calendar days from surgery to that date. Adverse events were assessed throughout the 2-month postoperative follow-up period. The safety assessment focused on complications considered potentially related to either the study intervention, including clinically relevant inflammatory or allergic reactions, bleeding attributable to the applied adjunct, thromboembolic events, wound complications considered intervention-related, reoperation related to the study treatment, or any other event judged by the treating team to be attributable to fibrin sealant or PRP. Additional exploratory postoperative outcomes included drain duration and cumulative closed-suction drainage volume. Drain duration was defined as the number of days from surgery to drain removal. Cumulative drainage volume was defined as the sum of daily drain output from surgery until drain removal. These drainage outcomes were summarized descriptively, and no formal between-group inferential analysis was performed.

Follow-up

Participants were scheduled for standardized postoperative assessments at approximately 1 week, 2 weeks, 1 month, and 2 months after surgery. At each visit, clinical examination and ultrasonographic evaluation were performed to assess postoperative fluid collections and seroma.

Ultrasonographic assessment and aspiration criteria

At each scheduled postoperative follow-up visit, a clinical examination was performed by the treating breast surgeon. Ultrasonographic assessment of the operative bed was performed by a specialist or a consultant radiologist. Ultrasonography was used to identify and quantify postoperative fluid collections within the breast, mastectomy bed, and/or axillary region. The ultrasound system automatically calculated the volume of any postoperative fluid collection identified during the examination, and the recorded volume was documented in the radiology report. Therapeutic aspiration was performed when a postoperative fluid collection was considered clinically significant. Indications included symptomatic swelling, pain or discomfort, wound or skin-flap tension, functional limitation, progressive enlargement of the collection, or a clinical judgment that drainage was required to prevent wound-related complications. Small asymptomatic collections without clinically relevant tension or functional impairment were managed conservatively and were not routinely aspirated. The decision to perform aspiration was made by the treating breast surgeon after consideration of both the clinical examination and the ultrasonographic findings. No isolated ultrasonographic volume measurement was used as the sole indication for aspiration.

Statistical Analysis:

Statistical analyses were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were summarized as frequencies and percentages. Continuous variables were summarized as mean $\pm$ standard deviation for approximately normally distributed data and as median with interquartile range for skewed data. Normally distributed continuous outcomes were compared using the independent-samples *t* test, with Welch's correction when the assumption of equal variance was not satisfied. Non-normally distributed continuous outcomes were compared using the Mann–Whitney *U* test. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. Treatment effects were reported with corresponding 95% confidence intervals wherever applicable. All tests were two-sided, with $P < 0.05$ considered statistically significant. Because the study was exploratory, statistical significance was interpreted alongside effect estimates and confidence intervals rather than as definitive evidence of treatment superiority. All analyses were performed according to the intention-to-treat principle, with participants analyzed according to their original randomized allocation. No adjustment for multiplicity was performed because the trial was exploratory. Accordingly, *P* values for secondary and subgroup analyses were interpreted as descriptive and hypothesis-generating, with emphasis placed on effect estimates and 95% confidence intervals.

3. RESULTS

Between December 2024 and December 2025, 100 patients undergoing breast cancer surgery were assessed for eligibility. Of these, 50 patients were excluded before randomization: 15 did not meet the inclusion criteria, 30 met one or more exclusion criteria, and 5 declined to participate. A total of 50 eligible patients were enrolled and randomized in a 1:1 ratio, with 25 allocated to the fibrin-sealant group and 25 allocated to the platelet-rich plasma (PRP) group. All randomized participants received the intervention to which they had been assigned. Accordingly, 25 patients in the fibrin-sealant group received topical VISTASEAL™ application, while 25 patients in the PRP group received autologous PRP applied to the

operative bed. Postoperative follow-up assessments were scheduled at 1 week, 2 weeks, 1 month, and 2 months. No participants were lost to follow-up, and complete outcome data were available for all randomized patients throughout the 2-month study period. All 50 randomized participants were included in the primary analysis according to the intention-to-treat principle, including 25 patients in the fibrin-sealant group and 25 patients in the PRP group. The same participants were included in the secondary outcome analyses. Participant flow through screening, randomization, allocation, follow-up, and analysis is presented in Figure 1. Baseline Characteristics. All 50 randomized participants were included in the baseline analysis, with 25 patients in the fibrin-sealant group and 25 in the platelet-rich plasma (PRP) group. The mean age was 52.48 ± 1.49 years in the fibrin-sealant group and 51.29 ± 1.48 years in the PRP group. The standardized mean difference (SMD) for age was 0.80, indicating an appreciable baseline imbalance despite randomization. Baseline characteristics are therefore presented descriptively rather than interpreted using significance testing. Tumor-stage distribution was identical between groups: 10 participants (40.0%) had stage I disease, 10 (40.0%) stage II disease, and 5 (20.0%) stage III disease in each group (SMD=0.00). Mastectomy was performed in 18/25 participants (72.0%) in the fibrin-sealant group and in 17/25 (68.0%) in the PRP group; breast-conserving surgery was performed in 7/25 (28.0%) and in 8/25 (32.0%), respectively (SMD for mastectomy =0.09). Across the entire study population, the mean age was 51.88 ± 1.59 years (range, 49–55 years). Twenty patients (40.0%) had stage I disease, 20 (40.0%) had stage II disease, and 10 (20.0%) had stage III disease. Thirty-five patients (70.0%) underwent mastectomy and 15 (30.0%) underwent breast-conserving surgery. All participants underwent level I–II axillary lymph-node dissection. The number of lymph nodes removed ranged from 12 to 16 in the fibrin-sealant group and from 12 to 20 in the PRP group. Latissimus dorsi flap reconstruction was performed in 2 participants (8.0%) in the fibrin-sealant group and in 3 (12.0%) in the PRP group, whereas oncoplastic breast surgery was performed in 7 (28.0%) and 8 (32.0%), respectively. Operative time ranged from 120 to 140 minutes in the fibrin-sealant group and from 120 to 180 minutes in the PRP group. Additional baseline and perioperative characteristics are summarized in Table 1.

Primary outcomes

Seroma incidence:

During the 2-month postoperative follow-up period, clinically significant seroma developed in 4 of 25 patients (16.0%) in the fibrin-sealant group and 5 of 25 patients (20.0%) in the PRP group. The absolute risk difference was –4.0 percentage points (95% CI, approximately –25.3 to 17.3 percentage points), corresponding to a relative risk of 0.80 (95% CI, 0.24 to 2.64). Fisher's exact test demonstrated no statistically significant difference in seroma incidence between the treatment groups ($P=1.000$). Because the confidence interval was wide and included both a potentially clinically relevant reduction and an increase in risk, the observed numerical difference should not be interpreted as evidence of the superiority of fibrin sealant over PRP.

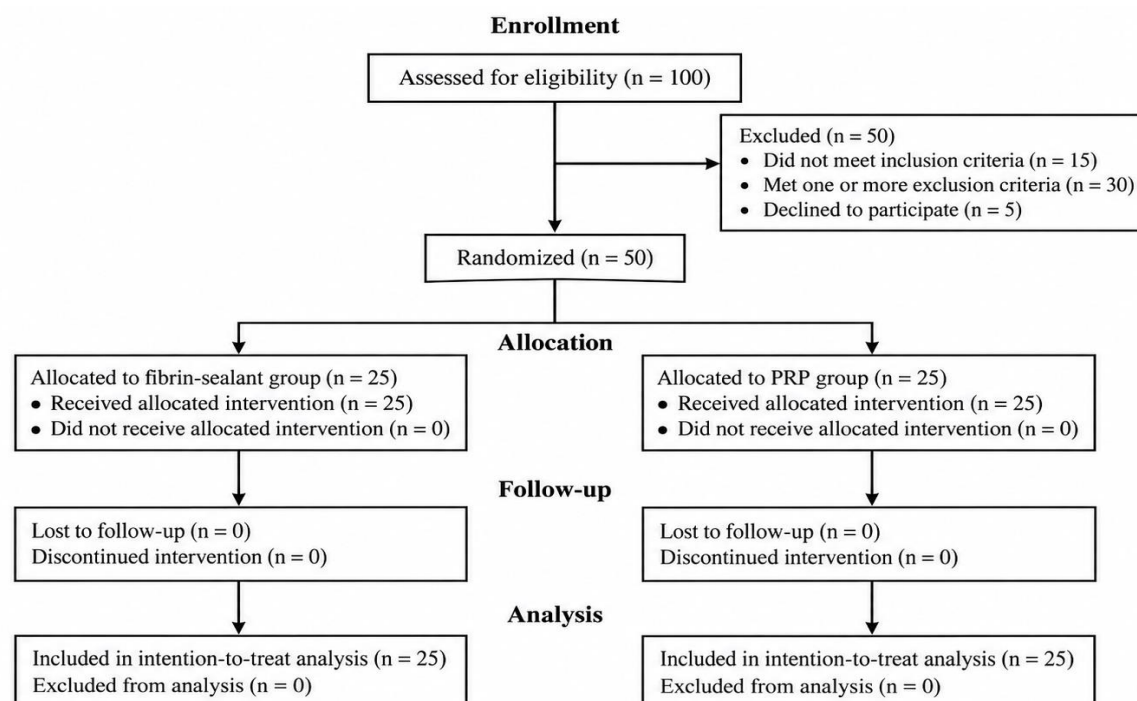


Figure 1. CONSORT flow diagram of participant recruitment, randomization, allocation, follow-up, and analysis. Of 100 patients assessed for eligibility, 50 were excluded and 50 were randomized 1:1 to fibrin sealant or platelet-rich plasma. All randomized participants received the allocated intervention, completed 2-month follow-up, and were included in the intention-to-treat analysis.

Postoperative fluid/seroma volume:

The postoperative fluid accumulation was assessed separately from the cumulative closed-suction drain output. The distribution of postoperative fluid-volume measurements was non-normal; therefore, the Mann–Whitney U test was used for the principal between-group comparison. The median postoperative fluid volume was 15.3 mL (IQR, 13.8–16.8) in the fibrin-sealant group and 18.7 mL (IQR, 16.7–20.7) in the PRP group ($P < 0.001$). For descriptive purposes, the corresponding mean $\pm$ SD values were 15.24 ± 1.26 mL and 18.62 ± 1.68 mL, respectively, yielding an unadjusted mean difference of -3.38 mL (95% CI, -4.23 to -2.53 mL). Postoperative drainage characteristics showed a similar descriptive pattern. Drain duration ranged from 12 to 15 days in the fibrin-sealant group and from 12 to 16 days in the PRP group. Cumulative drainage volume ranged from 500 to 675 mL in the fibrin-sealant group compared with 525 to 800 mL in the PRP group. Closed-suction drains were removed when the drainage volume decreased to <30 mL during the preceding 24 hours, provided that no clinical indication for continued drainage was present. Overall, the fibrin-sealant group demonstrated lower recorded postoperative fluid accumulation and a narrower range of cumulative drainage volume than the PRP group. However, because only ranges were available for cumulative drainage volume and drain duration, no formal between-group statistical comparison of these drainage outcomes was performed. Given the exploratory design and absence of a priori power calculation, these findings should be interpreted as hypothesis-generating rather than definitive evidence of superiority.

Post-Hoc exploratory analysis among patients developing clinically significant seroma

Among the 9 patients who developed clinically significant seroma, the mean seroma volume was 14.93 ± 1.44 mL in the fibrin-sealant group ($n=4$) and 18.70 ± 2.00 mL in the PRP group ($n=5$). The corresponding median values were 14.55 mL (IQR, 13.8–15.68) and 18.7 mL (IQR, 16.7–20.7), respectively. The mean difference was -3.78 mL (95% CI, -6.49 to -1.06 mL). Because of the very small subgroup sample size, the non-parametric between-group comparison did not reach conventional statistical significance (Mann–Whitney $P=0.063$). This subgroup analysis should therefore be regarded as exploratory.

Secondary outcomes

Postoperative discomfort:

Postoperative discomfort scores were statistically lower in the fibrin-sealant group, although the absolute difference was small. The median visual analogue scale score was 2.1 (IQR, 1.8–2.4) versus 2.4 (IQR, 2.1–2.7), respectively. The corresponding mean $\pm$ SD values were 2.09 ± 0.25 and 2.39 ± 0.25 , respectively. The unadjusted mean difference was -0.30 points (95% CI, -0.44 to -0.16). Because the distribution was non-normal, the Mann–Whitney U test was used for the principal comparison and demonstrated a statistically significant between-group difference ($P < 0.001$).

Time to functional recovery:

The median time to functional recovery was 15 days (IQR, 14–16) in the fibrin-sealant group and 16 days (IQR, 15–17) in the PRP group, representing a modest 1-day difference. Mean recovery times were 14.96 ± 0.84 days and 15.96 ± 0.84 days, respectively. The mean between-group difference was -1.00 day (95% CI, -1.48 to -0.52 days). The Mann–Whitney U test demonstrated a statistically significant difference between the groups ($P < 0.001$).

Adverse events:

No intervention-related adverse events were documented in either treatment group during the follow-up period. The primary and secondary clinical outcomes and corresponding between-group comparisons are summarized in Table 2.

Seroma aspiration:

Therapeutic aspiration was required in 4/25 participants (16.0%) in the fibrin-sealant group and 5/25 (20.0%) in the PRP group (RR 0.80, 95% CI 0.24–2.64; $P=1.000$). A total of 6 and 7 aspiration procedures were performed, respectively. The median number of aspiration sessions among affected patients was 1.5 in the fibrin-sealant group and 1.0 in the PRP group. There was no statistically significant difference in the number of aspiration sessions between the groups. When all randomized patients were analyzed according to the intention-to-treat principle, including zero aspirations for patients without clinically significant seroma, the mean number of therapeutic aspiration procedures was 0.24 ± 0.60 per patient in the fibrin-sealant group and 0.28 ± 0.61 per patient in the PRP group. The median was 0 (IQR, 0–0) in both groups, with no significant between-group difference. The proportion of patients requiring at least one therapeutic aspiration was therefore identical to the incidence of clinically significant seroma: 16.0% in the fibrin-sealant group versus 20.0% in the PRP group. Therapeutic aspiration requirements and the number of aspiration procedures in each treatment group are summarized in Table 3.

Table 1. Baseline demographic, oncologic, and surgical characteristics

Characteristic	Fibrin sealant (n=25)	PRP (n=25)	Overall (N=50)	Absolute SMD
Age, years, mean $\pm$ SD	52.48 $\pm$ 1.49	51.29 $\pm$ 1.48	51.88 $\pm$ 1.59	0.80
BMI, kg/m ² , range	25–38	27–40	25–40	—
Controlled diabetes mellitus, n (%)	8 (32.0%)	6 (24.0%)	14 (28.0%)	0.18
Current smoking, n (%)	0 (0.0%)	2 (8.0%)	2 (4.0%)	0.42
Stage I disease, n (%)	10 (40.0%)	10 (40.0%)	20 (40.0%)	0.00
Stage II disease, n (%)	10 (40.0%)	10 (40.0%)	20 (40.0%)	0.00
Stage III disease, n (%)	5 (20.0%)	5 (20.0%)	10 (20.0%)	0.00
Mastectomy, n (%)	18 (72.0%)	17 (68.0%)	35 (70.0%)	0.09
Breast-conserving surgery, n (%)	7 (28.0%)	8 (32.0%)	15 (30.0%)	0.09
Axillary lymph-node dissection, levels I–II, n (%)	25 (100%)	25 (100%)	50 (100%)	0.00
Number of lymph nodes removed, range	12–16	12–20	12–20	—
Latissimus dorsi flap reconstruction, n (%)	2 (8.0%)	3 (12.0%)	5 (10.0%)	0.13
Oncoplastic breast surgery, n (%)	7 (28.0%)	8 (32.0%)	15 (30.0%)	0.09

*ALND, axillary lymph-node dissection; BMI, body mass index; PRP, platelet-rich plasma; SD, standard deviation; SMD, standardized mean difference.

Table 2. Primary and secondary clinical outcomes.

Outcome	Fibrin sealant (n=25)	PRP (n=25)	Effect estimate (95% CI)	P value
Clinically significant seroma	4/25 (16.0%)	5/25 (20.0%)	RR 0.80 (0.24-2.64); RD -4.0 percentage points ($\approx$ -25.3 to 17.3)	1.000
Postoperative fluid volume, mL, median (IQR)	15.3 (13.8-16.8)	18.7 (16.7-20.7)	Descriptive mean difference -3.38 mL (-4.23 to -2.53)	<0.001*
Discomfort, VAS, median (IQR)	2.1 (1.8-2.4)	2.4 (2.1-2.7)	Descriptive mean difference -0.30 (-0.44 to -0.16)	<0.001*
Return to normal activity, days, median (IQR)	15 (14-16)	16 (15-17)	Descriptive mean difference -1.00 day (-1.48 to -0.52)	<0.001*
Intervention-related adverse events	0/25 (0%)	0/25 (0%)	—	—
Operative time, min, range	120–140	120–180	—	—†
Drain duration, days, range	12–15	12–16	—	—†
Cumulative drainage volume, mL, range	500–675	525–800	—	—†

*Mann–Whitney U test. Continuous outcomes are summarized as the median (IQR); mean differences and 95% confidence intervals are provided descriptively. RR, relative risk; RD, risk difference; IQR, interquartile range; VAS, visual analogue scale.

† Descriptive data only; no formal between-group inferential analysis was performed.

Table 3. Therapeutic Aspiration Outcomes

Outcome	Fibrin sealant (n=25)	PRP (n=25)	Effect / comparison	P value
Patients requiring therapeutic aspiration ≥ 1	4/25 (16.0%)	5/25 (20.0%)	RR 0.80 (95% CI 0.24–2.64)	1.000†

Total procedures	aspiration	6	7	—	—
Aspiration sessions among affected patients, mean ± SD		1.50 ± 0.58	1.40 ± 0.55	Mean difference 0.10 sessions (95% CI −0.81 to 1.01)	0.888*

Abbreviations: CI, confidence interval; PRP, platelet-rich plasma; RR, relative risk; SD, standard deviation.

† Fisher's exact test.

* Mann–Whitney U test was used for the principal comparison because aspiration counts were discrete and highly skewed.

4. DISCUSSION

This exploratory randomized controlled trial directly compared topical fibrin sealant with autologous platelet-rich plasma (PRP) for the prevention and reduction of postoperative seroma following breast cancer surgery. The principal finding was that fibrin sealant did not significantly reduce the incidence of clinically significant seroma compared with PRP, although the absolute incidence was numerically lower in the fibrin-sealant group (16.0% vs 20.0%). The estimated relative risk was 0.80, with a wide 95% confidence interval (0.24–2.64), while the absolute risk difference was −4.0 percentage points. These estimates indicate substantial uncertainty around the binary seroma outcome and do not support a definitive claim of superiority. In contrast, the recorded postoperative fluid-volume distribution was lower in the fibrin-sealant group. Across all randomized patients, the median postoperative fluid volume was 15.3 mL (IQR, 13.8–16.8) in the fibrin-sealant group compared with 18.7 mL (IQR, 16.7–20.7) in the PRP group. The corresponding mean difference was −3.38 mL (95% CI, −4.23 to −2.53 mL; $P < 0.001$). This finding suggests that fibrin sealant may reduce the magnitude of postoperative fluid accumulation even when it does not clearly prevent the occurrence of clinically significant seroma. Such a distinction between seroma incidence and seroma volume is clinically plausible because an intervention may decrease lymphatic or serous leakage without completely eliminating postoperative fluid collection. This pattern is broadly consistent with previous evidence regarding fibrin sealants in breast and axillary surgery. A meta-analysis of 23 randomized controlled trials involving 1,640 patients undergoing axillary dissection found no significant reduction in seroma incidence with fibrin sealants, but it demonstrated significant reductions in seroma volume, total drainage volume, and drainage duration [3]. Similarly, a systematic review and meta-analysis of 23 randomized trials examining axillary lymphatic morbidity reported reduced drainage output and duration of drainage without a significant reduction in postoperative lymphocele incidence [5]. These findings closely resemble the pattern observed in the present study, in which fibrin sealant was associated with lower postoperative fluid volume but not a statistically significant reduction in clinically significant seroma incidence. More recent evidence suggests that the magnitude of benefit may vary according to surgical technique, patient population, and study methodology. A 2026 systematic review and meta-analysis of fibrin sealants in breast cancer surgery reported a significant reduction in total drainage volume and a lower odds of seroma formation, although substantial heterogeneity was observed for drainage-volume outcomes [6]. In contrast, a broader contemporary meta-analysis of seroma-prevention strategies after mastectomy found that tissue adhesives, including fibrin-based products, produced comparatively modest and inconsistent reductions in seroma, whereas mechanical dead-space obliteration techniques such as quilting sutures and flap fixation demonstrated more consistent effects [15]. Other meta-analyses have likewise shown substantial reductions in postoperative seroma with quilting techniques [8, 9]. Thus, the present finding of a reduction in postoperative fluid accumulation without a clear reduction in seroma incidence remains biologically plausible and compatible with the wider literature. The biological mechanism of fibrin sealants provides a plausible explanation for these observations. Fibrin-based sealants reproduce the final phase of the coagulation process by combining fibrinogen and thrombin to generate a localized fibrin matrix. Applied across raw mastectomy, breast resection, and axillary surfaces, this matrix may enhance tissue adherence, seal small vascular and lymphatic channels, and reduce the potential space available for fluid accumulation. These mechanisms could reasonably reduce postoperative fluid production without completely preventing all clinically significant seromas [3,5,6]. PRP represents a mechanistically distinct approach. Autologous PRP contains concentrated platelets together with a range of platelet-derived growth factors and cytokines involved in tissue repair, angiogenesis, extracellular-matrix remodeling, and inflammatory regulation. However, clinical evidence specifically evaluating PRP for seroma prevention after breast surgery remains limited. A small, blinded patient-controlled study evaluating autologous platelet-leukocyte-enriched plasma in latissimus dorsi breast reconstruction found no significant reduction in drainage output, time to drain removal, or seroma incidence, illustrating the limited and inconsistent clinical evidence currently available [11]. This evidence gap provides a rationale for direct comparative studies such as the present randomized trial. Postoperative discomfort was statistically lower in the fibrin-sealant group. Median visual analogue scale scores were 2.1 (IQR, 1.8–2.4) with fibrin sealant and 2.4 (IQR, 2.1–2.7) with PRP, with a descriptive mean difference of −0.30 points (95% CI, −0.44 to −0.16; $P < 0.001$). Although statistically significant, a 0.30-point difference on a 10-point VAS is small and should not be interpreted as evidence of a clinically important analgesic benefit. Participants in the fibrin-sealant group achieved functional recovery approximately 1 day earlier than those receiving PRP. Median recovery time was 15 days (IQR, 14–16) and 16 days (IQR, 15–17), respectively, with a descriptive mean difference of −1.00 day (95% CI, −1.48 to

−0.52; $P < 0.001$). Although statistically significant within this dataset, the clinical relevance of this small difference is uncertain; it should be interpreted as a modest difference in time to functional recovery rather than evidence of superior postoperative recovery. The aspiration findings reinforce the interpretation of the seroma-incidence results. Therapeutic aspiration was required only in patients who developed clinically significant seroma. Four patients in the fibrin-sealant group and five patients in the PRP group required aspiration, corresponding to rates of 16.0% and 20.0%, respectively. Among affected patients, the mean number of aspiration sessions was 1.50 ± 0.58 in the fibrin-sealant group and 1.40 ± 0.55 in the PRP group, with no significant between-group difference. Thus, although fibrin sealant was associated with a lower postoperative fluid volume, it did not materially reduce the likelihood of requiring therapeutic aspiration or the number of aspiration procedures once a clinically significant seroma had developed. Drain management represents another important determinant of postoperative seroma. In the present study, closed-suction drainage was standardized across both groups, and drains were removed when output decreased to less than 30 mL during the preceding 24 hours. A systematic review and meta-analysis comparing early and late drain removal after breast cancer surgery found that earlier drain removal was associated with a significantly higher risk of seroma formation [17]. Standardizing the drainage protocol between treatment groups therefore reduces the likelihood that the observed differences in postoperative fluid accumulation were attributable to differential drain management. Descriptively, drain duration ranged from 12–15 days with fibrin sealant and 12–16 days with PRP, while cumulative drainage volumes ranged from 500–675 mL and 525–800 mL, respectively. Because only range data were available, these observations were not subjected to inferential comparisons. No intervention-related adverse events were documented in either treatment group during the 2-month follow-up. However, the small sample size and limited duration of follow-up preclude conclusions regarding uncommon or delayed adverse effects. Long-term safety is particularly relevant when considering PRP in patients undergoing cancer surgery. PRP contains biologically active growth factors, and theoretical concerns have been raised regarding whether these mediators could influence residual malignant cells or the tumor microenvironment. Reviews of PRP use in breast reconstruction after cancer surgery have therefore emphasized the need for caution and longer-term oncologic surveillance [13]. However, currently available clinical evidence has not demonstrated a clear recurrence signal. In a long-term follow-up study of 89-breast cancer patients in whom PRP was used to support wound healing after venous access-device removal, no recurrence was observed within the treated scar area during a median follow-up of 45 months [14]. These observations are reassuring but remain insufficient to establish definitive oncologic safety for intraoperative PRP application directly within a breast cancer surgical bed. Several limitations should be considered when interpreting these findings. First, the trial included only 50 participants and no formal *a priori* sample-size calculation was performed. The study was intentionally exploratory and therefore was not specifically powered to detect a prespecified difference in seroma incidence. This limitation is reflected in the wide confidence interval surrounding the relative risk estimate for clinically significant seroma. Accordingly, the lack of statistical significance for the binary endpoint should not be interpreted as evidence of equivalence between fibrin sealant and PRP. Second, because of the appreciable chance imbalance in age and the absence of sufficient covariate data for an adjusted sensitivity analysis (SMD approximately 0.80), some influence of baseline age imbalance on the continuous outcomes cannot be excluded. Third, the study included both mastectomy and breast-conserving surgery. Although the distribution of surgical procedures was similar between treatment groups, these procedures generate different degrees of tissue dissection, lymphatic disruption, and dead space and therefore may carry different baseline risks of seroma. Previous observational evidence has demonstrated that seroma incidence varies according to the type and extent of breast surgery [2]. The sample size of the present study was insufficient for adequately powered procedure-specific subgroup analysis. Fourth, although several clinically relevant seroma risk factors, including BMI, diabetes mellitus, smoking status, extent of axillary dissection, lymph-node yield, reconstruction, operative time, and drain duration, were available descriptively, some variables were available only as ranges rather than as complete patient-level measurements. Consequently, comprehensive multivariable adjustment for potential prognostic factors was not feasible. Fifth, complete blinding was not feasible because VISTASEAL and PRP were visually and technically distinguishable after allocation, and postoperative outcome assessors and ultrasonographers were not documented as blinded. This introduces potential detection bias, particularly for subjective secondary outcomes such as discomfort and return to normal activities. Allocation concealment until completion of surgical dissection and standardized postoperative assessment reduced, but did not eliminate, this risk. Sixth, postoperative follow-up was limited to 2 months. Although this interval was sufficient to capture early postoperative seroma and most immediate wound-related complications, it cannot address long-term wound outcomes, cosmetic results, cost-effectiveness, patient satisfaction, or oncologic safety. Longer-term follow-up would be particularly important when evaluating PRP in an oncologic surgical setting. Despite these limitations, the study has several strengths. It provides a direct randomized comparison of two biologically distinct intraoperative adjuncts, used concealed allocation, standardized treatment application, employed identical closed-suction drain-management protocols, incorporated ultrasonographic postoperative surveillance, achieved complete 2-month follow-up, and included all randomized participants in the intention-to-treat analysis. Importantly, these findings should not be interpreted as demonstrating overall superiority of fibrin sealant over PRP. Rather, they suggest a more nuanced pattern: fibrin sealant was associated with a lower postoperative fluid volume, slightly lower postoperative discomfort, and approximately 1 day shorter time to return to normal activities, whereas clinically significant seroma incidence, the need for therapeutic aspiration, and the number of aspiration sessions were similar between groups. This distinction is clinically relevant and is broadly consistent with previous evidence suggesting that fibrin sealants may influence postoperative fluid production more consistently than they

completely prevent seroma formation [3,5,6,15]. Future adequately powered, multicenter randomized trials should stratify participants according to the type of breast surgery and the extent of axillary treatment, incorporate established seroma risk factors, standardize and characterize PRP preparation, and provide longer follow-up. Future studies should evaluate cumulative drainage volume and drain duration using complete patient-level measurements and prespecified inferential analyses. Such studies would help determine whether the reductions in postoperative fluid accumulation and recovery time observed with fibrin sealant translate into clinically meaningful and economically justified advantages over autologous PRP.

5. CONCLUSION

In this exploratory randomized controlled trial, fibrin sealant and autologous platelet-rich plasma were associated with comparable rates of clinically significant postoperative seroma after breast cancer surgery. Although the incidence of seroma was numerically lower with fibrin sealant than with PRP, the between-group difference was small and not statistically significant. Fibrin sealant was associated with a lower recorded postoperative fluid volume, and small differences in postoperative discomfort and time to functional recovery. The requirement for therapeutic aspiration and the number of aspiration sessions among patients who developed clinically significant seroma were comparable between groups. These findings suggest that fibrin sealant may reduce the magnitude of postoperative fluid accumulation and modestly improve short-term recovery compared with autologous PRP, without clearly reducing the incidence of clinically significant seroma. Given the exploratory design, small sample size, and absence of a formal a priori power calculation, these findings should not be interpreted as definitive evidence of superiority. Larger, adequately powered multicenter randomized controlled trials with standardized surgical and PRP protocols, comprehensive assessment of seroma-related risk factors, and longer-term follow-up are warranted to confirm these findings and evaluate their clinical, economic, and oncologic implications.

Declarations

Reporting Guideline: The manuscript was prepared and reported with reference to the Consolidated Standards of Reporting Trials (CONSORT 2025) recommendations for randomized controlled trials. A completed CONSORT 2025 checklist and participant flow diagram are provided with the final submission.

Institutional Review Board Statement: The study protocol was reviewed and approved by the Institutional Review Board before initiation of recruitment (approval no. BURJ/RERC/2024/011). The study was conducted in accordance with the Declaration of Helsinki and applicable institutional requirements. Written informed consent was obtained from all participants before enrollment.

Data Availability Statement: The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable institutional, ethical, and patient-confidentiality requirements.

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