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The last dance of coupled plasma filtration adsorption (CPFA): Clinical outcomes, challenges, and perspectives in multiple organ support therapy

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Cristian Pedreros-Rosales[1,2], Pilar Musalem[2], Cristóbal Alvarado Livacic[3,4], Hans Müller-Ortiz[1,2] and Gonzalo Ramírez-Guerrero[2]

Abstract

Background: Coupled plasma filtration and adsorption (CPFA) is a non-selective extracorporeal technique designed to modulate systemic inflammation through plasma filtration combined with resin-based adsorption. While preclinical data were promising, randomized trials in septic shock yielded conflicting results and raised safety concerns, leading to its discontinuation. Nonetheless, selected patients might benefit from CPFA when adequately delivered.

Methods: We performed a retrospective, single-center observational study of 36 critically ill patients treated with CPFA between 2019 and 2022. A total of 56 CPFA sessions were analyzed, evaluating clinical indications, plasma-treated volume (VPT), hemodynamic changes, and clinical outcomes.

Results: The main indication was sepsis (75%), followed by rhabdomyolysis and intoxications (8% each). Most patients received one to two sessions, with a mean duration of 9 ± 1 h and a VPT of $10{,}103 \pm 4275$ mL. Survival at 72 h and 28 days was 85% and 61%, respectively, with no early deaths. Patients achieving a VPT $\geqslant$18% of estimated plasma volume had better 28-day survival (81% vs 42%, $p = 0.03$), although they had lower initial severity scores. A non-significant trend toward vasopressor reduction was observed. No major adverse events occurred.

Conclusion: In this cohort, CPFA was feasible and safe, with possible hemodynamic and survival benefits when a sufficient plasma-treated volume was reached. Patient selection and optimized treatment delivery appear crucial. However, the retrospective design and lack of a control group limit definitive conclusions. Future research should focus on more effective and targeted extracorporeal strategies for immune modulation in critically ill patients.

Keywords
coupled plasma filtration adsorption, multiple organ support therapy, sepsis, rhabdomyolysis, liver failure

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Introduction

Coupled plasma filtration and adsorption (CPFA) is an extracorporeal technique that combines plasma separation with adsorption in a resin cartridge, followed by reinfusion and hemofiltration to manage volume overload and remove water-soluble mediators.

Although initially designed for sepsis, the resin also removes cytokines, myoglobin, toxins, and certain drugs, expanding CPFA's indications beyond infections.[1] Nonetheless, uncertainties remain about its optimal use, particularly regarding treatment timing and the absence of biomarkers to predict benefit over other extracorporeal techniques. Based on current evidence, CPFA can be considered a multi-organ support option in scenarios such as sepsis, non-infectious inflammatory syndromes, liver

[1]Departamento de Medicina Interna, Facultad de Medicina, Universidad de Concepción, Concepción, Chile
[2]Nephrology Service, Hospital Las Higueras, Talcahuano, Chile
[3]Facultad de Medicina, Universidad Católica de la Santísima Concepción, Concepción, Chile
[4]Biomedical Research Unit, Hospital Las Higueras, Talcahuano, Chile

Corresponding author:
Gonzalo Ramírez-Guerrero, Nephrology Service, Las Higueras Hospital, Alto Horno 777, Talcahuano, Región del Bío Bío 4270918, Chile.
Email: ramirezguerrero.g@gmail.com

failure, rhabdomyolysis, autoimmune neurologic diseases, and intoxications.[2]

While clinical trials have shown no mortality reduction with CPFA in sepsis,[3] this does not negate its potential for improving intermediate outcomes. Observational studies suggest CPFA can enhance mean arterial pressure (MAP), reduce vasopressor needs, and improve oxygenation,[4–9] with effectiveness appearing to depend on the plasma volume treated (VPT), regardless of hypotension duration.[10]

Due to limited evidence and lack of consensus, CPFA use has declined in favor of newer hemoadsorption strategies. CPFA was implemented in 2019 at our center and has been used in critically ill patients with various inflammatory conditions. This study describes our experience with CPFA in the Critical Care Unit of Hospital Las Higueras de Talcahuano from 2019 to 2022, analyzing clinical and technical outcomes to assess its applicability in clinical practice.

Methods

Study design

This retrospective cohort study included patients who underwent CPFA in the Critical Care Unit at Las Higueras Hospital between January 2019 and October 2022. All indications followed a standardized multimodal protocol aimed at hemodynamic stabilization, guided by predefined clinical and laboratory parameters (see Supplemental Figure S2).

Patient data collection

Demographic and clinical data were collected before and during CPFA. Variables included:

- **Biometric Data**: Age, height, weight, and BMI
- **Comorbidities:** Hypertension, diabetes mellitus, and chronic kidney disease
- **Pre-CPFA Clinical Status:** AKI (KDIGO), SAPS II, SOFA score, cumulative fluid balance, cardiac index, CRP, albumin, indexed vascular resistance (RVSI), capillary leak index, AST, pH, and hemoglobin
- **Clinical Outcomes:** 28-day mortality, vasopressor use reduction, and duration of mechanical ventilation

CPFA treatment, anticoagulation, and mortality follow-up

All patients received CPFA using a standardized circuit, including a plasma filter, hemofilter, and Mediasorb® resin cartridge (see Supplemental Figure S1). Indications comprised sepsis (with or without AKI), intoxications, liver failure, rhabdomyolysis, and other inflammatory syndromes.

Patients were evaluated at baseline, during treatment (1–8 h), and at ICU discharge. Monitored parameters included arterial lactate (mmol/L), mean arterial pressure (MAP, mmHg), PaO_2/FiO_2 ratio, and vasoactive drug doses (norepinephrine, epinephrine, and vasopressin in µg/kg/min). At treatment end, plasma volume treated (VPT) was calculated; a VPT $\geqslant$18% was considered adequate, based on prior studies.[10,11]

Patients with VPT $<$18% were classified by reasons for failure: circuit clotting, technical or organizational issues, patient death, lack of trained staff, or family decision. Two anticoagulation strategies were used: systemic heparin and regional citrate. Mortality was assessed at 4, 6, 15, and 28 days. The rationale for CPFA use and selection criteria are shown in Supplemental Figure S2.

Statistical analysis

Continuous and categorical variables are expressed as mean $\pm$ standard deviation and frequency (%), respectively. Kaplan-Meier analysis was used to compare mortality between patients with VPT $<$18% and $\geqslant$18%. Potential mortality predictors were assessed using Cox regression, with results reported as hazard ratios (HR) and beta coefficients. Statistical significance was set at $p < 0.05$. Analyses were performed using SPSS version 26.

Ethics approval and consent to participate

The Scientific Ethics Committee of the Talcahuano Health Service approved the protocol and waived informed consent, as the study used anonymized retrospective data. Patient consent for publication was not applicable.

Results

A total of 36 critically ill patients underwent CPFA between January 2019 and October 2022 at Las Higueras Hospital. As shown in Table 1, the mean age was 53 $\pm$ 15 years, with 69% male. The mean BMI was 30 $\pm$ 7 kg/m². Hypertension (47%) and diabetes mellitus (28%) were the most common comorbidities. Regarding AKI severity, 83% were classified as KDIGO stage 3, while 17% had stages 1 or 2. The mean SAPS II was 58 $\pm$ 12, and SOFA was 10 $\pm$ 4. Prior to CPFA, the mean cumulative fluid balance was 1849 $\pm$ 4706 mL, RVSI 1229 $\pm$ 416, and the capillary leak index 98 $\pm$ 84. The right femoral vein was the most frequent vascular access (64%).

Indications and outcomes of CPFA treatment

CPFA was mainly indicated for sepsis (n=27, 75%), followed by rhabdomyolysis and intoxications (n=3 each, 8%), liver failure (n=1, 4%), and other inflammatory syndromes (n=1, 4%). In total, 56 sessions were administered,

Table 1. Baseline characteristics and pre-treatment clinical variables of patients undergoing CPFA.

Variables	Total	Survivors	Non-survivors	*p*-value
Age (years)	53.3 ± 14.0	52.9 ± 10.7	53.5 ± 15.9	0.862
Gender (M)	M: 34 (61%); F: 22 (39%)	M: 14 (64%); F: 8 (36%)	M: 20 (59%); F: 14 (41%)	0.999
Height (m)	1.6 ± 0.1	1.7 ± 0.1	1.6 ± 0.1	0.116
Weight (kg)	82.5 ± 18.0	79.4 ± 19.5	84.6 ± 17.0	0.309
BMI	30.9 ± 6.5	28.8 ± 7.1	32.3 ± 5.8	0.065
HTA	0.4 ± 0.5	0.3 ± 0.5	0.4 ± 0.5	0.630
DM	0.3 ± 0.5	0.2 ± 0.4	0.4 ± 0.5	0.314
SAPS II	55.5 ± 12.5	52.7 ± 16.4	57.3 ± 9.2	0.249
SOFA	10.8 ± 3.0	9.3 ± 2.4	11.8 ± 2.9	<0.001
Water balance (mL)	915.6 ± 4945	159.8 ± 5580	1452.0 ± 4457	0.373
Cardiac Index (L/min/m^2)	4.1 ± 1.9	4.3 ± 1.9	4.0 ± 2.0	0.744
SVRI (dyn s/cm^5 m^2)	1283.4 ± 498	1295.8 ± 589	1271.9 ± 422	0.909
C-Reactive protein (mg/dL)	22.6 ± 15.1	21.5 ± 15.1	23.3 ± 15.3	0.668
Albumin (g/L)	23.6 ± 8.0	23.6 ± 8.9	23.6 ± 7.5	0.988
Capillary Leakage Index	112.9 ± 96.6	98.8 ± 71.9	121.8 ± 109.3	0.364
AST (U/L)	256.2 ± 395.9	92.5 ± 180.7	352.5 ± 455.1	0.005
pH	7.3 ± 0.1	7.2 ± 0.2	7.3 ± 0.1	0.713
Hemoglobin (g/dL)	10.8 ± 2.5	10.9 ± 2.3	10.8 ± 2.6	0.912

AKI: acute kidney injury; AST: aspartate aminotransferase; BMI: body mass index; CPFA: coupled plasma filtration adsorption; CRP: C-reactive protein; DM: diabetes mellitus; HTA: hypertension; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; SVR: systemic vascular resistance index.

Summary of demographic data, comorbidities, and baseline clinical variables from 36 critically ill patients treated with coupled plasma filtration adsorption (CPFA). Results are stratified by 28-day survival status. Data are expressed as mean ± standard deviation or number (percentage), as appropriate. Statistical comparisons between survivors and non-survivors were performed using *t*-tests or chi-square tests.

with most patients (94%) receiving one or two treatments. Sessions lasted 9 ± 1 h on average, and the mean plasma-treated volume was 10,103 ± 4275 mL (Table 2).

Following treatment, a non-significant reduction in vasopressor requirements was observed. Norepinephrine decreased from 0.4 ± 0.2 to 0.3 ± 0.4 µg/kg/min (p=0.06); epinephrine from 0.2 ± 0.2 to 0.1 ± 0.2 µg/kg/min (p=0.16); and vasopressin from 0.3 ± 1.0 to 0.1 ± 0.2 µg/kg/min (p=0.12; Figure 1, Supplemental Table S1).

A plasma-treated volume ⩾18% was reached in 75% of patients. The remaining 25% failed to meet this target, primarily due to hemodynamic intolerance (67%) and technical issues (25%). Compared to the ⩾18% group, these patients had significantly lower baseline MAP (63 ± 5 vs 70 ± 11 mmHg, p=0.02) and higher SOFA scores (13 ± 3 vs 10 ± 3, p=0.02), indicating more severe illness.

Early mortality (<72 h) was 15%. Overall mortality at 28 days was 57%. As illustrated in Figure 2 and Figure 3, survival was significantly better in patients with VPT ⩾18%, with a mean survival of 20 ± 12 days versus 10.9 ± 2.6 days in the <18% group (p=0.03).

Discussion

Despite the high mortality risk of our patients (⩾50% by SOFA score), our cohort showed lower early mortality (15% at 72 h) compared to COMPACT-2 and ROMPA, where early deaths reached 30.2% and 40.6%, respectively.[12,13] This suggests CPFA might be safer than previously thought and that early mortality may reflect illness severity more than the therapy itself (Figure 3). Furthermore, survival was significantly better in patients with treated plasma volume (VPT) ⩾18%, potentially due to greater hemodynamic stabilization. It is also noteworthy that our median SOFA score (10 ± 4) was lower than in COMPACT-2 and ROMPA (median 12), which may partially explain our more favorable outcomes. Similarly, the Toraymyxin® device showed benefit specifically in patients with SOFA scores between 7 and 12, a range resembling our cohort.[14] These findings highlight the importance of proper patient selection and achieving a VPT >18% to optimize CPFA efficacy and safety in septic shock.

Although limited in size and design, our study provides real-world data on CPFA's technical execution, safety, and potential dose-response effects, which may guide future developments in extracorporeal therapies involving hemoadsorption.

Achieving a VPT ⩾18% was associated with improved survival, yet only 75% of patients reached this target. This aligns with Berlot et al.[10] and Livigni et al.,[11] who also found technical limitations a major hurdle for effective CPFA delivery. In our cohort, the main barriers were hemodynamic intolerance (67%) and technical issues

Table 2. Technical characteristics and treatment parameters of CPFA therapy.

Parameter	Value
Patient and treatment summary	
Number of patients	36
Total number of sessions	41
Patients with one session	31 (86%)
Patients with two sessions	5 (14%)
Severity classification of Acute Kidney Injury (AKI)	
KDIGO Stage 0–2 (non-severe AKI)	6 (17%)
KDIGO Stage 3 (severe AKI)	30 (83%)
Vascular access	
Right femoral vein	32 (89%)
Left femoral vein	4 (11%)
CPFA session characteristics	
Mean duration of CPFA sessions (h)	9 ± 1
Plasma flow rate (mL/min)	30–40
Blood flow rate (mL/min)	175 ± 34
Substitution flow (mL/h)	2509 ± 612
Dialysate flow (mL/h)	1593 ± 1186
Effluent volume (mL/h)	4102 ± 1604
Treated plasma volume (mL/kg/session)	151 ± 48
Total volume of treated plasma (mL/session)	10,103 ± 4275
Anticoagulation strategy	
Systemic heparin	9 (25%)
Regional citrate	27 (75%)

Overview of treatment characteristics, vascular access, CPFA session parameters, and anticoagulation strategies used in 36 critically ill patients undergoing coupled plasma filtration adsorption (CPFA). Data are expressed as a number (percentage) or mean ± standard deviation, as appropriate.

(25%). Those failing to reach VPT goals had lower baseline MAP and higher SOFA scores, indicating more severe illness and potentially lower suitability for CPFA. These challenges may be mitigated through early optimization of hemodynamics, reliable vascular access, and regional anticoagulation protocols.

Our cohort included patients with varied indications (e.g. sepsis, rhabdomyolysis, and liver failure), introducing heterogeneity that may affect interpretation. Although we considered a comparator group, matching proved unfeasible due to the highly selected nature of CPFA cases and lack of available controls with comparable severity and timing. This underscores the need for prospective multicenter studies or registries. At the time of data collection, CPFA was the only hemoadsorption technique in routine use at our institution; other devices such as CytoSorb® had not yet been adopted or approved locally.

Mortality versus intermediate outcomes

A key challenge in evaluating CPFA is selecting appropriate clinical endpoints. Mortality, though frequently used, is

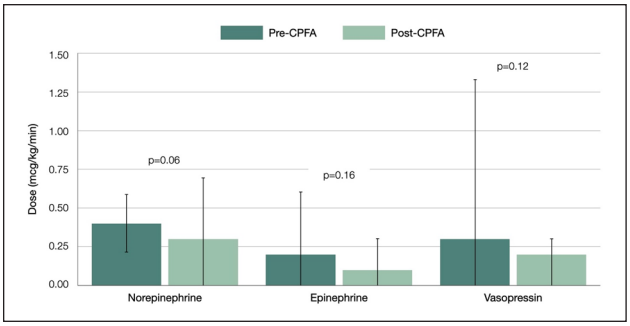


Figure 1. Vasoactive drug requirements before and after CPFA. Mean norepinephrine, epinephrine, and vasopressin doses before and after CPFA therapy. Although a downward trend was observed in all three agents following treatment, the differences were not statistically significant.

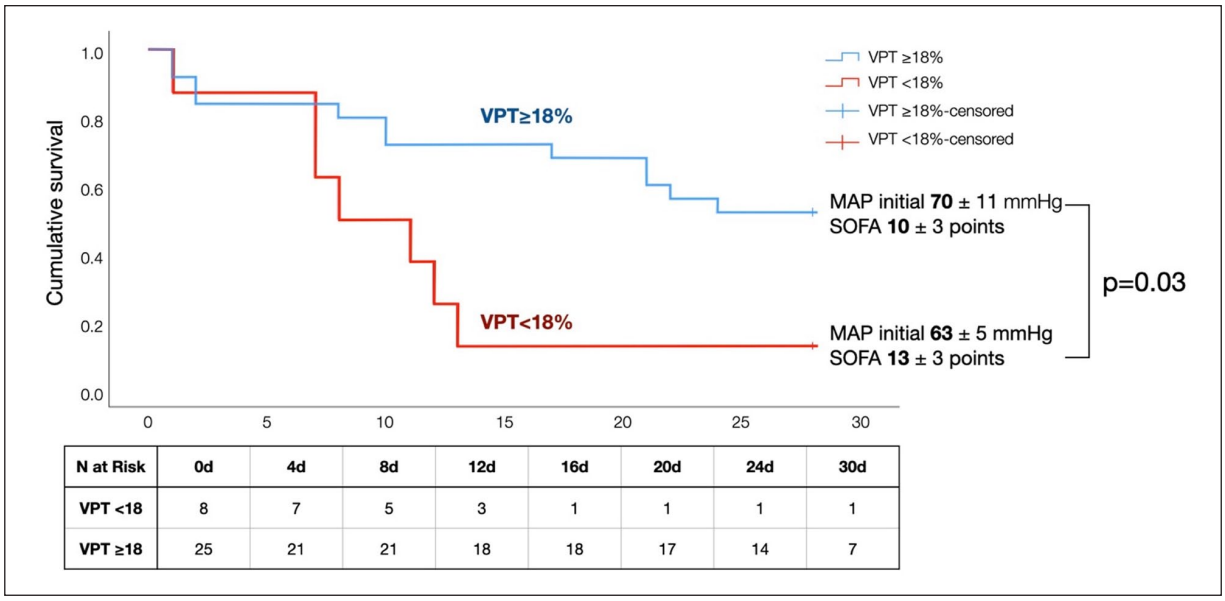
suboptimal in critically ill populations due to multifactorial influences and limited modifiability. In this setting, intermediate outcomes such as hemodynamic stabilization, vasopressor weaning, mechanical ventilation duration, and potential renal recovery may better capture therapeutic benefit.[15]

Our study supports viewing CPFA not as a mortality-reducing intervention, but as an adjunct in multi-organ support strategies aimed at stabilizing critically ill patients. Although we observed a trend toward lower vasopressor needs after CPFA, statistical significance was not reached, likely due to small sample size. Nevertheless, such trends may reflect either genuine improvement or natural evolution of illness. The observed reduction in vasoactive drugs (Figure 1), while modest, could still be clinically meaningful.

Limitations of the Mediasorb® cartridge

The Mediasorb® resin cartridge used in CPFA has not evolved significantly over the past decade, despite substantial advances in hemoadsorption technologies.[16,17] This stagnation may relate to the negative results in sepsis trials and subsequent safety concerns.[12] Technical improvements—such as enhanced solute clearance or optimized flow dynamics—could reinvigorate its performance, yet internal parameters like mass transfer zones and flow distribution remain poorly characterized.[18,19]

Moreover, several limitations of the Mediasorb® cartridge have been documented. Ronco et al.[5] described high circuit pressures and limited filtration rates as frequent technical challenges, potentially reducing treatment duration and increasing clotting risk. In a porcine model of septic shock, Sykora et al.[20]found no benefit from CPFA using Mediasorb®, and reported increased markers of oxidative and nitrosative stress, suggesting potential endothelial harm. Additionally, adsorbents with pore sizes >30 nm may reduce protein C and fibrinogen levels, disrupting coagulation and contributing to early circuit failure.[21]



N at Risk	0d	4d	8d	12d	16d	20d	24d	30d
VPT <18	8	7	5	3	1	1	1	1
VPT ≥18	25	21	21	18	18	17	14	7

Figure 2. Kaplan–Meier survival analysis according to plasma volume treated. Kaplan–Meier survival curves comparing 28-day survival in patients who achieved a plasma volume treated (VPT) ⩾18% versus those with VPT <18%. A significant survival advantage was observed in the higher VPT group.

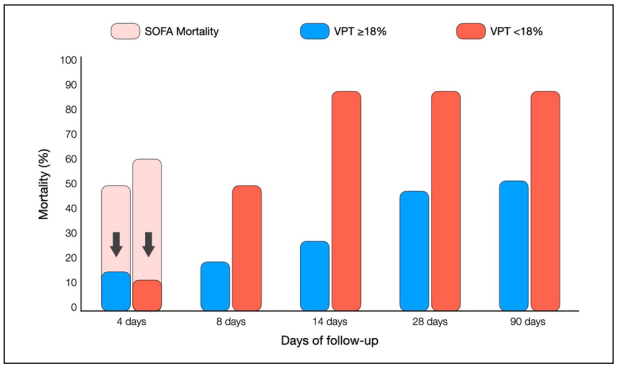


Figure 3. Observed early mortality versus SOFA-predicted mortality, stratified by plasma volume treated. Stacked bar chart comparing early mortality (<72 h) after CPFA with the mortality predicted by baseline SOFA scores. The chart illustrates that early mortality was lower than expected, particularly in patients who achieved a plasma volume treated (VPT) ⩾18%, suggesting a potential hemodynamic stabilizing effect of CPFA.

These findings highlight the need for improved cartridge materials that enhance solute removal without compromising vascular integrity or coagulation.

The rise of modern hemoadsorption

In contrast, modern hemoadsorption devices have rapidly advanced, targeting endotoxins, cytokines, and uremic toxins with greater specificity and safety, thereby displacing CPFA in most centers. Given their versatility and ease of integration into existing platforms, newer technologies are now preferred in both research and clinical settings. Although plasma adsorption remains conceptually attractive, the lack of innovation in CPFA has relegated its role to a niche context.

Study strengths and limitations

Our study has limitations. First, its retrospective design introduces selection bias and limits causality. Second, the sample size reduces generalizability and statistical power. Third, despite standardized protocols, heterogeneity in indications may have influenced outcomes. The small sample also constrains the ability to detect smaller but meaningful differences. Thus, observed associations should be interpreted cautiously, as hypothesis-generating rather than confirmatory.

Nonetheless, the study offers several strengths. It provides real-world data from a critically ill cohort, using a consistent CPFA protocol, thus enhancing internal validity. By focusing on intermediate rather than mortality outcomes, our findings reflect a more relevant perspective for extracorporeal therapy evaluation.

Importantly, these results may inform clinical decision-making and patient selection in centers where CPFA remains in use.

Conclusion

In this retrospective cohort, CPFA was feasible and generally well tolerated, with no major adverse events reported. Although a trend toward reduced vasopressor requirements was observed, it did not reach statistical

significance, and the extent of potential hemodynamic benefits remains uncertain.

Achieving an adequate plasma-treated volume may be important for maximizing therapeutic effect, but delivery was frequently limited by technical and clinical constraints. These observations underscore the relevance of patient selection and optimization of treatment logistics.

Given the limitations of CPFA—particularly regarding cartridge performance and delivery consistency—its use has declined in favor of more advanced hemoadsorption technologies. Future evaluation of extracorporeal therapies should prioritize intermediate outcomes over mortality.

Author contributions

CPR was responsible for conceptualization, methodology, supervision, and writing—original draft. PM and GRG contributed to data collection and curation, with GRG also involved in formal analysis and writing—review and editing. HMO supported the investigation and provided resources. CAL contributed to statistical analysis, validation, and visualization. All authors reviewed and approved the final version of the manuscript.

Declaration of conflicting interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: CPR has received honoraria for lectures from Fresenius Medical Care and Medtronic. GRG has received speaker fees from AstraZeneca, B. Braun, Baxter, Fresenius Medical Care, and Novo Nordisk. None of the other authors declare any competing interests. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article. The authors alone are responsible for the content and writing of this article.

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Ethical considerations

Biochemical and clinical parameters were collected with the approval of the Talcahuano Health Service's scientific ethics committee (approval number N°95.08.11.2022).

Consent to participate

The local ethics committee authorized waiver of informed consent due to the retrospective nature of the study and the anonymization of the data.

Consent for publication

The local ethics committee authorized waiver of informed consent due to the retrospective nature of the study and the anonymization of the data.

ORCID iD

Gonzalo Ramírez-Guerrero https://orcid.org/0000-0002-1696-9997

Data availability statement

All data generated or analyzed during this study are included in this published article.

Supplemental material

Supplemental material for this article is available online.

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