

Changes in Renal Venous Flow and Liberation from Renal Replacement Therapy in Patients with Acute Heart Failure

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Keywords

Cardiorenal syndromes · Congestive nephropathy · Intrarenal venous-flow patterns · Renal venous stasis index · Venous congestion

Abstract

Introduction: In acute heart failure (AHF), the factors associated with successful renal replacement therapy (RRT) discontinuation are largely undefined. We hypothesized

that improvements in Doppler-derived renal venous flow (RVF) waveforms may serve as indicators of recovering cardiorenal function associated with successful liberation from RRT. **Methods:** We performed a post hoc analysis of a prospective cohort study involving inpatients with AHF undergoing serial renal Doppler evaluations. Patients who received acute RRT were retained for analysis, with Doppler assessments conducted both before RRT initiation and after discontinuation. Successful RRT discontinuation was defined as RRT cessation without relapse for at least 14 days. Logistic regression was used to evaluate the association between changes in RVF markers – including intra-renal venous flow (IRVF) and the renal venous stasis index (RVSI) – and RRT discontinuation, along with echocardiographic and clinical data from pre- to post-RRT Doppler measurements. **Results:** Overall, 10/53 (19%) patients successfully discontinued RRT. Increases in the severity of IRVF patterns and RVSI were negatively associated with RRT discontinuation (IRVF per 1-pattern increase in severity: OR 0.01, 95% CI, <0.001–0.11; $p < 0.001$; RVSI per 0.1-unit increase: OR 0.11, 95% CI, 0.03–0.48; $p < 0.001$). Additionally, improvements in right ventricular function markers, such as the TAPSE/sPAP ratio (per 0.1 mm/mm Hg increase: OR 1.83, 95% CI, 1.03–3.32; $p = 0.049$), were associated with higher odds of RRT discontinuation. **Conclusions:** In AHF patients requiring acute RRT, improvements in RVF were associated with successful RRT discontinuation. Serial RVF assessment may offer a noninvasive means of capturing dynamic changes in cardiorenal syndrome physiology and renal recovery. Larger studies with more frequent and appropriately timed Doppler assessments are needed to determine whether RVF monitoring may guide RRT management in AHF.

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Introduction

Acute heart failure (AHF) is the leading cause of unplanned hospitalization in both the USA and Europe, with more than 90% of cases attributed to signs and symptoms of fluid overload [1]. Approximately 40% of patients experiencing AHF present with a type 1 cardiorenal syndrome (CRS) phenotype, characterized by acute kidney injury (AKI) secondary to AHF [2]. In cases of diuretic-resistant volume overload or worsening renal function, isolated ultrafiltration or renal replacement therapy (RRT) may be required to expedite decongestion [3]. To date, the clinical determinants of successful liberation from RRT in these patients remain unclear.

Doppler-derived renal venous flow (RVF), including both intra-renal venous flow (IRVF) patterns and the dimensionless renal venous stasis index (RVSI) (online suppl. Fig. 1; for all online suppl. material, see <https://doi.org/10.1159/000546851>), has emerged as a noninvasive method for assessing renal congestion. RVF abnormalities are associated with adverse cardiorenal outcomes, including RRT initiation [4, 5]. Since RVF reflects disease pathophysiology and severity across the continuum of heart failure (HF), we hypothesized that among HF patients requiring acute RRT, an improvement in RVF waveforms may serve as an indicator of recovering cardiorenal function associated with the successful discontinuation of RRT.

Methods

We conducted a post hoc analysis of a prospective observational cohort study, “Changes in Doppler-derived kidney venous flow and adverse cardiorenal outcomes in patients with heart failure” [4]. In the parent cohort, consecutive adult cardiology inpatients with HF admitted to the University Hospital Giessen and Marburg (Giessen, Germany) were prospectively enrolled and underwent serial renal Doppler assessments to evaluate RVF. Patients were referred to the consulting nephrologist if they had a history of diuretic resistance and reduced renal function (i.e., estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m²). A total of 216 patients were included in the parent cohort. For the current analysis, we included patients who received RRT, had serial Doppler data available, and did not have baseline chronic kidney disease (CKD) stage 5. These patients were subsequently followed up for additional 12 months (totaling 30 months post-admission) to evaluate long-term renal outcomes. In total, 53 patients met these criteria and were included in the present analysis.

As per study protocol, renal Doppler and echocardiography were performed at up to three time points: Doppler 1, when the patient was first seen by a nephrologist after referral; Doppler 2, 25–35 days later or, if RRT was initiated earlier, pre-RRT initiation, and Doppler 3, after RRT discontinuation when euvolemia and clinical recovery was achieved, or when RRT discontinuation was unlikely. In the present study, Doppler 2 was defined as the most recent Doppler performed pre-RRT initiation. Patients were classified as successfully liberated from RRT if they discontinued RRT and did not

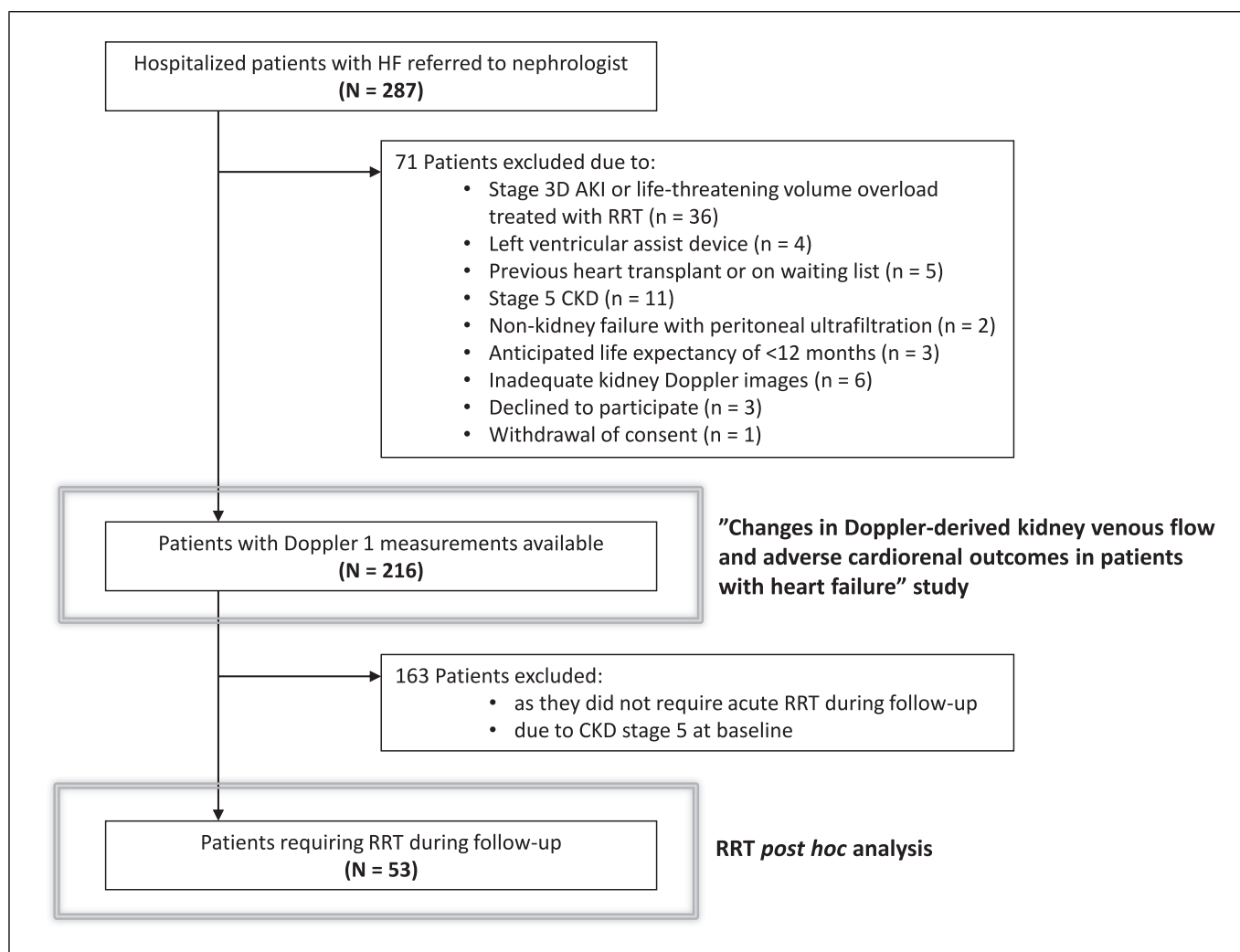


Fig. 1. Study flowchart. The flowchart of the observational study titled “Changes in Doppler-Derived Kidney Venous Flow and Adverse Cardiorenal Outcomes in Patients with Heart Failure” shows that 216 patients were included in the parent study. Among these, data from 53 patients were available for the RRT post hoc analysis. Stage 3D AKI, stage 3 acute kidney injury with dialysis; CKD, chronic kidney disease; HF, heart failure; RRT, renal replacement therapy.

receive RRT for at least 14 days (relapse-free period) after RRT discontinuation (see online suppl. Methods for rationale). Full details on the study methodology and statistical analyses are provided in the online supplementary material.

Statistical Analysis

Baseline was defined as the time of RRT initiation. All Doppler 2 measurements were collected prior to or up to the time of RRT initiation. If a patient did not undergo Doppler 2 measurements, then the date and values were imputed using last observation carried forward using the previous Doppler 1 measurements ($N = 2$). Patients were

followed up until they experienced RRT discontinuation. Patients were censored if they were lost to follow-up and died, or the end of the study was reached, whichever occurred first.

Continuous variables were summarized as mean $\pm$ SD or median (IQR) depending on the distribution, and categorical variables were expressed as n (%). Cumulative incidence estimates and Cox proportional hazard regression models were used to determine the relationship of RVSI and IRVF patterns pre-RRT with time to RRT discontinuation in patients undergoing RRT therapy. Correlations between changes in pre-to post-RRT Doppler measurements were evaluated using

Table 1. RRT outcome data

RRT outcome	Patients with RRT (N = 53)*
RRT indication	
Recurrent AHF with AKI and diuretic resistance	53 (100)
AKI criteria met for RRT initiation	
Serum creatinine	4 (7.6)
Urine output	21 (39.6)
Serum creatine and urine output	28 (52.8)
RRT modality	
Peritoneal dialysis	23 (43.4)
<i>Ascites absent</i>	6/23 (26.1)
<i>Ascites present</i>	17/23 (73.9)
Hemodialysis	30 (56.6)
<i>Ascites absent</i>	24/30 (80.0)
<i>Ascites present</i>	6/30 (20.0)
RRT outcome	
Kidney failure on maintenance dialysis	43 (81.1)
Discontinuation of acute RRT	10 (18.9)

Values are reported as numbers (%). CKD, chronic kidney disease; HF, heart failure; RRT, renal replacement therapy. *Among the N = 53 patients with acute RRT initiated during follow-up.

Pearson's correlation coefficient. The association between changes in RVSI and IRVF patterns from pre- to post-RRT Doppler measurements and RRT discontinuation at 2 years among patients with both measurements available were evaluated using logistic regression.

Results

A total of 53 patients were included in the final cohort for analysis (Fig. 1). Baseline patient characteristics at the time of Doppler 2 are shown in online supplementary Table S1. The median interval between Doppler 1 and Doppler 2 among those without missing Doppler 2 measurements was 31 (IQR, 25–48) days. The median interval between Doppler 2 measurements and RRT initiation was 13 (IQR, 4–70) days. All patients required acute RRT for AHF with AKI and diuretic-resistant fluid overload. Acute hemodialysis was the predominant RRT modality (Table 1). All patients had CKD stages 3–4 at baseline.

The median hospital length of stay was 15 days (IQR, 13–24). The average follow-up time after RRT initiation was 15.4 (SE, 1.08) months. Ten patients (19%) eventually discontinued RRT (see online suppl. Table S2; Fig. S2 for cumulative incidence estimates of RRT discontinuation), with Doppler 3 measurements obtained at a

median of 13 days (IQR, 5–29) following RRT discontinuation. In patients for whom RRT discontinuation was considered improbable despite achieving euvolemia and in whom Doppler 3 data were available ($n = 41$), Doppler 3 measurements were performed at a median of 38 days (IQR, 13–61) after RRT initiation. Among the 51 patients with available Doppler 3 data, the median duration between Doppler 2 and Doppler 3 was 64 days (IQR, 44–153). Individual patient data, including hospital length of stay, discharge status, and Doppler 3 follow-up location, are summarized in online supplementary Table S3.

When assessing Doppler measures pre-RRT initiation, patients who eventually discontinued RRT, as opposed to those who did not, were less likely to have ascites and exhibited higher indices of right ventricular (RV) dysfunction (Table 2). Neither an increase in severity of IRVF pattern nor an increase in RVSI severity was significantly associated with RRT discontinuation. Among the subset of patients with available right heart catheterization data (32.1%) during the index hospital stay, patients who discontinued RRT were more likely to have lower RAP and lower mPAP values pre-RRT (online suppl. Table S4).

Increases in severity of both IRVF patterns and RVSI from pre- to post-RRT Doppler were negatively associated with RRT discontinuation (IRVF per 1 pattern increase in severity change: odds ratio 0.01, 95% confidence interval, <0.001–0.11; $p < 0.001$, and RVSI per

Table 2. Univariable associations between pre-RRT Doppler measures and time to RRT discontinuation

Patient characteristic	HR (95% CI)	p value
RVSI (per 0.1 unit increase)*	0.82 (0.52–1.29)	0.39
IRVF pattern (per 1 pattern increase in severity)†	0.44 (0.13–1.52)	0.19
RRI (per 0.1 unit increase)	0.71 (0.16–3.09)	0.65
Age (per decade)	0.74 (0.49–1.11)	0.15
Male sex	0.39 (0.11–1.34)	0.13
Weight (per 5 kg increase)	1.05 (0.89–1.23)	0.56
BMI (per 5 kg/m ² increase)	1.46 (0.87–2.42)	0.15
Mean arterial pressure (per 5 mm Hg increase)	0.94 (0.70–1.28)	0.71
Pleural effusion	0.90 (0.19–4.22)	0.89
Ascites	0.20 (0.04–0.94)	0.042
Previous HF decompensation	0.22 (0.03–1.73)	0.15
Previous coronary revascularization	0.34 (0.09–1.32)	0.12
Diabetes	0.77 (0.22–2.72)	0.68
Loop diuretic dose (per 100 mg/day increase)	1.07 (0.90–1.28)	0.45
Laboratory data		
Serum sodium (per 5 mmol/L increase)	1.41 (0.69–2.87)	0.35
BNP (per 100 pg/mL increase)	0.83 (0.68–1.01)	0.056
Hemoglobin (per 10 g/dL increase)	0.74 (0.47–1.16)	0.19
Serum creatinine (per 1 mg/dL increase)	1.21 (0.69–2.13)	0.51
Cystatin C (per 1 mg/L increase)	1.07 (0.52–2.24)	0.85
eGFR _{cr-cys} (per 1 mL/min/1.73 m ² decrease)	0.98 (0.88–1.08)	0.64
Urea (per 10 mg/dL increase)	0.90 (0.78–1.03)	0.11
BUN/creatinine ratio (per 10 mg/dL increase)	0.28 (0.11–0.69)	0.006
Albuminuria (per 100 mg/day increase)	0.92 (0.68–1.24)	0.57
Urinary sodium excretion (per 10 mmol/day increase)	0.89 (0.78–1.02)	0.088
Echocardiography parameters		
LVEF (per 10% increase)	1.21 (0.80–1.83)	0.37
LA diameter (per 10 mm increase)	0.63 (0.22–1.80)	0.38
E/e' ratio (per 5 unit increase)	0.41 (0.12–1.38)	0.15
RA area (per 10 cm ² increase)	0.27 (0.11–0.69)	0.006
RV diameter (per 10 mm increase)	0.31 (0.13–0.75)	0.009
TAPSE (per 5 mm increase)	2.42 (0.68–8.60)	0.17
TAPSE/sPAP ratio (per 0.1 mm/mm Hg increase)	1.16 (0.55–2.47)	0.70
Tricuspid regurgitation (per 1 grade increase in severity)	0.82 (0.31–2.21)	0.70
IVC diameter (per 1 cm increase)	0.25 (0.05–1.24)	0.089

p values in bold denote significance at the 0.05 alpha level. BMI, body mass index; BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CI, confidence interval; E/e', ratio of mitral inflow velocity to lateral annular relaxation velocity; eGFR_{cr-cys}, estimated glomerular filtration rate (creatinine-cystatin C equation); HF, heart failure; HR, hazard ratio; IRVF, intra-renal venous flow; IVC, inferior vena cava; LA, left atrial; LVEF, left ventricular ejection fraction; RA, right atrial; RRT, renal replacement therapy; RV, right ventricular; RVSI, renal venous stasis index; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion. *RVSI was modeled as a linear term on a per 0.1-unit increase. †IRVF was modeled as an ordinal term on a per 1 pattern severity increase.

0.1-unit increase change: odds ratio 0.11, 95% confidence interval, 0.03–0.48; $p < 0.001$; Table 3, Fig. 2). Changes in both IRVF patterns and RVSI from pre- to post-RRT Doppler were also negatively correlated with change in eGFR_{creatinine-cystatin C equation} ($r = -0.37$, $p = 0.011$, and $r = -0.41$, $p = 0.005$, respectively; Fig. 3). Among other clinical parameters available at both pre- to post-RRT

Doppler, increases in RRI, loop diuretic dose, and inferior vena cava diameter were associated with a decreased chance of RRT discontinuation. Conversely, improvements in surrogate markers of renal and RV dysfunction (i.e., eGFR_{cr-cys}, blood urea nitrogen/creatinine ratio, tricuspid annular plane systolic excursion, and tricuspid annular plane systolic excursion/systolic pulmonary

Table 3. Univariable associations between pre- to post-RRT Doppler and RRT discontinuation status ($n = 51$ patients with both Doppler 2 and Doppler 3 measures available)

Change from pre- to post-RRT Doppler	OR (95% CI)	<i>p</i> value
RVSI (per 0.1-unit increase)*	0.11 (0.03–0.48)	<0.001
IRVF (per 1 pattern increase in severity)†	0.01 (<0.001–0.11)	<0.001
RRI (per 0.1 unit increase)	<0.001 (<0.001–0.07)	0.003
Weight (per 5 kg increase)	1.22 (0.68–2.21)	0.50
Mean arterial pressure (per 5 mm Hg increase)	1.03 (0.78–1.35)	0.86
Loop diuretic dose (per 100 mg/day increase)	0.79 (0.65–0.96)	0.020
Serum sodium (per 5 mmol/L increase)	1.03 (0.58–1.84)	0.92
BNP (per 100 pg/mL increase)	1.18 (0.94–1.48)	0.15
Serum creatinine (per 1 mg/dL increase)	0.52 (0.30–0.91)	0.023
Cystatin C (per 1 mg/L increase)	0.43 (0.22–0.83)	0.012
eGFR _{cr-cys} (per 1 mL/min/1.73 m ² increase)	1.09 (1.01–1.18)	0.023
Urea (per 10 mg/dL increase)	1.09 (0.97–1.23)	0.16
BUN/creatinine ratio (per 10 mg/dL increase)	3.91 (1.55–9.84)	0.004
24-h albuminuria (per 100 mg increase)	1.18 (0.75–1.86)	0.47
Urinary sodium excretion (per 10 mmol/day increase)	1.11 (0.98–1.26)	0.11
RA area (per 10 cm ² increase)	0.17 (0.014–1.91)	0.15
RV diameter (per 10 mm increase)	0.22 (0.043–1.17)	0.08
TAPSE (per 5 mm increase)	3.73 (1.02–13.63)	0.046
TAPSE/sPAP ratio (per 0.1 mm/mm Hg increase)	1.83 (1.03–3.32)	0.049
Tricuspid regurgitation (per 1 grade increase in severity)	0.35 (0.10–1.22)	0.10
IVC diameter (per 1 cm increase)	0.071 (0.008–0.63)	0.018

p values in bold denote significance at the 0.05 alpha level. BNP, B-type natriuretic peptide; BUN, blood urea nitrogen; CI, confidence interval; eGFR_{cr-cys}, estimated glomerular filtration rate (creatinine-cystatin C equation); IRVF, intra-renal venous flow; IVC, inferior vena cava; OR, odds ratio; RA, right atrial; RV, right ventricular; RRI, renal resistive index; RRT, renal replacement therapy; RVSI, renal venous stasis index; sPAP, systolic pulmonary arterial pressure; TAPSE, tricuspid annular plane systolic excursion. *RVSI was modeled as a linear term on a per 0.1-unit increase. †IRVF was modeled as an ordinal term on a per 1 pattern severity increase.

arterial pressure ratio) were associated with increased odds of RRT discontinuation.

Long-term renal data of patients who discontinued RRT are provided in online supplementary Table S5. RRT was reintroduced in 4 patients (40.0%) at a median of 240 days (IQR, 121–287).

Discussion

In patients with AHF and CKD at baseline requiring acute RRT, we found that improvements in RVF post-RRT, along with enhancements in surrogate markers of

RV dysfunction and/or fluid overload, were associated with successful RRT discontinuation. These findings underscore the importance of addressing worsening HF-related RV dysfunction and implementing effective decongestion strategies in the management of acute CRS [6].

There is growing interest in using venous excess ultrasound to interrogate splanchnic congestion patterns even in patients with “clinical euvolemia” despite elevated right-sided pressures [7, 8]. Our study adds to this growing body of literature, indicating that understanding RVF may offer additional value to existing measures, including clinical exams, natriuretic peptides, hemoconcentration, and right heart catheterization.

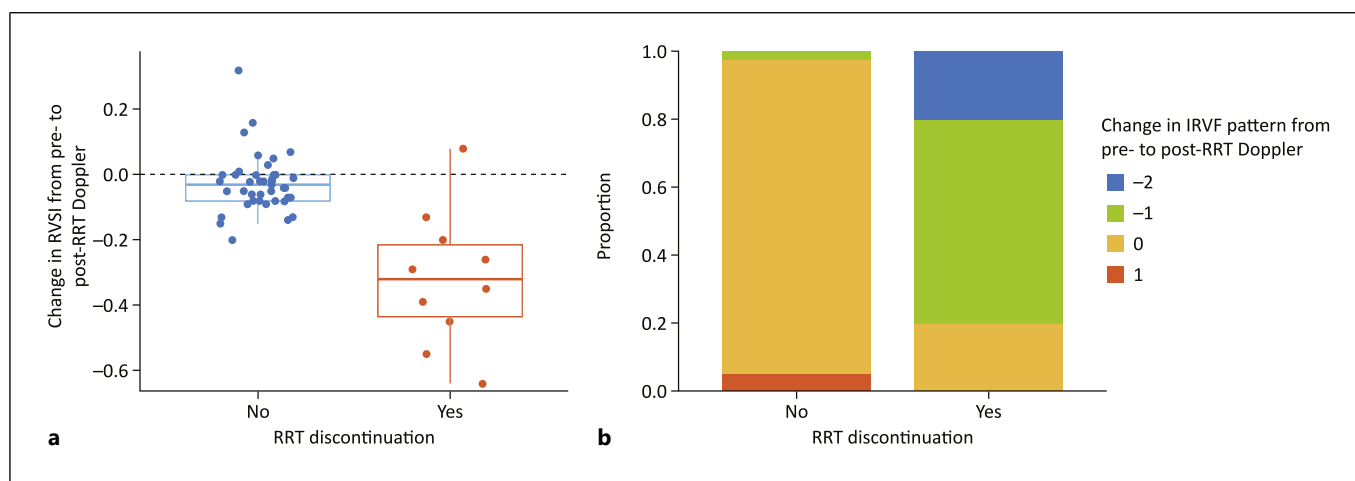


Fig. 2. Associations between change in RVSI (a) and IRVF (b) patterns from pre- to post-RRT Doppler discontinuation status. IRVF, intra-renal venous flow; RRT, renal replacement therapy; RVSI, renal venous stasis index.

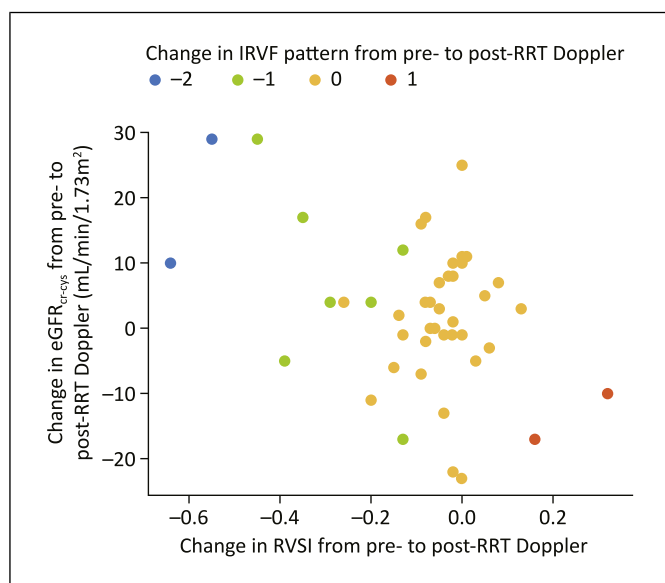


Fig. 3. Scatterplot of changes in eGFR_{cr-cys} versus changes in IRVF patterns and RVSI from pre- to post-RRT Doppler. The figure shows the relationship between changes in eGFR and changes in IRVF patterns and RVSI from pre- to post-RRT Doppler. Color coding is used to highlight changes in IRVF patterns between these two Doppler measurements. eGFR_{cr-cys}, estimated glomerular filtration rate (creatinine-cystatin C equation); IRVF, intra-renal venous flow; RVSI, renal venous stasis index.

Previous studies have focused on serum biomarkers (e.g., serum creatinine, cystatin C) and urinary output as indicators of renal recovery in general ICU patients [9]. In AHF, CA125 – but not NT-proBNP – has been in-

dependently associated with discontinuous IRVF patterns, suggesting its potential utility in identifying renal venous congestion [10]. Combining RVF assessment with biomarkers of tubular stress or injury (e.g., [TIMP-2]•[IGFBP7], KIM-1, NGAL) may help differentiate patients with structural kidney damage from those with functional, congestion-driven GFR decline. Such multimodal profiling could facilitate the identification of distinct subgroups within the cardiorenal spectrum – those more likely to recover after decongestion versus those at risk of progressive CKD due to renal parenchymal damage [11]. This strategy aligns with the emerging venous excess ultrasound framework, which emphasizes phenotyping venous congestion and tailoring decongestion strategies. However, this integrative approach remains largely untested and should be prioritized in future prospective studies.

The dynamic nature of RVF as a surrogate for renal congestion highlights its potential utility across the CRS spectrum, including guiding decisions on RRT trajectories. This noninvasive method provides real-time, organ-specific insights into renal hemodynamics and, when interpreted with clinical exam and AKI biomarkers, may support more precise clinical decision-making regarding renal recovery. Such an integrated approach could help avoid premature discontinuation of RRT, reduce unnecessary treatment prolongation, and ultimately improve patient outcomes.

For future research directions, larger prospective studies examining the timing and discontinuation of

acute RRT should consider integrating RVF monitoring. This inclusion would enable exploration of the prevalence of acute, undetected CRS and the potential effectiveness of individualized decongestion targets in enhancing renal recovery.

We acknowledge several limitations in this post hoc analysis, including the single-center design. The lack of standardization in the study protocol regarding the initiation of RRT, along with prespecified timepoints for RVF assessments intended to mitigate potential data loss due to varying patient referral timelines, also impacts the generalizability of our findings. Additionally, the timing of Doppler 3 assessments was variable and, in several cases, occurred after RRT discontinuation, limiting its utility as a predictive tool. Many factors influencing RRT discontinuation may not have been recorded, including the absence of timed urine collection. Thus, our results must be considered as hypothesis-generating only. Nonetheless, our study is the first to explore this research question.

In conclusion, our study suggests that serial RVF assessment may offer potential insights into changes in CRS physiology during RRT. However, given the preliminary nature of our findings and limitations in the timing of Doppler assessments, larger studies with more frequent and protocolized Doppler evaluations are warranted to confirm the clinical utility of RVF as a noninvasive tool to guide RRT discontinuation in patients with acute CRS.

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Statement of Ethics

This study protocol was reviewed and approved by the Ethik-Kommission des Fachbereichs Medizin, Klinikstrasse 29, 35392 Giessen, Germany, approval No. AZ 237/16. Written informed consent was obtained from the participants.

Conflict of Interest Statement

Khodr Tello discloses grants from the German Research Foundation and nonfinancial support from the University of Giessen during the conduct of the study and personal fees

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Author Contributions

The authors shared responsibility for study design, data collection, data analysis, and data interpretation, as well as preparation, review, and approval of the manuscript. F.H.-S. and L.V. share first authorship and contributed to the statistical analysis. F.H.-S. had full access to all data in the study and took final responsibility for the decision to submit for publication. K.B.K. is the senior author of the work. Study concept and design: F.H.-S., L.V., H.-W.B., C.R., and K.B.K. Literature research and clinical advice; acquisition, analysis, or interpretation of data; and critical revision of the manuscript for important intellectual content: F.H.-S., L.V., P.B., K.T., M.J.R., H.G., R.E., M.C.M., J.N., J.R.,

G.R.-G., G.Y., B.Y., M.H.R., C.R., B.A., F.G., H.A.G., W.S., H.-W.B., and K.B.K. Drafting of the manuscript: F.H.-S., L.V., and K.B.K. Study supervision: F.H.-S., H.-W.B., C.R., and K.B.K.

Data Availability Statement

The data that support the findings of this study are not publicly available as they contain information that could compromise the privacy of research participants. However, they are available from the corresponding author, F.H.-S., upon reasonable request.

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