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IV Pulmonary trunk reversible banding: Analysis of right ventricle acute hypertrophy in an intermittent loading experimental model

Bandagem reversível do tronco pulmonar IV: análise da hipertrofia aguda do ventrículo direito em modelo experimental de sobrecarga intermitente

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Abstract

Objectives: **Adjustable pulmonary trunk (PT) banding device may induce a more physiological ventricle retraining for the two-stage Jatene procedure. This experimental study evaluates theacute hypertrophy (96 hours) of the right ventricle (RV) submitted to intermittent systolic overload.**

Methods: **Five groups of seven young goats were distributed according to RV intermittent systolic overload duration (0, 24, 48, 72 and 96 hours). The zero-hour group served as a control group. Echocardiographic and hemodynamic evaluations were performed daily. After completing the training program of each group, the animals were sacrificed for water content and cardiac mass evaluation.**

Results: **There was a significant increase in RV free wall thickness starting with the 48-hour group ($p<0.05$). However, a decreased RV ejection fraction, associated with an important RV dilation and a significant increase in the RV volume-to-mass ratio was observed at 24-hour training period, when compared to 96-hour period ($p=0.003$), with subsequent recovery throughout the protocol. A 104.7 % increase in RV mass was observed in the 96-hour group, as compared to the control group, with no differences in water content between these two groups. The daily mean increase in RV mass during the study period was 21.6% ± 26.8 %. The rate of RV mass acquisition for the overall study period of intermittent systolic overload was 0.084 g/h ± 0.035 g/h.**

Conclusion: **Intermittent PT banding has allowed a significant RV mass acquisition in the 96-hour trained group. No myocardial water content changes were observed in this group, suggesting an increased myocardial protein synthesis.**

Descriptors: **Heart ventricles/physiopathology. Hypertrophy/physiopathology. Right ventricular hypertrophy. Transposition of great vessels/surgery. Cardiac surgical procedures/methods. Goats.**

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Resumo

***Objetivo:* A bandagem ajustável do tronco pulmonar (TP) pode proporcionar treinamento ventricular mais fisiológico para cirurgia de Jatene em dois estágios. Este estudo experimental analisa a hipertrofia aguda (96 horas) do ventrículo direito (VD) submetido à sobrecarga sistólica intermitente.**

***Método:* Cinco grupos de sete cabritos jovens foram dispostos conforme o tempo de sobrecarga sistólica do VD (0, 24, 48, 72 e 96 horas). O grupo zero hora funcionou como grupo controle. Avaliações ecocardiográficas e hemodinâmicas foram feitas diariamente. Os animais foram sacrificados para avaliação do conteúdo de água e pesagem das massas cardíacas.**

***Resultados:* Houve aumento da espessura do VD a partir de 48 horas de treinamento (p<0,05) e rebaixamento da fração de ejeção do VD, com dilatação importante desta câmara nas primeiras 24 horas do protocolo, recuperando-se posteriormente. Houve aumento da relação volume/massa nas primeiras 24 horas do protocolo, em relação ao momento 96 horas (p=0,003). A massa do VD apresentou aumento de 104,7% no grupo 96 horas em relação ao controle. Não houve diferença quanto ao conteúdo de água do VD. A média diária de aumento da massa do VD foi de 21,6% ± 26,8%. A taxa de ganho de massa muscular do VD para todo o período de estudo foi de 0,084 g/h ± 0,035 g/h.**

***Conclusão:* O protocolo de bandagem intermitente do TP permitiu ganho de massa muscular do VD, significativa no grupo de 96 horas de estudo. Esta hipertrofia não foi acompanhada de aumento no conteúdo de água, o que sugere maior síntese protéica nos tecidos cardíacos.**

***Descritores:* Ventrículos cardíacos/fisiopatologia. Hipertrofia/fisiopatologia. Hipertrofia ventricular direita. Transposição dos grandes vasos/cirurgia. Procedimentos cirúrgicos cardíacos/métodos. Cabras.**

INTRODUCTION

The establishment of the Jatene procedure as the best option for treatment of the transposition of large arteries (TGA) [1], as well as the well-studied concept about the right ventricle (RV)'s inability to maintain appropriate performance as a long-term systemic ventricle in atrial inversion operations or in congenitally corrected transposition of large arteries (CTTGA) [2,3], lead us to the following alternative: training of the hypotrophied left ventricle (LV), aiming to surgically recruit it for systemic circulation.

In 1977, before the Jatene procedure, Yacoub et. al. [4] described, for the first time, the idea of performing a ventricular preparation by banding the pulmonary trunk (PT) to a pulmonary-systemic shunt, aiming for LV hypertrophy as the first stage of the surgery, with a subsequent Jatene procedure months later. However, high rates of mortality connected to the procedure were described [5].

In 1989, Jonas et. al. [6] introduced a concept of rapid LV preparation by banding it to the pulmonary trunk for TGA correction in two stages, showing appropriate hypertrophy of this chamber in a mean period of nine days. However, the long-term evolution also showed ventricular dysfunction and dilatation in approximately 25% of the evaluated patients (aspects that were not observed in patients who were operated early without need for previous ventricular preparation) [7]. Other studies also showed that acute pressure overload can lead to cellular necrosis focus in the hypertrophied myocardium and consequently late ventricular dysfunction [8-11].

The best option for subpulmonary ventricle training for congenital cardiopathies with ventriculoarterial discordance still remains undefined. Intermittent overload periods with adjustable banding devices seem to be related to healthier hypertrophic processes [12,13]. However, a detailed analysis of the increase in subpulmonary ventricle mass that has undergone intermittent systolic overload has not yet been established. Thus, the aim of this study is to analyze the RV acute hyperthophy process in young goats that underwent intermittent systolic overload, in terms of hemodynamic, echocardiographic and morphological aspects at 24, 48, 72 and 96 hours.

METHODS

This study was carried out in the Experimental Division of the Heart Institute of Hospital das Clínicas, University of São Paulo Medical School, meeting the norms of Animal Experimentation in Teaching and Research of Animal Research Inspection Commission – COFIPA.

Four study groups with seven young goats each (between 30 and 60 days of age) were used for induction of RV systolic overload using an experimental model of reversible PT banding [14-16]. Each group underwent twelve hours of systematic stimuli of RV systolic overload, followed by 12 hours of resting divided in training groups of 24 hours (Group 24, weight: 9.64 Kg ± 0.95 Kg), 48 hours (Group 48,weight: 9.64 Kg ± 0.95 Kg), 72 hours (Group 72, weight: 8.76 Kg ± 1.17 Kg) and 96 (Group 96, weight: 8.13 Kg ± 0.75 Kg). A control group (group C – zero hours, weight: 7.65 Kg ± 1.88 Kg), also with seven animals with similar weight and age, was used to compare the cardiac mass and water volume of these animals to those from the study groups.

Preoperative evaluation

All animals underwent echocardiography exams and were previously examined by veterinarians to eliminate any animals with preexisting diseases. Animals with preoperative RV-PT gradients higher than or equal to 10mmHg were not selected.

Surgical Procedure

The animals were operated under general anesthesia and mechanical ventilation. They also were prepared for aseptic surgery through left lateral thoracothomy in 4th intercostal space After the opening of pericardial flap and exposition of outlet right ventricle, PT and descending thoracic aorta, previously heparinized catheters were implanted in these structures. The catheters were fixed with 5-0 polypropylene purse-string sutures and exteriorized and fixed to the thoracic skin wall. The pressures were measured using ACQ Knowledge software v.3.01 (Biopac Systems, Inc., Goleta, CA, USA).

Pulmonary Trunk Banding device

After dissection between the PT and the ascending aorta, the banding device is positioned in the PT immediately above the pulmonary valve, and is fixed to the PT adventitia in order to avoid its migration. The banding device used in this study represents the development and improvement of 15 years of this research line, working together with SILIMED (Rio de Janeiro, RJ). The proposed improvements resulted in the development of a completely hermetic adjustable banding device, which is thinner and more delicate, to be used for the treatment of several cardiopathies (Figure 1). After device implantation, thoracic water-sealed drainage was performed. The ribs were approximated and a layered suture of the soft parts was performed.

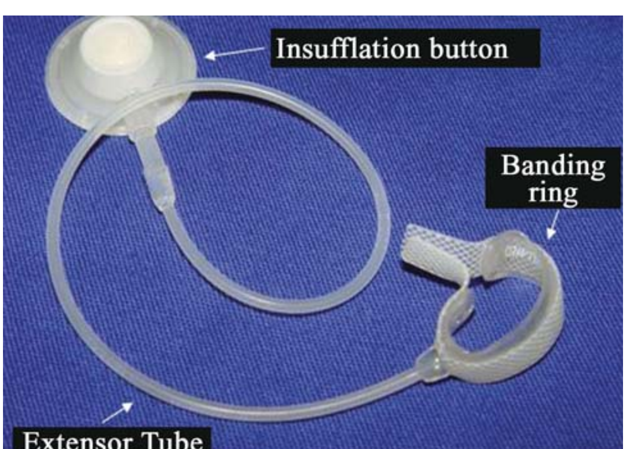

Fig. 1 – PT adjustable banding device used in the protocol, manufactured by SILIMED (Rio de Janeiro)

A preoperative antibiotic prophilaxy was performed in the animals and was spread out over the time of their stay in an animal care facility until the end of the study protocol of each group.

Device insufflation protocol

After 48 hours of total operation recovery, we initiated the ring intermittent inflation protocol (inflated in 12-hour blocks and then alternated with 12 hours of resting) for induction of RV progressive systolic stress, for 24 hours in the Group 24, for 48 hours in Group 48, and so on for all groups. The animals in Group 24 received the inflation only once in 12 hours. Before and after each stimulus, and at 12-hour intervals, and with the conscious animal immobilized on a special stretcher, the RV, PT and aortic basal pressures were measured. The ring inflation was performed with saline solution in an attempt to understand the pressure relationship of approximately 70% between the RV and the aorta, inasmuch as this did not drop the systemic systolic pressure by more than 10%, according to what was previously described in other studies [17-19].

In the case of any signs of instability of the animal, the banding volume would have been reduced to a tolerable level. The animals remained with RV systolic overload during the determined periods for each group, with progressive inflations at the maximum tolerated limit.

Echocardiographic study

All animals were submitted to echocardiographic evaluation by the same specialist (MCDA), awake and in esternal decubitus position in order to decrease interobserver variability. The examination was performed before the start of the protocol, as also after each inflation period in order to evaluate the RV hypertrophy process of all stimulated groups, as well as to record heart function in terms of RV ejection fraction (RVEF) and right ventricular diastolic volume [20]. The animals of the control group were also evaluated once before being euthanized.

Weighing of heart mass

After the closure of the protocol of each group, the animals were euthanized under general anesthesia, heparinization and induction of hyperpotassemia for resection of the heart. The epicardial fat was carefully resected and the ventricular and septal walls were separated following the Fulton et. al. technique [21]. Next, the RV, LV and interventricular septum were weighed in a digital balance (METTLER AE-200, Mettler-Toledo AG, Greifensee, Switzerland). Due to the variation in the weight of the animals, the measurements were standardized by indexing the weight of the heart muscle mass to the respective body weights of the animals, following the suggestions of Bishop & Cole [22]. The indexed weights were expressed in g/kg.

The animals of the control group also underwent the same protocol of ressection and weighing of the hearts.

Water volume of the tissues

Samples of each of the cardiac walls were harvested for water volume evaluation. Each sample was correctly identified and weighed. They were stored in appropriate containers and placed in an incubator (temperature of 55º-60ºC) for about 70 hours for dehydration. After this period, the dry weight of each sample was obtained. The percentage of water volume was then obtained and compared to that of the control group in order to clarify whether the increase of RV weight of the study groups should be associated with myocardial edema or with the gain of muscle mass.

Statistical analysis

The normal distribution of each variable was evaluated using the Kolmogorov-Smirnov test. Comparisons of hemodynamic, echocardiographic, morphological and morphofunctional variables were made through the analysis of variance (ANOVA) of one factor, with the respective times of 0,12, 24, 36, 48, 60, 72, 84 e 96 hours). Analysis of variance reaching the established significance level was performed by Bonferroni's test for multiple comparisons. Values are presented as means ± standard deviation. For all cases, the level of significance used was 5%. Statistical analyses were carried out by the softwares Prism v.4 (San Diego, CA, USA) and ESTATISTICA v.6 (Tulsa, OK , USA).

RESULTS

All animals completed the protocols of their specific group. Migration or rupture of the adjustable banding device was not observed in any of them. There were no observed statistical differences between the animals' body weights in the different groups (p=0,65).

Hemodynamic measurements

The animals showed progressively larger RV-PT gradients along the protocol parallel during the process of hypertrophy/ventricular adaptation (Figure 2). From an initial value of RV/PT pressure gradient of 36.6 mmHg ± 9.3 mmHg, the ventricles reached values of 80.0 mmHg ± 13.0 mmHg at the end of 96 hours of intermittent overload.

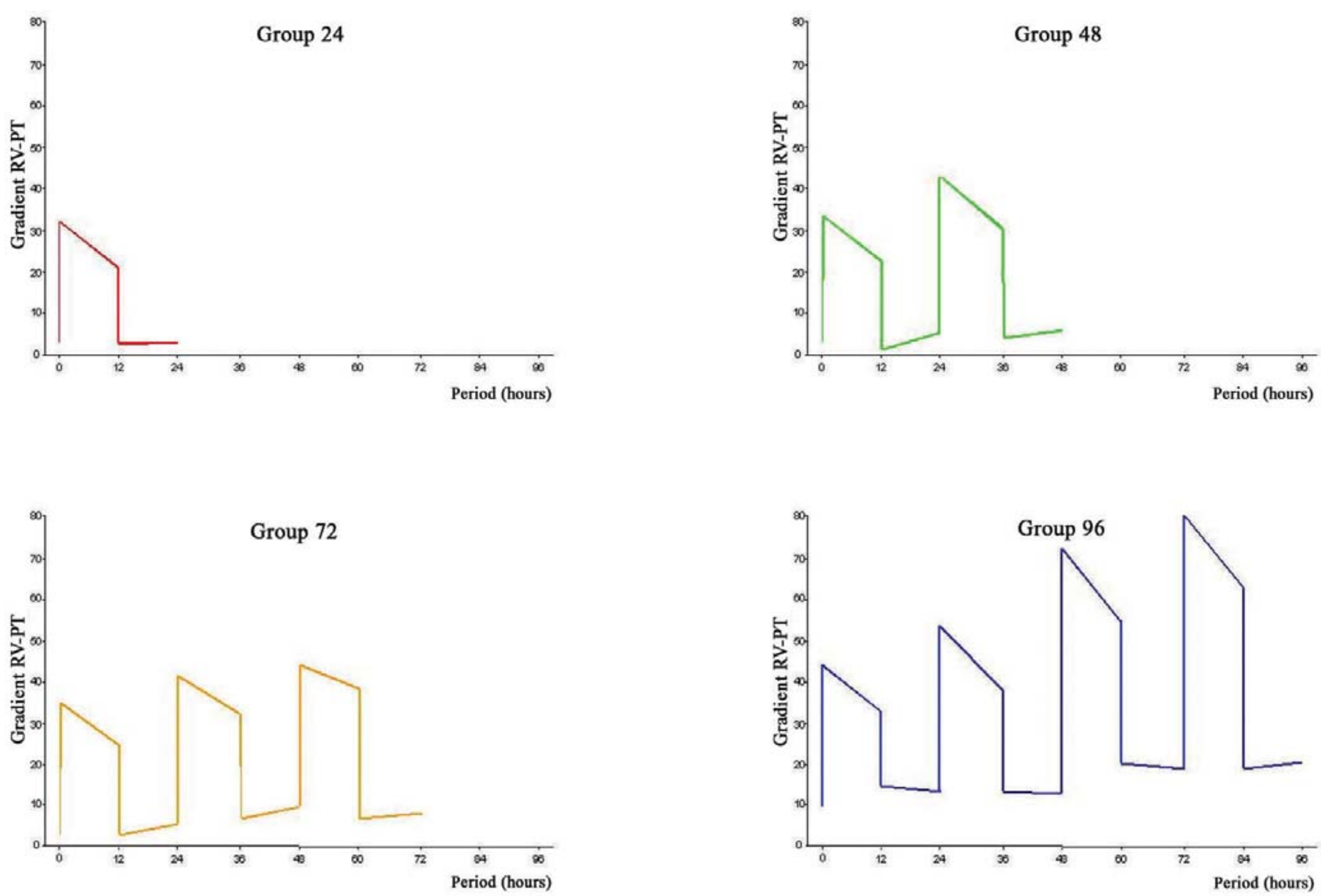

Fig. 2 – Demonstrative diagram of the intermittence of RV systolic overload in the four study groups

The pressure ratio of the animals RV/LV are shown in Figure 3. The ratios were significantly increased during all periods of RV systolic overload compared to the values found in base levels (p=0.0001). Paradoxically, the means of the periods of 60, 84 and 96 hours – periods in which the banding devices were deflated – were also significantly increased compared to the base values (p=0.05).

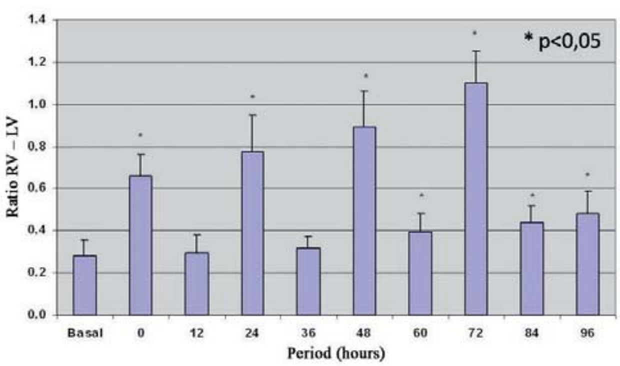

*Fig. 3 – RV/LV pressure ratio in the four study groups. Note the ratio intermittence in each period of 12 hours. Values = mean ± standard deviation. *p<0.05 vs. base values*

Group 24 in relation to the base period (p=0.0001). After 48 hours of overload, there was recovery of this parameter, reaching, at the end of the protocol, the value of 81.9% ± 30.4% of the RV end-diastolic base volume.

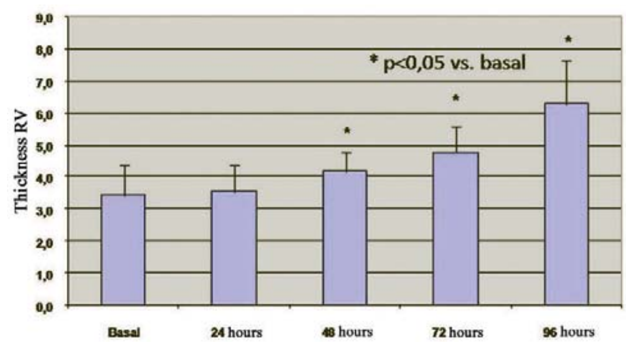

*Fig. 4 – The thickness of the RV wall presented significant increase from the period of 48 hours through the intermittent systolic overload protocol imposed upon the RV in the four study groups. n = 28 (base value and 24 hours); n = 21 (48 hours); n = 14 (72 hours); n = 7 (96 hours). Values (mm) = mean ± standard deviation. * = p<0.5 vs. base values*

Echocardiographic measurements

Neither the LV wall nor the ventricular septum presented alterations in thickness that were visible by echocardiogram during the protocol of RV intermitent systolic overload in four study groups. Figure 4 shows combined analysis of the animals' RV wall thickness during the protocol of intermittent systolic overload. Significant increase of this parameter was observed (48 hours after the initiation of intermittent overload) exceeding the values of septal and of LV thickness in the 96 hours of training (p<0.05).

The acute overload induction, despite of established resting periods, resulted in significative decrease of the animals RVEF, 24 hours after initiation of the intermittent systolic overload in relation to the base period (p=0.0001; from 0.68 ± 0.08 to 0.52 ± 0.21) with its significant recovery in the following periods (48, 72 and 96 hours).

Concomitantly to RVEF decrease, an increase in the RV final diastolic volume of 229.5% ± 133.4% was observed in Group 24 in relation to the base period.

Morphological measurements

The ventricular septum and the RV presented progressive increase of the weighed mass, as shown in Figure 5. The RV mass presented significant increase in Group 96 (1.76 g/kg ± 0.52 g/kg) in relation to the following groups: the control group, Group 24, Group 48, and Group 72 (p=0.0001). The ventricular septum mass also presented significant increase in Group 96 (1.44 g/kg ± 0.25 g/kg), when compared to the other groups (p.0.01). The LV mass did not present a significant increase during the protocol (p=0.14).

Daily mean of RV mass increase was 21.6% ± 26.8%, with a 104.7% mass gain in Group 96 compared to the control group. The rate of RV muscle mass increase in all periods of intermittent systolic overload was 0.084 g/h ± 0.035 g/h. Figure 6 shows the daily gain of RV muscle mass, indexed by body weight. The highest gain of ventricular mass was seen in Group 96.

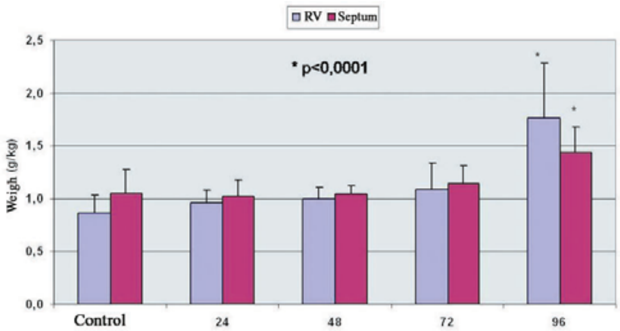

Fig. 5 – Septum and RV masses (indexed to body weight) evaluated during the intermittent systolic overload protocol, showing significant increase of both masses at the group 96 (p<0.0001). n=7

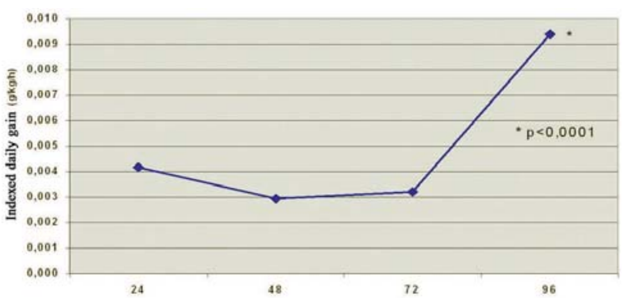

*Fig. 6 – Evolution of the daily muscle mass gain of the RV (indexed to body weight) during the intermittent systolic overload protocol, showing significant increase at the group 96. (p<0.0001) n=7. Values (g/kg/h) = mean ± Standard deviation.*p<0.0001*

Concerning the water volume of the RV, LF and septum muscle masses, increases in the RV (p=0.014) and septum (p=0.003) in Group 72 were found; though slight, the increases were significant when compared to the control group and Group 24. The RV and ventricular septum masses of Group 96 – which presented significative weight gain – did not present significative variation in water volume in relation to the control group.

Morphofunctional measurements

Figure 7 shows the RV's volume/mass relationship during the intermittent systolic overload protocol. Significant increase in the first 48 hours of protocol was observed in relation to Group 96 (p=0.006); Group 96 tended to have a lower volume/mass ratio when compared to the control group.

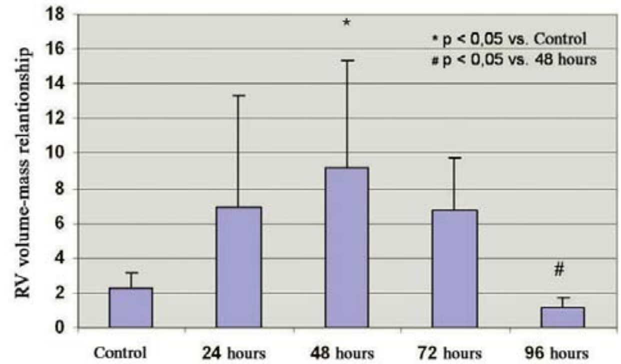

*Fig. 7 – Evolution of the volume/mass relationship of the RV during the intermittent systolic overload protocol, showing significant increase at the 48-hour mark. N = 7. Values (ml/g/kg) = mean ± Standard deviation * p < 0.05 vs. control group; # p < 0.05 vs. 48 hours*

The pressure generated on the myocardial wall is directly proportional to the result of the RV intracavitary pressure multiplied by volume/mass ratio of the RV [23]. Figure 8 shows the graphic elucidation of the RV's wall pressure during the systolic overload period (inflated cuff); it was significantly increased in Group 48 compared to Group 24 (p=0.003). From then on, keeping consistent with ventricular adaptation, this pressure presented a progressive decrease, reaching final values that were less than base values.

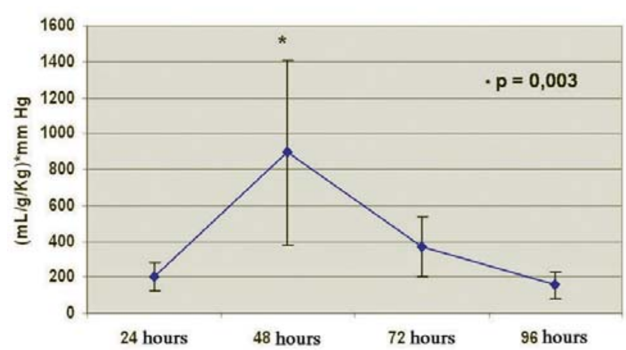

*Fig. 8 – Image of the RV pressure wall during the protocol of intermittent systolic overload. Values (mmHg.ml.g^{-1}. Kg^{-1}) = mean ± Standard deviation; * p=0.003*

DISCUSSION

This study was performed to establish, with the highest accracy possible, the daily gain patterns of a ventricular mass submitted to intermittent systolic overload and the degree of its hypertrophy by direct weighing of the myocardial muscle mass in groups with different periods of RV intermittent overload. During 96 hours of RV intermittent systolic overload, a significant increase in mass was observed at the end of protocol, reaching more than two times the gain of the control group (an increase of 104.7%). This fact indicates that the RV has rapid hypertrophic capacity in only four periods of 12 hours of systolic overload stimulus per day. The weighing of cardiac masses consistently shows the development of the hypertrophic process when compared to the echocardiographic estimation used in studies, such as that of Boutin et. al. [23].

Boutin et. al.'s study was a clinical study in Boston. With respect to the rapid preparation of the LV for the Jatene procedure in two stages, the LV mass reached its peak of hypertrophy in seven days, with a mean increase of 100% with an initial significant gain within 36 hours of continuous systolic overload. In some studies, the highest total overload in the continuous protocols (in relation to the intermittent protocols) results in a early and more accentuated hypertrophy. However, according to observations by Perrino et. al. [24], the higher and highest early mass gain seems to be associated with a higher myocardial dysfunction. The rate of increase in muscle mass of 0.08 g/h ± 0.04 g/h of this study was slightly larger than the values found by the echocardiographic evaluation of the Boston group in the rapid preparation for the Jatene procedure (0.06 g/h ± 0.04 g/h), despite less systolic overload time and consequently lesser energetic consumption by the myocardium [23]. It is likely that, after the early activation of hypertrophy genes, the mechanism of this hypertrophic process may lead to more favorable conditions during the resting periods and more transportation of oxygen.

Concerning the interventricular septum mass, a significant gain of 37% observed after 96 hours of training is corroborated by the findings of previous studies in our laboratory [13], which also failed to show echocardiographic alterations parallel to the hypertrophic process of this ventricular mass area.

Morphofunctional parameters

The capacity of the subpulmonary ventricle - prepared to support the systemic vascular resistance during the second stage of the Jatene procedure – primarily depends on the afterload to which it will be postoperatively submitted. Generally, the simple ventricular mass measurement is not enough to predict if the ventricle would be capable of anatomical correction of the TGA. Although the ventricular mass may be proportional to the body surface of the patient, the trained ventricle may still be poorly prepared for a connection to systemic circulation. The best situation would be to anticipate the volume/mass relationship to which the ventricle would be submitted in the postoperative of Jantene procedure, in order to use it as successfully prognostic index of the trained ventricle.

In this study, the volume/mass relationship of the RV presented maximum increase in the first 48 hours of intermittent overload with total recovery at the end of the protocol. This moment indicated a condition that is favorable for supporting the systemic circulation afterload. The improvement of this RV ratio contrasts with the findings about rapid preparation in the Boston clinical study, which indicated progressive increase of this parameter, reaching its maximum in a period of seven to ten days, characterizing the progressive ventricular dilatation observed until the moment of the Jatene procedure [23]. Normalization of RV dilatation in this study, associated with its significant mass gain may be attributed to the intermittent pattern of hypertrophic stimulus.

RV pressure was also analyzed in this study, as it is considered the best parameter of afterload submitted to the ventricle by banding and also the best paramater of energy use dispensed by the ventricle in a given moment. Although we have been observing that the induced RV-PT gradients and the RV/LV pressure relation have been progressively larger over time, the values of wall pressure did not comply with this tendency. We observed a peak of this parameter at the 48-hour mark, when the RV presented high intracavitary pressure with severe dilatation but without significant mass gain.

Later, a progressive decrease was observed in the subsequent periods due to the significant mass gain of the RV. This study clearly showed that the RV wall pressure is at its maximum in the initial periods of overload, with progressive decrease during **ventricular adaptation** through muscle hypertrophy and a decrease in final diastolic volume of the RV. The more hypertrophied heart— that is, the more conditioned muscle— would "suffer" less with the induced afterload.

In relation to myocardial water volume, the four periods of intermittent systolic overload caused significant RV and septum hypertrophy of Group 96, and was not followed by myocardial edema. It is likely that this increase of the aforementioned cardiac mass weight was due to increased protein synthesis, due the fact that there was no significant difference in the RV and septum myocardial water volume between Group 96 and and the control group.

Echocardiographic parameters

The intermittent systolic overload (imposed by the PT banding) allowed for a rapid RV hypertrophy; as a result, the thickness of its free wall superceded the thickness of the septum and LV walls, beginning at the 72-hour mark of the protocol. Paradoxically, the septum thickness did not show detectable hypertrophy in the echocardiogram during the protocol, which differs from the significant increase of the septa weighing in Group 96. Perhaps, this difference may be explained by the larger protein content and muscle density of the wall, even without the proportional macroscopic increase visible in the echocardiogram.

The decrease in the ejection fraction and the parallel increase of final RV diastolic volume occurring 24 hours after the RV intermittent systolic overload, especially in the Group 48 and Group 72, were not followed by a significant drop in systemic arterial pressure. In the rapid preparation protocol of the Boston group with fixed and continuous TP banding, the ventricular dysfunction was earlier and the recovery time was longer (12 hours and 84 hours, respectively) [23]. This fact may be explained by RV diastolic dysfunction with its contractile function largely unaffected, according as suggested by Gaynor et. al. [25]. These authors suggest compensatory mechanisms in atrial compliance in order to avoid systemic hemodynamic alterations.

In this study, the recovery from the ejection fraction and the RV final diastolic volume in the subsequent periods are probably related to the four intervals (12 hours) of rest between the periods of systolic overload, which induces remodeling and “healthier” myocardial hypertrophy of the RV. The periods of intermittent resting during the protocol may optimize the subendocardial coronary flow and, consequently, enlarge the quantity of substrates in the myocardial hypertrophic process, which limits the seriousness of a continuous systolic overload imposed upon the RV. This improvement in prerformance of the RV contrasts with the findings of Leeuwenburgh et al. [26], which showed a drop in the cardiac debt in protocol of PT chronic banding in young sheep, despite the increase of RV contractility. The authors concluded that the chronic banding of the RV causes an increase in RV relaxation and decrease of the diastolic compliance, both indicative of diastolic dysfunction of the RV.

Clinical implications

In this study, it was clear that the intermittent systolic overload of the RV caused a significant gain in muscle mass without the loss of contractile function. However, this kind of protocol was not still clinically applied in the Jatene procedure in two stages. It is still not known if this means of ventricular preparation - although it allows for significant hypertrophy of the RV - would be effective in preparing the ventricle for the anatomical correction with the proposed overload and time rate.

Evaluating some aspects that are commonly considered as effective ventricular preparation criteria, the systolic overload of this protocol would be enough and appropriate for ventricular preparation, due to the following facts:

- Within 24 hours of intermittent systolic overload, the RV already tolerated a pressure ratio higher than 0.75 in relation to the systemic ventricle;
- Within 72 hours, the RV thickness already had reached the values of the systemic ventricle;
- The ventricular function and the RV dilatation was also perfectly recovered within 72 hours;
- However, the gain of ventricular mass showed significance only within 96 hours; and,
- Within 96 hours, the volume/mass relationship tended to have values that were less than those of the control group.

Limitations of the study

Considering the limitations of clinical inferences from observations of an experimental group, we can not affirm that the behavior of the human heart with TGA would be exactly the same as what was observed in our experiment. In this study, the evaluated subpulmonary ventricle was the RV and not the LV, as in the TGA. On the other hand, the experiments with aortic banding in animals occur with mortality rates of 30%-50%. Furthermore, the aortic banding would submit the coronary system to high pressures, which may cause several repercussions. This experimental approach also would not correspond with reality because, in the TGA, the LV is connected to the pulmonary artery. In the case of adult patients with CTTGA, we can not affirm that the adaptive behavior of the heart will be the same, which could limit our conclusions about the subpulmonary ventricle preparation of this class of patients for the Jatene procedure in two stages. Studies with adult animals and the use of molecular biology to analyze the markers of the hypertrophic process certainly may be enlightening and may generate knowledge that would allow for a better understanding of the ventricular hypertrophic process that would offer the best ventrical training.

CONCLUSION

This study showed that the four periods of intermittent systolic overload caused significant septum and RV hypertrophy in the 96-hour group without myocardial edema. Therefore, this intermittent pattern of hypertrophy stimulus may decrease the time needed for ventricular preparation of 96 hours for patients with TGA beyond the neonatal period.

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