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Original Article

Assessing Splanchnic Compartment Using Portal Venous Doppler and Impact of Adding It to the EVEREST Score for Risk Assessment in Heart Failure

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ABSTRACT

Background: The Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan (EVEREST) score has proven useful for risk prediction in acute decompensated heart failure (ADHF). However, this score does not include the characterization of the splanchnic compartment, which has been involved in worsening heart failure. Refining this score by integrating an assessment of the splanchnic compartment would allow for a better risk assessment. Therefore, we aimed to characterize the patterns of portal vein pulsatility (PVP), an ultrasound metric used for the assessment of splanchnic compartment

RÉSUMÉ

Contexte : Le score EVEREST (*Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan*) s'avère utile pour la prévision du risque dans les cas d'insuffisance cardiaque décompensée aiguë (ICDA). Cependant, ce score ne permet pas de caractériser le compartiment splanchnique, impliqué dans l'aggravation de l'insuffisance cardiaque. Affiner ce score en y intégrant une évaluation du compartiment splanchnique permettrait une meilleure évaluation du risque. Par conséquent, nous avons entrepris de caractériser les profils de la pulsatilité du flux de la veine porte (PFVP)

Heart failure (HF) is the leading cause of hospitalization in patients aged more than 65 years in North America,[1,2] with up to 25% of decompensated patients being readmitted within the 30 days after discharge.[3] Signs and symptoms of congestion related to elevated filling pressure are the most common precipitants for decompensation,[4,5] and unresolved congestion after an episode of acute decompensated HF (ADHF) has been associated with an increased rate of readmissions.[6] Achieving effective decongestion before discharge is thus a priority in this context.[7,8] However, there is little agreement with regard to the optimal way of assessing effective decongestion during hospitalization and at discharge,[9] and therapeutic management guided by signs and symptoms relief has shown a lack of accuracy in this setting.[10]

Recent data demonstrate that increased filling pressures may occur in the absence of weight gain,[5,11] suggesting a potential role for abnormal volume redistribution from the splanchnic reservoir as an important contributor to decompensation.[12] Moreover, persistent splanchnic congestion at discharge could contribute to rapid recurrent decompensation through volume redistribution.[13] Therefore, integrating the assessment of the splanchnic compartment into a comprehensive evaluation of volume status may allow for a better volume management in patients with ADHF.

Portal vein flow assessment using abdominal ultrasonography and pulsed-wave Doppler has been suggested to provide a noninvasive evaluation of portal hypertension and splanchnic compartment.[14,15] A pulsatile pattern of portal venous flow is interpreted as the transmission of changes in right atrial pressure across the hepatic veins and the sinusoids to the portal vein.[16,17] Abnormal portal vein pulsatility (PVP) has been demonstrated to correlate with elevated right atrial pressures[18] and bowel edema in patients with HF,[19] suggesting the potential use of this metric as a noninvasive tool for the assessment of splanchnic compartment. Notably, increased venous congestion along with severe tricuspid

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Ethics Statement: The present research has adhered to the relevant ethical guidelines.

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and their determinants in patients with ADHF, to explore the relationships between abnormal patterns of PVP and outcomes, and to evaluate the added value of PVP to the EVEREST score for risk assessment in ADHF.

Methods: Portal vein flow was assessed prospectively on admission and at discharge in 95 patients with ADHF using pulsed-wave Doppler. Abnormal PVP was defined for values $\geq$ 50%. Cox proportional hazards models were used for the assessment of the relationship between PVP and outcomes.

Results: Overall, 64% of patients on admission and 24% at discharge had abnormal PVP. PVP on admission was inversely correlated with right ventricular function (tricuspid annular plane systolic excursion, $\rho = -0.434$) and pulmonary pressure ($\rho = 0.346$), $P < 0.05$. Although PVP was associated with all-cause mortality (hazard ratio, 1.028, $P < 0.001$), the addition of this metric to the EVEREST score had little effect on its C-index (0.813 vs 0.818) for risk assessment.

Conclusions: Abnormal PVP is frequent and associated with right ventricular dysfunction in ADHF. Although abnormal PVP identifies higher-risk patients, this metric does not improve the performance of the EVEREST score for risk assessment.

(mesure échographique permettant d'évaluer le compartiment splanchnique et ses déterminants dans les cas d'ICDA) afin d'examiner les relations entre les profils anormaux de la PFVP et les résultats, et afin d'évaluer la valeur ajoutée de la PFVP dans l'évaluation du risque faisant appel au score EVEREST chez des patients atteints d'ICDA.

Méthodologie : Le flux de la veine porte a été évalué prospectivement par échographie Doppler pulsée à l'admission et à la sortie de 95 patients atteints d'ICDA. La définition d'une PFVP anormale ciblait des valeurs de 50 % ou plus. Des modèles à risques proportionnels de Cox ont servi à évaluer la relation entre la PFVP et les résultats.

Résultats : Globalement, la PFVP était anormale à l'admission chez 64 % des patients et à la sortie chez 24 % des patients. Une corrélation inverse a été notée entre la PFVP à l'admission et la fonction ventriculaire droite (excursion annulaire horizontale systolique de la tricuspide, $\rho = -0{,}434$) ainsi que la pression pulmonaire ($\rho = -0{,}346$), $p < 0{,}05$. Bien que la PFVP ait été associée à la mortalité toutes causes confondues (rapport des risques instantanés de 1,028, $p < 0{,}001$), l'ajout de cette mesure au score EVEREST a eu peu d'effet sur son indice C (0,813 vs 0,818) pour l'évaluation du risque.

Conclusions : Une PFVP anormale est d'observation courante et se trouve associée à une dysfonctionn ventriculaire droite dans les cas d'ICDA. Bien qu'une PFVP anormale permette de déceler les patients qui présentent un risque plus élevé, son objectivation n'améliore pas la précision du score EVEREST dans l'évaluation du risque.

regurgitation (TR) related to right heart dysfunction, and altered compliance of the hepatic vascular bed are mechanisms suggested to result in portal hypertension and therefore lead to a markedly pulsatile portal flow.[16,20,21] This being said, the additive value of PVP to the clinical assessment of congestion using the Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan (EVEREST) score, a validated clinical score of congestion,[22] has never been evaluated in a population of patients with ADHF.

We hypothesize that integrating the assessment of splanchnic compartment using PVP to the EVEREST score would allow for a more accurate evaluation of volume status and a better postdischarge risk assessment. The objectives of the present work were to (1) characterize the patterns of PVP; an ultrasound metric used for the assessment of splanchnic compartment; and their determinants, in patients with ADHF; (2) explore the relationships between abnormal pattern of PVP and outcomes; and (3) evaluate the added value of PVP to the EVEREST score for risk assessment in ADHF.

Methods

Patient selection

Patients with signs and symptoms of ADHF, New York Heart Association (NYHA) functional class II to IV symptoms, and clinical signs of venous congestion managed with intravenous diuretics at the Montreal Heart Institute from April 2017 to November 2018 were evaluated for the present study. Patients were excluded if they had 1 of the following: acute coronary syndrome, uncontrolled arrhythmias, severe chronic kidney disease (baseline estimated glomerular filtration rate $<$ 15 mL/min/1.73 m^2 or chronic dialysis), severe anemia (defined as baseline haemoglobin values $<$ 90 g/L), sepsis, pulmonary embolism and any condition potentially interfering with the ability of free consent such cognitive dysfunction or delirium. The study was approved by the institutional ethics board, and all patients provided written informed consent.

Study design

Medical history (cardiovascular risk factors, known cardiomyopathy, history of atrial fibrillation [AF], or myocardial infarction), clinical (symptoms of HF, signs of venous and/or pulmonary congestion, NYHA class, potential precipitating factors), biochemical (renal and hepatic functions, cardiac biomarkers) and echocardiographic and abdominal ultrasonographic measurements were obtained prospectively after enrolment, within the first 24 hours after admission, and again at discharge. Patients were discharged as per usual care, at a time at which they were considered as euvolemic by the treating team. Ultrasonographic (cardiac and extracardiac) assessments were obtained in an independent fashion, the results of which were blinded from the treating team, and thus did not modify the treatment strategy. A single operator (NB), blinded to medical management, performed the ultrasound assessment. Echocardiographic assessment was performed at the bedside, according to current guidelines.[23] Left ventricular ejection fraction (LVEF) was assessed visually and using the Simpson's equation as per most recent guidelines, and right ventricular (RV) function was assessed using the tricuspid annular plane systolic excursion (TAPSE).[23-26] The simplified Bernoulli equation ($P = 4^* [TR_{max}]^2 +$ right atrial pressure estimate) was used to calculate pulmonary artery systolic pressure (PASP) using peak TR velocity, and inferior vena cava collapsibility index as an estimate for right atrial pressure.[7,26] Total diuretic dose was calculated in furosemide-equivalent upon the whole hospital stay (20 mg intravenous furosemide = 40 mg oral furosemide).

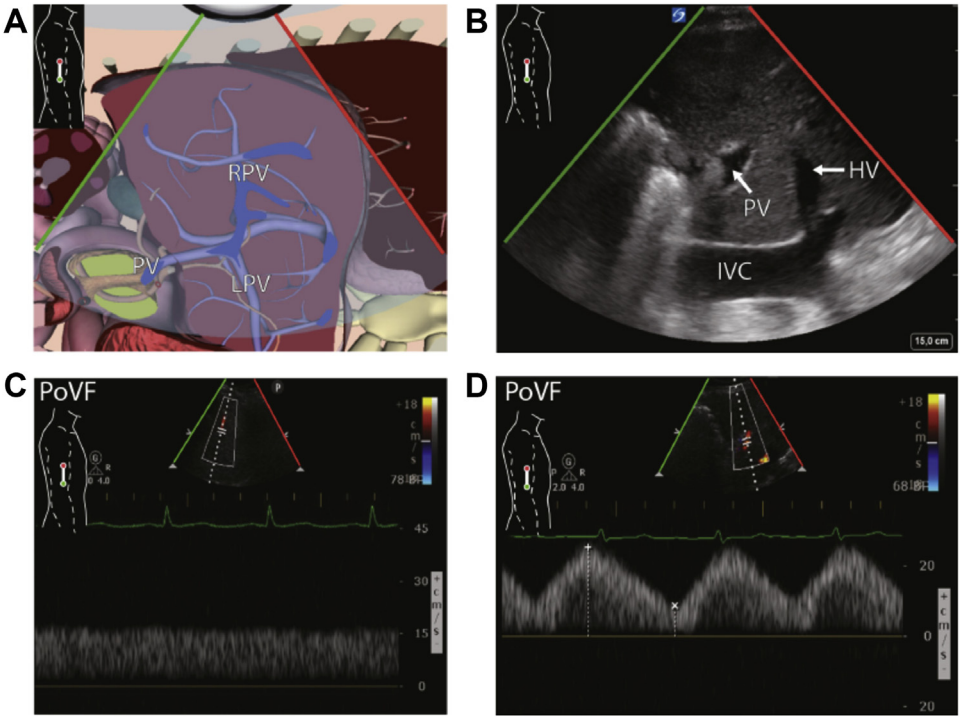

Figure 1. Bedside assessment of splanchnic compartment. (**A**) The cardiac probe is placed between the 9th and 11th intercostal right space (mid-axillary line, PV, LPV, RPV). (**B**) Direct visualization of the portal vein in 2-dimensional mode (PV, HV, IVC). (**C**) Normal portal venous flow is an anterograde flow, normally directed toward the liver, and continuous throughout the cardiac cycle. (**D**) In the setting of portal hypertension, portal venous flow appears biphasic, with a marked pulsatility allowing for the calculation of a portal vein pulsatility (PVP) ratio as follows: ([Vmax- Vmin]/Vmax), where Vmax stands for peak velocity and Vmin for nadir velocity recorded during the cardiac cycle. In the present work, a PVP ratio $\geq$ 50% was considered as abnormal. HV, hepatic vein; IVC, inferior vena cava; LPV, left portal vein; PoVF, portal venous flow; PV, portal vein; RPV, right portal vein.

Ultrasound protocol for the assessment of splanchnic compartment

Patterns of PVP were assessed using ultrasound interrogation of the portal vein and were obtained at the bedside as previously described[27] using a Sparq system (Philips Healthcare, Amsterdam, The Netherlands). Portal blood flow was measured from the right portal vein (extra-hepatic site). For patients in AF, measures were recorded during 5 consecutive cardiac cycles, and mean values were considered for analysis. Pulsatility was measured as follows: ((Vmax- Vmin)/Vmax), where Vmax stands for peak velocity and Vmin for nadir velocity recorded during the cardiac cycle.[27] Data from our center with regard to interobserver and intraobserver variability have been published and showed adequate interobserver agreement.[28] Figure 1 displays the ultrasound protocol for the assessment of splanchnic compartment using portal vein flow analysis.

Definitions

Patient weight was collected as per local practice as part of daily assessment. In-hospital changes in body weight were defined as the absolute difference between baseline (admission) and discharge in body weight (in kilograms). Although effective decongestion was defined by the treating team, the composite EVEREST score was assessed post hoc at admission and discharge. The EVEREST score (range, 0-18) has been developed upon patients included in the EVEREST trial and is based on the assessment of simple clinical parameters including dyspnea, orthopnea, jugular venous distension, rales, edema, and fatigue,[22] these parameters being prospectively collected by the research team. An EVEREST score < 2 has been proposed as a decongestion target at discharge in patients admitted with ADHF.[22,29] Persistent clinical congestion at discharge was thus defined as an EVEREST score ≥ 2 in the present work. The EVEREST score is detailed in Supplemental Table S1. Cardiac output was estimated using the following formula: cardiac output = 3.14 * left ventricular outflow tract (LVOT)-d^2/4 * LVOT-VTI * heart rate, LVOT diameter, mm), LVOT velocity-time integral (cm). RV systolic dysfunction was defined for TAPSE values $<$ 17 mm as per guidelines.[23] In the present work, markedly increased pulsatility of portal venous flow was used for a surrogate of portal hypertension, and a high pulsatility of portal flow ($\geq$50%) was considered as abnormal. Although debated, a pulsatility ratio of $\geq$ 50 has been suggested to provide the optimal balance between sensitivity and specificity for its association with elevated right atrial pressure.[20,21]

Statistical analysis

Results are presented using counts and percentages for categorical variables and mean $\pm$ standard deviation or median (interquartile range [IQR]) for continuous variables, where appropriate. In the present work, PVP is analyzed as continuous except for groups comparison and for the assessment of Kaplan–Meier curves where PVP is used as

Table 1. Baseline characteristics according to portal vein profiles on hospital admission and at discharge

Variables	All patients (N = 95)	PVP < 50% at admission (N = 34)	PVP ≥ 50% at admission (N = 61)	*P*	PVP < 50% at discharge (N = 72)	PVP ≥ 50% at discharge (N = 23)	*P*
Demographics							
Age, y	73.8 ± 11.5	73.5 ± 11.9	74.0 ± 11.4	0.857	74.3 ± 11.3	72.3 ± 12.5	0.516
Female (%, no)	27.4% (N = 26)	35.3% (N = 12)	23% (N = 14)	0.233	27.8% (N = 20)	26.1% (N = 6)	0.874
Hypertension (%, no)	75.8% (N = 72)	64.7% (N = 22)	82.0% (N = 50)	0.081	79.2% (N = 57)	65.2% (N = 15)	0.262
Diabetes (%, no)	49.5% (N = 47)	50.0% (N = 17)	49.2% (N = 30)	0.939	55.6% (N = 40)	30.4% (N = 7)	0.054
AF (%, no)	68.4% (N = 65)	58.8% (N = 20)	73.8% (N = 45)	0.169	62.5% (N = 45)	87.0% (N = 20)	0.038
Medication at baseline							
β-Blockers (%, no)	81.1% (N = 77)	79.4% (N = 27)	82.0% (N = 50)	0.789	81.9% (N = 59)	78.3% (N = 18)	0.762
ACEi-ARB-ARNI (%, no)	56.8% (N = 54)	58.8% (N = 20)	55.7% (N = 34)	0.831	56.9% (N = 41)	56.5% (N = 13)	0.972
MRA (%, no)	37.9% (N = 36)	35.3% (N = 12)	39.3% (N = 24)	0.826	33.3% (N = 24)	52.2% (N = 12)	0.139
Loop diuretics (%, no)	66.3% (N = 63)	55.9% (N = 19)	72.1% (N = 44)	0.119	62.5% (N = 45)	78.3% (N = 18)	0.209
Dose of loop diuretics, mg per day	42.1 ± 50.5	25.0 ± 36.7	51.6 ± 54.8	0.006	39.0 ± 50.4	51.7 ± 50.6	0.133
Clinical characteristics at baseline							
JVD (cmH_2O)	15.8 ± 4.3	14.5 ± 4.8	16.5 ± 3.9	0.011	15.0 ± 4.0	18.1 ± 4.3	0.005
Peripheral edema (%, no)	86.3% (N = 82)	85.3% (N = 29)	86.9% (N = 53)	0.829	86.1% (N = 62)	87.0% (N = 20)	0.918
NYHA:							
2 (%, no)	20.0% (N = 19)	29.4% (N = 10)	14.8% (N = 9)	0.011	22.2% (N = 16)	13.0% (N = 3)	0.379
3 (%, no)	66.3% (N = 63)	47.1% (N = 16)	77.0% (N = 47)		62.5% (N = 45)	78.3% (N = 18)	
4 (%, no)	13.7% (N = 13)	23.5% (N = 8)	8.2% (N = 5)		15.3% (N = 11)	8.7% (N = 2)	
EVEREST score at baseline	11.3 ± 1.9	11.1 ± 2.4	11.4 ± 1.6	0.527	11.2 ± 2.0	11.5 ± 1.4	0.440
Laboratory findings at baselin0065							
Creatinine, μmol/L	128.7 ± 45.7	118.4 ± 41.4	134.4 ± 47.3	0.033	127.7 ± 46.5	131.7 ± 44.2	0.495
eGFR, mL/min/1.73 m^2	45.7 ± 13.0	48.9 ± 12.8	44.0 ± 13.0	0.078	46.3 ± 13.1	43.9 ± 12.9	0.447
Hs-TnT, ng/mL	49.6 ± 46.2	35.4 ± 22.1	57.7 ± 53.9	0.006	46.7 ± 41.9	58.6 ± 57.6	0.371
NT-proBNP, ng/L	4480.0 (2536.0-7536.0)	4375.0 (2083.0-6303.0)	4619.0 (2619.0-9523.0)	0.380	4366.0 (2515.0-7380.0)	5680.0 (2702.0-10676.0)	0.390
Bilirubin, mg/dL	20.9 ± 14.3	16.5 ± 10.7	23.5 ± 15.6	0.015	18.5 ± 11.3	28.4 ± 19.5	0.010
Ultrasound findings at baseline							
LVEF, %	40.5 ± 16.3	43.6 ± 18.9	38.7 ± 14.5	0.195	41.0 ± 16.8	38.9 ± 14.7	0.564
LVEF > 50% (%, no)	37.9% (N = 36)	55.9% (N = 19)	27.9% (N = 17)	0.009	41.7% (N = 30)	26.1% (N = 6)	0.222
Cardiac output, L/min	4.5 ± 1.8	4.7 ± 1.6	4.5 ± 1.8	0.548	4.5 ± 1.7	4.5 ± 1.3	0.880
Normal RV function (%, no)	57.0% (N = 49)	82.8% (N = 24)	43.9% (N = 25)	0.001	67.2% (N = 43)	27.3% (N = 6)	0.002
TAPSE, mm	17.5 ± 5.6	20.5 ± 5.2	15.9 ± 5.2	<0.001	18.8 ± 5.2	13.4 ± 5.0	<0.001
TR grade at admission							
0 (%, no)	2.1% (N = 2)	2.9% (N = 1)	1.6% (N = 1)	0.002	2.8% (N = 2)	0	0.001
1 (%, no)	16.8% (N = 16)	35.3% (N = 12)	6.6% (N = 4)		22.2% (N = 16)	0	
2 (%, no)	35.8% (N = 34)	38.2% (N = 13)	34.4% (N = 21)		41.7% (N = 30)	17.4% (N = 4)	
3 (%, no)	36.8% (N = 35)	20.6% (N = 7)	45.9% (N = 28)		29.2% (N = 21)	60.9% (N = 14)	
4 (%, no)	8.4% (N = 8)	2.9% (N = 1)	11.5% (N = 7)		4.2% (N = 3)	21.7% (N = 5)	
IVC collapse > 50% (%, no)	25.3% (N = 24)	47.1% (N = 16)	13.1% (N = 8)	< 0.001	31.9% (N = 23)	4.3% (N = 1)	0.006
PASP, mm Hg	53.3 ± 14.4	45.7 ± 15.8	57.7 ± 11.6	0.001	52.0 ± 14.9	58.6 ± 11.2	0.067
PVP, %	57.9 ± 26.5	30.6 ± 10.4	73.1 ± 19.7	< 0.001	49.4 ± 22.3	84.6 ± 20.4	< 0.001
Abnormal PVP (%, no)	64.2% (N = 61)	0	100% (N = 61)	—	52.8% (N = 38)	100% (N = 23)	< 0.001

Results are presented using counts and percentages for categorical variables and mean ± standard deviation (SD) for continuous variables. For NT-proBNP, results are presented as median [interquartile range (IQR)].

ACEi, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; eGFR, estimated glomerular filtration rate; EVERST, Efficacy of Vasopressin Antagonism in Heart Failure: Outcome Study with Tolvaptan; IVC, inferior vena cava; JVD, jugular venous distension; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N terminal pro-brain natriuretic peptide; PASP, pulmonary artery systolic pressure; PVP, portal vein pulsatility; TAPSE, tricuspid annular plane systolic excursion.

The EVEREST score (range, 0-18) is based on the assessment of simple clinical parameters including dyspnea, orthopnea, JVD, rales, edema, and fatigue.

Normal RV systolic function relates to TAPSE values ≥ 17 mm.

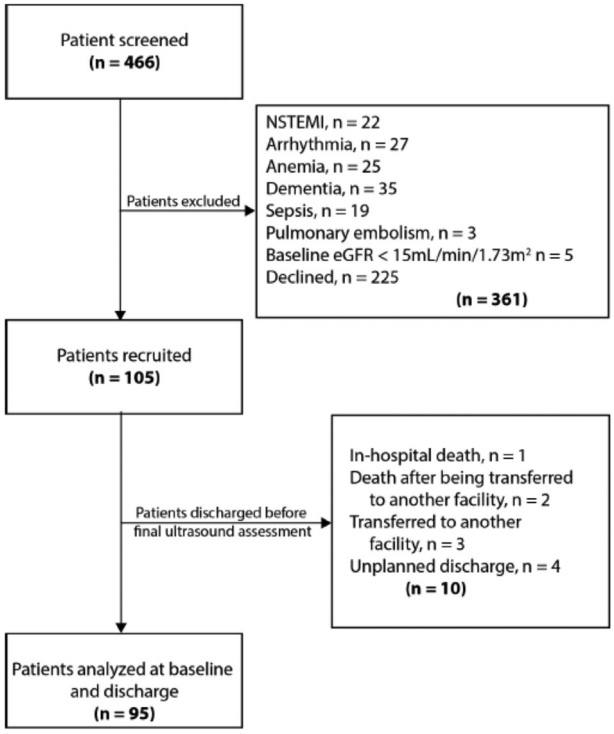

Figure 2. Selection process.

categorical (< vs > 50%). To investigate the characteristics of patients according to their PVP at admission, patients were compared according to whether they had a PVP $\geq$ or < 50% at baseline. The groups were compared using chi-square or exact Fisher test for categorical variables, and Student *t* tests or Mann–Whitney *U* tests for continuous variables, as appropriate. To elucidate the relationships between PVP and clinical, biological, and ultrasound parameters, Spearman's correlations were assessed. The relationships between the EVEREST score, PVP at discharge and clinical outcomes (all-cause mortality and all-cause hospitalization, all-cause mortality alone, and all-cause hospitalization alone) were assessed using Cox proportional hazards models, adjustments being made for sex, age, LVEF, and creatinine. In addition, C-indices were calculated to quantify the added value of PVP to the EVEREST score for risk assessment. The Kaplan–Meier method with the log-rank test was used to draw and compare the survival curves in patients with abnormal vs normal PVP pattern after decongestive therapy. All analyses were conducted using SPSS version 24 (IBM, Armonk, NY), and *P* values < 0.05 were considered to be statistically significant.

Results

Baseline characteristics

Baseline characteristics are detailed in Table 1. Of 466 patients screened, 95 had a systematic assessment of their splanchnic compartment on admission and again at discharge (Fig. 2). Patients were predominantly male (73%) with a mean age of 74 years. They were mostly in NYHA functional class 3 (66%), and had signs of congestion on clinical examination (86% had peripheral edema and jugular venous distension was 16 cmH_2O). Creatinine was 129 µmol/L, N terminal pro-brain natriuretic peptide was 4480 ng/L, and LVEF was 41%. Mean TAPSE values were 17.5 ± 5.6 mm, PASP was 53 mm Hg, and 64% of patients displayed abnormal PVP.

Characteristics of patients according to PVP patterns

When compared with patients with normal portal vein pattern on hospital admission (ie, PVP < 50%), those with PVP $\geq$ 50% appeared to have more advanced cardiomyopathy with a more severe RV dysfunction (TAPSE 16 vs 20 mm), more severe TR, and higher pulmonary pressures (PASP 58 vs 46 mm Hg), all $P < 0.05$ (Table 1). They also had higher levels of circulating cardiac high-sensitivity troponin (58 vs 35 ng/L) and bilirubin (24 vs 17 µmol/L) when compared with patients with normal portal vein pattern, both $P < 0.05$ (Table 1). At discharge, 24% patients still had abnormal PVP. Again, patients with abnormal PVP at discharge had more RV dysfunction (TAPSE 13 vs 19 mm, $P < 0.001$) and more moderate-severe TR (83% vs 33%, $P = 0.001$) when compared with patients with normal PVP pattern. Other characteristics are detailed in Table 2.

Determinants of abnormal PVP on admission and discharge

Abnormal PVP on admission was correlated with parameters of RV systolic function (TAPSE, $\rho = -0.434$, $P < 0.001$) and pulmonary pressure ($\rho = 0.346$, $P = 0.002$). TAPSE at discharge ($\rho = -0.401$, $P < 0.001$) was the only parameter significantly correlated with abnormal PVP at discharge. No significant association was demonstrated between PVP on admission or at discharge, and parameters of LV function including LVEF and cardiac output.

Abnormal PVP at discharge and clinical outcomes

Morbidity and mortality were high, with 70% (N = 67) of patients dying or being hospitalized during a median period of 174 (IQR, 52-407) days of follow-up (Table 2). Patients with abnormal PVP at discharge had significantly higher rates of all-cause mortality when compared to those without (39% vs 18%, $P = 0.024$ by the log-rank test) (Table 2). Patients with abnormal PVP at discharge did not have significantly higher rates of hospitalization or of the combination of hospitalization or mortality when compared with patients with normal PVP pattern at discharge (both $P > 0.05$ by the log-rank test). PVP was significantly associated with mortality (hazard ratio [HR], 1.028; 95% confidence interval [CI], 1.012-1.044; $P < 0.001$ unadjusted, and HR, 1.032, 95% CI, 1.014-1.049; $P < 0.001$ adjusted for age, sex, LVEF and creatinine) (Table 3 and Supplemental Table S2). No significant association was found between abnormal PVP pattern at discharge and hospitalizations from all-causes or with all-cause deaths or hospitalizations (Table 3 and Supplemental Table S2).

EVEREST score, PVP at discharge, and outcomes

The EVEREST score at discharge was associated (unadjusted and adjusted for age, sex, LVEF, and creatinine) with the mortality (adjusted HR, 1.694; 95% CI, 1.362-2.106; *P*

Table 2. In-hospital and discharge characteristics according to portal vein profiles on hospital admission and at discharge

Variables	All patients (N = 95)	PVP < 50% at admission (N = 34)	PVP ≥ 50% at admission (N = 61)	*P*	PVP < 50% at discharge (N = 72)	PVP ≥ 50% at discharge (N = 23)	*P*
In-hospital characteristics							
Hospital length of stay, d	7.5 ± 7.2	6.7 ± 7.4	8.0 ± 7.1	0.413	7.2 ± 7.5	10.2 ± 3.5	0.193
Total furosemide, mg	480.0 (280.0-960.0)	360.0 (240.0-645.0)	640.0 (320.0-1210.0)	0.012	400.0240.0-720.0)	780.0 (400.0-1440.0)	0.008
In-hospital changes in body weight, kg	−4.1 ± 4.2	−2.6 ± 2.7	−5.0 ± 4.7	0.004	−3.5 ± 3.3	−6.1 ± 5.8	0.047
Congestion at discharge							
JVD (cm H_2O)	8.1 ± 2.8	6.8 ± 1.8	8.8 ± 3.0	< 0.001	7.4 ± 2.1	10.2 ± 3.5	0.002
EVEREST score	2.9 ± 2.3	2.6 ± 1.9	3.3 ± 2.5	0.026	2.5 ± 2.2	4.1 ± 2.5	0.011
EVEREST score ≥ 2 (%, no)	69.5% (N = 66)	50.0% (N = 17)	77% (N = 47)	0.039	62.5% (N = 45)	91.3% (N = 21)	0.009
Medication at discharge							
β-Blockers (%, no)	84% (N = 79)	82.4% (N = 28)	85.0% (N = 51)	0.774	84.7% (N = 61)	81.8% (N = 18)	0.745
ACEi-ARB-ARNI (%, no)	58.5% (N = 55)	61.8% (N = 21)	56.7% (N = 34)	0.669	59.7% (N = 43)	54.5% (N = 12)	0.805
MRA (%, no)	73.7% (N = 70)	73.5% (N = 25)	73.8% (N = 45)	0.980	76.4% (N = 5)	65.2% (N = 15)	0.292
Loop diuretics (%, no)	93.7% (N = 89)	94.1% (N = 32)	93.4% (N = 57)	0.897	94.4% (N = 68)	91.3% (N = 21)	0.630
Dose of loop diuretics (%, no)	76.1 ± 62.6	53.8 ± 44.4	88.5 ± 67.9	0.003	68.1 ± 58.5	100.8 ± 69.6	0.042
Laboratory findings at discharge							
Creatinine, μmol/L	137.4 ± 53.3	124.2 ± 45.2	144.7 ± 56.3	0.056	136.9 ± 56.5	138.9 ± 42.5	0.355
eGFR, mL/min/1.73 m^2	43.6 ± 14.5	45.9 ± 15.1	42.3 ± 14.1	0.259	44.3 ± 15.3	41.3 ± 11.6	0.317
NT-proBNP, ng/L	3368 (1544-5710)	2445 (1338-5190)	3790 (1792-5974)	0.199	2936 (1356-5614)	4940 (2064-6060)	0.210
Ultrasound assessment at discharge							
LVEF, %	42.7 ± 15.6	45.3 ± 17.7	41.5 ± 14.6	0.318	42.3 ± 16.0	43.7 ± 14.9	0.698
Cardiac output, L/min	4.7 ± 1.3	4.8 ± 1.3	4.7 ± 1.3	0.815	4.8 ± 1.3	4.5 ± 1.3	0.319
Normal RV function (%, no)	62.0% (N = 57)	75.9% (N = 22)	55.6% (N = 35)	0.050	72.3% (N = 47)	37.0% (N = 10)	0.002
TAPSE, mm	18.3 ± 5.9	20.4 ± 5.6	17.4 ± 5.8	0.023	19.8 ± 5.3	14.8 ± 5.7	<0.001
TR grade at admission:							
0 (%, no)	6.3% (N = 6)	8.8% (N = 3)	4.9% (N = 3)		8.3% (N = 6)	0	
1 (%, no)	33.6% (N = 32)	52.9% (N = 18)	22.9% (N = 14)		44.4% (N = 32)	0	
2 (%, no)	37.8% (N = 36)	29.4% (N = 10)	42.6% (N = 26)		41.6% (N = 30)	26.0% (N = 6)	
3 (%, no)	16.8% (N = 16)	8.8% (N = 3)	21.3% (N = 13)		5.5% (N = 4)	52.1% (N = 12)	
4 (%, no)	5.2% (N = 5)	0	8.1% (N = 5)	0.013	0	21.7% (N = 5)	<0.001
IVC collapse > 50% (%, no)	61.1% (N = 58)	88.2% (N = 30)	45.9% (N = 28)	<0.001	75.0% (N = 54)	17.4% (N = 4)	< 0.001
PASP, mm Hg	42.33 ± 13.4	38.0 ± 13.1	44.5 ± 13.1	0.023	39.3 ± 12.5	50.8 ± 12.5	0.001
PVP, %	34.2% ± 25.7	16.8% ± 11.8	43.9% ± 26.9	< 0.001	22.4% ± 13.5	71.3 ± 18.3	< 0.001
Abnormal PVP (%, no)	24.2% (N = 23)	0	37.7% (N = 23)	< 0.001	—	—	—
Outcomes							
All-cause deaths and all-cause hospitalizations (%, no)	70.5% (N = 67)	64.7% (N = 22)	73.8% (N = 45)	—	65.3% (N = 47)	87.0% (N = 20)	—
All-cause deaths (%, no)	23.2% (N = 22)	14.7% (N = 5)	27.9% (N = 17)	—	18.1% (N = 13)	39.1% (N = 9)	—
All-cause hospitalizations (%, no)	65.3% (N = 62)	61.8% (N = 21)	67.2% (N = 41)	—	61.1% (N = 44)	78.3% (N = 18)	—

The EVEREST score (range 0-18) is based on the assessment of simple clinical parameters including dyspnea, orthopnea, JVD, rales, edema, and fatigue. Results are presented using counts and percentages for categorical variables and mean ± standard deviation (SD) for continuous variables. For NT-proBNP and total furosemide, results are presented as median [IQR].

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; eGFR, estimated glomerular filtration rate; IVC, inferior vena cava; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NT-proBNP, N terminal pro-brain natriuretic peptide; PVP, portal vein pulsatility.

Table 3. Associations between congestion status at discharge and clinical outcomes

	Unadjusted						Adjusted*					
	All-cause deaths and hospitalizations		All-cause deaths		All-cause hospitalizations		All-cause deaths and hospitalizations		All-cause deaths		All-cause hospitalizations	
Outcomes	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
EVEREST at discharge	1.193 (1.091-1.305)	< 0.001	1.591 (1.361-1.859)	< 0.001	1.160 (1.053-1.278)	0.003	1.265 (1.101-1.455)	0.001	1.694 (1.362-2.106)	< 0.001	1.220 (1.055-1.411)	0.007
PVP at discharge	1.009 (0.999-1.019)	0.071	1.028 (1.012-1.044)	< 0.001	1.005 (0.994-1.016)	0.370	1.008 (0.998-1.019)	0.126	1.032 (1.014-1.049)	<0.001	1.004 (0.993-1.015)	0.488

CI, confidence interval; HR, hazard ratio; PVP, portal vein pulsatility.
*Adjusted for sex, age, LVEF, and creatinine.

< 0.001) (Table 3 and Supplemental Table S2), hospitalization (adjusted HR, 1.220; 95% CI, 1.055-1.411; $P = 0.007$) and the combination of mortality or hospitalization (adjusted HR, 1.265; 95% CI, 1.101-1.455; $P = 0.001$) (Table 3).

In a bivariate Cox model including the EVEREST score and PVP at discharge, PVP was no longer associated with mortality (HR, 1.013; $P = 0.114$) (Supplemental Table S3). Adding PVP to the EVEREST score had little impact on the C-index (0.813 vs 0.818) for the prediction of all-cause mortality and no impact for the prediction of all-cause deaths or hospitalization (C-index 0.630 vs 0.621), and all-cause hospitalization (C-index 0.617 vs 0.613) (Supplemental Table S4). Although there were significant differences in terms of survival (log-rank = 0.024) according to PVP pattern at discharge (Fig. 3B), survival curves according tended to separate late during follow-up (Fig. 3A-C).

Discussion

This study finds that abnormal PVP pattern, defined as PVP $\geq$ 50%, is highly prevalent in a population of patients hospitalized with ADHF and that it is most closely associated with RV dysfunction. After decongestive therapy, abnormal PVP at discharge is less frequent than an increased EVEREST score ($\geq$2) and may occur in different patients. Patients with abnormal PVP at discharge may have poorer long-term clinical outcomes when compared with those with normal PVP pattern. Systematic assessment of PVP did not improve the discrimination of the EVEREST score, nor did adding it to the EVEREST score significantly improve its C-index for predicting all-cause mortality postdischarge in patients with ADHF (C-index 0.813 vs 0.818).

PVP on admission and discharge, and their determinants

In this study, we demonstrate that abnormal PVP is highly prevalent among patients admitted with ADHF, with 64% of patients displaying features of abnormal PVP at hospital admission, which is in line with data from the literature.[19,30] After decongestive therapy and at the time of hospital discharge, 24% still had abnormal PVP despite the clinical team having deemed the patient ready for discharge.

Measures of RV dysfunction were strongly correlated with abnormal PVP at admission, and again with abnormal PVP at discharge. RV function appears to be a key determinant of the interactions between the failing heart and the splanchnic circulation. RV dysfunction in patients with HF has notably been associated with poorer outcomes[31] and has shown to be a major predisposing factor to cardiac cachexia[32] and the cardiorenal syndrome.[33] Notably, in patients with ADHF, recent data demonstrated similar hemodynamic features across the whole spectrum of LVEF with the role of the RV, when it comes to the acute impacts of congestion, proven to be independent of HF phenotype.[34] These results reinforce the fact that deleterious effects of venous congestion may be exerted independently of other determinants of poor prognosis in HF (LVEF, comorbidities).[34]

Abnormal PVP at discharge and outcomes in ADHF

In this study, associations between PVP at discharge and outcomes were explored, and there was an association between all-cause mortality and abnormal PVP in this patient population. Splanchnic compartment has recently been demonstrated

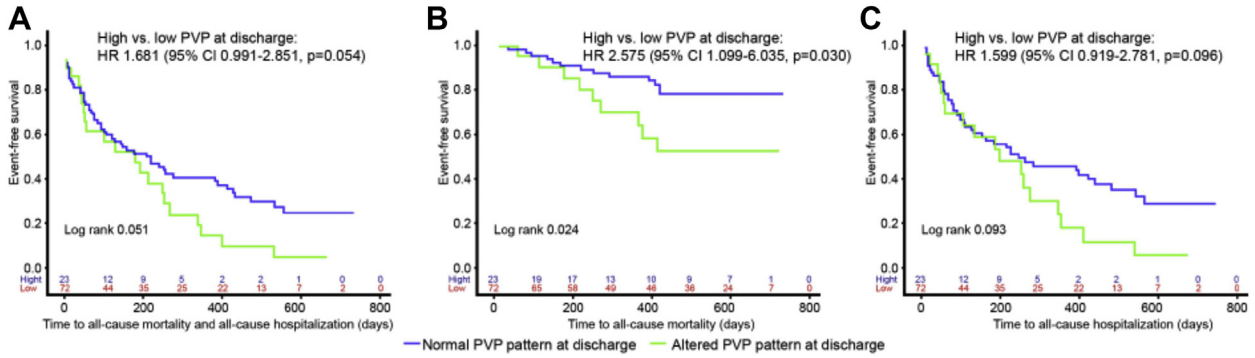

Figure 3. (**A**) Event-free survival for all-cause mortality and hospitalization according to high PVP at discharge. Log-rank 0.051. (**B**) Event-free survival for all-cause mortality according to high PVP at discharge. Log-rank 0.024. (**C**) Event-free survival for all-cause hospitalization according to congestion profiles at discharge for all-cause hospitalization alone. Log-rank 0.093.

to be an important determinant of the abdominal contribution to cardio-renal interactions, playing a major role in worsening renal function in patients with HF,[33] as well as a key player in the increased inflammatory activation attributable to HF.[32] As such, the assessment of PVP patterns may potentially add novel insights into the comprehension of the complex pathophysiology underlying the transition process leading patients with HF from a compensated to a decompensated state and improve our understanding of changes in splanchnic capacitance in patients with HF.[12] Moreover, this noninvasive technique may enrich the concept of abnormal fluid distribution as an important precipitating factor for decompensation in HF[12] and may help guide new therapeutic approaches in this setting.[35] Nevertheless, although abnormal PVP was associated with mortality, it was not significantly associated with either hospitalization or the combination of hospitalization and mortality, suggesting that although important, it is only one part of a more complex syndrome in patients with ADHF. Furthermore, survival curves separate late, suggesting that abnormal PVP after decongestive therapy did not translate into a higher number of events during the short-term. Whether this observation describes a specific pathophysiological pattern by which portal hypertension may participate into the prognosis of HF remains unclear.

PVP vs the EVEREST score in predicting clinical outcomes in ADHF

In this study, despite the clinical team deeming the patients ready for hospital discharge, 70% of patients still had an EVEREST score of $\geq$ 2, indicating persistent congestion, whereas 24% had abnormal PVP. Considering the proven relationship between persistent congestion at discharge and poor outcomes, this finding suggests that the high morbidity and mortality of the patients included in this study is at least partially related to incomplete decongestive therapy. There was a poor correlation between the PVP and the EVEREST score suggesting a loose relationship, meaning that an increase in one of these measurements can occur without the other and that more patients have an elevated EVEREST score at discharge than abnormal PVP. Nevertheless, despite both measures having predictive value for poor outcomes combining them does not appear to have additive value (in terms of discrimination) in predicting outcomes.

Limitations

The sample size and the number of events were limited, which may limit the strength of our conclusions; however, this is the largest study on the use of portal vein interrogation performed at admission and after decongestive therapy in 95 patients with ADHF. The most unstable patients requiring intensive care unit admission or severe renal failure were not screened, as were patients with mild HF who were not admitted to hospital. Noninvasive assessment of LV filling pressure was not prospectively assessed in the present work. Using PVP assessment as a surrogate for portal hypertension or splanchnic congestion remains debated because the pulsatility ratio might not only reflect volume status within splanchnic compartment but also be influenced by splanchnic venous compliance and intrahepatic pressure/resistance. Our definition of abnormal PVP used a cutoff of 50% because this value has been used in the most recent literature data, although various cutoff values have also been used in other settings. However, in assessing PVP's relationship with outcomes in this study, continuous values were used, suggesting that the use of other cutoffs would have had limited impact on our findings.

Conclusion

In patients with ADHF, we demonstrate that abnormal PVP is highly prevalent at hospital admission, most closely associated with RV dysfunction, and frequently responds to decongestive therapy. It is less frequently present at hospital discharge than an increased EVEREST score and not always present in the same patients. Patients with abnormal PVP at discharge were at a higher risk for mortality, but the addition of PVP values did not significantly improve the predictive value of the EVEREST score for mortality nor was its predictive value as good as that of the EVEREST score.

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References

1. Roger VL, Weston SA, Redfield MM, et al. Trends in heart failure incidence and survival in a community-based population. JAMA 2004;292:344-50.
2. Benjamin EJ, Virani SS, Callaway CW, et al. Heart disease and stroke statistics-2018 update: a report from the American Heart Association. Circulation 2018;137:e67-492.
3. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009;360:1418-28.
4. Lala A, McNulty SE, Mentz RJ, et al. Relief and Recurrence of Congestion During and After Hospitalization for Acute Heart Failure: Insights From Diuretic Optimization Strategy Evaluation in Acute Decompensated Heart Failure (DOSE-AHF) and Cardiorenal Rescue Study in Acute Decompensated Heart Failure (CARESS-HF). Circ Heart Fail 2015;8:741-8.
5. Zile MR, Bennett TD, St John Sutton M, et al. Transition from chronic compensated to acute decompensated heart failure: pathophysiological insights obtained from continuous monitoring of intracardiac pressures. Circulation 2008;118:1433-41.
6. Costanzo MR, Jessup M. Treatment of congestion in heart failure with diuretics and extracorporeal therapies: effects on symptoms, renal function, and prognosis. Heart Fail Rev 2012;17:313-24.
7. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129-200.
8. Writing Committee M, Yancy CW, Jessup M, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. Circulation 2013;128:e240-327.
9. Gheorghiade M, Follath F, Ponikowski P, et al. Assessing and grading congestion in acute heart failure: a scientific statement from the acute heart failure committee of the heart failure association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. Eur J Heart Fail 2010;12:423-33.
10. Kociol RD, McNulty SE, Hernandez AF, et al. Markers of decongestion, dyspnea relief, and clinical outcomes among patients hospitalized with acute heart failure. Circ Heart Fail 2013;6:240-5.
11. Androne AS, Hryniewicz K, Hudaihed A, et al. Relation of unrecognized hypervolemia in chronic heart failure to clinical status, hemodynamics, and patient outcomes. Am J Cardiol 2004;93:1254-9.
12. Fudim M, Hernandez AF, Felker GM. Role of volume redistribution in the congestion of heart failure. J Am Heart Assoc 2017;6.
13. Fallick C, Sobotka PA, Dunlap ME. Sympathetically mediated changes in capacitance: redistribution of the venous reservoir as a cause of decompensation. Circ Heart Fail 2011;4:669-75.
14. Catalano D, Caruso G, DiFazzio S, et al. Portal vein pulsatility ratio and heart failure. J Clin Ultrasound 1998;26:27-31.
15. Styczynski G, Milewska A, Marczewska M, et al. Echocardiographic correlates of abnormal liver tests in patients with exacerbation of chronic heart failure. J Am Soc Echocardiogr 2016;29:132-9.
16. Wachsberg RH, Needleman L, Wilson DJ. Portal vein pulsatility in normal and cirrhotic adults without cardiac disease. J Clin Ultrasound 1995;23:3-15.
17. Gallix BP, Taourel P, Dauzat M, et al. Flow pulsatility in the portal venous system: a study of Doppler sonography in healthy adults. AJR Am J Roentgenol 1997;169:141-4.
18. Hu JT, Yang SS, Lai YC, Shih CY, Chang CW. Percentage of peak-to-peak pulsatility of portal blood flow can predict right-sided congestive heart failure. World J Gastroenterol 2003;9:1828-31.
19. Ikeda Y, Ishii S, Yazaki M, et al. Portal congestion and intestinal edema in hospitalized patients with heart failure. Heart Vessels 2018;33:740-51.
20. Duerinckx AJ, Grant EG, Perrella RR, Szeto A, Tessler FN. The pulsatile portal vein in cases of congestive heart failure: correlation of duplex Doppler findings with right atrial pressures. Radiology 1990;176:655-8.
21. Hosoki T, Arisawa J, Marukawa T, et al. Portal blood flow in congestive heart failure: pulsed duplex sonographic findings. Radiology 1990;174(3 Pt 1):733-6.
22. Ambrosy AP, Pang PS, Khan S, et al. Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVEREST trial. Eur Heart J 2013;34:835-43.
23. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2015;16:233-70.
24. Konstam MA, Kiernan MS, Bernstein D, et al. Evaluation and management of right-sided heart failure: a scientific statement from the American Heart Association. Circulation 2018;137:e578-622.
25. Lai WW, Gauvreau K, Rivera ES, et al. Accuracy of guideline recommendations for two-dimensional quantification of the right ventricle by echocardiography. Int J Cardiovasc Imaging 2008;24:691-8.
26. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685-713. quiz 86-8.
27. Denault AY, Beaubien-Souligny W, Elmi-Sarabi M, et al. Clinical significance of portal hypertension diagnosed with bedside ultrasound after cardiac surgery. Anesth Analg 2017;124:1109-15.
28. Beaubien-Souligny W, Benkreira A, Robillard P, et al. Alterations in portal vein flow and intrarenal venous flow are associated with acute kidney injury after cardiac surgery: a prospective observational cohort study. J Am Heart Assoc 2018;7:e009961.
29. Girerd N, Seronde MF, Coiro S, et al. Integrative assessment of congestion in heart failure throughout the patient journey. JACC Heart Fail 2018;6:273-85.

30. Goncalvesova E, Lesny P, Luknar M, Solik P, Varga I. Changes of portal flow in heart failure patients with liver congestion. Bratisl Lek Listy 2010;111:635-9.

31. Melenovsky V, Kotrc M, Borlaug BA, et al. Relationships between right ventricular function, body composition, and prognosis in advanced heart failure. J Am Coll Cardiol 2013;62:1660-70.

32. Valentova M, von Haehling S, Bauditz J, et al. Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. Eur Heart J 2016;37:1684-91.

33. Verbrugge FH, Dupont M, Steels P, et al. Abdominal contributions to cardiorenal dysfunction in congestive heart failure. J Am Coll Cardiol 2013;62:485-95.

34. Van Aelst LNL, Arrigo M, Placido R, et al. Acutely decompensated heart failure with preserved and reduced ejection fraction present with comparable haemodynamic congestion. Eur J Heart Fail 2018;20:738-47.

35. Fudim M, Jones WS, Boortz-Marx RL, et al. Splanchnic nerve block for acute heart failure. Circulation 2018;138:951-3.

Supplementary Material

To access the supplementary material accompanying this article, visit *CJC Open* at https://www.cjcopen.ca/ and at https://doi.org/10.1016/j.cjco.2020.03.012.