Echocardiographic Evaluation of Left Ventricular Filling Pressure in Patients With Heart Failure With Preserved Ejection Fraction: Usefulness of Inferior Vena Cava Measurements and 2016 EACVI/ASE Recommendations

EMMANUELLE BERTHELOT, MD,[1,2] PATRICK JOURDAIN, MD,[1,2] MINH TAM BAILLY, MD,[1,2] AMIR BOUCHACHI, MD,[1,2] BARNABAS GELLEN, MD, PhD,[3] ALEXANDRA ROUQUETTE, MD, PhD,[4] THIBAUD DAMY, MD, PhD,[5] PHILIPPE HERVÉ, MD,[6] DENIS CHEMLA, MD, PhD,[1,7] AND PATRICK ASSAYAG, MD, PhD[1,2]

Le Kremlin-Bicêtre, Poitiers, Paris, Le Plessis Robinson, and Créteil, France

ABSTRACT

Context: The left ventricular filling pressure (LVFP) is correlated to right atrial pressure (RAP) in heart failure. We compared diagnostic value of the inferior vena cava (IVC) measurements to the one of the 2016 echocardiographic recommendations to estimate LVFP in patients with suspected heart failure with preserved ejection fraction (HFpEF).

Methods: Invasive hemodynamics and echocardiography were obtained within 48 hours in 132 consecutive patients with left ventricular ejection fraction ≥50%, and suspected pulmonary hypertension. Increased LVFP was defined by a pulmonary artery wedge pressure (PAWP) >15 mmHg.

Results: Of 83 patients in sinus rhythm, a score of the 2016 recommendations ≥ 2 (E/e′ ratio >14 and/or tricuspid regurgitation velocity >2.8 m/s and/or indexed left atrial volume>34 mL /m^2) had a positive predictive value (PPV) of 63% for PAWP>15 mmHg, whereas a dilated IVC (>2.1 cm) and/or non-collapsible (≤50%) had a PPV of 82%. The net reclassification improvement was 0.39 ($P < .05$). In atrial fibrillation (AF), a dilated and/or non-collapsible IVC had an 86% PPV for PAWP>15 mmHg. The correlation between RAP and PAWP was 0.60, with 75.7% concordance (100/132) between dichotomized pressures (both RAP>8 mmHg and PAWP>15 mmHg and vice versa).

Conclusion: The IVC size and collapsibility is valuable to identify patients with HFpEF with high LVFP in both sinus rhythm and AF. (*J Cardiac Fail 2020;26:507−514*)

Key Words: Heart failure, left ventricular filling pressure, diagnosis, echocardiography, right heart catheterization.

Transthoracic echocardiography (TTE) is a key examination for the evaluation of left ventricular filling pressure (LVFP).[1] The noninvasive diagnosis of an abnormal increase in LVFP by TTE remains difficult to interpret in a significant proportion of patients.[2−4] However, the TTE-based estimation of LVFP is important for several reasons. It is a key element for the diagnosis, treatment guidance, and prognostic evaluation of heart failure (HF).[5] Although heart catheterization is the reference method to measure LVFP, this invasive procedure cannot be routinely performed, with TTE therefore remaining the first-line method.[1] European Association of Cardiovascular Imaging/American Society of Echocardiography (EACVI/ASE) guidelines have proposed a TTE-based algorithm taking into account several parameters for the evaluation of LVFP.[6] The algorithm has been tested in different populations, namely in patients with HF referred for hemodynamic evaluation and in patients referred for further exploration in unexplained dyspnea.[7−9]

From the [1]University Paris-Saclay, Le Kremlin-Bicêtre, France; [2]AP-HP, Service de Cardiologie, Hôpital Bicêtre, Le Kremlin-Bicêtre, France; [3]Service de Cardiologie, ELSAN−Polyclinique de Poitiers, Poitiers, France; [4]AP-HP, Service de Santé Publique et Epidémiologie, Hôpital Bicêtre, Le Kremlin-Bicêtre, France. CESP, INSERM, University Paris-Saclay, UVSQ, Université Paris-Saclay, Paris, France; [5]AP-HP, Henry Mondor Hospital; Department of Cardiology; Heart Failure and Amyloidosis Unit, INSERM/UPEC: U955, GRC Amyloid Research Institute, Créteil, France; [6]Department of Thoracic Surgery, Marie Lannelongue Hospital, Le Plessis Robinson, France and [7]AP-HP, Service de physiologie, Hôpital Bicêtre, Le Kremlin-Bicêtre, France.

Manuscript received June 11, 2019; revised manuscript received January 9, 2020; revised manuscript accepted January 23, 2020.

Reprint requests: Emmanuelle Berthelot, MD, Praticien hospitalierService de Cardiologie, Pôle ThoraxHôpital Bicêtre, APHP 78, rue du Général Leclerc, 94270 Le Kremlin Bicêtre, France. Tel: +33145213735; Fax: +33145213293. E-mail: emmanuelle.berthelot@aphp.fr

See page 513 for disclosure information.

1071-9164/$ - see front matter

© *2020 Elsevier Inc. All rights reserved.*

https://doi.org/10.1016/j.cardfail.2020.01.018

Right atrial pressure (RAP) is significantly correlated with pulmonary artery wedge pressure (PAWP) and LVFP.[10−12] RAP is most commonly estimated by inferior vena cava (IVC) diameter measurement and the relative magnitude of inspiratory collapse.[12] Increased RAP leads to IVC dilatation and/or reduced IVC collapse with inspiration. Few studies have tested the usefulness of IVC evaluation for LVFP estimation.[10−12] A recent study has highlighted the prognostic value of IVC dilatation in HF.[12]

Our study aimed at evaluating the performance of the updated 2016 EACVI/ASE diastolic function guidelines and of IVC measurements for the estimation of LVFP in patients referred for right heart catheterization (RHC) to explore suspected pulmonary hypertension at our center in patients with suspected HF with preserved ejection fraction (HFpEF). We also compared the diagnostic accuracy in sinus rhythm and in patients with atrial fibrillation (AF).

Methods

Between 2015 and 2018, 132 patients with suspected HFpEF were identified based on HF symptoms (New York Heart Association [NYHA] class ≥II), a left ventricular ejection fraction (LVEF) ≥50%, and suspicion of pulmonary hypertension on a previous echocardiogram (defined as tricuspid regurgitation [TR] velocity >2.8 m/s and/or right ventricular [RV] dilatation without other cause), who were referred to the catheterization laboratory, Hôpital Bicêtre, APHP, France, for routine RHC. Inclusion criteria were TTE and RHC performed within 48 hours without changes in medication, and a suspected HFpEF. Exclusion criteria were all patients with moderate to severe mitral, tricuspid or aortic valve disease, and all patients with pulmonary hypertension of precapillary origin, ie, mean pulmonary pressure (mPAP) ≥ 25 mmHg and PAWP ≤ 15 mmHg at RHC. The investigation was in line with the principles of the Helsinki Declaration, and was approved by the local ethics committee.

Echocardiography

Echocardiographic images were prospectively acquired in a supine position and according to a specific protocol with a Vivid 9 echocardiograph (GE, Horten, Norway). The images were recorded over 3 consecutive cardiac cycles. In patients with AF, a mean of 5 cycles were analyzed. An off-line analysis was performed with an Echopac system by a single observer (E.B.) who was blinded to the cardiac catheterization results. Cardiac structures were evaluated including heart dimensions and left and right ventricular and atrial heart thicknesses and volumes.[13] LV systolic function and left atrial volume were evaluated by the Simpson method. LV mass was assessed in M mode. Pulsed early mitral Doppler flow (E and A wave) and tissue Doppler velocities (e′) at the septal and lateral mitral annulus were recorded and the mean E/e′ ratio was calculated. Measurements were also done for the maximum speed of TR. For all patients, we applied the updated diastolic function guidelines that analyses E/A ratio, E wave value, the E/e′ ratio, TR velocity (TRV), and left atrial volume. The 2016 recommendations permitted the determination of "normal LVFP", "elevated LVFP", and in some cases were not able to determine LVFP. In parallel, patients were analyzed for the size and collapsibility of the IVC.

The subcostal view was used when feasible for imaging the IVC, with the IVC viewed in its long axis. Measurement of IVC diameter was made at end-expiration and just proximal to the junction of the hepatic veins that lie ∼0.5 to 3.0 cm proximal to the ostium of the right atrium. M-mode was used for measurement when possible. When the IVC was not perpendicular to the cursor, IVC diameter was measured in 2D. To accurately assess IVC collapse, the respiratory-induced variations of the IVC diameter were measured with the respiration, ensuring that the change in diameter does not reflect a translation of the IVC into another plane as recommended.[14,15] In our study, we defined 2 groups depending on IVC size and collapsibility. The first group with an IVC diameter ≤ 2.1 cm and collapses >50% was the "normal LVFP" group, and the second group with an IVC diameter >2.1 cm and/or collapses ≤ 50% was the "high LVFP" group. These groups were defined according to the recommendations.[14] Interobserver variability was tested in our patients. All measurements were performed in accordance with recommendations for structure and function evaluation.

Invasive Hemodynamic Measurements

All patients had a medical indication of RHC based on the European pulmonary hypertension recommendations.[16] The time interval between echocardiography and RHC ranged from 5 to 48 hours. The RHC was performed after patients signed an informed consent. A catheter with a 7 F balloon was used to measure RAP, PAP, and PAWP, which were measured on both sides by remote exhalation to minimize potential errors related to pressure variations and air bubbles. Catheterization data were acquired through automated measurement and all curves were reviewed off-line by an experienced catheterizer. For pressure measurements, the intra-observer and interobserver variability has been tested on 14 patients in a previous study and each was <5%.[17] In the present study, the interobserver variability was tested on 36 patients and the inter-rater agreement kappa coefficient of PAWP measurement between both readers was 0.91.

The wedge position was verified by fluoroscopy and changes in the waveform. Wedge pressure was measured at the end of expiration according to an initial validation using PAWP as a surrogate measure of LVFP.[18] A PAWP ≤ 15 mmHg indicates a normal LVFP and a PAWP > 15 mmHg indicates high LVFP. Patients with mPAP ≥ 25 mmHg and PAWP > 15 mmHg were diagnosed as "post-capillary hypertension due to HFpEF".

Statistical Analysis

Quantitative continuous variables are presented as mean ± SD (normal distribution) or median (1st and 3rd quartiles;

non-normal distribution). Categorical variables are presented by numbers (%). We calculated sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive values (NPV) and positive likelihood ratio (PLR). PLR was calculated as Se/(1 − Sp). When PLR is >10 the discriminating property is high, 5−10 moderate, 2−5 mild, and <2 weak.[19] To quantify how well a new model reclassifies subjects, either appropriately or inappropriately, compared with another model, the net reclassification improvement (NRI) is a good index.[20,21] The NRI is a statistical tool proposed to assess improvement in model performance offered by a new method of classification compared with a reference one. The NRI indicates how much more frequently appropriate reclassification occurs than inappropriate reclassification using a new model of classification. The NRI is based on reclassification tables constructed separately for participants with and without the interest event, and quantifies the correct movement in categories, upward for events and downward for non-events. Define upward movement (up) as a change into higher category based on the new algorithm and downward movement (down) as a change in the opposite direction. The NRI is defined as follows: NRI= P(up|event)−P(down|event)+P (down|non-event)−P(up|non-event). The null hypothesis for NRI = 0 is tested using Z statistic following McNemar asymptotic test for correlated proportions. In our study, the comparison is between an original model (2016 recommendations) and a new model which is the study of IVC size and collapsibility. NRI is composed of subjects with and without events. In our study, the event is the PAWP > 15 mmHg and the nonevent PAWP ≤ 15 mmHg. Subject with events who are correctly classified by IVC methods are assigned a +1. Subjects without events who are incorrectly classified by IVC method are assigned a −1. Subjects well classified either with both methods are assigned a 0.[20] The NRI values vary between 0 and 1. A result >0.25 is a non-weak improvement. Concerning hemodynamic data, the relationship between RAP and PAWP was assessed using Pearson correlation. Mean RAP and PAWP values were dichotomized as RAP < 8 or ≥ 8 mmHg and PAWP ≤ 15 or > 15 mmHg.[14,16] The agreement of right- and left-sided filling pressures, dichotomized as normal versus high, was calculated as the percentage of patients with both elevated RAP and elevated PAWP and patients with both normal RAP and normal PAWP. The percentage of patients with discordant pressures was also calculated (elevated PAWP but normal RAP or vice versa).[12] Statistical analysis was performed by Medcalc software. Statistical significance was defined as a 2-tailed $P < .05$ for all tests.

Results

Study Population

The baseline characteristics of the 132 patients included in the study are described in Tables 1 and 2. Patients with PAWP> 15 mmHg were more often in stages 3 or 4 of the NYHA class, were more often hospitalized for HF, had more often AF, and were more often on diuretics treatment.

Table 1. Patients Characteristics

	Overall	PAWP ≤ 15 mmHg	PAWP > 15 mmHg	*P*
	N = 132	N = 40 (30%)	N = 92 (70%)	
Demographics				
Age (y)	70±11	72±10	69±11	.107
Gender (female) (%)	85 (64%)	25 (63%)	60 (65%)	.961
Heart rate (BPM)	78±18	76±15	80±19	.270
BMI (kg/m^2)	32±7	30±7	33±8	.038
NYHA class 3 or 4 (%)	71 (54%)	10 (25%)	66 (72%)	<.001
Systolic blood pressure (mmHg)	139±24	137±25	140±24	.677
Diastolic blood pressure (mmHg)	75±13	75±12	75±13	.803
Medical history				
Atrial fibrillation (%)	49 (37%)	9 (22%)	40 (43%)	.057
Coronary disease (%)	21 (16%)	7 (18%)	14 (15%)	.940
Previous HF hospitalization (%)	32 (24%)	5 (12%)	27 (29%)	<.001
Arterial hypertension (%)	88 (67%)	31 (77%)	57 (63%)	.084
Diabetes (%)	53 (40%)	16 (40%)	37 (40%)	.932
Dyslipidemia (%)	36 (27%)	14 (35%)	22 (24%)	.333
Smoker status (%)	33 (25%)	15 (39%)	18 (20%)	.048
Sleep apnea syndrome (%)	33 (25%)	6 (13%)	27 (29%)	.042
Medical use at admission				
Diuretics (%)	99 (75%)	25 (62%)	74 (80%)	<.001
Beta blockers (%)	55 (42%)	13 (33%)	42 (46%)	.195
ACE inh-ARB (%)	75 (57%)	22 (55%)	53 (58%)	.628
Laboratory assessment at admission				
BNP (pg/mL)	289±252	232±278	313±211	.239
BNP >400 pg/mL	29 (22%)	9 (22%)	20 (22%)	.895
GFR (Cockcroft, mL/min)	88±40	84±49	89±35	.856
Hb (g/dL)	12.7±1.9	13,0±2.1	12.5±1.8	0.452
Hematocrit (%)	42±12	42±13	42±12	0.896

Data are presented as mean ± SD or number (%). BMI, body mass index; ACE-inh, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers; Hb, hemoglobin; GFR, glomerular filtration rate.

Table 2. Echocardiographic and Hemodynamic Characteristics of Patients

	Overall	PAWP ≤ 15 mmHG	PAWP > 15 mmHg	*P*
	132	40	92	
Echocardiography				
Ejection fraction (%)	58±8	60±7	57±8	.127
IV sept thickness (mm)	11±1	10±1	11±1	.562
LV mass index (g/m^2)	86±28	75±19	91±30	.019
LV end-diastolic diameter (mm)	46±3	45±5	47±3	.120
E wave (cm/s)	99±30	86±28	105±28	.006
E ≤ 50 cm/s (%)	5 (4%)	4 (10%)	1 (2%)	.052
E/A ratio	1.48±1.03	1.35±1.23	1.53±0.88	.128
E/A ≥ 2 (%)	15 (11%)	4 (10%)	11 (12%)	.081
A wave (cm/s)	77±32	79±31	76±36	.176
e′ lat (cm/s)	10±3	10±3	10±3	.921
e′ sept (cm/s)	8±4	8±4	7±4	.256
E/e′ median	10±4	9±3	11±4	.049
LA vol index (mL/m^2)	41±25	36±21	43±26	<.001
TAPSE (mm)	19±7	19±6	19±7	.936
TRV (m/s)	3.3±0.6	2.8±0.5	3.5±0.6	<.001
IVC (mm)	19±6	15±5	20±6	<.001
IVC collapsibility >50% (%)	46 (35%)	26 (65%)	20 (22%)	<.001
RHC				
mPAP, mmHG	39±19	34±19	42±20	<.001
PAWP, mmHg	18 ±3	12±2	23±4	NA
RAP, mmHg	14±6	10±3	16±6	<.001
CO, L/min	5.54±1.74	5.22±1.48	5.86±1.96	.556

Data are presented as mean ± SD or median [interquartile range] or number (%). LA, left atrial; IV sept, interventricular septum; TAPSE, tricuspid annular plane systolic excursion; CO, cardiac output; NA, not applicable.

Mean brain natriuretic peptide (BNP) level was not significantly different in the 2 groups. Patients with PAWP> 15 mmHg (n=92) had a higher LV mass index, mitral E-wave, indexed left atrial volume (LAV) and maximum TRV and a more important IVC dilatation. Thirty-seven percent of patients had AF at inclusion. Maximum E wave velocity was available in 96% of patients and E/A was analyzable in 81/83 patients in sinus rhythm. Using the 2016 recommendations, LVFP "could not be determined" in 37% of the patients, all in AF. IVC size and collapsibility were analyzable in 92% of patients and the LVFP could be determined in 100% of the analyzable cases. The Pearson correlation coefficient between IVC maximal size and RAP was 0.58, and the coefficient between IVC collapsibility and RAP was −0.44 (each $P < .001$).

Identification of Patients With PAWP ≥ 15 mmHg (n=92)

In sinus rhythm, an "E/A ratio≥2" had a PPV of 79% for PAWP > 15 mmHg. Se was 39% and Sp 84%. In patients with "E/A<2", the sum of the criteria (E/e′ ratio> 14, maximal systolic TRV > 2.8 m/s and indexed left atrial volume (LAV)> 34 mL/m^2) ≥ 2 had a PPV of 63% for PAWP> 15 mmHg. Se was 48% and Sp was 50%. An "IVC dilatation >2.1 cm and/or collapse≤ 50%" had a PPV of 82%, Se was 69% and Sp was 74%. In patients with AF, the use of the 2016 recommendations is not recommended according to the guidelines.[6] In this case, an "IVC dilatation >2.1 cm and/or collapse ≤ 50%" had a PPV of 86%, Se was 74% and Sp was 75% (Table 3).

Table 3. Sensitivity, Specificity, and Predictive Value of Echographic Parameters for PAWP >15 mmHg

	Se	Sp	PPV	NPV	LHR
Sinus rhythm					
2016 recommendations					
E/A ≥2	39%	84%	79%	47%	2.43
If E/A <2, ≥2 positive criteria • E/e' >14 • TRV > 2.8 m/s • LA vol index >34 mL/m^2	48%	50%	63%	35%	0.96
IVC proposal					
Dilatation and/or non-collapsible IVC	69%	74%	82%	61%	2.65
Atrial fibrillation					
2016 recommendations Not applicable*					
IVC proposal tested					
Dilatation and/or non-collapsible IVC	74%	75%	86%	37%	2.96

LA, left atrial; LHR, likelihood ratio.
*The 2016 recommendations were not tested because it is discouraged in patients with AF.

Identification of Patients With PAWP ≤ 15 mmHg (n= 40)

In sinus rhythm, the criteria "E/A ≤ 0. 8 and E < 50 cm/s" had a PPV of 100%, Se was 58% and Sp was 100%. When these criteria were not analyzable, the sum of the criteria (E/e′ ratio, TRV, and indexed LAV) < 2 had a PPV of 36% for PAWP ≤ 15 mmHg, Se was 34% and Sp was 65%. An "IVC diameter ≤ 2.1 cm and collapses > 50%" had a PPV of 82% to predict PAWP ≤ 15 mmHg, Se was 55% and Sp was 69%.

Table 4. Sensitivity, Specificity, and Predictive Value of Echographic Parameters for PAWP ≤15 mmHg

	Se	Sp	PPV	NPV	LHR
Sinus rhythm					
2016 recommendations					
E<50 and E/A ≤ 0.8 If E> 50 cm/s or 0.8<E/A<2, <2 positive criteria • E/e′ > 14 • TRV >2.8 m/s • LA vol index >34 mL/m^2	58% 34%	100% 65%	100% 36%	13% 64%	NA 0.97
IVC proposal tested					
Thin/collapsible IVC Atrial fibrillation	55%	69%	82%	65%	2.77
2016 recommendations Not applicable*					
IVC proposal tested					
Thin/collapsible IVC	52%	86%	63%	86%	3.71

LHR, likelihood ratio.
*The 2016 recommendations were not tested because it is discouraged in patients with AF.

In patients with AF, the use of 2016 recommendations is not applicable. An "IVC diameter ≤ 2.1 cm and collapses >50%" had a PPV of 63%, Se was 52% and Sp was 86% (Table 4).

Net Reclassification Index

All 83 patients in sinus rhythm had analyzable TTE data including IVC measurements. Among patients with PAWP > 15 mmHg, 46 patients were correctly classified using the IVC analysis, and 9 patients were misclassified. Using the 2016 recommendations, 28 patients were correctly classified, and 27 patients were misclassified. Among patients with PAWP ≤15 mmHg, 15 patients were correctly classified using the IVC analysis, and 13 patients were misclassified. Using the 2016 recommendations, 12 patients were correctly classified, and 16 patients were misclassified. The NRI value was 0.39, thus favoring the study of the vena cava ($P < .05$; Table 5).

Relationship Between Invasively Measured Right- and Left-Sided Filling Pressures

There was a positive relationship between IVC size and RAP (Pearson correlation coefficient 0.583; $P < .001$; Fig. 1a), and between IVC size and PAWP (0.539; $P < .001$; Fig. 1c). There was a negative relationship between IVC maximal over minimal size ratio and RAP (−0.438; $P < .001$; Fig. 1b), between IVC maximal over minimal size ratio and PAWP (−0.405; $P < .001$; Fig. 1d) and between RAP and PAWP (−0.405; $P < .001$; Fig. 1e). There was 75.7% concordance between dichotomized pressures (100/132 patients). Indeed, 87 patients had both high RAP and high PAWP and 13 patients had both normal RAP and normal PAWP. Conversely, 24.2% patients (32/132) had discordant dichotomized pressure, namely 27 patients with normal PAWP, but high RAP, and 5 patients with high PAWP but normal RAP.

Table 5. Net Reclassification Improvement Table Comparing 2016 Recommendations and Study of the IVC of Patients in Sinus Rhythm

Hemodynamic PAWP > 15 mmHg Hemodynamic PAWP ≤ 15 mmHg		2016 recommendations		
		Elevated LVFP	Normal LVFP	Total
Proposal with IVC study	Elevated LVFP	23 8	23 5	59
	Normal LVFP	5 8	4 7	24
Total		44	39	83

Yellow indicates the results for hemodynamic PAWP >15 mmHg for each noninvasive methods; blue indicates the results for hemodynamic PAWP ≤15 mmHg for each noninvasive methods.

Discussion

The data shows that in our patients with suspected HFpEF, the 2016 recommendations for filling pressure evaluation algorithm is not always accurate for estimating the invasively measured PAWP and is relatively complex. For a long time, a non-invasive and reliable evaluation of LVFP has been a difficult and important issue.

In the past, the recommendations for evaluation of LVFP[22] were validated, with studies showing a good correlation between E/e' and PAWP,[23,24] including in patients with HFpEF studied separately.[25] Other more recent studies have questioned the accuracy of E/e' for the estimation of LVFP because a correlation coefficient between the 2 values does not allow for analysis of the exact performance of a test.[26] LA size is increased and LA function is impaired in HFpEF.[27,28] These 2 left atrium parameters are also an important prognostic factor in HF.[28] However, only 1 study showed a good correlation between LA size and LVFP elevation.[29] Studies are controversial regarding the evaluation of PAPs by maximum speed of TR with echocardiography, and its relationship with the values obtained by RHC.[30,31] No studies have shown a relationship between maximum speed of TR and PAWP. Notably, in our study the BNP did not differ between groups, which supports the hypothesis that BNP level is not the best parameter for indicating filling pressure, as suggested in previous studies.[32] Natriuretic peptide level is partly due to the stretching of myocardial fibers, but is also partly due to other phenomenon like fibrosis and hypertrophy. In this last case, natriuretic peptide level is more a marker of structural disease than hypervolemia.

Three recent studies have evaluated the performance of the 2016 recommendations for estimation of LVFP and the results showed a moderate predictive value for estimation

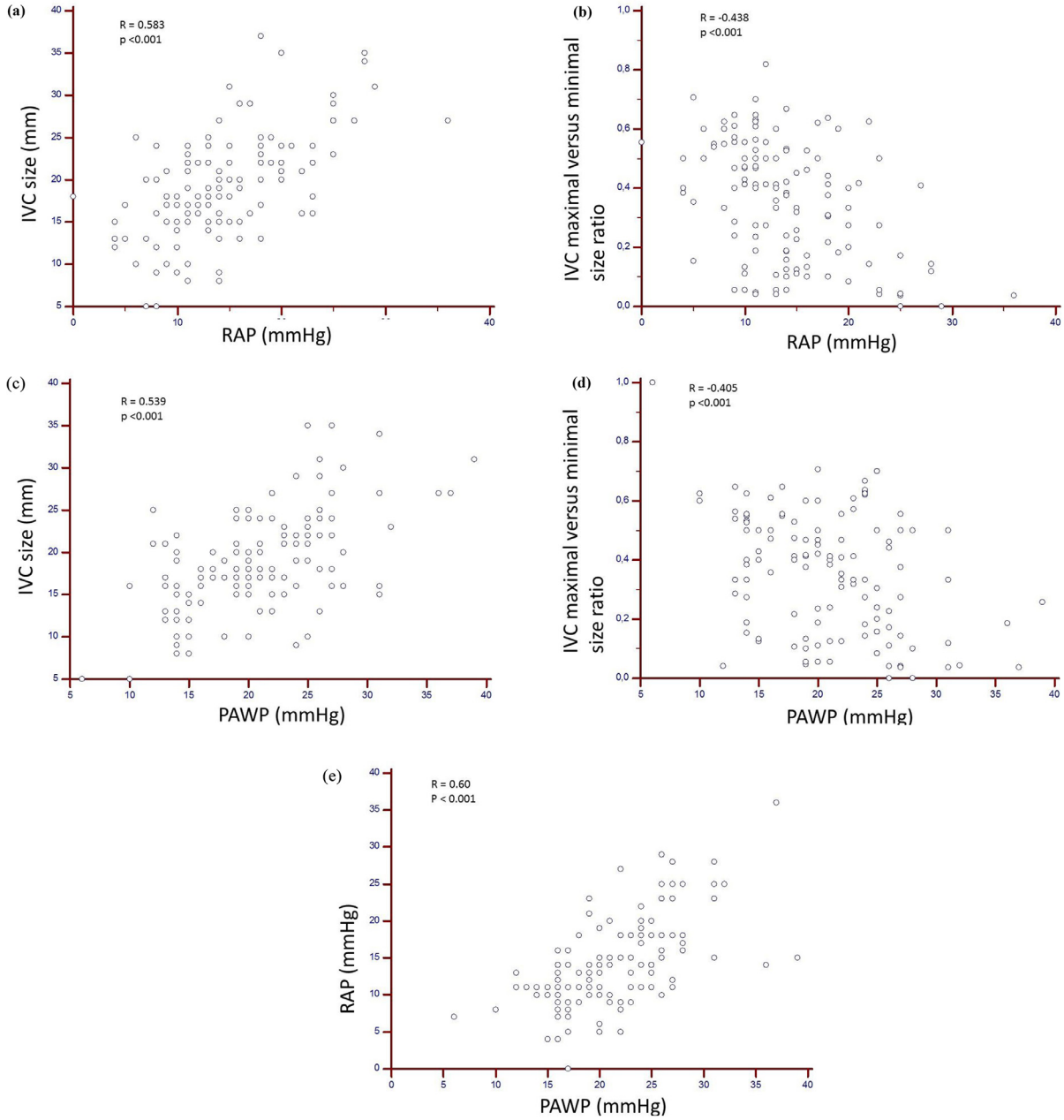


Fig. 1. (a) Scatterplot of the relationship between RAP and IVC maximal size. (b) Scatterplot of the relationship between RAP and IVC maximal versus minimal size ratio. (c) Scatterplot of the relationship between PAWP and IVC maximal size. (d) Scatterplot of the relationship between PAWP and IVC maximal versus minimal size ratio. (e) Scatterplot of the relationship between RAP and PAWP.

of invasively acquired PAWP. In the first study, only correlation coefficients between invasive and non invasive LVFP evaluation were studied.[7] In the second study, only 65% of patients with low echo LVFP had low LVFP at catheterization and 79% of patients with echo increased LVFP had high LVFP at catheterization.[8] In the third study, the correlation coefficient between the mean E/e′ ratio and PAWP was r = 0.24 (P= .019), and between the indexed LAV and PAWP was r = 0.20 (P = .11).[9] Applying the algorithm recommended in the updated 2016 guidelines, the diagnostic accuracy of elevated LAP by echocardiography was 87% for the overall study group compared with 72% by clinical assessment alone (P < .001). Among the 241 patients with LVEF ≥50%, the impact of echocardiographic assessment of LAP was good, with a diagnostic accuracy of 84% compared with 64% by clinical assessment alone (P < .001).[7,8]

Our study supports the helpfulness of an analysis of the E wave and E/A ratio as recommended in the 2016 recommendations. We found that all patients with E/A ≤ 0. 8 and E < 50 cm/s had normal PAWP (sensitivity and PPV of 100%). However, this result concerns only 4/132 patients. Our study shows that the performance of the analysis of E/e′ ratio, LA volume and peak TRV was a reasonably good

value for assessing elevated PAWP (Table 4). When analyzing the E/A $\geq$ 2 ratio, the PPV is 79% for detecting a PAWP $\geq$ 15 mmHg and concerns only 19/132 patients (Table 3).

The present IVC analysis may be viewed as an additional use of the existing data from conventional echocardiographic examination. Although the combined criteria/algorithms are directly aimed at determining the left ventricular filling pressure, we took advantage of the RAP versus PAWP relationship to indirectly estimate the left ventricular filling pressure. Several studies have documented a good correlation between RAP and PAWP,[10,11] as also observed in our study. Furthermore, we documented good agreement of right- and left-sided filling pressure obtained from right catheterization and dichotomized as normal versus high, and the 75.7% concordance was fully consistent with previous findings.[12] Finally, assessment of IVC is well known to significantly correlate with RAP, as also documented in our study.

Thus, in our study, the analysis of IVC was related to PAWP elevation, and demonstrated better positive and negative predictive values, and a better test likelihood ratio than the 2016 recommendations analyses. For LVFP evaluation, calculation of NRI (0.39) favors utilization of IVC for evaluating PAWP elevation of patients in sinus rhythm.

Importantly, another advantage of our new proposal is that it may theoretically apply to all patients while the currently published criteria/algorithms for directly assessing the LVFP may not be universally applicable in every patient. Indeed, AF remains a difficult case for the estimation of LVFP.[33,34] In the 2016 recommendations, there are no specific guidelines addressing this situation. Importantly, our study found that the analysis of the IVC had a good PPV for evaluation of LVFP in patients with AF. In the Hummel et al[9] study, the correlation between the echo parameters and hemodynamic estimation was lower in AF than in sinus rhythm, but the PPV of the echo parameters was not studied in this population. Overall, analysis of the size and collapsibility of the IVC was the most reliable parameter when the hemodynamic LVFP is either high or normal, whatever the rhythm (sinus or AF).

Strengths of the study

We recorded echo and RHC within 48 hours, without changing medications. We had a sample of 132 patients, which is a reasonably large sample of patients with hemodynamic and echo evaluation over a short time period. We tested the patients in sinus rhythm and in AF. We tested and proposed a simple parameter to indirectly estimate noninvasive LVFP and we found that the study of the IVC had good performance.

Limitations of the Study

First, we retrospectively analyzed patients prospectively enrolled in our center and the results pertain strictly to the population under study. Our monocentric study explored a particular population represented by patients referred for RHC at our center with finally normal hemodynamic results or post-capillary pulmonary hypertension related to HFpEF. As a result, only patients with dyspnea and a TRV >2.8 m/s or RV dilatation on a previous echo were included. This selection is the consequence of the ethics related to the indication of RHC. It could be that adding IVC size and collapse would be less informative in a more generalized population with dyspnea. However, this is an avoidable limitation when invasive hemodynamics and echocardiographic are compared. Second, there may be an unavoidable variability of cardiac catheterization measurements in patients with AF. Third, we used PAWP to estimate left heart filling pressure but did not measure left ventricular end diastolic pressure (LVEDP).[18] Finally, the correlations between invasively measured RAP and IVC size and collapsibility are at best only modest (Pearson correlation coefficients 0.44−0.58).

Clinical Perspectives

For evaluation of LVFP in patients with HFpEF, the 2016 recommendations must be used with caution. Our study favors analysis of IVC size and collapsibility in addition to the recommendations for detection of normal or elevated filling pressure for both sinus rhythm and AF because it is reliable and easy to use.

Acknowledgement

The authors thank Centres Mémoire de Ressources et de Recherche (CMRR) Paris Nord Ile-de-France for online help in calculation.

Disclosures

The authors declare no disclosure for this work, and no grant funding.

References

1. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, 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 J Heart Fail 2016;18:891–975.
2. Galderisi M, Lancellotti P, Donal E, Cardim N, Edvardsen T, Habib G, et al. European multicentre validation study of the accuracy of E/e' ratio in estimating invasive left ventricular filling pressure: EURO-FILLING study. Eur Heart J Cardiovasc Imaging 2014;15:810–6.
3. Gellen B, Canoui-Poitrine F, Lesault PF, Le Thuaut A, Lim P, Gueret P, et al. Usefulness of tissue Doppler imaging for assessing left ventricular filling pressure in patients with stable severe systolic heart failure. Am J Cardil 2013;112:1619–24.
4. Santos AB, Kraigher-Krainer E, Gupta DK, Claggett B, Zile MR, Pieske B, et al. PARAMOUNT Investigators: impaired left atrial function in heart failure with preserved ejection fraction. Eur J Heart Fail 2014;16:1096–103.
5. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. N Engl J Med. 2006;355:251–9.

6. Nagueh SF, Smiseth OA, Appleton CP, Byrd B.F. 3rd, Dokainish H, Edvardsen T, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2016;29:277–314.
7. Andersen OS, Smiseth OA, Dokainish H, Abudiab MM, Schutt RC, Kumar A, et al. Estimating left ventricular filling pressure by echocardiography. J AmCollCardiol 2017;69:1937–48.
8. Lancellotti P, Galderisi M, Edvardsen T, Donal E, Goliasch G, Cardim N, et al. Echo-Doppler estimation of left ventricular filling pressure: results of the multicentre EACVI Euro-Filling study. Eur Heart J Cardiovasc Imaging 2017;18:961–8.
9. Hummel YM, Liu LCY, Lam CSP, Fonseca-Munoz DF, Damman K, Rienstra M, et al. Echocardiographic estimation of left ventricular and pulmonary pressures in patients with heart failure and preserved ejection fraction: a study utilizing simultaneous echocardiography and invasive measurements. Eur J Heart Fail 2017;19:1651–60.
10. Drazner MH, Prasad A, Ayers C, Markham DW, Hastings J, Bhella PS, et al. The relationship of right- and left-sided filling pressures in patients with heart failure and a preserved ejection fraction. Circ Heart Fail 2010;3:202–6.
11. Nagueh SF, Smiseth OA, Dokainish H, Andersen OS, Abudiab MM, Schutt RC, Kumar A, Gude E, Sato K, Harb SC, Klein AL. Mean right atrial pressure for estimation of left ventricular filling pressure in patients with normal left ventricular ejection fraction: invasive and noninvasive validation. J Am SocEchocardiogr 2018;31:799–806.
12. Brinkley D.M. Jr, Ho KKL, Drazner MH, Kociol RD. The prognostic value of the relationship between right atrial and pulmonary capillary wedge pressure in diverse cardiovascular conditions. Am Heart J 2018;199:31–6.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, 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.
14. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, 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.
15. Brennan JM, Blair JE, Goonewardena S, Ronan A, Shah D, Vasaiwala S, et al. Reappraisal of the use of inferior vena cava for estimating right atrial pressure. J Am Soc Echocardiogr 2007;20:857–61.
16. Galiè N, Humbert M, Vachiery JL, Gibbs S, Lang I, Torbicki A, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 2016;37:67–119.
17. Castelain V, Hervé P, Lecarpentier Y, Duroux P, Simonneau G, Chemla D. Pulmonary artery pulse pressure and wave reflection in chronic pulmonary thromboembolism and primary pulmonary hypertension. J Am Coll Cardiol 2001;37:1085–92.
18. Hemnes AR, Opotowsky AR, Assad TR, Xu M, Doss LN, Farber-Eger E, Wells QS, et al. Features associated with discordance between pulmonary arterial wedge pressure and left ventricular end diastolic pressure in clinical practice: implications for pulmonary hypertension classification. Chest 2018;154:1099–107.
19. Pewsner D, Battaglia M, Minder C, Marx A, Bucher H, Egger M. Ruling a diagnosis in and out with "SpPIn" and "SnNOut": a note of caution. BMJ 2004;329:209–13.
20. Pencina MJ, D'Agostino RB, Sr., D'Agostino RB, Jr., Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med 2008;27:188–90.
21. Pencina MJ, D'Agostino RB, Sr., Steyerberg EW. Extensions of net reclassification improvement calculations to measure usefulness of new biomarkers. Stat Med 2011;30:11–21.
22. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. J Am Soc Echocardiogr 2009;22:107–33.
23. Dokainish H, Zoghbi WA, Lakkis NM, Al-Bakshy F, Dhir M, Quinones MA, et al. Optimal noninvasive assessment of left ventricular filling pressures: a comparison of tissue Doppler echocardiography and B-type natriuretic peptide in patients with pulmonary artery catheters. Circulation 2004;109:2432–9.
24. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, Redfield MM, et al. Clinical utility of Doppler echocardiography and tissue Doppler imaging in the estimation of left ventricular filling pressures: a comparative simultaneous Doppler-catheterization study. Circulation 2000;102:1788–94.
25. Kasner M, Westermann D, Steendijk P, Gaub R, Wilkenshoff U, Weitmann K, et al. Utility of Doppler echocardiography and tissue Doppler imaging in the estimation of diastolic function in heart failure with normal ejection fraction: a comparative Doppler-conductance catheterization study. Circulation 2007;116:637–47.
26. Santos M, Rivero J, McCullough SD, West E, Opotowsky AR, Waxman AB, et al. E/e' ratio in patients with unexplained dyspnea: lack of accuracy in estimating left ventricular filling pressure. Circ Heart Fail 2015;8:749–56.
27. Kurt M, Wang J, Torre-Amione G, Nagueh SF. Left atrial function in diastolic heart failure. Circ Cardiovasc Imaging 2009;2:10–5.
28. Abhayaratna WP, Seward JB, Appleton CP, Douglas PS, Oh JK, Tajik AJ, et al. Left atrial size: physiologic determinants and clinical applications. J Am Coll Cardiol 2006;47:2357–63.
29. Hsiao SH, Lin KL, Chiou KR. Comparison of left atrial volume parameters in detecting left ventricular diastolic dysfunction versus tissue Doppler recordings. Am J Cardiol 2012;109:748–55.
30. Pozzoli M, Capomolla S, Pinna G, Cobelli F, Tavazzi L. Doppler echocardiography reliably predicts pulmonary artery wedge pressure in patients with chronic heart failure with and without mitral regurgitation. J Am Coll Cardiol 1996;27:883.
31. Amsallem M, Sternbach JM, Adigopula S, Kobayashi Y, Vu TA, Zamanian R, et al. Addressing the controversy of estimating pulmonary arterial pressure by echocardiography. J Am Soc Echocardiogr 2016;29:93–102.
32. Van Aelst LNL, Arrigo M, Placido R, Akiyama E, Girerd N, Zannad F, et al. Acutely decompensated heart failure with preserved and reduced ejection fraction present with comparable hemodynamic congestion. Eur J Heart Failure 2018;20:738–47.
33. Chirillo F, Brunazzi MC, Barbiero M, Giavarina D, Pasqualini M, Franceschini-Grisolia E, et al. Estimating mean pulmonary wedge pressure in patients with chronic atrial fibrillation from transthoracic Doppler indexes of mitral and pulmonary venous flow velocity. J Am CollCardiol 1997;30:19–26.
34. Sohn DW, Song JM, Zo JH, Chai IH, Kim HS, Chun HG, Kim HC. Mitral annulus velocity in the evaluation of left ventricular diastolic function in atrial fibrillation. J Am SocEchocardiogr 1999;12:927–31.