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Case Report

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Biological Mechanisms and Therapeutic Potential of PRP-Fibrin Glue in Managing Refractory Pleural Effusion Following Cardiac Surgery: Insights from a Pilot Study

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Abstract

Introduction: Refractory pleural effusion (RPE) is a serious postoperative complication of cardiac surgery that often persists despite conventional chest tube drainage. Platelet-rich plasma fibrin glue (PRP-FG), a biologically active sealant with hemostatic and regenerative properties, has previously shown efficacy in reducing morbidity in postoperative chylothorax and pneumothorax. This clinical trial aimed to evaluate the safety and therapeutic efficacy of intrapleural PRP-FG in patients with RPE unresponsive to standard thoracostomy management.

Case Presentation: In this pilot clinical trial, 19 patients with unilateral or bilateral RPE resistant to standard therapy were treated with intrapleural PRP-FG. Treatment success was defined as pleural drainage of <50 mL/day for two consecutive days within one week post-intervention, accompanied by symptomatic improvement.

The mean age was 43.6 ± 19.6 years; 52.6% of patients had undergone coronary artery bypass grafting (CABG), and 36.8% had undergone congenital cardiac surgery. PRP-FG administration led to a significant reduction in effusion volume (624.2 ± 275.0 mL to 25.0 ± 20.1 mL; mean difference 599.2 mL, $p < 0.001$; Cohen's d = 2.29). Five patients (26.3%) required a second application, and three (15.8%) required a third for complete resolution. No major adverse events or recurrence were observed during the six-month follow-up; minor, self-limited effects included pleuritic pain and transient dyspnea. One patient with uncontrolled diabetes died from a sternal wound infection unrelated to PRP-FG.

Conclusion: Intrapleural PRP-FG appears to be a safe, effective, and minimally invasive therapy for RPE following cardiac surgery. These promising findings warrant confirmation in larger multicenter studies with longer follow-up to establish its long-term efficacy and clinical applicability.

Keywords: Pleural effusion; Cardiac surgery; Platelet-rich plasma; Fibrin glue; Coronary artery bypass grafting; Cardiology; Surgery.

1. Introduction

Refractory pleural effusion (RPE) is a serious postoperative complication after cardiac surgery, frequently resulting in extended hospitalization, increased morbidity, and higher healthcare costs (1-3). Although most pleural effusions are transient and resolve spontaneously, approximately 5–10% of patients develop sizable refractory effusions within 30 days post-surgery, requiring invasive interventions such as decortication when standard therapies, such as therapeutic tube thoracostomy, thoracentesis, or pharmacologic therapies, fail (2,4,5). In a comprehensive cross-sectional study of 11,037 cardiac surgery patients by Schiefenhövel et al. (6), 1,254 (11.4% of the total cohort) underwent at least one additional thoracentesis or chest tube placement during their hospital stay (6). Recent studies highlight that 83% of these effusions have multifactorial etiologies, including post-cardiac injury syndrome, pulmonary embolism, and congestive heart failure (CHF) (7,8). Pleural effusions are classified according to their timing as perioperative (within the first week), early (within the first month), late (2–12 months post-surgery), and persistent (lasting beyond six months). Notably, approximately 40% of patients develop pleural effusion immediately after surgery (4,9). Hemorrhagic effusions are typically managed with therapeutic tube thoracostomy, while non-hemorrhagic effusions may be managed with other interventions such as anti-inflammatory agents, sclerosing agents, or prolonged drainage (2,4).

The persistence of RPE is a clinical challenge, particularly when traditional treatments prove ineffective over time. Refractory effusions may delay recovery, increase morbidity and mortality, and contribute significantly to healthcare costs for both patients and the healthcare system (2,3,6). Furthermore, the prolonged physical and emotional burden of persistent effusions can negatively impact patients' mental health, potentially leading to anxiety and depression (10).

Platelet-rich plasma fibrin glue (PRP-FG) is well-known for its role in tissue repair and wound healing (11,12). Recently, PRP-FG has been successfully used to treat postoperative complications such as chylothorax after esophagectomy, chylothorax following cavopulmonary connections, and persistent pneumothorax after congenital cardiac surgery (13–15).

Building on these successes, this pilot study aims to explore the application of PRP-FG in managing recalcitrant pleural effusions following cardiac surgery. This approach was employed as a last resort after conventional treatments failed. Here, we present 19 cases of postoperative pleural effusion resistant to standard thoracostomy treatment, which were successfully treated using PRP-FG.

2. Case Presentation

Study design and setting

This pilot study was conducted at Imam Reza Hospital, Mashhad University of Medical Sciences, Iran, between 2020 and 2024, and included patients who developed unilateral or bilateral RPE following cardiac surgery and failed to respond to conventional conservative management.

Patient Selection

Nineteen patients with persistent pleural effusion after cardiac surgery were enrolled in this study. Inclusion criteria required that patients had undergone cardiac surgery (e.g., CABG, valve repair, or congenital heart surgery) and had a documented diagnosis of pleural effusion refractory to standard treatment, as confirmed by two cardiac surgeons or fellows. Patients were considered refractory if they continued to exhibit pleural drainage exceeding 100 mL/day despite therapeutic thoracostomy, diuretics, anti-inflammatory therapy, and prolonged observation.

Exclusion criteria included patients with preoperative pleural effusion resulting from underlying conditions such as (CHF), chronic kidney disease (CKD), hepatic cirrhosis, or malignancy. Patients with a history of connective tissue disorders or significant asbestos exposure were also excluded. Additionally, individuals who were hemodynamically unstable at the time of evaluation or those who declined to provide informed consent were not eligible for inclusion.

Data Collection

Demographic and clinical characteristics, including age, sex, body mass index (BMI), smoking history, renal function status, type of surgery, and initial pleural effusion characteristics, were collected from hospital records. Laboratory results, imaging studies (chest X-ray and (CT) scan), and procedural details were documented. Data collection was facilitated through the Hospital Information System (HIS), archived medical records, and direct patient interviews.

Postoperative Management and Initial Conservative Treatment

For all patients requiring chest tube placement due to pleural effusion, at least one standard mediastinal chest tube (Soroush Nasr Biotech, Iran) was inserted on the affected side via a subcostal approach and connected to a vacuum system for postoperative blood evacuation. In cases of significant postoperative pleural effusion necessitating further intervention beyond routine drainage, a secondary thoracentesis or an additional chest tube was placed in the anterior axillary line via mini-thoracotomy by the (ICU) team

or a surgical resident. Chest tube drainage was subsequently managed under the supervision of cardiothoracic surgeons.

Conservative management included continued thoracostomy drainage to maintain lung function and ensure adequate pulmonary expansion. Medical therapy consisted of diuretics, non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids, administered in accordance with established ICU protocols. Nutritional support was tailored to individual patient needs, with protein-rich, fat-restricted, or diabetic diets provided to promote healing and reduce fluid retention. Monitoring involved daily documentation of chest tube output by trained nursing staff, along with serial chest X-rays and ultrasonographic imaging to assess the progression of pleural effusion; computed tomography CT scans were performed when clinically indicated.

Patients who did not respond to one week of conservative management were offered PRP-FG pleurodesis before considering surgical intervention.

Preparation of platelet-rich plasma fibrin glue

Allogenic PRP-FG was derived from blood obtained from a blood bank, following standard protocols described in previous studies (13–15). Aprotinin was omitted to prevent anaphylactic shock. Peripheral blood (400 mL) was collected from a donor with a matching ABO blood type, and rigorous viral safety tests were conducted. Red blood cells (RBCs) were removed by centrifugation at 2000 rpm for 8 minutes to obtain platelet-containing plasma. The resulting plasma was then centrifuged at 4000 rpm for 15 minutes, which allowed the platelets to sediment.

The supernatant plasma was removed, and the platelet pellet was resuspended in a small volume of plasma to obtain concentrated PRP (10 mL).

Fibrinogen was extracted from the separated plasma using cryoprecipitation. After freezing at -70°C and following thawing at 4°C, fibrinogen concentrate (20 mL) was prepared by centrifugation at 6500 × g for 5 minutes. The concentrated PRP was combined with fibrinogen (30 mL).

Thrombin was generated from the plasma isolated during the second centrifugation step. Ionic strength and pH were adjusted to precipitate prothrombin. The resulting precipitate was separated by centrifugation and dissolved in a calcium ion solution, resulting in a final volume of 5 mL of thrombin solution. Before administration, the concentrated PRP, fibrinogen, and thrombin were thoroughly mixed.

Intervention with Platelet-Rich Plasma Fibrin Glue

Although the risk of anaphylaxis was extremely low and nearly negligible, a resuscitation and anaphylaxis management kit was readily available at the patient's bedside to ensure safety. As the first step, the proper functionality of the chest tube was confirmed before injection. Aseptic conditions were maintained in an isolated room in the intensive care unit ICU while injecting PRP-FG into patients. The pleural space was injected under the supervision of a cardiac surgeon with PRP-FG (5–7 mL/kg) through a placed chest tube. To enable the smooth passage of the liquid and prevent clot formation, 5 mL of isotonic saline solution was used to flush the chest tube. The chest tube was clamped for 30 minutes, and the patient's position was changed every 5 minutes by medical staff to circulate the mixture throughout the pleural cavity. To monitor clotting time, 5 mL of PRP-FG was collected using a small syringe. After 30 minutes, when the PRP-FG sample was entirely clotted, the chest tube was opened and left on a water seal. Patients were instructed to remain immobile and lie down for 2 hours.

Follow-Up and Outcome Assessment

The primary outcome was treatment success, defined as a reduction in pleural effusion volume to <50 mL/day for two consecutive days within one week post-treatment, confirmed by clinical and imaging assessments. Secondary outcomes included symptom resolution, adverse effects related to PRP-FG, duration of hospitalization, and recurrence rates over a six-month follow-up period.

Patients were monitored for drainage reduction and symptom improvement. Treatment success was defined as: 1) pleural drainage <50 mL/day for two consecutive days within one week, and 2) no recurrence of effusion within six months on the affected side.

If effusion persists after one week, the PRP-FG injection was repeated with the same volume through the chest tube. The intervention was considered successful if the effusion was <50 mL/day for two consecutive days after another week. Patients who failed two applications were considered for surgical intervention. In patients with bilateral pleural effusion, PRP-FG was initially injected on one side, and after the effusion ceases, a second injection was administered on the other untreated side. Patients were followed for at least for six months, either by telephone or in person at the clinic, and were asked to provide any further work-up and documentation for better monitoring through online communication services.

Statistical Analysis

Data analysis was performed using SPSS version 26 (IBM Corp., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) for

normally distributed data or as median with interquartile range (IQR) for non-normal distributions, as determined by the Kolmogorov–Smirnov test. Categorical variables were summarized as frequencies and percentages. Comparisons between groups were conducted using the independent-samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-parametric data. Associations between categorical variables were evaluated using the Chi-square test or Fisher's exact test when appropriate. Paired comparisons of pre- and post-intervention data were analyzed using the paired t-test for normally distributed variables or the Wilcoxon signed-rank test for non-parametric variables. Statistical significance was defined as $p < 0.05$ (two-tailed). Effect size for the primary outcome was calculated using Cohen's d to quantify the magnitude of the treatment effect.

A total of 19 patients were assessed for eligibility (Figure 1). No patients were excluded, and all were randomized. The nineteen patients were allocated to the intervention group andreceived the assigned treatment. No patients were allocated to a control group due to ethical considerations. Ultimately, all19 patients were included in the final analysis.

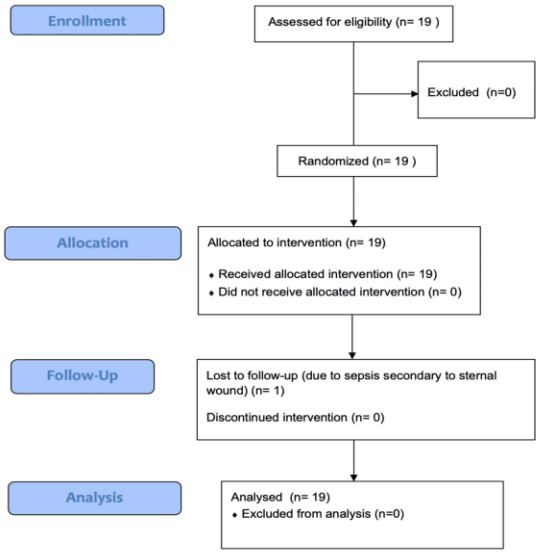

Figure 1. CONSORT 2010 flow diagram of the study participants.

The demographic and clinical characteristics of patients are shown in Table 1. The mean age of the participants was 43.58±19.58 (mean±SD) with a range of 7 to 78 years. Among them, two patients (10.5%) were under the age of 18 years.

Table 1. Baseline characteristics of patients enrolled in the study (N = 19).

Characteristic	Category	Value / n (%)
Gender	Female	10 (52.6)
	Male	9 (47.4)
Age (years)	Mean ± SD	43.6 ± 19.6
	Range	7–78
Smoking history	Yes	10 (52.6)
	No	9 (47.4)
Renal function	Normal	12 (63.2)
	Impaired	7 (36.8)
Type of surgery	CABG	10 (52.6)
	Valve repair / Congenital	9 (47.4)
Pleural effusion	Right	8 (42.1)
	Left	5 (26.3)
	Bilateral	6 (31.6)

Data are presented as mean ± standard deviation (SD) or number (percentage).
CABG, coronary artery bypass grafting.

Among the 19 patients, 10 (52.6%) underwent CABG, 7 (36.8%) underwent congenital cardiac surgery, 1 (5.2%) underwent isolated mitral valve repair, and 1 (5.2%) underwent combined congenital and valvular surgery (ASD + TR), as summarized in Table 2.

The mean age differed significantly between the two surgical groups, with patients in the valve/congenital group being younger (26.9 ± 12.7 years) than those who underwent CABG (58.6 ± 6.0 years; $p < 0.001$). A history of smoking was significantly more frequent among CABG patients (8 [80%]) than among those in the valve/congenital group (2 [22.2%]; $p = 0.012$). Renal function did not differ significantly between the two groups ($p = 0.75$).As shown in Table 3, pleural effusion volume decreased markedly following PRP-FG therapy (mean difference = 599 mL, $p < 0.001$), corresponding to a large effect size (Cohen's $d = 2.29$). All patients demonstrated clinical and radiologic improvement, with drainage volumes declining to <50 mL/day after treatment. Five patients (26.3%) required a second PRP-FG application, and three (15.8%) required a third to achieve complete resolution. Following successful pleurodesis, 18 patients were discharged, and chest tubes were removed within two days. One female patient with poorly controlled diabetes died one month later due to a sternal wound infection unrelated to PRP-FG; notably, she had exhibited no signs of dyspnea, effusion recurrence, or procedure-related complications prior to death.

Table 2. Comparison of baseline characteristics between CABG and valve/congenital surgery groups.

Variable	Category	Valve/ Congenital (n = 9)	CABG (n = 10)	p-value

Gender	Male	4 (44.4)	5 (50.0)	0.82[a]
	Female	5 (55.6)	5 (50.0)	
Age (years)	—	26.9 ± 12.7	58.6 ± 6.0	<0.001[b]
History of smoking	No	7 (77.8)	2 (20.0)	0.012[a]
	Yes	2 (22.2)	8 (80.0)	
Renal dysfunction	No	6 (66.7)	6 (60.0)	0.75[a]
	Yes	3 (33.3)	4 (40.0)	
Pleural effusion	Bilateral	3 (33.3)	3 (30.0)	0.72[a]
	Left	3 (33.3)	2 (20.0)	
	Right	3 (33.3)	5 (50.0)	
Number of PRP-FG injections	1	5 (55.6)	6 (60.0)	0.75[a]
	2	3 (33.3)	2 (20.0)	
	3	1 (11.1)	2 (20.0)	

Data are presented as mean ± standard deviation or number (percentage).
[a] Chi-square test; [b] Independent-samples t-test.
CABG = coronary artery bypass grafting; PRP-FG = platelet-rich plasma fibrin glue.

Table 3. The comparison of pleural effusion volume before and after the intervention.

Variable	Before treatment(mL*)	End of treatment(mL)	p-value	95% CI for Mean Difference	Cohen's d (Effect Size)
Mean ± SD	624.21 ± 275.02	25.00 ± 20.07	< 0.001	[473.31, 725.11]	2.29
Sample Size (N)	19				

During the observation period, no serious adverse effects related to PRP-FG injections were reported. However, some patients experienced minor side effects immediately after the injection, such as pleuritic pain and dyspnea. These symptoms were effectively managed with analgesics and oxygen therapy. All discharged patients were monitored for a minimum of six months, during which no recurrence of pleural effusion was observed.

To provide further insights, detailed case studies of three patients are presented, offering a comprehensive understanding of individual treatment responses and clinical outcomes.

Case 1

A 29-year-old woman with hypothyroidism and no history of smoking or alcohol use was admitted to Imam Reza Hospital (Mashhad, Iran) in October 2023 with complaints of palpitations. On admission, she was tachycardic (113 beats/min) with normal blood pressure (110/87 mmHg) and an oxygen saturation of 92% on room air. Lung auscultation was clear bilaterally, and initial laboratory results were unremarkable. Transthoracic echocardiography identified a secundum-type atrial septal defect (ASD) with severe tricuspid regurgitation (TR) and a reduced ejection fraction of 40%. The patient underwent surgical repair via a mini-right thoracotomy with femoral cannulation, which included ASD closure using a pericardial patch and TR repair via the bicuspidization technique. Six hours post-surgery, she developed cardiac tamponade, necessitating drainage in the operating room. Three days later, a chest X-ray revealed a massive right-sided pleural effusion (800 mL), accompanied by oxygen saturation levels dropping below 89% without supplemental oxygen. A chest tube was inserted, draining over 700 mL of serous fluid daily for a week. Despite conservative management, the effusion persisted.

Given the refractory nature of the pleural effusion, PRP-FG was administered in the affected area in two

separate applications, spaced one week apart. This intervention led to a significant reduction in pleural fluid drainage (less than 50 mL/day) within a few days without any serious adverse effects. The patient showed marked clinical improvement and was discharged in stable condition after a one-week observation period. Figure 2 illustrates chest X-rays before and after PRP-FG administration, demonstrating the resolution of the pleural effusion. At her six-month follow-up clinic visit, the patient reported no complications or recurrence of symptoms, and no serious issues were noted during the follow-up period.

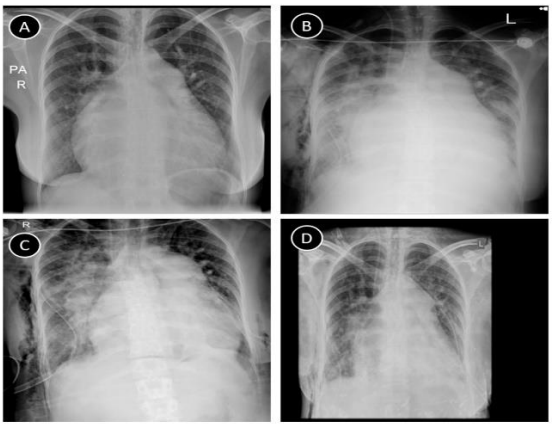

Figure 2. Chest radiographs of Case 1: (A) preoperative image; (B) postoperative image showing cardiac tamponade; (C) following tube thoracostomy placement; (D) four days after intrapleural platelet-rich plasma fibrin glue (PRP-FG) administration, demonstrating remarkable resolution of the pleural effusion.

Case 2

A 66-year-old man with a medical history of hypertension, type 2 diabetes mellitus, dyslipidemia, and chronic tobacco use underwent elective CABG in July 2023 after angiography revealed three-vessel coronary artery disease. Two weeks postoperatively, he presented to our center with progressive dyspnea.

On admission, he appeared lethargic, with bilateral lower-limb edema and weak peripheral pulses. Vital signs showed a blood pressure of 140/90 mmHg, heart rate of 100 beats/min, and oxygen saturation of 90% on room air. Laboratory evaluation demonstrated leukocytosis (13.8 × 10^6/L), hyperglycemia (223 mg/dL), mildly elevated serum creatinine (1.6 mg/dL), and hypoalbuminemia (2.7 g/dL). Imaging, including chest radiography and ultrasound, confirmed bilateral pleural effusions;hencs, bilateral chest tubes were inserted via thoracostomy.

Despite one week of optimized conservative therapy, drainage remained excessive (>400 mL/day). Intrapleural PRP-FG therapy was therefore initiated. The patient received one PRP-FG instillation through the right chest tube, followed by a second application to the same side after one week. Given the bilateral pleural involvement, an additional PRP-FG instillation was performed on the left side two weeks after the initial dose. Drainage volumes on both sides decreased to <50 mL/day within two days of the final administration.

The patient exhibited rapid clinical and radiologic improvement and was discharged in stable condition. At the six-month follow-up, he remained asymptomatic, with no recurrence of effusion or treatment-related complications. Figure 3 demonstrates chest radiographs obtained before and after PRP-FG therapy, showing complete resolution of the bilateral effusions.

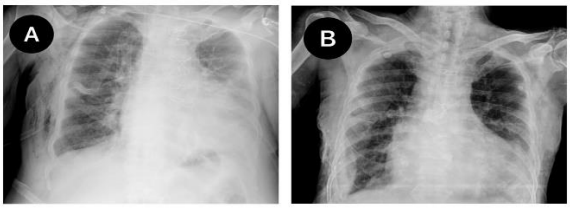

Figure 3. Chest radiographs of Case 2: (A) two weeks after cardiac surgery, showing bilateral pleural effusion and dyspnea; (B) two days after intrapleural platelet-rich plasma fibrin glue (PRP-FG) administration, demonstrating marked radiologic improvement.

Case 3

A 61-year-old woman with dyslipidemia and long-term tobacco use, suggestive of chronic obstructive pulmonary disease (COPD), underwent CABG in September 2023 following an acute myocardial infarction.

During the three months postoperatively, she developed progressively worsening dyspnea and orthopnea and was admitted for further evaluation. On admission, her vital signs were stable. Chest radiography revealed a large right-sided pleural effusion (~1100 mL) (Figure 4A)
; hence a chest tube was inserted.

CT angiography demonstrated filling defects in the segmental branches of both pulmonary arteries and the right interlobar branches, consistent with pulmonary embolism. She was managed according to pulmonary embolism protocols, including anticoagulation and diuretic therapy, while pleural drainage was continued. Despite one week of medical management, drainage remained high (~800 mL/day) with no sign of improvement.

Intrapleural PRP-FG therapy was therefore initiated, administered in two sessions, spaced one week apart. Within two days of the first instillation, drainage markedly decreased, accompanied by substantial

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radiologic improvement (Figure 4B). The patient's respiratory status improved significantly, and she remained clinically stable throughout follow-up. At follow-up, the patient reported only mild dyspnea attributed to pre-existing COPD; however,showed overall significant improvement in respiratory status compared to her preoperative condition, with notable compliance to her medication regimen.

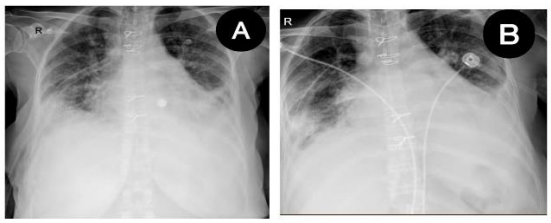

Figure 4. Chest radiographs of Case 3: (A) on admission, showing a large right-sided pleural effusion; (B) two days after the first intrapleural platelet-rich plasma fibrin glue (PRP-FG) administration, demonstrating marked resolution of the effusion.

3. Discussion

RPE after cardiac surgery remains a significant postoperative challenge, with no standardized treatment algorithm currently available. Although pleural effusion is a common finding in the early postoperative period, only a small subset (7–10%) of patients develop persistent effusions that cause clinically significant symptoms, most often dyspnea rather than pain or fever (16). However, recent studies have reported that up to 15% of patients develop pleural effusions requiring interventional management (4,17). The optimal duration of conservative therapy remains a topic of debate and varies based on factors such as the volume of pleural fluid drainage and other clinical indicators that influence the urgency of definitive treatment. prolonged chest tube drainage carries significant risks, including an increased likelihood of infection, electrolyte imbalances, nutritional deficiencies, and even higher mortality rates (3,18). Additionally, extended drainage may reduce patients' tolerance for subsequent surgical interventions, further complicating their clinical management. Current treatment paradigms generally follow a stepwise approach, beginning with conservative measures, such as therapeutic thoracostomy, diuretics, colchicine, and anti-inflammatory agents, before escalation to more invasive procedures when indicated (4,17,19).

In this pilot study, PRP-FG was evaluated as a novel, biologically based approach for RPE unresponsive to standard therapy. Fibrin sealants have long been recognized for their hemostatic and adhesive properties, initially used in cardiovascular surgery to control bleeding and later expanded to gastrointestinal anastomosis and wound healing (20–22). However, their role in pleurodesis remains largely unexplored. Our findings demonstrate that PRP-FG effectively reduced pleural drainage in all patients, with mean effusion volume decreasing from 624 ± 275 mL to 25 ± 20 mL ($p < 0.001$; Cohen's $d = 2.29$). Notably, five patients required a second application, yet no patient experienced recurrence within the six-month follow-up period. Importantly, no severe adverse effects were reported. Althouhg minor side effects such as transient pleuritic pain and mild dyspnea were observed, these symptoms were self-limited and resolved without additional intervention.

Josa et al. reported an 18.7% mortality rate among cardiac surgery patients due to pulmonary embolism (23). Notably, in our Case 3, despite the co-occurrence of pulmonary embolism and pleural effusion, the patient was successfully treated with PRP-FG therapy. Light et al. (2016) reported a predominance of left-sided effusions following CABG, whereas our study did not observe a statistically significant laterality difference, likely attributed to the small sample size (5). Notably,two patients in our study initially presented with unilateral right-sided pleural effusion. Following successful PRP-FG treatment, they were readmitted two months later with recurrent pleural effusion, but on the contralateral (left) side. Importantly, the side previously treated with PRP-FG remained free of effusion. Both patients were ultimately discharged successfully after receiving a second round of PRP-FG therapy on the left side.

The success of PRP-FG in this study may be attributed to its dual mechanism of action: fibrin glue provides a physical barrier to prevent fluid leakage, while PRP stimulates a biological healing response, promoting the formation of stable pleural adhesions (12,14,21,22,24,25). Compared to surgical interventions such as thoracotomy and pleurectomy, PRP-FG pleurodesis offers a less invasive and cost-effective alternative. Furthermore, unlike chemical pleurodesis, which relies on inflammatory agents such as talc or doxycycline and can cause significant discomfort or dangerous side effects, PRP-FG is a biocompatible option with minimal inflammatory response (26).

The PRP-FG administration procedure is cost-effective when compared to other invasive procedures such as thoracotomy. It does not require any additional invasive procedures, as it can be administered through a chest tube already in place to drain pleural effusion. Moreover, this technique is easily and safely repeatable to achieve therapeutic results, unlike other invasive procedures.

To the best of our knowledge, this is the first study to

investigate the use of PRP-FG for the management of postoperative RPE after cardiac surgery. Our results are consistent with recent studies conducted by the author demonstrating the utility of PRP-FG in managing other postoperative complications such as chylothorax and pneumothorax (13–15).

Ethical constraints imposed certain limitations on our study.Withholding a potentially beneficial treatment (PRP-FG) from a control group raised ethical concerns. In such cases, where established interventions (medical therapy, thoracentesis, and observation) are ineffective, patients might require more invasive procedures such as thoracotomy and decortication, which can carry a higher risk of complications and mortality (2). Additionally, the short follow-up period limited our ability to assess the long-term safety and effectiveness of PRP-FG therapy.

Multicenter studies with larger sample sizes and longer follow-up periods are recommended to validate our findings and provide more robust evidence for the efficacy and safety in managing postoperative pleural effusion.

In summary, this pilot study suggests that PRP-FG is a safe, effective, and minimally invasive option for managing refractory pleural effusion after cardiac surgery. Administration of PRP-FG led to a significant reduction in pleural drainage and rapid symptomatic improvement, with no major adverse events or recurrence observed during six-month follow-up. The treatment was well tolerated, easily repeatable, and offered a cost-effective alternative when conventional therapies fail. Larger multicenter studies with longer follow-up are warranted to confirm its long-term efficacy and to define its role in future clinical practice.

Acknowledgments

None

Ethical Considerations and Compliance with Ethical Guidelines

Ethical approval was obtained from the Mashhad University of Medical Sciences Ethics Committee (IR.MUMS.REC.1399.235), and all patients or their legal guardians provided written informed consent before participation. The trial was registered on ClinicalTrials.gov (Identifier: NCT06449131).
A control group was not included, as withholding the intervention from a subset of patients would have been unethical, given that the treatment was considered a last-resort therapeutic approach.

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

AI Using Declaration

During the preparation of this work, the authors used ChatGPT in order to check the grammar and improve readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Author's contributions

Author contribution: DHA, MAT, and AAM designed and performed the experiments. YM and MJ-N wrote the manuscript, and AAM, MHM, HH, PAT,RR, MJ-N, and MRN revised the manuscript. YM, and MRN carried out the data analysis. All authors reviewed, considered, and approved the manuscript.

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