SUPPLEMENTAL MATERIAL

Appendix

Details of PURSUIT-HFpEF registry

The OCVC-Heart Failure Investigators

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Table S1. Baseline clinical characteristics divided with RHC-PAC tertiles

	all patients	tertile 1: RHC-PAC < 2.51	tertile 2: 2.51 ≤ RHC-PAC < 3.88	tertile 3: 3.88 ≤ RHC-PAC	P-value
N	167	55	56	56	
Age, years	81 (74–86)	83 (78–87)	82 (74–85)	79 (70–84)	0.005
gender, female	88 (53)	39 (71)	29 (52)	20 (36)	0.001
general condition at discharge					
BMI, kg/m^2	21.2 (19.0–23.4)	19.7 (18.1–22.4)	22.1 (19.6–23.4)	21.7 (19.4–24.6)	0.004
SBP, mmHg	123 (110–133)	121 (108–130)	122 (107–134)	129 (113–133)	0.083
DBP, mmHg	64 (56–73)	66 (55–73)	64 (57–73)	65 (56–74)	0.928
Heart rate	69 (61–77)	68 (60–78)	67 (60–78)	71 (61–77)	0.768
AF	49 (29)	19 (35)	11 (20)	19 (34)	0.148
GNRI	92 (85–100)	89 (83–96)	94 (87–100)	93 (86–103)	0.032
6MWD, m	253 (149–336)	255 (158–319)	205 (101–340)	290 (160–400)	0.266
NYHA I / II / III / IV	41 /122/ 4/ 0	15 / 37 / 3 / 0	8 / 47 / 1 / 0	18 / 38 / 0 / 0	0.066
laboratory examination at discharge					
Hemoglobin, g/dL	11.8 (10.1–13.1)	11.8 (10.6–13.1)	11.5 (9.8–13.2)	11.8 (10.3–13.3)	0.666
Hematocrit, %	36 (31–40)	36 (32–40)	35 (30–40)	35 (32–39)	0.767
Serum total protein, g/dL	6.8 (6.2–7.2)	6.6 (6.2–7.2)	6.8 (6.3–7.2)	6.9 (6.2–7.3)	0.805
Serum albumin, g/dL	3.5 (3.2–3.8)	3.4 (3.1–3.7)	3.5 (3.1–3.8)	3.5 (3.2–3.8)	0.652
eGFR, mL/min/1.73m^2	44 (29–58)	40 (26–51)	40 (26–64)	50 (37–57)	0.064
NT-proBNP, ng/L	1020 (473–2600)	1430 (618–3808)	1210 (384–2628)	726 (381–1410)	0.009
CRP, mg/dL	0.35 (0.12–1.01)	0.31 (0.11–0.93)	0.48 (0.15–1.12)	0.26 (0.11–1.21)	0.615
Echocardiographic variables at discharge					
Echocardiography examined day	13 (10–17)	14 (12–17)	14 (11–18)	12 (9–15)	0.037
LVDd, mm	47 (42–51)	43 (40–48)	47 (43–50)	49 (45–54)	< 0.001
LVEDV (m-Simpson), mL	89 (63–110)	69 (56–93)	92 (69–109)	99 (71–125)	< 0.001

LVEDVI (m-Simpson), mL/m^2	53 (43–72)	51 (41–69)	62 (46–73)	59 (44–83)	0.060
LVEF (m-Simpson), %	61 (56–66)	59 (55–64)	61 (56–66)	62 (56–68)	0.415
SV, mL	51 (39–67)	42 (33–54)	57 (42–68)	60 (42–77)	< 0.001
LAD, mm	43 (39–48)	44 (38–48)	43 (39–46)	44 (39–49)	0.412
LAVI, mL/m^2	50 (39–63)	55 (41–71)	48 (38–60)	48 (38–62)	0.200
E/e'	12.6 (9.7–16.0)	13.7 (10.4–20.0)	11.2 (9.5–15.5)	11.3 (9.4–15.3)	0.092
RVD, mm	31 (28–36)	29 (26–36)	31 (26–36)	32 (29–38)	0.233
TAPSE, mm	17.8 (14.6–21.5)	16.8 (12.6–19.7)	18.3 (14.2–21.9)	18.7 (15.1–23.0)	0.012
TRPG, mmHg	26 (20–32)	28 (23–36)	26 (21–32)	22 (19–28)	0.003
PASP, mmHg	30 (24–36)	33 (28–40)	30 (25–36)	27 (23–32)	0.007
PAPP, mmHg	18 (14–22)	20 (17–24)	18 (15–21)	16 (14–19)	0.007
TAPSE/PASP, mm/mmHg	0.58 (0.45–0.77)	0.49 (0.39–0.66)	0.64 (0.47–0.77)	0.68 (0.49–0.98)	0.001
PAC, mL/mmHg	2.82 (2.00–3.98)	2.19 (1.66–2.86)	3.06 (2.34–3.89)	3.61 (2.30–5.31)	< 0.001
Mitral regurgitation (none / trace / mild / moderate)	11 / 65 / 74 /17	3 / 16 / 29 / 7	3 / 28 / 23 / 2	5 / 21 / 22 / 8	0.181
Tricuspid regurgitation (none / trace / mild / moderate / severe)	4 / 72 / 72 /18 / 1	1 / 15 / 28 / 10 / 1	2 / 25 / 26 / 3 / 0	1 / 32 / 18 / 5 / 0	0.054
Aortic stenosis (none / mild)	160 / 7	52 / 3	54 / 2	54 / 2	0.850
Mitral stenosis (none / mild)	165 / 2	53 / 2	56 / 0	56 / 0	0.127
Right Heart Catheterization					
RHC examined day	10 (7–13)	10 (7–13)	11 (8–14)	9 (6–13)	0.231
Heart rate at RHC	70 (60–77)	74 (60–83)	69 (63–76)	67 (58–73)	0.027
mean RAP, mmHg	6 (3–9)	8 (4–11)	5 (4–8)	6 (3–8)	0.011
RVEDP, mmHg	6 (4–10)	7 (4–11)	6 (4–11)	6 (5–10)	0.472
PASP, mmHg	32 (27–40)	39 (31–49)	32 (27–36)	28 (22–33)	< 0.001
PADP, mmHg	14 (9–18)	16 (9–21)	13 (10–16)	12 (9–18)	0.113
PAMP, mmHg	21 (17–25)	24 (21–30)	20 (17–24)	18 (14–23)	< 0.001
PAPP, mmHg	19 (14–25)	25 (18–32)	20 (16–23)	14 (12–19)	< 0.001
PAWP, mmHg	13 (9–18)	15 (12–21)	12 (9–17)	11 (6–17)	< 0.001
SV, mL	60 (46–74)	46 (36–62)	59 (47–72)	71 (60–94)	< 0.001
CO, L/min	4.0 (3.1–4.9)	3.2 (2.5–4.2)	3.9 (3.2–4.6)	4.7 (3.9–5.5)	< 0.001
PVR, dyne*sec*cm^{-5}	157 (106–209)	200 (152–253)	168 (124–209)	121 (81–150)	< 0.001
RHC-PAC, mL/mmHg	3.00 (2.31–4.27)	2.00 (1.65–2.31)	3.00 (2.61–3.37)	4.66 (4.626–5.55)	< 0.001

Values are given as median (IQR) or n (%).

Age is given on admission and all the others except right heart catheterization are at discharge. GNRI was calculated as:

$$14.89 \times [serum\ albmin] + 41.7 \times \frac{[body\ mass\ index]}{22}$$

Abbreviations: 6MWD, 6-minutes walking distance; AF, atrial fibrillation; BMI, body mass index; CO, cardiac output; CRP, C-reactive protein; DBP, diastolic blood pressure; PAC, pulmonary artery capacitance estimated with echocardiography; E/e', The ratio of mitral peak velocity of early filling E to the velocity of mitral annulus early diastolic motion e'; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; LAD, left atrial dimension; LAVI, left atrial dimension index; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVEDV, left ventricular end-diastolic volume; LVEDVI, left ventricular end-diastolic volume index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York heart failure functional class; PAC, pulmonary artery capacitance estimated with echocardiography; PAMP, pulmonary artery mean pressure; PAPP, pulmonary artery pulse pressure; PASP, pulmonary artery systolic pressure; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC, right heart catheterization; RHC-PAC, pulmonary artery capacitance measured with right heart catheterization; RVD, basal right ventricular linear dimension; RVEDP, right ventricular end-diastolic pressure; SBP, systolic blood pressure; SV, stroke volume; TAPSE, tricuspid annular plane systolic excursion; TRPG, tricuspid valve regurgitation pressure gradient

Between-group comparisons were performed using Kruskal–Wallis test or Pearson's chi-squared test.

Table S2. Baseline Clinical Characteristics of patients with and without RHC-PAC

	all patients	RHC-PAC obtained	RHC-PAC not obtained	P value
N	705	167	538	
Age, years	83 (78–87)	81 (74–86)	84 (77–88)	< 0.001
gender, female	389 (55)	88 (53)	301 (56)	0.460
prior HF hospitalization	168 (24)	36 (22)	132 (25)	0.385
comorbidities				
Hypertension	599 (85)	144 (86)	455 (85)	0.670
Diabetes	227 (32)	62 (37)	165 (31)	0.121
Dyslipidemia	286 (41)	80 (48)	206 (39)	0.032
Hyperuricemia	227 (32)	73 (44)	154 (29)	< 0.001
CKD	278 (40)	82 (49)	196 (37)	0.004
COPD	55 (8)	18 (11)	37 (7)	0.099
malignancy	84 (12)	10 (6)	74 (14)	0.007
general condition at discharge				
BMI, kg/m^2	21.3 (18.9–23.9)	21.2 (19.0–23.4)	21.3 (18.9–24.0)	0.677
SBP, mmHg	119 (107–130)	123 (110–133)	118 (106–129)	0.004
DBP, mmHg	65 (57–74)	64 (56–73)	65 (58–74)	0.447
Heart rate	70 (61–79)	69 (61–77)	70 (61–80)	0.267
AF	273 (39)	49 (29)	224 (42)	0.004

GNRI	92 (85–99)	92 (85–100)	91 (85–98)	0.413
6MWD, m	250 (154–335)	253 (149–336)	250 (155–332)	0.909
NYHA I / II / III / IV	262 / 433 / 41 / 1	41 /122/ 4/ 0	209 / 291 / 34 / 1	< 0.001
laboratory examination at discharge				
Hemoglobin, g/dL	11.3 (10.1–12.8)	11.8 (10.1–13.1)	11.2 (10.1–12.6)	0.045
Hematocrit, %	34 (31–39)	36 (31–40)	34 (31–38)	0.105
Serum total protein, g/dL	6.6 (6.2–7.1)	6.8 (6.2–7.2)	6.6 (6.2–7.1)	0.056
Serum albumin, g/dL	3.4 (3.1–3.7)	3.5 (3.2–3.8)	3.4 (3.1–3.7)	0.041
eGFR, mL/min/1.73m^2	44 (30–55)	44 (29–58)	43 (31–55)	0.568
NT-proBNP, ng/L	1057 (466–2372)	1020 (473–2600)	1057 (465–2335)	0.692
CRP, mg/dL	0.26 (0.11–0.75)	0.35 (0.12–1.01)	0.24 (0.10–0.63)	0.027
Echocardiographic variables at discharge				
Echocardiography examined day	14 (10–19)	13 (10–17)	14 (10-19)	0.972
LVDd, mm	45 (41–50)	47 (42–51)	45 (41–49)	0.009
LVEF (m-Simpson), %	61 (55–66)	61 (56–66)	61 (55–66)	0.674
SV, mL	46 (35–61)	51 (39–67)	45 (34–59)	< 0.001
LAD, mm	44 (39-49)	43 (39–48)	44 (39-49)	0.165
LAVI, mL/m^2	50 (37–65)	50 (39–63)	50 (36–65)	0.750
E/e'	12.5 (9.6–16.6)	12.6 (9.7–16.0)	12.5 (9.6–16.7)	0.803
RVD, mm	32 (28–36)	31 (28–36)	33 (28–36)	0.026
TAPSE, mm	17.3 (14.4–20.4)	17.8 (14.6–21.5)	17.2 (14.3–20.0)	0.180
TRPG, mmHg	27 (22–32)	26 (20–32)	27 (22–32)	0.041

PASP, mmHg	31 (26–38)	30 (24–36)	31 (26–38)	0.029
PAPP, mmHg	19 (15–23)	18 (14–22)	19 (16–23)	0.029
TAPSE/PASP, mm/mmHg	0.54 (0.42–0.72)	0.58 (0.45–0.77)	0.54 (0.42–0.70)	0.009
PAC, mL/mmHg	2.52 (1.78–3.32)	2.82 (2.00–3.98)	2.42 (1.73–3.20)	< 0.001
Mitral valve regurgitation (none / trace / mild / moderate)	38 / 232 /310 /125	11 / 65 / 74 /17	27 / 167 / 236 / 108	0.018
Tricuspid valve regurgitation (none / trace / mild / moderate / severe)	12 / 235 / 301 / 141 / 16	4 / 72 / 72 /18 / 1	8 / 163 / 229 / 123 / 15	0.001
Aortic valve stenosis (none / mild)	657 / 48	160 / 7	497 / 41	0.124
Mitral valve stenosis (none / mild)	690 / 15	165 / 2	525 / 13	0.340
Medication at discharge				
Antiplatelet	193 (27)	60 (36)	133 (25)	0.004
ACE inhibitor or ARB	387 (55)	82 (49)	305 (57)	0.085
Calcium channel blocker	342 (49)	87 (52)	255 (47)	0.259
β-blocker	397 (56)	104 (63)	293 (54)	0.063
loop diuretics	567 (80)	143 (86)	424 (78)	0.052
tolvaptan	111 (16)	34 (20)	77 (14)	0.061
aldosterone antagonist	295 (42)	73 (44)	222 (41)	0.575
anticoagulant	440 (62)	95 (57)	345 (64)	0.092

Values are given as median (IQR) or n (%).

Age and comorbidities are given on admission and all the others are at discharge. GNRI was calculated as:

$$14.89 \times [serum\ albmin] + 41.7 \times \frac{[body\ mass\ index]}{22}$$

Abbreviations: 6MWD, 6-minutes walking distance; ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; DBP, diastolic blood pressure; E/e', The ratio of mitral peak velocity of early filling E to the velocity of mitral annulus early diastolic motion e'; eGFR, estimated glomerular filtration rate; GNRI, Geriatric Nutritional Risk Index; HF, heart failure; LAD, left atrial dimension; LAVI, left atrial dimension index; LVDd, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-B-type natriuretic peptide; NYHA, New York heart failure functional class; PAC, pulmonary artery capacitance; PAPP, pulmonary artery pulse pressure; PASP, pulmonary artery systolic pressure; RVD, basal right ventricular linear dimension; SBP, systolic blood pressure; SV, stroke volume; TAPSE, tricuspid annular plane systolic excursion; TRPG, tricuspid valve regurgitation pressure gradient

Between-group comparisons were performed using Kruskal–Wallis test or Pearson's chi-squared test.
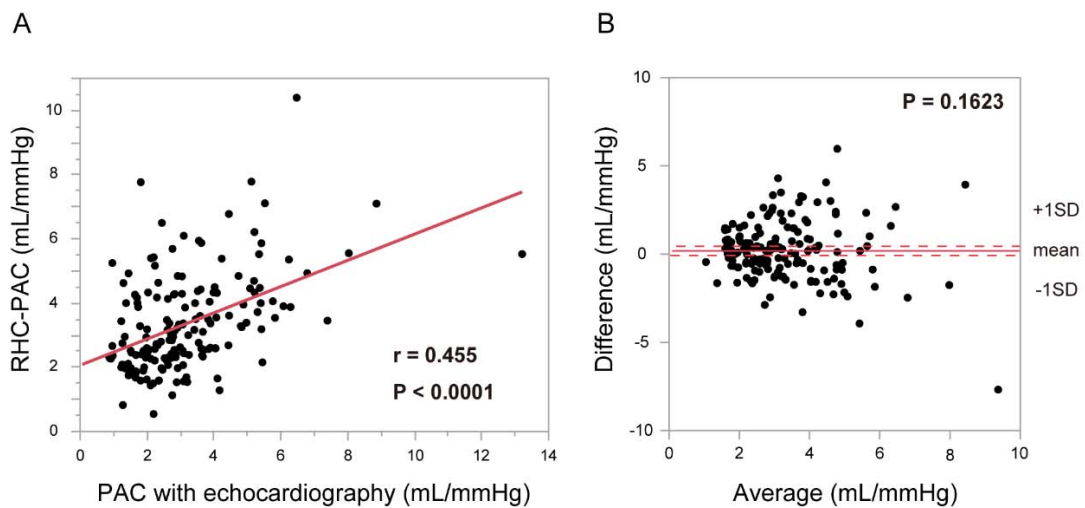
Table S3. Firth's penalized Cox regression model for prognostic prediction of primary endpoint with RHC-PAC

	Hazard ratio	Lower 95% CI	Upper 95% CI	P-value
Univariable Cox regression				
RHC-PAC, 1-mL/mmHg increments	0.71737875	0.53181805	0.93212049	0.01096244
Multivariable Cox regression				
Model 1				
PAWP, 1-mmHg increments	1.02601948	0.95611505	1.09609356	0.46582646
RAP, 1-mmHg increments	0.97960514	0.87120734	1.10105714	0.73140940
PVR, 1-dyne*sec*cm^{-5} increments	0.99939252	0.99560331	1.00253958	0.72784528
RHC-PAC, 1-mL/mmHg increments	0.71883795	0.50443914	0.98191005	0.03706094
Model 2				
Age, 1-year increments	1.01646969	0.97624612	1.06692205	0.45851959
Female	0.90947510	0.46537297	1.79816293	0.78176114
NT-proBNP, 1-ng/L increments	1.00007064	1.00002436	1.00010639	0.00637700
RHC-PAC, 1-mL/mmHg increments	0.73056984	0.53330803	0.96532015	0.02579811

Firth's penalized Cox proportional hazard models of RHC-PAC for composite endpoint. The composite endpoint was defined as all-cause mortality or heart failure re-hospitalization. Multivariable Cox regression for primary endpoint was performed using covariates as follows: (model 1) hemodynamic parameters of PAWP, RAP and PVR, (model 2) clinical aspects of age, gender, and NT-proBNP, respectively.

Abbreviations: NT-proBNP, N-terminal pro-B-type natriuretic peptide; PAWP, pulmonary artery wedge pressure; PVR, pulmonary vascular resistance; RAP, right atrial pressure; RHC-PAC, pulmonary artery capacitance calculated with right heart catheterization

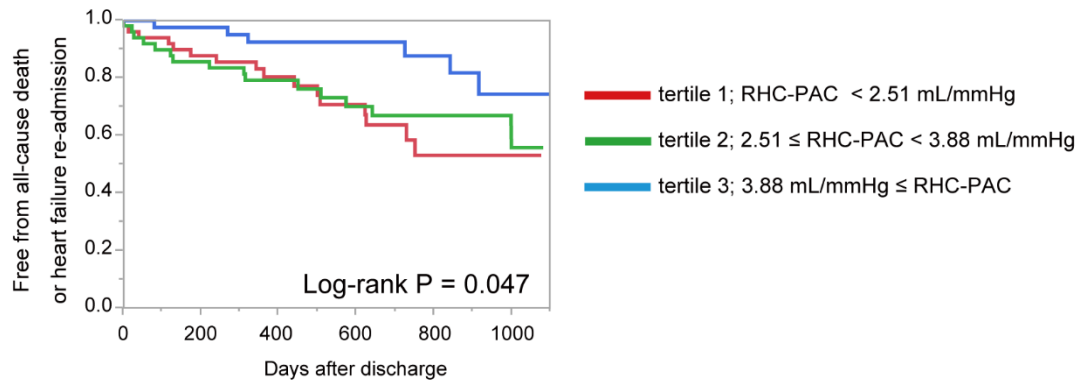**Figure S1. Correlation of PAC with echocardiography and with right heart catheterization**

(A) The analysis of the correlation provides an r value of 0.455 with a *P* < 0.0001 (n = 167). (B) Bland and Altman analysis showed that the difference was not significant (mean difference ± standard error; 0.18 ± 0.13 mL/mmHg, *P* = 0.1623)

Abbreviation: PAC; pulmonary artery capacitance, RHC; right heart catheterization, SD; standard deviation

Figure S2. Kaplan-Meier survival curves of PAC with right heart

catheterization

Kaplan-Meier survival curves for prediction of composite endpoint of RHC-PAC

tertiles.

Abbreviations: RHC-PAC, pulmonary artery capacitance calculated with right heart

catheterization