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Paper Accepted¹

ISSN Online 2406-0895

Original Article / Оригинални рад

Qiuyan Zhang[#], Tingting Wu[#], Xiao Fang^{*}

Association of Donabedian-based management with short-term outcomes in dialysis-independent survivors of acute kidney injury receiving continuous renal replacement therapy

Повезаност управљања заснованог на Донабедијановом моделу са краткорочним исходима код преживелих болесника са акутним оштећењем бубрега, независних од дијализе, лечених континуираном бубрежном надоместном терапијом

Nanjing Medical University, Nanjing First Hospital, Department of Emergency Intensive Care Unit, Nanjing, Jiangsu, China

[#]Contributed to the work equally

Received: September 11, 2025

Revised: September 9, 2026

Accepted: September 16, 2026

Online First: October 12, 2026

DOI: <https://doi.org/10.2298/SARH250911084Z>

¹**Accepted papers** are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the *Serbian Archives of Medicine*. They have not yet been copy-edited and/or formatted in the publication house style, and the text may be changed before the final publication.

Although accepted papers do not yet have all the accompanying bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: the author's last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI; e.g.: Petrović P, Jovanović J. The title of the article. *Srp Arh Celok Lek*. Online First, February 2017.

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***Correspondence to:**

Xiao FANG

Nanjing Medical University, Nanjing First Hospital, Department of Emergency Intensive Care Unit, No.68 Changle Road, Qinhuai District, Nanjing, 210000 Jiangsu, China.

E-mail: 13813076310@163.com

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SUMMARY

Introduction /Aim This study evaluated the association between implementation of a Donabedian-based management protocol and short-term laboratory, renal-function, urine-output, and fluid-management outcomes in patients with acute kidney injury receiving continuous renal replacement therapy.

Methods This retrospective before-and-after cohort study screened 155 consecutive patients aged ≥ 50 years with KDIGO-defined acute kidney injury who received continuous renal replacement therapy between January 2021 and January 2025. The analytical cohort comprised 100 patients who survived to hospital discharge, recovered sufficient kidney function to remain dialysis-independent at discharge, and had complete baseline and 72-h data; 43 patients treated from January 2021 to December 2022 constituted the routine group, whereas 57 patients treated after protocol implementation, from January 2023 to January 2025, constituted the intervention group. The primary outcome was serum IL-6 concentration 72 h after continuous renal replacement therapy initiation; secondary outcomes included other inflammatory and stress-response biomarkers, blood-gas and coagulation indices, renal-function markers, serial urine output, fluid-balance compliance, and ICU length of stay.

Results Of the 155 patients who received continuous renal replacement therapy, 110 survived to discharge, corresponding to an overall hospital survival rate of 71.0%; 100 dialysis-independent survivors were included in the comparative analysis. At 72 h, serum IL-6 was lower in the intervention group than in the routine group (60.39 ± 16.37 vs. 73.89 ± 18.04 pg/mL; $P < 0.001$). After adjustment for baseline IL-6, age, sex, sepsis, the sequential organ failure assessment (SOFA) score, vasopressor support, baseline urine output, and baseline serum creatinine, the adjusted between-group difference was -13.21 pg/mL (95% confidence interval, -20.34 to -6.07 ; $P < 0.001$). The intervention group also had more favorable inflammatory, stress-response, blood-gas, coagulation, renal-function, urine-output, and fluid-balance indices, although ICU length of stay was slightly longer (13.84 ± 3.67 vs. 12.40 ± 3.43 days; $p = 0.047$).

Conclusions Among selected hospital survivors who were dialysis-independent at discharge, Donabedian-based management was associated with more favorable 72-h laboratory, urine-output, and fluid-management outcomes, but not with a shorter ICU stay; survivor selection, the before-and-after design, and the multicomponent nature of the protocol preclude causal interpretation.

Keywords: acute renal failure; continuous blood purification; Donabedian model; inflammatory response; stress response

САЖЕТАК

Увод /Циљ Циљ овог истраживања био је да се процени повезаност између примене протокола управљања заснованог на Донабедијановом моделу и краткорочних лабораторијских показатеља, параметара бубрежне функције (БФ), диурезе и управљања течним билансом код болесника са акутним оштећењем бубрега који су лечени континуираном бубрежном надоместном терапијом (КБНТ).

Методе У овој ретроспективној кохортној студији пре и после увођења протокола прегледано је 155 узастопних болесника старости ≥ 50 година са акутним оштећењем бубрега дефинисаним према критеријумима КДИГО, који су примали КБНТ у периоду од јануара 2021. до 2025. године. Аналитичку кохорту чинило је 100 болесника који су преживели до отпуста из болнице, повратили довољну БФ да при отпусту не зависе од дијализе и имали потпуне почетне податке и податке након 72 часа. Рутинску групу чинила су 43 болесника лечена од јануара 2021. до децембра 2022. године, док је интервентну групу чинило 57 болесника лечених након увођења протокола, од јануара 2023. до 2025. године. Примарни исход била је концентрација интерлеукина 6 у серуму 72 часа након започињања КБНТ. Секундарни исходи обухватали су остале инфламаторне и стресне биомаркере, параметре гасне анализе крви и коагулације, показатеље БФ, серијски праћену диурезу, усклађеност са циљним билансом течности и дужину боравка у јединици интензивне неге (ЈИН).

Резултати Од 155 болесника који су примали КБНТ, 110 је преживело до отпуста из болнице, што одговара укупној стопи болничког преживљавања од 71%; у упоредну анализу укључено је 100 преживелих болесника који при отпусту нису зависили од дијализе. Након 72 часа, концентрација интерлеукина 6 у серуму била је нижа у интервентној него у рутинској групи ($60,39 \pm 16,37$ према $73,89 \pm 18,04$ pg/mL; $p < 0,001$). Након прилагођавања за почетну концентрацију интерлеукина 6, старост, пол, сепсу, СОФА скор, примену вазопресора, почетну диурезу и почетну концентрацију серумског креатинина, прилагођена разлика између група износила је $-13,21$ pg/mL (95% интервал поверења: $-20,34$ до $-6,07$; $p < 0,001$). Интервентна група је такође имала повољније инфламаторне и стресне биомаркере, параметре гасне анализе крви, коагулације, БФ, диурезе и течног биланса, иако је боравак у ЈИН био нешто дужи ($13,84 \pm 3,67$ према $12,40 \pm 3,43$ дана; $p = 0,047$).

Закључак Код одабраних болесника који су преживели до отпуста и нису зависили од дијализе, управљање засновано на Донабедијановом моделу било је повезано са повољнијим лабораторијским показатељима, већом диурезом и бољим управљањем течним билансом након 72 часа, али не и са краћим боравком у ЈИН. Селекција преживелих болесника, дизајн студије пре и после увођења протокола и вишеккомпонентна природа интервенције онемогућавају узрочно тумачење резултата.

Кључне речи: акутно оштећење бубрега;
континуирана бубрежна надоместна терапија;
Донабедијанов модел; унапређење квалитета;
инфламаторни одговор

INTRODUCTION

Acute kidney injury (AKI) is a frequent and clinically heterogeneous complication in critically ill patients. In the multinational AKI-EPI study [1], 57.3% of general ICU patients met the complete KDIGO criteria for AKI, whereas the EPIS-AKI study reported postoperative AKI in 18.4% of patients undergoing major surgery followed by ICU or high-dependency care [2]. AKI commonly occurs in association with sepsis, major surgery, cardiac dysfunction, hemodynamic instability, nephrotoxic exposure, and pre-existing comorbidity; these factors may influence inflammatory activation, neuroendocrine stress, urine output, kidney recovery, and mortality [3]. Continuous renal replacement therapy provides sustained control of solute concentrations, acid-base status, electrolytes, and fluid balance in hemodynamically unstable patients. Nevertheless, its clinical effects remain strongly dependent on the underlying illness, disease severity, treatment prescription, and quality of care delivery, and available evidence does not establish a consistent hospital-mortality advantage over intermittent hemodialysis [4]. The structure–process–outcome framework for evaluating healthcare quality was first described by Avedis Donabedian in 1966 and was subsequently developed into a widely used approach for examining how organizational resources and care processes relate to patient outcomes [5].

Holmes et al. [6] applied Donabedian's framework to the development of laboratory-based indicators for monitoring AKI-related healthcare outcomes, demonstrating how routinely collected serum creatinine data may support quality measurement and service improvement. Their study did not, however, evaluate a patient-level Donabedian-based treatment protocol or demonstrate improved survival.

Accordingly, this retrospective before-and-after study compared inflammatory and stress-response biomarkers, blood-gas and coagulation indices, renal-function markers, serial urine output, fluid-balance compliance, and ICU length of stay between patients treated before and after implementation of a Donabedian-based management protocol. Because the study did not include mechanistic experiments, mediation analyses, or sufficiently frequent biomarker measurements to determine an optimal intervention time, the findings were interpreted as associations with protocol implementation rather than evidence of mechanism or causality.

METHODS

This single-center retrospective before-and-after cohort study screened 155 consecutive patients aged ≥ 50 years who met the KDIGO diagnostic criteria for AKI [7] and received continuous renal replacement therapy at Nanjing First Hospital between January 2021 and January 2025. Continuous renal replacement therapy (CRRT) was administered during hospitalization; the eligibility criterion requiring treatment for at least 24 hours did not imply continuation of CRRT after discharge. Patients treated from January 2021 to December 2022, before implementation of the Donabedian-based protocol, constituted the routine-period cohort, whereas those treated from January 2023 to January 2025, after protocol implementation, constituted the intervention-period cohort. The analytical cohort was restricted to patients who survived to hospital discharge, recovered sufficient kidney function to remain dialysis-independent at discharge, and had complete baseline and 72-hour outcome data. Patients with stage 5 chronic kidney disease or end-stage kidney disease, maintenance dialysis before admission, previous kidney transplantation, advanced malignancy, Child–Pugh class C liver failure, or uncorrectable severe coagulopathy were excluded. Of the 155 patients initially treated with CRRT, 45 died before hospital discharge; among the 110 survivors, six remained

dialysis-dependent at discharge and four lacked complete 72-h data, leaving 100 patients for analysis, including 43 in the routine group and 57 in the intervention group. The complete participant selection flowchart is presented in Figure 1.

Clinical data collection

Demographic and clinical data were extracted from the electronic medical records using a predefined data-collection form. Variables included age, sex, body mass index, primary reason for ICU admission, major comorbidities, baseline mean arterial pressure, heart rate, SOFA score, vasopressor support, invasive mechanical ventilation, nephrotoxic-agent exposure within the preceding 7 days, cumulative fluid balance during the 24 h before CRRT, clinical evidence of volume overload, urine output during the 6 h before CRRT, and total CRRT duration. Urine output was measured hourly from the urinary catheter and summarized at baseline and at 24, 48, and 72 h after CRRT initiation.

CRRT initiation and discontinuation

In both study periods, the decision to initiate CRRT and the initial prescription were made jointly by the attending intensivist and a consulting nephrologist. CRRT was initiated when AKI was accompanied by one or more of the following institutional indications: refractory hyperkalemia, severe metabolic acidosis, pulmonary edema or clinically important fluid overload unresponsive to medical treatment, uremic complications, or persistent oliguria with progressive azotemia. Treatment decisions were based on the overall clinical context rather than on a single serum creatinine or BUN threshold.

CRRT was discontinued when the patient maintained hemodynamic stability without escalating vasoactive support, electrolyte and acid-base abnormalities remained controlled, urine output reached at least 0.5 mL/kg/h for 24 h, serum creatinine was stable or decreasing, and fluid balance could be maintained without extracorporeal support. None of the 100 patients in the analytical cohort was transferred to intermittent hemodialysis before dialysis liberation; patients who remained dependent on any form of kidney replacement therapy at discharge were not included in the analytical cohort.

METHODS

Routine management: CRRT was delivered using a multiFiltrate system (Fresenius Medical Care, Bad Homburg, Germany), a 1.0-m² polysulfone hemofilter, and a 12-Fr, 15-cm double-lumen catheter. Care was delivered by the standard ICU medical and nursing team under the staffing, training, and competency arrangements in place during the routine-management period; CRRT initiation and initial prescription remained the joint responsibility of the attending intensivist and consulting nephrologist. Monitoring was limited to vital signs and serum creatinine (Scr)/blood urea nitrogen (BUN), without ultrasound or central venous pressure (CVP) assessment. Anticoagulation followed a fixed low-molecular-weight heparin (LMWH) regimen, with a bolus dose of 20 U/kg and a maintenance dose of 0.5 U/kg/h. Blood flow rates were maintained between 150 and 180 mL/min, while replacement fluid was delivered at 40 mL/kg/h. The target fluid balance was a net negative balance of 300–500 mL per day.

Intervention management: CRRT was delivered using a multiFiltratePRO system (Fresenius Medical Care, Bad Homburg, Germany), with integrated hematocrit, blood-gas, and volumetric-monitoring functions, a 1.3-m² AN69ST membrane, and a 12-Fr, 15-cm double-

lumen catheter. A 1.3 m² AN69 ST membrane and 12Fr/15 cm dual-lumen catheter were utilized. The enhanced training formed part of the hospital's institutional CRRT competency-certification program. Attending physicians completed at least 20 h of training in CRRT principles, anticoagulation, prescription adjustment, and complication management, whereas specialized nurses completed at least 40 h of training in circuit preparation, parameter configuration, alarm management, vascular-access care, and fluid-volume control. Certification required a written examination score of at least 80%, successful completion of a simulation-based assessment, and satisfactory direct observation during three supervised CRRT procedures before independent practice was permitted. The protocol standardized the variables that required assessment and the permissible ranges for treatment adjustment rather than imposing an identical prescription on every patient. Blood flow, effluent dose, anticoagulation, and net-fluid-removal targets were individually adjusted according to hemodynamic status, urine output, cumulative fluid balance, acid-base and electrolyte findings, solute control, bleeding risk, and treatment tolerance. Deviations from the predefined ranges were permitted for immediate safety concerns, required approval by the attending intensivist, and were documented in the medical record. Pre-CBP (≤ 2 h), volume status was assessed via integrated ultrasound and CVP analysis, aiming for a daily net negative balance of 500–1000 mL, with a lower target (≤ 300 mL) in specific cases. Additionally, anticoagulation therapy was determined after thorough assessment of the patient's coagulation function and individualized bleeding risk. For low-risk patients, a regimen involving LMWH was implemented: a loading dose of 30 U/kg intravenously, followed by a maintenance infusion of 1 U/kg/h. Activated partial thromboplastin time (APTT) measurements were performed at 4-hour intervals, maintaining levels within 45–65 seconds. For patients at high bleeding risk or with active bleeding, regional citrate anticoagulation was performed using 4% trisodium citrate and calcium-free replacement fluid. Citrate was infused prefilter at an initial rate of 1.5 mL/h for each 1 mL/min of blood flow

and was subsequently titrated to maintain post-filter ionized calcium at 0.2–0.4 mmol/L. Calcium gluconate was infused through a separate line and adjusted to maintain systemic ionized calcium at 0.9–1.1 mmol/L [8]. The baseline blood flow was 180–200 mL/min (titrated down to 150 mL/min for systolic blood pressure < 90 mmHg). Replacement-fluid flow was initiated at 35–40 mL/kg/h and adjusted within a prespecified range of 35–50 mL/kg/h according to solute control, acid-base and electrolyte status, hemodynamic tolerance, urine output, and fluid-balance requirements. Persistent hyperkalemia, metabolic acidosis, or inadequate solute control prompted temporary escalation, whereas hemodynamic instability, electrolyte depletion, or excessive negative fluid balance prompted dose reduction. Serial IL-6 measurements were analyzed as study outcomes and were not used as stand-alone triggers for CRRT prescription changes. The routine group received a fixed rate of 40 mL/kg/h. The CPB protocol involved: 1) constant tracking of physiological parameters with hourly documentation of blood pressure (via invasive arterial monitoring), heart rate, respiratory rate, and oxygen saturation, 2) periodic four-hour laboratory evaluations of blood gases and electrolytes, 3) rapid-response protocols ensuring sub-15-minute reactions to therapeutic emergencies including hHemofilter thrombosis, hypotension, or bleeding incidents, followed by evidence-based countermeasures. Functional assessment of vascular access was performed 48–72 hours after treatment initiation. Catheter thrombosis identified by ultrasonography and blood flow <150 mL/min constituted indications for catheter withdrawal. Patients qualified for discharge when meeting these criteria: Scr levels decreased to $< 1.5 \times$ baseline, maintained urine output > 1.0 mL/kg/h for 24 hours, and no serious complications occurred. Discharge preparations involved dietary guidance, medication instructions, and follow-up scheduling. Subsequent monitoring occurred at 1/3/6/12 months through clinic visits or phone follow-ups.

Sample collection and testing

Arterial or venous blood samples were collected within two hours before CRRT initiation and at a fixed assessment point 72 hours after CRRT initiation. The 72-hour sample was not defined in relation to completion of a single circuit or CRRT weaning; if CRRT had been discontinued before 72 hours, the sample was still collected at the scheduled 72-hour time point. The following tests were performed:

Inflammatory cytokines (interleukin [IL]-6, tumor necrosis factor [TNF]- α , IL-1 β , IL-10) were analyzed via enzyme-linked immunosorbent assay (ELISA; R&D Systems, Minneapolis, MN, USA), following the kit instructions precisely.

Stress response biomarkers (cortisol [Cor], norepinephrine [NE], epinephrine [E]) were quantified via the Siemens ADVIA Centaur XP chemiluminescent immunoassay system.

Blood gas function (pH, lactate, base excess [BE]) was measured with the ABL90 FLEX system (Radiometer, Denmark).

Coagulation parameters (APTT, D-Dimer, platelet count [PLT]) were measured using the Sysmex CS-5100 automated coagulation analyzer and the Sysmex XN-9000 automated hematology analyzer.

Renal-function markers, including serum creatinine and BUN, were measured using a Beckman Coulter AU5800 automated chemistry analyzer.

Additionally, the fluid balance compliance rate was calculated as (compliant cases / total patients) $\times$ 100%.

Outcomes and sample-size assessment

The primary outcome was serum IL-6 concentration 72 h after CRRT initiation. Secondary outcomes included IL-1 β , TNF- α , IL-10, cortisol, norepinephrine, epinephrine, pH, lactate, base excess, APTT, D-dimer, platelet count, serum creatinine, BUN, urine output at 24, 48, and 72 h, fluid-balance compliance, and ICU length of stay. Fluid-balance compliance was defined as achievement of the individualized 24-h net-fluid target, within a tolerance of ± 100 mL, on at least two of the first three CRRT days.

Sample-size adequacy was assessed using PASS version 15.0 for a two-sided independent-samples comparison. Assuming a standardized effect size of 0.58, a two-sided α level of 0.05, 80% statistical power, and an allocation ratio of 1.33, the minimum required sample was 98 patients, comprising 42 patients in the routine group and 56 in the intervention group. The analytical cohort of 43 and 57 patients, respectively, met this requirement.

Statistical analysis

Statistical analyses were performed using SPSS version 32.0. Distributional assumptions were assessed using the Shapiro–Wilk test and inspection of residual plots. Normally distributed continuous variables are presented as mean $\pm$ standard deviation and were compared using independent-samples t tests between groups and paired t tests within groups. Non-normally distributed variables are presented as median and interquartile range and were analyzed using Mann–Whitney U tests or Wilcoxon signed-rank tests, as appropriate. Categorical variables are presented as numbers and percentages and were compared using chi-square or Fisher's exact tests.

The primary outcome was additionally analyzed using analysis of covariance, with 72-h IL-6 as the dependent variable, management group as the fixed factor, and baseline IL-6, age, sex,

sepsis, baseline SOFA score, vasopressor support, baseline urine output, and baseline serum creatinine as prespecified covariates. Serial urine-output measurements were analyzed using a mixed-effects model with fixed effects for group, time, and the group-by-time interaction and a patient-level random intercept. Secondary-outcome analyses were exploratory, and their P values were not adjusted for multiple comparisons. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Participant selection

During the study period, 155 consecutive patients with AKI received CRRT. Forty-five patients died before hospital discharge, resulting in an overall hospital survival rate of 71.0% (110/155). Of the 110 survivors, six remained dialysis-dependent at discharge and four lacked complete 72-h outcome data; the final analytical cohort therefore comprised 100 dialysis-independent survivors, including 43 patients in the routine group and 57 in the intervention group.

Patients' baseline clinical characteristics

Baseline demographic, clinical, physiological, and laboratory characteristics are summarized in Table 1. The distributions of primary ICU admission diagnoses were similar between groups, including sepsis in 18 of 43 patients in the routine group and 23 of 57 patients in the intervention group (41.9% vs. 40.4%; $p = 0.879$). No statistically significant differences were observed in age, sex, body mass index, major comorbidities, SOFA score, vasopressor support, mechanical ventilation, nephrotoxic exposure, baseline hemodynamics, urine output, fluid balance, or selected laboratory indices ($p > 0.05$). Nevertheless, the absence of statistically significant

differences was not interpreted as proof that the non-randomized groups were clinically equivalent.

CRRT prescription and treatment characteristics

As expected from the protocol definitions, the groups differed in equipment, membrane type, initial blood-flow rate, prescribed effluent dose, target net-fluid removal, and anticoagulation strategy (Table 2). The intervention group had a higher initial blood-flow rate and a larger prescribed net-fluid-removal target, whereas regional citrate anticoagulation was used in 18 intervention-group patients and in no routine-group patient. Total CRRT duration did not differ significantly between groups (72.80 ± 20.10 vs. 71.60 ± 18.90 h; $p = 0.762$). These prescription differences were components of the management intervention rather than baseline patient imbalances.

Alterations and comparisons of inflammatory responses

Pretreatment inflammatory-marker values were comparable between groups ($p > 0.05$). At 72 h, the intervention group had lower IL-1 β , IL-6, and TNF- α concentrations and a higher IL-10 concentration than the routine group ($p < 0.05$; Figure 2). Serum IL-6 was 60.39 ± 16.37 pg/mL in the intervention group and 73.89 ± 18.04 pg/mL in the routine group ($p < 0.001$). After adjustment for baseline IL-6, age, sex, sepsis, SOFA score, vasopressor support, baseline urine output, and baseline serum creatinine, the adjusted between-group difference remained -13.21 pg/mL (95% confidence interval, -20.34 to -6.07 ; $p < 0.001$).

Changes and comparative evaluation of stress responses

At 72 h, cortisol, norepinephrine, and epinephrine concentrations were lower in the intervention group than in the routine group (all $p < 0.05$; Figure 3). These findings indicate an association between protocol implementation and lower 72-h stress-response biomarker levels.

Variations and comparisons in blood gas function

When examining the blood gas function of the two patient groups, it was found that the baseline levels of pH, lactate, and BE were consistent ($p > 0.05$). Post-treatment, the pH values in both groups showed no marked alterations ($p > 0.05$), yet lactate decreased and BE rose in each group ($p < 0.05$). At 72 h, the intervention group had a lower lactate concentration and a higher base-excess value than the routine group (both $p < 0.05$; Figure 4), whereas pH did not differ significantly between groups.

Comparative analysis of coagulation function alterations

APTT increased significantly from baseline in both groups and was lower in the intervention group than in the routine group at 72 h (46.94 ± 5.18 vs. 51 ± 7.86 s; $p = 0.002$). D-dimer decreased in both groups and was lower in the intervention group at 72 h (2.60 ± 1.06 vs. 3.68 ± 0.75 $\mu\text{g/mL}$; $p < 0.001$), whereas platelet counts decreased in both groups but remained higher in the intervention group (162.54 ± 14.23 vs. $146.26 \pm 18.82 \times 10^9/\text{L}$; $p < 0.001$; Figure 5).

These results indicate more favorable 72-h coagulation indices but do not establish a reduction in clinical bleeding risk because bleeding events were not evaluated.

Urine-output trajectory

Baseline urine output did not differ significantly between groups ($p = 0.489$). Urine output increased over time in both groups and was higher in the intervention group at 24, 48, and 72 h; the group-by-time interaction was statistically significant ($p < 0.001$). At 72 h, urine output was 0.91 ± 0.19 mL/kg/h in the intervention group and 0.74 ± 0.20 mL/kg/h in the routine group ($p < 0.001$; Table 3).

Variations and comparisons in renal function

Serum creatinine and BUN decreased significantly from baseline in both groups. At 72 h, the intervention group had lower serum creatinine (258.88 ± 30.79 vs. 281.86 ± 51.55 $\mu\text{mol/L}$; $p = 0.007$) and BUN (12.05 ± 4.46 vs. 16.88 ± 3.98 mmol/L ; $p < 0.001$), together with a higher fluid-balance compliance rate (91.23% vs. 72.09% ; $p = 0.012$). ICU length of stay was slightly longer in the intervention group than in the routine group (13.84 ± 3.67 vs. 12.40 ± 3.43 days; $p = 0.047$; Table 3), indicating that the more favorable laboratory and fluid-management findings were not accompanied by a shorter ICU stay.

DISCUSSION

In this retrospective before-and-after cohort of dialysis-independent hospital survivors, implementation of a Donabedian-based management protocol was associated with more favorable 72-h inflammatory, stress-response, blood-gas, coagulation, renal-function, urine-output, and fluid-management indicators. The protocol simultaneously changed several structural and process components, including equipment, membrane type, staff training, monitoring intensity, anticoagulation, and fluid-management procedures; consequently, the observed differences cannot be attributed to the Donabedian framework or to any individual component in isolation. Moreover, the more favorable laboratory findings were not accompanied by a shorter ICU stay.

At 72 h, the intervention group had lower pro-inflammatory-marker concentrations and a higher IL-10 concentration than the routine group. Because sepsis is a major determinant of inflammatory-marker levels, its distribution was examined explicitly and was similar between groups (41.9% vs. 40.4% ; $p = 0.879$); sepsis was also included in the adjusted primary-outcome

model. The adjusted association with 72-h IL-6 remained statistically significant, although residual confounding from infection severity, source control, antimicrobial treatment, and other unmeasured factors cannot be excluded. Differences in membrane characteristics, device-assisted monitoring, treatment prescription, and fluid management may have contributed collectively to the observed biomarker patterns; however, membrane type and equipment were inseparable from the wider intervention bundle, and the present study was not designed to compare individual products. Besides, the dynamic modification of replacement-fluid flow based on solute control, acid-base and electrolyte status, hemodynamic tolerance, urine output, and fluid-balance requirements and the precise control of fluid volume using ultrasound alongside CVP may have facilitated inflammatory-mediator clearance and reduced volume overload, thereby potentially attenuating the inflammation–stress cycle [9]. Related studies of AN69ST-based hemofiltration in patients with severe sepsis have reported reductions in circulating inflammatory markers, although differences in patient populations and treatment protocols limit direct comparison with the present cohort [10]. Similarly, the stress hormones like Cor and NE, as well as E, saw a greater drop in levels in the observation group compared to the routine group. This finding may partly relate to the adsorptive and biocompatibility characteristics of the AN69ST membrane, which may reduce blood–membrane interaction and inflammatory stimulation; however, membrane type was only one component of the broader management protocol [11]. In the meantime, dynamic fluid-balance management and individualized anticoagulation may have contributed to greater hemodynamic stability and reduced treatment-related physiological stress, thereby potentially limiting excessive activation of the HPA axis. In the present cohort, the intervention group showed a lower 72-h lactate concentration and a higher base-excess value, together with a lower APTT, lower D-dimer concentration, and a smaller decline in platelet count than the routine group. Urine output also increased more rapidly during the first 72 h. These findings describe laboratory and

physiological differences but cannot establish superior anticoagulation safety or durable kidney recovery, because clinical bleeding, circuit lifespan, recurrent AKI, and post-discharge kidney outcomes were not evaluated. The integrated blood-gas monitoring function of the CRRT system may have allowed earlier recognition of acid-base changes and more timely prescription adjustment than routine intermittent laboratory monitoring. Similarly, titration of regional citrate anticoagulation according to blood flow and ionized-calcium measurements is intended to maintain circuit patency while limiting bleeding risk; however, filter lifespan and clinical bleeding events were not recorded in the present study, and these potential benefits could not be evaluated directly [12]. Finally, the intervention group had a higher fluid-balance compliance rate and more favorable 72-h renal-function indices than the routine group. The lower 72-h serum creatinine and BUN values, higher urine output, and greater fluid-balance compliance may reflect the combined effects of protocolized volume assessment and treatment delivery; however, the present data do not demonstrate renal tubular regeneration or identify the independent contribution of the membrane, device, staffing model, or prescription strategy. Moreover, dynamic fluid management based on urine output and ultrasound assessment may help reduce secondary renal stress associated with volume overload.

These findings support further prospective evaluation of structured quality-management protocols during CRRT but do not justify routine adoption of the complete intervention bundle or any specific device or membrane without confirmation of its clinical effectiveness, safety, resource requirements, and cost-effectiveness. Moreover, regular assessments should be conducted to evaluate the medical staff's proficiency in dynamic monitoring techniques.

However, several limitations should be considered. First, the retrospective, non-randomized before-and-after design is susceptible to selection bias, residual confounding, and temporal bias; because management group was determined by calendar period, secular changes in

staffing, equipment, clinical experience, infection management, supportive care, and treatment practice cannot be separated completely from the association with the Donabedian-based protocol. Second, the analytical cohort was restricted to patients who survived to discharge and became dialysis-independent, which introduced substantial survivor and selection bias and limits applicability to the complete population of patients receiving CRRT. Third, although the revised analysis included ICU admission diagnosis, comorbidities, SOFA score, vasopressor support, mechanical ventilation, fluid status, nephrotoxic exposure, and urine output, unmeasured differences in infection severity, antimicrobial treatment, source control, cardiac function, and clinician decision-making may remain. Fourth, the intervention was implemented as a multicomponent bundle, and the independent effects of equipment, membrane, staff training, monitoring, anticoagulation, and fluid-management procedures could not be isolated. Fifth, the study focused principally on 72-h outcomes; ICU stay was not shortened, and mortality, dialysis dependence in the complete CRRT cohort, sustained kidney recovery, readmission, quality of life, recurrent AKI, and long-term adverse events were not evaluated as comparative outcomes. Finally, no prespecified subgroup analyses were performed according to AKI etiology, sepsis severity, anticoagulation strategy, or illness-severity category, and cost-effectiveness was not assessed.

CONCLUSION

Among selected hospital survivors who were dialysis-independent at discharge, implementation of a Donabedian-based management protocol was associated with more favorable 72-h inflammatory, stress-response, coagulation, renal-function, urine-output, and fluid-management indicators, but not with a shorter ICU stay. These findings suggest that structured organization and monitoring may contribute to short-term differences in care-related

outcomes; however, the before-and-after design, survivor selection, temporal confounding, and simultaneous modification of multiple treatment components preclude causal attribution. Prospective multicenter studies with concurrent controls and clinically important long-term outcomes are required.

Ethics: This retrospective study was approved by the Ethics Committee of Nanjing First Hospital (No. KY20230829-03) and was conducted in accordance with the Declaration of Helsinki. Because the study used de-identified clinical data and involved no additional intervention or patient contact, the requirement for written informed consent was waived by the Ethics Committee.

ACKNOWLEDGEMENTS

Not applicable.

Author contributions: X.F. conceived and designed the study, QY.Z. wrote and revised the manuscript, TT.W. collected and analyzed data, X.F. supervised the study, QY.Z. and TT.W. made equal contributions in this work as co-first authors. All authors read and approved the final submitted manuscript.

Consent to Publish: All authors gave final approval of the version to be published.

Funding: No funds, grants, or other support was received.

Conflict of interest: None declared.

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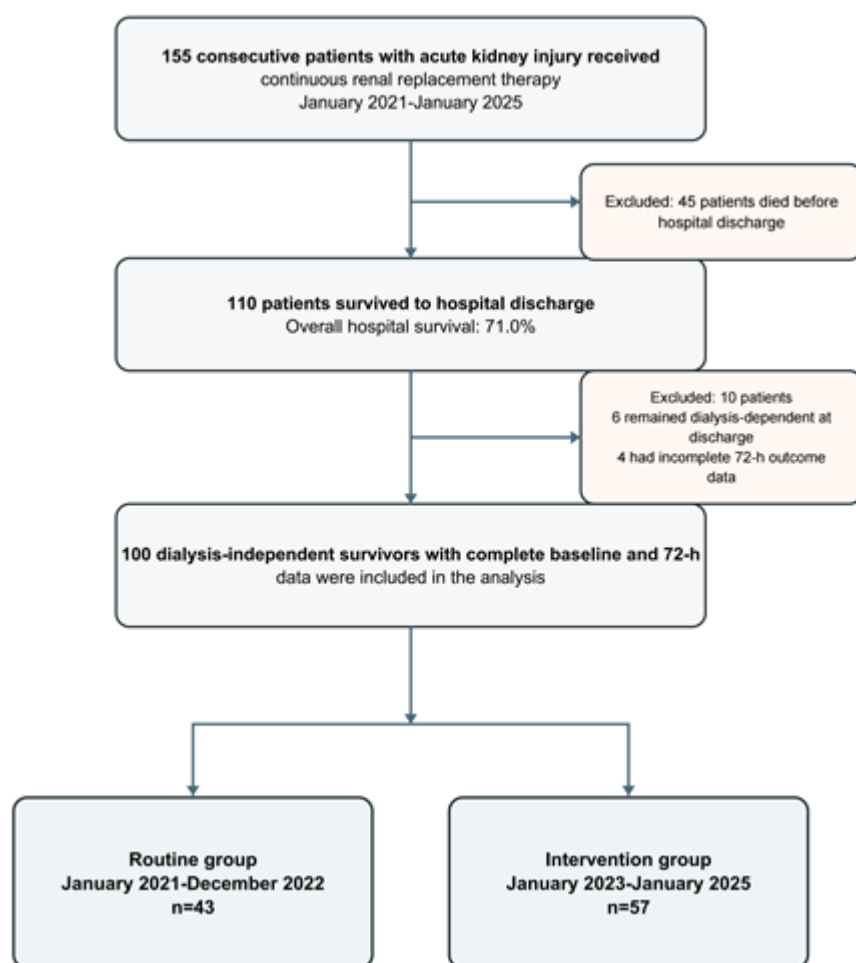


Figure 1. Flow diagram of cohort selection and allocation according to the management protocol in use during each calendar period

Table 1. Baseline demographic, clinical, physiological, and laboratory characteristics

Characteristic	Routine group (n = 43)	Intervention group (n = 57)	p
Age, years	65.02 ± 5.24	64.58 ± 3.66	0.619
Male sex, n (%)	35 (81.4)	50 (87.7)	0.381
Body mass index, kg/m ²	23.80 ± 3.20	23.53 ± 3.03	0.665
Obesity, n (%)	7 (16.3)	8 (14)	0.756
Primary reason for Intensive care unit admission, n (%)			0.999
Sepsis	18 (41.9)	23 (40.4)	
Major noncardiac surgery or trauma	8 (18.6)	11 (19.3)	
Cardiac surgery	7 (16.3)	9 (15.8)	
Acute heart failure or cardiogenic shock	6 (14)	8 (14)	
Other	4 (9.3)	6 (10.5)	
Hypertension, n (%)	25 (58.1)	31 (54.4)	0.708
Diabetes mellitus, n (%)	15 (34.9)	18 (31.6)	0.728
Chronic cardiovascular disease, n (%)	12 (27.9)	14 (24.6)	0.706
Pre-existing chronic kidney disease stages 1–4, n (%)	7 (16.3)	10 (17.5)	0.868
Mean arterial pressure, mmHg	68.20 ± 8.70	69 ± 9.10	0.658
Heart rate, beats/min	101.50 ± 16.30	99.70 ± 15.80	0.579
Sequential organ failure assessment score	10.91 ± 3.07	10.50 ± 2.99	0.495
Vasopressor support, n (%)	24 (55.8)	31 (54.4)	0.887
Mechanical ventilation, n (%)	27 (62.8)	35 (61.4)	0.887
Nephrotoxic-agent exposure, n (%)	14 (32.6)	17 (29.8)	0.77
Clinical volume overload, n (%)	20 (46.5)	25 (43.9)	0.792
Urine output before continuous renal replacement therapy, mL/kg/h	0.27 ± 0.15	0.29 ± 0.16	0.489
Positive fluid balance during preceding 24 hours, mL	2050 ± 850	1984 ± 810	0.696
Serum creatinine, µmol/L	333.12 ± 54.55	341.25 ± 67.06	0.518
Blood urea nitrogen, mmol/L	23.38 ± 4.98	22.84 ± 4.19	0.557
Interleukin-6, pg/mL	150.39 ± 31.79	151.92 ± 33.97	0.819
Lactate, mmol/L	5.75 ± 1.48	5.71 ± 1.72	0.899

Table 2. Continuous renal replacement therapy systems, initial prescription, and treatment characteristic

Characteristic	Routine group (n = 43)	Intervention group (n = 57)	p
Age, years	65.02 ± 5.24	64.58 ± 3.66	0.619
Male sex, n (%)	35 (81.4)	50 (87.7)	0.381
Body mass index, kg/m ²	23.80 ± 3.20	23.53 ± 3.03	0.665
Obesity, n (%)	7 (16.3)	8 (14)	0.756
Primary reason for Intensive care unit admission, n (%)			0.999
Sepsis	18 (41.9)	23 (40.4)	
Major noncardiac surgery or trauma	8 (18.6)	11 (19.3)	
Cardiac surgery	7 (16.3)	9 (15.8)	
Acute heart failure or cardiogenic shock	6 (14)	8 (14)	
Other	4 (9.3)	6 (10.5)	
Hypertension, n (%)	25 (58.1)	31 (54.4)	0.708
Diabetes mellitus, n (%)	15 (34.9)	18 (31.6)	0.728
Chronic cardiovascular disease, n (%)	12 (27.9)	14 (24.6)	0.706
Pre-existing chronic kidney disease stages 1–4, n (%)	7 (16.3)	10 (17.5)	0.868
Mean arterial pressure, mmHg	68.20 ± 8.70	69 ± 9.10	0.658
Heart rate, beats/min	101.50 ± 16.30	99.70 ± 15.80	0.579
Sequential organ failure assessment score	10.91 ± 3.07	10.50 ± 2.99	0.495
Vasopressor support, n (%)	24 (55.8)	31 (54.4)	0.887
Mechanical ventilation, n (%)	27 (62.8)	35 (61.4)	0.887
Nephrotoxic-agent exposure, n (%)	14 (32.6)	17 (29.8)	0.77
Clinical volume overload, n (%)	20 (46.5)	25 (43.9)	0.792
Urine output before continuous renal replacement therapy, mL/kg/h	0.27 ± 0.15	0.29 ± 0.16	0.489
Positive fluid balance during preceding 24 hours, mL	2050 ± 850	1984 ± 810	0.696
Serum creatinine, µmol/L	333.12 ± 54.55	341.25 ± 67.06	0.518
Blood urea nitrogen, mmol/L	23.38 ± 4.98	22.84 ± 4.19	0.557
Interleukin-6, pg/mL	150.39 ± 31.79	151.92 ± 33.97	0.819
Lactate, mmol/L	5.75 ± 1.48	5.71 ± 1.72	0.899

Table 3. Urine-output trajectory, renal-function indices, and short-term clinical outcomes

Outcome	Routine group (n = 43)	Intervention group (n = 57)	p
Urine output before continuous renal replacement therapy, mL/kg/h	0.27 ± 0.15	0.29 ± 0.16	0.489
Urine output at 24 hours, mL/kg/h	0.40 ± 0.19	0.48 ± 0.21	0.035
Urine output at 48 hours, mL/kg/h	0.59 ± 0.18	0.69 ± 0.21	0.009
Urine output at 72 hours, mL/kg/h	0.74 ± 0.20	0.91 ± 0.19	<0.001
Serum creatinine before continuous renal replacement therapy, µmol/L	333.12 ± 54.55	341.25 ± 67.06	0.518
Serum creatinine at 72 hours, µmol/L	281.86 ± 51.55	258.88 ± 30.79	0.007
Blood urea nitrogen before continuous renal replacement therapy, mmol/L	23.38 ± 4.98	22.84 ± 4.19	0.557
Blood urea nitrogen at 72 hours, mmol/L	16.88 ± 3.98	12.05 ± 4.46	< 0.001
Fluid-balance compliance, n (%)	31 (72.09)	52 (91.23)	0.012
Intensive care unit length of stay, days	12.40 ± 3.43	13.84 ± 3.67	0.047

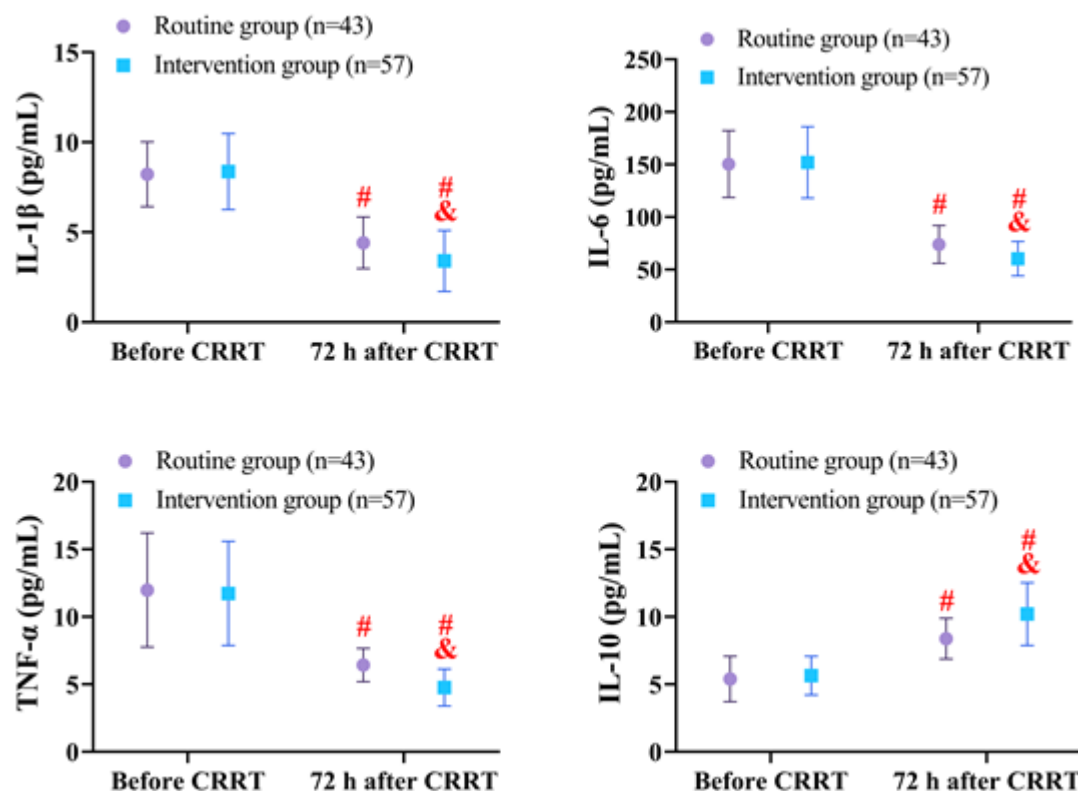


Figure 2. The levels of pro-inflammatory factors (IL-6, TNF- α , IL-1 β) and anti-inflammatory factors (IL-10) before and after treatment were compared between the two groups. a: IL-1 β , b: IL-6, c: TNF- α , d: IL-10;

& $p < 0.05$ – the difference between the observation group and the conventional group after treatment was statistically significant (independent sample t);

$p < 0.05$ – statistically significant difference before and after treatment within the group (paired t-test)

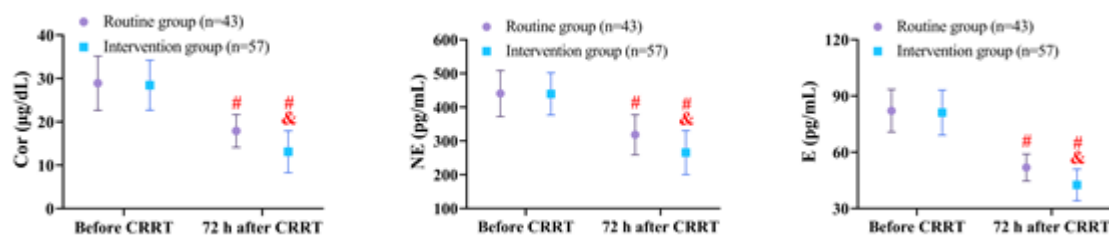


Figure 3. Comparison of stress hormone (Cor, NE, E) levels between the two groups before and after treatment. a: Cor, b: NE, c: E;

&p < 0.05 – the difference between the observation group and the conventional group after treatment was statistically significant (independent sample t);

#p < 0.05 – statistically significant difference before and after treatment within the group (paired t test)

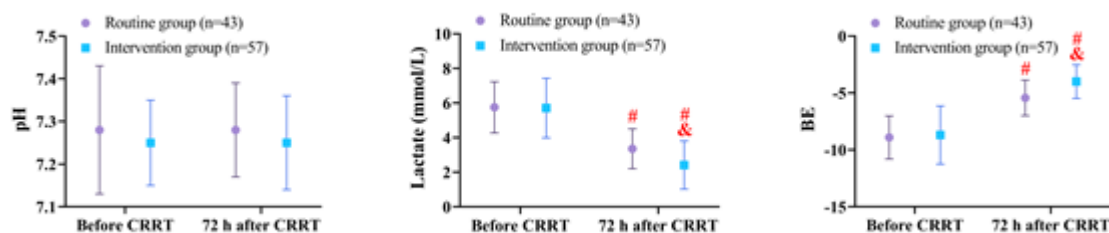


Figure 4. Comparison of blood pH, lactate, and BE levels before and after treatment in the two groups. a: pH, b: lactate, c: BE;

&p < 0.05 – the difference between the observation group and the conventional group after treatment was statistically significant (independent sample t);

#p < 0.05 – statistically significant difference before and after treatment within the group (paired t test)

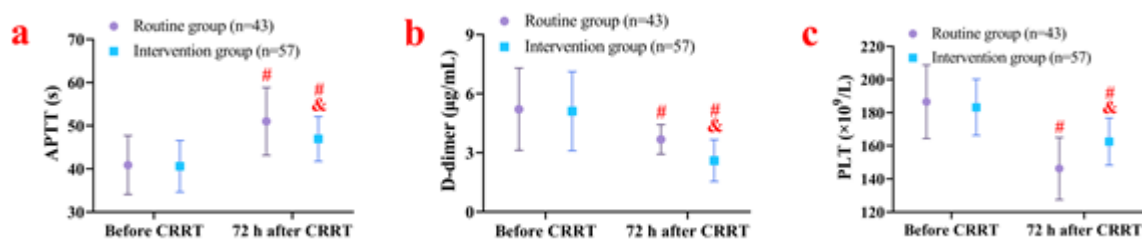


Figure 5. Comparison of APTT, D-dimer, and PLT levels before and after treatment in the two groups. a: APTT, b: D-dimer, c: PLT;

&p < 0.05 – the difference between the observation group and the conventional group after treatment was statistically significant (independent sample t);

#p < 0.05 – statistically significant difference before and after treatment within the group (paired t test)