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# Extent of jugular venous distension and lower extremity edema are the best tools from history and physical examination to identify heart failure exacerbation

## Introduction

Congestion is the hallmark of heart failure (HF) and therefore evaluation for congestion and its severity is the cornerstone in managing HF patients. Congestion not only leads to symptoms and signs of HF but is also linked to HF progression [1] and is associated with post-discharge morbidity and mortality [2]. It is known that many patients hospitalized with HF are not optimally decongested at time of discharge [3], leading to re-hospitalization due to HF decompensation. In a recent analysis of the Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial, Cooper et al. found that post-discharge outcomes of patients with HF were mainly driven by persistent congestion (higher right and left-sided filling pressures) [4]. Thus, the most reliable way to reduce HF admission and readmission is to monitor severity of congestion and optimally treat it.

The congestion cascade begins days to weeks prior to symptom onset with subclinical rise of left and right-sided filling pressures (hemodynamic congestion), which is followed by redistribution of fluids in the extravascular space and visceral organs (organ congestion), ultimately leading to symptoms and signs

of volume overload (clinical congestion) [5]; therefore, it is prudent to recognize the onset of clinical congestion early enough to allow medication adjustment and/or hospitalization if necessary. Validity of physical signs in the diagnosis of HF decompensation has been acknowledged a long time ago [6], but the correlation of these signs with direct hemodynamic measurements has rarely been reported.

It is unknown whether subjective symptoms versus objective physical examination signs of volume overload are more important for the diagnosis of HF decompensation among patients with left ventricular systolic dysfunction. We have recently shown the value of a simple physical examination sign, the positive hepatojugular reflux (HJR), in its ability to identify the degree of congestion through its strong association with inferior vena cava diameter and central hemodynamic parameters of volume overload: the pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP), in addition to its ability to predict post-discharge outcomes [7]. Herein, we aimed to provide a more detailed assessment of the value of history and physical examination in identifying degree of congestion. In a recent study, the sum of PCWP + RAP was used as

a measure of congestion as it reflects both right and left ventricular performance [8]. We utilized this criterion to grade the severity of congestion, and compare patient symptoms and signs of volume overload according to the sum of PCWP and RAP, in order to identify the best tools for evaluation of degree of congestion in HF.

## Methods

This study is a retrospective analysis of a limited access dataset from the ESCAPE trial provided by the National Heart, Lung and Blood Institute (NHLBI) [9]. The ESCAPE trial enrolled 433 patients hospitalized with acute HF, and compared outcomes of groups of patients whose care was guided by pulmonary artery catheters (PAC) versus those managed by clinical assessment alone. The following were the study inclusion criteria: hospitalization for decompensated HF within the previous year, urgent visit to the emergency department, treatment during the previous month with 160 mg of furosemide or its equivalent, experiencing at least 3 months of HF symptoms despite being on angiotensin-converting enzyme inhibitors and diuretics, systolic blood pressure  $\leq 125$  mmHg, and left ventricular ejection fraction  $\leq 30\%$  in

**Table 1** Comparison of baseline clinical, laboratory and echocardiographic characteristics among patients enrolled in the ESCAPE trial according to tertiles of combined pulmonary capillary wedge pressure and right atrial pressure

	Tertile 1 PCWP + RAP < 31 mm Hg (n = 58)	Tertile 2 PCWP + RAP = 31–42 mm Hg (n = 65)	Tertile 3 PCWP + RAP > 42 mm Hg (n = 64)	P-value
<i>Demographics</i>				
Age (years, median, IQR)	59 (50, 67)	58 (49, 67)	55 (46, 63)	0.380
Men % (n)	67.2 (39/58)	70.8 (46/65)	84.4 (54/64)	0.069
White % (n)	65.5 (38/58)	58.5 (38/65)	53.1 (34/64)	0.380
Black % (n)	29.3 (17/58)	29.2 (19/65)	26.6 (17/64)	0.927
BMI (Kg/m <sup>2</sup> , median, IQR)	28.2 (23.9, 33.9)	25.4 (22.5, 31.1)	28.8 (25.2, 32.5)	0.087
<i>Comorbidities</i>				
Ischemic etiology of HF % (n)	55.2 (32/58)	56.9 (37/65)	46.9 (30/64)	0.478
Idiopathic etiology of HF % (n)	36.2 (21/58)	30.8 (20/65)	39.1 (25/64)	0.606
Atrial fibrillation % (n)	31 (18/58)	24.6 (16/65)	31.3 (20/64)	0.643
CABG % (n)	10.3 (6/58)	6.2 (4/65)	3.1 (2/64)	0.255
Stroke % (n)	10.3 (6/58)	15.4 (10/65)	7.8 (5/64)	0.383
Hypertension % (n)	58.6 (34/58)	49.2 (32/65)	40.6 (26/64)	0.139
DM on insulin % (n)	20.7 (12/58)	15.4 (10/65)	14.1 (9/64)	0.586
Malignancy % (n)	6.9 (4/58)	9.2 (6/65)	3.1 (2/64)	0.362
COPD % (n)	19 (11/58)	16.9 (11/65)	12.5 (8/64)	0.606
Depression % (n)	22.4 (13/58)	15.4 (10/65)	25 (16/64)	0.381
<i>Laboratory variables</i>				
BNP pg/ml (median, IQR)	423 (211, 681)	707 (368, 1430)	737 (236, 1305)	0.016
BUN mg/dl (median, IQR)	27 (17, 36)	27 (19, 47)	34 (23, 49)	0.022
Creatinine mg/dl (median, IQR)	1.4 (0.9, 1.7)	1.3 (1, 1.8)	1.5 (1.2, 2)	0.156
Total bilirubin mg/dl (median, IQR)	0.6 (0.4, 1.1)	0.9 (0.6, 1.3)	0.9 (0.3, 1.4)	0.301
Na meq/l (median, IQR)	137 (136, 140)	138 (134, 140)	136 (133, 138)	0.015
Hct % (median, IQR)	38 (33, 40)	39 (36, 41)	38 (35, 42)	0.082
<i>Echocardiography</i>				
EF % (median, IQR)	19 (14, 30)	23 (14, 30)	14 (10, 21)	0.005
LVEDD (median, IQR)	6.4 (5.9, 6.9)	6.3 (5.8, 7.3)	6.6 (5.9, 7.6)	0.284
LVESD (mm, m ± SD)	5.6 (4.8, 6.4)	5.8 (5, 6.5)	6 (5.3, 7.1)	0.049
IVC inspiration cm (median, IQR)	0.8 (0.4, 1.7)	1.8 (1, 2.3)	2 (1.6, 2.5)	<0.001
IVC expiration cm (median, IQR)	1.9 (1.2, 2.3)	2.2 (1.7, 2.6)	2.7 (2.2, 3)	<0.001

BMI body mass index, HF heart failure, CABG coronary artery bypass graft, DM diabetes mellitus, COPD chronic obstructive pulmonary disease, BNP B-type natriuretic peptide, LVEDD left ventricular end-diastolic dimension, LVESD left ventricular end-systolic dimension, IVC inferior vena cava, IQR interquartile range, SD standard deviation, PCWP pulmonary capillary wedge pressure, RAP right atrial pressure, EF ejection fraction, Hct hematocrit, BUN blood urea nitrogen

addition to at least one symptom and one sign of congestion. The study concluded that the use of PAC did not improve or worsen HF outcomes.

The objective of the current analysis was to identify the best history and physical examination components that predict the severity of HF exacerbation. The ESCAPE trial is ideal for such analysis as it comprised variables of the history and physical examination at multiple time points including hospital admission. Variables of HF decompensation related to patient history included dyspnea, orthopnea and fatigue. The study also contained detailed physical examination findings including the presence of rales, S3 gallop, jugular venous distension (JVD), lower extremity edema, HJR, hepatomegaly and ascites. These variables were also dichotomized according to the severity of history and physical examination sign (for example, dyspnea and fatigue were graded from 1–3 and orthopnea was graded from 1–5). We determined the severity of HF exacerbation in each patient by the sum of PCWP and RAP on admission, which assesses the degree of pulmonary and systemic congestion, respectively, and therefore only patients who were managed via PAC were included in the current analysis. Cases were divided into tertiles according to the sum of PCWP and RAP on admission. History and physical examination variables of congestion were examined across tertiles.

## Statistical analysis

Primary analysis compared history and physical examination signs of congestion across tertiles of PCWP + RAP. Categorical variables were compared using the  $\chi^2$ -test and results were summarized as counts and percentages. Continuous variables were compared using the Kruskal-Wallis test because of non-normality of distribution (assessed using the Shapiro-Wilk test) and results were presented as median and interquartile range (IQR). The ability of the magnitude of the combined value of PCWP and RAP on admission to predict all-cause mortality and rehospitalization for HF, both at 6 months after randomization was assessed

## Abstract · Zusammenfassung

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### Extent of jugular venous distension and lower extremity edema are the best tools from history and physical examination to identify heart failure exacerbation

#### Abstract

**Introduction.** We aimed to identify the best tools from history and physical examination that predict severity of heart failure (HF) exacerbation among patients with an ejection fraction (EF)  $\leq 30\%$ .

**Methods.** Patients enrolled in the ESCAPE trial were divided into tertiles according to the combined value of pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP) which we used as a marker of volume loading of both pulmonary and systemic compartments. Variables of congestion from history and physical examination were examined across tertiles.

**Results.** There were significant differences across tertiles (tertile 1: PCWP + RAP  $< 31$  mm Hg, tertile 2: PCWP + RAP 31–42 mm Hg and tertile 3: PCWP + RAP  $> 42$  mm Hg) with respect to baseline B-type

natriuretic peptide ( $P = 0.016$ ), blood urea nitrogen ( $P = 0.022$ ), sodium ( $P = 0.015$ ), left ventricular ejection fraction ( $P = 0.005$ ), and inferior vena cava diameter during inspiration ( $P < 0.001$ ) and expiration ( $P < 0.001$ ). With respect to variables of congestion from history and physical examination, we found significant differences across tertiles predominantly in signs of right sided failure, specifically, the frequency of jugular venous distension (JVD,  $P < 0.001$ ) and JVD  $> 12 \text{ cmH}_2\text{O}$  ( $p < 0.001$ ), lower extremity edema ( $P = 0.001$ ) and lower extremity edema of at least grade 2+ ( $P = 0.029$ ), and positive hepatojugular reflux (HJR,  $P = 0.022$ ) but no differences in patients' symptoms such as degree of dyspnea, orthopnoea or fatigue. With regards to post-discharge outcomes, there was a significant difference across

tertiles in all-cause mortality ( $P = 0.029$ ) and rehospitalization for HF ( $P = 0.031$ ) at 6 months following randomization. Receiver operator characteristic curves showed that admission PCWP + RAP had an area under the curve of 0.623 ( $P = 0.0075$ ) and 0.617 ( $P = 0.0048$ ), respectively, in predicting 6-month all-cause mortality and rehospitalization for HF.

**Conclusion.** The presence and extent of JVD and lower extremity edema, and a positive HJR are better than other signs and symptoms in identifying severity of HF exacerbation among patients with EF  $\leq 30\%$ .

#### Keywords

Congestion · Pulmonary artery catheterization · Pulmonary capillary wedge pressure · Atrial pressure · Retrospective study

### Ausmaß der jugularvenösen Distension und Ödeme der unteren Extremität als beste Parameter aus der Anamnese und körperlichen Untersuchung zur Identifizierung einer Verschlechterung der Herzinsuffizienz

#### Zusammenfassung

**Einleitung.** Ziel ist es, die besten Instrumente aus der Anamnese und körperlichen Untersuchung zu identifizieren, welche die Schwere der Verschlimmerung einer Herzinsuffizienz (HF) bei Patienten mit einer Ejektionsfraktion (EF)  $\leq 30\%$  vorhersagen.

**Methoden.** Die in die ESCAPE-Studie eingeschlossenen Patienten wurden in Terzilen eingeteilt hinsichtlich der kombinierten Werte des pulmonalkapillären Verschlussdrucks („pulmonary capillary wedge pressure“, PCWP) und des rechtsatrialen Drucks („right atrial pressure“, RAP), die als Marker des Ladevolumens sowohl der pulmonalen als auch der systemischen Kompartimente verwendet wurden. Variablen der Kongestion aus der Anamnese und körperlichen Untersuchung wurden in allen Terzilen untersucht.

**Ergebnisse.** Zwischen den Terzilen gab es signifikante Unterschiede (Terzil 1: PCWP + RAP  $< 31$  mmHg, Terzil 2: PCWP + RAP 31–42 mmHg und Terzil 3: PCWP + RAP

$> 42$  mmHg) hinsichtlich des Ausgangswerts des natriuretischen Peptids Typ B ( $p = 0.016$ ), des Harnstoffstickstoffs im Blut ( $p = 0.022$ ), des Natriums ( $p = 0.015$ ), der linksventrikulären Ejektionsfraktion ( $p = 0.005$ ) sowie des Durchmessers der V. cava inferior während der Einatmung ( $p < 0.001$ ) und Ausatmung ( $p < 0.001$ ). Bezuglich der Variablen einer Kongestion aus der Anamnese und körperlichen Untersuchung stellen wir vor allem bei Anzeichen der Rechtsherzinsuffizienz, insbesondere bei der Häufigkeit einer jugularvenösen Distension (JVD;  $p < 0.001$ ) und JVD  $> 12 \text{ cmH}_2\text{O}$  ( $p < 0.001$ ), bei Ödemen der unteren Extremität ( $p = 0.001$ ), Ödemen der unteren Extremität  $>$  Grad 2 ( $p = 0.029$ ) und positivem hepatojugulärem Reflux (HJR;  $p = 0.022$ ), signifikante Unterschiede bei den Terzilen fest. Bei den Symptomen der Patienten, wie dem Grad der Dyspnoe, Orthopnoe oder Fatigue, gab es jedoch keine Unterschiede. Bezuglich der Ergebnisse

nach Entlassung gab es einen signifikanten Unterschied zwischen den Terzilen in der Mortalität jeglicher Ursache ( $p = 0.029$ ) und Rehospitalisation wegen HF ( $p = 0.031$ ) jeweils 6 Monate nach der Randomisierung. Die Receiver-Operating-Characteristic-Kurven zeigten, dass der Ausgangswert von PCWP + RAP bei der Prädiktion der Mortalität jeglicher Ursache und Rehospitalisation wegen HF eine „area under the curve“ von 0,623 ( $p = 0.0075$ ) bzw. 0,617 ( $p = 0.0048$ ) zeigte.

**Schlussfolgerung.** Vorliegen und Ausmaß von JVD und Ödemen der unteren Extremität sowie ein positiver HJR sind zur Identifizierung der Schwere einer HF-Verschlechterung bei Patienten mit einer EF  $\leq 30\%$  besser geeignet als andere Anzeichen und Symptome.

#### Schlüsselwörter

Kongestion · Pulmonalarterienkatheterisierung · Pulmonalkapillärer Verschlussdruck · Vorhofdruck · Retrospektive Studie

**Table 2** Comparison of history and physical examination findings among patients enrolled in the ESCAPE trial according to tertiles of combined pulmonary capillary wedge pressure and right atrial pressure

	Tertile 1 PCWP + RAP < 31 mm Hg (n = 58)	Tertile 2 PCWP + RAP = 31–42 mm Hg (n = 65)	Tertile 1 PCWP + RAP > 42 mm Hg (n = 64)	P-value
<i>History</i>				
<i>Dyspnea</i>				
Dyspnea grade 1 % (n)	12.1 (7/58)	13.8 (9/65)	7.8 (5/64)	0.539
Dyspnea grade 2 % (n)	31 (18/58)	29.2 (19/65)	28.1 (18/64)	0.939
Dyspnea grade 3 % (n)	55.2 (32/58)	56.9 (37/65)	62.5 (40/64)	0.688
<i>Orthopnea</i>				
Orthopnea grade 1 % (n)	15.5 (9/58)	7.7 (5/65)	6.3 (4/63)	0.187
Orthopnea grade 2 % (n)	8.6 (5/58)	7.7 (5/65)	6.3 (4/63)	0.892
Orthopnea grade 3 % (n)	39.7 (23/58)	49.2 (32/65)	44.4 (28/63)	0.566
Orthopnea grade 4 % (n)	24.1 (14/58)	18.5 (12/65)	25.4 (16/63)	0.607
Orthopnea grade 5 % (n)	12.1 (7/58)	16.9 (11/65)	17.5 (11/63)	0.670
<i>Fatigue</i>				
Fatigue grade 1 % (n)	10.3 (6/58)	6.2 (4/65)	3.1 (2/64)	0.265
Fatigue grade 2 % (n)	27.6 (16/58)	20 (13/65)	32.8 (21/64)	0.255
Fatigue grade 3 % (n)	60.3 (35/58)	72.3 (47/65)	64.1 (41/64)	0.354
<i>NYHA class</i>				
NYHA class III % (n)	8.6 (5/58)	7.7 (5/65)	14.1 (9/64)	0.438
NYHA class IV % (n)	91.4 (53/58)	92.3 (60/65)	85.9 (55/64)	0.438
<i>Physical examination</i>				
JVD % (n)	76.8 (43/58)	95.2 (60/63)	98.4 (61/62)	<0.001
JVP > 12 cm % (n)	35.7 (20/56)	50.8 (32/63)	82.3 (51/62)	<0.001
Positive HJR % (n)	67.9 (38/56)	85.7 (54/63)	85.5 (53/62)	0.022
Hepatomegaly % (n)	41.4 (24/58)	59.4 (38/64)	59.4 (38/64)	0.074
Ascitis % (n)	22.4 (13/58)	32.3 (21/65)	48.4 (31/64)	0.009
LE edema % (n)	46.6 (27/58)	72.3 (47/65)	78.1 (50/64)	0.001
LE edema at least 2 + % (n)	25.9 (15/58)	46.2 (30/65)	46.9 (30/64)	0.029
Rales % (n)	46.6 (27/58)	50.8 (33/65)	54.7 (35/64)	0.668
S3 gallop % (n)	62.1 (36/58)	61.5 (40/65)	62.5 (40/64)	0.994
Respiratory rate/min (median, IQR)	20 (18, 22)	20 (18, 23)	20 (18, 22)	0.128
6MWD m (median, IQR)	604 (300, 968)	550 (249, 950)	583 (384, 973)	0.890

NYHA New York Heart Association, JVD jugular venous distension, JVP jugular venous pressure, HJR hepatojugular reflux, LE lower extremity, 6MWD 6-minute walk distance, IQR interquartile range, LE lower extremity

using receiver operating characteristics (ROC) curves. Optimum cut-off values of PCWP + RAP were those that provided the highest combined sensitivity and specificity for predicting the outcome. P-values for the trend across tertiles were examined via linear regression analysis for continuous variables and  $\chi^2$ -test linear-by-linear association for categorical variables. Other than ROC curve analysis which was performed via MedCalc software (MedCalc, Ostend, Belgium), the rest of the statistical analysis was performed using IBM SPSS 21.0 statistical software (IBM SPSS version 21.0. Armonk, NY). All statistical significance was assessed using a 2-sided P-values. A P-value < 0.05 was considered statistically significant.

## Results

### Baseline characteristics

A total of 187 cases that were randomized to receive PAC and had data available for both PCWP and RAP were included in our analysis. These cases were divided into tertiles according to the combined value of PCWP and RAP as follows: tertile 1: PCWP + RAP < 31 mm Hg, tertile 2: PCWP + RAP 31–42 mm Hg and tertile 3: PCWP + RAP > 42 mm Hg. There were significant differences across tertiles with regards to baseline B-type natriuretic peptide (BNP) levels ( $P = 0.016$ ), blood urea nitrogen (BUN,  $P = 0.022$ ), sodium ( $P = 0.015$ ), left ventricular ejection fraction ( $P = 0.005$ ), left ventricular end-systolic dimension ( $P = 0.049$ ), and the diameter of inferior vena cava during inspiration ( $P < 0.001$ ) and expiration ( $P < 0.001$ ). Comparison of baseline characteristics among patients enrolled in the ESCAPE trial according to tertiles of PCWP + RAP is listed in Table 1.

### Best history and physical examination tools that predict the degree of congestion

With regards to patient history, there was no significant differences across tertiles of PCWP + RAP in the degree of dyspnea (grades 1–3), orthopnea (grades 1–5) or fatigue (grades 1–3). With regards to

**Table 3** Short and intermediate term outcomes of patients enrolled in the ESCAPE trial according to tertiles of combined pulmonary capillary wedge pressure and right atrial pressure

	Tertile 1 PCWP + RAP < 31 mm Hg (n = 58)	Tertile 2 PCWP + RAP = 31–42 mm Hg (n = 65)	Tertile 3 PCWP + RAP > 42 mm Hg (n = 64)	P-value	P-trend
6-month mortality % (n)	10.3 (6/58)	24.6 (16/65)	29.7 (19/64)	0.029	0.011
6-month rehospitalization % (n)	50 (29/58)	53.8 (35/65)	60.9 (39/64)	0.465	–
Rehospitalization for HF % (n)	32.8 (19/58)	36.9 (24/65)	54.7 (35/64)	0.031	0.013
Composite endpoint of death, cardiac rehosp., cardiac transplant % (n)	36.2 (21/58)	55.4 (36/65)	65.6 (42/64)	0.004	0.001
Composite endpoint of death, any rehosp., cardiac transplant % (n)	53.4 (31/58)	69.2 (45/65)	76.6 (49/64)	0.022	0.007
Number of hospitalizations (median, IQR)	1.5 (1, 3)	2 (1, 2)	2 (1, 3)	0.373	–
Duration of initial hospitalization (days, median, IQR)	6 (4, 10)	7 (5, 13)	9 (6, 13)	0.02	0.157
Duration in-hospital during 1 <sup>st</sup> month (days, median, IQR)	4 (3, 11)	6 (4, 12)	8 (6, 15)	0.001	0.01
Duration in-hospital during 6-months (days, median, IQR)	11 (4, 19)	11 (6, 23)	12 (8, 26)	0.066	–

physical examination on hospital admission, there were significant differences across tertiles in the frequency of JVD ( $P < 0.001$ ), or extent of JVD  $> 12 \text{ cmH}_2\text{O}$  ( $P < 0.001$ ), the presence of lower extremity edema ( $P = 0.001$ ) and lower extremity edema at least 2+ ( $P = 0.029$ ), a positive HJR ( $P = 0.022$ ) and the presence of ascitis ( $P = 0.009$ ). There were no differences across tertiles of PCWP + RAP in direct signs of elevated left sided filling pressures specifically the presence of rales and S3 gallop. A comparison of symptoms and signs of volume overload across tertiles of PCWP + RAP is listed in **Table 2**.

### Post-discharge outcomes according to admission PCWP + RAP

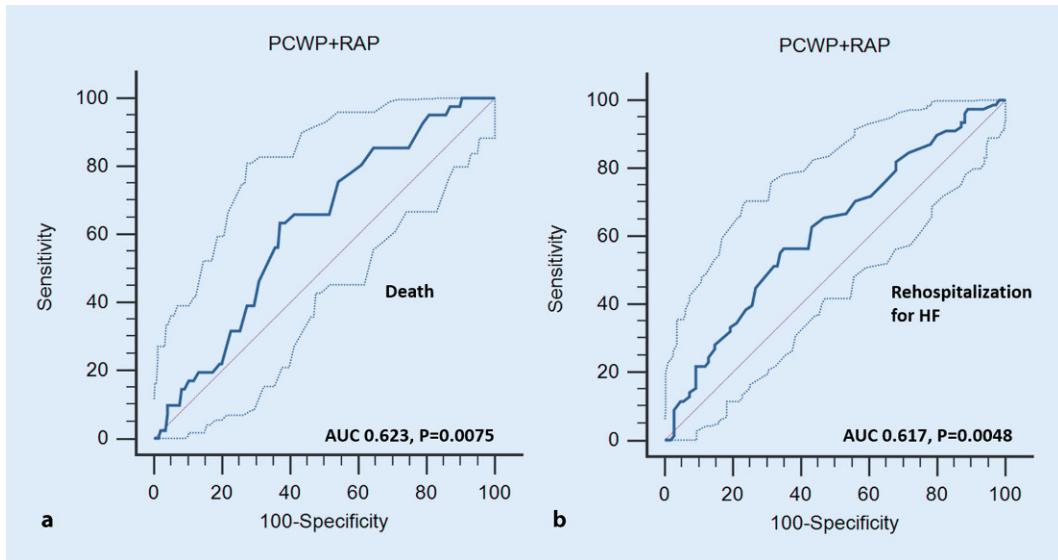
There was a significant difference across tertiles of PCWP + RAP with regards to 6-month all-cause mortality ( $P = 0.029$ ), rehospitalization for HF ( $P = 0.031$ ), composite end-point of death, cardiac rehospitalization and cardiac transplantation ( $P = 0.004$ ), composite end-point of death, any rehospitalization and cardiac transplantation ( $P = 0.022$ ), and total duration in-hospital in the first 30 days ( $P = 0.001$ ). Using linear regression and Chi-square linear-by-linear association, we found a significant increasing trend across tertiles of PCWP + RAP with regards to the aforementioned end-points. Comparison of post-discharge outcomes

(and trends) across tertiles of PCWP + RAP is listed in **Table 3**.

ROC curves showed that PCWP + RAP on admission had an AUC of 0.623 (95% CI 0.550–0.693,  $P = 0.0075$ ) in predicting 6-month all-cause mortality. An optimal cutoff criterion of PCWP + RAP  $\geq 40 \text{ mm Hg}$  had the highest combined sensitivity (63.4%) and specificity (63%) in predicting mortality (**Fig. 1**, panel a). Also, PCWP + RAP also had an AUC of 0.617 (95% CI 0.544–0.687,  $P = 0.0048$ ) in predicting rehospitalization for HF, and an optimal cutoff criterion of PCWP + RAP  $> 38 \text{ mm Hg}$  had the highest combined sensitivity (56.4%) and specificity (65.1%) (**Fig. 1**, panel b).

### Discussion

We have shown in this analysis that certain physical examination signs of congestion such as JVD, a positive HJR, and the amount of lower extremity edema, determine the severity of congestion among patients with HF exacerbation. The JVD not only reflects increased right sided filling pressures but was also shown to be the main clinical sign to indirectly detect elevated leftsided pressures due to the high degree of concordance between right and leftsided chambers in over two thirds of HF patients [10]. JVD was also independently associated with higher short and long-term mortality [11]. The extent of lower extremity edema is one of the important signs used in monitoring and managing HF patients. Although the importance of lower extremity edema was minimized in the Framingham criteria for diagnosing HF due to its low specificity, it is more important in guiding therapy of already established HF cases. The HJR is an underutilized, simple physical examination sign with high intraobserver agreement of approximately 97% [12] that was found previously by our group to correlate well with other physical examination signs of congestion, BNP level, as well as the PCWP and RAP [7]. In our cohort, ascites was present at baseline with increasing frequency across tertiles of PCWP + RAP (22.4% of patients in first tertile of PCWP + RAP had ascites vs. 32.3% of patients in tertile 2 vs. 48.4% in tertile 3,  $P = 0.009$ ). Those with ascites



**Fig. 1** ▲ ROC curves showing the ability of the sum of pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP) on hospital admission of patients with systolic HF in predicting death (panel a) and rehospitalization for heart failure (panel b), both at 6 months (AUC area under the curve)

were most likely to have grade 1 (trace ascites, 20% of the cases included in our analysis), followed by grade 2 (moderate ascites, 13%) and less likely to have grade 3 (massive ascites, 1.6%); therefore, if present only modest amount of ascites is expected in HF exacerbations even with more severe congestion.

Not surprisingly, we did not find any value for conventional clinical signs of increased left sided filling pressure (e.g. rales and S3 gallop) in predicting the degree of congestion. It is known that patients with chronic HF often lack pulmonary rales despite elevated left-sided filling pressures due to chronic lymphatic hypertrophy, which prevents alveolar edema development despite high interstitial pressures [13]. Symptoms of volume overload, such as dyspnea, orthopnea and fatigue and their severity were also not associated with the degree of congestion. In fact, we have previously shown from an analysis of the ESCAPE trial that symptoms in HF correlate poorly with objective parameters of congestion [14]. Moreover, the ESCAPE trial enrolled patients with acute systolic HF with advanced symptoms and approximately 90% of patients included in our analysis had New York Heart Association class IV symptoms, thereby limiting the diagnostic value of symptoms of volume overload in predicting severity of congestion in this dataset.

We used the combined sum of PCWP and RAP as a measure of congestion as

it represents volume loading of both the pulmonary and systemic compartments and is thus an index of biventricular performance [15]. A recent study illustrated the prognostic effect of PCWP + RAP obtained post-treatment on survival and readmission at 6 months [8], and our analysis similarly confirms the prognostic effect of this marker on hospital admission in predicting morbidity and mortality. The misperception that the physical examination provides limited information compared with modern diagnostic tools has led to a gradual decline in emphasis of the value of physical examination in HF. The significant association that we found between the presence and magnitude of JVD and lower extremity edema, a positive HJR, and PAC-derived intracardiac pressures, highlights the value of these physical examination tools in evaluating patients with HF, and to guide medication adjustment and decision for hospitalization.

## Conclusion

We have shown the importance of certain physical examination signs in identifying the severity of HF exacerbation. Specifically, these are signs of more severe systemic congestion and include the extent of JVD, lower extremity edema and a positive HJR. Those signs correlated well with central hemodynamic markers of congestion measured via the PAC. Neither the physical examination signs of

pulmonary congestion such as S3 gallop and the presence and extent of rales, nor HF symptoms, such as dyspnea, orthopnea or fatigue were valuable in determining the degree of congestion during HF exacerbation. The study further highlights the value of physical examination skills in acute HF.

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## Compliance with ethical guidelines

**Conflict of interests.** H.R.Omar and M.Guglin declare that they have no competing interests.

This article does not contain any studies with human participants or animals performed by any of the authors.

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Die Dietmar-Hopp-Stiftung unterstützt den Neubau mit weiteren 100 Millionen Euro.</p> <p data-bbox="1049 713 1429 1347">„Die Herzmedizin entwickelt sich in allen Bereichen mit großer Dynamik, was in den letzten Jahren zu einer bemerkenswerten Ausweitung von Behandlungsmöglichkeiten geführt hat. Viele Therapien werden heute bereits in interdisziplinären Herzteams gemeinsam geplant und durchgeführt“, erläuterte Professor Dr. Hugo A. Katus, Sprecher des Herzzentrums am Universitätsklinikum Heidelberg. Im neuen Gebäude werde nun zusammengeführt, was zusammengehört, und das betreffe alle Facetten der Herzmedizin – von der Notfall- und Intensivmedizin über die Bildgebung bis zu gemeinsamen Behandlungsstrategien bei angeborenen Herzfehlern, Erkrankungen der Herzkappen, Rhythmusstörungen und der Implantation elektrischer Unterstützungssysteme sowie bei der Herztransplantation.</p> <p data-bbox="1049 1383 1429 1784">Das neue Herzzentrum kann zudem noch mit einer weiteren Besonderheit aufwarten: Es wird modellhaft als vollständig digitales Krankenhaus entworfen und in einem angeschlossenen Forschungsinstitut, das zeitgleich neben dem Neubau des Herzzentrums errichtet wird, begleitet. Von den Möglichkeiten der Digitalisierung versprechen sich die Wissenschaftler weitere Fortschritte in der personalisierten Herzmedizin, denn schon heute werden in der Kardiologie umfassende Datenmengen aus molekularen Analysen verarbeitet.</p> <p data-bbox="1112 1854 1429 1945"><b>Quelle:</b> Universitätsklinikums Heidelberg, <a href="http://www.klinikum.uni-heidelberg.de">www.klinikum.uni-heidelberg.de</a></p>