Long-Term Outcomes and Prognostic Determinants After Balloon Pulmonary Angioplasty in Chronic Thromboembolic Pulmonary Hypertension: A Binational Cohort Study

Yoichi Sugiyama[1,2,3,4,5], Hiromi Matsubara[5,6], Philippe Brenot[1,7], Mitja Jevnikar[1,2,3], Hiroto Shimokawahara[5], Olivier Sitbon[1,2,3], Gerald Simonneau[1,2,3], Elie Fadel[1,3,8], Marc. Humbert[1,2,3], Xavier Jaïs[1,2,3]

Affiliations

1. Université Paris-Saclay, School of Medicine, Le Kremlin-Bicêtre, France.
2. Assistance Publique - Hôpitaux de Paris (AP-HP), Department of Respiratory and Intensive Care Medicine, FHU Cournand, ERN-LUNG, Hôpital Bicêtre, Le Kremlin-Bicêtre, France
3. INSERM UMR_S 1358 HPPIT «Pulmonary Hypertension: Pathophysiology and Novel Therapies», Le Plessis-Robinson, France.
4. Division of Cardiovascular Medicine, Department of Medicine, Kurume University School of Medicine, Kurume, Japan.
5. Department of Cardiology, National Hospital Organization Okayama Medical Center – Okayama, Japan.
6. Department of Clinical Science, National Hospital Organization Okayama Medical Center – Okayama, Japan.
7. Department of Radiology, Hôpital Marie Lannelongue, Le Plessis-Robinson, France.
8. Department of Thoracic Surgery and Heart-Lung Transplantation, Hôpital Marie Lannelongue, Le Plessis-Robinson, France.

Introduction

- Balloon pulmonary angioplasty (BPA) is an established treatment for patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH) and for those with residual pulmonary hypertension after pulmonary endarterectomy.
  (Humbert M, et al. Euro Heart J (2022) 00, 1–114.)
- While short- and long-term outcomes after BPA have been reported, data beyond five years remain scarce, and prognostic determinants as well as post-procedural treatment targets have not been clearly defined.
  (Delcroix M, et al. Circulation. 2024;150:1354–1365.)

Methods

- We conducted a binational retrospective cohort study including consecutive patients with CTEPH treated with BPA between 2004 and 2023 in Japan (National Hospital Organization Okayama Medical Center: NHO Okayama Medical Center) and France (French Reference Center for Pulmonary Hypertension).
- Long-term survival was assessed using Kaplan–Meier analyses and multivariable Cox regression models, and pre-procedural clinical and haemodynamic parameters as well as post-procedural haemodynamic variables, were evaluated as potential prognostic determinants of long-term outcomes.

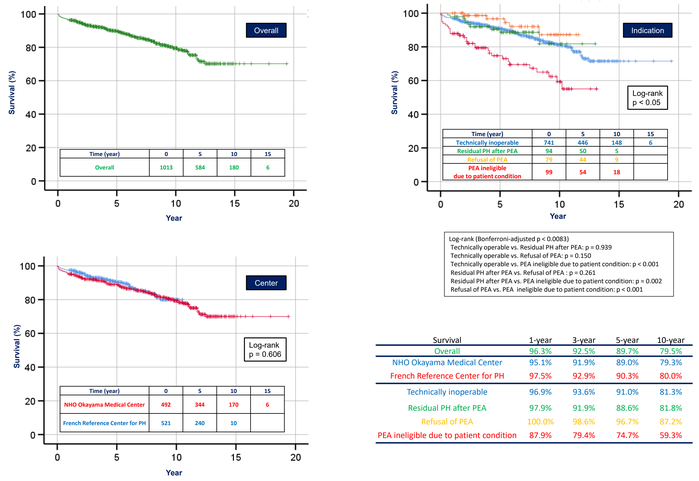
Results: Patients' characteristics

	Overall (%)
Patients	1013 (100%)
Sex distribution, male: female	352 (34.7%) : 661 (65.3%)
Age	64.2 ± 13.6
Body weight	64.7 ± 17.4
Time from last RHC before BPA to end of study (Observation period), years	5.8 [3.0-9.0]
Patient history	
Acute pulmonary embolism	503 (49.7%)
Associated medical conditions	
Malignant disorders* and myeloproliferative disorders†	141 (13.9%)
Splenectomy	55 (5.4%)
Antiphospholipid syndrome	26 (2.6%)
Sickle cell disease	14 (1.4%)
Thyroid disease	90 (8.9%)
Indication for BPA	
Technically inoperable	741 (73.1%)
Residual pulmonary hypertension after surgery	94 (9.3%)
Refusal of surgery	79 (7.8%)
Surgery ineligible due to patient condition	99 (9.8%)

	Overall (%)
Evaluations before BPA	
WHO-functional class, I/II/III/IV	19/348/536/110
6-minute walk distance, m	335.8 ± 130.0
BNP, pg/ml	72.6 [27.7-252.1]
Mean RAP, mmHg	7.1 ± 4.2
Mean PAP, mmHg	40.2 ± 11.3
Cardiac output, L/min	4.7 ± 1.5
Cardiac index, L/min/m^2	2.8 ± 0.7
PVR, wood units	7.4 ± 4.0
Mean PAWP, mmHg	9.1 ± 3.7
SvO_2, %	63.6 ± 9.0
PH targeted drugs before BPA	
PH-targeted drugs	628 (62.0%)
Oral monotherapy	241 (23.8%)
Oral combination therapy	264 (26.1%)
Parenteral Prostaglandin I_2	123 (12.1%)

*: Malignant disorder is defined as solid cancers and histological malignancies.
†: Myeloproliferative disorder is defined as polycythemia, essential thrombocythemia, myelofibrosis, and chronic myelogenous leukemia.

Results: Long-term survivals



Log-rank (Bonferroni-adjusted p < 0.0083)
Technically operable vs. Residual PH after PEA: p = 0.939
Technically operable vs. Refusal of PEA: p = 0.150
Technically operable vs. PEA ineligible due to patient condition: p < 0.001
Residual PH after PEA vs. Refusal of PEA : p = 0.261
Residual PH after PEA vs. PEA ineligible due to patient condition: p = 0.002
Refusal of PEA vs. PEA ineligible due to patient condition: p < 0.001

Survival	1-year	3-year	5-year	10-year
Overall	96.3%	92.5%	89.7%	79.5%
NHO Okayama Medical Center	95.1%	91.9%	89.0%	79.3%
French Reference Center for PH	97.5%	92.9%	90.3%	80.0%
Technically inoperable	96.9%	93.6%	91.0%	81.3%
Residual PH after PEA	97.9%	91.9%	88.6%	81.8%
Refusal of PEA	100.0%	98.6%	96.7%	87.2%
PEA ineligible due to patient condition	87.9%	79.4%	74.7%	59.3%

Results: Pre-BPA factors associated with long-term survival

(sex- and age-corrected analysis for all patients)

	Univariate β	Univariate Hazard ratio (95% CI)	Univariate p-value	Multivariate β	Multivariate Hazard ratio (95% CI)	Multivariate p-value
Patient history						
Acute pulmonoary embolism	0.072	1.074 [0.771-1.498]	0.671			
Comorbidity						
Psychiatric disease	0.536	1.710 [1.161-2.518]	0.007			0.105
Connective tissue disease	0.225	1.252 [0.656 -2.388]	0.496			
Associated medical conditions						
Malignant disorders and Myeloproliferative disorders	0.902	2.464 [1.686-3.601]	<0.001			
Malignant disorders	0.955	2.599 [1.769-3.817]	<0.001			
Malignant disorders treated within the two years prior to BPA	1.608	4.993 [3.176-7.848]	<0.001	1.58	4.856 [2.907-8.110]	<0.001
Malignant disorders treated before the two years prior to BPA	0.132	1.141 [0.631-2.064]	0.663			
Solid cancer	0.932	2.540 [1.717-3.757]	<0.001			
Splenectomy	0.501	1.650 [0.902-3.019]	0.104			
Antiphospholipid syndrome	0.542	1.719 [0.628 -4.704]	0.291			
Pacemaker	-0.766	0.465 [0.065-3.327]	0.446			
Sickle cell disease	0.826	2.285 [0.558-9.362]	0.251			
Thyroid disease	0.343	1.409 [0.834-2.379]	0.200			
Totally implantable central venous access systems	0.450	1.569 [0.733-3.359]	0.246			
Data at last evaluation before BPA						
WHO-functional class III or IV	0.800	2.226 [1.470-3.371]	<0.001			0.364
6-minute walk distance, m	-0.004	0.996 [0.995-0.997]	<0.001	-0.004	0.996 [0.994-0.997]	<0.001
BNP*, pg/dl	0.266	1.304 [1.137-1.496]	<0.001			
Mean RAP, mmHg	0.070	1.072 [1.033-1.112]	<0.001			0.542
Mean PAP, mmHg	0.018	1.018 [1.004-1.033]	0.011			
Cardiac output, L/min	-0.034	0.966 [0.853-1.095]	0.590			
Cardiac index, L/min/m^2	0.026	1.027 [0.819-1.288]	0.819			
PVR, wood units	0.055	1.057 [1.019-1.095]	0.003			0.388
Mean PAWP, mmHg	0.002	1.002 [0.957-1.048]	0.938			
Heart rate, /min	0.001	1.001 [0.988-1.014]	0.878			
SvO_2, %	-0.042	0.959 [0.942-0.976]	<0.001			

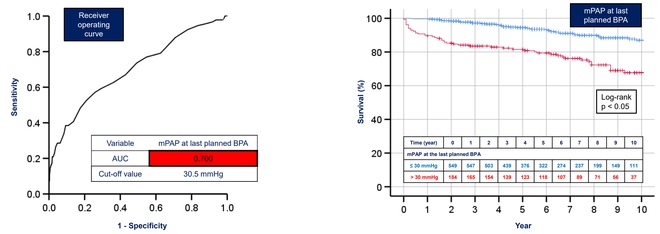
*Log-transformed value was used.

Results: Post-BPA factors associated with 10-year survival

(sex- and age-corrected analysis for technically inoperable CTEPH patients)

	Univariate β	Univariate Hazard ratio (95% CI)	Univariate p-value	Multivariate β	Multivariate Hazard ratio (95% CI)	Multivariate p-value
Patient history						
Acute pulmonoary embolism	-0.197	0.821 [0.537-1.256]	0.364			
Comorbidity						
Psychiatric disease	0.370	1.448 [0.881-2.379]	0.144			
Connective tissue disease	-0.050	0.951 [0.348-2.600]	0.922			
Associated medical conditions						
Malignant disorders and Myeloproliferative disorders	0.938	2.556 [1.576-4.144]	<0.001			
Malignant disorders	1.010	2.747 [1.676-4.502]	<0.001			
Malignant disorders treated within the two years prior to BPA	1.695	5.449 [2.995-9.912]	<0.001	2.142	8.517 [4.556-1.592x10]	<0.001
Malignant disorders treated before the two years prior to BPA	0.257	1.293 [0.624-2.679]	0.489			
Solid cancer	0.949	2.584 [1.551-4.303]	<0.001			
Splenectomy	0.622	1.863 [0.966-3.593]	0.063			
Antiphospholipid syndrome	0.545	1.724 [0.421-7.056]	0.449			
Pacemaker	-0.027	0.973 [0.135-7.027]	0.978			
Sickle cell disease	0.985	2.678 [0.645-1.112x10]	0.175			
Thyroid disease	0.216	1.242 [0.639-2.414]	0.524			
Totally implantable central venous access systems	0.575	1.777 [0.775-4.073]	0.175			
Hemodynamics at last planned BPA						
Mean RAP, mmHg	0.155	1.167 [1.102-1.236]	<0.001	0.082	1.085 [1.014-1.161]	0.001
Mean PAP, mmHg	0.083	1.086 [1.067-1.106]	<0.001	0.085	1.088 [1.062-1.116]	<0.001
Cardiac output, L/min	-0.009	0.991 [0.854-1.150]	0.901			
Cardiac index, L/min/m^2	0.000	1.000 [0.752-1.329]	0.998			
PVR, wood units	0.169	1.184 [1.131-1.239]	<0.001			
Mean PAWP, mmHg	0.089	1.093 [1.030-1.161]	0.003			0.195
Heart rate, /min	0.015	1.015 [0.996-1.034]	0.131			
SvO_2, %	-0.061	0.941 [0.913-0.970]	<0.001			
Complication	0.389	1.475 [0.964-2.258]	0.073			
Severe lung injury	0.974	2.648 [1.535-4.569]	<0.001			0.289

Results: 10-year survival in technically operable CTEPH



Conclusions

- BPA was associated with excellent long-term survival in patients with CTEPH.
- Haemodynamic status at the last planned BPA session, particularly achievement of mean pulmonary arterial pressure ≤30 mmHg, emerged as a clinically relevant treatment target, supporting a goal-oriented BPA strategy in technically inoperable patients.

Contact

E-mail: Yoichi Sugiyama; sugiyama_youichi@kurume-u.ac.jp