International Journal of Cardiology 197 (2015) 227–234

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Is there a place for intra-aortic balloon counterpulsation support in acute right ventricular failure by pressure-overload?☆

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ARTICLE INFO

Article history:
Received 18 February 2015
Received in revised form 7 May 2015
Accepted 22 June 2015
Available online 27 June 2015

Keywords:
IABP
RV failure
Pressure overload
Hemodynamics

ABSTRACT

Background: Most therapeutic strategies for acute right ventricular failure (RVF) by pressure-overload are directed to improve cardiac output and coronary perfusion pressure by vasopressive agents. The eventual role of intra-aortic balloon counterpulsation (IABP) support remains questionable. This study investigates the contribution of IABP for acute RVF by pressure-overload, in comparison with phenylephrine (PE) and norepinephrine (NOR).
Methods: Acute RVF is induced by fixed pulmonary artery constriction in 6 pigs, pursuing a 50% reduction of cardiac output. Assessment of the treatment interventions included biventricular PV-loop analysis, and continuous measurement of aortic and right coronary artery flow.
Results: Restoration of baseline cardiac output was only observed by administration of NOR (Baseline = 3.82 ± 1.52 ml/min — RVF = 2.03 ± 0.59 ml/min — IABP = 2.45 ± 0.62 ml/min — PE = 2.98 ± 0.63 ml/min — NOR = 3.95 ± 0.73 ml/min, $p < 0.001$). NOR had most effect on biventricular contractility (PRSW-slope-RV: IABP +24% — PE +59% — NOR +208%, $p < 0.001$ and PRSW-slope-LV: IABP +36% — PE +53% — NOR +196%, $p < 0.001$), heart rate acceleration (IABP +7% — PE +12% — NOR +51%, $p < 0.001$), and RCA flow (IABP +31% — PE +58% — NOR +180%, $p < 0.001$), concomitant to a higher increase of LV-to-RV pressure ratio (IABP: +7% versus −3%, PE: +36% versus +8%, NOR: +101% versus 42%). The hemodynamic contribution of IABP was limited, unless a modest improvement of LV compliance during PE and NOR infusion.
Conclusion: In a model of acute pressure-overload RV failure, IABP appears to offer limited hemodynamic benefit. The administration of norepinephrine is most effective to correct systemic output and myocardial perfusion through adding an inotropic and chronotropic effect to systemic vasopression.

1. Introduction

Acute right ventricular failure by increased afterload is a common cause of circulatory insufficiency in the clinical setting of pulmonary embolism or pulmonary hypertension after heart transplantation. Several pathophysiological mechanisms have been accounted for the hemodynamic deterioration as the acute RV stretch leading primarily to decreased RV output, and compromising the LV function by the altered ventricular interdependence [1,2]. The contribution of ischemia is more debatable. The increased RV wall stress during acute ventricular dilation entails subendocardial RV ischemia, whereas the systemic hypotension further enhances the disturbed oxygen balance of the afterloaded RV by decreasing the coronary driving pressure and disruption of coronary autoregulation [3,4]. However, recent research has shown that ischemia does not seem to trigger pressure overload-induced RV dysfunction as long as adequate coronary perfusion pressure is maintained [5].

Most therapeutic strategies for pressure-induced RV failure are aiming to restore cardiac output through improving the ventricular interaction and increasing coronary perfusion pressure by use of systemic vasopressors [6,7]. Sometimes, ongoing hemodynamic deterioration during the interval awaiting for the efficacy of the target therapy, might ask for more advanced heart failure assistance. Based on the well-known advantages, i.e. systolic LV unloading and improved coronary perfusion during diastole, additional support by IABP warrants further study in these conditions of circulatory failure when particularly the RV is the predominantly failing ventricle. So far, the contribution of IABP as stand-alone therapy in this setting has been studied occasionally, yielding inconclusive results. Darrah et al. found a significant improvement of cardiac function during IABP support for RV failure, without clearly identifying the underlying mechanism [8]. Otherwise,

Abbreviations: RV, right ventricle; LV, left ventricle; PE, phenylephrine; NOR, norepinephrine; IABP, intra-aortic balloon pump; RCA, right coronary artery; RVF, right ventricular failure; ESV(P), end-systolic volume(pressure); EDV(P), end-diastolic volume(pressure); CO, cardiac output; PRSW, preload-recruitable stroke work.

☆ Statement of authorship: all authors take the responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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http://dx.doi.org/10.1016/j.ijcard.2015.06.092
0167-5273/

Liakopoulos et al. could not demonstrate any beneficial effect on RV performance with IAPB alone, whereas its application permitted to reduce the dosage of phenylephrine, which was more effective in this study [9]. In neither of both studies, the effect on myocardial blood flow was analyzed instantaneously.

This study aims to investigate the hemodynamic effectiveness of IABP in an animal model of acute RV failure by pressure-overload, through analysis of biventricular performance, systemic hemodynamics and coronary flow. In analogy to the current clinical approach based on the use of vasopressive agents, its adjunct effect was compared to the administration of phenylephrine as α-agonist, and to norepinephrine as a more potent agent with α- and β_1-activity.

2. Material and methods

The study protocol was performed according to the standards of "The guide for the Care and Use of Laboratory Animals" published by the National Institutes of Health (publication 85–23, revised 1996) and approved by the ethical committee for animal research of the Ghent University (ECD 13/30).

2.1. Experimental preparation

Seven landrace pigs (weight 55(1) kg) were included in the study. Following premedication with intramuscular tiletamine and zolazepam, in a combined solution with xylazine 2% (0.2 ml/kg), anesthesia was induced with intravenous propofol 3 mg/kg, sufentanil 0.005 mg/kg and rocuronium bromide 1 mg/kg. After endotracheal intubation, the animals were mechanically ventilated with FiO2 40% and tidal volume of 0.1–0.15 l/kg. Anesthesia was maintained with continuous sevoflurane ET 2.5% administered through the AnaConda® system (Sedana Medical, Sundbyberg, Sweden), and eventually additional boluses of sufentanil 0.005 mg/kg. Basic monitoring included electrocardiogram, body temperature and ventilatory CO2 emission through capnography. Oxygenation was controlled by arterial blood gas sampling. A central venous line was inserted via the external jugular vein, for isotonic saline infusion at a constant rate of 3–5 ml/kg/h. The left carotid artery was punctured with a 8.5 F catheter, through which a 7 F dual-field pressure–volume catheter (CD Leycom, Zoetermeer, Netherlands) was introduced into the LV. The left femoral artery was exposed for insertion of a 34 cc intra-aortic balloon catheter (Sensation IAB catheter, Maquet Getinge Group, Rastatt, Germany) through a 9 F introducer sheet, and positioned into the descending aorta under fluoroscopic control. The IABP was then connected to the counterpulsation unit (CS300, Maquet Getinge Group) and adjusted for maximal pressure augmentation during ECG-mediated T-wave triggering.

The heart was exposed through midline sternotomy and longitudinal opening of the pericardium. A second 7 F dual-field pressure–volume catheter (CD Leycom, Zoetermeer, Netherlands) was inserted into the RV via puncture of the right ventricular outflow tract. The pulmonary artery was encircled with an umbilical tape with tourniquet for controlled pulmonary artery constriction. A 18-mm perivascular flow probe (Transonic Systems, Ithaca, NY, USA) was put around the ascending aorta for continuous measurement of cardiac output. A 3.0-mm flow probe (Transonic Systems) was placed around the proximal RCA for coronary flow analysis. A second tourniquet was placed at the inferior vena cava for pre-load modulation during hemodynamic measurements. Both pressure–volume catheters were connected to the Sigma M module for simultaneous biventricular loop recording and digitized at 250 Hz for on-line computer analysis with the Conduct NT software (CD Leycom). Acquisition of pressure and volume data was obtained at end-expiration. Volume calibration was performed by integration of slope factor α for cardiac output, and by parallel conductance during injection of 0.02 ml/kg hypertonic saline. Baseline measurements included the determination of ventricular volumes and pressures in end-systole and end-diastole, with subsequent calculation of stroke volume (SV), ejection fraction (EF) and systemic vascular resistance. Continuous arterial pressure was obtained from the IABP line. Pulmonary artery pressure monitoring was not performed because of poor reliability through conflict during experimental pulmonary artery constriction. Based on the instantaneous pressure–volume relationship changes during transient occlusion of the inferior vena cava, the contractility of LV and RV was quantified by the M_w-slope of the PRSW, as most reliable load-independent index of contractility. Evaluation of diastolic function was based on passive ventricular compliance, expressed as chamber stiffness-constant β, derived from the exponential fit of the end-diastolic pressure–volume curve. Only recordings with less than 10% heart rate change and a correlation–coefficient of the linear regression line $r^2 > 0.90$ were considered eligible.

Table 1
Systemic and ventricular hemodynamic data.

	Baseline	RVF	+ IABP	+ PE	+ PE + IABP	+ NOR	+ NOR + IABP	p-Value Friedman
Right ventricle								
ESP (mm Hg)	24 (2)	64 (4) *	62 (6)	69 (6)	67 (5)	89 (4) #,†	87 (6) #,†	0.003
EDP (mm Hg)	5 (1)	10 (2) *	9 (2)	11 (2)	10 (2)	13 (2)#,†	12 (2)	0.004
ESV (ml)	33 (2)	81 (7) *	78 (8)	76 (7)	72 (6)	59 (6) #,‡	57 (5) #,‡	<0.0001
EDV (ml)	94 (6)	120 (13) *	119 (13)	117 (12)	111 (11)	101 (10)#	102 (10)#	0.012
SV (ml)	61 (6)	39 (7) *	41 (7)	41 (6)	39 (6)	42 (6)	45 (6)	0.18
EF (%)	64 (3)	32 (3) *	33 (4)	34 (3)	35 (3)	41 (3)#,‡	43 (3)#,‡	<0.001
SW (ml/mm Hg)	893 (91)	545 (72) *	582 (131)	892 (200)	935 (175)	1243 (144)#,†	1419 (171)#,†	<0.0001
Mw-slope (Mw.s/ml)	17.6 (2.0)	10.9 (1.2) *	13.7 (2.2)	17.3 (2.5) #	16.7 (2.4) #	33.5 (4.5) #,‡	32.7 (4.0) #,‡	0.001
β (ml^{-1})	0.06 (0.01)	0.14 (0.02)*	0.10 (0.01)	0.14 (0.02)	0.14 (0.02)	0.18 (0.01) #,†	0.16 (0.01)	0.03
Left ventricle								
ESP (mm Hg)	81 (4)	54 (4) *	57 (5)	71 (4) #,§	72 (5) #,§	103 (9)#,‡	101 (10)#,‡	<0.0001
EDP (mm Hg)	10 (1)	5 (1) *	6 (1)	7 (1)#	7 (1)#	9 (1)#,†	9 (1)#,†	0.023
ESV (ml)	33 (4)	35 (5)	34 (5)	33 (4)	31 (4)	28 (4)	27 (4) #	0.045
EDV (ml)	90 (4)	54 (8) *	55 (7)	54 (6)	53 (6)	49 (5)	48 (6)	0.38
SV (ml)	57 (3)	19 (3) *	20 (2)	22 (2)	23 (3)	21 (3)	22 (3)	0.65
EF (%)	64 (3)	35 (1) *	37 (1)	40 (1)	43 (2)#	44 (4)#	46 (4)#,†	0.007
SW (ml/mm Hg)	2294 (241)	1466 (264)*	1642 (316)	2038 (286)#,§	2130 (267)#,§	3151 (360)#,‡	3203 (384)#,‡	<0.0001
Mw-slope (Mw · s/ml)	77.3 (15.2)	40.5 (6.5)*	56.2 (11.6) #	63.4 (13.8) #	72.8 (12.2) #	103.6 (13.0) #,‡	106.7 (14.7) #,‡	0.008
β (ml^{-1})	0.21 (0.03)	0.15 (0.03)	0.15 (0.02)	0.21 (0.02) #,§	0.17 (0.03) #,§§	0.35 (0.09) #,‡	0.29 (0.06) #,‡,§§	0.003
Systemic parameters								
HR (bpm)	80 (6)	86 (3)	92 (4)	97 (6)	101 (5)	130 (7)#,‡	130 (6)#,‡	<0.0001
CO (ml/min)	3.8 (0.6)	2.0 (0.2)*	2.4 (0.3) #	3.0 (0.3) #,§	3.2 (0.2) #,§	4.0 (0.3) #,‡	4.0 (0.3) #,‡	<0.001
RCA flow (ml/min)	38.8 (6.4)	34.0 (4.8)	44.3 (6.9) #	52.8 (7.8) #	55.5 (7.2) #	92.2 (13.7) #,‡	91.7 (12.9) #,‡	<0.001
SVR (dyn · s · m^{-5})	817 (76)	1168 (118)	1118 (113)	1324 (215)	1266 (229)	1571 (328)	1464 (300)	0.81

Data represent mean and SEM.
$p < 0.05$ of Friedman test represents a significant difference for the comparison between treatments and RVF (not to baseline).
ESP = end-systolic pressure, EDP = end-diastolic pressure, ESV = end-systolic volume, EDV = end-diastolic volume, SV = stroke volume, EF = ejection fraction, SW = stroke work, SVR = systemic vascular resistance, HR = heart rate, Mw-slope = regression slope of preload-recruitable stroke work, β = myocardial stiffness constant, CO = cardiac output, RCA = right coronary artery.
* $p < 0.05$ for difference between Baseline and RVF.
# $p < 0.05$ for difference between Treatment and RVF.
† $p < 0.05$ for difference in-between Treatment arms NOR/NOR + IABP and IABP.
‡ $p < 0.05$ for difference in-between Treatment NOR/NOR + IABP and other Treatments.
§ $p < 0.05$ for difference in-between Treatment PE/PE + IABP and IABP.
§§ $p < 0.05$ for difference in-between Treatment PE and PE + IABP, and Treatment NOR and NOR + IABP.