Title: REGIONAL MYOCARDIAL ISCHEMIA DEVELOPS DURING ACUTE PULMONARY HYPERTENSION WHEN RIGHT CORONARY ARTERY STENOSIS IS PRESENT

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Introduction. During increased right ventricular (RV) afterload, RV performance might critically depend on adequate coronary blood flow. Accordingly, the aim of this study was to evaluate the effects of an acute increase in RV afterload on global and regional RV function during right coronary artery (RCA) stenosis.

Methods. 9 open-chest, closed-pericardium, ventilated (FiO_2 1.0), and anesthetized (fentanyl and pentobarbital) dogs (21-34 kg) were studied. RCA blood flow (CBF) and pulmonary artery flow (PAF) were determined by electromagnetic flow probes, and regional RV myocardial performance by sonomicrometry. Piezoelectric crystals were inserted in the RV inflow tract (IT) within the territory of the RCA, and the RV outflow tract (OT). The ultrasonic signals were analyzed for end diastolic segment lengths (SL_{ED}), minimum, maximum and end systolic SL (SL_Smin, SL_Smax, SL_{ES}) and minimum diastolic SL (SL_Dmin). From these values systolic shortening, paradoxical systolic lengthening, and post systolic shortening were derived. 20 g of autologous sartorius muscle were chopped finely and suspended in 100 ml of normal saline containing 2000 U of heparin. - Protocol: After control measurements (C), RCA stenosis (S) to the point of abolished reactive hyperemia was induced by a cuff occluder placed around the RCA. Pulmonary hypertension (PH) was induced by repeated injections of small volumes of the muscle suspension via femoral vein until mean PA pressure (PAP) had approx. doubled. Subsequently, the stenosis was released, and measurements were repeated (PH Ø S) after CBF had stabilized following reactive hyperemia. Data were analyzed by Friedman's statistic and Wilcoxon signed-rank test.

Results. There were no significant ($p>0.05$) differences between C and S (Tables 1 and 2). PH was associated with increases in PAP, pulmonary vascular resistance (PVR), heart rate (HR), RVEDP and $PaCO_2$, and with decreases in PAF, stroke volume (SV), mean aortic pressure (AoP), PaO_2, and pH. In the RVOT, diastolic and systolic SL increased, but the contraction pattern remained qualitatively normal. In marked contrast, in the RVIT systolic shortening (ΔSL_{SS}) ceased, and paradoxical systolic lengthening (ΔSL_{SL}) and post systolic shortening (ΔSL_{PS}) developed in 8 animals. This was associated with a 60% decrease in CBF. Upon release of the stenosis, CBF increased fourfold, myocardial performance of the IT normalized, and AoP, PAF, and SV improved.

Discussion. These results indicate that severe regional RV myocardial dysfunction may develop during only moderate acute PH when RCA stenosis is present. Systolic lengthening and post systolic shortening indicate myocardial ischemia. Regional ischemia with subsequent worsening of global hemodynamics (PAF, SV, AoP) appears to have been secondary to insufficient blood supply. This is suggested by the findings that (a) CBF fell despite evidence of increased myocardial O_2 demand (increased RV dimensions and pressures, HR, PAP, and PVR), (b) a qualitatively normal contraction pattern was preserved in the normally perfused area of the RVOT, and (c) upon release of the stenosis with its resultant fourfold increase in CBF, contraction pattern in the RVIT normalized and global hemodynamics improved. The critically stenosed and thus, close to maximally dilated RCA seems unable to increase or even preserve flow when wall tension increases, and diastolic filling time and coronary perfusion pressure decrease. In conclusion, during increased RV afterload global and regional RV performance depend critically on adequate CBF. In this model, creation of the stenosis had no effect on resting CBF or on global or regional RV performance. Thus, patients although not exhibiting clinical symptoms of coronary insufficiency at rest, may develop severe regional myocardial dysfunction during only mild increases in PAP.

TABLE 1. GLOBAL HEMODYNAMICS AND GAS EXCHANGE

Variable	Control	Stenosis	PH	PH Ø S
PAP(mmHg)	11±1	11±1	21±1*	18±1*
PVR(units)	2.5±0.3	2.6±0.2	11.2±1.3*	7.8±0.7*
PAF(l/min)	1.6±0.2	1.7±0.2	1.4±0.2*	1.7±0.2*
HR(/min)	103±5	103±7	139±8*	122±6*
SV(ml/beat)	16±1	16±2	10±1*	14±1*
RVEDP(mmHg)	4.0±0.3	4.3±0.4	5.3±0.6*	4.3±0.6*
CBF(ml/min)	13±1	12±1	5±1*	20±2*
AoP(mmHg)	97±4	96±2	79±6*	94±2*
PaO_2(mmHg)	528±14	520±18	367±45*	427±47
$PaCO_2$(mmHg)	33±1	33±1	41±2*	40±2*
pH	7.44±0.01	7.44±0.01	7.35±0.02*	7.37±0.01*

Means ± SE. PH = pulmonary hypertension. PH Ø S = PH without stenosis. * = $p<0.05$ compared to preceding value. (See text for further abbreviations.)

TABLE 2. REGIONAL RV MYOCARDIAL PERFORMANCE

Variable	Control	Stenosis	PH	PH Ø S
RVIT				
SL_{ED}(mm)	10.0±0.4	10.0±0.3	10.9±0.4*	10.5±0.4*
SL_Smax(mm)	9.8±0.4	9.9±0.4	11.6±0.5*	10.5±0.4*
SL_Smin(mm)	8.5±0.3	8.5±0.3	10.9±0.4*	9.2±0.4*
SL_{ES}(mm)	9.0±0.4	8.9±0.4	11.0±0.5*	9.2±0.4*
SL_Dmin(mm)	9.0±0.4	8.9±0.4	10.4±0.4*	9.2±0.4*
ΔSL_{SS}(%)	14.6±1.2	14.5±1.4	0.0±1.2*	12.5±1.5*
ΔSL_{SL}(%)	0	0	6.7±0.9*	0.1±1.2*
ΔSL_{PS}(%)	0	0	5.0±1.2*	0*
RVOT				
SL_{ED}(mm)	9.3±0.4	9.4±0.4	9.9±0.4*	9.6±0.4*
SL_Smax(mm)	9.4±0.4	9.5±0.4	10.0±0.5*	9.7±0.4*
SL_Smin(mm)	7.9±0.3	7.9±0.3	8.5±0.4*	8.3±0.3*
SL_{ES}(mm)	8.0±0.3	8.0±0.3	8.7±0.4*	8.3±0.3*
SL_Dmin(mm)	8.0±0.3	8.0±0.3	8.6±0.3*	8.3±0.3*
ΔSL_{SS}(%)	15.0±1.1	15.7±0.8	13.3±1.8	13.5±1.0
ΔSL_{SL}(%)	0.2±0.2	0	0.2±0.2	0
ΔSL_{PS}(%)	0.2±0.2	0.2±0.2	1.0±0.4	0.4±0.3

Means ± SE. ΔSL_{SS} = systolic shortening. ΔSL_{SL} paradoxical systolic lengthening. ΔSL_{PS} = post systolic shortening. * = $p<0.05$ compared to preceding value. (See Table 1 and text for further abbreviations.)