

Transcatheter implantation of self-expandable valved prosthesis in outlet right ventricle an experimental study in pigs

Estudo experimental do implante transcater de prótese valvada autoexpansível na via de saída do ventrículo direito em porcos

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Abstract

Introduction: Patients with congenital heart disease who underwent pulmonary valvotomy or surgery to open the pulmonary valve ring are prone to develop residual pulmonary insufficiency or stenosis that may lead to right heart failure with clinical deterioration. These children require multiple interventions throughout their lives, which impose a high rate of morbidity and mortality.

Objective: To develop a less invasive technique for implantation of a valved prosthesis through the right ventricle.

Methods: The valved prosthesis consists of an auto-expanding metal stent built with nitinol, surrounded with polyester, where the three leaflets of bovine pericardium were mounted. Twelve pigs were used to perform the implants. Echocardiographic control was performed immediately after implantation and one, four, eight and 12 weeks.

Results: One animal showed reflux of moderate to severe and three mild reflux. Transvalvular gradients measured before implantation ranged from 3 to 6 mmHg and that soon after the implant was increased, ranging from 7 to 45 mmHg. There was a decrease in these gradients during follow up and in only four of the twelve animals the gradients were above 20 mmHg. Thrombus formation occurred in the prosthesis of six animals, and this was the most frequent complication.

Conclusion: These findings highlight the need for studies with the use of anticoagulants and antiplatelet, an attempt to reduce this event. The study aims to contribute for the start of the use of prosthetic heart valves that could be implanted through minimally invasive techniques without the use of cardiopulmonary bypass.

Descriptors: Pulmonary Valve Insufficiency. Pulmonary Surgical Procedures. Pulmonary Valve Stenosis.

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Resumo

Introdução: Nos pacientes portadores de cardiopatias congênitas que foram submetidos à valvotomia pulmonar ou cirurgias de ampliação com o uso do anel da válvula pulmonar, a insuficiência ou estenose pulmonar residual pode acarretar falência cardíaca direita com deterioração clínica. Essas crianças necessitam de múltiplas intervenções ao longo de suas vidas, que impõem uma elevada taxa de morbidade e mortalidade.

Objetivo: Desenvolvimento de uma técnica menos invasiva para implante de uma prótese valvada através do ventrículo direito.

Métodos: A prótese valvada consiste em um anel metálico construído com nitinol autoexpansível, revestida de poliéster, onde três cúspides de pericárdio bovino foram montadas. Doze porcos foram utilizados para a realização dos implantes. Foi realizado controle ecocardiográfico imediatamente após o implante e com uma, quatro, oito e 12 semanas.

Resultados: Um animal apresentou refluxo de grau moderado a importante e outros três refluxo de grau leve. Os gradientes transvalvares medidos antes do implante variavam entre 3 a 6 mmHg, sendo que, logo após o implante, houve aumento dos gradientes que variaram de 7 a 45 mmHg. Houve queda desses gradientes, sendo que em apenas quatro dos 12 animais os gradientes estavam acima de 20 mmHg. Em seis animais, ocorreu a formação de trombo na prótese, sendo esta a complicação mais frequente.

Conclusão: Esses achados evidenciam a necessidade da realização de estudos com a utilização de anticoagulantes e ou antiagregantes plaquetários na tentativa de diminuir esse evento. O estudo pretende apresentar subsídios para o início do emprego de próteses valvares que poderiam ser implantadas através de técnicas menos invasivas.

Descritores: Valva Pulmonar. Insuficiência da Valva Pulmonar. Estenose da Valva Pulmonar. Anormalidades Congênitas. Cardiopatia congênita.

INTRODUCTION

The extraordinary advances in cardiac surgery in non-invasive diagnostic and intensive care over the past 50 years have a worldwide growth in the number of patients with congenital heart disease who reach adolescence and adulthood. It is expected that approximately 85% of children born with congenital heart defects will survive to adulthood, and with the continued improvement in surgical techniques, this number may increase further in the next two decades [1]. It is estimated that currently there are around 856,000 adults with congenital heart disease in the United States of America [2].

The dysfunction of right ventricular outflow tract (RVOT) with pulmonary stenosis or insufficiency is a condition often found in the follow-up of patients, children and adults undergoing repair of complex congenital heart disease, especially in diseases that present with some degree of obstruction to pulmonary flow, either subvalvular, valvular or supra-valvular. As a rule, these patients require enlargement of the RVOT for correction, either by expanding this or the interposition of valved conduits between the right ventricle and pulmonary artery. In follow-up of patients with pulmonary stenosis, varying degrees of pulmonary insufficiency are found in more than 70% of patients, regardless of the technique used in its correction [3-6]. The same is true for patients undergoing repair of tetralogy of Fallot, which are almost invariably present with pulmonary insufficiency, which may be important in moderate to 50% of cases [7].

The residual pulmonary insufficiency in the early postoperative period of the diseases that require the

RVOT enlargement or pulmonary valvuloplasty was long assumed to be a normal consequence, with benign evolution and acceptable in the early stages of congenital heart surgery. However, follow-up studies have shown long-term hemodynamic deleterious effects on right and left ventricular function [8,9], which results in decreased ability to exercise, which often precedes the onset of symptoms of heart failure, dyspnea, arrhythmias and sudden death [10,11].

The surgical indications for pulmonary valve replacement in these patients is a challenge. The use of cardiopulmonary bypass (CPB) may exacerbate the dysfunction of the right ventricle, with worsening symptoms and decreased survival in the postoperative period. Valve replacement options consist of performance of prosthetic implants, both metallic or biological prosthesis in the interposition of a homograft, xenograft or simple enlargement of the outflow in young children. Regardless of the technique used for the treatment, these children require multiple interventions throughout their lives, which imposes a high rate of morbidity and mortality.

Percutaneous treatment of RVOT dysfunction has emerged as an alternative to conventional surgical treatment. Initial studies were developed by Bonhoeffer et al. [12] in 2000, with the use of bovine jugular vein mounted on a balloon expandable stent made of stainless steel, for percutaneous implantation. From this initial study, the first series of cases in humans have demonstrated the applicability of this method for the treatment of patients with severe pulmonary regurgitation and or residual pulmonary stenosis, with low rates of morbidity and mortality [13-16].

This study aims to develop a less invasive technique for implantation of a prosthetic valve in the RVOT without use of cardiopulmonary bypass, by transcatheter via through the right ventricle.

The experimental protocol was performed at the Center for Research and Training in Surgery (CETEC), Hospital Israelita Albert Einstein (Figure 1). This research center in experimental surgery has all the resources necessary to perform the project as a team of anesthesiologists, anesthesia machines, echocardiography and fluoroscopy (arch in "C"), plus all the infrastructure to accommodate and follow the animals after implant.

The models of stent valves are produced in partnership with the private sector and Braile Biomédica, a Brazilian company with extensive experience in commercial bioprostheses and stents.



Fig. 1. Bovine pericardial valve prosthesis coated with polyester

The valve prosthesis consists of a metal ring, in conformation with "Z", built with nitinol (alloy of nickel and titanium) selfexpandable, coated with polyester, where three bovine pericardial leaflets were mounted to form a valve. The prostheses were made with bovine pericardium, and fixed in glutaraldehyde (Figure 1). The prostheses were produced in four sizes with 20, 22, 24 and 26 millimeters (mm) in diameter. The devices were tested in flow replicates, with hemodynamic performance and durability comparable to commercially available bioprostheses and released for human use.

The device was implanted through the right ventricle of the animal, according to the technique described below.

To perform the echocardiographic and hemodynamic measures an echocardiography device - Envisor C Philips Medical Systems (Eindhoven, the Netherlands) was used.

Measurements of the diameter of the RVOT, just below the pulmonary valve ring, a cut in short axis of the pulmonary artery to the level of the aortic valve were performed.

Assessments of hemodynamic and echocardiographic measurements were performed before and immediately after implantation. The measurements were repeated with one, four, eight and twelve weeks of follow-up.

Histological evaluation was performed after removal of the prosthesis.

Preparation of animals

All animals were treated according to international ethical principles and those prepared by the Brazilian College of Animal Experimentation (COBEA), by the Ethics Committee on Animal Use (CEUA/Einstein).

Twelve Large White pigs, all castrated males, three months old and weighing 25-32 kg were used to perform the implants.

All animals were fasted for 12 hours - solid and water - for 6 hours prior to the procedure.

The choice of prosthesis size was based on the diameter of the pulmonary valve annulus, which was measured, using transthoracic echocardiography immediately after general anesthesia of the animal. The diameter of the pulmonary ring was added 20% to ensure a good coupling of the prosthesis to the walls of the pulmonary artery. Thus, in 11 of 12 animals, the measurements were almost 20 mm, and a 24mm prosthesis was used. In an animal with an annulus diameter of 17 mm, we chose to use a prosthesis size 22 (22 mm diameter).

After general anesthesia and tracheal intubation, median sternotomy was performed, followed by pericardiectomy and confection of purse-string suture with 5-0 green polyester yarn in the anterior right ventricle (near the RVOT) for insertion of the prosthesis (Figure 2). Puncture of the right ventricle with large-bore needle and passage of guidewire into the distal pulmonary artery were performed, followed by insertion of a pig-tail catheter. Pulmonary arteriography was performed for localization of the pulmonary valve. Pig-tail-type catheter was then replaced by rigid guide wire on which the release device of the prosthesis was placed (Figure 3). Releasing of the prosthesis was performed in the position of the pulmonary valve with the aid of fluoroscopy and echocardiography (Figure 4).

After implantation, we performed measurements of pressures in the right chamber, followed by arteriography to confirm the absence of pulmonary valve regurgitation.

Postoperative follow-up was performed with echocardiographic measurements of transvalvular gradients with one, four, eight and 12 weeks.

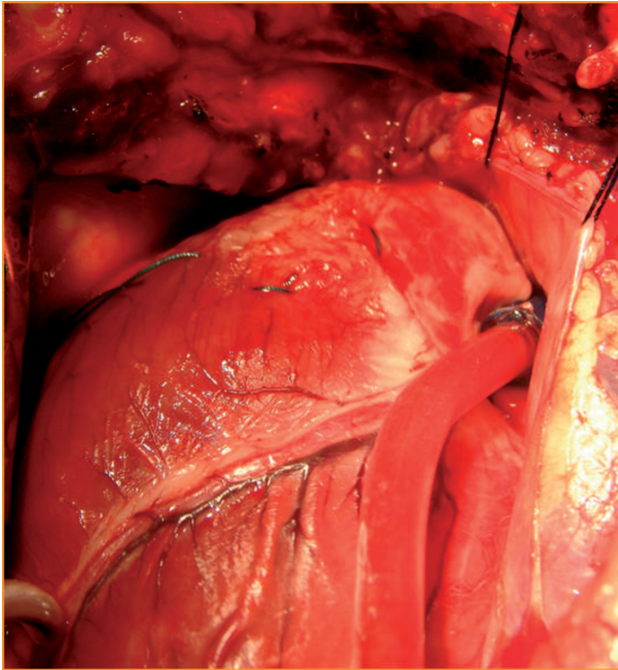


Fig. 2. Right ventricle anterior side.

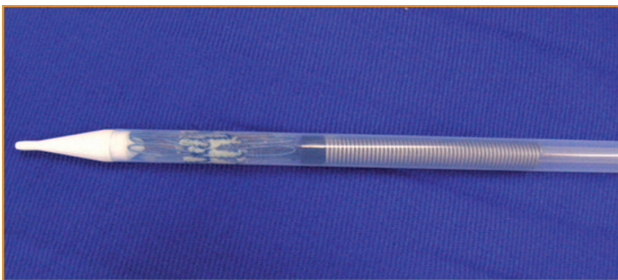


Fig. 3. Device (introducer) prepared containing the prosthesis to the implant

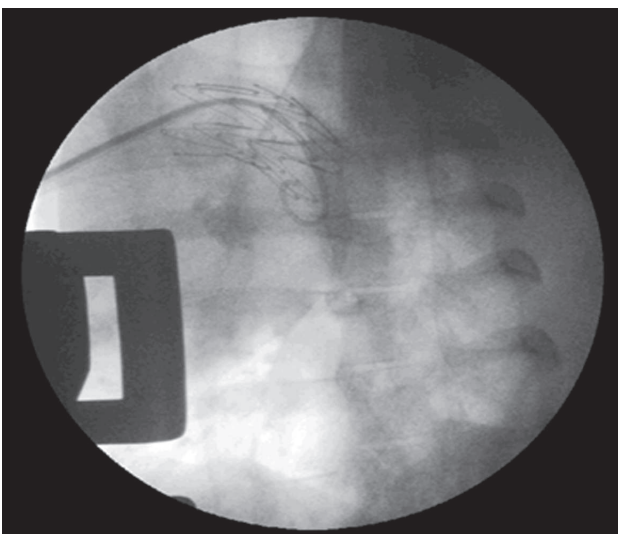


Fig. 4. Radioscopic image of the valve placed after the implant

After removal of the prosthesis, all were washed with saline solution (NaCl) 0.9% and fixed in formalin, and then subjected to macroscopic and histopathological analysis.

RESULTS

All prostheses were implanted with the intention of the native pulmonary valve was pressed against the walls of the pulmonary artery. However, accidentally, in three animals the prosthesis was implanted in the pulmonary artery trunk.

Eleven of the 12 implanted prostheses proved to be competent to angiography after implantation. Only in one animal perivalvar leak was present shortly after implantation, this being quantified as moderate to severe, or three crosses on a scale of one to four (where one means minimal regurgitation, and four major reflux).

Periprosthetic reflux was observed in five of the following twelve animals, and there was only a moderate to severe reflux, this soon after the implant, as mentioned above. The other four animals showed only a mild (+4/+), which was diagnosed in the first week in three animals, and in the fourth week in one of them. In one of the animals showed reflux in the first week, there was regression of reflux in the fourth week of follow-up. In one animal, the reflux was detected after migration of the prosthesis from its initial position to the pulmonary artery, in other animals, reflux was not preceded or accompanied by other changes. The presence of reflux did not affect the evolution of these animals.

Migration of the prosthesis was diagnosed in two animals, both in the first week of follow-up, leading to the appearance of mild reflux (+4/+) in one of the animals, as previously reported.

The echocardiographic evaluation showed thrombus formation on the prosthesis in six of 12 animals. Of these, in one animal, the thrombus was diagnosed in the first week of follow-up, and in five other animals, the diagnosis was confirmed in the fourth week of follow-up. In three animals, the presence of thrombus resonated with increased gradient of 15 to 42 mmHg, from 17 to 24 mmHg and from 8 to 45 mmHg, respectively.

Two animals were found dead in the stalls, one with 31 days and another with 85 days of follow-up. In none of these animals there was thrombus formation in the prosthesis on autopsy. In one of these animals occurred minimal regurgitation (+4/+), which was diagnosed the day before the finding of death. Two other animals have evolved presenting surgical wound infection, both sacrificed at 11 and 17 days postoperatively, respectively. Also, in these animals there was no thrombus on the prosthesis or evidence of dysfunction at autopsy.

There was considerable increase in the gradients between the right ventricle and pulmonary artery, immediately after implantation of the prosthesis. The values of the gradients pre-implantation ranged from 3 to 6 mmHg (mean 4.1 mmHg), which have risen from 7 to 45 mmHg (mean 18.6 mmHg) after implantation. The echocardiographic measurements during follow-up showed a gradual decrease in the values of pulmonary gradients, and in only four of 12 animals, the gradients remained above 20 mmHg (23, 24, 42 and 59) (Figure 5).

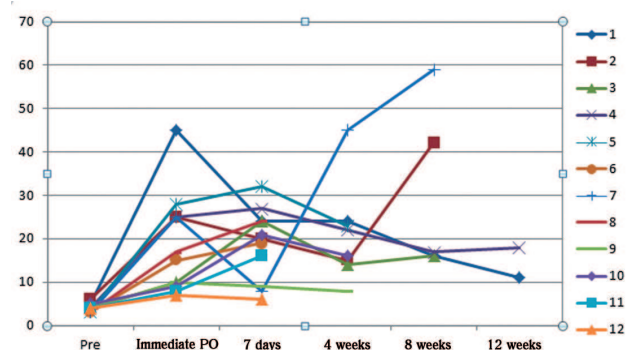


Fig. 5. Evolution of the gradient (in mmHg) through the prosthesis during the follow-up

Macroscopic analysis performed showed good fixation of the prosthesis to the wall of the pulmonary artery. Presence of macroscopic thrombus was observed in six of 12 animals at autopsy, as diagnosed by echocardiography, and it has been described previously. Microscopy showed a satisfactory outcome, with little inflammatory infiltrate in the valve leaflets.

DISCUSSION

RVOT dysfunction represents a major problem in patients undergoing surgery for congenital heart diseases, especially where there is need for reconstruction of the RVOT. This regurgitation can lead to severe right ventricular dysfunction [17]. Sometimes, the right ventricular dysfunction can be reversed when the valve replacement is performed. However, if the replacement is performed later, these changes can be permanent [18].

The pulmonary valve replacement is recommended in patients with deterioration of clinical or objective signs of right ventricular dysfunction. The surgical procedure, with the pulmonary valve replacement (or RVOT), is the strategy used that is able to improve clinical status and patient survival. However, the cardiopulmonary bypass used for valve replacement may worsen right ventricular dysfunction, and the risks inherent in a reoperation, reducing the clinical benefit of valve replacement [19].

For pulmonary valve replacement, various materials can be used, the most frequent are the homografts, porcine pulmonary valves and prostheses made from bovine pericardium. Another material widely used in recent years is from the bovine jugular vein, which has shown good results [20-22].

More recently, the percutaneous treatment of pulmonary insufficiency has shown a promising field, with the possibility of correction of pulmonary insufficiency without the adverse effects and risks associated with the conventional CPB [12].

Together with the private sector, we developed a prosthetic valve consisted of a nitinol stent covered with polyester, in which a bovine pericardial valve was mounted. Percutaneous treatment of valvular dysfunction and aortic stenosis has been performed widely throughout the world, including our institution [23-25].

In our study, nine of 12 animals underwent implantation of heart valve prosthesis successfully. In three animals, the prosthesis was introduced accidentally in the pulmonary artery trunk. However, none of these had reflux immediately after the implant, or graft dysfunction during the follow-up. Different from the reported by Bonhoeffer et al. [12] in their experimental study in sheep, in which the animals who received stents out of the preconized location, covering the pulmonary valve, and presenting dysfunction of the prosthesis.

Five of 12 animals showed perivalvar reflux after implantation, and in one the reflux was graded as moderate to severe just after implantation, although the prosthesis has been released in the correct position (pulmonary valve). One explanation for the development of reflux may be inadequate estimation of the size of the pulmonary annulus. This animal received a 24mm prosthesis (20% above the pulmonary annulus diameter), a size considered by us to provide adequate radial force sufficient to maintain the prosthesis coapted to the pulmonary artery wall. In the other four animals, reflux grade was estimated as minimal (+/4+), causing no clinical consequences to animals, these results comparable to those presented by other authors [12].

Migration of the prosthesis to the pulmonary artery occurred in two animals, both in the first week, and in one patient presented minimal regurgitation (+/4+), also without effect. One hypothesis for the migration of the device would once again be an underestimation of the diameter of the pulmonary annulus, which would result in a choice of prosthesis with insufficient size, thus providing lower radial force to the prosthesis, which would facilitate its migration. The diameter of the prostheses used were both 24 mm diameter retaining 20% above the pulmonary annulus measured prior to implantation (20 mm in two animals).

The formation of thrombus on the prosthesis was the most frequent complication, affecting six of the twelve animals. In one animal, the thrombus was evidenced in the first week, in the other five the diagnosis was performed in the fourth week of follow-up. Of the six animals with thrombus, in three there was a higher gradient in the lung to more than 20 mmHg (24, 42 and 45). The high rate of thrombosis found can be explained by factors such as the tendency to hypercoagulability found in pigs, the presence of low flow in the right heart chambers and the possible presence of bacterial endocarditis by contamination at the time of implantation, as reported by others [12]. These findings highlight the need for studies with the use of anticoagulants or antiplatelet agents in an attempt to reduce this event and an special care in aseptic handling during implantation.

Despite the high rate of thrombosis found in our study, the possibility of treatment via transcatheter pulmonary valve dysfunction without the need for extracorporeal circulation, with less invasive technique may benefit a large proportion of pediatric and adult patients in the coming years. The prostheses presented in this study are available in a variety of sizes, which allows the treatment of patients with different degrees of dilation of the RVOT, an advantage over the prosthesis on the market today [26].

The study aims to provide subsidies to the beginning of the use of prosthetic heart valves that could be implanted through less invasive techniques for the treatment of RVOT dysfunction, commonly seen in postoperative pediatric cardiac surgery.

We believe that the development of such devices with national technology could benefit a large number of children and young adults suffering from dysfunction of the RVOT and require frequent surgical interventions.

REFERENCES

1. Moller JH, Taubert KA, Allen HD, Clark EB, Lauer RM. Cardiovascular health and disease in children: current status. A Special Writing Group from the Task Force on Children and Youth, American Heart Association. *Circulation*. 1994;89(2):923-30.
2. Bureau USC. *Annual estimates of the population by selected age groups and sex for the United States*. In: Bureau USC, ed. Washington;2004.
3. Chen CR, Cheng TO, Huang T, Zhou YL, Chen JY, Huang YG, et al. Percutaneous balloon valvuloplasty for pulmonic stenosis in adolescents and adults. *N Engl J Med*. 1996;335(1):21-5.
4. Griffith BP, Hardesty RL, Siewers RD, Lerberg DB, Ferson PF, Bahnson HT. Pulmonary valvulotomy alone for pulmonary stenosis: results in children with and without muscular infundibular hypertrophy. *J Thorac Cardiovasc Surg*. 1982;83(4):577-83.
5. Hayes CJ, Gersony WM, Driscoll DJ, Keane JF, Kidd L, O'Fallon WM, et al. Second natural history study of congenital heart defects. Results of treatment of patients with pulmonary valvar stenosis. *Circulation*. 1993;87(2 Suppl):I28-37.
6. O'Connor BK, Beekman RH, Lindauer A, Rocchini A. Intermediate-term outcome after pulmonary balloon valvuloplasty: comparison with a matched surgical control group. *J Am Coll Cardiol*. 1992;20(1):169-73.
7. Oliver Ruiz JM. Congenital heart disease in adults: residua, sequelae, and complications of cardiac defects repaired at an early age. *Rev Esp Cardiol*. 2003;56(1):73-88.
8. Therrien J, Siu SC, Harris L, Dore A, Niwa K, Janousek J, et al. Impact of pulmonary valve replacement on arrhythmia propensity late after repair of tetralogy of Fallot. *Circulation*. 2001;103(20):2489-94.
9. Therrien J, Marx GR, Gatzoulis MA. Late problems in tetralogy of Fallot: recognition, management, and prevention. *Cardiol Clin*. 2002;20(3):395-404.
10. Carvalho JS, Shinebourne EA, Busst C, Rigby ML, Redington AN. Exercise capacity after complete repair of tetralogy of Fallot: deleterious effects of residual pulmonary regurgitation. *Br Heart J*. 1992;67(6):470-3.
11. Marie PY, Marçon F, Brunotte F, Briançon S, Danchin N, Worms AM, et al. Right ventricular overload and induced sustained ventricular tachycardia in operatively "repaired" tetralogy of Fallot. *Am J Cardiol*. 1992;69(8):785-9.
12. Bonhoeffer P, Boudjemline Y, Saliba Z, Hausse AO, Aggoun Y, Bonnet D, et al. Transcatheter implantation of a bovine valve in pulmonary position: a lamb study. *Circulation*. 2000;102(7):813-6.
13. Bonhoeffer P, Boudjemline Y, Saliba Z, Merckx J, Aggoun Y, Bonnet D, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet*. 2000;356(9239):1403-5.
14. Bonhoeffer P, Boudjemline Y, Qureshi SA, Le Bidois J, Iserin L, Acar P, et al. Percutaneous insertion of the pulmonary valve. *J Am Coll Cardiol*. 2002;39(10):1664-9.
15. Khambadkone S, Coats L, Taylor A, Boudjemline Y, Derrick G, Tsang V, et al. Percutaneous pulmonary valve implantation in humans: results in 59 consecutive patients. *Circulation*. 2005;112(8):1189-97.
16. Lurz P, Coats L, Khambadkone S, Nordmeyer J, Boudjemline Y, Schievano S, et al. Percutaneous pulmonary valve

- implantation: impact of evolving technology and learning curve on clinical outcome. *Circulation*. 2008;117(15):1964-72.
17. Bove EL, Byrum CJ, Thomas FD, Kavey RE, Sondheimer HM, Blackman MS, et al. The influence of pulmonary insufficiency on ventricular function following repair of tetralogy of Fallot. Evaluation using radionuclide ventriculography. *J Thorac Cardiovasc Surg*. 1983;85(5):691-6.
 18. Therrien J, Provost Y, Merchant N, Williams W, Colman J, Webb G. Optimal timing for pulmonary valve replacement in adults after tetralogy of Fallot repair. *Am J Cardiol*. 2005;95(6):779-82.
 19. Bove EL, Kavey RE, Byrum CJ, Sondheimer HM, Blackman MS, Thomas FD. Improved right ventricular function following late pulmonary valve replacement for residual pulmonary insufficiency or stenosis. *J Thorac Cardiovasc Surg*. 1985;90(1):50-5.
 20. Boethig D, Thies W, Hecker H, Breyman T. Mid term course after pediatric right ventricular outflow tract reconstruction: a comparison of homografts, porcine xenografts and Contegras. *Eur J Cardiothorac Surg*. 2005;27(1):58-66.
 21. Boethig D, Goerler H, Westhoff-Bleck M, Ono M, Daiber A, Haverich A, et al. Evaluation of 188 consecutive homografts implanted in pulmonary position after 20 years. *Eur J Cardiothorac Surg*. 2007;32(1):133-42.
 22. Boethig D, Breyman T. Contegra pulmonary valved conduits cause no relevant hemolysis. *J Card Surg*. 2004;19(5):420-5.
 23. Gaia DF, Palma JH, Souza JA, Guilhen JC, Telis A, Fischer CH, et al. Off-pump transapical balloon-expandable aortic valve endoprosthesis implantation. *Rev Bras Cir Cardiovasc*. 2009;24(2):233-8.
 24. Chiam PT, Ruiz CE. Percutaneous transcatheter aortic valve implantation: assessing results, judging outcomes, and planning trials: the interventionalist perspective. *JACC Cardiovasc Interv*. 2008;1(4):341-50.
 25. Van Brabant H, Neyt M. Safety of percutaneous aortic valve insertion. A systematic review. *BMC Cardiovasc Disord*. 2009;9:45.
 26. Zahn EM, Hellenbrand WE, Lock JE, McElhinney DB. Implantation of the melody transcatheter pulmonary valve in patients with a dysfunctional right ventricular outflow tract conduit early results from the U.S. Clinical trial. *J Am Coll Cardiol*. 2009;54(18):1722-9.