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Melody transcatheter valve: Histopathology and clinical implications of nine explanted devices

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ABSTRACT

Objectives: We examined interventionally implanted valved Melody conduits after surgical explantation by means of histology and immunohistochemistry and matched these findings with clinical data in order to assess in vivo biocompatibility and to identify risk factors for graft failure.
Methods: 9 Melody valves had been implanted in 8 patients (pulmonary n = 7, tricuspid position n = 1). Indication for explantation included significant obstruction in 7 patients and valve insufficiency in 1 patient. 4 of 8 patients had suffered from endocarditis. Mean interval between implantation and explantation was 3.2 (1.8–5.2) years. All explants were worked up using a uniform protocol with fixation in formalin and embedding in methylmethacrylate.
Results: All but one valve of the explanted Melody grafts were thin and histologically intact without any pathological findings. Complete neo-endothelialization could be demonstrated by means of immunohistochemistry. All 4 Melody valves from patients with endocarditis showed dense granulocytic infiltrations, 3 of these showed thrombotic material within the valves.
Conclusion: This report covers the first series of explanted Melody valves from humans applying a uniform protocol for histopathological examination. Good biocompatibility of the Melody valves could be demonstrated after a mid-term follow-up. Factors for graft failure included endocarditis, outgrowth, and residual stenosis. These findings may have significant implications for the implant procedure as well as care of the patients during long-term follow-up.

1. Introduction

Implantation of the Melody transcatheter pulmonary valve (Medtronic Inc., Minneapolis, MN, USA) has evolved as an interventional treatment for dysfunctional right ventricular outflow tract conduits allowing delay of surgical therapy [1–5]. In rare cases, successful implantation in tricuspid position has also been reported [6–8].

The Melody valve consists of a bovine jugular vein valve, sutured within a laser-welded platinum-iridium stent with gold brazing of the welds. With the goal to postpone surgical replacement and to prolong the life span of a conduit, the 'Instruction for Use' manual (Medtronic Inc., Minneapolis, MN, USA) states an intended lifetime for the transcatheter valve of two years. However, clinical experience has shown that most Melody valves achieve a longer implantation time.

Since the first percutaneous pulmonary valve implantation reported in 2000 [9], now more than 7500 cases have been performed worldwide. Several reports have identified Melody valve stent fractures and residual or recurrent stenosis as major risk factors for re-intervention. Nevertheless, data on explanted Melody valves including clinical circumstances are limited [10–12].

Therefore, there is a lack of knowledge about local tissue reactions of Melody valves after implantation into the human circulation. Description of the histopathology of explanted Melody valves is limited to very few patients who suffered from infective endocarditis [13,14].

As we are not aware of preclinical animal studies, the purpose of our study was (a) to characterize biocompatibility of the Melody valve in a series of eight patients after surgical explantation and (b) to correlate these findings with indications for explantation and clinical data at the time of implantation and during follow-up. As incomplete endothelialization and thrombogenesis have been proposed as potential risk factors

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for endocarditis after device closure of atrial septal defects [15–17], we focused our attention on endothelialization, thrombogenesis, neointimal proliferation, inflammation, and formation of cellular and extracellular matrix components in the explanted Melody valves.

2. Patients and methods

2.1. Patients

Nine Melody valves from eight patients were included in the study. The implantation procedure and surgical device explantation had been performed in three centers in Germany and the Netherlands. Patients' histories as well as data from echocardiography and cardiac catheterization were obtained from medical records. Patient characteristics at the time of implantation are summarized in Table 1.

In seven patients the valve had been implanted in a dysfunctional right ventricular outflow tract (RVOT), one of these patients had already received a second Melody valve as a valve-in-valve procedure 17 months after initial implant due to significant stenosis of the first Melody valve. Melody valves had been implanted in 4 homografts and 3 Hancock conduits (Medtronic Inc., Minneapolis, USA) for significant RVOT obstruction with documented calcifications. In addition, relevant regurgitation of the conduit had been documented in three of these patients. Pre-stenting had been performed in all but one of the patients prior to placement of the Melody valve. Apposition to the chest wall after implantation of the Melody valve had been documented in each case. Recoil of the valved stent had been noted only once; in this case pre-stenting had been performed with 2 bare metal CP-stents (patient 1).

One Melody valve had been implanted in tricuspid position in a patient for severe insufficiency of a bioprosthetic valve (Mosaic 25 mm; Medtronic Inc., Minneapolis, USA). This patient had undergone several surgical procedures for a double outlet right ventricle with ventricular septal defect including reconstruction and finally replacement of the tricuspid valve.

Indications for explantation of the valved conduit had been established on individual basis by the local team of pediatric cardiologists and surgeons. Mean interval from implantation to explantation was 3.2 ± 1.3 years. Clinical data at the time of explantation of the Melody valve are summarized in Table 2.

In all 7 patients with a Melody valve in pulmonary position, significant stenosis was present. Melody valve regurgitation was documented and graded less than moderate in 3 of 7 and was never considered the primary reason for explantation in any of the patients. Additional indication for surgery included an outgrown conduit (18 mm Hancock conduits) in 2 patients, the need for mechanical aortic valve replacement at the same time in another 2 patients, and repeated stent fractures after a valve-in-valve procedure in one patient, respectively.

Four patients suffered from endocarditis and three had completed treatment according to international guidelines prior to surgical explantation of the valved conduit. One of the patients presented with a fulminant course and required urgent surgery (patient 8). Vegetations within the Melody graft, the truncal valve, and adjacent to the VSD-patch were evident.

All patients had received acetylsalicylic acid for 6–12 months following implantation of Melody valves. None of the patients was still on acetylsalicylic acid at the time of explantation.

The study was approved by an institutional review committee. Informed consent was obtained in all patients and data were processed and documented according to the Declaration of Helsinki.

2.2. Tissue preparation

After surgical removal and flushing with normal saline, tissue specimen containing the valved conduit was placed in formalin for fixation. Extended histopathological and immunohistological work-up following a predefined protocol was performed at a single center (Georg-August-

Table 1
Baseline characteristics and clinical data at percutaneous pulmonary valve implantation (PPVI).

Baseline					Implantation								
Patient	Gender	Underlying diagnosis	Number of previous surgeries	Type of RVOT conduit	Calcification of the conduit	Indication for PPVI	Age at PPVI	Catheter systolic PV gradient at PPVI		Pre-stent	Melody valve insufficiency post PPVI	Apposition to chest wall	Recoil
			Closed/open[a]		Y/N		Years	Pre-mm Hg	Post-mm Hg	Y/N, type[b]	Grade[c]	Y/N	Y/N
1	M	Truncus arteriosus	0/3	Homograft 23 mm	Y	PS	12.3	45	32	Y, 2 bare CP	1	Y	Y
2	F	TOF/PA	1/1	Homograft 18 mm	Y	PS/PI	11.8	55	35	Y, Melody	0	Y	N
3	M	Valvular aortic stenosis	0/2	Homograft 22 mm	Y	PS	19.6	43	32	Y, MaxLD	0	Y	N
4	M	TOF/PA	0/1	Hancock 18 mm	Y	PS	14.7	61	37	N	0	Y	N
5	F	DORV, VSD	1/4	Mosaic bioprosthesis 25 mm	Y	TI	31.2	TI	–	Y, bare CP	1	–	N
6	M	TOF	1/2	Hancock 18 mm	Y	PS/PI	12.3	31	13	Y, MaxLD	1	Y	N
7	M	TOF/PA	0/3	Hancock 20 mm	Y	PS	23.2	51	29	Y, MaxLD	0	Y	N
8	M	Truncus arteriosus	0/2	Homograft 19 mm	Y	PS/PI	20.8	46	28	Y, MaxLD	0	Y	N
Mean + SD			Median 0/2				18.2 ± 6.2	47.4 ± 9.6	29.4 ± 7.9				

Abbreviations: RVOT = right ventricular outflow tract; m = male; f = female; TOF = tetralogy of Fallot; PA = pulmonary atresia; DORV = double outlet right ventricle; VSD = ventricular septal defect; PS = pulmonary stenosis; PI = pulmonary valve insufficiency; TI = tricuspid valve insufficiency; SD = standard deviation.

[a] Closed = heart surgery without cardiopulmonary bypass; open = heart surgery with cardiopulmonary bypass.

[b] CP = Cheatham-Platinum stent (NuMED Inc., Hopkinton, NY, USA); MaxLD = Max LD stent (EV3, Plymouth, MN, USA).

[c] PI grade: 1 = trivial, 2 = mild, 3 = moderate, 4 = severe.