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Supplemental Material S1: The OCVC-Heart Failure Investigators

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SUPPLEMENTARY METHODS

Haemodynamic assessments

Because right heart catheterisation (RHC) was not mandatory in the PURSUIT-HFpEF study, there was no standardized procedure protocol for RHC as a study, and the choice of sheath, catheter, and access site was at the discretion of individual hospitals and physicians.

Therefore, practice may differ. The following measurements were obtained: systolic, diastolic, and mean pulmonary artery pressures (sPAP, dPAP, and mPAP, respectively); pulmonary artery wedge pressure (PAWP); right atrial pressure (RAP); and cardiac output (CO). Generally, the midpoint between precordial level and bed surface level in the supine position was used to establish the zero value. The method to confirm the wedge position was chosen at the discretion of the performing physician. Mean PAWP was calculated over the entire cardiac cycle including V waves. In most patients, CO was measured using the thermodilution technique. In the case of missing values for thermodilution CO, measurements using the indirect Fick method were used for analysis. The diastolic pulmonary artery pressure gradient (DPG) was calculated as the difference between dPAP and PAWP.

Pulmonary vascular resistance (PVR) was calculated as $(\text{mPAP} - \text{PAWP}) / \text{CO}$ and expressed as Wood unit.

Echocardiographic assessments

Of 219 patients, echocardiographic data at discharge were not available in 3 patients (2 in non-PH group and 1 in Ipc-PH group). The number of patients with missing data for each echocardiographic variable in Table 2 was as follows: 19 patients for left ventricular (LV) volumetry by modified Simpson method; 2 for LV mass; 2 for early diastolic mitral inflow (E) velocity; 80 for late diastolic mitral inflow (A) velocity; 44 for deceleration time (DcT); 9 for medial early diastolic mitral annular tissue velocity (e'); 13 for lateral e' ; 14 for E/e' ; 35 for right ventricular end-diastolic dimension (RVDD); 22 for tricuspid annular plane systolic excursion (TAPSE); 36 for TAPSE/SPAP. E/e' using mean value of medial and lateral e' was available for analysis in 147 patients in non-PH, 40 in Ipc-PH, 7 in precapillary PH, and 8 in Cpc-PH. SPAP was an estimate of systolic PAP on echocardiography: the sum of tricuspid regurgitant pressure gradient (TRPG) and an estimate of RAP obtained from the diameter and collapsibility of the inferior vena cava. RAP was estimated to be 3 mmHg when IVC diameter ≤ 2.1 cm that collapsed $>50\%$ with a sniff, 15 mmHg when IVC diameter > 2.1 cm that collapsed $< 50\%$ with a sniff. When the IVC diameter and collapse rate did not meet any of above criteria, RAP was estimated to be 8 mmHg.¹

Table S1. Patient characteristics on admission comparing the study cohort with patients**who did not undergo RHC**

	Patients who did not undergo RHC (n=634)	Study cohort (n=219)	p value*
Age, years	83 (77-88)	81 (75-85)	<0.001
Male	284 (45)	101 (46)	0.753
Hypertension	533 (84)	190 (87)	0.443
Diabetes mellitus	200 (32)	83 (38)	0.095
Dyslipidaemia	249 (40)	101 (47)	0.079
Coronary artery disease	123 (20)	43 (20)	0.921
eGFR, mL/min/1.73 m ²	43.7 (29.8-57.7)	44.7 (28.5-60.0)	0.803
NT-pro-BNP, pg/mL	3090 (1658-5783)	4230 (1985-8020)	0.002
LVDD, mm	46 ± 6	47 ± 7	0.053
LV ejection fraction, %	61 ± 7	60 ± 7	0.112
Estimated SPAP	43 (34-54)	44 (34-52)	0.783
SPAP > 35mmHg	377 (72)	136 (71)	0.926
Initial HF treatment			
NIPPV usage	57 (9)	54 (25)	<0.001

Intubation	8 (1)	7 (3)	0.073
Dobutamine	16 (3)	1 (0.5)	0.088
Intravenous PDE3I	1 (0.2)	2 (0.9)	0.163
Carperitide	150 (24)	44 (20)	0.304
Intravenous nitrates	132 (21)	120 (55)	<0.001
Intravenous CCB	31 (5)	44 (20)	<0.001
Diuretics (continuous iv)	138 (22)	143 (66)	<0.001
Diuretics (bolus iv)	340 (54)	132 (61)	0.082

Values are shown as mean±SD, median (IQR) or n (%).

* Analysis of variance or the Mann-Whitney test for continuous variables and the Fisher's exact test for categorical variables were used.

CCB, calcium channel blocker; eGFR, estimated glomerular filtration rate; HF, heart failure; iv, intravenous infusion; LV, left ventricular; LVDD, LV end-diastolic dimension; NIPPV, non-invasive positive pressure ventilation; NT-pro-BNP, N-terminal probrain natriuretic peptide; PDE3I, phosphodiesterase-3 inhibitor; RHC, right heart catheterization; SPAP, systolic pulmonary artery pressure estimated on echocardiography.

Table S2. Haemodynamic parameters associated with PH categories according to the 2015 ESC/ERS definition of PH

	Non-PH	Ipc-PH	Precapillary PH	Cpc-PH	p value
	n=159	n=44	n=7	n=9	
Days from admission to RHC	11 (7-14)	10 (7-13)	13 (12-14)	12 (10-18)	0.238
Heart rate, bpm	70 (61-78)	66 (59-75)	80 (57-98)	69 (60-90)	0.376
Systolic blood pressure, mmHg	131 (118-147)	135 (119-169)	145 (133-154)	136 (102-142)	0.404
Diastolic blood pressure, mmHg	62 (53-70)	64 (50-73)	67 (50-80)	57 (52-61)	0.641
Systolic PAP, mmHg	29 (24-33)	43 (38-49) *	46 (35-51) *	49 (38-65) *	<0.001
Diastolic PAP, mmHg	11 (8-14)	20 (16-22) *	18 (14-24) *	24 (20-27) *	<0.001
Mean PAP, mmHg	18 (14-21)	28 (26-31) *	29 (26-31) *	30 (28-41) *	<0.001
PAWP, mmHg	10 (7-13)	21 (18-25) *	14 (13-15) †	19 (16-24) *,‡	<0.001
RAP, mmHg	5 (3-7)	10 (8-13) *	8 (7-10) *	10 (9-15) *	<0.001

Cardiac output, L/min	3.8 (3.0-4.7)	4.2 (3.7-5.1)	4.5 (3.0-8.5)	3.2 (2.7-4.2)	0.057
Cardiac index, L/min/m ²	2.5 (2.1-3.1)	2.7 (2.3-3.2)	3.5 (2.3-5.8)	2.4 (2.1-3.2)	0.206
DPG, mmHg	1 (-2-3)	-3 (-6-2) *	5 (1-10) †	3 (-1-5)	<0.001
PVR, Wood units	1.9 (1.2-2.6)	1.7 (1.2-2.1)	3.2 (2.2-3.7) †	3.6 (3.1-4.6) *, †	<0.001

Values are shown as median (IQR).

* p < 0.05 vs. non-PH, † p < 0.05 vs. Ipc-PH, ‡ p < 0.05 vs. Precapillary PH.

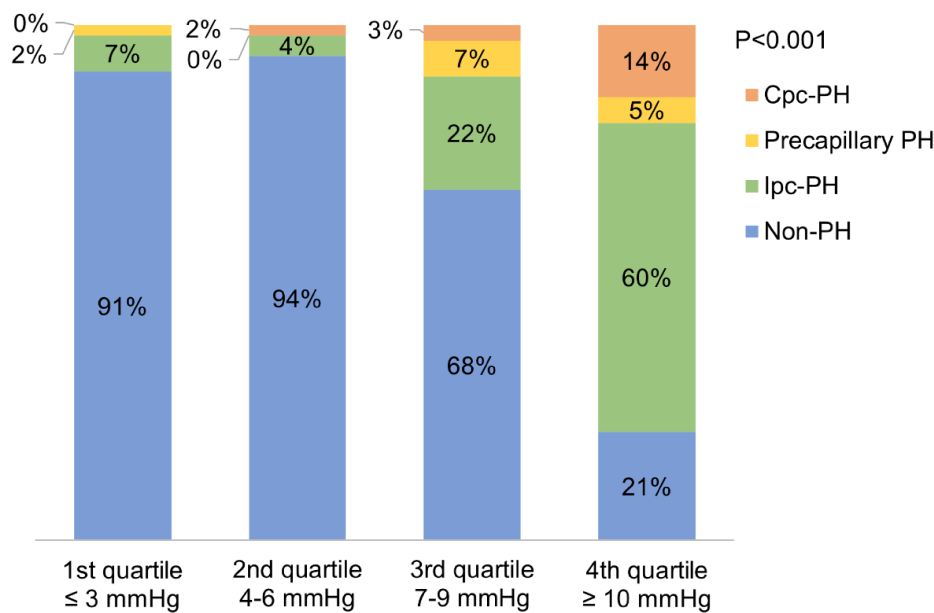
Bpm, beats per minute; Cpc-PH, combined postcapillary and precapillary pulmonary hypertension; DPG, diastolic pressure gradient; Ipc-PH, isolated postcapillary pulmonary hypertension; PAP, pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC, right heart catheterisation.

Table S3. PH categories according to the 2022 ESC/ERS guidelines

Categories according to the 2022 definition ²	
Non-PH	mPAP \leq 20 mmHg
Precapillary PH	mPAP $>$ 20 mmHg, PAWP \leq 15 mmHg, and PVR $>$ 2 WU
Ipc-PH	mPAP $>$ 20 mmHg, PAWP $>$ 15 mmHg, and PVR \leq 2 WU
Cpc-PH	mPAP $>$ 20 mmHg, PAWP $>$ 15 mmHg, and PVR $>$ 2 WU
Unclassified PH	mPAP $>$ 20 mmHg, PAWP \leq 15 mmHg, and PVR \leq 2 WU

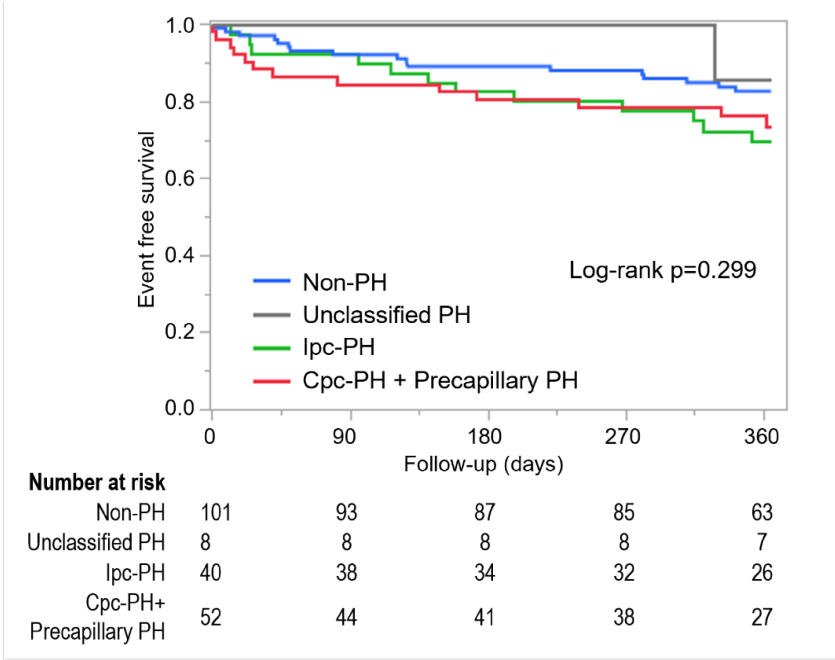
Cpc-PH, combined postcapillary and precapillary pulmonary hypertension; ESC/ERS, European Society of Cardiology/the European Respiratory Society; Ipc-PH, isolated postcapillary pulmonary hypertension; mPAP, mean pulmonary artery pressure; PAWP, pulmonary artery wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; WU, Wood unit.

Figure S1. Prevalence of PH categories associated with RAP quartiles according to the 2015 ESC/ERS definition of PH



The prevalence of PH categories was significantly different across the RAP quartiles. The PH with the precapillary component was most frequently observed in the highest RAP quartile (19%). Cpc-PH, combined postcapillary and precapillary pulmonary hypertension; ESC/ERS, European Society of Cardiology/the European Respiratory Society; Ipc-PH, isolated postcapillary pulmonary hypertension; PH, pulmonary hypertension; RAP, right atrial pressure.

Figure S2. Kaplan–Meier curves for the prediction of all cause death and HF hospitalisation by PH categories according to the 2022 ESC/ERS definition of PH



Applying the ESC/ERS 2022 definition, which adopts a lower threshold of PVR of > 2 Wood units for the definition of precapillary PH, clinical outcomes 1 year after discharge did not differ across the PH groups.

Cpc-PH, combined postcapillary and precapillary pulmonary hypertension; HF, heart failure; ESC/ERS, European Society of Cardiology/the European Respiratory Society; Ipc-PH, isolated postcapillary pulmonary hypertension; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

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