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Efficacy of double filtration plasmapheresis in hyperlipidemia acute pancreatitis: a retrospective observational study

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Abstract

Background This study examines the role and effectiveness of double filtration plasmapheresis (DFPP) in managing hyperlipidemiclipidemic acute pancreatitis (HLAP).

Methods Comparative analysis was conducted between two groups: one treated with DFPP and one without. Comparative parameters included blood lipid levels, inflammatory factors, vital signs, disease severity scores, and complication rates.

Results A total of 97 HLAP patients were included in the study. Within-group analysis revealed significant pre- and post-treatment changes in total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), white blood cell count (WBC), neutrophil percentage (N%), systemic immune-inflammation index (SII), mean arterial pressure (MAP), bedside index for severity in acute pancreatitis (BISAP), and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores in the DFPP group ($P < 0.05$). In contrast, the without DFPP group showed significant changes in TC, TG, LDL-C, WBC, N%, SII, systemic inflammation response index (SIRI), panimmune-inflammation value (PIV), respiration rate (RR), and APACHE II scores ($P < 0.05$). Significant differences in TC, TG, HDL-C, LDL-C, and RR were found between the DFPP and without DFPP groups ($P < 0.05$). The DFPP group exhibited greater reductions in TG levels and more individual variability. In terms of complications, the rate of systemic inflammatory response syndrome (SIRS) differed significantly between the groups ($P < 0.05$).

Conclusions DFPP can significantly improve short-term outcomes, reduce lipid levels, and reduce the incidence of complications such as SIRS in HLAP patients compared with those not receiving DFPP treatment. The clinical utility of DFPP is considerable, and further exploration and implementation of this method are warranted.

Keywords Double filtration plasmapheresis, Hyperlipidemic acute pancreatitis, Treatment outcome

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Introduction

The global incidence of acute pancreatitis (AP) is increasing [1], primarily due to factors such as gallstones, alcohol intake, and hypertriglyceridaemia (HTG). Notably, in China, the incidence of HLAP cases has surpassed the incidence of alcohol-related AP, becoming the second most common cause, a shift attributed to improved living conditions and dietary changes [2].

The trend of AP increasingly affects younger individuals, who often present with multiple comorbidities and exhibit rapid disease progression, increasing the likelihood of severe complications, including SIRS, persistent organ failure, and increased mortality [3]. The lack of uniform treatment protocols further complicates the management of this disease. Studies suggest that TG and their lipolytic byproducts, free fatty acids (FFAs), contribute toxically to pancreatic health and are significantly correlated with both the frequency and severity of AP [4]. Consequently, early and effective reduction of elevated TG and FFA levels is posited to mitigate pancreatic damage and enhance patient outcomes. Effective management strategies for lowering serum TG levels include non-invasive and invasive approaches. Non-invasive methods include administering lipid-lowering agents, insulin, and heparin. In contrast, invasive methods include various blood purification techniques, such as blood perfusion, plasma exchange (PE), and continuous renal replacement therapy [5]. Notably, these interventions primarily yield transient effects on lipoproteins. Over the past decade, PE has been recognised as particularly efficacious in rapidly reducing TG levels in severe cases of HLAP. DFPP represents a semi-selective approach in which the concept is based on a dual filtration system: the first filter is the standard PE filter that separates blood cells from their plasma components; the second filter, with smaller pores, allows the passage of proteins with diameters smaller than 0.15 nm, thus excluding lipid-binding proteins [6]. Moreover, clinical investigations have demonstrated the superiority of DFPP over PE in effectively lowering TG levels.

Despite the continuous debate about the efficiency of DFPP in treating HLAP and the limited experience with therapy, DFPP has become a first-choice treatment in our centre due to its advantages over particular challenges, such as plasma shortages and allergic reactions. However, most previous studies on DFPP treatment for HLAP have focused primarily on limited indicators, such as lipid profiles or basic inflammatory markers [7, 8]. This study expands the scope by incorporating vital signs, disease severity scores, and novel inflammatory markers such as SII, SIRI, and PIV. These markers provide a more comprehensive perspective of the inflammatory response and immune status, offering deeper insights into the therapeutic effects of DFPP.

This study aimed to assess the clinical efficacy of DFPP in treating HLAP compared with conventional pharmacological treatments based on treatment outcome analysis of HLAP patients admitted to our hospital. This approach holds promise for offering more effective clinical treatment to patients with HLAP.

Methods

Study design

In this retrospective study, the clinical records of patients diagnosed with HLAP at the Department of Gastroenterology, Yan'an Hospital Affiliated to Kunming Medical University, between January 2019 and April 2024 were reviewed. The inclusion criteria included consistent upper AP with elevated blood amylase and/or lipase levels exceeding three times the upper normal limit and supporting imaging findings [9]. A confirmed AP diagnosis required at least two of these criteria to be met, in addition to serum TG levels reaching or exceeding 11.3 mmol/L. Exclusion criteria included cases with other aetiologies, such as biliary disorders, alcohol consumption, trauma, or malignancies; severely incomplete records; recurrent hospitalisations for HLAP; pregnancy; age younger than 18 years or older than 70 years; and those unable to undergo DFPP. Detailed clinical profiles, including age, sex, BMI, and pre-existing conditions such as diabetes and hypertension, were compiled for all participants.

Ethical approval for the study was obtained from the Ethics Committee, and informed consent was obtained from all participants. Each participant was also given a detailed explanation of the study's objectives and potential risks.

Treatment methods

The participants were divided into two groups based on the treatment received: the with DFPP group and the without DFPP group.

Without DFPP group: Patients were primarily treated with fenofibrate for lipid reduction, and some received low-molecular-weight heparin or insulin once contraindications were excluded.

DFPP group: In addition to standard pharmacotherapy for pancreatitis, these patients underwent DFPP treatment. DFPP was administered twice within 24 to 48 h after admission, following informed consent from patients and their families. ① Extracorporeal circulation: Vascular access was established using the Seldinger technique, employing a Haemodialysis Machine DX-10 from Jianfan and plasma separators from Asahi Kasei Medical Co., Ltd.: a plasma separator (first filter, PE-80) and a plasma component separator (second filter, EC-4A20). ② Treatment parameters: The blood flow rate was maintained at 120–130 mL/min. The plasma separation rate

was 20–25% of the blood flow through the first filter and 10–20% of this rate in the second filter. ③ Replacement fluids: 250 mL of 4% human albumin for the first group (200 mL of 0.9% sodium chloride injection + 10 g human albumin) and 250 mL of 0.9% sodium chloride injection for the second group. ④ Anticoagulation: The system was pre-flushed with heparinised saline, and regular heparin was administered during treatment, with dosage adjustments made based on coagulation function. Treatment was immediately discontinued if bleeding risks were identified. ⑤ DFPP sessions: Each patient in the DFPP group received two treatment sessions, processing 4–10 L of plasma each, lasting 2–4 h, as determined by the blood purification team according to the patient's condition. DFPP was discontinued once symptoms of AP were alleviated and serum TG levels fell below 11.3 mmol/L.

Observation and evaluation indicators

The following indicators were collected for both patient groups upon admission and on the third day after admission: ① Lipid Levels: TC, TG, LDL-C, and HDL-C; ② Inflammatory Markers: CRP, PCT, WBC count, N%, PIV, SIRI, and SII; ③ Basic Vital Signs: P, RR, and MAP; ④ Disease Scores: APACHE II score and BISAP score; and ⑤ Complications: SIRS, sepsis, AKI, respiratory failure, APFC, and ANC.

Note: ① The APACHE II score is a scoring system that includes acute physiological indicators, Glasgow Coma Scale points, age, chronic health factors, and a total of 15 items. Scores of ≥ 8 points indicate that moderate to severe AP (MSAP) or severe AP (SAP) should be considered. ② The BISAP score includes age, mental status, blood urea nitrogen level, SIRS, and pleural effusion. A score of ≥ 3 suggests the consideration of MSAP or SAP. ③ Calculation of PIV: PIV = neutrophil count × platelet count × monocyte count/lymphocyte count. ④ Calculation of the SIRI: SIRI = neutrophil count × monocyte count/lymphocyte count. ⑤ Calculation of the SII: SII = absolute neutrophil count × absolute platelet count/absolute lymphocyte count.

Statistical analysis

Analytical tests for normally distributed continuous variables involved independent and paired samples t tests for intergroup and intragroup comparisons. For skewed distributions, intergroup and intragroup analyses utilised the Wilcoxon rank-sum and paired Wilcoxon rank-sum tests, respectively. Categorical data were analysed using Pearson's chi-square test, with Fisher's exact test applied when appropriate. All statistical analyses were conducted using SPSS software version 26.0, and a P value of < 0.05 was considered statistically significant.

Results

Selection process for study subjects

This retrospective cohort study assessed 319 patients diagnosed with AP and HTG (serum TG > 1.70 mmol/L) based on inclusion and exclusion criteria. Among these patients, 167 were diagnosed with HLAP, and 152 were diagnosed with AP complicated by HTG. Within the HLAP group, 4 patients had two admissions, 2 were pregnant, 36 had severely incomplete data, 26 had AP due to other causes, and 2 could not tolerate DFPP treatment, resulting in 70 exclusions. Consequently, 97 patients were included in the study cohort, comprising 49 in the with DFPP group and 48 in the without DFPP group (Fig. 1).

Baseline characteristics of study subjects

The comparative analysis revealed no significant differences in sex, age, BMI, or medical history, including diabetes and hypertension, between the groups treated with and without DFPP ($P > 0.05$). For additional details, see Table 1.

Analysis of laboratory parameters, vital signs, and severity scoring for acute pancreatitis between the with DFPP group and the without DFPP group

Before Treatment: In the DFPP group, TG levels were 20.41 (14.21, 26.86) mmol/L, and LDL-C levels were 2.22 (1.57, 2.92) mmol/L. In the Without DFPP group, the TG level was 17.23 (13.82, 19.76) mmol/L, and the LDL-C level was 1.65 (1.47, 2.25) mmol/L. The differences in TG and LDL-C between the groups were statistically significant ($P < 0.05$), with higher levels observed in the DFPP group prior to treatment. However, the other indicators, such as TC, HDL-C, PCT, WBC, N%, CRP, SII, SIRI, PIV, MAP, P, RR, BISAP score, and APACHE II score, did not reach statistical significance ($P > 0.05$).

After treatment, in the DFPP group, the TC level was 3.03 (2.25, 3.97) mmol/L, TG level was 2.93 (2.16, 3.86) mmol/L, HDL-C level was 0.41 (0.30, 0.51) mmol/L, LDL-C level was 1.26 (0.85, 2.09) mmol/L, PCT level was 0.19 (0.11, 0.40) ng/mL, P was 78.00 (74.00, 82.00) time/min, RR was 19.00 (19.00, 19.00) time/min, and BISAP score was 0.00 (0.00, 0.00). In contrast, in the without DFPP group, the TC level was 6.64 (4.90, 8.70) mmol/L, the TG level was 4.95 (3.95, 7.46) mmol/L, the HDL-C level was 0.63 (0.51, 0.70) mmol/L, the LDL-C level was 2.95 (2.30, 4.05) mmol/L, the PCT level was 0.44 (0.15, 1.04) ng/mL, the P was 80.00 (78.50, 87.00) time/min, the RR was 19.00 (18.00, 19.00) time/min, and the BISAP score was 0.00 (0.00, 1.00). Significant differences in lipid profiles were observed posttreatment; the DFPP group presented lower levels of TC, TG, HDL-C, and LDL-C than those untreated ($P < 0.05$). Other laboratory markers, such as the WBC count, N%, CRP, SII, SIRI,

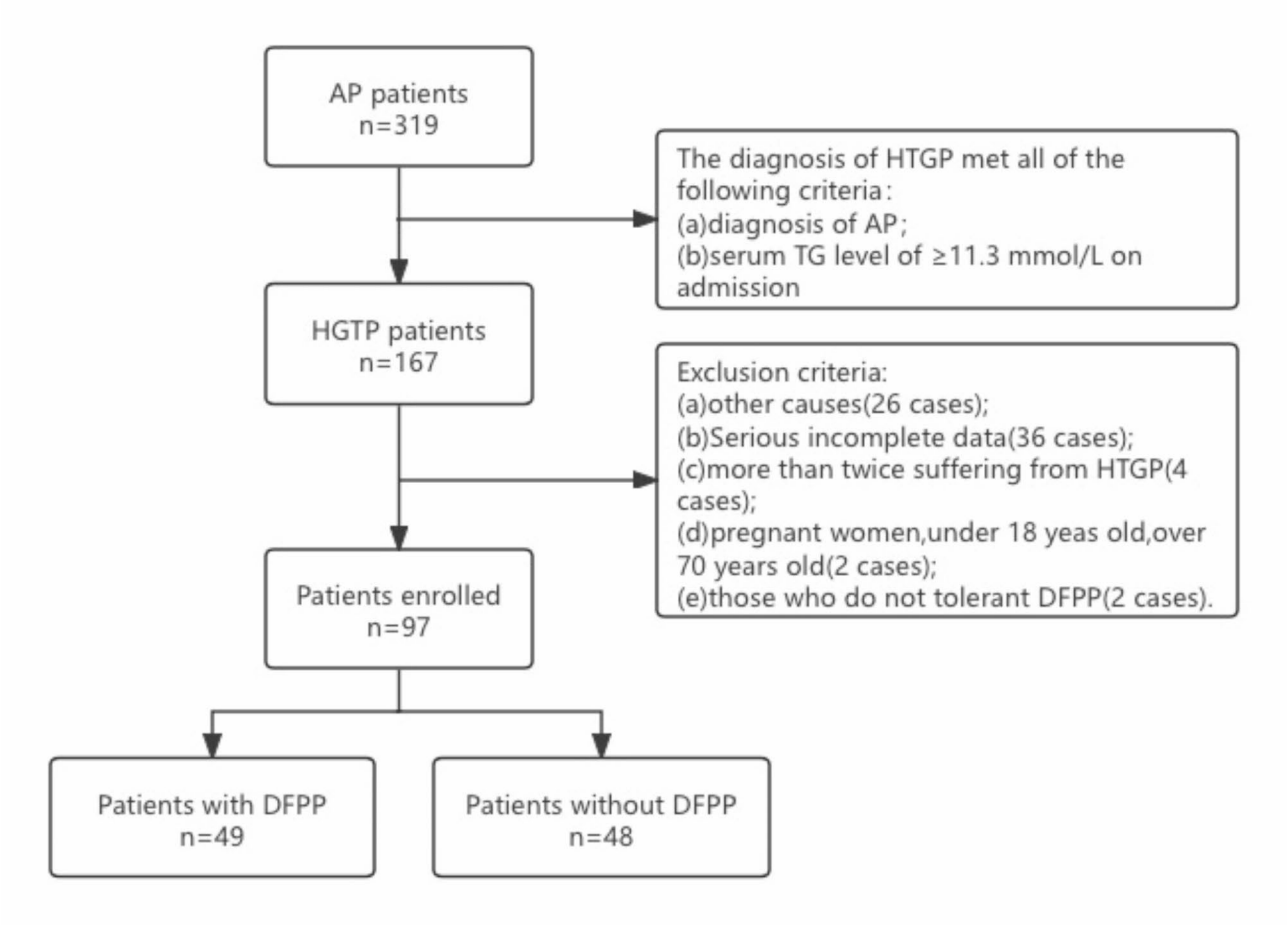

Fig. 1 Selection process for study subjects

Table 1 Baseline characteristics of patients

Variable	With DFPP group (*n* = 49)	Without DFPP group(*n* = 48)	*P*
Gender, *n* (%)			0.211
Male	40.00 (81.63%)	34.00 (70.83%)	
Female	9.00 (18.37%)	14.00 (29.17%)	
Age, median (IQR), years	39.61 ± 11.50	40.42 ± 10.45	0.719
BMI, median (IQR), kg/m^2	26.00 (23.90, 30.00)	25.95 (23.50, 29.40)	0.897
Comorbidity, *n* (%)			
Type 2 diabetes mellitus			0.153
No	29.00 (59.18%)	35.00 (72.92%)	
Yes	20.00 (40.82%)	13.00 (27.08%)	
Hypertension			0.341
No	37.00 (75.51%)	40.00 (83.33%)	
Yes	12.00 (24.49%)	8.00 (16.67%)	

and PIV, did not differ significantly between the groups ($P > 0.05$) (Table 2).

Analysis of Laboratory parameters within the with DFPP and without DFPP groups

With DFPP Group: significant pre- and post-treatment differences were observed in lipid levels, inflammatory markers, and clinical scores ($P < 0.05$). Notable changes included reductions in TC, TG, HDL-C, LDL-C, WBC, N%, and the SII and improved MAP, BISAP, and APACHE II scores. No significant changes were detected in PCT or CRP levels ($P > 0.05$).

Without DFPP Group: Conversely, the Without DFPP group showed significant pre- and post-treatment

Table 2 Differences in laboratory indicators, basic vital signs and severity scoring for acute pancreatitis between two groups

Variable	Pre Treatment			Post Treatment		
	With DFPP group($n=49$)	Without DFPP group($n=48$)	*P*	With DFPP group($n=49$)	Without DFPP group($n=48$)	*P*
TC, median(IQR), mmol/L	9.94 (7.71, 13.33)	9.43 (7.53, 11.28)	0.308	3.03 (2.25, 3.97)	6.64 (4.90, 8.70)	< 0.001***
TG, median(IQR), mmol/L	20.41 (14.21, 26.86)	17.23 (13.82, 19.76)	0.017*	2.93 (2.16, 3.86)	4.95 (3.95, 7.46)	< 0.001***
HDL, median(IQR), mmol/L	0.61 (0.52, 0.66)	0.61 (0.54, 0.73)	0.479	0.41 (0.30, 0.51)	0.63 (0.51, 0.70)	< 0.001***
LDL, median(IQR), mmol/L	2.22 (1.57, 2.92)	1.65 (1.47, 2.25)	0.040*	1.26 (0.85, 2.09)	2.95 (2.30, 4.05)	< 0.001***
PCT, median(IQR), ng/mL	0.13 (0.06, 0.41)	0.17 (0.09, 0.93)	0.181	0.19 (0.11, 0.40)	0.44 (0.15, 1.04)	0.005**
WBC, median(IQR), $\times 10^9$/L	11.55 (9.86, 14.15)	11.54 (8.99, 13.84)	0.743	8.36 (6.81, 10.86)	8.67 (5.50, 12.59)	0.843
N%, median(IQR),	83.00 (76.50, 85.80)	80.65 (74.95, 84.55)	0.188	72.25 (63.05, 77.25)	69.25 (55.10, 77.30)	0.379
CRP, median(IQR), mg/L	78.63 (52.76, 113.65)	86.14 (32.09, 128.41)	0.934	63.19 (28.61, 107.94)	48.14 (15.33, 94.89)	0.475
SII, median(IQR)	1,359.93 (959.00, 2,269.31)	1,180.62 (749.10, 2,098.11)	0.256	750.66 (416.19, 1,326.19)	673.30 (330.29, 1,215.68)	0.420
SIRI, median(IQR)	4.35 (2.96, 6.04)	4.24 (2.60, 7.15)	0.871	2.77 (1.39, 4.93)	2.05 (0.76, 4.40)	0.144
PIV, median(IQR)	887.76 (502.78, 1,303.55)	835.84 (464.87, 1,589.27)	0.882	440.94 (227.79, 1,074.22)	486.81 (157.80, 1,153.42)	0.470
MAP, median (IQR), mmHg	92.00 (86.67, 103.33)	87.67 (83.33, 95.00)	0.128	83.33 (83.33, 90.00)	86.67 (80.67, 90.00)	0.857
P, median (IQR), time/min	88.00 (78.00, 98.00)	85.50 (78.00, 100.00)	0.951	78.00 (74.00, 82.00)	80.00 (78.50, 87.00)	0.026*
RR, median (IQR), time/min	19.00 (19.00, 19.00)	19.00 (19.00, 19.00)	0.520	19.00 (19.00, 19.00)	19.00 (18.00, 19.00)	< 0.001***
BISAP Score, median (IQR)	1.00 (0.00, 1.00)	1.00 (0.00, 2.00)	0.369	0.00 (0.00, 0.00)	0.00 (0.00, 1.00)	0.018*
APACHE II score, median (IQR)	1.00 (1.00, 2.00)	1.00 (0.00, 2.00)	0.869	1.00 (0.00, 1.00)	0.00 (0.00, 2.00)	0.827

Note: [1]Median (Q1, Q3), [2]*$P<0.05$; **$P<0.01$; ***$P<0.001$。MAP = Diastolic Pressure + 1/3 (Systolic Pressure - Diastolic Pressure) (mmHg)

differences in TC, TG, LDL-C, WBC, N%, SII, SIRI, PIV, RR, and APACHE II scores ($P < 0.05$). HDL-C, PCT, and CRP remained unchanged ($P > 0.05$) (Table 3).

Comparison of pre- and post-treatment differences in laboratory parameters, basic vital signs, and severity scoring for acute pancreatitis between the with DFPP group and the Without DFPP group

When the changes in pre- and post-treatment values between the two groups were compared, the DFPP group showed a decrease in TC of -7.09 (-9.42, -4.76) mmol/L, TG of -17.40 (-24.51, -11.43) mmol/L, HDL-C of -0.22 (-0.34, -0.06) mmol/L, LDL-C of -0.92 (-1.66, -0.36) mmol/L, and RR of 0.00 (0.00, 0.00) time/min. In contrast, the Without DFPP group exhibited changes in TC of -2.54 (-4.59, -1.29) mmol/L, TG of -11.06 (-13.19, -8.46) mmol/L, HDL-C of -0.01 (-0.14, 0.11) mmol/L, LDL-C of -1.21 (-0.28, 1.93) mmol/L, and RR of 0.00 (-1.00, 0.00) time/min. The differences between these data points were statistically significant, with the DFPP group showing greater changes ($P < 0.05$). Other parameters, such as PCT, WBC, N%, CRP, SII scores, SIRI scores, PIV, MAP, P, BISAP scores, and APACHE II scores, were not significantly different ($P > 0.05$) (Table 4).

Comparison of complications between the with DFPP group and the without DFPP group

An analysis of local and systemic complications between the DFPP group and the Without DFPP group revealed notable differences in the occurrence of SIRS. In the DFPP group, the incidence was 17.00 (34.69%) compared with 32.00 (66.67%) in the Without DFPP group, indicating a statistically significant difference ($P < 0.05$). There were no significant differences in complications such as sepsis, AKI, APFC, or ANC between the groups ($P > 0.05$) (Table 5).

Comparison of TG reduction between the with DFPP group and the without DFPP group

As shown in Fig. 2, the DFPP group presented a higher median TG level and a broader range of values, including several outliers, with the highest value approaching 70. This finding reflects significant variability in TG levels among individuals in this group. In contrast, the Without DFPP group had a notably lower median TG level, with a more concentrated data distribution and fewer outliers, with the highest outlier being close to 20. Notably, the DFPP group presented a more significant reduction in TG levels, albeit with greater individual variability, indicating that DFPP may exert a more pronounced effect on TG reduction.

Discussion

HLAP is a form of AP caused by HTG, yet the exact pathophysiological mechanisms remain unclear. The role of HTG in the onset and progression of HLAP is critical, primarily due to the toxic effects of FFAs released from TG hydrolysis on pancreatic cells. Additionally, hyperlipidemia increases blood viscosity, and FFAs can stimulate platelets to secrete thromboxane, further developing localised microemboli and damaging capillaries. These factors exacerbate disturbances in the microcirculation, directly contributing to the disease process. Furthermore, it has been shown that there is a rare genetic susceptibility whereby extreme increases in TG can lead to pancreatitis, such as in multifactorial chylomicronaemia syndrome [10]. HTG might also facilitate the transformation of pancreatic cells from apoptosis to necrosis, further aggravating HLAP [11]. As a result, HLAP usually presents with more serious symptoms and a higher incidence of MODS than pancreatitis caused by other factors. Therefore, rapidly decreasing TG levels in the short term to break this vicious cycle is crucial in HLAP treatment. While previous studies on DFPP treatment for HLAP have focused primarily on limited indicators, such as lipid profiles or basic inflammatory markers, this study offers a more comprehensive analysis. This study evaluated a broader range of parameters, including blood lipid levels, inflammatory factors, vital signs, disease severity scores, and complication rates. Additionally, novel inflammatory markers such as SII, SIRI, and PIV were incorporated, providing deeper insights into the inflammatory response and immune status of patients. This approach allows for a more thorough and clinically meaningful evaluation of DFPP efficacy and its potential advantages in treating HLAP.

This research examined the alterations in key indicators among HLAP patients subjected to DFPP treatment compared to those who underwent standard medical interventions to evaluate the efficacy of DFPP. The analysis revealed no substantial differences between the groups in terms of age, sex, BMI, or pre-existing health conditions. However, as shown in Table 1, both the With DFPP group (average BMI 26 kg/m^2) and the Without DFPP group (average BMI 25.95 kg/m^2) fell within the overweight category (BMI: 24–27.9 kg/m^2). Research indicates that a BMI ≥ 25 kg/m^2 increases the risk of SAP [12]. Additionally, this study found that HLAP patients were predominantly male, which may be associated with more prevalent unhealthy lifestyle habits among men. The average age of the study population was 40.6 years, indicating a trend towards younger individuals developing HLAP, potentially due to unhealthy dietary and lifestyle choices.

The current literature suggests maintaining the serum TG level below 5.6 mmol/L as an optimal target [13, 14].

Table 3 Within-group differences in laboratory indicators, basic vital signs, and severity scoring for acute pancreatitis

	With DFPP group($n=49$)			Without DFPP group($n=48$)		
Variable	**Pre Treatment**	**Post Treatment**	***P***	**Pre Treatment**	**Post Treatment**	***P***
TC, median(IQR), mmol/L	9.94 (7.71, 13.33)	3.03 (2.25, 3.97)	< 0.001***	9.43 (7.53, 11.28)	6.64 (4.90, 8.70)	< 0.001***
TG, median(IQR), mmol/L	20.41 (14.21, 26.86)	2.93 (2.16, 3.86)	< 0.001***	17.23 (13.82, 19.76)	4.95 (3.95, 7.46)	< 0.001***
HDL, median(IQR), mmol/L	0.61 (0.52, 0.66)	0.41 (0.30, 0.51)	< 0.001***	0.61 (0.54, 0.73)	0.63 (0.51, 0.70)	0.595
LDL, median(IQR), mmol/L	2.22 (1.57, 2.92)	1.26 (0.85, 2.09)	< 0.001***	1.65 (1.47, 2.25)	2.95 (2.30, 4.05)	< 0.001***
PCT, median(IQR), ng/mL	0.13 (0.06, 0.41)	0.19 (0.11, 0.40)	0.326	0.17 (0.09, 0.93)	0.44 (0.15, 1.04)	0.480
WBC, median(IQR), $\times 10^9$/L	11.55 (9.86, 14.15)	8.36 (6.81, 10.86)	< 0.001***	11.54 (8.99, 13.84)	8.67 (5.50, 12.59)	< 0.001***
N%, median(IQR),	83.00 (76.50, 85.80)	72.25 (63.05, 77.25)	< 0.001***	80.65 (74.95, 84.55)	69.25 (55.10, 77.30)	< 0.001***
CRP, median(IQR), mg/L	78.63 (52.76, 113.65)	63.19 (28.61, 107.94)	0.098	86.14 (32.09, 128.41)	48.14 (15.33, 94.89)	0.118
SII, median(IQR)	1,359.93 (959.00, 2,269.31)	750.66 (416.19, 1,326.19)	< 0.001***	1,180.62 (749.10, 2,098.11)	673.30 (330.29, 1,215.68)	< 0.001***
SIRI, median(IQR)	4.35 (2.96, 6.04)	2.77 (1.39, 4.93)	0.011*	4.24 (2.60, 7.15)	2.05 (0.76, 4.40)	< 0.001***
PIV, median(IQR)	887.76 (502.78, 1,303.55)	440.94 (227.79, 1,074.22)	0.017*	835.84 (464.87, 1,589.27)	486.81 (157.80, 1,153.42)	< 0.001***
MAP, median (IQR), mmHg	92.00 (86.67, 103.33)	83.33 (83.33, 90.00)	< 0.001***	87.67 (83.33, 95.00)	86.67 (80.67, 90.00)	0.037*
P, median (IQR), time/min	88.00 (78.00, 98.00)	78.00 (74.00, 82.00)	0.004**	85.50 (78.00, 100.00)	80.00 (78.50, 87.00)	0.030*
RR, median (IQR), time/min	19.00 (19.00, 19.00)	19.00 (19.00, 19.00)	0.020*	19.00 (19.00, 19.00)	19.00 (18.00, 19.00)	< 0.001***
BISAP Score, median (IQR)	1.00 (0.00, 1.00)	0.00 (0.00, 0.00)	< 0.001***	1.00 (0.00, 2.00)	0.00 (0.00, 1.00)	0.003**
APACHE II score, median (IQR)	1.00 (1.00, 2.00)	1.00 (0.00, 1.00)	< 0.001***	1.00 (0.00, 2.00)	0.00 (0.00, 2.00)	< 0.001***

Note: [1]Median (Q1, Q3)。 [2]*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

Table 4 Differences in laboratory indicators and basic vital signs pre- and post-treatment

Variable	With DFPP group($n=49$)	Without DFPP group($n=48$)	*P*
ΔTC, median(IQR), mmol/L	-7.09 (-9.42, -4.76)	-2.54 (-4.59, -1.29)	< 0.001***
ΔTG, median(IQR), mmol/L	-17.40 (-24.51, -11.43)	-11.06 (-13.19, -8.46)	< 0.001***
ΔHDL, median(IQR), mmol/L	-0.22 (-0.34, -0.06)	-0.01 (-0.14, 0.11)	< 0.001***
ΔLDL, median(IQR), mmol/L	-0.92 (-1.66, -0.36)	1.21 (0.28, 1.93)	< 0.001***
ΔPCT, median(IQR), ng/mL	0.04 (-0.04, 0.10)	0.04 (-0.32, 0.78)	0.568
ΔWBC, median(IQR), $\times 10^9$/L	-2.15 (-4.11, 0.16)	-2.56 (-5.22, -0.56)	0.519
ΔN%, median(IQR),	-8.95 (-15.40, -5.40)	-10.00 (-21.85, -5.90)	0.517
ΔCRP, median(IQR), mg/L	-10.04 (-58.06, 28.12)	-17.88 (-67.84, 20.53)	0.991
ΔSII, median(IQR)	-513.43 (-1,250.37, -191.07)	-572.54 (-1,123.78, -189.53)	0.712
ΔSIRI, median(IQR)	-0.84 (-3.23, 0.55)	-2.40 (-3.49, -0.79)	0.071
ΔPIV, median(IQR)	-203.27 (-721.23, 42.55)	-368.57 (-872.99, -87.94)	0.304
ΔMAP, median (IQR), mmHg	-8.66 (-16.67, 1.00)	-3.34 (-13.00, 3.34)	0.154
ΔP, median (IQR), time/min	-6.00 (-20.00, 3.00)	-6.50 (-20.00, 5.50)	0.566
ΔRR, median (IQR), time/min	0.00 (0.00, 0.00)	0.00 (-1.00, 0.00)	0.008**
ΔBISAP Score, median (IQR)	0.00 (-1.00, 0.00)	0.00 (-1.00, 0.00)	0.524
ΔAPACHE II score, median (IQR)	0.00 (-1.00, 0.00)	0.00 (-1.00, 0.00)	0.715

Note: Median (Q1, Q3), *$P<0.05$; **$P<0.01$; ***$P<0.001$

Table 5 Comparison of complications between the with DFPP group and the without DFPP group

Complications	With DFPP group($n=49$)	Without DFPP group($n=48$)	*P*
SIRS, *n* (%)	17.00 (34.69%)	32.00 (66.67%)	0.002**
Sepsis, *n* (%)	2.00 (4.08%)	3.00 (6.25%)	0.678
AKI, *n* (%)	0.00 (0.00%)	2.00 (4.17%)	0.242
Respiratory failure, *n* (%)	0.00 (0.00%)	2.00 (4.17%)	0.242
APFC, *n* (%)	37.00 (75.51%)	38.00 (79.17%)	0.667
ANC, *n* (%)	12.00 (24.49%)	12.00 (25.00%)	0.954

Note: *$P<0.05$; **$P<0.01$; ***$P<0.001$

DFPP reduces the need for fresh frozen plasma, minimising the risks associated with blood product transfusions. Traditional treatments for lipid reduction can be slow and limited in efficacy, and long-term use may impair liver function in patients. In contrast, DFPP can selectively remove pathogenic proteins, lipid metabolites, and inflammatory cytokines from plasma, thereby interrupting the progression of SIRS and improving patient prognosis. Additionally, DFPP treatment necessitates reduced fresh frozen plasma usage, diminishing the likelihood of allergic reactions and infections related to blood products. Lu et al. [15] reported that DFPP treatment rapidly and effectively lowers TG levels in HLAP patients compared with conservative treatment. Chang et al.'s study [16] indicated that patients who underwent DFPP within the first 24 h of hospitalisation experienced significant reductions in serum levels of TG, TC, and LDL-C. Specifically, TG levels decreased by an average of 71.2%, and 36.2% of patients achieved safe TG thresholds (TG < 5.65 mmol/L). In alignment with these findings, our study demonstrated that the baseline serum TG levels in the DFPP-treated group were significantly greater than those in the untreated group. However, following two DFPP sessions, TG levels decreased by approximately 85.6%. DFPP thus proved more effective at rapidly lowering TG levels than traditional pharmacological treatments, significantly reducing serum TC, HDL-C, and LDL-C levels posttreatment. Moreover, DFPP treatment can reduce disease-related complications [15, 16]. Our findings revealed a significant decrease in SIRS incidence among patients who received early DFPP treatment. This suggests that early initiation of DFPP for HLAP patients can effectively halt SIRS progression, reduce complications, shorten disease duration, and improve overall prognosis.

The BISAP scoring system is widely implemented in clinical practice to evaluate pancreatic necrosis and the associated mortality risk [17]. The analysis revealed no significant differences in BISAP scores between the two groups before treatment. However, after DFPP intervention, the BISAP scores of the treatment group were markedly lower than those of the untreated group. These findings suggest that DFPP not only rapidly reduces serum TG levels but also significantly decreases the rates of pancreatic necrosis and mortality, thus lowering the

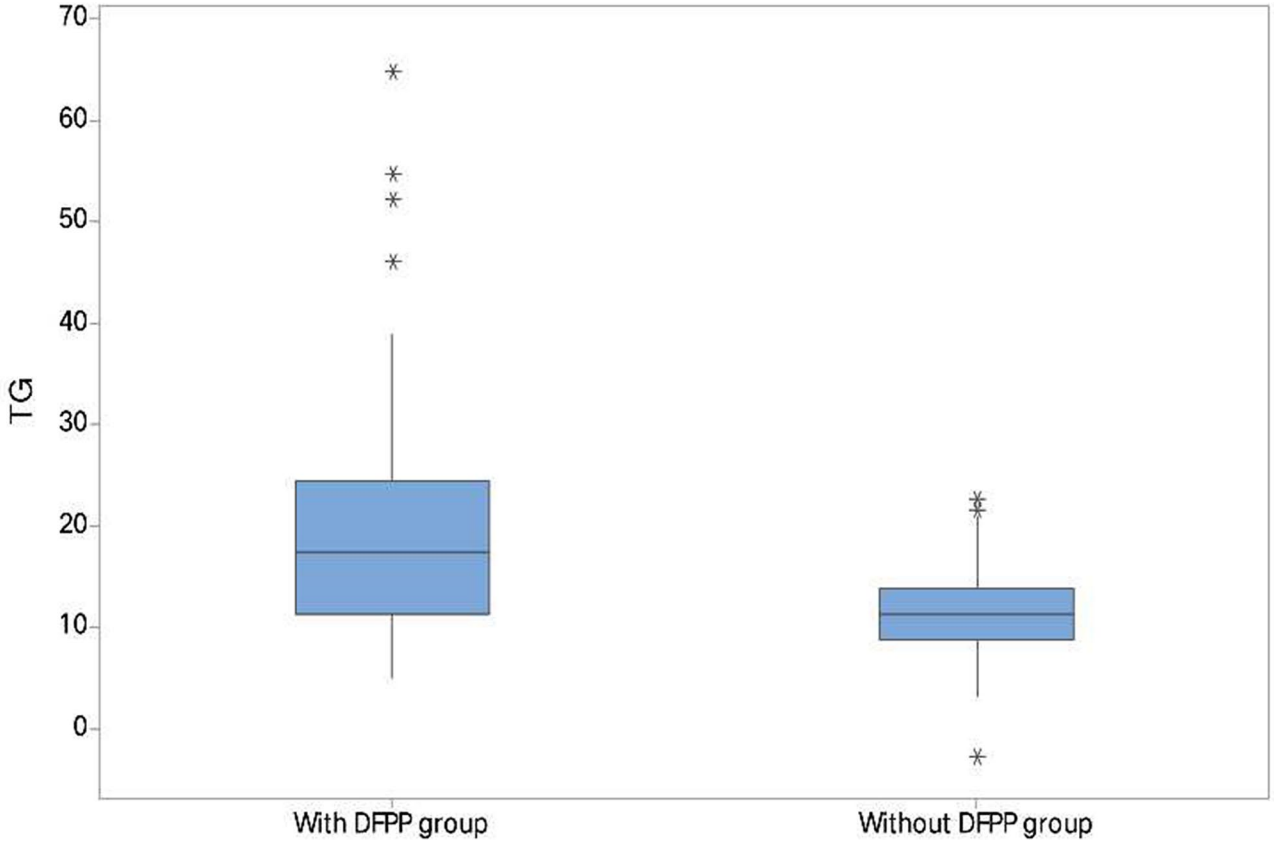

Fig. 2 Pre- and post-treatment comparison of TG levels in study cohort

risk of severe complications. Additionally, APACHE II scores were recorded for both cohorts before and after treatment. This score assesses the severity of illness and the associated mortality risk among critically ill individuals. As most study participants were in the early stages of their illness, there was no significant deterioration in their condition, resulting in stable APACHE II scores.

Moreover, DFPP has demonstrated benefits in reducing the levels of inflammatory markers. In this study, baseline inflammatory markers (PCT, WBC, N%, and CRP) exceeded normal ranges for both groups prior to treatment. After treatment, significant reductions in WBC, N%, and CRP levels were observed, whereas PCT levels tended to increase. This could be attributed to most patients being admitted within 24 h of symptom onset, potentially before initial serum PCT levels peak. Moreover, the increase in serum PCT levels was markedly less evident in the DFPP-treated cohort than in the control group, with posttreatment PCT levels significantly lower in the DFPP group. Given the critical role of inflammatory responses in AP, the SII and SIRI are emerging as potential biomarkers for predicting disease severity in AP patients [18]. An innovative biomarker, PIV is derived by accounting for counts of peripheral blood lymphocytes, neutrophils, monocytes, and platelets, incorporating a comprehensive spectrum of proinflammatory cells. This biomarker thus offers a more complete reflection of the body's inflammatory state and immune status. The study revealed that after treatment, the SII, SIRI, and PIV values of both groups were lower than those before treatment, with a greater reduction in the DFPP group. Although DFPP did not have a significant advantage over non-DFPP treatment in reducing inflammatory marker levels, the study results still provide a basis to suggest that DFPP contributes to diminishing inflammatory marker levels and blocking the disease course in patients receiving HLAP treatment.

Study strengths

Building on prior research, this study offers a comprehensive evaluation of DFPP in the short-term management of HLAP. It incorporates several novel immunoinflammatory markers, such as the SII, SIRI, and PIV. By integrating vital signs, disease severity scores, and complication rates, this multidimensional analysis provides a nuanced understanding of DFPP's underlying mechanisms in correcting dyslipidemic abnormalities, modulating systemic inflammation, and mitigating complications. These findings demonstrate that DFPP effectively lowers TG levels, significantly reduces the incidence of SIRS, and improves

short-term clinical outcomes, thereby providing more robust evidence for its potential role as a promising alternative to conventional therapeutic strategies.

Limitations

The study's retrospective, single-centre design limits generalisability and the small sample size may introduce bias. The lack of long-term follow-up prevents the assessment of the lasting effects of DFPP. Additionally, the lack of significant differences in the levels of inflammatory markers between the groups suggests that further research is needed.

Conclusions

In conclusion, this study highlights the efficacy of early DFPP intervention in HLAP patients for rapidly reducing serum TG levels, potentially mitigating the cycle of hypertriglyceridemia-induced pancreatic damage. Furthermore, DFPP has shown potential in reducing the incidence of SIRS and improving short-term outcomes. These findings indicate that DFPP could be a valuable therapeutic option for managing HLAP, especially in severe cases where traditional treatments may be less effective. These findings underscore the clinical importance of DFPP in improving patient prognosis by addressing both underlying hypertriglyceridemia and inflammatory complications, thereby offering a more efficient treatment approach than traditional therapies.

Despite these promising results, the study has several limitations. The retrospective, single-centre design limits the generalisability of the findings, and the relatively small sample size may introduce bias. Furthermore, while DFPP has demonstrated notable short-term efficacy, the lack of long-term follow-up prevents us from assessing its ability to maintain TG control and its impact on long-term prognosis. Additionally, the levels of inflammatory markers, while reduced, did not significantly differ from those in the group without DFPP, suggesting the need for further exploration of the role of DFPP in modulating inflammatory responses.

This study provides valuable insights into how DFPP can improve the clinical management of HLAP. By rapidly lowering TG levels and mitigating the progression of SIRS, DFPP can potentially reduce complications, shorten hospital stays, and improve patient outcomes. These findings have direct implications for clinical practice, suggesting that DFPP should be considered a front-line therapeutic option for HLAP patients, especially when conventional treatments are inadequate.

Abbreviations

DFPP	Double Filtrati on Plasmapheresis
HLAP	Hyperlipidemic Acute Pancreatitis
AP	Acute Pancreatitis
TG	Triglycerides
TC	Total Cholesterol
HDL-C	High-Density Lipoprotein Cholesterol
LDL-C	Low-Density Lipoprotein Cholesterol
WBC	White Blood Cell Count
N%	Neutrophil Percentage
SII	Systemic Immune-Inflammation Index
SIRI	Systemic Inflammation Response Index
PIV	Pan-Immune-Inflammation Value
MAP	Mean Arterial Pressure
RR	Respiration Rate
BISAP	Bedside Index for Severity in Acute Pancreatitis
APACHE II	Acute Physiology and Chronic Health Evaluation II
SIRS	Systemic Inflammatory Response Syndrome
PE	Plasma Exchange
FFA	Free Fatty Acids
MODS	Multiple Organ Dysfunction Syndrome
AKI	Acute Kidney Injury
APFC	Acute Peripancreatic Fluid Collection
ANC	Acute Necrotic Collection
PCT	Procalcitonin
BMI	Body Mass Index
IV	Intravenous
HTG	Hypertriglyceridemia

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Author contributions

Conception and study design: R. Qin, M.H. Yang, L.F. Zhou, H. wang; Data curation and analysis: Y.B. Liu, R. Ding, X.J. Chen, F. Zhang, Y.T. Liu, H.P. Jia, Y.Y. Duan; Research support: R. Qin, H. wang; Manuscript; original draft preparation: R. Qin, Y.B. Liu, L.F. Zhou, Y. Huang; Manuscript; review and editing: L.F. Zhou, H. wang; Supervision: R. Qin, L.F. Zhou, H. wang; Final approval of manuscript: all authors.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

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