

Dysfunction of the Pulmonary Homograft Used in the Reconstruction of the Right Ventricle Exit Tract

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Abstract

Background: The pulmonary homograft has been used as an option in the correction of congenital cardiopathy with obstruction of the right ventricle exit tract. The long term results, however, are little satisfactory.

Objective: Identify the risk factors associated to the dysfunction and the pulmonary homograft failure.

Methods: Study with children submitted to the enlargement of the exit tract of the right ventricle with pulmonary homograft. The clinical, surgical, evolutional and morphological aspects of the prosthesis variables were analyzed as risk factors.

Results: The final sample of 75 patients with median age at the surgery of 22 months, varying from 1-157 months, presented 13 patients (17.0%) who developed dysfunction of the homograft, characterized by stenosis or severe pulmonary insufficiency. The occurrence time between the homograft implant and the detection of the dysfunction was of 45 ± 20 months. When the size of the homograft was smaller than 21 mm and the Z score of the pulmonary valva is lower than zero, or higher than three, the risk factors were considered for the dysfunction occurrence.

Conclusion: The pulmonary homograft smaller than 21 mm and the inadequate pulmonary valva for the age and weight of the patient are determining factors for the prosthesis dysfunction. (*Arq Bras Cardiol* 2011; 96(1): 2-7)

Keywords: Transplantation, homologous/physiopathology; heart ventricles; heart defects, congenital/surgery.

Introduction

The use of homograft in the surgical treatment of the congenital cardiopathies started in the 60's, with Rastelli et al (1964) and Ross and Somerville (1966). In the first years, the high calcification and stenosis rate of the graft caused the search for different combinations of materials for the reconstruction surgeries¹.

From the 80's, with the improvement of the techniques of preparation and conservation, the homograft became the chosen material in several services¹. Despite this, the literature has still been showing the need for surgical changing due to the occurrence of stenosis or prosthesis insufficiency.

The pediatric cardiac surgery service of *Santa Casa de Curitiba* has been using, since the 90's, the pulmonary or aortic homograft in the correction of the congenital cardiopathies, obtaining good result,

The reconstruction of the exit path of the right ventricle with pulmonary homograft would have a better evolution in the medium and long term.

The objective of the study was to evaluate the influence of several risk factors recognized in the literature for the occurrence of dysfunction of the homograft in a sample of operated patients with graft developed in our group.

Material and methods

For this study, 90 patients were evaluated, operated in the 1998-2005 period, who used cryopreserved pulmonary type homograft in the reconstruction of the exit pathway of the right ventricle, or in the replacement of a heterograft placed in this position in a previous surgery.

The cryopreserved pulmonary homograft was provided by the Human Cardiac Valvas Bank of *Santa Casa de Curitiba*.

The patients using the pulmonary homograft in the reconstruction of the left exit tract, as in the Norwood surgeries and in the interruption of the aortic arch or in the surgeries of cavopulmonary anastomosis were excluded from this study. In addition to those with incomplete data in their records.

In their records, the data related to gender, cardiopathy type, presence of change in the pulmonary tree, blood type, age in the first visit and at the moment of the surgery, previous surgery, time of outpatient follow-up and result of the tests performed in the institution, such as color echocardiogram doppler and cardiac catheterism were collected.

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The analyzed data of the surgical part were: homograft sizes, donator's blood type, Z value of the pulmonary valva, the maintenance of the homograft integrity, the extracorporeal time and the aortic clamping time. The post-surgery data were: the intercurrents during the stay in the intensive care unit and the occurrence of death in the immediate post-surgery.

The Z value of the pulmonary valva relates the homograft size in millimeters with the body surface of the patient. The Z value of the pulmonary valva equal to zero means the ideal size of the homograft for the patient's body surface. The negative and positive values mean a less or greater standard deviation from the ideal value,

The pulmonary homograft integrity can be altered by the surgeon, decreasing the valva ring size, removing one of the cusps or replacing the cusps by a monocuspid of homograft, or other material.

The surgeries were performed by the same surgical team and some patients, before the total correction surgery, required palliative surgeries.

From the outpatient follow-up, it was analyzed the insufficiency or the pulmonary stenosis, measured by means of echocardiographic tests and classified as mild, moderate and severe. The insufficiency or severe stenosis of the homograft was designated as dysfunction.

The severe insufficiency was considered as regurgitation that encompasses totally the diameter of the pulmonary ring and with diastolic reflux in the color Doppler in branches of the pulmonary arteries. The severe stenosis was considered as an instantaneous and maximum systolic gradient in the Doppler, superior to 50 mmHg,

The existence of reflux with discreet amplitude of the ring was defined as mild pulmonary insufficiency. The moderate pulmonary insufficiency was defined when there was regurgitation of around half of the diameter of the valva ring, with diastolic reflux in the color Doppler in the trunk of the pulmonary artery. The mild pulmonary stenosis was considered in the presence of the maximum instantaneous pulmonary systolic gradient in the Doppler inferior to 30 mmHg and moderate between 30-50 mmHg,

It was considered as homograft failure the need to change the pulmonary homograft by surgery due to its dysfunction (insufficiency or severe stenosis).

For comparing the time curves up to the occurrence of the homograft dysfunction, it was used the Log-rank test. The cases that until the last echocardiographic evaluation did not present homograft dysfunction were considered as censored. In the univariate analysis, the variables gender, age at the time of the surgery, cardiopathy type, homograft size, Z value of the pulmonary valva, blood compatibility, anatomy change of the pulmonary tree, previous surgery, extracorporeal time and aortic clamping time were analyzed.

For the joint evaluation of factors, a Cox's regression model was adjusted and the relative risk values were estimated, as well as 95.0% confidence intervals. Kaplan-Meier curves were built for presenting the time curves for the homograft dysfunction. Values of $p < 0.05$ indicated statistical significance. The data

were organized in an Excel worksheet and analyzed with the use of the computing software Statistica v.8.0.

Results

The records of 92 patients submitted to surgical correction of the cardiopathy with the use of the cryopreserved pulmonary homograft in the right ventricle exit tract were analyzed.

The average age of the patients in the first visit was 14.3 ± 4.2 months. Forty patients received care in the first month of life and 66 during the first year of life. From the patients, 56% were females.

The cardiopathies are listed in Table 1. The patients with tetralogy of Fallot, who used the pulmonary homograft, were those with agenesis of the pulmonary valva or with hypoplasia of ring and pulmonary trunk.

The outpatient follow-up of these patients was 106 ± 62.7 months, with median of 89 months, varying from 24 months to 272 months.

The average age of the patients at the moment of the surgery of the cardiopathy correction was $40,3 \pm 42,3$ months, with median of 22 months, varying from 1 month to 157 months. Thirty per cent of the sample (28 cases) were operated before being one year old, with variation in the total correction ages as per the cardiopathy.

In 8 patients, the exchange of a bovine pericardium tube was performed in a previous surgery by a pulmonary homograft, around 110.5 ± 24.3 months after the initial surgery.

In 46.0% of the patients, the pulmonary tree showed changes as branch stenosis, absence of branch, aneurysmatic pulmonary branches or presence of pulmonary systemic side effects.

The pulmonary homograft used in the surgeries varied in size from 12 to 26 mm, with average of 21.5 ± 3.2 mm and median of 22 mm. The Z value of the pulmonary valva varied from less than one to 5, with average of 2.8 ± 1.4 and median

Table 1 - Table with the cardiopathy types, number of patients, age in the first visit and age when total correction surgery was performed

Cardiopathy	Number of patients	Age in the first visit, in months (median)	Age on the correction surgery, in months (median)
Pulmonary atresia + IVC	26	4	23
Tetralogy of Fallot	24	15 *	21.5
Truncus arteriosus	17	2	3
TGA + IVC and VPS	16	1.5	41.5
TGA corrected + IVC + VPS	6	15.5*	61.5
Valva pulmonay stenosis	3	0.5	132

IVC - interventricular communication; TGA - transposition of great arteries; VPS - valva pulmonay stenosis; (*) some patients are sent to the service older, after the palliative surgery or clinical observation.

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of 3. Fifty seven per cent of the homografts had their Z value between 0 and plus 3.

The integrity of the pulmonary homograft when inserted, varied as per the patient. In 11 cases (12.0% of the sample), there was a change in the pulmonary homograft for better adaptability: 9 cases used a monocuspid of the homograft and two cases a monocuspid of goretex.

In 47 patients, a hemashield ceiling or bovine pericardium, to make the connection of the right ventricle with the pulmonary homograft. In 30.0% of the patients there was blood compatibility between the donator of the homograft and the receptor.

In 56.0% of the patients, the extracorporeal time was above 120 minutes, with average of 135 ± 44.6 minutes. In 62,0% of the cases, the clamping time of the aorta was kept over 80 minutes, with average of 99.5 ± 34.2 minutes.

There were 17 early deaths, 11 of them by failure of multiple organs and two late deaths.

The pulmonary homograft dysfunction in the outpatient evaluation was present in 13 patients (17.0% of the sample) and, from these, 5 were submitted to surgical change of the homograft.

Ten patients presented severe stenosis of the pulmonary homograft with average systolic gradient of 67 ± 22 mmHg, varying from 50 mmHg to 127 mmHg, and three patients had severe pulmonary insufficiency.

For the patients with homograft dysfunction, the surgery time up to the occurrence of the dysfunction was in average

45.4 ± 20.3 months with median of 36 months, varying from 7 to 86 months.

For three years, the survival free from dysfunction was of 90.0%, for 5 years, was of 84.0% and, for 7 years, it was of 80.0%. The survival free from homograft surgical exchange was for 3 years, of 96.0%, for 5 years, was of 94.0% and for 7 years of 93.0%.

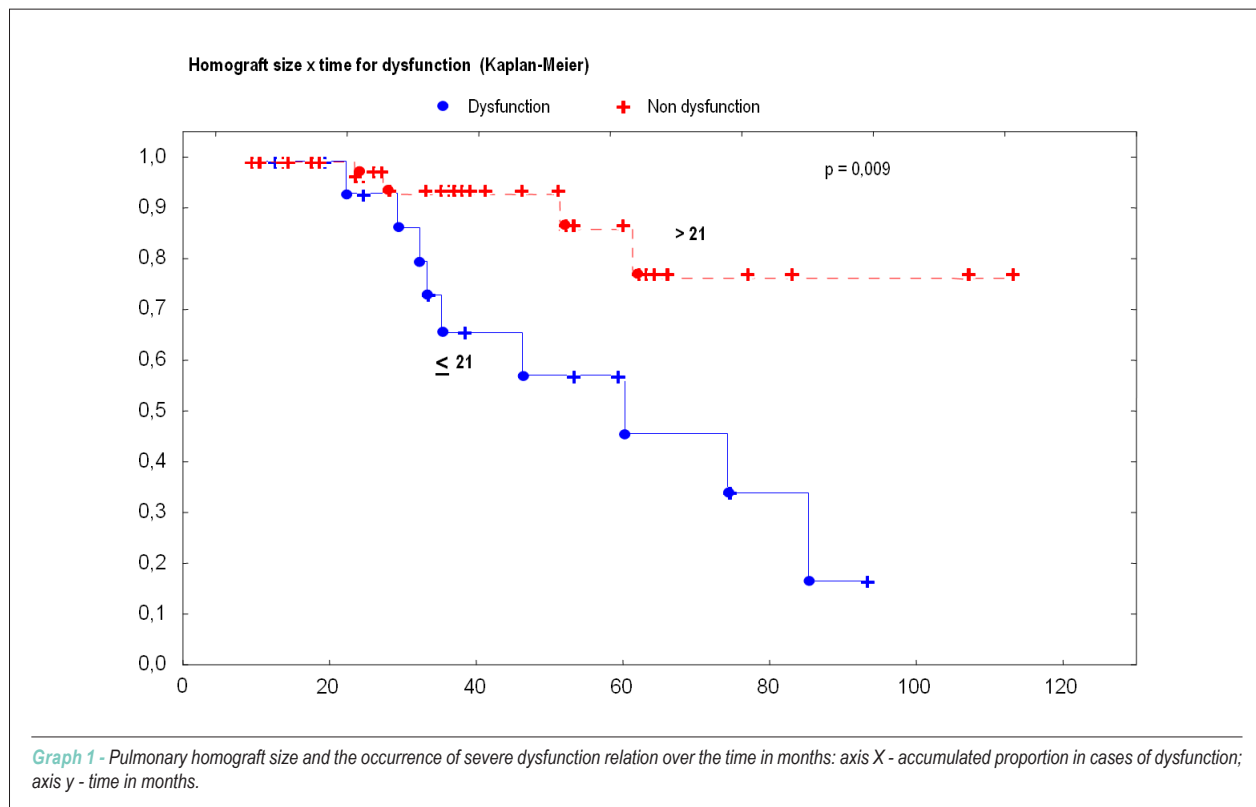
Only the size of the homograft, equal or smaller than 21 mm, was involved in severe dysfunction of the homograft, having a survival free from dysfunction in 5 years of 45.0% for this size and of 80.0% for the homograft over 21 mm ($p = 0.009$) (Graph 1).

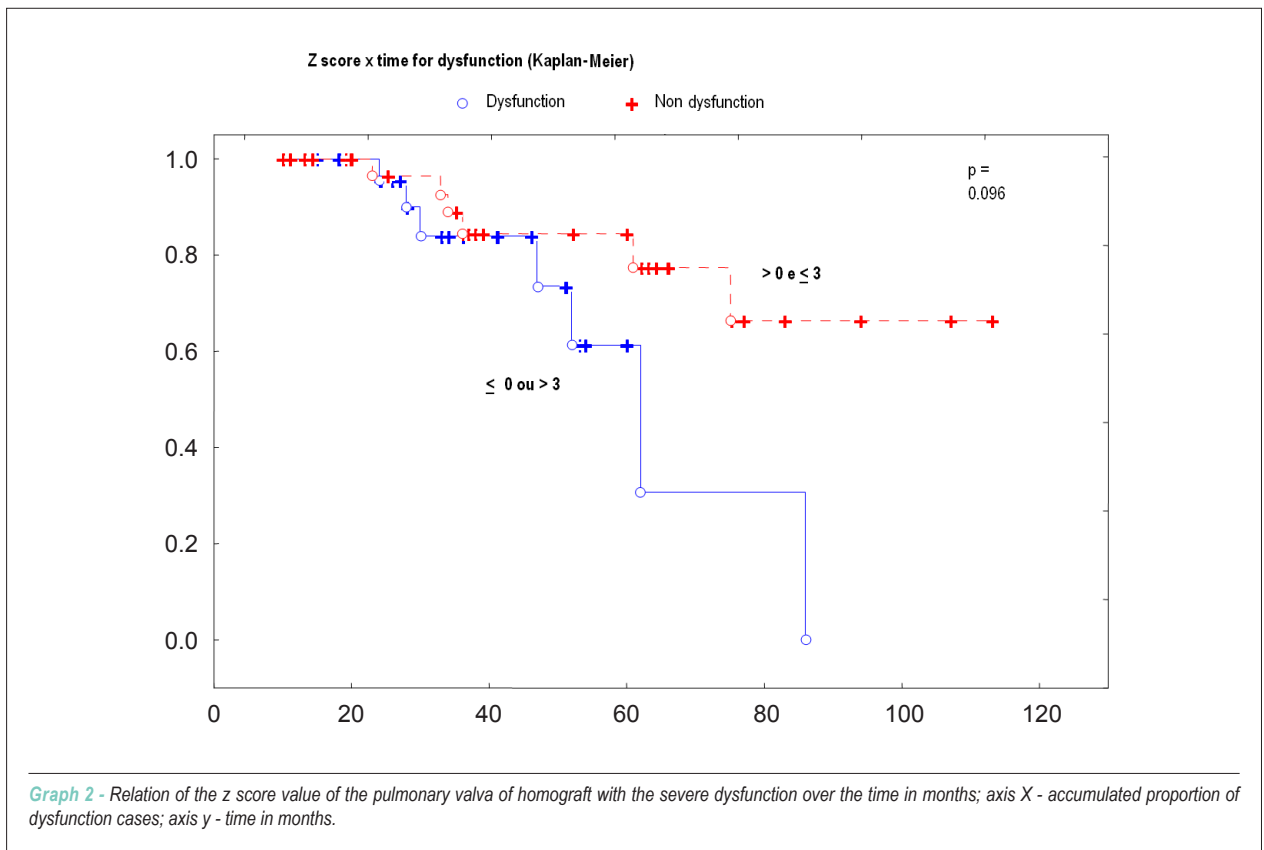
The Z value of the pulmonary valva revealed that, for the measures between zero and plus three, the rate for the dysfunction occurrence in 5 years was of 22.0%, and, for the measures below zero or above plus three, was 65,0% ($p = 0.09$) (Graph 2).

In Cox's regression, the variable involved in the homograft dysfunction was the size, when the homograft with size inferior or equal to 21 mm had a risk 3,7 times higher than the homograft dysfunction over 21 mm (table 2).

Discussion

In the last years, the cardiac surgery service of Santa Casa de Curitiba chose to use the pulmonary homograft for reconstructing the right ventricle exit tract due to its technical advantages and the good clinical and surgical results of the already operated patients^{2,3}.





Graph 2 - Relation of the z score value of the pulmonary valva of homograft with the severe dysfunction over the time in months; axis X - accumulated proportion of dysfunction cases; axis y - time in months.

Table 2 - Variables related to the dysfunction and its relative risk with confidence interval 95.0%

Variable	P value	RR	CI 95,0%
Homograft size	0.031	3.7	1.1-12.4
Z value of the pulmonary valva	0.187	2.1	0.7-6.5
Clamping time	0.367	1.8	0.5-6.7

RR - relative risk; CI - confidence index.

The option of this service for the use of the pulmonary homograft, in such position, is based on studies that show that the aortic homograft in pulmonary position presents higher index of calcification due to its composition rich in elastin⁴⁻¹⁵.

From the surgical point of view, the pulmonary homograft is available in small sizes, has higher hemostatic capacity, higher ductility and handling easiness for the surgeon, their branches can be used for enlarging the stenotic areas in the pulmonary arteries, does not need chronic anticoagulation, presents higher resistance to endocarditis and has a potential feasibility for the second repair^{5,7,10,11,15-18}.

In the majority of the cases, the deterioration of the homograft takes place by stenosis due to the calcification¹. The rate of homograft failure varies as per the study, being in 5 years between 10.0-40.0%^{5,14} of the implanted homografts and, in 10 years, between 46.0-65.0%^{4,7}.

Of the risk factors involved in the deterioration of the

homograft, the cardiopathy type is one of them. Forbes et al¹⁹, Bando et al⁹ and Dearanie et al⁴ found a higher failure rate of the homograft associated to the cardiopathies as *truncus arteriosus*, transposition of the great arteries with pulmonary stenosis and double exit pathway from the right ventricle; however, in this study, there was no homograft durability correlation with the type of cardiopathy.

In young people, the insertion of the homograft it is considered a risk factor for the conduit failure^{4,5,8,9,12,14,15,18-21}. The reasons for this are diverse and, among them, the accelerated growth pattern of the children, the use of homografts of smaller sizes and the immunological response exacerbate in the children. In our study, there was no difference in the durability of the homografts inserted in children below and above one year old.

One of the most discussed points is the size of the homograft used and its influence in the durability. The pulmonary homograft small in size is associated to a higher dysfunction rate and surgical exchange^{4,5,14,15,18,19,21-24}.

Our study demonstrated that the use of a pulmonary homograft smaller than 21 mm has a higher probability of dysfunction, that is, the homograft below 21 mm has 3.7 times more risk of developing dysfunction than the one above 21 mm. The survival free from dysfunction in 5 years, for a homograft inferior to 21 mm is of 55.0% and, above 21 mm, is of 85.0%.

Other studies have already related that the homograft size is a risk factor for dysfunction. Bielefeld et al¹⁵ demonstrated that

the occurrence of the dysfunction in the homograft above 20 mm is low. Razzouke et al²⁹ affirms that the homograft above 24 mm has a higher survival free from surgical exchange and Boethige et al²⁰ shows that the homograft below 20 mm is less durable in children and develops stenosis gradient more quickly.

The small Z value of the pulmonary valva is also involved in the homograft dysfunction^{7,8,20}. The higher dysfunction rate in our study was for a Z value below zero and above plus three, that is, the best results were obtained when the size of the pulmonary valva was between zero and plus three Z value. Thus, some centers, including our Service, has been using a homograft with the biggest number possible for the children, trying to compensate the natural growth of them with a valva of biggest size and decrease the incidence of dysfunction and surgical exchange^{7,14,20,21,25,26}.

In this study, other risk factors for dysfunction of the prosthesis known in the literature such as blood compatibility between donator and receptor, change in the anatomy of the pulmonary tree, cardiac surgery with previous enlargement, use of integral homograft or a replacement of one of its parts, patient sex, extracorporeal time and the age at the surgery did not have influence in the durability of the homograft.

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Conclusion

The use of pulmonary homograft for the enlargement of the right ventricle exit tract presents good results, with a dysfunction rate of 17.0% of the cases. This study showed lower chance of dysfunction with implant of a pulmonary homograft over 21 mm and a Z value of pulmonary valva between zero and plus three.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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