



Current diagnosis and management of chronic thromboembolic pulmonary hypertension

Results from a European Prospective Registry

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CTEPH Registry - Rationale

Today, epidemiological data from **large, multicenter registries** are only available for **PAH** :

- **Rich S et al.** *Ann Int Med* 1987
(NIH Prospective Registry of **194** incident & prevalent cases)
- **Peacock AJ et al.** *Eur Respir J* 2007
(Scottish Retrospective Registry of **374** cases)
- **Thenappan T et al.** *Eur Respir J* 2007
(US Prospective Registry of **578** incident & prevalent cases)
- **Benza R et al.** *Circulation* 2010
(US prospective REVEAL Registry of **2967** incident & prevalent cases)
- **Humbert M et al.** *Eur Respir J* 2010
(French Prospective Registry of **674** of incident & prevalent cases)

CTEPH Registry – Objectives

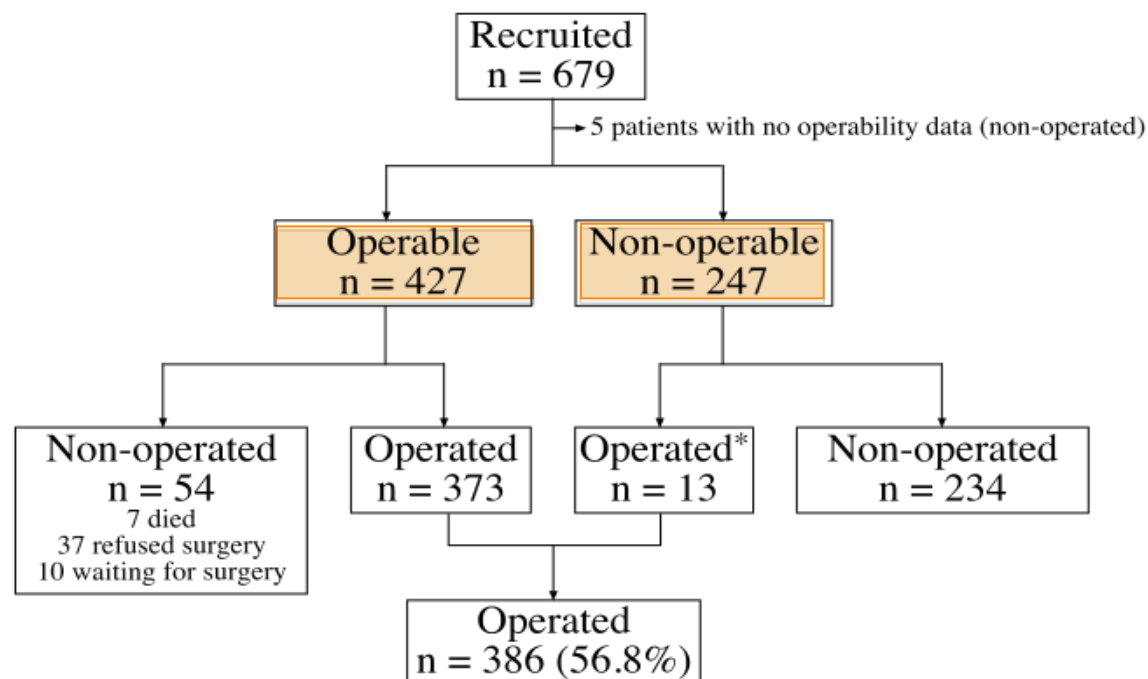
- collect information on medical history of CTEPH patients
- characterize and differentiate operable vs. non-operable patients
- describe and analyze therapeutic practices
- Report postoperative outcomes

CTEPH Registry - Inclusion Criteria

- incident cases (diagnosis < 6 months prior to inclusion)
- diagnosis „CTEPH“ confirmed by specific investigations and imaging
- no PAH-specific treatment prior to diagnosis
- at least 3 months of anticoagulation

Patient disposition

**27 CTEPH centers (26 European, 1 Canadian)
Enrollment 2/2007 to 1/2009)**



* Patients initially deemed non-operable but finally operated

Symptoms at diagnosis

| | <i>All patients</i> N = 679 | <i>Operable patients*</i> N = 427 | <i>Non-operable patients*</i> N = 247 |
|--|--------------------------------|--------------------------------------|--|
| Median time from symptoms to diagnosis (months) | 14.1 | 14.9 | 13.1 |
| Dyspnoea (N, %) | 673 (99.1) | 424 (99.3) | 244 (98.8) |
| Fatigue (N, %) | 214 (31.5) | 127 (29.7) | 87 (35.2) |
| Dizziness (N, %) | 38 (5.6) | 24 (5.6) | 14 (5.7) |
| Chest pain (N, %) | 104 (15.3) | 67 (15.7) | 36 (14.6) |
| Hemoptysis (N, %) | 30 (4.%) | 18 (4.2) | 11 (4.5) |
| Syncope (N, %) | 93 (13.7) | 66 (15.5) | 27 (10.9) |

* In 5 patients no data were available on operability

Patient characteristics at diagnosis

| | <i>All patients</i> | <i>Operable patients*</i> | <i>Non-operable patients*</i> | <i>p-value</i> |
|-------------------------------|--------------------------------|--------------------------------|--------------------------------|----------------|
| | <i>N = 679</i> | <i>N = 427</i> | <i>N = 247</i> | |
| Gender (% male) | 50.1% | 53.4 | 44.5 | 0.0308 |
| Ethnicity (% white) | 95.9% | 95.3 | 96.7 | 0.4277 |
| Age, years [range] | 63 [18;86] | 61 [18;84] | 67 [21;86] | < 0.0001 |
| Weight, kg [range] | 75 [38;162] | 76 [38;162] | 73 [39;140] | 0.0161 |
| NYHA class (%III/ %IV) | 68.6/12.8 | 67.7/12.6 | 70.4/12.6 | 0.4908/1.0000 |
| 6MWD m, [range] | 329 [11;700] <i>n = 589</i> | 340 [20;700] <i>n = 373</i> | 315 [11;695] <i>n = 214</i> | 0.0219 |
| Blood group non-0 (%) | 76.0 <i>n = 366</i> | 79.5 <i>n = 249</i> | 68.4 <i>n = 117</i> | 0.0255 |

History of VTE at diagnosis

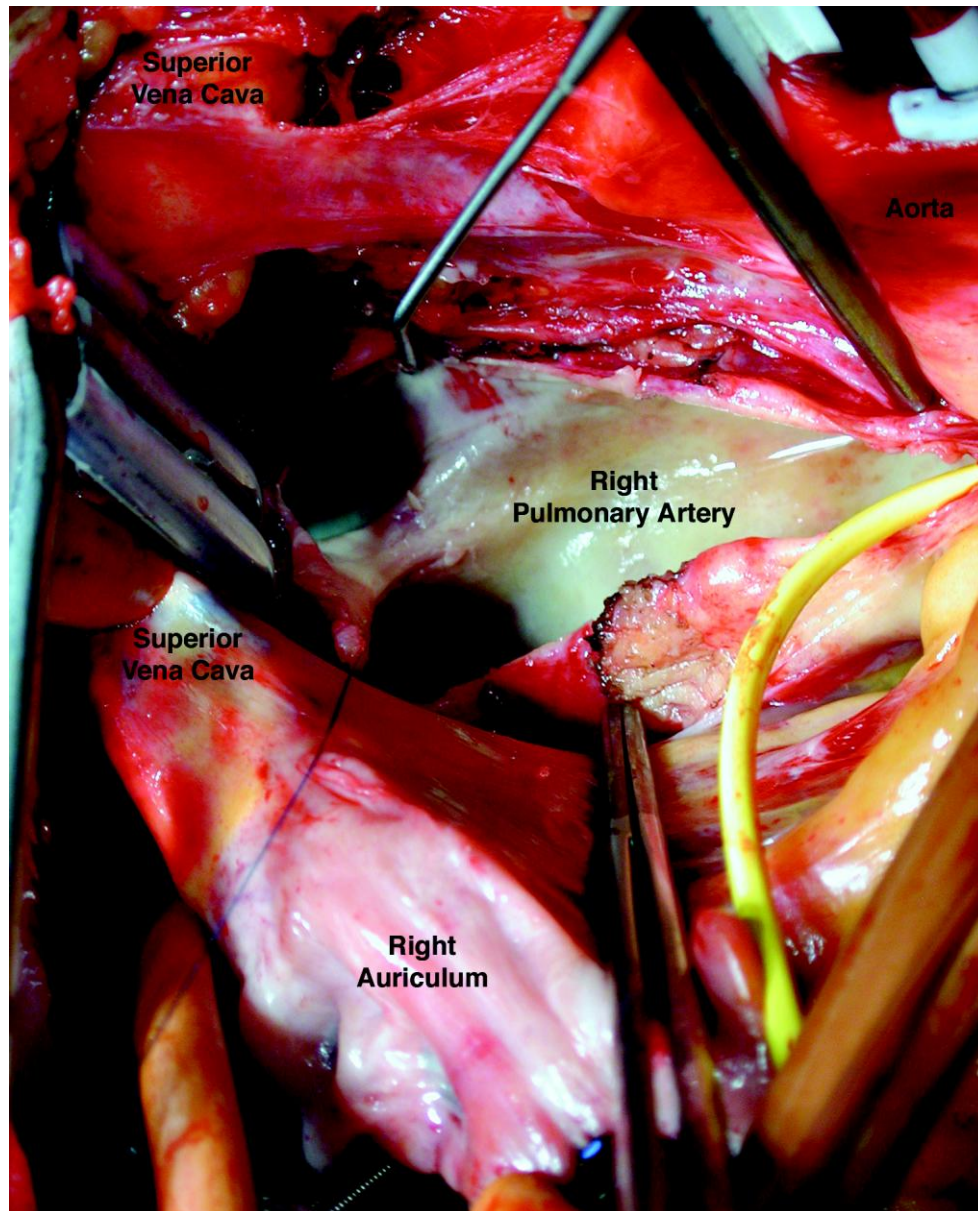
| | All patients N = 679 | Operable patients* N = 427 | Non-operable patients* N = 247 | p-value |
|---|-------------------------|-------------------------------|--------------------------------------|---------|
| Confirmed previous acute PE (%) | 74.8 n = 678 | 77.5 n = 427 | 70.0 n = 247 | 0.0344 |
| PE diagnosed more than twice (%) | 8.7 n = 469 | 10.6 n = 303 | 5.5 n = 163 | 0.0856 |
| Size of previous PE reported as 'massive' (%) | 40.8 n = 240 | 47.1 n = 155 | 29.4 n = 85 | 0.0090 |
| Confirmed previous DVT (%) | 56.1 n = 426 | 60.4 n = 280 | 49.0 n = 143 | 0.0295 |
| Acute PE and DVT (%) | 55.4 | 59.3 | 48.9 | 0.0477 |
| Acute PE no DVT (%) | 42.6 n = 413 | 39.3 n = 270 | 48.2 n = 141 | 0.0926 |
| Thrombolytic treatment (%) | 14.4 n = 404 | 18.5 n = 265 | 6.6 n = 137 | 0.0009 |
| Vena cava filter implanted (%) | 12.4 n = 491 | 13.7 n = 322 | 10.2 n = 166 | 0.3139 |

Diagnostic evaluations - 1

| | <i>All patients</i> N = 679 | <i>Operable patients*</i> N = 427 | <i>Non-operable patients*</i> N = 247 |
|--|--------------------------------|--------------------------------------|--|
| Right heart catheterization <i>median</i> <i>[range]</i> | | | |
| <i>mPAP</i> [†] (mm Hg) | 47 [14; 81] n = 669 | 47 [17; 80] n = 423 | 47 [14; 81] n = 244 |
| <i>PVR</i> [‡] (dyn.s.cm ⁻⁵) | 709 [97; 2880] n = 604 | 717 [97; 2682] n = 381 | 691 [148; 2880] n = 221 |
| <i>Cardiac index</i> (L.min ⁻¹ .m ⁻²) | 2.2 [0.9; 7.0] n = 632 | 2.2 [0.9; 7.0] n = 404 | 2.3 [1.1; 5.1] n = 227 |
| Scintigraphy (%) | | | |
| <i>Perfusion scan abnormal</i> | 98.7% n = 535 | 99.4% n = 344 | 97.4% n = 189 |
| <i>Ventilation scan abnormal</i> | 19.0% n = 484 | 17.5% n = 314 | 22.0% n = 168 |

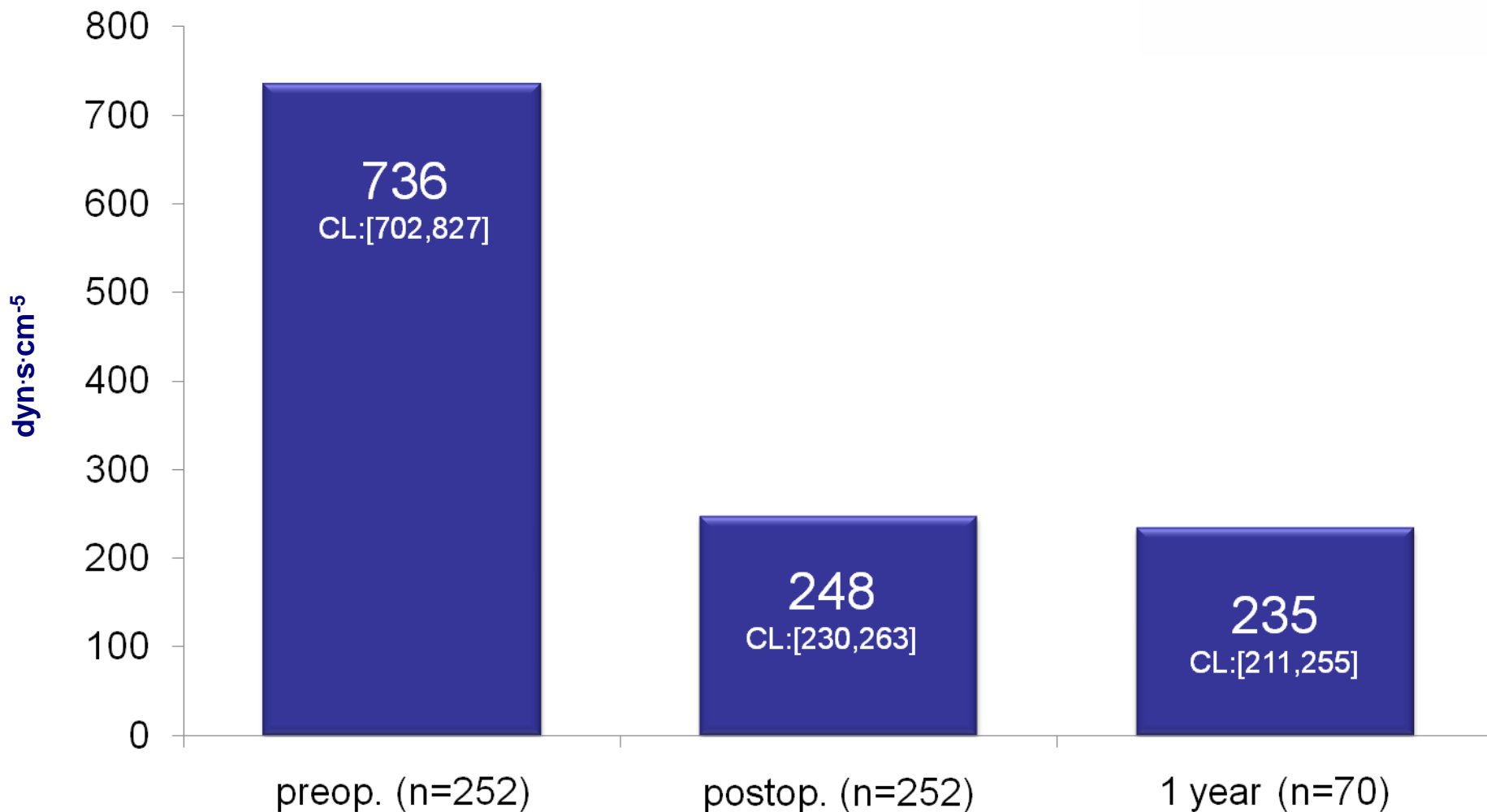
Diagnostic evaluations - 2

| | <i>All patients</i> N = 679 | <i>Operable patients*</i> N = 427 | <i>Non-operable patients*</i> N = 247 |
|---------------------------------------|--------------------------------|--------------------------------------|--|
| Angiography (%) | | | |
| <i>Proximal lesions</i> | 63.0% n = 552 | 70.9% n = 358 | 48.2% n = 191 |
| CT scan (%) | | | |
| <i>Proximal lesions</i> | 60.4% n = 541 | 70.1% n = 345 | 43.0% n = 193 |
| <i>Dilation of bronchial arteries</i> | 68.4% n = 345 | 75.0% n = 216 | 57.0% n = 128 |
| <i>Mosaic perfusion pattern</i> | 76.6% n = 414 | 82.4% n = 261 | 67.1% n = 152 |

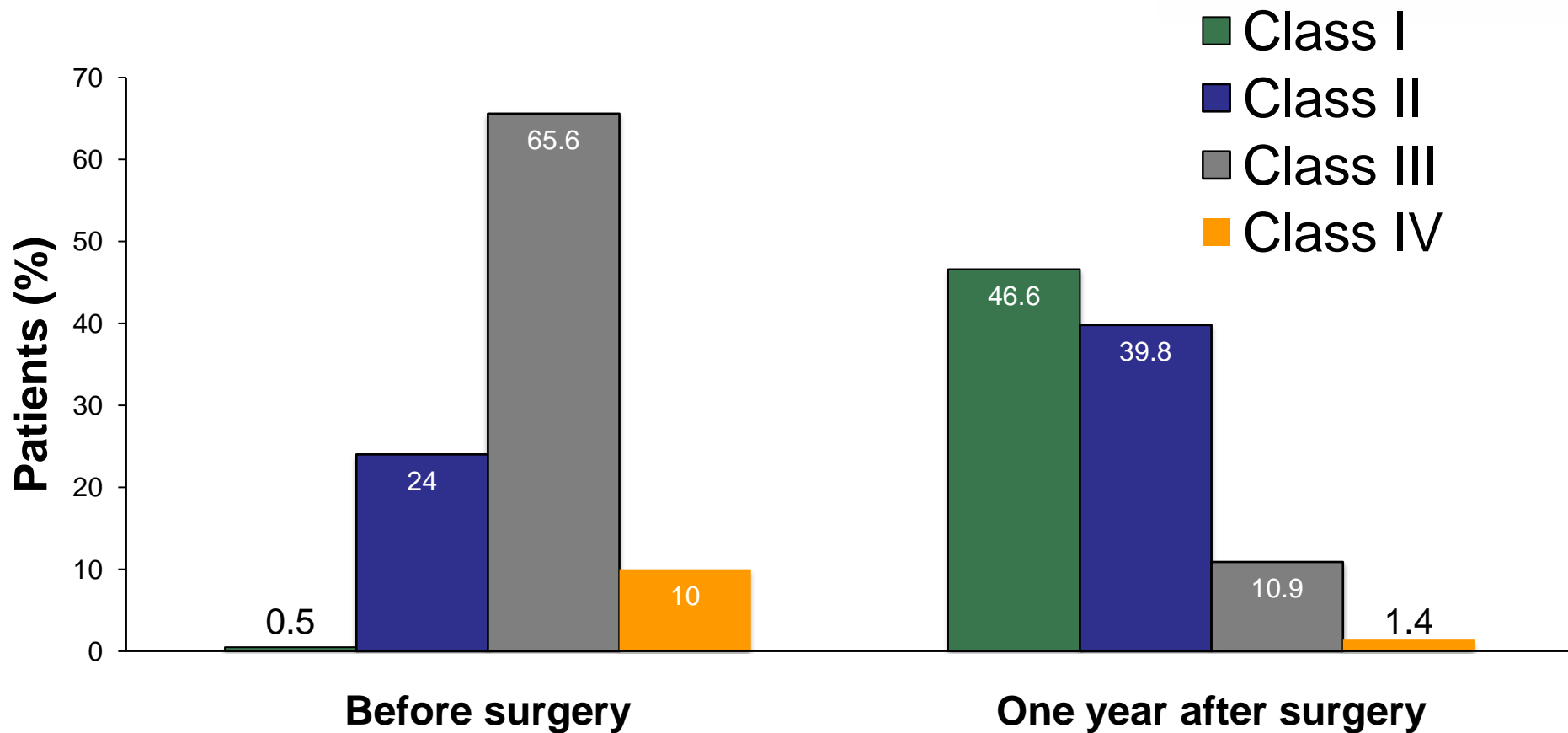


Courtesy
Walter
Klepetko

Pulmonary Vascular Resistance



NYHA Functional Class



Deaths at 1 year

| All patients | | Operable patients* | | Non-operable Patients* | |
|---------------|----------------|--------------------|--------------|------------------------|----------------|
| 62/679 (9.1%) | | 36/427 (8.4%) | | 26/247 (10.5%) | |
| Operated | Non-operated | Operated | Non-operated | Operated | Non-operated |
| 30/386 (7.8%) | 32/293 (10.9%) | 29/373 (7.8%) | 7/54 (13.0%) | 1/13 (7.7%) | 25/234 (10.7%) |

Medical therapy initiated at diagnosis

| | All patients N = 679 | Operable patients* N = 427 | Non-operable patients* N = 247 |
|---|-------------------------|-------------------------------|--------------------------------------|
| Anticoagulants (%) | 99.3% | 100% | 99.6% |
| PAH-specific therapy (%) | 37.9% n = 676 | 28.3% n = 427 | 53.8% n = 247 |
| <i>phosphodiesterase type V inhibitor</i> | 17.5% | 16.2% | 19.4% |
| <i>endothelin receptor antagonist</i> | 21.7% | 12.2% | 37.7% |
| <i>prostacyclin analogue</i> | 2.7% | 1.6% | 4.5% |
| <i>Combination therapies</i> | 4.0% | 1.6% | 7.7% |

Summary of current diagnosis and management of CTEPH in Europe

- Perfusion scintigraphy, conventional and CT pulmonary angiography are main tools to diagnose CTEPH
- In specialized centers, the surgical management of incident, newly diagnosed CTEPH patients provides in hospital death rates of <5%.
- However, at least 36% of all patients are inoperable
- About 40% of all newly diagnosed patients are started on PAH vasodilator treatments

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