Reversible pulmonary trunk banding: VII. Stress echocardiographic assessment of rapid ventricular hypertrophy in young goats

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Background: Ventricle retraining with abrupt systolic overload can cause myocardial edema and necrosis, followed by late ventricular failure. Intermittent systolic overload could minimize the inadequacy of conventional pulmonary artery banding. The present study compared ventricle function under dobutamine stress in 2 protocols of systolic overload in young goats.

Methods: Nineteen young goats were divided into 3 groups: sham (n = 7; no systolic pressure overload), continuous (n = 6; systolic overload maintained for 96 hours), and intermittent (n = 6; 4 periods of 12-hour systolic overload, paired with a 12-hour resting period). Echocardiographic and hemodynamic evaluations were performed daily. The myocardial performance index and ejection fraction were evaluated at rest and during dobutamine stress. The goats were then killed for morphologic evaluation.

Results: The intermittent group underwent less systolic overload than the continuous group ($P < .05$). Nevertheless, both groups had increased right ventricular and septal masses compared with the sham group ($P < .0002$). Echocardiography revealed a major increase in right ventricular wall thickness in the intermittent group (+64.8% ± 23.37%) compared with the continuous group (+43.9% ± 19.26%; $P = .015$). Only the continuous group remained with significant right ventricular dilation throughout the protocol ($P < .001$). The intermittent group had a significantly better myocardial performance index at the end of the protocol, under resting and dobutamine infusion, compared with the continuous group ($P < .012$).

Conclusions: Both systolic overload protocols have induced rapid right ventricular hypertrophy. However, only the intermittent group had better preservation of right ventricular function at the end of the protocol, both at rest and during dobutamine infusion. (J Thorac Cardiovasc Surg 2013;145:1345-51)

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In developing countries, the number of patients with transposition of the great arteries (TGA) presenting beyond the neonatal period is still considerable. In this scenario, complete anatomic repair must be preceded by left ventricle retraining with pulmonary artery banding, to enable the ventricle to handle the systemic circulation. Concern is increasing about the quality of subpulmonary ventricle retraining, aiming at the most physiologic hypertrophic process to avoid late ventricular dysfunction.[1]

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Previous studies have looked for better alternatives to subpulmonary ventricle retraining. It has been demonstrated in a young animal model that intermittent systolic overload, in agreement with athletic philosophy, has promoted more prominent hypertrophy, compared with continuous systolic overload.[2,3] However, these studies assessed global right ventricular (RV) systolic function only at rest, without showing any significant differences between the systolic overload protocols.

Nevertheless, the evaluation of RV function is difficult to image because of its complex morphology. Although cardiac magnetic resonance imaging is currently considered the reference technique for RV volumetry and calculation of the ejection fraction, various echocardiographic parameters can provide reliable information on RV dimensions and RV systolic and diastolic function in daily clinical practice.[4] Therefore, the myocardial performance index (MPI) has been proposed as a relatively simple method to assess the combined systolic and diastolic performance of the right ventricle simultaneously, at rest and under dobutamine stress.[5]

The present study aimed at a more detailed echocardiographic assessment of subpulmonary ventricular function in 2 different protocols of systolic overload, using MPI and a pharmacologic stress technique.

ET/BS

Abbreviations and Acronyms

LV	= left ventricular
MPI	= myocardial performance index
PAB	= pulmonary artery banding
PT	= pulmonary trunk
RV	= right ventricular
RVEDV	= RV end-diastolic volume
RVEF	= RV ejection fraction
RVMPI	= RV myocardial performance index
TGA	= transposition of the great arteries

METHODS

Nineteen young goats, aged 30 to 60 days were enrolled in the present study and divided into 3 groups of comparable weight ($P = .84$): sham (n = 7; weight, 12.00 ± 2.65 kg), continuous (n = 6; weight, 11.27 ± 3.20 kg), and intermittent (n = 6; weight, 11.98 ± 1.07 kg). All goats received humane care in accordance with the guidelines established by the Brazilian College of Animal Experimentation. The ethics committee for research protocols at the University of São Paulo School of Medicine reviewed and approved the present study (CAPPesq 0664/09).

ANESTHESIA

Anesthesia was induced with intramuscular ketamine (20 mg/kg) and maintained with ketamine (1 mg/kg intravenously) and nembutal (5 mg/kg intravenously) on demand. The goats were intubated and mechanically ventilated (Harvard 708, South Natick, Mass). An electrocardiogram was recorded and blood pressure measurements were taken with computer software (ACQknowledge, version 3.01; Biopac Systems, Inc, Goleta, Calif). Antibiotic therapy (cephazolin 500 mg intravenously and gentamicin 40 mg intramuscularly) was administered just before the operation and maintained during the protocol. Digoxin (0.01 mg/kg) and heparin (5000 IU) were also administered throughout the protocol. All the goats were extubated right after the surgical procedure and remained ambulatory and breathing spontaneously throughout the protocol.

SURGICAL PROCEDURE

The chest was opened at the fourth left intercostal space to expose the RV outflow tract, after lung retraction. A 17-gauge heparinized catheter was inserted in the RV outflow tract, pulmonary trunk (PT), and descending aorta for pressure measurements at specific intervals during the entire study. The adjustable pulmonary artery banding (PAB) system (SILIMED; Silicone e Instrumental Medico-Cirurgico e Hospitalar Ltda, Rio de Janeiro, Brazil) was implanted just beyond the pulmonary valve, as previously described.[6]

RV SYSTOLIC OVERLOAD PROTOCOL

RV training was begun after a 72-hour convalescence period with percutaneous PAB insufflation with saline solution to achieve an RV/systemic pressure ratio of 0.7, limited by a 10% decrease in systolic blood pressure. Readjustments were made every morning throughout the protocol. If systemic hypotension and/or respiratory distress developed after PAB inflation, it was deflated to a volume compatible with RV tolerance and maintenance of goat hemodynamics. A 96-hour study period has been previously established as the minimum time required for cardiac masses equalization in young goats.[7]

Continuous Group Protocol

In the continuous group, the goats remained with continuous systolic overload for 96 hours, with daily assessment to keep the RV/aortic pressure ratio at 0.7. Hemodynamic data were collected once daily (mornings) during PAB readjustments.

Intermittent Group Protocol

In the intermittent group, the goats underwent 4 daytime periods of 12-hour systolic overload, alternating with a 12-hour nighttime resting period. Hemodynamic data were collected every 12 hours, during PAB readjustments.

Sham Group Protocol

In the sham group, the PAB system was maintained deflated during the entire protocol. Hemodynamic data were collected once daily (mornings).

ECHOCARDIOGRAPHY

All the goats while under light sedation (ketamine 15 mg intramuscularly) were examined by a single experienced observer preoperatively and daily throughout the study and monitored continuously with surface electrocardiography. The following echocardiographic parameters were studied using multifrequency transducers (7.5 and 2.5 MHz, Acuson Cypress; Siemens, Erlagen, Germany): left ventricular (LV), RV, and ventricular septum wall thicknesses, RV end-diastolic volume (RVEDV) and RV end-systolic volume, RV end-diastolic diameter, RV ejection fraction (RVEF), and RV MPI (RVMPI).

Because of the keel structure of the goat thorax, the RV free wall thickness was taken from the parasternal long-axis 4-chamber view and from the parasternal short-axis view (at basal and papillary muscle levels), where the limits of the RV free wall were more easily obtained. The LV end-diastolic posterior and septal wall thicknesses were measured through the parasternal long-axis view, at the level of the mitral valve leaflet tips. All the wall thicknesses were measured using 2-dimensional technique, under resting conditions.

Also, from the long-axis, 4-chamber view, the RVEF was measured by the modified Simpson rule. The RVMPI was calculated from pulsed wave Doppler of RV inflow and outflow tracts, positioning the sample volume at the level of the tricuspid and pulmonary valve leaflet tips, respectively, as previously described by Ishii and colleagues.[8] This index