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Transcatheter closure and prognosis of coronary artery fistulae in heart transplant recipients

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Introduction

Coronary artery fistulae (CAF) represent an abnormal communication bypassing the myocardial capillary bed between a coronary artery and either a cardiac chamber (coronary-cameral CAF) or a vascular structure from systemic or pulmonary circulation (coronary-vascular CAF). CAF represent a congenital anomaly in 0.2% of the population, but are more frequently found in heart transplant recipients (8%), mostly as coronary-right ventricle (RV) CAF caused by endomyocardial biopsy used for monitoring of rejection[1,2]. Other complications of myocardial biopsy include perforation of the RV wall and tricuspid valve damage[2]. Several case reports have shown successful transcatheter closure of CAF[3,4]. We aimed to analyse the indications for transcatheter closure and the long-term prognosis of CAF in heart transplant recipients.

Methods

All patients aged ≥18 years who were transplanted at the Erasmus Medical Center, Rotterdam, from the start of the heart transplantation (HT) programme in June 1984 until January 2018 were included in the study. Clinical data after transplantation were prospectively collected from the start from clinical records and office visits with permission from the patients. The institutional board approved the use of anonymised data for the present study.

Rejection was monitored by endomyocardial biopsy obtained percutaneously. All biopsies were performed on the RV septum under fluoroscopic guidance using a 50 cm Jawz™ 2.2 mm bioptome (Argon Medical Devices, Frisco, TX, USA) inserted through a 7 Fr sheath placed into the right internal jugular or right femoral vein. In the first decade of the HT programme each patient underwent 30 to 40 biopsies, while in the last decades the number of biopsies decreased to 15 to 20 for each patient. Coronary angiography (CAG) was performed per protocol every year until 1990. After 1990, CAG was performed at the 1st year and the 4th year after transplantation. Thereafter, patients annually underwent single-photon emission computed tomography (SPECT) for assessment of ischaemia, or cardiac CT angiography. Follow-up CAG was only performed in case of ischaemia. All coronary angiograms were reviewed independently by two cardiologists. The incidence of CAF to the RV was calculated from all heart transplant recipients who had at least one CAG.

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STATISTICAL ANALYSIS

Data were analysed using SPSS software, Version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables are presented as mean±standard deviation (SD) and were compared using the Student's t-test. Non-parametric variables were compared using the chi-square test. Cumulative survival was estimated according to the Kaplan-Meier method and compared using the log-rank test; $p<0.05$ was considered statistically significant.

Results

From a total of 711 heart transplant recipients, there were 565 adult patients who underwent at least one CAG and were included in the analysis. Forty-one patients (7.3%) had coronary-RV CAF. The clinical characteristics of the transplanted patients with and without CAF are presented in **Table 1**. There was no difference in the age of the recipient or the donor, the number of rejection episodes, coronary allograft vasculopathy and development of heart failure between the two groups. Of the eight cardiac deaths in the group of patients with CAF, seven were due to cardiac allograft vasculopathy, while one death was caused by severe aortic valve stenosis.

Table 1. Characteristics of heart transplant recipients with and without CAF.

		CAF (n=41)	No CAF (n=524)	*p*-value
Age at transplant, years (mean±SD)		48.8±9.7	49±11	0.80
Female gender, n (%)		14 (34)	140 (29)	0.11
Donor age, years (mean±SD)		37.9±13.6	34±13	0.11
Number biopsies/ patient (mean±SD)	1984-1990	22±6.2	30±6.5	0.08
	1991-2000	17.3±4.9	20±4.3	0.06
	2001-2018	15.6±4	15.4±3	0.80
Follow-up after transplant, years (mean±SD)		11.4±5.9	10±6	0.18
Rejection episodes (mean±SD)		1.5±1.3	2±2	0.79
Coronary allograft vasculopathy, n (%)		8 (19.5)	133 (25)	0.26
Myocardial infarction, n (%)		4 (9.8)	64 (12.2)	0.43
Revascularisation for coronary allograft vasculopathy, n (%)		5 (12.2)	82 (15.6)	0.37
Heart failure, n (%)		2 (5)	56 (10.7)	0.18
Cardiac death, n (%)		8 (19.5)	110 (21)	0.50

The anatomic distribution of CAF is presented in **Figure 1**. Of the four untreated fistulae originating from the left anterior descending (LAD) artery, two remained unchanged, while two disappeared at follow-up due to cardiac allograft vasculopathy. The characteristics of the individual patients with CAF from the LAD who underwent transcatheter intervention are presented in **Table 2**. **Moving image 1** and **Moving image 2** show transcatheter closure of CAF in patient 7. CAF closure by covered stent or coils for myocardial ischaemia preserved the patency of the LAD during a follow-up of 10±4 years. The survival of patients with CAF was not different from the whole HT cohort **(Figure 2)**.

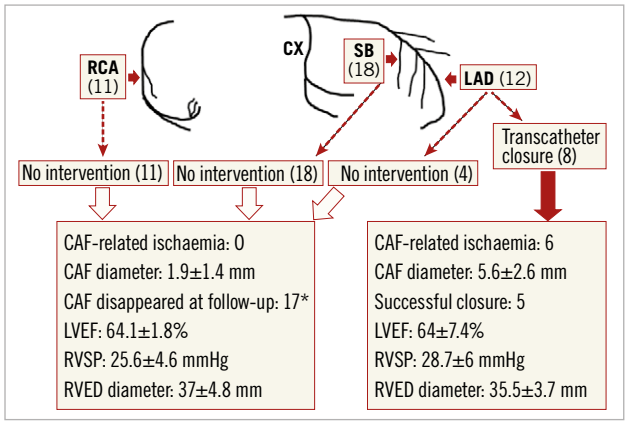

Figure 1. *Distribution of CAF (number of patients) and treatment. *Follow-up CAG was performed in only 27 patients in the No intervention group. CX: circumflex coronary artery; LVEF: left ventricle ejection fraction; RVED diameter: right ventricular end-diastolic diameter at the tricuspid annular plane; RVSP: right ventricular systolic pressure, measured by right heart catheterisation; SB: septal branches*

Discussion

Although the incidence of coronary-RV CAF was 7.3%, CAF-related clinical events occurred in only six patients (1%), caused by impaired perfusion of the distal LAD. Fistulae originating from the LAD could be clinically diagnosed by the presence of a continuous cardiac murmur peaking in diastole.

Historically, right-sided volume overload due to left-right shunt, myocardial ischaemia, and aneurysmal dilatation of the proximal coronary artery were potential indications for CAF closure[3,4]. In the first decade of the transplantation programme at our centre, the indication for transcatheter closure was progressive dilatation of the proximal LAD. However, in the absence of ischaemia, the

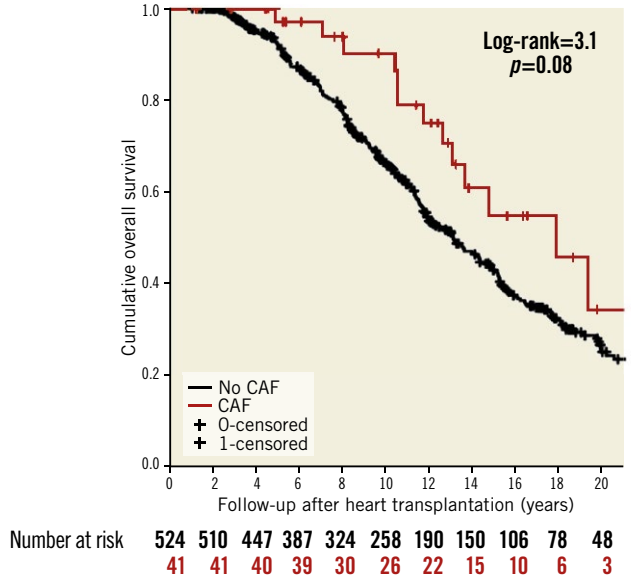

Figure 2. *Cumulative overall survival of patients with CAF and without CAF.*

Table 2. Description of patients with transcatheter closure of CAF.

	Year HT	Origin of CAF	Indication for CAF closure	Year of closure	Intervention	Follow-up
1	1986	LAD	Dilatation LAD, shunt ratio=1.3	1992	Coils, unsuccessful (2 embolised to RV)	2004 CAG: occlusion LAD 2013 death
2	1996	LAD	Dilatation LAD, shunt ratio=1.1	1997	Covered stent (unsuccessful due to tortuosity LAD)	2001 CAG: aneurysmal LAD 2016 SPECT: negative
3	1999	LAD	SPECT: ischaemia	2010	Amplatzer plug 8 mm (small residual shunt)	2012 severe aortic stenosis 2012 death
4	2001	LAD	SPECT: ischaemia	2005	Covered stent	2018 CT: LAD open
5	2002	LAD	STEMI during biopsy	2002	Covered stent	2017 CAG: in-stent intimal hyperplasia FFR 0.82
6	2007	LAD	SPECT: ischaemia	2008	Coils	2018 CAG: LAD open PCI with DES
7	2007	LAD	STEMI during biopsy	2008	Coils + covered stent*	2016 CAG: in-stent restenosis
8	2014	LAD	Arrhythmia MRI: ischaemia	2014	Covered stent	2018 CAG: LAD open

*Moving image 1, Moving image 2. DES: drug-eluting stent; FFR: fractional flow reserve; MRI: magnetic resonance imaging; PCI: percutaneous coronary intervention

need for CAF closure is questionable as many fistulae disappear at follow-up due to either a small calibre or development of coronary allograft vasculopathy. Even when CAF from the LAD persisted in some patients in the long term, they did not develop RV failure. Two patients with CAF developed heart failure with preserved ejection fraction due to cardiac allograft vasculopathy.

Limitations

Follow-up CAG was not available in all patients with CAF. Left-right shunt measurement was performed in only a few patients, which hampered the evaluation of CAF haemodynamics. The low number of CAF did not permit a multivariate analysis to detect risk factors.

Conclusion

The majority of CAF after HT are asymptomatic. Transcatheter closure is indicated for myocardial ischaemia and to maintain the coronary patency in the long term. Overall CAF does not affect survival after heart transplantation.

Impact on daily practice

Transcatheter closure of CAF is indicated for myocardial ischaemia due to coronary steal. The long-term outcome after heart transplantation is not affected by the presence of CAF.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Moving image 1. Coronary-RV CAF in patient 7.

Moving image 2. CAF closure by coils and covered stent.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00191