Cardiology in the Young

cambridge.org/cty

Coronary artery fistulas after paediatric heart transplantation

Elisabet Camprubi-Tubella[1], Ferrán Gran-Ipiña[2] and Pedro Betrián-Blasco[1]

[1]Pediatric Cardiology and Pediatric Cardiac Surgery Department, Pediatric Interventional Cardiology Unit. Hospital Vall Hebrón, Barcelona, Spain and [2]Pediatric Cardiology and Pediatric Cardiac Surgery Department, Pediatric Heart Transplant Unit. Hospital Vall Hebrón, Barcelona, Spain

ABSTRACT

Coronary artery fistulas have been described in patients after heart transplantation more often than in the normal population. We reviewed our centre's database between 2008 and 2020. Thirty patients had coronary angiography and 13 showed non-cameral coronary artery fistulas in their first coronary angiography. Distribution, degree and evolution of the fistulas and characteristics of transplant procedure, patient and immunosuppressive treatments were analysed.

Case report

Coronary artery fistulas have been described in patients after heart transplantation more often than in the normal population.[1] Our aim was to review the incidence, anatomy, and evolution of coronary fistulas in our paediatric heart transplant patients.

Our centre's database of paediatric heart transplant patients was reviewed retrospectively. All the patients transplanted between 2008 and 2020 with at least one coronarography during their follow-up were included and every coronary angiography was reviewed focusing on the presence of coronary artery fistulas, number, anatomic distribution, ending structure, size, and flow amount. Categorical data are reported as frequencies and percentages and have been analysed using the Fisher's exact test. The continuous variables are reported as median and interquartile range.

During this period, a total of 50 patients were transplanted and 30 of them had at least 1coronary angiography. The median age at the transplant was 8.2 years (SIQR 5.3 years). The reason for the transplant was 73.3% cardiomyopathy, 23.3% congenital, and 3.3% retransplantation. All of them had at least one coronary angiography in the first 3years after heart transplantation, with median time until the first procedure of 1 year (SIQR 0.6) and median of two coronary angiographies during follow-up. Median follow-up of 5.3 years (SIQR 3.2). Table 1 describes the characteristics of the patients with coronary artery fistulas and Table 2 summarises the characteristics of the fistulas. A total of 13 (43.3%) patients had at least 1 coronary artery fistula on the first coronarography: 8 (61.5%) presented just one fistula, 2 (16.6%) two fistulas, 1 (12%) three fistulas, and 1 more than three. According to the importance of their flow, fistulas were classified as small in 7 patients (58.3%), medium in 4 (30.7%), and large in 2 (16.6%), with one of the large ones causing dilatation of the coronary arteries as a collateral effect. Their origin was the anterior descending coronary artery in 9, right coronary artery in 5, and the circumflex artery in 3, and 78.9% of them were terminated at the ipsilateral lung field. Two patients presented a second fistula draining to the pulmonary artery. Two fistulas to systemic thoracic arteries were identified. None of them presented any symptoms of cardiac dysfunction, nor electrocardiogram or echocardiography ischaemic signs. A second coronarography was performed in 7 patients, a median of 22 months after the first one. In 2 patients the amount of fistulas flow significantly decreased, and in 1 case, even disappeared.

Compared to the previous descriptions of this finding, we didn't find any statistically significant difference in the sex, age at heart transplant, indication for heart transplant, induction agent, immunosuppressant treatment nor median time of follow-up between the group with fistulas and the one without. In contrast to what is suggested in the literature, we have not found any statistically significant difference in the ischaemia time. No relationship has been found between the characteristics of the fistulas and mortality or retransplantation either.

Discussion

Coronary artery fistulas are a rare coronary anomaly,[4] and is found in 0.2% of patients undergoing coronary angiography. Although heart transplantation has been associated with a higher frequency of this finding.[2]

In the literature, coronary-to-right ventricle fistulas in heart transplant patients is suggested to be a secondary effect of myocardial biopsies performed on them.[2] More recent reports show

Brief Report

Cite this article: Camprubi-Tubella E, Gran-Ipiña F, and Betrián-Blasco P (2022) Coronary artery fistulas after paediatric heart transplantation. *Cardiology in the Young* **32**: 312–314. doi: 10.1017/S1047951121002729

Received: 6 April 2021
Revised: 21 June 2021
Accepted: 23 June 2021
First published online: 29 July 2021

Keywords:
Coronary fistula; coronary bypass; cardiac transplant; children

Author for correspondence:
Elisabet Camprubi Tubella, Pediatric Cardiology and Pediatric Cardiac Surgery Department, Hospital Universitario Vall Hebrón, Passeig de la Vall d'Hebrón, 119-129, 08035 Barcelona, Spain. Tel: +34 934 89 30 00; Fax: +34932746001.
E-mail: ecamprubi.ebre.ics@gencat.cat

CAMBRIDGE UNIVERSITY PRESS

Table 1. Characteristics of the patients.

Case	Age at heart Tx (years)	Aetiology	Blood type	Age donor	Ischaemia time (min)	Induction drug	Immunosuppressant treatment	Time Tx first catheterism (years)	Nº fistulas first	Grade	Origin	Destination	Second catheterism (time after Tx)	Evolution	Follow-up years	Nº catheterism total
1	15	CONG	A+	16	190	BAS	TC/MM/COR	2.5	1	Small	LAD	Lung field	No	No control	11.3	1
2	13	CMOP	0+	32	245	ATG	TC/EV/COR	0.7	1	Small	Circ.	Lung field	1	Same	8.9	5
3	6	CMOP	0+	23	255	ATG	TC/EV/COR	0.5	1	Small	LAD	Lung field	0.5	Same	8.7	7
4	10	CMOP	0+	1.5	210	ATG	TC/MM/EV/COR	1	1	Moderate	RCA	Lung field	5	Same	8.3	2
5	13	CMOP	A+	16	253	BAS	TC/MM/COR	0.5	1	Moderate	LAD	Lung field	3	Same	5.1	2
6	2	CMOP	B+	28	206	ATG	TC/MM/COR	0.9	2	Small	RCA	Lung field	1	Same	4.84	2
										Moderate	Thoracic	LAD		Regressed		
7	14	CONG	A+	U	194	ATG	TC/MM/COR	1.25	1	Small	LAD	Lung field	0.8	Regressed	4.38	2
										Moderate	Circ.	Lung field	No	No control		1
8	6	CONG	A+	9	U	BAS	TC/MM/EV/COR	2	3	Small	RCA	Lung field			4.15	
										Large	LAD	RPA				
9	14	CMOP	A+	38	270	BAS	TAC/MM/COR	0.4	2	Small	LAD	Lung field	2,2	Same	2.75	2
										Small	Circ.	Lung field		Regressed		
10	8	CMOP	0+	U	220	BAS	TC/MM/COR	0.75	1	Small	RCA	Lung field	No	No control	2.3	1
11	6	CMOP	0+	14	165	BAS	TC/MM/COR	1.6	1	Small	LAD	MPA	No	No control	1.72	1
										Large	CD	Lung field	No	No Control		1
12	1	CMOP	AB+	3	U	ATG	TC/MM/COR	0.5	> 3	Large	CI	Lung field			0.65	
										Large	Thoracic	LAD				
13	1.6	CMOP	A+	0.4	242	BAS	TC/MM	7	1	Moderate	LAD	Lung field	No	No control	7	1

ATG = Thymoglobulin; BAS = Basiliximab; Circ=Circumflex; CMOP = Cardiomyopathy; CONG = Congenital; COR = Corticosteroids; EV = Everolimus; LAD = Left anterior descending; MM = Mycophenolate; MPA = Main Pulmonary Artery; RCA = Right Coronary Artery; RPA = Right Pulmonary Artery; TC = Tacrolimus; TX = Transplant; U = Unknown

Table 2. Characteristics of the fistulas.

Nº fistulas first catheterism	Grade	Origin	Destination	Evolution
1 (9, 69.3%)	Small (7, 58.3%)	LAD (9, 47.3%)	Lung field (15, 78.9%)	Regressed (3, 15.7%)
2 (2, 15.3%)	Moderate (4, 30.7%)	RCA (5, 26.3%)	MPA (1, 5.2%)	Same (6, 31.5%)
3 (1, 7.7%)	Large (2, 16.6%)	Circumflex (3, 15.7%)	RPA (1, 5.2%)	No control (10, 52.6%)
>3 (1, 7.7%)		Thoracic artery (2, 10.5%)	LAD (2, 10.5%)	

LAD = Left anterior descending; MPA = Main Pulmonary Artery; RCA = Right Coronary Artery; RPA = Right Pulmonary Artery

an important number of patients with fistulas connecting to other places, and some new potential mechanisms have been suggested, including angiogenesis secondary to the post-cardiac transplant inflammatory state, surgical trauma, and hypoxia.[2]

We report a series of paediatric heart recipients with coronary artery fistulas connecting the donor's heart with structures from recipients. We describe two cases of coronary artery fistulas connecting the graft to systemic arteries of the receptor, a very unfrequent finding in pediatrics, as previously reported.[3]

We found a similar incidence of coronary artery fistulas (43.3%) than previous descriptions,[1] as well as a similar distribution of the fistula, but with a higher percentage of medium/large fistulas (47.3%). Also, as shown in the multicentre series of Allen et al.,[1] all the non-cameral coronary artery fistulas were discovered on the first angiography and tended to disappear or decrease its size during the follow-up. We have also not found any correlation between non-cameral coronary artery fistulas and any adverse outcome or requirement of intervention.

Although the aim of our study was not to find out the possible mechanisms of the fistula's formation, we can't avoid thinking over the causes of that neoangiogenesis. Given that the fistulas are already present in the first coronarography, its appearance should be closely related to the changes that happen during the transplant procedure. A suitable hypothesis would be that the great post-inflammatory state that occurs after a transplant surgery, stimulates vascular growth factors, and has a determinant role in stimulating angiogenesis, and so, the formation of fistulas. This hypothesis would also agree with the downregulation of the fistula's flow or its disappearance on the control coronary angiographies, because as we distance from the transplant, the organism tends to return to its basal state and the pro-inflammatory state decreases.

It is worth mentioning the main limitation of our study is a low size sample, making it very difficult to reach any statistical significance of the relation between fistula formation and the studied factors. Another limitation would also be the study has been done retrospectively and some patients have a short time of follow-up, so in many cases, we have just one coronary angiography.

In conclusion, non-cameral coronary artery fistulas after heart transplant in the paediatric population are not an uncommon finding, but those draining to systemic arteries seem to be less common. It would be necessary to carry out larger studies to better establish how frequent this finding is and if there are any involved factors. All fistulas showed involutional tendency. The main pathophysiological hypothesis for fistula formation is a great post-transplant pro-inflammatory state. No statistically significant relationship between non-cameral coronary artery fistulas and any of the studied factors were found, neither any relationship with mortality nor loss of the graft.

Acknowledgements. We would also like to acknowledge the invaluable contributions made by Dr. Paola Dolader (Pediatric Cardiac transplant unit) and Dr. Raul Abella (Pediatric Cardiac Surgery) and his surgical team.

Financial support. This research received no specific grant from any funding agency, commercial, or not-for-profit sectors.

Conflict of interest. None.

Ethical standards. The authors assert that all procedures contributing to this work were in accordance with the ethical standards of the institutional research committee and with the 1975 Helsinki Declaration and its later amendments or comparable ethical standards.

References

1. Allen KY, Goldstein BH, Pahl E, et al. Non-cameral coronary artery fistulae after pediatric cardiac transplantation: A multicenter study. J Heart Lung Transplant 2012; 31: 744–749. https://doi.org/10.1016/j.healun.2012.02.026.
2. Wei J, Azarbal B, Singh S, et al. Frequency of coronary artery fistulae is increased after orthotopic heart transplantation. J Heart Lung Transpl 2013; 32: 744–746. https://doi.org/10.1016/j.healun.2013.04.009.
3. Camprubí-Tubella E, Albert-Brotons DC,Betrián-Blasco P. Spontaneous "Coronary Bypass" in a Paediatric Transplanted Heart. Pediatr Cardiol 2020; 41: 217–219. https://doi.org/10.1007/s00246-019-02278-x.
4. Zaban NB, Elshershari H, Hoyer MH. Early and late presentation of coronary artery fistula: a possible natural progression?. Cardiol Young 2019; 29: 1407–1409. https://doi.org/10.1017/S1047951119002142.

https://doi.org/10.1017/S1047951121002729 Published online by Cambridge University Press