

# The report of the first 12 cases of heart transplantation among children at shahid rajaei heart center

## Abstract

**Purpose:** In the present report, the baseline information and outcome of heart transplantation surgeries among 12 children in our hospital as the first referral heart center for this operation were described.

**Methods:** Twelve patients aged less than 14years that underwent heart transplantation from 2012 to 2015 at Shahid Rajaei Heart Center were retrospectively reviewed.

**Results:** One of the transplanted patients was positive for cytomegalovirus antigen two months after the surgery that was successfully treated. Another patient was diagnosed as giardia-related diarrhea two weeks after grafting that was completely improved. One of the patients suffered renal aspergillus abscess 10months later that was finally discharged after complete treatment. With respect to graft rejection, 2 cases suffered rejection that both improved fortunately and were discharged after treatment. Only one patient died early due to C and S proteins deficiency and coagulation problems. Although the patient was undertreated with ECMO protocol, he died due to brain death after a week of transplantation.

**Conclusion:** In our short-term experience, we could achieve an appropriate procedural outcome with low death rate and controlled postoperative complications following heart transplantation in our required children.

Volume 6 Issue 5 - 2016

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**Received:** August 29, 2016 | **Published:** October 04, 2016

## Introduction

According to the registry of the International Society for Heart and Lung Transplantation, 350 to 500 heart transplantations have been annually performed entire the world.<sup>1</sup> About 512 heart transplantations were planned in children only in 2015. Despite available evidences on the use of stem cells in renewal of the cells, heart transplantation has still remained as the best way to extend the life and to improve symptoms in patients with end-stage heart failure.<sup>2</sup> Heart transplantation in children continues to face more problems than adults because of the possibility of more scar as well as more technical problems encountered due to some congenital malformations.<sup>3</sup> The main indications for heart transplantation in children include cardiomyopathy, correctable congenital defects but with high risk (such as, IAA, severe sub-aortic stenosis, critical aortic stenosis with severe endocardial fibroelastosis, and Ebsteins anomaly in symptomatic infants), refractory heart failure after heart surgery in the past, cardiac allograft vasculopathy, or with chronic function. The most common cause of transplantation in neonates is congenital heart disease and in older children is cardiomyopathy.<sup>4</sup> The first heart transplantation at Shahid Rajaei Heart Center was performed in 2012 on a 14-year-old child with dilated cardiomyopathy. Because of the severe side effects, the program was stopped for two years, but it was started again with performing eleven heart transplantation surgeries within a year that are all described in the present case series.

## Methods

Twelve patients aged less than 14years that underwent heart transplantation from 2012 to 2015 at Shahid Rajaei Heart Center

were retrospectively reviewed. The main indications of this surgery included heart failure refractory to medical therapy and require a high dose inotropes that all patients were scheduled for emergency surgery. The method of surgery was based on the bicaval technique and aortic cannulation for extracorporeal circulation using mild hypothermia (30degrees C). Immunosuppression was performed based on the CHOP (children hospital of Philadelphia) protocol by administrating solumedrol (15mg/kg) and mycophenolate mofetil (600mg/m<sup>2</sup>) one hour before operation. After transplantation, all patients were medicated with mycophenolate, solumedrol, ATG, and tacrolimus and also the prophylactic regimen for cytomegalovirus was also considered using ganciclovir and for pneumocystis using cotrimoxazole. The patients were also followed-up for assessment of acute or chronic graft rejection and also probable postoperative infectious complications evident by echocardiography, chest X-ray, electrocardiography, and also laboratory findings such as assessing the levels of tacrolimus and cytomegalovirus antigens. For all patients, endomyocardial biopsy was performed to check acute graft rejection at the end of the first week and then serially. All patients had NYHA class III to IV and were treated with heart failure medications.

## Results

As shown in Table 1, in total, 12 patients (7 male and 5 female) in the age range of 22 months to 14years were described. Of those, 2 were in the age range 2 to 3years and others were in the age range 9 to 14years. The mean body weight was 29.7kg ranged 9 to 52kg with the mean height of 134.6cm ranged 81 to 165cm. Six patients had the blood group of A+, 5 had the blood group of O+, and one patient had the blood group of B+. The mean time of intubation after ICU

admission was 13.95hours ranged 4 to 168hours. The average time for decreasing the level of troponin to less than 2 units was 59hours ranged 24 to 168hours. The mean pump time was 120.6min ranged 80 to 165min. Among the patients underwent heart transplantation, 10 had the serum pro-BNP level less than 25000 and in other two patients, this marker raised to higher than 25000. Regarding liver functional status, only one patient had impaired liver function preoperatively.

The baseline preoperative diagnoses included idiopathic cardiomyopathy (7 cases), Noncompaction left ventricular (3 cases), myocarditis (1 case), and myocarditis plus Noncompaction left ventricular (1 case). Three patients underwent invasive treatment procedures including surgical ASD occlusion (1 case), interventional ASD occlusion using Amplatzer (1 case), and ablation with the primary diagnosis of Noncompaction left ventricular (Wolff Parkinson White with Atrioventricular nodal tachycardia). Regarding postoperative complications, one of the transplanted patients was positive for cytomegalovirus antigen two months after the surgery that was treated with ganciclovir intravenous and then with valcyclovir orally. Another patient was diagnosed as giardia-related diarrhea two weeks after grafting that was treated with furazolidone, metronidazole, and IVIG that was completely improved. One of the patients suffered renal aspergillus abscess 10months later that was initially treated with itraconazole that was inevitably changed to caspofungin and voriconazole leading

significant improvement evidenced by negative urine analysis and also reducing the size of mass in CT scan. The patient was finally discharged with voriconazole. The same patient referred again with the evidences of graft rejection 20months later with suspected pneumonia that was assessed by bronchoalveolar lavage leading the final diagnosis of CMV(cytomegalovirus), PCP(pneumocystis carini), and mycoplasmosis infections. The patients was then medicated with a combination of cotrimoxazole, dapsone, Azithromycin, and ganciclovir led to negative bronchoalveolar lavage after 11days of treatment.

With respect to graft rejection, 2 cases suffered rejection. One of the patients (a 14-year old child) had rejection 20months after grafting with the pathological report of cellular graft that was finally treated with pulse therapy with methyl prednisolone, ATG(anti-thymocyte globulin), and IVIG. Another 12-year old child had hyper acute rejection (Antibody mediated) plus cellular rejection that was presented with drug-refractory arrhythmias on ICU admission. The patient was initially treated with prednisolone and ATG (anti-thymocyte globulin) that was then undertreated with ECMO, plasmapheresis, and rituximab. Fortunately, both cases of rejection improved and were discharged after treatment (Table 2). Only one patient died early due to C and S proteins deficiency and coagulation problems. Although the patient was undertreated with ECMO protocol, he died due to brain death after a week of transplantation.

**Table 1** Baseline characteristics of the study population

No	Age	Sex	Weight kg	Height cm	Liver Function Test	Time of Intubation	Pump Hour time	Pro BNP	Blood Group	Preoperative Diagnosis
1	14	M	30	130	Normal	16	90	> 2500	A+	Dilated cardiomyopathy
2	2	M	13	97	Normal	4	138	< 2500	A+	Dilated cardiomyopathy
3	11	M	40	150	Normal	10	80	< 2500	O+	Myocarditis
4	12	F	39	154	normal	72	115	< 2500	O+	Myocarditis+ Left ventricular noncompaction
5	<2	M	9	81	normal	4.5	96	< 2500	O+	Dilated cardiomyopathy
6	11	F	35	155	Impaired	17	121	< 2500	A+	Left ventricular noncompaction
7	10	F	30	130	normal	11	155	< 2500	B+	Myocarditis+ Left ventricular noncompaction
8	14	F	52	165	normal	4	100	> 2500	A+	Left ventricular noncompaction
9	9	M	21	130	normal	7	165	< 2500	A+	Left ventricular noncompaction
10	14	F	35	160	normal	6	115	< 2500	A+	Dilated cardiomyopathy
11	9	M	30	134	normal	12	160	>25000	O+	Dilated cardiomyopathy
12	11	M	23	130	normal	4	113	<25000	O+	Dilated cardiomyopathy

**Table 2** Postoperative outcome

Complication	Number	Action	Time of occurrence (after graft)
Pericardial effusion	1	pericardiocentesis	5 days
Renal failure	1	Peritoneal dialysis	3 days
	1	Peritoneal dialysis	19 days
RV dysfunction	2	Diuretic administration	Immediately
Reaction to cellcept	1	Discontinuation of cellcept and administration of Azathioprine	3 months
Reaction to cellcept	1	Discontinuation of cellcept and administration of Azathioprine	3 months
Polyradiculopathy	1	IVIG	1.5 years
ECMO	1	Coagulopathy	Immediately
	1	hyper acute rejection	Rituximab

## Discussion

Since 1985 that Bailey et al. reported the first successful pediatric heart transplantation, the number of these operation dramatically rose.<sup>5,6</sup> Several studies reported different mortality and survival rates among transplanted patients. The first pediatric heart transplantation

surgery in Iran was done about three years ago on a 14-year old boy led to several postoperative problems and considerable complications. Thus, this surgery stopped for three years and was begun again after that so totally 12 heart transplantation operations were performed till now. The patients were thus followed-up for maximum one year. Among our reported patients, death was reported only in a patient

who suffered S and C proteins deficiency and coagulation problems. In a study by Sarris et al on 72 patients who were scheduled for heart transplantation between 1977 and 1993, 1, 5, and 10 survival rates were estimated to be 75%, 60%, and 50% respectively. They showed the most frequent causes for death in the patients as infections, graft rejection, graft-related coronary disease, and pulmonary hypertension.<sup>7</sup> As presented by the International Society for Heart and Lung Transplantation (ISHLT) in 2002, 1, 5, and 10 survival rates were 77%, 68%, and 57% respectively.<sup>6</sup> We stated our pediatric heart transplantation on patients with dilated cardiomyopathy and NCLV (Noncompaction left ventricular) with minimized predicted postoperative complications and therefore the transplantation surgery on those patients with underlying congenital heart anomalies were postponed to the near future because of their related complications and complexity. Because of the difference in the learning curves of the two pointed groups, the statistics on mortality and survival of the patients in the two groups can be very discrepant. In surveys by Groetzner et al.,<sup>8</sup> and by Miana et al.,<sup>9</sup> the most prevalent reason for long-term death was postoperative infections and graft rejection. Given that most studies focused on long-term follow up of patients and also employed new immunosuppressive therapies as well as used new and quick diagnostic techniques for postoperative complications, we expected lower mortality as well as higher improvement rates following heart transplantation in children that was also revealed in our observation in a short-term follow-up time. The start of heart transplantation among children in our country needs to frequent following-up and also to minute assessments to achieve better procedural outcome. The likelihood of transplantation-related malignancies and graft-related vascular disorders (GVD) and also need to reoperation after many years are the major problems of such operation in the future. The number of heart transplantations among children in our hospital as the first referral hospital for this surgery in Iran is considerably low because of lower donors compared to the adults leading high mortality and morbidity among children in the heart transplant waiting list.

## Conclusion

In our short-term experience, we could achieve an appropriate procedural outcome with low death rate and controlled postoperative complications following heart transplantation in our required children.

## Acknowledgments

None.

## Conflicts of interest

Author declares there are no conflicts of interest.

## Funding

None.

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