Pulmonary artery radiofrequency ablation in an acute porcine model of pulmonary arterial hypertension

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Introduction: Pulmonary hemodynamics improvement after pulmonary artery denervation (PADN) was demonstrated in PAH. Questions arise regarding PADN perioperative effectiveness and the accuracy of the target nerves damage. The aim of the study was to evaluate whether PADN decreases pulmonary artery pressure (PAP) in acute thromboxane A2 (U46619)–induced PAH, and damages PA perivascular nerve fibers.

Materials and methods: 10 male Landrace swine (34.7±5.1 kg). In 6 swine acute reversible target mean PAP of 40 mm Hg was induced with synthetic thromboxane A2 infusion (U46619). Control group: 4 swine with PADN. Hemodynamics was assessed throughout the study, PAH modeling was done before and 20 min after PADN (radiofrequency energy, 40 Watts), followed by pathology and immunohistochemical studies.

Results: The mean number of RF applications was 17.5±3.6. Pulmonary embolism (PE) was observed after PADN in 3 swine with U46619 infusion, which were excluded. There was no differences in mPAP, PVR and U46619 dosage after PADN in PAH model (12.3±3.5 vs 12.1±1 mm Hg, p=0.2; 150.4±48.7 vs 129.2±64.1 dynes s cm^{-5}; p=0.2; 24.9±3.3 vs 22.4±4.1 mcg; p=0.18; respectively). Similar hemodynamic results were observed in the control group after PADN (mPAP; p=0.3; PVR; p=0.58). S100 expression was evident in the majority of RFA PA species and in some species loss in tyrosine hydroxylase and M1 acetylcholine receptors expression was detected with no hemodynamic correlation.

Conclusions: PADN using an electrophysiological catheter with unipolar energy does not lead to an acute PA perivascular nerve fibers destruction and detectable mPAP changes in U46619-induced PAH. Delayed nerve damage might be attributable to PADN effects observed in previous studies.

Table 1 . Hemodynamic parameters at baseline, on PAH modeling I and PAH modeling II with U46619 infusion after PADN

		Baseline/PH1/PH2 modeling with U46619 (mcg*kgr^{-1})		HR, *beats/min.*	mBP, *mm Hg*	mPAP, *mm Hg*	PVR, *dynes/s/sm^{-5}*
Swine №1**	baseline	Time to target PH, min	U46619 dosage for target PH (mcg*kg^{-1})	86	60	12	251,2
	PH1	20	0,2	98	69	45	1753,6
	PH2	5	0,1	108	36	20	804
Swine №2	baseline			95	69	14	198,1
	PH1	35	0,175	94	71	37	1054,5
	PH2	30	0,15	90	70	35	1020,5
Swine №3	baseline			84	56	11	100,8
	PH1	25	0,15	109	102	40	532
	PH2	25	0,15	108	90	40	462,4
Swine №4**	baseline			112	67	7	92,2
	PH1	25	0,15	109	85	40	494,5
	PH2	25	0,15	94	65	40	823
Swine №5	baseline			90	73	18	152,5
	PH1	25	0,12	128	78	39	484,2
	PH2	20	0,1	115	60	40	1139
Swine № 6*	baseline			108	69	16	87,3
	PH1	20	0,1	129	91	42	306,1
	PH2 not done due to PE						

Footnote: *- thrombotic occlusion of the main left PA confirmed with angiopulmonography immediately after PA RFA. PAH modeling II was not conducted. ** - pulmonary embolism revealed on autopsy study; PA RFA – pulmonary artery radiofrequency ablation; HR - heart rate; mBP - mean arterial pressure; mPAP - mean pulmonary artery pressure; PVR - pulmonary vascular resistance.

Table 2 . Hemodynamic parameters at baseline and after PADN in animals with PAH modeling and without PE and animals without PAH modeling.

Baseline/after PA RFA		Ablations number	HR, *beats/min.*	mBP, *mm Hg*	mPAP, *mm Hg*	PVR, *dynes/s/sm^{-5}*
Swine № 2*	baseline	13	95	69	14	198,1
	after PA RFA		92	75	12	175,08
Swine № 3*	baseline	14	84	56	11	100,8
	after PA RFA		91	77	11	56
Swine № 5*	baseline	15	90	73	18	152,5
	After PA RFA		102	78	13	156,65
Swine № 7	baseline	21	75	59	15	249.8
	after PA RFA		85	56	14	171.7
Swine № 8	baseline	21	75	59	11	106.57
	after PA RFA		85	58	28	317
Swine № 9	baseline	21	106	72	9	93
	after PA RFA		114	60	11	71
Swine № 10	baseline	22	105	67	12	109
	after PA RFA		96	50	11	149.7

Footnote: *- swine with PAH U46619 induced without pulmonary embolism (PE); PADN – pulmonary artery denervation; HR - heart rate; mBP - mean arterial pressure; mPAP - mean pulmonary artery pressure; PVR - pulmonary vascular resistance