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Changes in the Inferior Vena Cava Are More Sensitive Than Venous Pressure During Fluid Removal: A Proof-of-Concept Study

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ABSTRACT

Background: Congestion is central to the pathophysiology of heart failure (HF); thus, tracking congestion is crucial for the management of patients with HF. In this study we aimed to compare changes in inferior vena cava diameter (IVCD) with venous pressure following manipulation of volume status during ultrafiltration in patients with cardiac dysfunction.

Methods and Results: Patients with stable hemodialysis and with systolic or diastolic dysfunction were studied. Central venous pressure (CVP) and peripheral venous pressure (PVP) were measured before and after hemodialysis. IVCD and PVP were measured simultaneously just before dialysis, 3 times during dialysis and immediately after dialysis. Changes in IVCD and PVP were compared at each timepoint with ultrafiltration volumes. We analyzed 30 hemodialysis sessions from 20 patients. PVP was validated as a surrogate for CVP. Mean ultrafiltration volume was 2102 $\pm$ 667 mL. IVCD discriminated better ultrafiltration volumes $\leq$ 500 mL or $\leq$ 750 mL than PVP (AUC 0.80 vs 0.62, and 0.80 vs 0.56, respectively; both $P < 0.01$). IVCD appeared to track better ultrafiltration volume ($P < 0.01$) and hemoconcentration ($P < 0.05$) than PVP. Changes in IVCD were of greater magnitude than those of PVP (average change from predialysis: -58 $\pm$ 30% vs -28 $\pm$ 21%; $P < 0.001$).

Conclusions: In patients undergoing ultrafiltration, changes in IVCD tracked changes in volume status better than venous pressure. (*J Cardiac Fail 2022;00:1–10*)

Key Words: Heart failure, congestion, inferior vena cava, venous pressure.

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Congestion is central to the pathophysiology and symptoms of heart failure (HF),[1–3] and acute decompensated HF (ADHF) is primarily a disease of congestion rather than low cardiac output.[4–7] ADHF accounts for more than half of all HF related expenditures, and HF represents 1 of the most common causes of death and hospitalizations in the United States.[8–10] As such, tracking congestion is crucial for the management of patients with HF.

Most congestion-monitoring systems measure elevations in pulmonary and systemic venous pressure as indicators of congestion.[11–13] The remarkable compliance of the venous system may provide a superior readout of volume status because large changes in venous volume occur with minimal changes in pressure, at least in the linear-compliant range of the venous pressure/volume relationship.[14–16] Theoretically, measurements of venous distension in the inferior vena cava (IVC) could be a noninvasive, earlier and more sensitive indicator of congestion before venous and intracardiac pressures rise.[17,18]

To investigate this hypothesis, we previously tested a novel sensor that measures IVC cross-sectional area in proof-of-concept experiments in an animal model.[19] In these experiments, IVC changes were significantly more sensitive than cardiac filling pressures following manipulation of intravascular volume, vascular tone and cardiac dysfunction in sheep.[19] Here we evaluate the potential for IVC diameter (IVCD) to track volume status, comparing it with directly measured venous pressure during fluid removal with hemodialysis in humans with cardiac dysfunction.

Methods

Patient Population

Patients in the hemodialysis program at our institution were enrolled into a prospective cohort study. Inclusion criteria included (1) chronic hemodialysis (patients with hemodialysis vintage $>$ 3 months); (2) functional central venous dialysis catheter; (3) average weight gain $\geq$ 3% of their dry weight between hemodialysis sessions; (4) the presence of systolic and/or diastolic ventricular dysfunction. Systolic dysfunction was defined as a left ventricular ejection fraction below 50%. Diastolic dysfunction was diagnosed based on the functional, morphological and biomarker criteria of the consensus recommendation of the Heart Failure Association of the European Society of Cardiology.[20] Patients with nonoptimal acoustic windows for viewing the inferior vena cava that prevented capturing images of acceptable quality were excluded. This study was approved by the research committee of our institution, and all patients provided written informed consent.

Hemodialysis Sessions

Patients in the hemodialysis program receive postdilution hemodiafiltration therapy 3 times per week. On the day of the study, patients arrived at the hemodialysis unit at 7 AM and were asked to eat their breakfast before they were weighed. Patients were not allowed to eat or drink after they were weighed. Patients were weighed just before the beginning of the hemodialysis session and were included in the study only if they had gained $\geq$ 3% of their dry body weight since the previous hemodialysis session. After patients were weighed, they were placed in a hemodialysis chair, and the head elevation was set to approximately 30 degrees. The position in the hemodialysis chair and the head elevation were maintained during the entire study and across all the study participants such that all measurements were standardized and not affected by changes in body position. Details of IVCD measurements are described below. After that, an experienced nurse placed a peripheral IV catheter in the upper extremity and took baseline blood samples. The IV catheter was heparinized, and the peripheral venous pressure (PVP) was measured as described below. Finally, the central venous dialysis catheter was opened, and the central venous pressure (CVP) was measured just before the patients were connected to the hemodialysis machine. The treating nephrologist set the ultrafiltration volume based on the weight gain plus 400 mL, which is the volume of crystalloid that patients receive based on the circuit volume.

Five timepoints were established for measurement of the parameters of interest: predialysis, intradialysis 1, intradialysis 2, intradialysis 3, and postdialysis (Fig. 1). For the 3 intradialysis timepoints, the length of the dialysis session was divided by 3 to create equal time periods. During each of these 5 timepoints, we measured the IVCD and the PVP and recorded the ultrafiltration volume and hemoglobin measured by the hemodialysis machine. At the end of hemodialysis, the total ultrafiltration volume was recorded, and the patients were weighed. Changes in IVCD and PVP were compared with ultrafiltration from predialysis to intradialysis 1, intradialysis 1 to intradialysis 2, intradialysis 2 to intradialysis 3, and intradialysis 3 to postdialysis. In a sensitivity analysis, only changes in IVCD and PVP from predialysis to intradialysis 1 were examined because during this time patients experienced the greatest changes in their fluid status; approximately 400 mL of blood left the intravascular space to fill

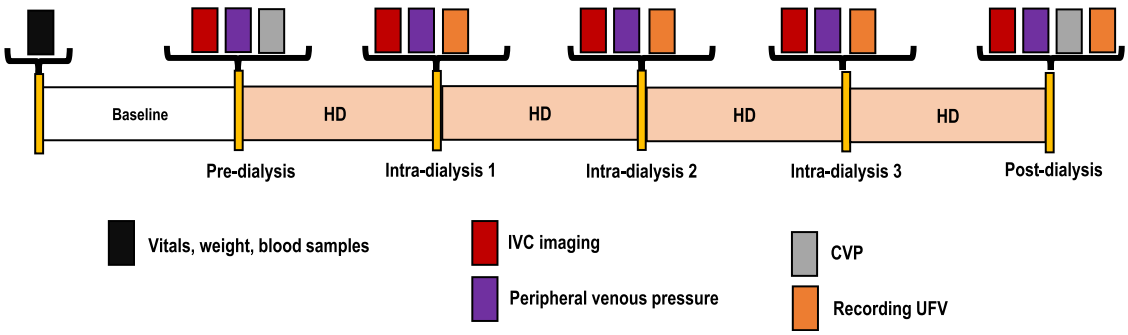

Fig. 1. Study flow diagram. Five timepoints were established to measure IVCD (red boxes) and PVP (purple boxes): predialysis, intradialysis 1, intradialysis 2, intradialysis 3, and postdialysis. Changes in IVCD and PVP were compared with ultrafiltration volume from predialysis to intradialysis 1, intradialysis 1 to intradialysis 2, intradialysis 2 to intradialysis 3, and intradialysis 3 to postdialysis. PVP was measured at the same time as CVP (gray boxes) at predialysis and postdialysis. CVP, central venous pressure; HD, hemodialysis; IVCD, inferior vena cava diameter; PVP, peripheral venous pressures; UFV, ultrafiltration volume.

the hemodialysis circuit, and they were also exposed to ultrafiltration.

Measurements of the IVC

Several measurements of the IVCD were performed at 5 points, as described above. Patients were placed in the hemodialysis chair, as described above, and stayed in the same position across all timepoints. The IVCD was measured in a subcostal or lateral view (5th intercostal space crossing the anterior axillary line), depending on image quality. All measurements were made with the IVC displayed in the longitudinal view. The following measurements of the IVCD were taken in each timepoint: maximum diameter and minimum diameter during normal respiration; maximum diameter during a breath hold after a normal inspiration; and the minimum diameter during a sniff. All measurements were done in triplicate, and average values were used for the final analysis. A total of 60 measurements were taken per patient (12 measurements [3 for each of the 4 dimensions described above] at each of the 5 timepoints), representing 1800 measurements during the study. All measurements were done by the same operator, a cardiologist with level III training in echocardiography. Intraobserver variability for maximum and minimum IVCD was obtained by analysis of 10 randomly selected cases by the same observer 2 months apart, and the intraclass correlation coefficient was 0.95 and 0.96 for maximum and minimum IVCD, respectively. The mean difference between measurements was 0.5 ± 0.9 mm and 0.3 ± 0.5 mm, respectively.

Central and Peripheral Venous Pressures

CVP and PVP were taken with the patient in the same position as for the IVCD measurements so as to establish comparable conditions. PVP and CVP measurements were taken sequentially by the same transducer. For the PVP measurement, the peripheral venous catheter was placed in the antecubital vein (18−22 gauge) and connected directly to the pressure line of the transducer. Measurements were taken at end-expiration using standard transducers after being zeroed at the phlebostatic axis. The patient's arm was placed such that the position of the peripheral catheter was at the level of the right atrium. Continuity of the peripheral intravenous line with the central venous system was assessed by demonstrating augmentation of the venous pressure after manual circumferential occlusion of the extremity proximal to the catheter, as described previously.[21] To obtain the CVP measurement, the hemodialysis' central venous catheter was attached via an extension set to a standard transducer positioned at the phlebostatic axis with the same procedure as described for the PVP. The transducer was connected to a monitor, where the CVP was read, and the mean CVP was recorded.

PVP was measured at each of the 5 timepoints described previously (predialysis, intradialysis 1, intradialysis 2, intradialysis 3, and postdialysis). Because the central venous catheter was used for dialysis, CVP was measured only at predialysis and postdialysis.

Hemoconcentration

The hemodialysis machine measures hemoglobin levels during the hemodialysis session. We recorded hemoglobin values at each timepoint. Changes in hemoglobin were analyzed from intradialysis1 to intradialysis 2, and from intradialysis 2 to intradialysis 3. Change in hemoglobin from predialysis to intradialysis1 was not included because using hemoconcentration as a surrogate for change in intravascular volume requires a stable red cell mass, which was not met because blood was leaving the

intravascular space to fill the ~400 cc circuit. Likewise, changes in hemoglobin from the intradialysis 3 to the postdialysis were also not included because approximately 400 mL of priming solution mixed with blood were returned to the patient at the end of the dialysis. Hemoconcentration was analyzed as the difference between 2 consecutive timepoints.

Statistical Analysis

Data that were approximately normally distributed are presented as mean ± standard deviation, and data with skewed distribution are shown as median with interquartile ranges (IQRs). Categorical values are presented as frequencies and percentages. IVCD and PVP were compared in 3 different ways: (1) The diagnostic utility of PVP vs IVCD measurements to determine changes in the ultrafiltration volume was evaluated by comparing the area under the curve from receiver-operating characteristic analyses by using the DeLong method; (2) IVCD and PVP (both in percent changes from baseline, given that they are in different units [mm vs mmHg]) were compared with ultrafiltration volume. Linear mixed models were used to account for the absence of independence of observations. The dependent variable was the percent change; fixed effects were ultrafiltration volume (continuous variable), a binary variable that was coded as 1 for IVCD and 2 for PVP, and their interaction term. Mixed models were a 3-level model with random intercepts by: (1) a variable identifying each patient and (2) a variable identifying each hemodialysis session, with the variable identifying each patient nested within the variable identifying each hemodialysis session. To capture the nonlinear association between ultrafiltration volume and IVCD or PVP, variables were modeled with a restricted cubic spline function with 3 knots and presented graphically. The locations of the knots were determined by the percentiles recommended by Harrell. Because 3 knots were chosen, percentiles were 10, 50 and 90. (3) The magnitude of percent change between IVCD and PVP was analyzed with linear mixed models; percent change in IVCD or PVP from predialysis to each of the other timepoints was the dependent variable, and a binary variable defining IVCD vs PVP was the independent variable (fixed effects). Random intercepts included (1) a variable identifying each patient; (2) a variable identifying each hemodialysis session; (3) a variable identifying each timepoint. Finally, linear mixed models were used to estimate correlation coefficients for the association between IVCD or PVP with hemoconcentration, and the correlation coefficients were compared by using the Meng test. A 2-tailed P value < 0.05 was considered statistically significant. Analyses were performed using Stata 17.0 (StataCorp, College Station, TX).

Results

Patient Population

A total of 20 patients were included in the analysis. Baseline characteristics are presented in Table 1. Eleven (55%) patients had left ventricular ejection fraction < 50%, and all patients fulfilled echocardiographic criteria for diastolic dysfunction. The left atrium was, on average, dilated (> 34 mL/m^2), and all patients had increased NT-proBNP levels (median 3541, IQR 1811–6377 pg/mL).

Hemodialysis Characteristics

We collected data from 30 hemodialysis sessions (Table 2). We included 10 patients during 2 different hemodialysis sessions, and 10 additional patients

Table 1. Baseline Patients Characteristics

Variable	n = 20
Age (years)	37 (30−46)
Female	13 (65%)
Weight (kg)	56.4±12.0
Body mass index (kg/m^2)	21.7 (20.3−23.4)
Functional class (NYHA)	
I	14 (70%)
II	5 (25%)
III	1 (5%)
Time in hemodialysis therapy (years)	3 (2−5)
Etiology of CKD	
Idiopathic	7 (35%)
Systemic lupus erythematosus	5 (25%)
Pre-eclampsia	2 (10%)
Other	6 (30%)
Comorbidities and baseline laboratory levels	
Diabetes	1 (5%)
Hypertension	11 (55%)
Smoker	6 (30%)
Hemoglobin (g/dL)	9.3±2.35
Hematocrit (%)	28.7±7.29
Proteins (g/dL)	6.7±0.58
Albumin g/dL)	3.9±0.32
NT-proBNP (pg/mL)	3541 (1811−6377)
Echocardiographic parameters	
End diastolic volume (mL/m^2)	62.1±18.1
Left ventricular ejection fraction (%)	49±8
Patients with LVEF <50%	11 (55%)
Left ventricular geometry	
Normal	4 (20%)
Concentric remodeling	6 (30%)
Concentric hypertrophy	8 (40%)
Eccentric hypertrophy	2 (10%)
Diastolic dysfunction	
Grade I	15 (75%)
Grade II	4 (20%)
Grade III	1 (5%)
Left atrium volume (mL/m^2)	36 ± 11

Data are presented as median (quartile 1−3), mean ± SD, or n (%).

CKD, chronic kidney disease; LVEF, left ventricular ejection fraction; NT-proBNP, N terminal pro natriuretic peptide; NYHA, New York Heart Association.

Table 2. Hemodialysis Sessions Characteristics

Characteristic	N = 30
Weight predialysis (kg)	56.9±11.6
Weight postdialysis (kg)	54.9±11.1
Central venous pressure predialysis (mmHg)	11±2
Central venous pressure postdialysis (mmHg)	7±3
Peripheral venous pressure predialysis (mmHg)	11±2
Peripheral venous pressure postdialysis (mmHg)	8 ± 3
Ultrafiltration volume (mL)	2101.5±666.8
Time of the hemodialysis session (min)	185 (185−190)
Systolic blood pressure predialysis (mmHg)	138 (118−154)
Systolic blood pressure post dialysis (mmHg)	121 (113−147)

Data are presented as median (quartile 1−3) or mean ± SD.

were included once. The median time of the hemodialysis session was 185 (185−190) minutes, and the mean ultrafiltration volume during this time was 2102 ± 667 mL. The mean weight loss from pre- to postdialysis was 2.0 ± 1.0 kg, representing 3.7% ± 1.0% of their dry body weight. The ultrafiltration volume at each timepoint was: predialysis to intradialysis 1 = 772 ± 261 mL; intradialysis 1 to intradialysis 2 = 670 ± 268 mL; intradialysis 2 to intradialysis 3 = 586 ± 148 mL; and intradialysis 3 to postdialysis 73 ± 230 mL. Note that the from intradialysis 3 to postdialysis, the ultrafiltration volume approached 0 because of the 400 mL of the blood/crystalloid returned to the patient from the circuit.

Validation of PVP as a Surrogate for CVP

CVP was successfully measured in 90% of sessions through the dialysis catheter, and PVP was successfully measured in 93% of the hemodialysis sessions. CVP and PVP showed a strong correlation: R = 0.94 ($P < 0.001$) (Supplementary Fig. 1). The mean difference between CVP and PVP was -0.31 mmHg (95% CI -0.80−0.19 mmHg).

Association Between IVC Parameters, PVP and Ultrafiltration Volume

At baseline, prior to dialysis, maximum and minimum IVCDs during normal respiration were 16.6 ± 3.7 mm and 12.6 ± 4.8 mm, respectively. IVCD during the sniff maneuver (minimum diameter) was 10.9 ± 3.8 mm. Mean CVP and PVP at baseline were 11 ± 2 mmHg. Changes in maximum and minimum IVCD and PVP during dialysis are described in Supplementary Table 1. Changes in IVCD (maximum and minimum) better discriminated changes in ultrafiltration volumes ≤ 500 mL or ≤ 750 mL compared with PVP in receiver operating curve analysis ($P<$ 0.01 for all comparisons) (Fig. 2). Likewise, when analyzing the ultrafiltration volume at all timepoints during dialysis, changes in IVCD (maximum and minimum) were statistically different from changes in PVP, and they appeared to track better with ultrafiltration volume than changes in PVP ($P<$ 0.01 for both comparisons) (Fig. 3). In addition, changes in IVCD were more sensitive (ie, of greater relative magnitude) than PVP when analyzing changes from predialysis to each of the other timepoints mentioned previously (average change for IVCD minimum: -58% ± 30%; average change for IVCD maximum: -35% ± 22%; average change for PVP: -28±21%; $P < 0.001$ for both IVCD maximum and minimum compared with PVP) (Fig. 4).

Importantly, when examining the time from predialysis to intradialysis 1 (the greatest change in fluid status), the changes in IVCD were of greater relative magnitude than the respective changes in PVP, as shown in Fig. 4 ($P<$ 0.01 for both maximum and minimum diameter). Changes in IVCD (maximum and minimum) were statistically different from changes in PVP ($P<$ 0.05 for both) and appeared to track better ultrafiltration volume compared with changes in PVP (Supplementary Fig. 2).

Association Between IVC Parameters, PVP and Hemoconcentration

Mean hemoglobin at intradialysis 1 was 9.7 ± 1.9 mg/dL, at intra-dialysis 2 was 10.5 ± 2.0 mg/dL and intradialysis 3 was 11.0 ± 2.3 mg/dL. Changes in IVCD correlated with hemoconcentration (IVCD max: R = -0.33; P= 0.011; IVCD min: R = -0.54; P= 0.003) better than change in PVP (R = 0.14; P= 0.68; P= 0.02 for between parameter comparison of IVCD min vs PVP).

Discussion

We measured changes of IVCD and PVP during fluid manipulations in patients on dialysis and with cardiac dysfunction. The principal finding was that changes in IVCD were more sensitive (ie, of greater relative magnitude) than changes in PVP, and they also more reliably tracked the ultrafiltration volume. These proof-of-concept findings are in alignment with our prior findings in animals and the known compliant physiology of venous vasculature. Measurements based on IVC size may offer significant advantages for earlier detection of congestion compared with pressure-based monitoring, and this hypothesis warrants testing in clinical trials (Visual Take-Home Graphic).

The finding that IVC size changes are more sensitive than changes in venous pressure is expected, based on the well-established physiology of the venous system, at least in the lower range of venous dimensions. The venous vasculature is approximately 30 times more compliant than the arterial vasculature and contains ~70% of the total blood

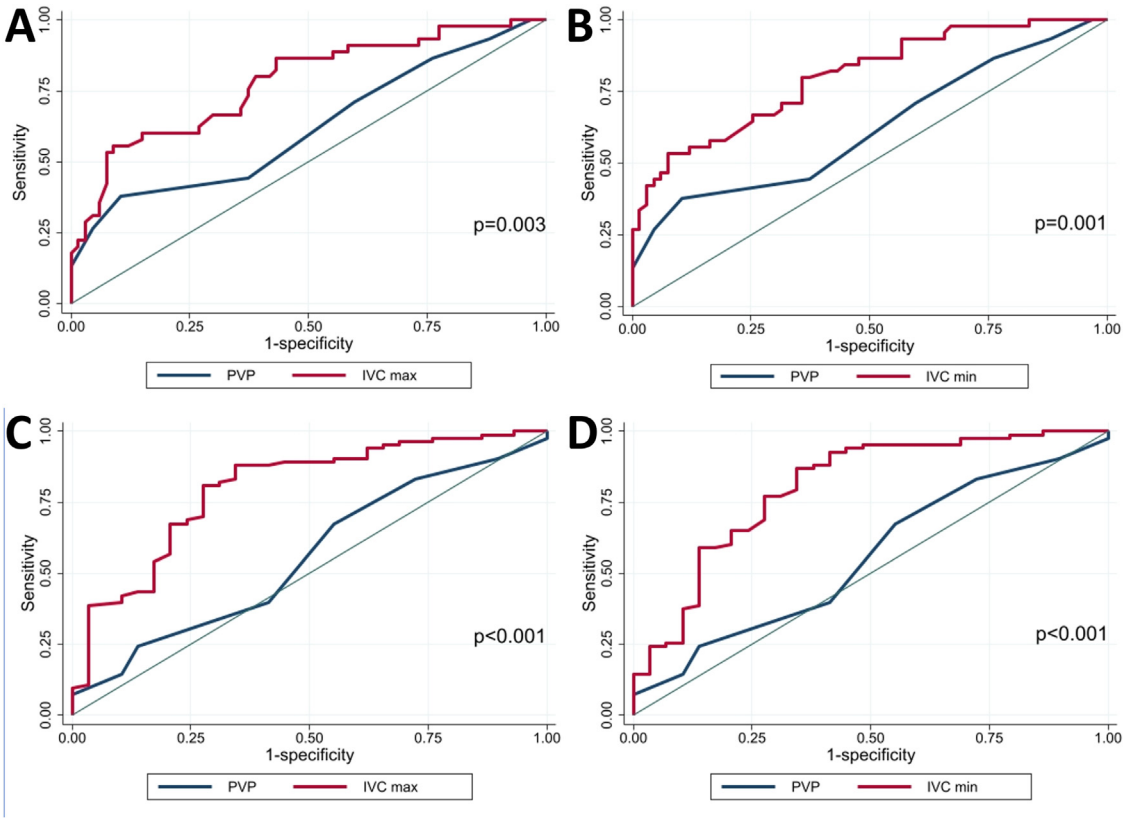

Fig. 2. Discrimination capacity of IVC diameters and PVP for ultrafiltration volumes. A and B show the discrimination capacity of IVC diameter and PVP for an ultrafiltration volume < 500 mL. Changes in IVC maximum diameter (A, AUC 0.78) or minimum diameter (B, AUC 0.80) discriminated better an ultrafiltration volume < 500 mL compared with PVP (AUC 0.62); *P*= 0.003 for IVC maximum diameter vs PVP; *P*= 0.001 for IVC minimum diameter vs PVP. C and D show the discrimination capacity of IVC diameter and PVP for an ultrafiltration volume < 750mL. Changes in IVC maximum diameter (C, AUC 0.80) or minimum diameter (D, AUC 0.80) discriminated better an ultrafiltration volume < 750 mL compared with PVP (AUC 0.56); *P*< 0.001 for both IVC maximum diameter or IVC minimum diameter vs PVP. For a volume < 750 mL, the optimal cut-off value for PVP was -1.5 mmHg (sensitivity 67%, specificity 45%); for IVCD maximum, it was -2.1 mm (sensitivity 82%, specificity 74%); and for IVCD minimum, it was -3.1 mm (sensitivity 85%, specificity 65%).

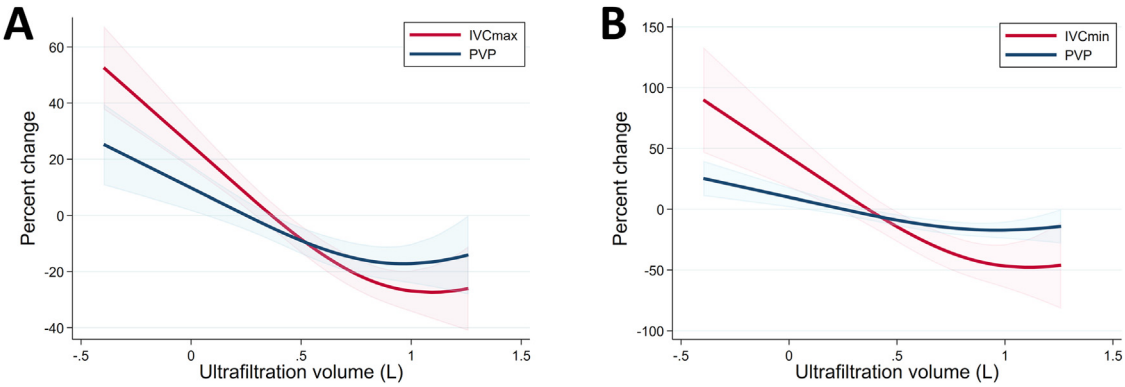

Fig. 3. Association between IVC diameter changes, PVP changes and ultrafiltration volume. Changes in IVC maximum diameter (left panel) and changes in IVC minimum diameter (right panel) tracked better ultrafiltration volume compared with changes in PVP (blue lines) during hemodialysis (*P* interaction <0.01 for both). Note that the x axis (change in volume) goes from 1500 mL to -400 mL. Negative numbers mean a net positive balance, which occurred in some patients from intradialysis 3 to postdialysis, when approximately 400 mL of priming solution mixed with blood were returned to the patient; if the volume of ultrafiltration during this period was lower than 400 mL, the balance was net positive.

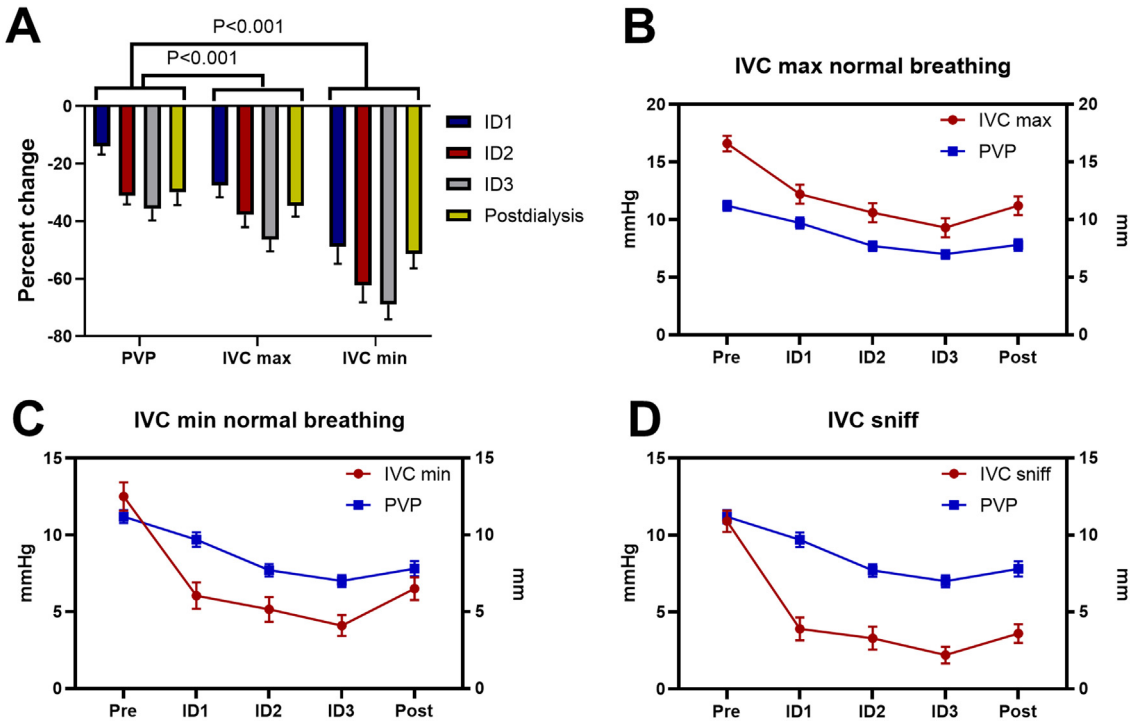

Fig. 4. A, Comparison between changes in IVC diameter and PVP from predialysis to subsequent timepoints. Changes in IVC maximum or minimum diameter are compared with changes in PVP (all in percent change) from predialysis to each of the subsequent timepoints (intradialysis 1, intradialysis 2, intradialysis 3, and postdialysis). Panels B, C and D (red lines) show IVC maximum diameter during normal respiration, minimum diameter during normal respiration, and minimum diameter during sniff, respectively. PVP is shown in the same figures in blue. Data are presented as mean and SEM across the 5 timepoints. Changes in IVC max or IVC min were of greater magnitude than changes in PVP in A ($P < 0.001$ for both). Changes in IVC from predialysis to intradialysis 1 appeared to be the greatest. ID, intradialysis; IVC, inferior vena cava; PVP, peripheral venous pressure.

volume. Due to this compliance, pressure and volume are relatively disassociated until the capacitance is exceeded by large changes in volume or a change in the vasculature tone. In alignment with this physiology, measures such as pulmonary capillary wedge pressure and CVP have consistently demonstrated minimal correlation with measures of venous volume (ie, circulating blood volume and intravenous fluid administration).[22] Congruently, in our present study, IVCD was more sensitive and specific for detecting small changes in ultrafiltration volume than was peripheral venous pressure.

Previous preclinical proof-of-concept studies validated the discordant relationship between changes in IVC and CVP.[19,22] During experiments involving administering IV fluid, venous vasodilator therapy and inducing acute HF with rapid ventricular pacing, an implantable sensor measuring IVC area was more sensitive than hemodynamic monitoring parameters, including CVP. These findings indicated that IVC measures can detect both venous-volume changes, due to fluid administration and redistribution, earlier than pressure-based measures. Our present findings validate the superior sensitivity of IVC size to detect changes with changes in total blood volume following ultrafiltration.

The transition from compensated to symptomatic decompensated HF is preceded by a rise in venous pressures prior to symptom onset.[23] Importantly, this change in venous pressure often occurs without measurable change in total body volume as indicated by weight change.[23–25] Implantable pulmonary artery-based pressure monitoring systems have demonstrated the ability to reduce hospitalizations due to HF by detecting these changes in pressure and tailoring diuretic and vasodilatory therapies to treat the underlying venous congestion. However, the absolute rate of HF events remained high; death or HF hospitalization occurred in more than 30% of patients at 1 year.[12,13,26] Following the theory behind these interventions, devices serially monitoring IVC size changes may be a strategy for earlier detection of congestion prior to changes in vascular pressure. This hypothesis warrants testing by chronic IVC remote monitoring in patients with HF. The FUTURE-HF trial (NCT04203576) is testing the feasibility and safety of FIRE1 device monitoring IVC size in patients with HF.

Several limitations should be noted. Congestion is a slow process on the timescale of days, and we studied acute changes in volume status. Nevertheless,

hemodialysis provides the opportunity to investigate fluid changes on a much faster time scale, improving the signal-to-noise ratio and potentially decreasing other factors that may affect IVC and filling pressure, independent of volume status. We studied patients undergoing chronic hemodialysis in whom vascular calcifications and other changes may independently influence venous pressure-volume relationships. However, these changes should diminish vasculature capacitance, making pressure a more sensitive measure of volume changes, which would be expected to bias the present results toward the null. Yet this represents a limitation because patients with acute HF may show differing venous compliance. IVCD was not severely enlarged at baseline; however, patients had, on average, lower body surface areas, and it has been suggested that IVCD is independently associated with body surface area. In fact, in patients with lower body surface areas, an IVCD of 17 mm was suggested as optimal cutoff point to define increased right atrial pressure.[27] We manipulated blood volume via ultrafiltration, which may not be representative of changes in venous volumes during the transition to decompensated HF. The present study does not show whether changes in IVC would remain more sensitive than PVP: (1) in gradual volume gain as would occur in outpatients with HF; (2) in patients admitted with ADHF and higher CVP on admission; (3) in patients whose net fluid loss was greater than 3 L during inpatient stay. We studied a relatively young population, and only 1 patient had diabetes; therefore, we cannot generalize our findings to regular hemodialysis cohorts, in whom diabetes mellitus is the main cause of kidney disease. Likewise, our findings cannot be directly translated to patients with HF without kidney failure but they warrant further investigation in such patients with HF. Changes in IVC are not a pure reflection of change in total blood volume and likely are influenced to variable degrees by venous capacitance, IVC compliance and tone, and transmural pressure. "Normal" IVC size has interpatient variability, limiting an absolute value indicative of congestion; thus, normalization to each patient as well as serial changes may be required for interpretation. The study was not blinded to the operator measuring the IVCD.

Conclusion

In conclusion, this proof-of-concept study in humans is consistent with our previously reported animal study, which showed that changes in IVC are more sensitive than changes in filling pressures during manipulation of volume status. Thus, the study supports the concept that monitoring the IVC may have value in the management of patients with chronic HF.

Lay Summary

Tracking congestion (too much fluid in the body) is key for the management of patients with heart failure. In this study, patients with stable hemodialysis were studied. We measured the inferior vena cava diameter and the peripheral venous pressure during ultrafiltration (removal of extra fluids from the body). Inferior vena cava diameter appeared to track better ultrafiltration volume than peripheral venous pressure. Possibly, monitoring inferior vena cava size changes may be a strategy for earlier detection of congestion. This hypothesis warrants testing chronic inferior vena cava monitoring in patients with heart failure.

Funding Source

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Conflicts of Interest

ZLC receives research funding from AstraZeneca and Cumberland Pharmaceuticals. MM is a consultant for Baxter, Astra Zeneca, Lilly-Boehringer. She has received research support from the Renal Research Institute (Fresenius Medical Center). AM reports personal fees from Orion, Roche, Adrenomed and Fire 1 and grants and personal fees from 4TEEN4, Abbott, Roche and Sphyngotec. DB reports institutional grant support from Fire1. MRC provides consultancy advice to AstraZeneca, Servier, Roche Diagnostics, Fire1, Medtronic & Abbott. MF was supported by the National Heart, Lung, and Blood Institute (NHLBI) (K23HL151744). He receives consulting fees from Fire1. KD reports being speaker and consultancy fees from Abbott, Boehringer Ingelheim, Astra Zeneca, Fire1. BAB has received research support from R01 HL128526 and U01 HL160226, from the National Institutes of Health (NIH), and W81XWH2210245, from the United States Department of Defense, as well as research grants from AstraZeneca, Axon, GlaxoSmithKline, Medtronic, Mesoblast, Novo Nordisk, and Tenax Therapeutics. BAB has received consulting fees from Actelion, Amgen, Aria, Axon Therapies, BD, Boehringer Ingelheim, Cytokinetics, Edwards Lifesciences, Eli Lilly, Imbria, Janssen, Merck, Novo Nordisk, NGM, NXT, and VADovations. BAB is named inventor on an issued patent (US Patent no. 10,307,179) for the tools and approach for a minimally invasive pericardial modification procedure to treat heart failure. JMT reports grants and/or personal fees from 3ive labs, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Astra Zeneca, Novartis, Cardionomic, MagentaMed, Reprieve inc., FIRE1, W.L. Gore, Sanofi, Sequana Medical, Otsuka,

Abbott, Merck, Windtree Therapeutics, Lexicon pharmaceuticals, Precardia, Relypsa, Regeneron, BD, Edwards life sciences, and Lilly. In addition, JMT has a patent Treatment of diuretic resistance issued to Yale and Corvidia Therapeutics Inc, a patent Methods for measuring renalase issued to Yale, and a patent Treatment of diuretic resistance pending with Reprieve inc. JBIM reports personal fees from Boehringer Ingelheim, AstraZeneca, Novartis, Translational Catalyst, Merck, Moksha8, and Servier. The other authors report no conflicts relevant to the content of this manuscript.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2022.09.012.

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