Effects of milrinone and epinephrine or dopamine on biventricular function and hemodynamics in right heart failure after pulmonary regurgitation

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Hyldebrandt JA, Agger P, Sivén E, Wemmelund KB, Heiberg J, Frederiksen CA, Ravn HB. Effects of milrinone and epinephrine or dopamine on biventricular function and hemodynamics in right heart failure after pulmonary regurgitation. Am J Physiol Heart Circ Physiol 309: H860–H866, 2015. First published June 19, 2015; doi:10.1152/ajpheart.00384.2015.—Right ventricular failure (RVF) due to pulmonary regurgitation is a common sequel of congenital heart disease and is associated with high mortality rates. The scientific evidence behind the management of RVF secondary to pulmonary regurgitation (PR) is limited and often ignores the biventricular aspects of RV dysfunction. The aim of this study was to compare the effects of milrinone with epinephrine and dopamine in a model of right ventricular failure secondary to pulmonary regurgitation.

Research Design and Methods

Hypothetical right ventricular outflow tract obstruction was induced by surgically disabling the pulmonary valve leaflets in 23 Danish landrace piglets weighing 5 kg (aged 2 wk) by disabling the apposition of 2 of 3 valve leaflets (1). The animals were reexamined after 79 (SD 7) days, at which point they had developed right ventricular dysfunction. Twenty-three animals with normal pulmonary valve function served as controls (16). The Danish landrace pig

Pulmonary regurgitation was surgically established in 23 Danish landrace piglets weighing 5 kg (aged 2 wk) by disabling the apposition of 2 of 3 valve leaflets (1). The animals were reexamined after 79 (SD 7) days, at which point they had developed right ventricular dysfunction. Twenty-three animals with normal pulmonary valve function served as controls (16). The Danish landrace pig
can be sexually active at age 4 mo, and the animals were therefore in late childhood/early adulthood at the time of examination.

**Induction of RV heart failure.** The investigation conformed to the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH Publication No. 85-23, revised 1996) and was approved by the Danish Animal Experiments Inspectorate, license number: 2012-15-2934-00219.

The animals were premedicated and anesthesia was induced using standard procedures as previously described (16). Pancuronium 0.1 mg/kg (Actavis, Munich, Germany) was administered to achieve muscle relaxation. Prior to surgery, the animals were given prophylactic antibiotics, penicillin 100,000 IU (Ceva Animal Health, Vejle, Denmark) im, and analgesia, flunixin 25 mg (MSD Animal Health, Ballerup, Denmark) im. Over the following 5 days, the veterinary technicians administered 25 mg flunixin po and 100,000 IU penicillin im once daily and paracetamol 250 mg (Actavis, Gentofte, Denmark) po twice daily.

**Reexamination.** On the day of reexamination, the animals were anesthetized using the same protocol, omitting pancuronium to avoid tachycardia. To avoid arrhythmias, the animals were given amiroidone 5 mg/kg (Cordarone, Sanofi-Aventis, Denmark) infused over 10 min prior to the intervention and at least 60 min prior to baseline measurements. The animals were ventilated (S/5 Avance Datex Ohmed, GE Healthcare) with a tidal volume of 10 ml/kg, respiration rate of 14, fraction of inspiratory oxygen of 35%, and positive end-expiratory pressure of 4 cmH2O. Ventilation was adjusted to maintain partial pressure of carbon dioxide in the arterial blood at ~40 mmHg. Arterial blood gases were analyzed (ABL, Radiometer, Denmark) every 30 min to ensure normal ventilation and oxygenation. Body temperature was maintained within the normal range (38–39°C) using a warming blanket. Hydration was maintained with isotonic sodium chloride (4 ml·kg\(^{-1}\)·h\(^{-1}\)), and an isotonic sodium-chloride infusion administered to match the urine output in the previous 30 min. Because there was no difference in urine output between the groups, the amount of administered fluid was equal. The animals had previously been examined using an identical anesthetic protocol (16).

Four sheaths were inserted bilaterally into the jugular veins and carotid arteries. The animals were given 150 IU/kg of heparin prior to catheter insertion to avoid clotting of the sheaths.

**Hemodynamics measurements.** A Swan-Ganz catheter (7.5F CCOmbo, Edwards Lifescience, Irvine, CA) was inserted in the pulmonary artery to continuously measure CO and mixed-venous oxygen saturation (SVO\(_2\), %). CO, stroke volume (SV), and ventricular volumes were indexed to body surface area (BSA, m\(^2\)) using the formula: 0.0734·(body weight, kg\(^{0.656}\)) (17). Mean arterial pressure (MAP, mmHg), mean pulmonary artery pressure (mPAP, mmHg), and central venous pressure (CVP, mmHg) were continuously recorded using pressure transducers (TruWave, Edwards Lifescience, Germany) throughout the experiment. Heart rate (HR, beats/min) was derived from the arterial pressure curve.

**Calculations.** The systemic vascular resistance index (SVRI, dyn·s·cm\(^{-5}\)·kg\(^{-1}\)) and pulmonary vascular resistance index (PVR, dyn·s·cm\(^{-5}\)·kg\(^{-1}\)) were calculated as 80[(MAP – CVP)/CO]·kg and 80[(mPAP – LV minimum pressure (P\(_{min}\))/CO]·kg, respectively.

**Ventricular measurements.** Guided by fluoroscopy, pressure-volume catheters (Ventric-Cath 510, Millar instruments) were inserted antegrade into the right ventricle and retrograde into the left ventricle. Volumes were calibrated using an alpha correctional value, and parallel wall conductance was determined using the hypertonic saline method (9). Calibration and preload occlusion measurements were performed for each ventricle with the other catheter disconnected to avoid the possibility of cross-talk. A Fogarty occlusion catheter (Boston Scientific, Denmark) was positioned in the inferior caval vein to induce preload reduction.

Maximum rate of pressure change (dP/d\(_{max}\), mmHg/s), the slope of preload recruitable stroke work (PRSW, mmHg·ml·ml\(^{-1}\)), and maximum ventricular pressure (P\(_{max}\)) were used as measures of systolic function. The end-diastolic pressure-volume relationship (EDPVR, mmHg/ml) was used as a parameter for ventricular stiffness, and the isovolumic relaxation constant (Weiss method) (tau, ms) was used as the parameter for active diastolic relaxation. Tau was only determined for the left ventricle because a right ventricle with PR lacks an isovolumetric phase. Arterial elastance (Ea, mmHg/ml) was determined as a measure of afterload. End-diastolic volume was determined for both ventricles and indexed to BSA (EDVI, ml/m\(^2\)). Signals were sampled by an MPVS Ultra (Millar Instruments), processed in PowerLab 16/35 (ADInstruments, UK), and recorded at 2 kHz and analyzed in LabChart 7 Pro (ADInstruments, UK).

**Assessment of septum deviation.** Echocardiography was performed using a Vivid S6 system (GE Healthcare, Horten, Norway), equipped with a M4S phased-array transducer (GE Healthcare). One investigator obtained echocardiographic images of all pulmonary artery-banded animals in the parasternal short-axis view profiling the ventricular septum. Another investigator quantified the ventricular septal position, in a blinded manner, using the eccentricity index (EI) in diastole and systole (26). A value of 1.0 defined the normal circular left ventricle.

**Experimental protocol.** After a 60-min stabilization period, the animals were treated with milrinone (Sanofi-Aventis, Hoersholm, Denmark) using a loading dose of 5 µg·kg\(^{-1}\)·min\(^{-1}\) over 10 min and followed by an infusion of 0.5 µg·kg\(^{-1}\)·min\(^{-1}\). The animals were randomized to treatment with incremental doses of either epinephrine (Nynomed, Roskilde, Denmark) at 0.04, 0.06, and 0.08 µg·kg\(^{-1}\)·min\(^{-1}\) or dopamine (Orion Pharma, Nivå, Denmark) at 4, 6, and 8 µg·kg\(^{-1}\)·min\(^{-1}\), with each step lasting 30 min (Fig. 1). Stable hemodynamics were a prerequisite before recording data.

**Statistics.** Differences between pulmonary artery-banded animals and controls were assessed with a two-tailed Student’s \(t\)-test for normally distributed data with equal variances, Welch’s \(t\)-test for normally distributed data with unequal variances, and Wilcoxon rank-sum test for nonparametric data. The assumptions of normal distribution and equal variance were tested using quantile-quantile plots and a variance-ratio test.

Differences between the baseline and post-milrinone treatment were analyzed using a two-tailed paired Student’s \(t\)-test, or Wilcoxon matched-pairs signed rank test in the case of nonparametric data. To test the hypothesis that there was no difference between epinephrine-treated and dopamine-treated animals with increasing doses, repeated-measures ANOVA was used to determine between-group
differences (epinephrine vs. dopamine) and dose-dependent differences. The assumptions of the model were confirmed by inspecting scatterplots of the residuals vs. fitted values and normal quantile plots of the residuals. Nonnormally distributed data were transformed to a logarithmic scale to ensure normality and constant variance. The data were analyzed to determine whether there were significant differences between the epinephrine and dopamine groups at baseline and post-milrinone infusion to ensure data comparability. Correlations between parameters were tested using the Pearson correlation coefficient and the square of the sample correlation coefficient ($r^2$), and significance values were reported. The data were reported as the mean and SD. A $P$ value $<0.05$ was considered statistically significant. All variables are graphically presented on the original scale of measurement.

**RESULTS**

Pulmonary regurgitation was induced in 23 pigs, of which 16 survived until the time of reexamination. At that time, all of the animals suffered from RV failure as demonstrated by tachypnea and lower activity compared with controls.

**Effects of pulmonary regurgitation.** Seventy-nine days after the induction of PR, the RV-EDVI increased by 33% ($P = 0.006$), while the LV-EDVI volume remained stable. A significant decrease of 58% ($P = 0.003$) in RV contractility was observed, despite the fact that RV $P_{\text{max}}$ and mPAP were unchanged. In contrast, LV-Pmax was significantly reduced, by 18% ($P = 0.002$).

A 15% decrease in MAP ($P = 0.01$) and 28% decrease in CI ($P < 0.0001$) were observed concomitantly with a significant decrease of 36% in $SvO_2$ ($P < 0.0001$).

There was reduced systolic function after 10 wk with PR, as indicated by a significantly reduced RV-PRSW ($P < 0.01$), but otherwise, the main diastolic function was unaltered. Ventricular compliance was decreased in both ventricles, primarily in the RV, with a 137% increase in RV-EDPVR ($P = 0.0006$). LV impairment was associated with a marked displacement of the interventricular septum, and the eccentricity index was $E_{\text{dia}} = 1.14$ in the PR animals (Table 1). A strong correlation was found between SVI and LV-EDVI ($r^2 = 0.65, P = 0.0002$), and a weak correlation was found between SVI and RV-EDVI ($r^2 = 0.29, P = 0.03$). No correlation was found between SVI and RV-PRSW ($r^2 = 0.02, P = 0.5$) or LV-PRSW ($r^2 = 0.05, P = 0.4$) (Fig. 2).

**Effects of milrinone.** Milrinone significantly increased CI ($P < 0.0001$), $SvO_2$ ($P = 0.02$), and HR ($P < 0.0001$), but SVI remained stable (Table 2). Despite a significant fall in SVRI ($P = 0.0002$), the MAP was unchanged. The vasodilating effects were equal in the systemic and pulmonary systems, as indicated by an equal PVRI/SVRI ratio. Ea was unchanged in both ventricles. In terms of contractility, RV-PRSW increased by 32% ($P = 0.002$) but was unaffected in the LV. Active relaxation in diastole (tau) was improved in both ventricles, while ventricular compliance (EDPVR) remained unchanged in both the RV and LV (Table 3).

**Effects of dopamine and epinephrine.** Both catecholamines increased CI and $SvO_2$ significantly, but there was no significant difference between the two interventions. The increase in CI was related to an increase in HR, as SVI remained unaltered both following dopamine and epinephrine. MAP was significantly higher in the dopamine-treated animals compared with epinephrine-treated animals ($P = 0.009$) and was associated with a significantly higher SVRI in the dopamine-treated animals. Likewise, mPAP and PVRI were significantly higher in the dopamine-treated animals ($P < 0.0001$) and SVRI remained stable (Table 2). Despite a significant fall in MAP, $SvO_2$ and $SvO_2$% was significantly higher in the dopamine-treated animals compared with the epinephrine group, and a higher $P_{\text{max}}$ was observed in the LV following dopamine infusion (Fig. 3).
DISCUSSION

Seventy-nine days after PR was established, right ventricular failure had developed, with increased RV EDVI and ventricular stiffness associated with severely impaired RV contractility and diastolic function, while LV contractility was preserved. The increase in RV EDV shifted the interventricular septum towards the LV, and in association with these findings, a decrease in LV Pmax, MAP, CI, and SvO2 was observed. Milrinone increased contractility in the failing RV, but not in the LV, whereas a lusitropic effect was observed in both ventricles. The inodilator significantly improved CI and SvO2 and reduced SVRI while maintaining MAP. Intravenous infusions of either epinephrine or dopamine further increased CI, HR, SvO2, and biventricular contractility equally in a dosedependent manner. Dopamine-treated animals had a greater vasopressor effect in both the systemic and pulmonary circulation.

Table 2. Effects of milrinone, epinephrine, and dopamine treatment on hemodynamics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Milrinone</th>
<th>Inotrope</th>
<th>Inotrope Baseline</th>
<th>Inotrope Level 1</th>
<th>Inotrope Level 2</th>
<th>Inotrope Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>CI, l·min⁻¹·m⁻²</td>
<td>3.5 (0.5)</td>
<td>4.0 (0.5)**</td>
<td>IPI</td>
<td>4.1 (0.6)</td>
<td>5.1 (1.1)</td>
<td>5.8 (1.3)</td>
<td>6.5 (1.4)††</td>
</tr>
<tr>
<td>SVI, ml/m²</td>
<td>48 (8)</td>
<td>49 (7)</td>
<td>DA</td>
<td>4.0 (0.5)</td>
<td>4.9 (0.8)</td>
<td>5.4 (0.9)</td>
<td>5.8 (0.9)††</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>74 (12)</td>
<td>84 (14)**</td>
<td>DA</td>
<td>85 (4)</td>
<td>116 (14)</td>
<td>128 (15)</td>
<td>137 (12)††</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>70 (13)</td>
<td>69 (14)</td>
<td>DA</td>
<td>66 (8)</td>
<td>68 (11)</td>
<td>63 (10)</td>
<td>61 (11)‡</td>
</tr>
<tr>
<td>SVRI, 80·dyn·s·cm⁻⁵·m⁻²</td>
<td>1,444 (316)</td>
<td>1,246 (271)*</td>
<td>EPI</td>
<td>1192 (154)</td>
<td>999 (253)</td>
<td>819 (172)</td>
<td>61 (11)§</td>
</tr>
<tr>
<td>LV Ea, ml/mmHg</td>
<td>2.88 (1.01)</td>
<td>2.8 (0.98)</td>
<td>DA</td>
<td>2.71 (1.05)</td>
<td>2.32 (0.76)</td>
<td>2.28 (0.85)</td>
<td>2.61 (1.45)</td>
</tr>
<tr>
<td>mPAP, mmHg</td>
<td>16 (2)</td>
<td>17 (3)</td>
<td>DA</td>
<td>17 (3)</td>
<td>19 (3)§</td>
<td>19 (2)#</td>
<td>20 (3)++</td>
</tr>
<tr>
<td>PVRI, dyn·s·cm⁻⁵·m⁻²</td>
<td>277 (87)</td>
<td>257 (88)</td>
<td>EPI</td>
<td>244 (76)</td>
<td>193 (60)</td>
<td>185 (60)</td>
<td>160 (24)††</td>
</tr>
<tr>
<td>RV Ea, ml/mmHg</td>
<td>0.87 (0.25)</td>
<td>0.85 (0.22)</td>
<td>DA</td>
<td>267 (85)</td>
<td>267 (85)</td>
<td>261 (60)</td>
<td>241 (58)</td>
</tr>
<tr>
<td>SvO2, %</td>
<td>56 (8)</td>
<td>60 (8)*</td>
<td>EPI</td>
<td>80 (1.17)</td>
<td>102 (0.36)</td>
<td>99 (0.32)</td>
<td>1.04 (0.3)</td>
</tr>
<tr>
<td>CVP, mmHg</td>
<td>3.7 (3)</td>
<td>3 (6)*</td>
<td>DA</td>
<td>7 (3)</td>
<td>6 (3)</td>
<td>6 (3)</td>
<td>5 (2)</td>
</tr>
</tbody>
</table>

Data are means (SD). Epinephrine (EPI) level 1: 0.04 μg·kg⁻¹·min⁻¹; level 2: 0.06 μg·kg⁻¹·min⁻¹; level 3: 0.08 μg·kg⁻¹·min⁻¹. Dopamine (DA) level 1: 4 μg·kg⁻¹·min⁻¹; level 2: 6 μg·kg⁻¹·min⁻¹; level 3: 8 μg·kg⁻¹·min⁻¹. CVP, central venous pressure. *P < 0.05, **P < 0.0001 vs. baseline. Dose-dependent change from milrinone: †P < 0.05. ††P < 0.0001. Significant difference in effect of epinephrine and dopamine: §§P < 0.05, §§§P < 0.0001. Significant difference between epinephrine and dopamine at this inotrope level: #P < 0.05.
Following 11 wk of PR, the classical features of right heart failure secondary to volume overload were pronounced, with right ventricular dilatation (4–6, 10, 19, 20, 24, 27), decreased RV contractility (20), reduced compliance (2–4, 20), a leftward septal shift in the diastolic phase, and compromised LV pressure generation (1, 19). The degree of change in RV EDVI and LV EDVI was close to what have been described as the difference in healthy adults and patients with repaired tetralogy of Fallot (28). Previous studies have mainly focused on the surgical or catheter-based treatment options, particularly valve replacement to correct the underlying cause (10, 19, 27). This study’s main objective was to evaluate the effect of medical treatment in patients admitted with RV failure in the presence of volume overload.

The effect of chronic PR on RV contractility has previously been determined by echocardiography using tissue Doppler. Although isovolumetric acceleration has been found to be a reliable measure of RV contractility (30), Kjaergaard and colleagues found no significant changes in isovolumetric acceleration, indicating preserved contractility in pigs after 3 mo of free PR (19). These observations were continued despite the fact that animals had developed severe RV dilatation and an increased eccentricity index, similar to the present study. In this respect, one of the strengths of this study is the load-independent evaluation of biventricular contractility, and accurate determination of changes in ventricular volumes (4) using the conductance catheter technique. Using the latter technique, we observed severely decreased RV contractility, as indicated by PRSW. This is in accordance with the results from studies by Bove and colleagues in animals with surgically induced pulmonary valve incompetence (4, 5). The discrepancy between the two methodologies emphasizes the difficulty of noninvasively assessing RV failure, as noted by the Kjaergaard group (19); in experimental animal models, RV contractility should ideally be evaluated with invasive techniques.

### Table 3. Effects of milrinone, epinephrine, and dopamine treatment on biventricular diastolic function

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Milrinone</th>
<th>Milrinone Inotrope</th>
<th>Milrinone Inotrope Level 1</th>
<th>Milrinone Inotrope Level 2</th>
<th>Milrinone Inotrope Level 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV tau, ms</td>
<td>73 (25)</td>
<td>62 (20)*</td>
<td>EPI 62 (24)</td>
<td>53 (18)</td>
<td>44 (20)</td>
<td>48 (21)†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DA 63 (18)</td>
<td>60 (18)</td>
<td>51 (21)</td>
<td>51 (20)†</td>
</tr>
<tr>
<td>LV tau, ms</td>
<td>39 (6)</td>
<td>36 (5)**</td>
<td>EPI 35 (6)</td>
<td>28 (5)</td>
<td>27 (6)</td>
<td>28 (7)††</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DA 37 (5)</td>
<td>32 (6)</td>
<td>29 (5)</td>
<td>28 (5)††</td>
</tr>
<tr>
<td>RV EDPVR, ml·mmHg</td>
<td>0.38 (0.19)</td>
<td>0.31 (0.16)</td>
<td>EPI 0.32 (0.17)</td>
<td>0.31 (0.22)</td>
<td>0.27 (0.15)</td>
<td>0.28 (0.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DA 0.3 (0.16)</td>
<td>0.41 (0.32)</td>
<td>0.27 (0.11)</td>
<td>0.39 (0.23)</td>
</tr>
<tr>
<td>LV EDPVR, ml·mmHg</td>
<td>0.27 (0.1)</td>
<td>0.26 (0.12)</td>
<td>EPI 0.31 (0.15)</td>
<td>0.29 (0.15)</td>
<td>0.23 (0.13)</td>
<td>0.26 (0.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DA 0.22 (0.08)</td>
<td>0.25 (0.05)</td>
<td>0.28 (0.1)</td>
<td>0.26 (0.06)</td>
</tr>
</tbody>
</table>

Data are means (SD). Epinephrine (EPI) level 1: 0.04 μg·kg⁻¹·min⁻¹; level 2: 0.06 μg·kg⁻¹·min⁻¹; level 3: 0.08 μg·kg⁻¹·min⁻¹. Dopamine (DA) level 1: 4 μg·kg⁻¹·min⁻¹; level 2: 6 μg·kg⁻¹·min⁻¹; level 3: 8 μg·kg⁻¹·min⁻¹. EDPVR, end-diastolic pressure-volume relationship. Milrinone vs. baseline: *P < 0.05, **P < 0.0001. Dose-dependent change from milrinone: †P < 0.05, ††P < 0.0001.
Milrinone is currently used in many pediatric cardiac centers as the primary inodilator after cardiac surgery irrespective of right or left ventricle failure (15, 31). Milrinone significantly increased CI and SvO$_2$ and caused a better off-loading of the RV, as demonstrated by a decrease in CVP. These beneficial changes were primarily due to increased contractility in the RV and the chronotropic effect of the drug. Despite the improvement in active relaxation, ventricular compliance was unaltered, resulting in no SVI improvement. Despite a significant decrease in SVRI, MAP remained stable during the milrinone infusion, but the prolonged decrease in SVRI after the initiation of catecholamines is most likely related to a progression of the vasodilatory effect of the drug (22).

This is the first study in which catecholamines have been investigated for RV failure secondary to RV dilation. Dopamine and epinephrine, two of the most commonly used inotropes, were studied in combination with milrinone (31). The choice of catecholamines was based on frequency of use (31), comparable chronotropic effects, and differentiated vasocnstrictor potency (23).

Hemodynamically, both catecholamines significantly increased CI and SvO$_2$ but did not significantly change SVI, indicating that the increase in CI was mainly related to an increase in the heart rate, in accordance with previous observations (20). The catecholamines were expected to have comparable chronotropic effects, whereas epinephrine is considered to be superior in terms of its inotropic potency, and dopamine has a more marked vasopressor effect (23). In terms of contractility, no significant difference was found between the two drugs in combination with milrinone. Although SVRI and MAP were higher in the dopamine-treated animals, SVRI decreased in both groups over time. This decrease is most likely related to an extended effect of milrinone.

Milrinone could not increase SVI, either alone or in combination with a catecholamine, despite great improvements in biventricular contractility. This observation is in accordance with recent studies that have demonstrated the importance of the interventricular relation during RV failure (2, 3, 18). In case of increased RV afterload, the interventricular septum is shifted towards the left ventricle in both systole and diastole. Apitz and colleagues (2) have previously shown how increases in LV afterload will improve CI in acute RV pressure-overload; however, their study did not include a study of biventricular volumes or eccentricity index. Our results are in accordance with this, and we further showed how increases in contractility alone cannot improve SVI, since only the chronotropic effect of the catecholamines had a positive influence on CI. This is the first study describing these observations with RV failure secondary to PR, and underlines the importance of LV afterload and the interventricular relationship in patients with pressure-overloaded RV failure.

There are a number of limitations that need to be considered in the present study. First, echocardiography was not performed during or after the infusion of milrinone and catecholamines. Although the determination of biventricular volumes provided insight into the ventricular-ventricular relation, we cannot conclude whether the eccentricity index approached normalization or further deteriorated after administration of catecholamines. A longer observation period would have improved the external validity; however, prolonged anesthesia would have influenced cardiac function and hemodynamics, interfering with the interpretation of measurements.

Conclusions. The present study demonstrated that in RV failure secondary to volume overload after pulmonary regurgitation, milrinone significantly improved CI, SvO$_2$, and CVP and increased contractility in the failing RV. The addition of epinephrine or dopamine further increased CI and SvO$_2$ and biventricular contractility, but higher MAP values were observed in dopamine-treated animals. Neither of the catecholamines could improve SVI, due to its strong correlation to LV EDVI rather than contractility.

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DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

REFERENCES


