

Risk assessment in medically treated Chronic Thromboembolic Pulmonary Hypertension patients

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Take home message: The risk stratification for PAH of the current European PH guidelines may allow survival prediction in medically treated CTEPH patients (136 characters).

Table S1. Characteristics of the patients included into the baseline risk stratification group (analysis included only patients for whom all risk score variables were available, n=318)

	N	All n=318	Low risk n=37 (12%)	Intermediate risk n=229 (72%)	High risk n=52 (16%)
Age (years)		71 ± 11	62 ± 11	71 ± 11	73 ± 10
Gender, % female		53%	49%	54%	54%
BMI (kg/m ²)	296	29 ± 6	28 ± 5	29 ± 7	28 ± 5
CTEPH status (n; %)					
Post PEA		17 (5%)	5 (14%)	12 (5%)	0 (0%)
Surgically inoperable		155 (49%)	17 (46%)	119 (52%)	19 (37%)
Medically inoperable		48 (15%)	3 (8%)	37 (16%)	8 (15%)
Accessible		23 (7%)	4 (11%)	10 (4%)	9 (17%)
Refused surgery		47 (15%)	5 (14%)	31 (14%)	11 (21%)
Operability unknown		28 (9%)	3 (8%)	20 (9%)	5 (9%)
WHO FC Class I/II/III/IV, %		1/15/72/12	0/62/38/0	1/10/82/7	0/0/54/46
6MWD (m)		300 ± 129	445 ± 101	304 ± 115	183 ± 88
NTproBNP (ng/L) Median (Q1; Q3)	258	1379 (344; 3,413)	108 (73; 249)	1275 (383; 2,586)	3975 (3411; 6,444)
BNP (ng/L)	60	140 (53; 450)	31 (22; 59)	152 (57; 382)	603 (482; 699)
Haemodynamics					
RAP (mmHg)		8 ± 6	4 ± 3	8 ± 6	12 ± 5
PAPm (mmHg)		41 ± 10	36 ± 9	40 ± 10	47 ± 10
PAWP (mmHg)		9 ± 4	8 ± 3	9 ± 4	10 ± 3
CI (l/min/m ²)		2.2 ± 0.8	2.9 ± 0.6	2.3 ± 0.8	1.6 ± 0.4
PVR (dyn·s·cm ⁻⁵)	316	698 ± 365	400 ± 167	656 ± 298	1104 ± 419
SvO ₂ (%)		63 ± 9	71 ± 5	64 ± 8	54 ± 6
Comorbidities					
Any comorbidities	265	92%	97%	91%	93%
CHD	251	18%	13%	19%	17%
AHT	256	62%	56%	63%	61%
DM	259	16%	0%	17%	24%
OSAS	231	11%	23%	10%	5%
VTE	249	75%	78%	75%	73%
Thyroid disease	237	22%	30%	22%	13%

<i>Atrial fibrillation</i>	317	10%	0%	11%	14%
Initial therapy (within 6 months after diagnosis)					
<i>ERA</i>		28%	27%	27%	35%
<i>PDE5i</i>		39%	38%	38%	40%
<i>sGCs</i>		36%	46%	36%	27%
<i>PCA</i>		0.3%	0%	0%	2%
<i>Monotherapy</i>		96%	86%	97%	96%
<i>Combination therapy</i>		4%	14%	3%	4%
<i>Anticoagulation</i>		97%	100%	97%	98%

Table S2. Characteristics of the patients with surgically inoperable CTEPH included into the baseline risk stratification group (n=248)

	N	All n=248	Low risk n=37 (15%)	Intermediate risk n=176 (71%)	High risk n=35 (14%)
Age (years)		68 ± 12	64 ± 10	69 ± 12	67 ± 14
Gender, % female		53%	46%	53%	57%
BMI (kg/m ²)	226	28 ± 6	28 ± 4	29 ± 6	28 ± 7
WHO FC Class I/II/III/IV, %	247	0/14/73/13	0/49/51/0	1/9/82/8	0/0/50/50
6MWD (m)	209	307 ± 130	421 ± 105	306 ± 117	167 ± 88
NTproBNP (ng/L) Median (Q1; Q3)	172	1,366 (356; 3,438)	110 (67; 270)	1,334 (432; 2,970)	3,855 (2,644; 7,528)
BNP (ng/L)	37	207 (57; 456)	31 (22; 45)	208 (78; 444)	536 (486; 670)
Haemodynamics					
RAP (mmHg)	236	8 ± 6	4 ± 3	8 ± 6	14 ± 5
PAPm (mmHg)		41 ± 12	35 ± 9	41 ± 11	49 ± 13
PAWP (mmHg)		9 ± 4	9 ± 3	9 ± 4	10 ± 3
CI (l/min/m ²)	236	2.3 ± 0.9	3.0 ± 0.5	2.3 ± 0.9	1.6 ± 0.3
PVR (dyn·s·cm ⁻⁵)	243	700 ± 411	367 ± 136	675 ± 322	1,188 ± 553
SvO ₂ (%)	229	64 ± 9	71 ± 5	64 ± 9	54 ± 6
Comorbidities					
Any comorbidities	202	93%	94%	93%	87%
CHD	196	19%	9%	21%	23%
AHT	197	59%	62%	61%	48%
DM	198	16%	9%	16%	19%
OSAS	186	9%	14%	9%	0%
VTE	199	77%	69%	79%	77%
Thyroid disease	183	15%	17%	16%	7%
Atrial fibrillation		10%	3%	11%	11%
Initial therapy (within 6 months after diagnosis)					
ERA		28%	19%	27%	40%

<i>PDE5i</i>		47%	43%	47%	51%
<i>sGCs</i>		29%	38%	30%	20%
<i>PCA</i>		0.4%	0%	0%	3%
<i>Monotherapy</i>		93%	92%	94%	86%
<i>Combination therapy</i>		7%	8%	6%	14%
<i>Anticoagulation</i>		98%	100%	97%	100%

Table S3. Variables obtained at baseline for the baseline risk stratification group (n=561), and at baseline and at 3 months to 2 years follow up for the follow-up risk stratification group (n=231)

	Baseline group at baseline n=561	Follow up group at baseline n=231	Follow up group at follow up N=231
Age (years)	69 ± 13	68 ± 14	69 ± 14
Gender, % female	54%	55%	-
BMI (kg/m ²)	28 ± 6	28 ± 6	28 ± 6
CTEPH status (n; %)			
<i>Post PEA</i>	30 (5%)	17 (7%)	-
<i>Surgically inoperable</i>	248 (44%)	107 (46%)	-
<i>Medically inoperable</i>	84 (15%)	32 (14%)	-
<i>Accessible</i>	48 (9%)	15 (7%)	-
<i>Refused surgery</i>	73 (13%)	35 (15%)	-
<i>Operability unknown</i>	78 (14%)	25 (11%)	-
WHO FC Class I/II/III/IV, %	0/15/72/13	0/18/69/13	4/31/61/4
6MWD (m)	302 ± 126	319 ± 129	318 ± 132
NTproBNP (ng/L) Median (Q1; Q3)	1,402 (352; 3,565)	1,266 (284; 3,477)	867 (227; 2,082)
BNP (ng/L)	186 (53; 486)	166 (52; 465)	145 (70; 324)
Haemodynamics			
<i>RAP (mmHg)</i>	8 ± 5	9 ± 6	8 ± 6
<i>PAPm (mmHg)</i>	42 ± 11	42 ± 11	40 ± 10
<i>PAWP (mmHg)</i>	9 ± 4	9 ± 4	9 ± 4
<i>CI (l/min/m²)</i>	2.2 ± 0.8	2.2 ± 0.7	2.3 ± 0.8
<i>PVR (dyn·s·cm⁻⁵)</i>	734 ± 387	727 ± 380	654 ± 374
<i>SvO₂ (%)</i>	63 ± 9	62 ± 9	63 ± 8
Comorbidities (from inclusion)			
<i>Any comorbidities</i>	91%	90%	-
<i>CHD</i>	20%	23%	-
<i>AHT</i>	59%	57%	-
<i>DM</i>	16%	13%	-
<i>OSAS</i>	9%	11%	-

<i>VTE</i>	72%	69%	-
<i>Thyroid disease</i>	20%	25%	-
<i>Atrial fibrillation</i>	8%	10%	-
Therapy (at baseline and at time of FU risk evaluation)			
<i>ERA</i>	24%	36%	40%
<i>PDE5i</i>	42%	41%	49%
<i>sGCs</i>	37%	27%	28%
<i>PCA</i>	1%	1%	2%
<i>no therapy</i>	0%	0%	3%
<i>Monotherapy</i>	93%	92%	71%
<i>Combination therapy</i>	7%	8%	26%
<i>Anticoagulation</i>	97%	98%	97%

Table S4. Characteristics of the patients with 0 to 3 low risk criteria at baseline (n=368)

	N	All n=368	Low risk criteria = 0 n=236 (64%)	Low risk criteria = 1 n=85 (23%)	Low risk criteria = 2 n=35 (10%)	Low risk criteria = 3 n=12 (3%)
Age (years)		70 ± 12	73 ± 10	68 ± 11	62 ± 14	57 ± 12
Gender, % female		52%	56%	54%	34%	17%
BMI (kg/m ²)	346	28 ± 6	28 ± 6	29 ± 7	27 ± 6	26 ± 4
CTEPH status (n; %)						
<i>Post PEA</i>		21 (6%)	11 (5%)	3 (4%)	5 (14%)	2 (17%)
<i>Surgically inoperable</i>		173 (47%)	108 (46%)	42 (49%)	17 (49%)	6 (50%)
<i>Medically inoperable</i>		54 (15%)	39 (17%)	13 (15%)	2 (6%)	0 (0%)
<i>Accessible</i>		30 (8%)	21 (9%)	4 (5%)	4 (11%)	1 (8%)
<i>Refused surgery</i>		53 (14%)	35 (15%)	11 (13%)	6 (17%)	1 (8%)
<i>Operability unknown</i>		37 (10%)	22 (9%)	12 (14%)	1 (3%)	2 (17%)
WHO FC Class I/II/III/IV, %		1/15/73/12	0/0/84/16	0/21/72/7	6/69/23/3	0/100/0/0
6MWD (m)		298 ± 131	248 ± 98	335 ± 115	467 ± 97	552 ± 80
NT-proBNP (ng/L) Median (Q1; Q3)	300	1385 (343; 3,436)	2503 (1121; 4,173)	290 (124; 1,547)	263 (88; 687)	94 (75; 130)
BNP (ng/L) Median (Q1; Q3)	69	140 (51; 456)	226 (105; 499)	40 (17; 96)	139 (23; 630)	22 (22; 22)
Haemodynamics						
<i>RAP (mmHg)</i>		8 ± 6	9 ± 6	7 ± 4	6 ± 5	7 ± 5
<i>PAPm (mmHg)</i>		41 ± 11	43 ± 10	38 ± 10	36 ± 9	34 ± 10
<i>PAWP (mmHg)</i>		9 ± 4	9 ± 4	9 ± 4	8 ± 4	8 ± 4
<i>CI (l/min/m²)</i>		2.2 ± 0.8	2.1 ± 0.8	2.5 ± 0.8	2.4 ± 0.7	2.9 ± 0.6
<i>PVR (dyn·s·cm⁻⁵)</i>		708 ± 366	805 ± 379	566 ± 290	522 ± 216	380 ± 144
<i>SvO₂ (%)</i>		63 ± 9	61 ± 8	68 ± 7	64 ± 12	73 ± 4
Comorbidities (from inclusion)						
<i>Any comorbidities</i>	310	93%	93%	93%	86%	91%
<i>CHD</i>	292	19%	19%	19%	17%	18%
<i>AHT</i>	298	63%	67%	63%	48%	46%
<i>DM</i>	302	16%	18%	17%	7%	0%
<i>OSAS</i>	270	11%	9%	13%	14%	14%

<i>VTE</i>	293	73%	71%	76%	72%	82%
<i>Thyroid disease</i>	277	21%	18%	28%	23%	20%
<i>Atrial fibrillation</i>	310	9%	13%	2%	0%	0%
Initial therapy (within 6 months after diagnosis)						
<i>ERA</i>		28%	28%	28%	31%	17%
<i>PDE5i</i>		39%	43%	34%	26%	33%
<i>sGCs</i>		36%	32%	39%	46%	58%
<i>PCA</i>		1%	1%	0%	0%	0%
<i>Monotherapy</i>		95%	95%	95%	97%	92%
<i>Combination therapy</i>		5%	5%	5%	3%	8%
<i>Anticoagulation</i>		97%	98%	92%	100%	100%

Table S5. Characteristics of the patients with 0 to 3 low risk criteria at 3 months to 2 years follow-up (n=199)

	N	All n=199	Low risk criteria = 0 n=95 (48%)	Low risk criteria = 1 n=64 (32%)	Low risk criteria = 2 n=23 (12%)	Low risk criteria = 3 n=17 (9%)
Age (years)		69 ± 14	72 ± 11	72 ± 14	58 ± 17	60 ± 13
Gender, % female		55%	59%	58%	44%	35%
BMI (kg/m ²)	140	29 ± 7	29 ± 6	29 ± 8	28 ± 6	27 ± 4
CTEPH status (n; %)						
<i>Post PEA</i>		15 (8%)	4 (4%)	6 (9%)	2 (9%)	3 (18%)
<i>Surgically inoperable</i>		91 (46%)	49 (52%)	22 (34%)	12 (52%)	8 (47%)
<i>Medically inoperable</i>		29 (15%)	16 (17%)	12 (19%)	0	1 (6%)
<i>Accessible</i>		13 (7%)	4 (4%)	5 (8%)	1 (4%)	3 (18%)
<i>Refused surgery</i>		30 (15%)	15 (16%)	7 (11%)	6 (26%)	2 (12%)
<i>Operability unknown</i>		21 (11%)	7 (7%)	12 (19%)	2 (9%)	0
WHO FC Class I/II/III/IV, %		4/33/59/4	0/0/93/7	0/58/41/2	13/70/17/0	29/71/0/0
6MWD (m)		320 ± 131	255 ± 94	307 ± 92	459 ± 107	540 ± 82
NTproBNP (ng/L) Median (Q1; Q3)	166	997 (207; 2,194)	1948 (997; 3,967)	505 (186; 1,385)	257 (128; 838)	87 (71; 106)
BNP (ng/L) Median (Q1; Q3)	34	145 (71; 324)	176 (112; 337)	113 (27; 324)	63 (48; 84)	11 (-; -)
Haemodynamics						
<i>RAP (mmHg)</i>	29	8 ± 5	9 ± 5	5 ± 3	7 ± 1	5 ± 1
<i>PAPm (mmHg)</i>	31	38 ± 9	41 ± 7	35 ± 10	28 ± 11	30 ± 15
<i>PAWP (mmHg)</i>	30	9 ± 4	10 ± 4	7 ± 3	13 ± 0	9 ± 1
<i>CI (l/min/m²)</i>	31	2.1 ± 0.6	1.9 ± 0.6	2.2 ± 0.5	2.4 ± 0.6	2.8 ± 0.4
<i>PVR (dyn·s·cm⁻⁵)</i>	31	708 ± 430	843 ± 424	540 ± 190	205 ± 86	309 ± 221
<i>SvO₂ (%)</i>	29	62 ± 9	61 ± 10	68 ± 3	71 ± 1	-
Comorbidities (from inclusion)						
<i>Any comorbidities</i>	163	90%	94%	95%	73%	73%
<i>CHD</i>	153	25%	25%	33%	14%	7%
<i>AHT</i>	160	58%	57%	62%	47%	60%
<i>DM</i>	159	14%	19%	13%	7%	0%

<i>OSAS</i>	135	11%	8%	15%	7%	18%
<i>VTE</i>	146	69%	72%	71%	64%	47%
<i>Thyroid disease</i>	139	25%	25%	24%	23%	31%
<i>Atrial fibrillation</i>	195	10%	14%	8%	0%	6%
Therapy (at time of FU risk evaluation)						
<i>ERA</i>		36%	47%	20%	44%	24%
<i>PDE5i</i>		49%	53%	52%	44%	29%
<i>sGCs</i>		28%	23%	31%	17%	53%
<i>PCA</i>		1%	0%	2%	4%	0%
<i>No therapy</i>		3%	0%	5%	4%	6%
<i>Monotherapy</i>		78%	73%	83%	83%	82%
<i>Combination therapy</i>		20%	27%	13%	13%	12%
<i>Anticoagulation</i>		97%	95%	98%	96%	100%