

Table S1. Clinical characteristics and outcomes in female vs male CTEPH Patients.

Variables	Female (n=160)	Male (n=190)	P value
Characteristics			
Age	54.7±13.8	50.7±15.4	0.012
BMI (kg/m ²)	23.6±3.3	24.1±3.7	0.178
Smoking	2 (1.3)	101 (53.2)	<0.001
Alcohol Drinking	0 (0.0)	60 (31.6)	<0.001
History of VTE	113 (70.6)	157 (82.6)	0.008
Time from first symptom to diagnosis (months)	24.4 [9.1,60.78]	24.3 [7.5,48.7]	0.449
WHO FC III/IV	108 (67.5)	105 (55.3)	0.020
6MWD (m)	377 [342,442]	406.5 [342,453]	0.053
Hemodynamics			
Systolic PAP (mmHg)	84.7±23.6	82.9±21.2	0.446
Diastolic PAP (mmHg)	31.0 [25.5,36.5]	31.0 [25.0,37.0]	0.961
mean PAP (mmHg)	50.6±13.0	49.3±11.9	0.315
mean RAP (mmHg)	7.0 [4.0,10.0]	8.0 [6.0,11.0]	0.007
PAWP (mmHg)	10.0 [8.0,12.0]	10.0 [8.0,12.0]	0.116
PVR (Wood units)	9.68 [6.81,12.66]	8.07 [5.93,11.11]	0.004
CO (L/min)	4.32 [3.69,4.96]	4.66 [3.90,5.40]	0.005
CI (L/(min.m ²))	2.47 [2.14,2.90]	2.47 [2.08,2.80]	0.516
SvO ₂ (%)	61.1 [56.9,65.9]	63.5 [59.6,68.5]	0.002
Laboratory tests			
HGB (g/L)	143.0 [129.0,155.0]	155.0 [144.0,166.0]	<0.001
WBC (×10 ⁹)	5.71 [4.81,6.97]	6.33 [5.10,7.54]	0.005
PLT (×10 ⁹)	199.0 [162.0,258.5]	182.0 [146.0,223.0]	0.001
NT-proBNP (ng/ml)	1318.75 [350.00,2867.65]	1129.50 [362.00,2824.00]	0.802
D-dimer (µg/ml)	0.42 [0.22,0.82]	0.58 [0.23,1.14]	0.018
ALT (IU/L)	20.0 [13.0,35.0]	25.0 [18.0,35.0]	0.001
AST (IU/L)	24.0 [19.0,31.0]	25.0 [20.0,32.0]	0.493
TB (µmol/L)	18.07 [12.90,27.57]	21.50 [15.64,32.70]	0.003
DB (µmol/L)	3.90 [2.87,7.40]	4.85 [3.20,7.95]	0.029
Creatinine (µmol/L)	70.15 [61.00,80.07]	88.96 [77.40,97.39]	<0.001
Uric acid (µmol/L)	381.46 [301.10,465.56]	449.37 [373.06,534.80]	<0.001
SaO ₂ (%)	89.4 [86.6,92.5]	90.9 [88.7,93.9]	0.001
Comorbidities			
Thrombophilia	8 (5.0)	23 (12.1)	0.020
APS	12 (7.5)	14 (7.4)	0.963
CHD	6 (3.8)	17 (9.0)	0.05
DM	4 (2.5)	8 (4.2)	0.381
Hypertension	37 (23.1)	47 (24.7)	0.725
Cancer	3 (1.9)	1 (0.5)	0.336

Anemia	14 (8.8)	14 (7.4)	0.635
Targeted drug at diagnosis			0.528
No drugs	8 (5.0)	15 (7.9)	
Monotherapy	54 (33.8)	65 (34.2)	
Combination therapy	98 (61.3)	110 (57.9)	
Main treatment modality			0.038
Targeted drug	49 (30.6)	57 (30.0)	
PEA	46 (28.8)	77 (40.5)	
BPA	65 (40.6)	56 (29.5)	
Anticoagulants			0.043
Warfarin	55 (34.6)	86 (45.3)	
NOAC	104 (65.4)	104 (54.7)	
Death	22 (13.8)	23 (12.1)	0.647

Data are presented as mean±SD or n (%) or median [IQR].

CTEPH: chronic thromboembolic pulmonary hypertension; BMI: Body mass index ; VTE: Venous Thrombus Embolism; WHO FC: WHO function class; 6MWD: 6-minutes walking distance; PAP: pulmonary artery pressure; RAP: right atrial pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance; CO: cardiac output; CI: cardiac index; SvO₂: mixed venous oxygen saturation; HGB: hemoglobin; WBC: white blood cell; PLT: platelet; NT-proBNP : N-terminal pro brain natriuretic peptide; ALT: alanine aminotransferase; AST: aspartic transaminase; TB: total bilirubin; DB: direct bilirubin; Sao₂: arterial oxygen saturation; APS: antiphospholipid syndrome; CHD: coronary heart disease; DM: Diabetes mellitus ; PEA: pulmonary endarterectomy; BPA: balloon pulmonary angioplasty; NOAC: novel oral anticoagulants.

Table S2. Univariate COX proportional hazards regression analysis of risk factors for mortality in female patients.

Variables	HR	95% CI	P value
Characteristics			
Age	1.00	0.97-1.03	0.831
BMI (kg/m ²)	0.91	0.80-1.04	0.156
Smoking	0.00	(0,inf)	0.993
Alcohol Drinking	—	—	—
History of VTE	0.61	0.26-1.42	0.255
Time from first symptom to diagnosis (months)	1.00	1.00-1.01	0.192
WHO FC III/IV	1.31	0.51-3.34	0.578
6MWD/20 (m)	0.92	0.86-0.99	0.018
Hemodynamics			
Systolic PAP (mmHg)	1.00	0.98-1.02	0.773
Diastolic PAP (mmHg)	1.01	0.96-1.06	0.743
mean PAP (mmHg)	1.01	0.98-1.04	0.612
mean RAP (mmHg)	1.04	0.96-1.13	0.364
PAWP (mmHg)	1.06	0.95-1.19	0.271

PVR (Wood units)	1.05	0.96-1.14	0.290
CO (L/min)	0.82	0.56-1.21	0.316
CI (L/(min.m ²))	0.82	0.41-1.64	0.565
SvO ₂ (%)	0.94	0.90-0.98	0.006
Laboratory tests			
HGB (g/L)	0.98	0.97-1.00	0.053
PLT (×10 ⁹)	1.00	0.99-1.00	0.431
NT-proBNP/500 (ng/ml)	1.07	1.01-1.13	0.017
D-dimer (μg/ml)	1.06	0.88-1.27	0.554
TB (μmol/L)	1.01	0.99-1.04	0.268
DB (μmol/L)	1.05	0.99-1.11	0.102
Creatinine (μmol/L)	1.01	1.00-1.03	0.119
Uric acid (μmol/L)	1.00	1.00-1.01	0.520
Sao ₂ (%)	1.00	0.93-1.07	0.994
Comorbidities			
Thrombophilia	0.95	0.13-7.09	0.960
APS	0.93	0.12-7.04	0.946
CHD	3.36	0.78-14.57	0.105
DM	1.35	0.18-10.17	0.769
Hypertension	0.64	0.22-1.91	0.427
Cancer	9.34	1.13-76.90	0.038
Anemia	2.80	1.02-7.70	0.046
Targeted drug	1.10	0.54-2.27	0.791
Main treatment modality			
Targeted drug	Ref	Ref	
PEA	0.38	0.13-1.17	0.091
BPA	0.30	0.10-0.91	0.033
Anticoagulants			
Warfarin	Ref	Ref	
NOAC	1.57	0.63-3.91	0.333

BMI: Body mass index ; VTE: Venous Thrombus Embolism; WHO FC: WHO function class; 6MWD: 6-minutes walking distance; PAP: pulmonary artery pressure; RAP: right atrial pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance; CO: cardiac output; CI: cardiac index; SvO₂: mixed venous oxygen saturation; HGB: hemoglobin; WBC: white blood cell; PLT: platelet; NT-proBNP : N-terminal pro brain natriuretic peptide; ALT: alanine aminotransferase; AST: aspartic transaminase; TB: total bilirubin; DB: direct bilirubin; Sao₂: arterial oxygen saturation; APS: antiphospholipid syndrome; CHD: coronary heart disease; DM: Diabetes mellitus ; PEA: pulmonary endarterectomy; BPA: balloon pulmonary angioplasty; NOAC: novel oral anticoagulant; Ref: reference.

Table S3. Clinical characteristics of female CTEPH Patients in each treatment group.

Variables	Targeted drug (n=49)	PEA (n=46)	BPA (n=65)	<i>P1</i>	<i>P2</i>	<i>P3</i>
Characteristics						
Age	58.0±12.9	47.8±11.8	57.2 14.1	<0.001	0.758	<0.001
BMI (kg/m ²)	24.2±3.1	23.0±3.6	23.6±3.1	0.095	0.333	0.353
Smoking	0 (0.0)	1 (2.2)	1 (1.5)	0.484	>0.999	>0.999
Alcohol Drinking	0 (0.0)	0 (0.0)	0 (0.0)	-	-	-
History of VTE	34 (69.4)	33 (71.7)	46 (70.8)	0.826	0.873	0.912
Time from first symptom to diagnosis (months)	27.3 [12.2,60.4]	11.6 [6.13,36.53]	33.9 [12.2,73.6]	0.007	0.473	0.001
WHO FC III/IV	32 (65.3)	30 (65.2)	46 (70.8)	0.993	0.535	0.535
6MWD (m)	357.0 [342.0,442.0]	408.0 [342.0,443.0]	370.0 [327.0,442.0]	0.201	0.818	0.115
Hemodynamics						
Systolic PAP (mmHg)	86.3±23.0	81.8±23.6	85.5±24.3	0.342	0.847	0.426
Diastolic PAP (mmHg)	31.0 [26.0,39.0]	29.0 [23.0,33.0]	31.0 [27.0,38.0]	0.159	0.932	0.099
mean PAP (mmHg)	52.0±13.3	48.6±13.2	50.9±12.6	0.211	0.648	0.351
mean RAP (mmHg)	7.0 [5.0,11.0]	6.0 [4.0 ,9.0]	7.0 [4.0,10.0]	0.099	0.776	0.189
PAWP (mmHg)	9.0 [8.0,11.0]	10.0 [8.0,11.0]	10.0 [8.0,12.0]	0.922	0.519	0.357
PVR (Wood units)	10.3 [8.1,13.3]	8.26 [6.33,10.53]	9.41 [6.71,12.41]	0.053	0.312	0.262
CO (L/min)	4.10 [3.67,4.60]	4.38 [4.07,5.13]	4.17 [3.47,5.13]	0.032	0.405	0.238
CI (L/(min.m ²))	2.41 [2.17,2.72]	2.55[2.28,3.06]	2.52 [2.09,2.96]	0.069	0.725	0.405
Svo ₂ (%)	61.8 [57.7,65.1]	60.6 [56.3,65.5]	62.0 [55.9,67.5]	0.979	0.413	0.765
Laboratory tests						
HGB (g/L)	141.0[129.0,147.0]	141.0 [118.0,159.0]	145.0 [131.0,158.0]	0.829	0.279	0.563

WBC ($\times 10^9$)	5.63 [4.94,6.65]	5.73 [4.75,7.68]	5.78 [4.65,7.03]	0.663	0.891	0.664
PLT ($\times 10^9$)	192.0 [162.0,258.0]	216.5 [171.0,273.0]	198.0 [155.0,244.0]	0.214	0.742	0.135
NT-proBNP (ng/ml)	1396.80 [560.30,2877.30]	1579.5 [310.8,2688.0]	1186.0 [227.0,2941.0]	0.704	0.520	0.728
D-dimer ($\mu\text{g/ml}$)	0.38 [0.20,0.80]	0.56 [0.26,0.93]	0.36 [0.17,0.75]	0.153	0.961	0.097
ALT (IU/L)	22.0 [14.0,35.0]	26.0 [13.0,41.0]	16.5 [12.0,25.5]	0.520	0.173	0.128
AST (IU/L)	21.0 [18.0,31.0]	26.0 [21.0,32.0]	16.5 [12.0,25.5]	0.053	0.229	0.348
ALP (IU/L)	67.0 [54.0,77.0]	79.0 [63.0,100.0]	65.0 [53.0,81.0]	0.004	0.898	0.006
Total bilirubin ($\mu\text{mol/L}$)	20.00 [14.30,29.60]	14.21 [10.75,20.19]	18.30 [13.21,28.90]	0.009	0.375	0.072
Direct bilirubin ($\mu\text{mol/L}$)	3.60 [2.90,7.20]	3.10 [2.40,4.90]	4.58 [3.25,8.28]	0.115	0.160	0.007
Creatinine ($\mu\text{mol/L}$)	66.89 [55.90,73.66]	69.00 [60.31,80.07]	76.0 [66.8,84.0]	0.249	<0.001	0.032
Uric acid ($\mu\text{mol/L}$)	364.10 [284.7,446.44]	375.63 [286.64,459.51]	400.05 [337.50,467.28]	0.719	0.112	0.371
Sao ₂ (%)	89.4 [87.3,92.4]	90.0 [86.7,93.1]	89.3 [85.9,91.8]	0.718	0.413	0.302
Comorbidities						
Thrombophilia	1 (2.0)	4 (8.7)	3 (4.6)	0.195	0.633	0.446
APS	3 (6.1)	4 (8.7)	5 (7.7)	0.709	>0.999	>0.999
Coronary disease	4 (8.2)	0 (0.0)	2 (3.1)	0.118	0.400	0.510
Diabetes mellitus	2 (4.1)	0 (0.0)	2 (3.1)	0.495	>0.999	0.510
Hypertension	16 (32.7)	5 (10.9)	16 (24.6)	0.011	0.344	0.069
Gastrointestinal disease	2 (4.1)	1 (2.2)	7 (10.8)	>0.999	0.296	0.137
Chronic kidney disease	0 (0.0)	0 (0.0)	1 (1.5)	-	>0.999	>0.999
Cancer	2 (4.1)	0 (0.0)	1 (1.5)	0.495	0.576	>0.999

Hyperhomocysteinemia	11 (22.5)	4 (8.7)	36 (55.4)	0.066	<0.001	<0.001
Anemia	4 (8.2)	5 (10.9)	5 (7.7)	0.735	>0.999	0.739
Targeted drug at diagnosis				0.004	<0.001	0.044
No drugs	0 (0.0)	69 (13.0)	2 (3.1)			
Monotherapy	27 (55.1)	14 (30.4)	13 (20.0)			
Combination therapy	22 (44.9)	26 (56.5)	50 (76.9)			
Anticoagulants				0.847	<0.001	<0.001
Warfarin	22 (45.8)	22 (47.8)	11 (16.9)			
NOAC	26 (54.2)	24 (52.2)	54 (83.1)			
Combination Medicine						
Antiplatelet	3 (6.1)	1 (2.2)	4 (6.2)	0.618	>0.999	0.401
NASID	1 (2.0)	2 (4.4)	1 (1.5)	0.609	>0.999	0.569
Steroidhormones	1 (2.0)	5 (10.9)	4 (6.2)	0.104	0.389	0.485
CCB	1 (2.0)	0 (0.0)	1 (1.5)	>0.999	>0.999	>0.999
Diuretic	41 (83.7)	41 (89.1)	61 (93.9)	0.439	0.080	>0.999
Digoxin	26 (53.1)	28 (60.9)	41 (63.1)	0.443	0.282	0.813
IVC filter	4 (8.2)	11 (23.9)	4 (6.2)	0.035	0.724	0.007

Data are presented as mean±SD or n (%) or median [IQR]. CTEPH: chronic thromboembolic pulmonary hypertension; BMI: Body mass index ; VTE: Venous Thrombus Embolism; WHO FC: WHO function class; 6MWD: 6-minutes walking distance; PAP: pulmonary artery pressure; RAP: right atrial pressure; PAWP: pulmonary artery wedge pressure; PVR: pulmonary vascular resistance; CO: cardiac output; CI: cardiac index; SvO₂: mixed venous oxygen saturation; HGB: hemoglobin; WBC: white blood cell; PLT: platelet; NT-proBNP : N-terminal pro brain natriuretic peptide; ALT: alanine aminotransferase; AST: aspartic transaminase; TB: total bilirubin; DB: direct bilirubin; Sao₂: arterial oxygen saturation; APS: antiphospholipid syndrome; CHD: coronary heart disease; DM: Diabetes mellitus ; PEA: pulmonary endarterectomy; BPA: balloon pulmonary angioplasty; NOAC: novel oral anticoagulants. *P1*: the *P* value between patients receiving targeted drug along and patients receiving PEA; *P2*: the *P* value between patients receiving targeted drug along and patients receiving BPA; *P3*: the *P* value between patients receiving PEA and patients receiving BPA. *P* <0.017 (Bonferroni correction) was consider significance.

Table S4. The results of sensitivity analysis.

Variables	HR	95% CI	P value
Age	1.00	0.96-1.04	0.997
BMI (kg/m ²)	0.92	0.78-1.09	0.357
6MWD/20 (m)	0.96	0.89-1.04	0.310
Svo ₂ (%)	0.98	0.92-1.05	0.546
NT-proBNP/500 (ng/ml)	1.09	1.00-1.19	0.050
Cancer	4.97	0.48-51.76	0.180
Anemia	4.96	1.33-18.40	0.017
Time from first symptom to diagnosis (months)	1.00	0.99-1.01	0.689
Anticoagulants	1.67	0.61-4.57	0.317
Main treatment modality			
Targeted drug	Ref	Ref	-
PEA	0.25	0.06-0.99	0.049
BPA	0.13	0.03-0.60	0.009

Multivariate Cox analysis after adjusting the confounders (age and BMI) and survival-related factors. BMI: Body mass index; 6MWD/20: 6-min walk distance, per 20m increase in distance; SvO₂: mixed venous oxygen saturation; NT-proBNP/500: N-terminal pro-brain natriuretic peptide, per 500 ng/ml increase in concentration; PEA: pulmonary endarterectomy; BPA: balloon pulmonary angioplasty.