

# Left heart disease phenotype in elderly patients with pulmonary arterial hypertension: insights from the Italian PATRIARCA registry.

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**Table S1.** Patient enrolment across the PATRIARCA registry.

Center	Enrolled patients Included in the analysis	
	(N=180)	(N=69)
Cardiology, IRCCS Policlinico San Matteo, Pavia	56 (31)	23 (33)
Cardiology, IRCCS Policlinico San Martino, Genova	28 (16)	9 (13)
Cardiology, Ospedale San Gerardo, Monza	20 (11)	9 (13)
Cardiology, Ospedale di Bolzano	14 (8)	2 (3)
Cardiology, IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano	12 (7)	3 (4)
ASST Grande Ospedale Metropolitano Niguarda, Milano	12 (7)	8 (12)
Cardiology, Azienda sanitaria Universitaria Giuliano Isontina, Trieste	10 (6)	4 (6)
Cardiology, ASST degli Spedali Civili, Brescia	10 (6)	2 (3)
Cardiology, Ospedale di Circolo e Fondazione Macchi, Varese	9 (5)	4 (6)
Cardiology, ASST Papa Giovanni XXIII, Bergamo	5 (3)	3 (4)
Cardiology, Ospedale Maggiore della Carità, Novara	4 (2)	2 (3)

Patient enrollment across the 11 centers participating in the Italian multicenter PATRIARCA registry between December 1<sup>st</sup> 2019 and September 15th 2020.

Data are expressed as count (%).

**Table S2.** Baseline characteristics according to the presence of the main analysis clinical criteria suggestive for left heart disease.

	Overall (N=69)	No clinical LHD profile (N=63)	Clinical LHD phenotype (N=6)	P
Demographics				
Age at diagnosis, y	73 ± 4	73 ± 4	74 ± 3	0.58
Age at enrolment, years	77 ± 5	77 ± 4	77 ± 3	0.87
Female	44 (64)	42 (67)	2 (33)	0.12
Weight, Kg	64 ± 15	64 ± 15	70 ± 12	0.34
Height, cm	163 ± 9	162 ± 8	169 ± 11	0.07
BSA, m <sup>2</sup>	1.70 ± 0.22	1.69 ± 0.22	1.81 ± 0.18	0.21
BMI, Kg/m <sup>2</sup>	24 ± 5	24 ± 5	25 ± 4	0.82
Clinical and echocardiographic parameters				
WHO-FC I-II	32 (46)	30 (48)	2 (33)	0.38
Systemic hypertension	45 (65)	39 (62)	6 (100)	0.07
Diabetes	15 (22)	9 (14)	6 (100)	<0.001
CAD	17 (25)	12 (19)	5 (83)	0.003
Permanent AF	3 (4)	3 (5)	6 (100)	0.76
Pulmonary disease	31 (45)	27 (43)	4 (67)	0.25

CKD	26 (38)	21 (33)	5 (83)	<b>0.03</b>
Previous/current cancer	8 (12)	8 (13)	6 (100)	0.46
SBP, mmHg	124 ± 15	124 ± 14	122 ± 19	0.71
DBP, mmHg	72 ± 9	72 ± 9	67 ± 10	0.19
SO <sub>2</sub> , %	95 [93; 97]	95 [93; 97]	96 [88; 97]	1
6MWD, meters	304 ± 199	305 ± 123	290 ± 73	0.81
LVEF <50%	4 (6)	3 (5)	1 (17)	0.25
LVH	17 (25)	16 (25)	1 (17)	0.53
LA dilation	31 (45)	28 (44)	3 (50)	0.59
TAPSE, mm	20 ± 5	21 ± 4	17 ± 5	<b>0.03</b>
TRV, m/s	3.81 ± 0.76	3.78 ± 0.76	4.10 ± 0.74	0.32
TAPSE/TRV	5.6 ± 1.9	5.8 ± 1.9	4.1 ± 1.2	0.05
RVSP, mmHg	57 [42; 77]	57 [40; 75]	73 [45; 90]	0.29
RA dilation	53 (77)	47 (75)	6 (100)	0.25
Pericardial effusion	11 (16)	9 (14)	2 (33)	0.24
Most recent RHC				
RAP, mmHg	7 [4; 10]	7 [4; 10]	6 [2; 10]	0.58
mPAP, mmHg	41 ± 10	41 ± 11	41 ± 10	0.98
dPAP, mmHg	25 ± 9	26 ± 9	23 ± 6	0.58
sPAP, mmHg	70 ± 20	69 ± 20	74 ± 20	0.53
PAWP, mmHg	11 ± 4	12 ± 4	7 ± 2	<b>0.004</b>
RAP/PAWP ratio	0.60 [0.46; 0.75]	0.58 [0.41; 0.75]	0.73 [0.67; 1.00]	0.18
PVR, WU	7.39 ± 4.53	7.22 ± 4.54	9.14 ± 4.47	0.33
Cardiac output, L/min	4.59 ± 1.43	4.65 ± 1.46	4.04 ± 1.04	0.33
Cardiac index, L/min/m <sup>2</sup>	2.74 ± 0.81	2.78 ± 0.82	2.30 ± 0.62	0.17
Diagnosis to last RHC interval, months	15 [4; 33]	15 [4; 35]	13 [0; 23]	0.42
Treatment				
No PAH therapy	6 (9)	5 (8)	1 (17)	0.43
Bosentan	-	-	-	
Ambrisentan	17 (25)	16 (25)	1 (17)	0.54
Macitentan	32 (46)	29 (46)	3 (50)	0.61
ERA	49 (71)	45 (71)	4 (67)	0.57
Sildenafil	22 (32)	19 (30)	3 (50)	0.29
Tadalafil	25 (36)	24 (38)	1 (17)	0.29
Riociguat	3 (4)	3 (5)	0	0.76
PDE5i/GCs	50 (73)	46 (73)	4 (67)	0.53
Dual oral combination therapy	36 (52)	33 (52)	3 (50)	0.62
Selexipag	6 (9)	6 (10)	0	0.57
Treprostinil	-	-	-	
Epoprostenol i.v.	1 (1)	1 (2)	0	0.91

Inhaled iloprost	2 (3)	2 (3)	0	0.83
Beta blockers	9 (13)	7 (11)	2 (33)	0.17
RASi	23 (33)	21 (33)	2 (33)	0.69
MRA	32 (46)	26 (41)	6 (100)	<b>0.007</b>
Furosemide	57 (83)	51 (81)	6 (100)	0.24
Digoxin	6 (9)	6 (10)	0	0.57
Amiodarone	9 (13)	9 (14)	0	0.41
Warfarin	11 (16)	10 (16)	1 (17)	0.67
DOAC	11 (16)	10 (16)	1 (17)	0.67
SAPT	22 (32)	18 (29)	4 (67)	0.07
Statins	26 (38)	22 (35)	4 (67)	0.14
Ezetimibe	3 (4)	1 (2)	2 (33)	<b>0.02</b>
Antidiabetic drugs	12 (17)	6 (10)	6 (100)	<b>&lt;0.001</b>

Characteristics of patients with and without a left heart disease (LHD) phenotype according to the clinical criteria definition in the main analysis. Data are expressed as n (%), mean  $\pm$  SD or median [IQR], as appropriate.

*LHD*, left heart disease; *BSA*, body surface area; *BMI*, body mass index; *PAH*, pulmonary arterial hypertension; *WHO-FC*, World Health Organization functional class; *CAD*, coronary artery disease; *AF*, atrial fibrillation; *CKD*, chronic kidney disease; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *SO<sub>2</sub>*, oxygen saturation; *6MWD*, six minute walking distance; *LVEF*, left ventricular ejection fraction; *LVH*, left ventricular hypertrophy; *LA*, left atrium; *TAPSE*, tricuspid annular plane systolic excursion; *TRV*, tricuspid regurgitant velocity; *RVSP*, right ventricular systolic pressure; *RA*, right atrium; *RHC*, right heart catheterization; *RAP*, right atrial pressure; *mPAP*, *dPAP* and *sPAP* for mean, diastolic and systolic pulmonary artery pressure; *PAWP*, pulmonary artery wedge pressure; *PVR*, pulmonary vascular resistance; *ERA*, endothelin receptor antagonist; *PDE5i*, phosphodiesterase type 5 inhibitor; *GCs*, guanylate cyclase stimulator; *RASi*, renin-angiotensin system inhibitors; *MRA*, mineralcorticoid receptor antagonist; *DOAC*, direct oral anticoagulant; *SAPT*, single antiplatelet therapy.

**Table S3.** Baseline characteristics according to the presence of the main analysis hemodynamic criteria suggestive for left heart disease.

	Overall (N=69)	No hemodynamic LHD profile (N=52)	Hemodynamic LHD phenotype (N=17)	P
Demographics				
Age at diagnosis, y	73 ± 4	73 ± 4	73 ± 4	0.77
Age at enrollment, years	77 ± 5	77 ± 4	77 ± 4	0.83
Female	44 (64)	31 (60)	13 (77)	0.21
Weight, Kg	64 ± 15	63 ± 14	68 ± 18	0.31
Height, cm	163 ± 9	162 ± 10	163 ± 6	0.86
BSA, m <sup>2</sup>	1.70 ± 0.22	1.68 ± 0.22	1.74 ± 0.24	0.37
BMI, Kg/m <sup>2</sup>	24 ± 5	24 ± 4	25 ± 6	0.28
Clinical and echocardiographic parameters				
WHO-FC I-II	32 (46)	23 (44)	9 (53)	0.44
Systemic hypertension	45 (65)	33 (64)	12 (71)	0.59
Diabetes	15 (22)	12 (23)	3 (18)	0.75
CAD	17 (25)	13 (25)	4 (24)	0.90
Permanent AF	3 (4)	2 (4)	1 (6)	0.72
Pulmonary disease	31 (45)	26 (50)	5 (29)	0.14
CKD	26 (38)	17 (33)	9 (53)	0.09
Previous/current cancer	8 (12)	6 (12)	2 (12)	0.98
SBP, mmHg	124 ± 15	123 ± 15	124 ± 13	0.83
DBP, mmHg	72 ± 9	72 ± 9	71 ± 9	0.64
SO <sub>2</sub> , %	95 [93; 97]	95 [93; 97]	95 [94; 97]	0.75
6MWD, meters	304 ± 199	312 ± 112	274 ± 147	0.37
LVEF <50%	4 (6)	3 (6)	1 (6)	0.73
LVH	17 (25)	11 (21)	6 (35)	0.19
LA dilation	31 (45)	22 (42)	9 (53)	0.52
TAPSE, mm	20 ± 5	20 ± 5	20 ± 4	0.86
TRV, m/s	3.81 ± 0.76	3.93 ± 0.71	3.41 ± 0.80	<b>0.02</b>
TAPSE/TRV	5.6 ± 1.9	5.4 ± 1.8	6.4 ± 2.1	0.07
RVSP, mmHg	57 [42; 77]	62 [45; 83]	45 [36; 63]	<b>0.02</b>
RA dilation	53 (77)	40 (77)	13 (77)	0.91
Pericardial effusion	11 (16)	10 (19)	1 (6)	0.27
Most recent RHC				
RAP, mmHg	7 [4; 10]	6 [3; 10]	8 [7; 11]	<b>0.02</b>
mPAP, mmHg	41 ± 10	42 ± 11	37 ± 7	0.07
dPAP, mmHg	25 ± 9	26 ± 10	23 ± 6	0.20
sPAP, mmHg	70 ± 20	72 ± 21	62 ± 16	0.12
PAWP, mmHg	11 ± 4	10 ± 3	16 ± 2	<b>&lt;0.001</b>
RAP/PAWP ratio	0.60 [0.46; 0.75]	0.63 [0.45; 0.76]	0.53 [0.46; 0.73]	0.72
PVR, WU	7.39 ± 4.53	8.40 ± 4.73	4.29 ± 1.53	<b>0.001</b>

Cardiac output, L/min	4.59 ± 1.43	4.41 ± 1.50	5.14 ± 1.07	0.07
Cardiac index, L/min/m <sup>2</sup>	2.74 ± 0.81	2.62 ± 0.81	3.09 ± 0.75	<b>0.04</b>
Diagnosis to last RHC interval, months	15 [4; 33]	13 [2; 30]	18 [6; 52]	0.26
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Treatment				
No PAH therapy	6 (9)	5 (10)	1 (6)	0.64
Bosentan	-	-	-	
Ambrisentan	17 (25)	13 (25)	4 (24)	0.90
Macitentan	32 (46)	24 (46)	8 (47)	0.79
ERA	49 (71)	37 (71)	12 (71)	0.96
Sildenafil	22 (32)	14 (27)	8 (47)	0.12
Tadalafil	25 (36)	19 (37)	6 (35)	0.93
Riociguat	3 (4)	3 (6)	0	0.57
PDE5i/GCs	50 (73)	36 (69)	14 (82)	0.29
Dual oral combination therapy	36 (52)	26 (50)	10 (59)	0.53
Selexipag	6 (9)	4 (8)	2 (12)	0.63
Treprostinil	-	-	-	
Epoprostenol i.v.	1 (1)	1 (2)	0	0.75
Inhaled iloprost	2 (3)	2 (4)	0	0.57
Beta blockers	9 (13)	7 (14)	2 (12)	0.86
RASi	23 (33)	12 (23)	11 (65)	<b>0.002</b>
MRA	32 (46)	26 (50)	6 (35)	0.35
Furosemide	57 (83)	44 (85)	13 (77)	0.44
Digoxin	6 (9)	5 (10)	1 (6)	0.64
Amiodarone	9 (13)	4 (8)	5 (29)	<b>0.04</b>
Warfarin	11 (16)	9 (17)	2 (12)	0.65
DOAC	11 (16)	7 (14)	4 (24)	0.27
SAPT	22 (32)	16 (31)	6 (35)	0.73
Statins	26 (38)	17 (33)	9 (53)	0.14
Ezetimibe	3 (4)	3 (6)	0	0.57
Antidiabetic drugs	12 (17)	10 (19)	2 (12)	0.72

Characteristics of patients with and without a left heart disease (LHD) phenotype according to the haemodynamic criteria definition (used in both main and secondary analysis). Data are expressed as n (%), mean ± SD or median [IQR], as appropriate.

*LHD*, left heart disease; *BSA*, body surface area; *BMI*, body mass index; *PAH*, pulmonary arterial hypertension; *WHO-FC*, World Health Organization functional class; *CAD*, coronary artery disease; *AF*, atrial fibrillation; *CKD*, chronic kidney disease; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *SO<sub>2</sub>*, oxygen saturation; *6MWD*, six minute walking distance; *LVEF*, left ventricular ejection

fraction; *LVH*, left ventricular hypertrophy; *LA*, left atrium; *TAPSE*, tricuspid annular plane systolic excursion; *TRV*, tricuspid regurgitant velocity; *RVSP*, right ventricular systolic pressure; *RA*, right atrium; *RHC*, right heart catheterization; *RAP*, right atrial pressure; *mPAP*, *dPAP* and *sPAP* for mean, diastolic and systolic pulmonary artery pressure; *PAWP*, pulmonary artery wedge pressure; *PVR*, pulmonary vascular resistance; *ERA*, endothelin receptor antagonist; *PDE5i*, phosphodiesterase type 5 inhibitor; *GCs*, guanylate cyclase stimulator; *RASi*, renin-angiotensin system inhibitors; *MRA*, mineralcorticoid receptor antagonist; *DOAC*, direct oral anticoagulant; *SAPT*, single antiplatelet therapy.

**Table S4.** Baseline characteristics of the study population according to the secondary analysis.

	Overall (N=69)	No LHD profile (N=32)	LHD phenotype (N=37)	P
Demographics				
Age at diagnosis, y	73 ± 4	73 ± 4	73 ± 4	0.53
Age at enrolment, years	77 ± 5	76 ± 4	78 ± 3	0.12
Female	44 (64)	18 (56)	26 (70)	0.23
Weight, Kg	64 ± 15	62 ± 13	67 ± 16	0.16
Height, cm	163 ± 9	161 ± 9	164 ± 8	0.10
BSA, m <sup>2</sup>	1.70 ± 0.22	1.65 ± 0.21	1.74 ± 0.23	0.14
BMI, Kg/m <sup>2</sup>	24 ± 5	24 ± 4	25 ± 5	0.40
Clinical and echocardiographic parameters				
WHO-FC I-II	32 (46)	15 (47)	17 (46)	0.89
Systemic hypertension	45 (65)	17 (53)	28 (76)	0.05
Diabetes	15 (22)	2 (6)	13 (35)	<b>0.004</b>
CAD	17 (25)	6 (19)	11 (30)	0.29
Permanent AF	3 (4)	1 (3)	2 (5)	0.64
Pulmonary disease	31 (45)	17 (53)	14 (38)	0.20
CKD	26 (38)	5 (16)	21 (57)	<b>&lt;0.001</b>
Previous/current cancer	8 (12)	5 (16)	3 (8)	0.33
SBP, mmHg	124 ± 15	125 ± 16	123 ± 14	0.68
DBP, mmHg	72 ± 9	74 ± 9	70 ± 9	0.11
SO <sub>2</sub> , %	95 [93; 97]	94 [93; 96]	96 [94; 97]	0.31
6MWD, meters	304 ± 199	326 ± 131	279 ± 102	0.18
LVEF <50%	4 (6)	1 (3)	3 (8)	0.63
LVH	17 (25)	3 (9)	14 (38)	<b>0.005</b>
LA dilation	31 (45)	7 (22)	24 (65)	<b>0.001</b>
TAPSE, mm	20 ± 5	21 ± 5	20 ± 5	0.64
TRV, m/s	3.81 ± 0.76	3.87 ± 0.69	3.75 ± 0.82	0.53
TAPSE/TRV	5.6 ± 1.9	5.5 ± 1.9	5.7 ± 2.0	0.79
RVSP, mmHg	57 [42; 77]	65 [43; 77]	54 [40; 85]	0.50
RA dilation	53 (77)	24 (75)	29 (78)	0.29
Pericardial effusion	11 (16)	6 (19)	5 (14)	0.55
Most recent RHC				
RAP, mmHg	7 [4; 10]	5 [3; 8]	8 [5; 10]	<b>0.03</b>

mPAP, mmHg	41 ± 10	42 ± 12	40 ± 9	0.48
dPAP, mmHg	25 ± 9	27 ± 11	24 ± 7	0.16
sPAP, mmHg	70 ± 20	71 ± 21	68 ± 19	0.47
PAWP, mmHg	11 ± 4	10 ± 3	12 ± 5	0.64
RAP/PAWP ratio	0.60 [0.46; 0.75]	0.59 [0.39; 0.72]	0.64 [0.47; 0.81]	0.28
PVR, WU	7.39 ± 4.53	8.50 ± 5.26	6.42 ± 3.58	0.06
Cardiac output, L/min	4.59 ± 1.43	4.39 ± 1.66	4.77 ± 1.19	0.28
Cardiac index, L/min/m <sup>2</sup>	2.74 ± 0.81	2.63 ± 0.93	2.83 ± 0.70	0.32
Diagnosis to last RHC interval, months	15 [4; 33]	12 [4; 30]	18 [4; 38]	0.48
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Treatment				
No PAH therapy	6 (9)	2 (6)	4 (11)	0.50
Bosentan	-	-	-	
Ambrisentan	17 (25)	7 (22)	10 (27)	0.62
Macitentan	32 (46)	17 (53)	15 (41)	0.35
ERA	49 (71)	24 (75)	25 (68)	0.50
Sildenafil	22 (32)	9 (28)	13 (35)	0.53
Tadalafil	25 (36)	10 (31)	15 (41)	0.42
Riociguat	3 (4)	3 (9)	0	0.06
PDE5i/GCs	50 (73)	22 (69)	28 (76)	0.52
Dual oral combination therapy	36 (52)	16 (50)	20 (54)	0.74
Selexipag	6 (9)	3 (9)	3 (8)	0.85
Treprostinil	-	-	-	
Epoprostenol i.v.	1 (1)	1 (3)	0	0.29
Inhaled iloprost	2 (3)	1 (3)	1 (3)	0.92
Beta blockers	9 (13)	3 (9)	6 (16)	0.40
RASi	23 (33)	6 (19)	17 (46)	<b>0.02</b>
MRA	32 (46)	14 (44)	18 (49)	0.69
Furosemide	57 (83)	24 (75)	33 (89)	0.12
Digoxin	6 (9)	3 (9)	3 (8)	0.85
Amiodarone	9 (13)	4 (13)	5 (14)	0.87
Warfarin	11 (16)	5 (16)	6 (16)	0.91
DOAC	11 (16)	5 (16)	6 (16)	0.91
SAPT	22 (32)	7 (22)	15 (41)	0.10
Statins	26 (38)	11 (34)	15 (41)	0.60
Ezetimibe	3 (4)	0	3 (8)	0.10
Antidiabetic drugs	12 (17)	1 (3)	11 (30)	<b>0.004</b>

Characteristics of patients with and without a left heart disease (LHD) phenotype according to the secondary analysis criteria. Data are expressed as n (%), mean ± SD or median [IQR], as appropriate.

*LHD*, left heart disease; *BSA*, body surface area; *BMI*, body mass index; *PAH*, pulmonary arterial hypertension; *WHO-FC*, World Health Organization functional class; *CAD*, coronary artery disease; *AF*, atrial fibrillation; *CKD*, chronic kidney disease; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *SO<sub>2</sub>*, oxygen saturation; *6MWD*, six minute walking distance; *LVEF*, left ventricular ejection fraction; *LVH*, left ventricular hypertrophy; *LA*, left atrium; *TAPSE*, tricuspid annular plane systolic excursion; *TRV*, tricuspid regurgitant velocity; *RVSP*, right ventricular systolic pressure; *RA*, right atrium; *RHC*, right heart catheterization; *RAP*, right atrial pressure; *mPAP*, *dPAP* and *sPAP* for mean, diastolic and systolic pulmonary artery pressure; *PAWP*, pulmonary artery wedge pressure; *PVR*, pulmonary vascular resistance; *ERA*, endothelin receptor antagonist; *PDE5i*, phosphodiesterase type 5 inhibitor; *GCs*, guanylate cyclase stimulator; *RASi*, renin-angiotensin system inhibitors; *MRA*, mineralocorticoid receptor antagonist; *DOAC*, direct oral anticoagulant; *SAPT*, single antiplatelet therapy.

**Table S5.** Baseline characteristics of the study population according to the secondary analysis clinical criteria suggestive for left heart disease.

	Overall (N=69)	No LHD profile (N=40)	LHD phenotype (N=29)	P
Demographics				
Age at diagnosis, y	73 ± 4	72 ± 4	74 ± 4	0.11
Age at enrolment, years	77 ± 5	76 ± 4	78 ± 3	<b>0.03</b>
Female	44 (64)	23 (58)	21 (73)	0.20
Weight, Kg	64 ± 15	63 ± 13	67 ± 18	0.21
Height, cm	163 ± 9	161 ± 9	165 ± 9	0.09
BSA, m <sup>2</sup>	1.70 ± 0.22	1.67 ± 0.20	1.74 ± 0.25	0.19
BMI, Kg/m <sup>2</sup>	24 ± 5	24 ± 4	25 ± 6	0.55
Clinical and echocardiographic parameters				
WHO-FC I-II	32 (46)	20 (50)	12 (42)	0.66
Systemic hypertension	45 (65)	23 (58)	22 (76)	0.11
Diabetes	15 (22)	4 (10)	11 (38)	<b>0.005</b>
CAD	17 (25)	10 (25)	7 (24)	0.94
Permanent AF	3 (4)	1 (3)	2 (7)	0.38
Pulmonary disease	31 (45)	18 (45)	13 (45)	0.99
CKD	26 (38)	11 (28)	15 (52)	0.05
Previous/current cancer	8 (12)	7 (18)	1 (3)	0.07
SBP, mmHg	124 ± 15	123 ± 16	124 ± 14	0.80
DBP, mmHg	72 ± 9	73 ± 9	70 ± 9	0.33
SO <sub>2</sub> , %	95 [93; 97]	94 [93; 96]	97 [94; 97]	0.18
6MWD, meters	304 ± 199	315 ± 132	282 ± 89	0.38
LVEF <50%	4 (6)	1 (2)	3 (10)	0.36
LVH	17 (25)	3 (8)	14 (48)	<b>&lt;0.001</b>
LA dilation	31 (45)	7 (18)	24 (83)	<b>&lt;0.001</b>
TAPSE, mm	20 ± 5	20 ± 5	20 ± 4	0.80
TRV, m/s	3.81 ± 0.76	3.73 ± 0.76	3.92 ± 0.77	0.32
TAPSE/TRV	5.6 ± 1.9	5.8 ± 2.0	5.4 ± 1.9	0.42

RVSP, mmHg	57 [42; 77]	58 [40; 70]	57 [44; 89]	0.39
RA dilation	53 (77)	29 (73)	24 (83)	0.05
Pericardial effusion	11 (16)	7 (18)	4 (14)	0.68
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Most recent RHC				
RAP, mmHg	7 [4; 10]	6 [3; 8]	8 [6; 10]	0.05
mPAP, mmHg	41 ± 10	41 ± 11	41 ± 9	0.87
dPAP, mmHg	25 ± 9	26 ± 10	25 ± 7	0.71
sPAP, mmHg	70 ± 20	69 ± 20	70 ± 20	0.91
PAWP, mmHg	11 ± 4	11 ± 4	11 ± 5	0.91
RAP/PAWP ratio	0.60 [0.46; 0.75]	0.55 [0.35; 0.72]	0.67 [0.53; 0.83]	<b>0.04</b>
PVR, WU	7.39 ± 4.53	7.66 ± 5.05	7.00 ± 3.75	0.56
Cardiac output, L/min	4.59 ± 1.43	4.55 ± 1.63	4.65 ± 1.12	0.77
Cardiac index, L/min/m <sup>2</sup>	2.74 ± 0.81	2.74 ± 0.96	2.73 ± 0.58	0.97
Diagnosis to last RHC interval, months	15 [4; 33]	15 [5; 34]	15 [2; 32]	0.73
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Treatment				
No PAH therapy	6 (9)	2 (5)	4 (14)	0.20
Bosentan	-	-	-	
Ambrisentan	17 (25)	9 (23)	8 (28)	0.63
Macitentan	32 (46)	21 (53)	11 (38)	0.19
ERA	49 (71)	30 (75)	19 (66)	0.39
Sildenafil	22 (32)	14 (35)	8 (28)	0.51
Tadalafil	25 (36)	13 (33)	12 (41)	0.45
Riociguat	3 (4)	3 (8)	0	0.13
PDE5i/GCs	50 (73)	30 (75)	20 (69)	0.58
Dual oral combination therapy	36 (52)	22 (55)	14 (48)	0.58
Selexipag	6 (9)	4 (10)	2 (7)	0.65
Treprostinil	-	-	-	
Epoprostenol i.v.	1 (1)	1 (3)	0	0.40
Inhaled iloprost	2 (3)	1 (3)	1 (3)	0.82
Beta blockers	9 (13)	3 (8)	6 (21)	0.11
RASi	23 (33)	13 (33)	10 (35)	0.86
MRA	32 (46)	17 (43)	15 (52)	0.42
Furosemide	57 (83)	29 (73)	28 (97)	<b>0.009</b>
Digoxin	6 (9)	3 (8)	3 (10)	0.68
Amiodarone	9 (13)	7 (18)	2 (7)	0.22
Warfarin	11 (16)	6 (15)	5 (17)	0.75
DOAC	11 (16)	7 (18)	4 (14)	0.72
SAPT	22 (32)	10 (25)	12 (41)	0.15

Statins	26 (38)	17 (43)	9 (31)	0.33
Ezetimibe	3 (4)	0	3 (10)	<b>0.04</b>
Antidiabetic drugs	12 (17)	3 (8)	9 (31)	<b>0.01</b>

Characteristics of patients with and without a left heart disease (LHD) phenotype according to the clinical criteria of the secondary analysis. Data are expressed as n (%), mean  $\pm$  SD or median [IQR], as appropriate.

*LHD*, left heart disease; *BSA*, body surface area; *BMI*, body mass index; *PAH*, pulmonary arterial hypertension; *WHO-FC*, World Health Organization functional class; *CAD*, coronary artery disease; *AF*, atrial fibrillation; *CKD*, chronic kidney disease; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *SO<sub>2</sub>*, oxygen saturation; *6MWD*, six minute walking distance; *LVEF*, left ventricular ejection fraction; *LVH*, left ventricular hypertrophy; *LA*, left atrium; *TAPSE*, tricuspid annular plane systolic excursion; *TRV*, tricuspid regurgitant velocity; *RVSP*, right ventricular systolic pressure; *RA*, right atrium; *RHC*, right heart catheterization; *RAP*, right atrial pressure; *mPAP*, *dPAP* and *sPAP* for mean, diastolic and systolic pulmonary artery pressure; *PAWP*, pulmonary artery wedge pressure; *PVR*, pulmonary vascular resistance; *ERA*, endothelin receptor antagonist; *PDE5i*, phosphodiesterase type 5 inhibitor; *GCs*, guanylate cyclase stimulator; *RASi*, renin-angiotensin system inhibitors; *MRA*, mineralcorticoid receptor antagonist; *DOAC*, direct oral anticoagulant; *SAPT*, single antiplatelet therapy.