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Brief Report

The Effect of Decongestion on Intrarenal Venous Flow Patterns in Patients With Acute Heart Failure

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ABSTRACT

Background: Discontinuous intrarenal venous flow patterns, as assessed by renal Doppler ultrasound examination, are associated with changes in hemodynamics such as volume expansion and poorer diuretic response in patients with heart failure (HF). We aimed to study intrarenal venous and arterial flow patterns after decongestive treatment in patients with acute HF.

Methods and Results: Fifteen patients with acute HF were enrolled. Intrarenal venous and arterial flow patterns were assessed at baseline, 1 hour after administration of loop diuretics, at day 2 and day 3. Among patients hospitalized for acute HF, 13 (87%) had a discontinuous venous flow pattern at admission. After decongestive treatment, a significant improvement of the venous impedance index (P = .021) and venous discontinuity index (P = .004) was observed at day 3 compared with baseline. There was no effect on the intrarenal arterial flow patterns.

Conclusions: In patients who exhibit discontinuous renal venous flow patterns hospitalized for decongestive treatment owing to acute HF led to a normalization of intrarenal venous flow to a continuous pattern. (*J Cardiac Fail 2020;00:1−6*)

Keywords: Heart failure, intrarenal flow, decongestion.

Heart and kidney function are closely related, and in patients with heart failure (HF), renal dysfunction is common and is associated with poor outcomes.[1] An increase in the central venous pressure is one of the primary determinants of renal impairment and reduced diuretic efficacy in patients with HF.[2] Furthermore, signs and symptoms of fluid overload are one of the main targets of therapy by attempting to compensate for the disproportional neurohormonal activation and sodium retention.[3] The function of the kidney is therefore of the utmost importance in HF, yet pathophysiologic changes, such as increased venous pressure, have detrimental effects on the kidneys. Recently, assessment of intrarenal flow patterns using renal Doppler ultrasound examination has become of interest in patients with HF, where discontinuous flow has been suggested to be associated with congestion and decreased diuretic response.[4,5] The findings in the previously described studies warrant further investigations regarding intrarenal flow patterns in patients with acute HF to establish its value during decongestive treatment in patients with decompensated HF. We therefore aimed to study intrarenal venous and arterial flow after decongestive treatment in patients with acute HF. We hypothesized that effective decongestion in patients with acute HF would result in normalization of intrarenal venous flow without an effect on arterial flow.

Methods

Study Design and Study Population

In this observational exploratory study, we assessed intrarenal flow patterns at different time points during decongestive treatment in patients with acute HF. Patients were

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prospectively enrolled in a single tertiary HF clinic between October 2018 and February 2019. In general, subjects were eligible for enrollment if they were older than 18 years of age and able to provide written informed consent. Patients were only enrolled on week days during day time hours. For more specific inclusion and exclusion criteria, see Supplementary Table 1. A total of 15 patients with acute HF were enrolled. The study was carried out in accordance with the Declaration of Helsinki. The study protocol was approved by the local institutional review board, and all patients provided written informed consent.

Renal Ultrasound Assessments

Intrarenal flow patterns, both arterial and venous were assessed at baseline, 1 hour after administration of loop diuretics, at day 2, and day 3. Renal Doppler ultrasound examination was performed with the use of a commercially available system with a convex transducer frequency range of 2.5−5.0 MHz. Resting images were obtained in the left semilateral decubitus position where the right kidney was recorded. Color Doppler images were used to locate interlobar vessels. Pulsed Doppler waveforms of interlobar arteries and veins were recorded simultaneously. Intrarenal arterial flow, venous impedance index and flow patterns were obtained as described previously (Supplementary Methods and Supplementary Fig. 1).[5,6] All measurements were averaged over 3 cardiac cycles during sinus rhythm, or 5 cardiac cycles if patients were in atrial fibrillation. The treating physicians were blinded to the results of the renal ultrasound assessments. Renal ultrasound examination was performed by 2 clinicians; all images were analyzed by 1 clinician.

Statistical Analysis

Data are presented as mean ± standard deviation when normally distributed, as median (interquartile range [IQR]) when skewed and as frequencies (percentage) when categorical. Normality of variables was evaluated graphically using histograms and normal quantile−quantile plots. Baseline characteristics (Table 1) were analyzed using the independent samples *t* test for normally distributed variables and Mann−Whitney *U*test for skewed variables. The χ^2 test was used for categorical variables. Patients were divided into groups based on changes in venous flow, comparing patients with an improved venous flow pattern with those displaying no changes in venous flow patterns. Changes in intrarenal venous flow over time were analyzed using the Wilcoxon signed rank test for non-normally distributed values, and the McNemar test for categorical values. A 2-tailed *P* value of less than .05 was considered statistically significant. All analyses were performed using SPSS version 22 (IBM, Chicago, IL)

Results

A total of 15 patients with acute HF were enrolled. The median age of the enrolled patients with acute HF was 81 years, and 67% were male (Supplementary Table 2). All patients had signs and symptoms of congestion at time of enrollment, median N terminal pro blood natriuretic peptide was 3931 ng/L, median estimated glomerular filtration rate 50 mL/min/1.73 m^2, and median left ventricular ejection fraction 43.1%. HF was most commonly owing to ischemic heart disease (60%).

On admission, 13 patients (87%) had a discontinuous venous flow pattern (60% biphasic, 27% monophasic), and the median venous impedance index was 1.0 [IQR 1.0−1.0]. The median intrarenal resistance index was 0.6 [IQR 0.5−0.7], whereas the venous discontinuity index was 0.5 [IQR 0.2−0.6].

One hour after administration of intravenous loop diuretics there was no significant change in renal arterial or venous flow patterns (Supplementary Table 3). Over the following 2 days of decongestive therapy (Fig. 1), renal ultrasound values were assessed daily showing a significant improvement in renal venous flow patterns (median venous impedance index on day 3, 0.5 [IQR 0.4−1.0], $P = .021$ compared with baseline) and the venous discontinuity index (median venous discontinuous index on day 3, 0.0 [IQR 0.0−0.4], $P = .004$ compared with baseline). A total of 9 (60% of all patients, 69% of patients with discontinuous flow at baseline) patients showed an improvement in renal venous flow pattern after 2 days of decongestive treatment (Fig. 2 and Supplementary Fig. 2). When comparing the patients with an improvement in renal flow after 2 days versus no change, patients with an improvement had a significantly higher blood pressure, and more preserved renal function at baseline (all $P < .05$, Table 1). There was no difference in renal function at discharge, length of stay, diuretic dose at discharge, or weight change during the first 3 days of hospitalization.

No significant change in renal arterial flow patterns were observed over time (Supplementary table 3, Fig. 1).

Discussion

The present study was a proof-of-concept, exploratory study investigating the effect of decongestive treatment on renal arterial and venous flow patterns, as assessed by ultrasound examination. Our study showed that venous renal flow patterns were discontinuous in 87% of patients at admission for acute HF, improved significantly during decongestive therapy, and were normalized to a continuous venous flow pattern in a significant number of patients at discharge.

Renal Ultrasound Examinations in Acute HF

Limited data regarding intrarenal flow in patients with acute HF are available. The 2 largest studies investigating intrarenal flow in patients with HF enrolled patients with chronic HF, or inpatients with HF in which intrarenal flow was assessed at one time point. Iida et al[4] showed that impaired intrarenal venous flow was associated with higher right atrial pressure and poor prognosis. Unfortunately, signs and symptoms of congestion were not mentioned in this

Table 1. Patients With Acute HF With an Improvement in Renal Venous Flow Versus no Change From Baseline to Day 3

	Continuous Flow at Baseline	No Change	Improvement in Renal Venous Flow Pattern	*P* value No Change vs Improvement
n	2	4	9	
Demographics				
Sex (male)	100 (2)	100 (4)	44 (4)	.057
Age (years)	77 [73−81]	75 [70−82]	86 [77−90]	.053
SBP (mm Hg)	134 [120−147]	98 [94−118]	151 [129−163]	.007
DBP (mm Hg)	79 [63−94]	64 [57−68]	67 [66−79]	.313
HR (bpm)	93 [84−102]	56 [56−87]	64 [62−84]	.643
Edema				.367
None	0 (0)	0 (0)	0 (0)	
Minimal	0 (0)	0 (0)	11 (1)	
Above knee	100 (2)	100 (4)	89 (9)	
JVP	50 (1)	75 (3)	100 (9)	.118
Hepatomegaly	0 (0)	25 (1)	0 (0)	.118
Crepitations	100 (2)	25 (1)	78 (7)	.071
Orthopnea	50 (1)	75 (3)	89 (8)	.522
NYHA functional class	3 [2−3]	3 [3−4]	3 [3−3]	.206
Dyspnea VAS	55 [50−60]	55 [50−68]	75 [66−83]	.020
Comorbidities				
IHD	50 (1)	75 (3)	56 (5)	.506
AF	50 (1)	75 (3)	44 (4)	.308
DM	50 (1)	50 (2)	33 (3)	.569
Hypertension	100 (2)	75 (3)	67 (6)	.164
Renal failure	50 (1)	75 (3)	11 (1)	.522
Medications				
ACEi/ARB	50 (1)	100 (4)	89 (8)	.488
Beta-blockers	100 (2)	100 (4)	78 (7)	.305
MRA	50 (1)	50 (2)	33 (3)	.569
Diuretics	100 (2)	100 (4)	89 (8)	.488
Mg of bumetanide (or equivalent)	2.5 [1.0−4.0]	1.5 [0.6−4.3]	1.3 [0.6−2.5]	.999
Laboratory values				
Hb (g/dL)	13.8 [13.5−14.0]	11.2 [10.0−13.0]	11.7 [9.9−12.4]	.757
Urea (mg/dL)	40 [34−46]	132 [67−222]	57 [37−67]	.045
Creatinine (mg/dL)	1.3 [1.3−1.3]	2.1 [1.7−3.4]	1.2 [0.9−1.6]	.031
eGFR (mL/min/1.73 m^2)	52 [50−54]	32 [17−41]	56 [42−61]	.031
Sodium (mmol/L)	143 [142−143]	138 [136−141]	141 [137−142]	.533
Potassium (mmol/L)	4.1 [3.8−4.4]	4.6 [4.3−5.0]	4.1 [3.7−4.6]	.090
NT-proBNP (ng/L)	1951 [1910−1992]	7834 [2576−52,209]	5968 [3279−9413]	.440
Troponin (ng/L)	43 [35−50]	55 [36−94]	33 [22−51]	.216
Cardiac ultrasound examination				
LVEF (%)	25 [23−27]	43 [27−52]	44 [30−50]	.877
Left atrial volume/BSA mL/m^2	54 [52−56]	53 [35−76]	50 [45−74]	.877
LVESV/BSA (mL/m^2)	73 [41−105]	46 [29−88]	44 [33−67]	.758
LVEDV/BSA (mL/m^2)	96 [57−136]	87 [54−119]	79 [65−101]	.877
Stroke volume/BSA (mL/m^2)	28 [15−41]	31 [23−44]	34 [24−48]	.643
TAPSE (mm)	20 [15−24]	11 [11−14]	14 [11−20]	.405
RVSP (mm Hg)	30 [30−40]	39 [37−44]	50 [43−52]	.088
Moderate/severe mitral regurgitation	0 (0)	25 (1)	56 (5)	.308
Moderate/severe tricuspid regurgitation	0 (0)	50 (2)	33 (3)	.569
IVC diameter (mm)	26 [25−27]	26 [23−31]	23 [21−25]	.122
Collapse (>50%)	0 (0)	25 (1)	0 (0)	
Renal ultrasound examination				
RI	0.5 [0.5−0.6]	0.7 [0.6−0.7]	0.6 [0.6−0.7]	.782
VII	0.2 [0.2−0.2]	1.0 [1.0−1.0]	1.0 [1.0−1.0]	>.999
Continuous flow pattern	100 (2)	0 (0)	0 (0)	>.999
Biphasic	–	0 (0)	44 (4)	
Monophasic	–	100 (4)	56 (5)	
VDI	0 [0−0]	0.6 [0.4−0.6]	0.5 [0.3−0.6]	.165
Day 3 values				
Urea (mg/dL)	55 [49−61]	114 [67−225]	64 [42−79]	.088
Creatinine (mg/dL)	1.4 [1.2−1.6]	2.0 [1.6−3.2]	1.5 [1.1−1.6]	.089
eGFR (mL/min/1.73 m^2)	51 [40−61]	33 [19−45]	39 [31−60]	.185
RI	0.7 [0.6−0.7]	0.7 [0.5−0.7]	0.7 [0.5−0.7]	.758
VII	0.3 [0.3−0.4]	1.0 [1.0−1.0]	0.5 [0.3−0.8]	.023
Continuous flow pattern	100 (2)	0 (0)	78 (7)	.009
Biphasic	–	0 (0)	22 (2)	
Monophasic	–	100 (4)	0 (0)	
VDI	0 [0−0]	0.5 [0.4−0.6]	0 [0−0.1]	.003

(*continued*)

Table 1 (*Continued*)

	Continuous Flow at Baseline	No Change	Improvement in Renal Venous Flow Pattern	*P* value No Change vs Improvement
Weight change during first 3 days of hospitalization (kg)	3.0 [1.0−4.5]	2.6 [1.7−3.5]	2.2 [0.5−4.0]	.071
Discharge values				
Urea (mg/dL)	64 [58−69]	112 [74−198]	59 [44−90]	.064
Creatinine (mg/dL)	1.5 [1.4−1.6]	1.9 [1.0−2.3]	1.2 [0.8−1.6]	.280
eGFR (mL/min/1.73 m^2)	45 [41−49]	36 [26−69]	56 [35−66]	.395
Diuretic dose at discharge (mg of bumetanide or equivalent)	1.3 [1.0−1.5]	2.0 [0.9−2.0]	1.0 [1.0−1.0]	.272
Length of stay (days)	6.0 [5.0−7.0]	9.5 [5.5−18.5]	7.0 [5.0−9.0]	.587
Total dose of diuretics during hospitalization (intravenous mg of bumetanide or equivalent)	6.8 [5.5−8.0]	12.9 [5.1−46.6]	7.3 [5.3−10.3]	.315

ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; AF, atrial fibrillation; BMI, body mass index; BSA, body surface area; DBP, diastolic blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate (CKD-EPI); Hb, hemoglobin; HR, heart rate; IHD, ischemic heart disease; IVC, inferior vena cava; JVP, jugular venous pressure; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; MRA, mineralocorticoid antagonist; NT-proBNP, N terminal pro blood natriuretic peptide (Roche assay); NYHA, New York heart association; RI, resistance index; RVSP, right ventricular systolic pressure; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion; VAS, visual analog scale; VDI, venous discontinuity index; VII, venous impedance index.

Values are percent (n) or median [IQR] unless otherwise noted.

report, even though 151 patients were enrolled as inpatients during a hospitalization for HF. In 50 euvolemic patients with HF, Nijst et al[5] showed that after intravascular volume expansion, intrarenal venous flow was blunted in 50 chronic patients with HF, and discontinuous intrarenal venous flow was associated with a reduced diuretic response.

One of the hallmarks of acute HF is congestion, and restoration of euvolemia is, therefore, one of the main objectives of treatment. As such, assessment of intrarenal venous flow patterns during a hospitalization for acute HF might be of great interest to assess treatment effects, yet also study the association with renal function.

Our study serially assessed intrarenal arterial and venous flow patterns during a hospitalization for acute HF. We showed that, in patients admitted with acute HF, at admission 87% of patients had a discontinuous venous flow pattern before treatment. After decongestive treatment, intrarenal venous flow patterns improved significantly after 48 hours of treatment and normalized to a continuous pattern in approximately one-half of patients with previous discontinuous flow patterns. No significant changes in intrarenal arterial flow patterns were observed. Our results confirm the association of intrarenal venous flow and congestion as previously described by Nijst et al[5] in patients with chronic HF. Patients with an improvement in intrarenal venous flow over time did not receive significantly higher doses of diuretics compared with patients with no change in intrarenal venous flow, nor was there a difference in length of hospital stay. Patients with an improvement in renal venous flow patterns did, however, have better renal function at baseline, yet no difference in renal function was observed on day 3 or at discharge. This finding is in contrast with a study in patients with acute HF, where an improvement in renal function was unexpectedly associated with persistent evidence of renal congestion.[7] We

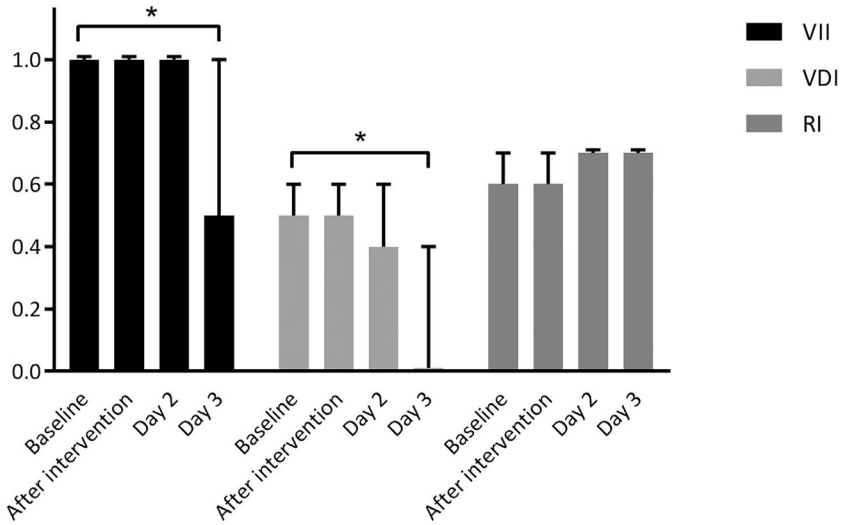

Fig. 1. Changes in arterial and venous flow following hemodynamic alterations. *$P < .05$. Figure shows median and IQRs. RI, resistance index, VDI, venous discontinuous index, VII, venous impedance index.

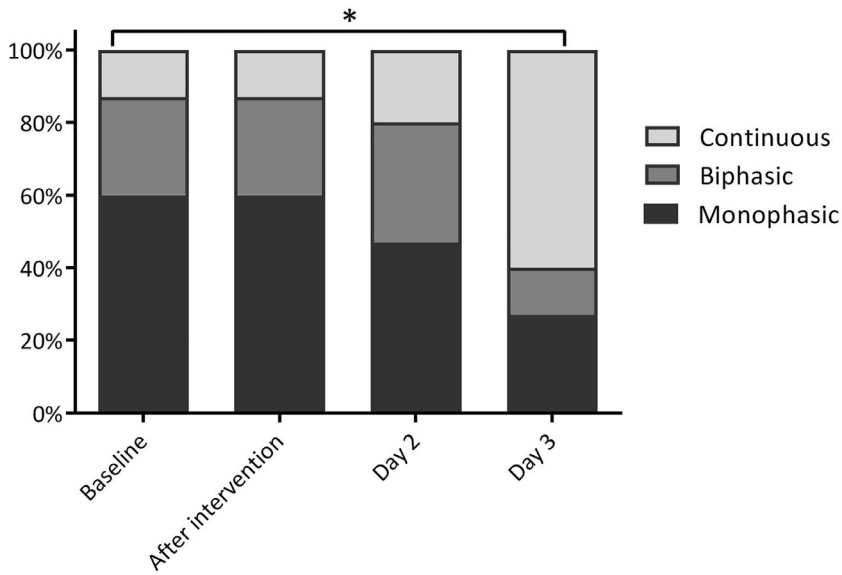

Fig. 2. Changes in percentages of continuous venous flow following hemodynamic alterations. *$P < .05$. AHF, acute heart failure, CRT, cardiac resynchronization therapy

did not see changes in renal flow parameters shortly after initiation of treatment. This finding suggests that significant hemodynamic, neurohumoral, and volume changes, as well as time, might be needed to (relatively) normalize intrarenal venous flow. Changes in venous capacitance alone, possibly induced by loop diuretic and vasodilator therapy, do not suffice.

Limitations and Future Perspectives

The limitations of our study include the limited number of patients enrolled in this small single-center exploratory study. Despite this small sample size, a post hoc power analysis showed a 61% power to detect a 2-tailed *P* value of less than .05 for an improvement in venous impedance index at day 3 compared with baseline. Intrarenal arterial flow was not invasively measured, nor correlated with the golden standard assessment of elevated filling pressures. Interobserver agreement was previously studied in our center and not repeated in this study.[5] Further studies are required to assess the value of intrarenal flow as a marker for diagnosis and treatment guidance in patients with HF. Assessment of intrarenal venous flow patterns using Doppler ultrasound examination has promising characteristics, because it is easily accessible, inexpensive, and safe, and can be performed at the bedside quickly providing additional information. The addition of renal venous flow to other echocardiographic or signs and symptoms of congestion in patients with acute HF might improve diagnosis and treatment.[8]

Conclusions

In patients who exhibit discontinuous renal venous flow patterns hospitalized for acute HF, decongestive therapy led to a normalization of intrarenal venous flow to a continuous pattern.

Disclosures

Drs Dauw, Somers, Damman, Nijst, Metalidis, and Dupont have nothing to disclose. Dr ter Maaten is supported by a grant from the UMCG (Mandema grant). Dr Martens is supported by a doctoral fellowship by the Research Foundation Flanders (FWO; grant no. 1127917N). Dr Martens and Dr Mullens are researchers for the Limburg Clinical Research Program UHasselt-ZOL-Jessa and supported by the Limburg Sterk Merk foundation, Hasselt University, Ziekenhuis Oost-Limburg, and Jessa Hospital.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2020.09.003.

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