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Coronary dominance patterns in hypoplastic left heart syndrome

Dominância coronariana na síndrome da hipoplasia do coração esquerdo

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Abstract

Introduction: **Although hypoplastic left heart syndrome (HLHS) is extensively studied this disease still has a high mortality rate compared to other diseases treated as univentricular physiology. In this context, morphological differences between phenotypes within the spectrum of HLHS may be recognized as risk factors, and their identification can assist in choosing treatment between subgroups.**

Objective: **To identify the most prevalent form of coronary artery dominance in HLHS in subgroups with atresia and mitral stenosis.**

Methods: **Analysis of the coronary anatomy according to the distribution of epicardial branches and the dominance patterns classified as right, left, or balanced (co-dominant). Control group was composed of nine specimens of morphologically normal hearts; the HLHS group consisted of nine specimens with MA and 24 specimens with MS. We applied Chi-square test for statistical analysis.**

Results: **There were significant differences between the two groups in relation to coronary artery dominance (÷2 = 9.298; *P* = 0.01). Left dominance was present in 75% of MS cases and the balanced (co-dominant) dominance was observed only in MS. In the control group, right dominance was observed in all cases (*P* <0.01).**

Conclusions: **Left dominance is more common in HLHS than in the control group of normal hearts and in HLHS. The left coronary dominance is more frequent in the subgroup with mitral stenosis.**

Descriptors: **Heart/anatomy & histology. Coronary vessels. Hypoplastic left heart syndrome. Heart defects, congenital.**

Resumo

Introdução: **Apesar de a síndrome do coração esquerdo hipoplásico (SCEH) ser extensamente estudada, esta doença ainda apresenta mortalidade elevada se comparada a outras doenças tratadas como fisiologia univentricular. Assim, diferenças morfológicas entre fenótipos dentro do espectro**

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This study was carried out at the Heart Institute (InCor), University of São Paulo Medical School, Brazil

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da SCEH podem ser fatores de risco e sua identificação pode auxiliar na escolha terapêutica entre os subgrupos anatômicos.

Objetivos: **Determinar a forma mais frequente de dominância coronariana em corações com SCEH nos subgrupos com atresia (AM) e estenose mitral (EM).**

Métodos: **Análise da anatomia coronariana de acordo com a distribuição dos ramos epicárdicos e o padrão de dominância, classificadas em direita, esquerda ou balanceada. O grupo controle foi composto por nove peças de corações morfologicamente normais. O grupo SCEH constituiu-se de nove peças com AM e 24 peças com EM. Para análise estatística foi utilizado o teste do qui-quadrado.**

Resultados: **Houve diferença significativa entre os dois grupos em relação à dominância coronariana (x^2= 9,298; *P*=0,01). A dominância esquerda esteve presente em 75% dos casos de EM, e a balanceada só foi observada na EM. No grupo controle, observou-se dominância direita em todos os casos (*P*<0,01).**

Conclusões: **A dominância esquerda é mais frequente na SCEH que no grupo controle de corações normais e, na SCEH, a dominância coronariana esquerda é mais frequente no subgrupo com EM.**

Descritores: **Coração/anatomia & histologia. Vasos coronários. Síndrome do coração esquerdo hipoplásico. Cardiopatias congênitas.**

INTRODUCTION

The hypoplastic left heart syndrome (HLHS) is a spectrum of cardiac malformations characterized by severe underdevelopment of the left heart complex and aorta. It includes both the left ventricular cavity and mass. At one end of the spectrum is the mitral and aortic atresia with absent/not detectable left ventricular cavity. At the other end are the cases with varying degrees of hypoplasia of the mitral and aortic valves and ventricular hypoplasia [1], leading to the impossibility of maintaining cardiac output and systemic perfusion by the left heart. In anatomic series, there is a predominance of the phenotype with a patent mitral valve (67%) [2].

Although the HLHS is extensively studied, the surgical treatment performed by the Norwood-type palliative surgery [3-4] or by the so-called hybrid procedures [5-6] has satisfactory results in many centers [7-8]. Nevertheless, this disease still has a high mortality rate between the first and second stage, when compared to other diseases treated as univentricular physiology. There has also been a lot of controversy over whether the subgroup patients with mitral stenosis and aortic atresia present a higher risk of death after the first stage of palliative surgery [9-11] due to factors related to myocardial perfusion or histological changes.

Although mortality from postoperative coronary heart disease is commonly caused by technical factors related to the aortic arch reconstruction [12], it can also be caused by intrinsic coronary abnormalities such as hypoplasia of the epicardial branches. In addition, the steal phenomenon of epicardial coronary flow by fistula is further considered an intrinsic coronary abnormality, particularly if it is associated with myocardial hypertrophy, as observed in the subgroup with mitral stenosis, which compromises myocardial perfusion [13]. These coronary fistulas usually arise from the left coronary artery branches [14].

In this context, morphological differences between phenotypes within the spectrum of HLHS may come to be recognized as limiting factors for a favorable postoperative course. Thus, their identification can possibly contribute to the therapeutic choice between the anatomical subgroups in near future.

Objective

To determine the most common form of coronary artery dominance in HLSH hearts in groups with mitral atresia and mitral stenosis.

METHODS

This study was approved by the Research and Ethics Committee of InCor-HCFMUSP. It received the protocol number 0786/09, and represents the partial result of the author's doctorate dissertation.

Selection of Anatomic Specimens

Anatomic specimens selection was carried out at the Museum of the Laboratory of Pathology; Heart Institute (InCor), University of São Paulo Medical School (InCor-HCFMUSP) according to the following criteria:

Inclusion Criterion

Anatomic specimens of HLHS obtained from deceased patients of both sexes under the age of 30 days.

Exclusion Criteria

- Anatomic specimens in which surgical procedures or the state of preservation prevented proper morphology identification.

- Age over 30 days.
- Other congenital anomalies with hypoplastic left ventricle but not with all criteria for HLHS.

Morphological Analysis

Anatomic specimens were classified according to their morphological diagnosis as follows:

I – group with mitral atresia (MA) associated with either atresia or stenosis of the aortic valve.

II – group with mitral stenosis (MS) associated with either atresia or stenosis of the aortic valve.

Anatomical Study

The gross examination of the epicardial coronary artery anatomy was done under a magnifying glass. The distribution of the major epicardial branches and the pattern of dominance were determined.

Coronary dominance was defined as the main artery (the right or the left) that supplies the posterior interventricular artery. Thus, it was classified as right, left or balanced (co-dominant) [15].

Control group consisted of nine specimens of morphologically normal hearts with from patients who died in the neonatal period due to non-cardiac causes.

HLHS group consisted of nine specimens with MA and 24 specimens with MS.

We used the Chi-square test for statistical analysis and *P* values less than 0.05 were considered statistically significant.

Table 1. Divisions between the morphological subgroups of hearts with HLHS

Morphologic subgroup	N
Mitral atresia and Aortic atresia	9
Mitral stenosis and Aortic atresia	13
Mitral stenosis and Aortic stenosis	11

HLHS = Hypoplastic Left Heart Syndrome

RESULTS

The numbers of hearts with HLHS in each morphological subgroup are shown in Table 1.

We found significant differences between the two groups in relation to coronary dominance ($\chi^2 = 9.298$; $P = 0.01$). Left dominance was present in 75% of MS cases. The balanced dominance (co-dominance) was observed in MS only. The distribution of data is shown in Table 2.

Comparisons with the control group

We did Chi-square tests including the controls. There was a statistically significant difference in the pattern of coronary dominance($P<0.01$), once the right dominance was only be observed in the control group.

DISCUSSION

The right coronary dominance is the most prevalent dominance pattern observed in normal humans [16,17], occurring in 72% of individuals [15]. In HLHS, the dominance has hardly been studied [18], and most studies analyzed their morphological and histological changes only [19-22].

In HLHS, the spatial distribution of the epicardial coronary vessels is similar to that of normal hearts [20]. The presence of coronary-cavitary fistulas, anomalous origin and tortuosity of the coronary arteries are related to complications and higher mortality [13].

The finding of coronary fistulas prevails in the hearts with mitral stenosis associated with aortic atresia [19]. Sauer et al. [21] showed that in hearts with mitral stenosis and aortic atresia, there is an association of 42% of coronary anomalies, such as thickening and tortuosity of the proximal left coronary artery in cases presenting associated endocardial fibroelastosis. The preoperative identification of such anomalies can avoid a direct injury or damage to the underlying areas in a surgery that involves the reconstruction of the aortic root [23].

Vida et al. [9] proposed that the patients' subgroup with mitral stenosis and aortic atresia should undergo

Table 2. Coronary dominance

			Dominance			Total
			Right	Left	Balanced	
		N	5	4	__	9
	MA	% within subgroup	55.6%	44.4%	__	100.0%
		n	2	18	4	24
Group	MS	% within subgroup	8.3%	75.0%	16.7%	100.0%
		n	7	22	4	33
Total		% within subgroup	21.2%	66.7%	12.1%	100.0%

MA = Mitral atresia group; MS = Mitral stenosis group preoperative cineangiocoronariography to define the magnitude of coronary-cavitary fistulas due to the greater surgical risk, suggesting heart transplantation or hybrid procedures as therapeutic options. Based on the study of their series of cases, the hospital mortality rate was significantly higher (29% vs 7.9%; *P*=0.002) in this subgroup compared to others. Coronary-cavitary communications were also associated with increased mortality (50% vs 6%; *P*=0.004).

Glatz et al. [10] conducted a retrospective study of 72 patients undergoing the Norwood procedure. They observed that the interstage mortality was higher in patients with aortic atresia and mitral stenosis. Thus, they correlated it to possible coronary abnormalities, such as thickening of the tunica media and ventricular-coronary connections. The abnormalities could predispose to ischemia and ventricular dysfunction, and also to potentially life-threatening arrhythmias. These authors consider the possibility that the Tuguo-Sano surgery, which interposes the tube between the right ventricle and the pulmonary trunk, if performed in the subgroup of patients with fistulas, could limit the flow steal during diastole to the pulmonary arteries to the detriment of the potentially vulnerable coronary arteries.

Considering the Brazilian experience, da Silva et al. [24] revealed no differences between the Norwood and Sano procedures. Some authors presume that the best results with the Sano technique would be more related to the increased experience of the groups than to hemodynamic peculiarities.

Sathanandam et al., [11] analyzing the 30-day survival in 100 patients undergoing Norwood-type surgery have obtained a 90%-success rate in the whole group and 89.9% in the subgroup with mitral stenosis and aortic atresia. At 60 days, they obtained 70% 70.4%, respectively without a significant difference. For these authors, the presence of coronary-cavitary fistulas had no effect on mortality.

Following the neonatal period, patients with HLHS have a similar outcome to other patients with single ventricle physiology [25].

Based on our present study, the left dominance was prevalent in HLHS. Hansel et al. [18], in an angiographic study also found that the left dominance had been more frequent in HLHS than in the normal population, although in the series studied the right dominance has prevailed. In that sample, the right dominance occurred in 51.2% of the patients, left dominance on 36.9%, and the balanced (co-dominance) in 11.9%. They, however, did not find statistically significant differences between the morphological groups. The left and balanced (co-dominance) dominances were significantly more common in the absence of the left ventricular cavity, in contrast to our findings where the left dominance was significantly higher in cases with mitral stenosis and detectable ventricular cavity.

The main clinical implication of our study is that patients with HLHS should be treated individually, considering the anatomical peculiarities. It is possible that patients with fistulas and left dominance have different prognosis and progression compared to those with fistulas but right dominance. However, the limitation of our study is to have been conducted using autopsy specimens. Thus, these hearts would presumably represent cases with the most severe morphological changes.

However, we support that it is possible for patients with coronary fistulas and left coronary dominance to have different prognosis and clinical evolution compared with patients with fistula and right coronary dominance. In order to support this statement, the total area of irrigated myocardium, its potential for ischemia, and secondary arrhythmias must be considered. These data will be evaluated in an ongoing histological investigation.

CONCLUSION

The data presented here, which result from the study of autopsy hearts, allowed us to conclude that the pattern of left dominance is more frequent in HLHS than in the control group with normal hearts, and even more prevalent in the subgroup with mitral stenosis.

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