Comparison of 2-years follow-up of optimal medical therapy versus balloon pulmonary angioplasty for inoperable chronic thromboembolic pulmonary hypertension

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Introduction: Balloon pulmonary angioplasty (BPA) has emerged as a therapeutic option for chronic thromboembolic pulmonary hypertension (CTEPH) considered ineligible for pulmonary endarterectomy (PEA). The initial publications showed very good short-term outcomes for the technique, but there are limited data regarding medium-term outcomes and its comparison with optimal medical treatment (OMT).

Objectives: To evaluate and compare the medium-term outcomes of OMT versus (vs) BPA in inoperable CTEPH.

Methods: Retrospective study of consecutive patients (pts) with CTEPH followed in a referral centre for Pulmonary Hypertension. Selected those pts considered ineligible for PEA and with at least 2 years of follow-up. Comparison between two treatment strategies: OMT alone [maximum tolerated doses of pulmonary vasodilator drugs (PVD), as indicated] vs BPA (pts who completed the program with or without OMT). Endpoint was a composite of all-cause death and unplanned right heart failure admission at 2-year.

Results: From 62 pts, 19 pts were included (11 pts were excluded due to recent diagnosis; 32 were submitted to EAP): mean age 65.0±15.3 years, 89.5% female. At diagnosis, all pts had functional capacity limitation and elevated serum NTproBNP levels (median value 1255.0 pg/mL). Mean pulmonary arterial pressure (mPAP) was 46.2±9.3 mmHg and pulmonary vascular resistance (PVR) 15.3±8.3 Wood units (WU). Concerning treatment, 12 pts (63.2%) underwent OMT alone. These pts had higher NTproBNP levels (2670.0 vs 538.0 pg/mL, $p<0.01$) and PVR values (19.7±7.6 vs 9.7±5.4 WU, p=0.01) and lower CI (1.6±0.3 vs 2.4±0.5 L/min/m^2, $p<0.01$), at baseline; the remaining basal features didn't differ among groups (Fig.A). At 2-year follow-up, pts submitted to BPA were under PVD in 71.4% of cases with a mean of 1±0.8 drugs per patient and no difference compared to OMT group (83.3%, 1.7±0.9 drugs per patient), although oxygen therapy was higher in medical group (50% vs 0%, p=0.04). A significant overall improvement was observed in BPA group (Table – A): all pts were in functional class I ($p<0.01$), no one had right ventricular dysfunction ($p<0.01$) and mPAP decreased to 25.1±6.7 mmHg (p=0.01) and RVP to 2.9±0.8 WU (p=0.01). Inversely, no change was observed in pts under OMT alone ($p>0.05$ in all, Table – A). Endpoint rate was 31.6% with all adverse events occurring in the OMT group (50% vs 0%, p=0.04). After adjustment by Cox regression, no difference in baseline or follow-up features besides treatment influenced the outcome. Kaplan-Meier analysis (Graphic – B) confirmed significant benefit of BPA in 2-year outcome occurrence (long rank 4.6, p=0.03).

Conclusions: BPA strategy seems to improve medium-term functional capacity, right ventricular function and haemodynamics and decrease oxygen therapy dependence in inoperable CTEPH. Pts under OMT alone have a poor prognosis. These data encourage the development and implementation of the technique for inoperable CTEPH.

A

Table. Comparison of 2-years follow-up of optimal medical therapy (OMT) versus balloon pulmonary angioplasty (BPA) for inoperable chronic thromboembolic pulmonary hypertension

Variables*	Baseline			2-year follow-up			Baseline vs. 2-year follow-up	
	OMT (n=12)	BPA (n=7)	p-value†	OMT (n=12)	BPA (n=7)	p-value†	OMT (n=12)	BPA (n=7)
Clinical characteristics								
Age (years)	63.2 ± 18.3	68.1 ± 8.3	p = 0.42					
Female Gender (*n*, %)	12 (100%)	5 (71.4%)	p = 0.12					
Limited functional class(*n*, %)*	12 (100%)	4 (57.1%)	p = 0.04	10 (83.3%)	0	p < 0.01	p = 0.99	p < 0.01
6MWT (m)	225.3	312.0	p = 0.19	284.2	430.0	p = 0.01	p = 0.33	p = 0.20
NT-proBNP (pg/mL)	2670.0	538.0	p < 0.01	2004.0	132.0	p < 0.01	p = 0.33	p = 0.06
Haemodynamics features								
Mean PAP (mmHg)	47.5 ± 2.6	44.4 ± 14.6	p = 0.60	46.5 ± 6.6	25.1 ± 6.7	p < 0.01	p = 0.92	p = 0.01
Mean RAP (mmHg)	9.6 ± 3.8	6.4 ± 4.0	p = 0.14	10.0 ± 7.2	5.7 ± 2.4	p = 0.17	p = 0.77	p = 0.61
PVR (uWood)	19.7 ± 7.6	9.7 ± 5.4	p = 0.01	13.3 ± 6.8	2.9 ± 0.8	p = 0.05	p = 0.23	p = 0.01
Cardiac output (L/min)	2.9 ± 1.0	4.4 ± 1.1	p = 0.01	3.7 ± 0.5	5.0 ± 1.3	p = 0.09	p = 0.38	p = 0.21
Cardiac index (L/min/m^2)	1.6 ± 0.3	2.4 ± 0.5	p < 0.01	2.2 ± 0.3	2.6 ± 0.5	p = 0.12	p = 0.12	p = 0.36
SvO_2 (%)	58.8 ± 12.5	69.3 ± 12.6	p = 0.16	66.1 ± 2.8	70.4 ± 4.7	p = 0.19	p = 0.99	p = 0.28
Echocardiographic features								
RV dysfunction (*n*, %)	6 (50%)	3 (42.9%)	p = 0.64	5 (41.7%)	0	p = 0.02	p = 0.08	p < 0.01

* Functional Classification according World Health Organization: I – without limitation of physical activity; II – slight limitation of physical activity; III – marked limitation of physical activity; IV – inability to carry out any physical activity without symptoms.

Continuous variables are expressed as mean± standard deviation with exception of NT-proBNP and 6MWT expressed as median

† After adjustment by Cox regression, no difference in baseline or follow-up features besides treatment influenced the outcome

BPA – Balloon Pulmonary Angioplasty; OMT – Optimal Medical Treatment; NT-proBNP – N-terminal pro-brain natriuretic peptide; PAP – Pulmonary Artery Pressure; PVR – Pulmonary Vascular Resistance; RAP – Right atrial pressure; RA – Right atrial; RV – Right ventricular; 6MWT – Six-minute walking test; SvO_2 – Mixed venous oxygen saturation.

B