



Changes in echocardiographic parameters of the donor's heart before and after heart transplantation and their relationship with post-transplant survival

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Background: Heart transplantation is now widely performed in China, but the current entry criteria for heart transplantation donors are simple and lack reliable standards; there are still no studies on the effect of preoperative echocardiographic parameters of heart transplantation donors on the prognosis of the recipient. Therefore, the aim of this study is twofold: (I) to observe the characteristics of changes in echocardiographic parameters of the donor's heart before and after heart transplantation and (II) to study the relationship between the changes in echocardiographic parameters of the donor's heart pre- and post-transplant and transplant recipient survival.

Methods: A total of 29 patients who underwent orthotopic heart transplant in our hospital from October 2016 to October 2019 were enrolled in this study. All recipients were followed up until April 2020. Echocardiographic data were collected pre-transplantation (donor) and at 1 week and 1 month post-transplant (recipient).

Results: Compared with the pretransplanted donor's heart, there was an increase in the interventricular septal diameter, left ventricular posterior wall diameter, right atrium diameter and right ventricular diameter, while a decrease was found in the tricuspid annular systolic displacement and tricuspid annular peak systolic velocity at 1 week post-transplant. The survival curve showed that the postoperative survival time in the right atrium/ventricle ≥ 32 mm group was better than that in the right atrium/ventricle < 32 mm group. The survival curve also showed that the postoperative survival time in the right atrium/ventricle enlargement < 2 mm group was better than that in the right atrium/ventricle enlargement ≥ 2 mm group.

Conclusions: In the early post-transplant period, ventricular myocardial thickening, right heart enlargement and a decrease in right heart function were observed in the post-transplanted heart compared to the pretransplanted donor's heart. Postoperative survival was higher among heart transplant patients who received a heart with right atrium/ventricle ≥ 32 mm. Postoperative survival was lower among heart transplant patients whose right atrium/ventricle was dilated ≥ 2 mm at 1 month postoperatively compared with the pretransplanted donor's heart.

Keywords: Heart transplant; echocardiographic parameters; donor's heart; survival

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Introduction

Heart transplantation is an important treatment for end-stage heart disease (1-3). The latest data from the International Society for Heart and Lung Transplantation show that the survival rate of patients after heart transplantation is 83% at 1 year and 72% at 5 years (4). After heart transplantation, perioperative death accounts for a relatively large proportion of deaths, and its main causes include right heart failure, left heart failure, rejection and infection (4). Therefore, the evaluation of the heart during the perioperative period of transplantation, including the structure of the heart, cardiac function, hemodynamics and rejection, is particularly important. Meanwhile, echocardiography can provide comprehensive information for assessing the structure and function of the donor's and recipient's hearts before transplantation and monitoring hemodynamics during the perioperative period and complications after transplantation and during follow-up (5-7).

Although echocardiography plays an irreplaceable role in heart transplantation, according to the International Society for Heart and Lung Transplantation Guidelines for the Management of Heart Transplant Recipients (8) and the Chinese Technical Specification for the Acquisition and Protection of Donor's Hearts in Heart Transplant (9), the only clear indicators related to the application of echocardiography in the process of screening donors for heart transplantation are as follows: (I) cardiac ultrasound without cardiac motion abnormalities showing good valve structure and function and mitral and aortic valves without anatomical or hemodynamic abnormalities; (II) left ventricular ejection fraction >50% is recommended; after hemodynamic stabilization under the application of positive inotropic drugs, ejection fraction <40% is not recommended for heart transplantation; (III) left ventricular myocardial thickness ≤ 13 mm is feasible for heart transplantation; mild left ventricular myocardial thickening (13-14 mm) without significant LV hypertrophy on ECG is acceptable (10-16). Thus, it can be seen that the evaluation of donors for heart transplantation is relatively simple according to these guidelines; there are insufficient criteria for echocardiographic precision indices in the application of

transplanted hearts.

There have been studies on echocardiographic to assess the condition of the recipient heart after heart transplantation (early, middle and late stage), but there are no studies on the effect of echocardiographic indices on the postoperative condition of the donors' heart before heart transplantation (17-19). Therefore, the aim of this study is twofold: (I) to observe the characteristics of changes in echocardiographic parameters of the donor's heart before and after heart transplantation and (II) to study the relationship between the changes in echocardiographic parameters of the donor's heart pre- and post-transplant and transplant recipient survival. As a result, contributions can be made to the development of appropriate echocardiographic evaluation criteria for the donor's heart and improvement in the survival rate of heart transplant recipients. We present the following article in accordance with the STROBE reporting checklist (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-592/rc>).

Methods

Study population

This study enrolled 29 patients (recipients) and 29 donors who underwent orthotopic heart transplantation in our hospital from October 2016 to October 2019. All recipients were followed up until April 2020. Donors who met the criteria for organ donation and recipients who received their organs were included in this study (8). General information of recipients and donors, such as sex, age, height, weight, race, smoking history, and drinking history, was recorded. The causes of heart failure were as follows: coronary heart disease, dilated cardiomyopathy, hypertrophic cardiomyopathy, congenital heart disease, among others. Treatments prior to transplantation included cardiopulmonary resuscitation, mechanical ventilation, coronary artery stenting (PCI), cardiac resynchronization therapy (CRT)/implantable defibrillator (ICD), extracorporeal membrane oxygenation (ECMO), and intra-aortic balloon pump (IABP). This study was approved by the human investigation committee of Sun Yat-sen Memorial Hospital (approval No. SYSEC-KY-

KS-2021-224) and was conformed to the provisions of the Declaration of Helsinki (as revised in 2013). Because of the retrospective nature of the research, the requirement for informed consent was waived.

Determining the data of the echocardiogram

In this study, the echocardiographic parameters of 29 cases of heart transplantation were recorded before heart transplantation, 1-week after heart transplantation, and 1 month after heart transplantation. For measurement of the indices, the subjects were placed in the left supine or supine position through the parasternal long-axis view of the left ventricle, parasternal short-axis view of the left ventricle, apical two-chamber, three-chamber, four-chamber and five-chamber views, and infraxiphoid two-chamber view. Based on the specific purpose of this study, the following echocardiographic parameters were measured in standard section: left ventricular end diastolic diameter (LVEDd), interventricular septal diameter (IVSd), left ventricular posterior wall diameter (LVPWd), left atrium diameter (LA), ascending aorta diameter (AAO), aortic root diameter (AOR), pulmonary artery diameter (PA), right atrium diameter (RA), right ventricle diameter (RV), left ventricle ejection fraction (LVEF, measured by Simpson's biplane method), tricuspid regurgitation velocity (TR), mitral Inflow E-wave peak velocity (MVE), mitral Inflow A-wave peak velocity (MVA), blood velocity of pulmonary valve (PV), blood velocity of aortic valve (AV); tricuspid annular peak systolic velocity (S'); and tricuspid annular plane systolic excursion (TAPSE). Additionally, pericardial effusion was observed and measured in each section. The above measurements are referenced according to The American Society of Echocardiography Recommendations for Cardiac Chamber Quantification in Adults: A quick reference guide from the ASE workflow and LAB management task force [2018] (20) and China Echocardiography Measurement Guidelines for Adults [2016] (21). The echocardiographic parameters were recorded for both donors and recipients before heart transplantation and at 1 week and 1 month post-transplant.

This study observed the survival of patients 36 months post-transplant and survival at 3 months after surgery was used as the basis for grouping.

Statistical analysis

All echocardiographic parameters were tested for normality.

The SPSS 21.0 software package (IBM, Armonk City, New York, United State) was used to process the data \pm standard deviation ($\bar{x}\pm s$). The independent sample *t*-test or paired sample *t*-test was used for comparisons between groups. The counting data are expressed as frequencies (%). Kaplan-Meier survival curves and log-rank tests were used for survival analysis, in which $P<0.05$ on both sides was considered statistically significant.

Results

Baseline data of clinical and echocardiographic parameters of heart transplantation donors and recipients

From October 2016 to October 2019, 29 cases of orthotopic heart transplantation were performed in our hospital. The basic clinical data for 29 cases (recipients) of orthotopic heart transplant are shown in *Table 1*, including 18 males and 11 females, aged 12 to 78 years (44.34 ± 16.80 years), 6 patients with a history of smoking, 2 patients with diabetes mellitus, and 1 patient with history of chronic hepatitis B. The primary diseases included dilated cardiomyopathy in 19 cases, coronary atherosclerotic cardiomyopathy in 4 cases, arrhythmogenic right ventricular cardiomyopathy in 3 cases, hyperthyroid cardiomyopathy in 1 case, hypertrophic cardiomyopathy in 1 case and viral myocarditis in 1 case. Among them, 6 patients received ECMO, 6 patients received CRT or ICD, 3 patients underwent PCI, 3 patients underwent IABP, and 1 patient underwent cardiopulmonary resuscitation.

All recipients were followed up until April 2020. Among them, 23 patients (79.31%) survived for more than 3 months, and 6 recipients died within 3 months post-transplant. Among the 6 deaths, 3 were due to postoperative right heart failure, two were secondary to postoperative infection, and 1 occurred due to complications of ECMO.

The preoperative echocardiographic parameters for all heart transplant recipients are shown in *Table 2*.

Comparison of echocardiographic parameters before and after heart transplantation

The results of the comparison of echocardiographic parameters of the donor hearts before transplantation and 1 week post-transplant are as follows (*Table 3*): the LA (28.90 ± 4.09 vs. 35.21 ± 6.09 mm, $P<0.001$), LVPWd (9.69 ± 1.39 vs. 10.96 ± 1.77 mm, $P<0.001$), IVSd (9.79 ± 1.54 vs. 10.85 ± 1.80 mm, $P=0.001$), PV (94.05 ± 18.47 vs.

Table 1 General information of 29 heart transplant patients

General information	n=29
Age (years)	44.34±16.80
Male, n (%)	18 (62.06)
Smoking history, n (%)	6 (20.69)
Diabetes, n (%)	2 (6.90)
Chronic viral hepatitis B, n (%)	1 (3.45)
Heart failure causes, n (%)	
Dilated cardiomyopathy	19 (65.52)
Coronary heart disease	4 (13.79)
Arrhythmogenic right ventricular cardiomyopathy	3 (10.34)
Hyperthyroid heart disease	1 (3.45)
Hypertrophic cardiomyopathy	1 (3.45)
Viral myocarditis	1 (3.45)
Preoperative ECMO, n (%)	6 (20.69)
Preoperative CRTD/ICD, n (%)	6 (20.69)
Preoperative PCI, n (%)	3 (10.34)
Preoperative IABP, n (%)	3 (10.34)
Preoperative CPR, n (%)	1 (3.45)

PCI, percutaneous coronary intervention; CRTD, cardiac resynchronization therapy and defibrillator; ICD, implantable cardioverter defibrillator; ECMO, extracorporeal membrane oxygenation; IABP, intra-aortic balloon pump.

127.90±51.55 mm, $P=0.022$), RA (35.21±3.46 vs. 38.61±5.45 mm, $P=0.001$) and RV (34.17±3.85 vs. 37.39±5.91 mm, $P=0.004$) were increased at 1 week post-transplant; the TAPSE (19.83±4.02 vs. 10.54±2.90 mm, $P<0.001$) and S' (14.68±3.01 vs. 8.19±2.62 mm, $P<0.001$) decreased at 1 week post-transplant (*Figure 1*); There was no significant difference in AOR, AAO, LVDd, PA, LVEF, AV, MVE, MVA or TR between the pre- and post-transplanted hearts.

The results of the comparison of echocardiographic parameters of the donor hearts before heart transplantation and 1 month post-transplant are as follows (*Table 4*): the LA (28.90±4.09 vs. 35.00±4.97 mm, $P<0.001$), LVPWd (9.69±1.39 vs. 10.62±1.58 mm, $P=0.003$), IVSd (9.79±1.54 vs. 10.64±1.66 mm, $P=0.018$) and PV (94.05±18.47 vs. 116.88±24.51 mm, $P=0.020$) were increased at 1 month after heart transplant; The TAPSE (19.83±4.02 vs. 12.35±3.14 mm, $P<0.001$) and MV-A (76.25±25.13 vs. 48.40±13.36 mm, $P=0.036$) were significantly decreased at 1 month

Table 2 Preoperative echocardiographic parameters in 29 heart transplant patients

Parameters	Value
AOR (mm)	19.96±2.51
AAO (mm)	29.11±5.52
LA (mm)	43.96±10.19
LVDd (mm)	66.75±14.58
LVPWd (mm)	7.85±1.81
IVSd (mm)	8.26±2.41
RVDd (mm)	30.16±11.99
RA (mm)	51.11±10.44
RV (mm)	48.26±9.88
PA (mm)	26.88±4.71
AV (cm/s)	103.50±31.45
PV (cm/s)	76.08±27.51
MVE (cm/s)	106.93±50.89
MVA (cm/s)	70.88±39.62
TR (cm/s)	261.45±68.77
TAPSE (mm)	13.63±4.49
S' (cm/s)	7.47±1.66
LVEF (%)	26.50±11.31

AOR, aortic root; AAO, ascending aorta; LVDd, left ventricle diastolic diameter; LVEF, left ventricle ejection fraction; LA, left atrium; IVSd, interventricular septum; LVPWd, left ventricle posterior-wall diameter; PA, pulmonary artery; PV, blood velocity of pulmonary valve; AV, blood velocity of aortic valve; RA, right atrium; RV, right ventricle; MVE, mitral Inflow E-wave peak velocity; MVA, mitral Inflow A-wave peak velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation velocity; S', tricuspid annular peak systolic velocity.

after heart transplant; there was no significant difference in RA, RV, S', AOR, AAO, LVDd, PA, LVEF, AV, MVE, or TR between the pre- and post-transplanted hearts.

The relationship between the donor's preoperative echocardiographic parameters and survival after heart transplant

The patients were divided into a survival group and a death group according to their 3-month survival status. The donor's preoperative RA was larger in the survival group than in the death group (36.00±3.21 vs. 32.17±

Table 3 The comparison of echocardiographic parameters of donor hearts before transplantation and 1 week post-transplant

Echocardiographic parameters	Donors before heart transplantation	1 week after heart transplantation	P value
AOR (mm)	20.10±1.37	19.86±1.28	>0.05
AAO (mm)	27.89±3.38	27.58±2.72	>0.05
LA (mm)	28.90±4.09	35.21±6.09	<0.001
LVDd (mm)	44.14±4.46	43.29±4.59	>0.05
LVPWd (mm)	9.69±1.39	10.96±1.77	<0.001
IVSd (mm)	9.79±1.54	10.85±1.80	0.001
RA (mm)	35.21±3.46	38.61±5.45	0.001
RV (mm)	34.17±3.85	37.39±5.91	0.004
PA (mm)	21.04±2.24	22.73±2.40	>0.05
LVEF (%)	64.10±4.39	65.75±6.01	>0.05
AV (cm/s)	119.05±30.01	121.08±20.79	>0.05
PV (cm/s)	94.05±18.47	127.90±51.55	0.022
MVE (cm/s)	88.18±23.72	94.25±30.40	>0.05
MVA (cm/s)	76.25±25.13	50.20±12.22	>0.05
TR (cm/s)	207.90±36.24	243.10±41.26	>0.05
TAPSE (mm)	19.83±4.02	10.54±2.90	<0.001
S' (cm/s)	14.68±3.01	8.19±2.62	<0.001

AOR, aortic root; AAO, ascending aorta; LVDd, left ventricle diastolic diameter; LVEF, left ventricle ejection fraction; LA, left atrium; IVSd, interventricular septum; LVPWd, left ventricle posterior-wall diameter; PA, pulmonary artery; PV, blood velocity of pulmonary valve; AV, blood velocity of aortic valve; RA, right atrium; RV, right ventricle; MVE, mitral Inflow E-wave peak velocity; MVA, mitral Inflow A-wave peak velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation velocity; S', tricuspid annular peak systolic velocity.

2.79 mm, $P=0.013$). The donor's preoperative RV was larger in the survival group than in the death group (34.96 ± 3.77 vs. 31.17 ± 2.64 mm, $P=0.029$). There was no significant difference in AOR, AAO, LA, LVDd, LVPWd, IVSD, LVEF, PA, AV, PV, MVE, MVA, TR, TAPSE or S' (*Table 5, Figure 2*).

According to the donors' preoperative RA size, the heart transplant recipients were divided into the RA ≥ 32 mm group and the RA < 32 mm group. The Kaplan-Meier survival curve is shown in *Figure 3*. The log-rank test resulted in $P=0.034$. The postoperative survival of the RA ≥ 32 mm group was better than that of the RA < 32 mm group.

According to the preoperative RV size of the donors, the heart transplant recipients were divided into the RV ≥ 32 mm group and the RV < 32 mm group. The Kaplan-Meier survival curve is shown in *Figure 4*. The log-rank

test resulted in $P=0.017$. The postoperative survival of the RV ≥ 32 mm group was better than that of the RV < 32 mm group.

According to the survival status at 3 months post-transplant, the recipients were divided into a survival group and a death group. A comparison of the difference between the postoperative 1 month and donor heart echocardiographic parameters in the survival group and death group (23 patients survived more than 3 months; 1 patient survived less than 2 weeks) is shown in *Table 6, Figure 5*. The difference in Δ RA between the postoperative 1 month hearts and donor hearts before transplantation was less in the survival group than in the death group (-0.22 ± 6.10 vs. 4.40 ± 1.14 mm, $P=0.020$). The difference in Δ RV between the postoperative 1 month hearts and donor hearts before transplantation was less in the survival group than in the death group (0.70 ± 7.35 vs. 5.20 ± 2.05 mm, $P=0.019$).

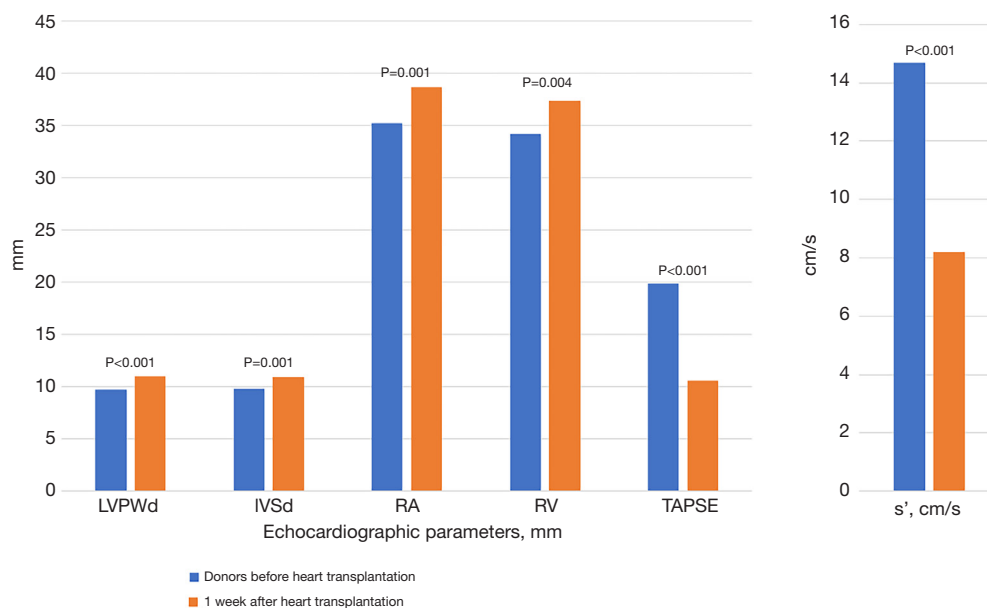


Figure 1 The comparison of echocardiographic parameters (LVPWd, IVSd, RA, RV, TAPSE, S') of donor hearts before transplantation and 1 week post-transplant. LVPWd, left ventricle posterior-wall diameter; IVSd, interventricular septum; RA, right atrium; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; S', tricuspid annular peak systolic velocity.

One month after heart transplant, the changes in RA were measured by echocardiography. The patients were divided into two groups: the RA enlargement ≥ 2 mm group and the RA enlargement < 2 mm group (comparison with donor hearts before transplantation). The Kaplan-Meier survival curve is shown in *Figure 6*. The log-rank test resulted in $P=0.013$. The postoperative survival time of the group with RA enlargement < 2 mm was better than that of the group with RA enlargement ≥ 2 mm.

One month after heart transplantation, the changes in RV were measured by echocardiography. The patients were divided into two groups: the RV enlargement ≥ 2 mm group and the RV enlargement < 2 mm group (comparison with the donor's heart before transplantation). The Kaplan-Meier survival curve is shown in *Figure 7*. The log-rank test resulted in $P=0.022$. The survival time of the group with RV enlargement < 2 mm was better than that of the group with RV enlargement ≥ 2 mm.

Discussion

Characteristics of changes in echocardiographic parameters before and after heart transplantation

After heart transplantation, the donor's heart forms a new

relationship with the recipient. The implanted donor's heart needs to adapt to the new environment of the recipient as well as the application of immunosuppressive drugs. Maladaptation can easily lead to changes in the size and function of the heart chambers of the transplanted heart. LVPWd and IVSd increase, and ventricular wall hypertrophy occurs after heart transplantation. In the early stage of heart transplantation, cardiac hypertrophy is mainly considered to be associated with the immunoproliferative response of cardiomyocytes, interstitial edema, and myocardial ischemia (22). The donor's heart is in an ischemic state during surgical excision, preservation, and transportation. Cardiomyocytes consume a large amount of ATP, which leads to dysfunction of $\text{Na}^+\text{-K}^+\text{-ATPase}$. Then, Na^+ , Ca^{2+} and water enter the cells, eventually leading to the onset of cell swelling and degeneration. When circulation is restored to the donor's heart after surgery, myocardial reperfusion causes the cells to produce large amounts of oxygen radicals, which can lead to swelling and degeneration of the cells (23). With the degenerative necrosis of myocardial cells and the subsidence of interstitial edema, the thickness of the left ventricular wall decreases (24). Liu *et al.* (25) found that the IVSd and LVPWd peaked at 7 d after transplantation in 29 patients, beginning on the first day post-transplant and gradually decreasing thereafter.

Table 4 The comparison of echocardiographic parameters before heart transplantation and 1 month post-transplant

Echocardiographic parameters	Donors before heart transplantation	1 month after heart transplantation	P value
AOR (mm)	20.10±1.37	20.38±1.58	>0.05
AAO (mm)	27.89±3.38	28.67±3.33	>0.05
LA (mm)	28.90±4.09	35.00±4.97	<0.001
LVDd (mm)	44.14±4.46	43.29±4.96	>0.05
LVPWd (mm)	9.69±1.39	10.62±1.58	0.003
IVSd (mm)	9.79±1.54	10.64±1.66	0.018
RA (mm)	35.21±3.46	35.89±5.24	>0.05
RV (mm)	34.17±3.85	35.79±5.88	>0.05
PA (mm)	21.04±2.24	33.74±31.22	>0.05
EF (%)	64.10±4.39	64.86±3.58	>0.05
AV (cm/s)	119.05±30.01	115.06±20.02	>0.05
PV (cm/s)	94.05±18.47	116.88±24.51	0.020
MVE (cm/s)	88.18±23.72	82.88±24.11	>0.05
MVA (cm/s)	76.25±25.13	48.40±13.36	0.036
TR (cm/s)	207.90±36.24	239.45±45.39	>0.05
TAPSE (mm)	19.83±4.02	12.35±3.14	<0.001
S' (cm/s)	14.68±3.01	13.64±21.09	>0.05

AOR, aortic root; AAO, ascending aorta; LVDd, left ventricle diastolic diameter; LVEF, left ventricle ejection fraction; LA, left atrium; IVSd, interventricular septum; LVPWd, left ventricle posterior-wall diameter; PA, pulmonary artery; PV, blood velocity of pulmonary valve; AV, blood velocity of aortic valve; RA, right atrium; RV, right ventricle; MVE, mitral Inflow E-wave peak velocity; MVA, mitral Inflow A-wave peak velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation velocity; S', tricuspid annular peak systolic velocity.

If thickening persists into the middle and late postoperative periods, chronic rejection may be occurring (26,27). Our study found that the LVPWd and IVSd of the heart increased 1 week after surgery compared to preoperative values, which is similar to findings in other studies.

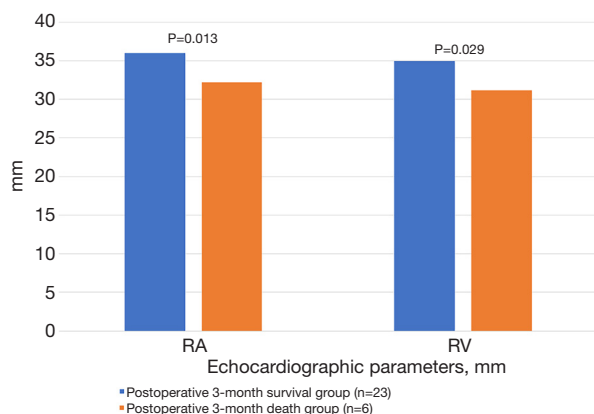
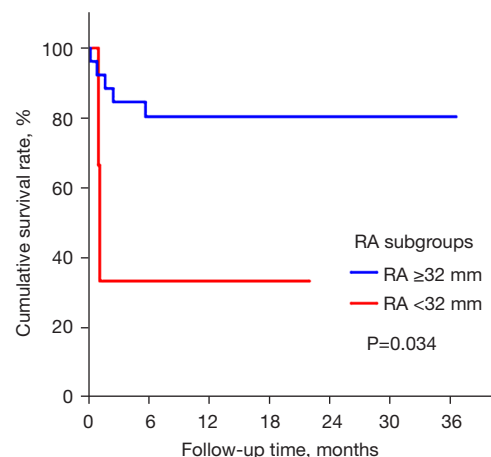
In this study, we found that the RA and RV increased at 1 week after transplantation compared to preoperative values, but the RA and RV did not increase significantly at 1 month after surgery compared to preoperative values, suggesting a recovery of dilatation of the right heart system. Fang *et al.* (28) found that elevated pulmonary artery pressure and transient enlargement and hypertrophy of the right heart system occurred early after heart transplantation. Bhatia *et al.* (29) also found that the right heart system enlarged early after transplantation, but the right ventricular size basically returned to normal and was relatively stable approximately 1 month after surgery. The results of the present study are consistent with this process. While right ventricular enlargement occurs after heart transplantation,

the left ventricle does not increase significantly under the same conditions. Possible mechanisms for this phenomenon include the following: (I) anatomical and physiological factors: The right ventricular myocardium is thinner than the left ventricular myocardium, has a lower compensatory capacity for pressure and is also more sensitive to various physiological and pathological changes and ischemia-reperfusion injury (30-32); (II) high preoperative pulmonary artery pressure in the recipient: patients receiving heart transplant have preoperative heart failure due to various causes. Long-term left heart failure leads to pulmonary circulation stasis and increased pulmonary small vessel resistance, and the normal transplanted heart has not adapted to pulmonary hypertension, thus leading to right heart failure (33). Young applied transesophageal ultrasound and found that patients with preoperative pulmonary hypertension resumed circulation soon after enlargement of the right heart system occurred in the donor's heart (34). A study has shown that it takes approximately 2 weeks for

Table 5 Comparison of donors' preoperative echocardiographic parameters between the survival group and death group at 3 months post-transplant

Echocardiographic parameters	Postoperative 3-month survival group (n=23)	Postoperative 3-month death group (n=6)	P value
AOR (mm)	20.13±1.39	20.00±1.41	>0.05
AAO (mm)	27.91±2.99	27.83±4.92	>0.05
LA (mm)	29.09±4.21	28.17±3.87	>0.05
LVDd (mm)	44.26±4.14	43.67±5.99	>0.05
LVPWd (mm)	9.70±1.22	9.67±2.07	>0.05
IVSd (mm)	9.74±1.48	10.00±1.90	>0.05
RA (mm)	36.00±3.21	32.17±2.79	0.013
RV (mm)	34.96±3.77	31.17±2.64	0.029
LVEF (%)	64.17±4.60	68.83±3.87	>0.05
PA (mm)	21.09±2.43	20.80±1.30	>0.05
AV (cm/s)	118.24±30.04	123.67±36.75	>0.05
PV (cm/s)	90.82±17.07	112.33±17.90	>0.05
MVE (cm/s)	88.59±23.42	86.80±27.49	>0.05
MVA (cm/s)	72.38±26.46	91.75±9.98	>0.05
TAPSE (mm)	19.83±4.03	19.83±4.36	>0.05
S' (cm/s)	14.59±3.19	15.00±2.00	>0.05

AOR, aortic root; AAO, ascending aorta; LVDd, left ventricle diastolic diameter; LVEF, left ventricle ejection fraction; LA, left atrium; IVSd, interventricular septum; LVPWd, left ventricle posterior-wall diameter; PA, pulmonary artery; PV, blood velocity of pulmonary valve; AV, blood velocity of aortic valve; RA, right atrium; RV, right ventricle; MVE, mitral Inflow E-wave peak velocity; MVA, mitral Inflow A-wave peak velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation velocity; S', tricuspid annular peak systolic velocity.

**Figure 2** Comparison of donors' preoperative echocardiographic parameters (RA, RV) between the survival group and death group at 3 months post-transplant. RA, right atrium; RV, right ventricle.**Figure 3** Comparison of survival curves between the RA ≥32 mm group and RA <32 mm group. RA, right atrium.

the right ventricle to gradually adapt to the pulmonary vascular resistance of the recipient using pulmonary vasodilator therapy in the post-transplant period (35); (III) surgical anastomosis: the presence of stenosis in the pulmonary artery anastomosis of the transplanted heart

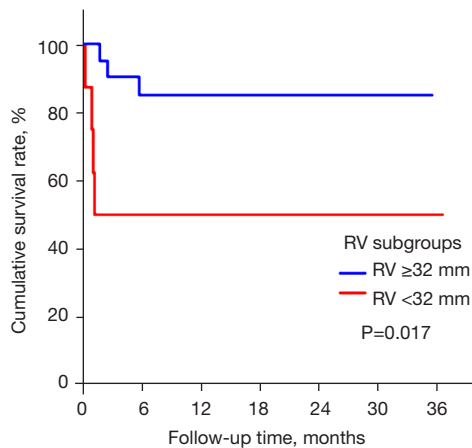


Figure 4 Comparison of survival curves between the RV ≥ 32 mm group and the RV < 32 mm group. RV, right ventricle.

increases the afterload of the right ventricle and enlarges the right heart, probably because of the preoperative pulmonary hypertension, thickening of the pulmonary artery vessel diameter, and local paradoxical motion after anastomosis with the pulmonary artery vessel of the normal donor's heart, which is a technically difficult challenge in the transplantation procedure (25); (IV) high-dose glucocorticoids lead to water and sodium retention: preoperative cardiac failure in transplant recipients leaves the body in an edematous state, and post-transplant immunosuppressive therapy requires high-dose glucocorticoids. The greater the amount of glucocorticoids used, the more pronounced the increase in blood volume due to water and sodium retention. The right heart preload is increased, and the right heart enlargement is more pronounced (15); (V) abnormal cardiac and renal reflexes after denervation: in normal hearts, when the volume load is increased, the volume receptors in the atria are stimulated, and then the renin-angiotensin-aldosterone system (RAAS) and antidiuretic hormone are reflexively inhibited, which inhibits sympathetic afferents to the renal vasculature and exerts diuretic and natriuretic effects to reduce the

Table 6 Comparison of changes in echocardiographic parameters of donor hearts in the survival and death groups at 3 months post-transplant

Echocardiographic parameters	Postoperative 3-month survival group (n=23)			Postoperative 3-month death group (n=5)			P value
	Donor's heart before transplant	1 month after heart transplant	Difference Δ	Donor's heart before transplantation	1 month after heart transplant	Difference Δ	
AOR (mm)	20.13 \pm 1.39	20.32 \pm 1.64	0.18 \pm 1.56	20.00 \pm 1.41	21.00 \pm 0.00	2.00 \pm 1.41	>0.05
AAO (mm)	27.91 \pm 2.99	28.59 \pm 3.45	0.90 \pm 3.33	27.83 \pm 4.92	29.50 \pm 2.12	3.50 \pm 0.71	>0.05
LA (mm)	29.09 \pm 4.21	34.91 \pm 5.39	5.83 \pm 5.33	28.17 \pm 3.87	35.40 \pm 2.61	7.20 \pm 5.45	>0.05
LVDd (mm)	44.26 \pm 4.14	44.04 \pm 4.96	-1.22 \pm 5.94	43.67 \pm 5.99	44.40 \pm 5.37	1.40 \pm 2.07	>0.05
LVPWd (mm)	9.70 \pm 1.22	10.41 \pm 1.56	0.82 \pm 1.44	9.67 \pm 2.07	11.75 \pm 1.26	1.25 \pm 0.96	>0.05
IVSd (mm)	9.74 \pm 1.48	10.52 \pm 1.68	0.78 \pm 1.91	10.00 \pm 1.90	11.20 \pm 1.64	1.20 \pm 1.30	>0.05
RA (mm)	36.00 \pm 3.21	35.78 \pm 5.73	-0.22 \pm 6.10	32.17 \pm 2.79	36.40 \pm 2.70	4.40 \pm 1.14	0.020
RV (mm)	34.96 \pm 3.77	35.65 \pm 6.41	0.70 \pm 7.35	31.17 \pm 2.64	36.40 \pm 2.70	5.20 \pm 2.05	0.019
LVEF (%)	64.17 \pm 4.60	65.26 \pm 3.76	1.09 \pm 5.13	68.83 \pm 3.87	63.00 \pm 1.87	-1.99 \pm 6.00	>0.05
PA (mm)	21.09 \pm 2.43	35.56 \pm 33.8	14.50 \pm 33.2	20.80 \pm 1.30	24.00 \pm 3.00	2.50 \pm 2.12	>0.05
TAPSE (mm)	19.83 \pm 4.03	12.36 \pm 3.35	-7.45 \pm 4.93	19.83 \pm 4.36	12.25 \pm 1.89	-9.00 \pm 3.61	>0.05
S' (cm/s)	14.59 \pm 3.19	13.93 \pm 22.0	-0.60 \pm 22.32	15.00 \pm 2.00	10.50 \pm 2.12	-6.00 \pm 2.83	>0.05

AOR, aortic root; AAO, ascending aorta; LVDd, left ventricle diastolic diameter; LVEF, left ventricle ejection fraction; LA, left atrium; IVSd, interventricular septum; LVPWd, left ventricle posterior-wall diameter; PA, pulmonary artery; PV, blood velocity of pulmonary valve; AV, blood velocity of aortic valve; RA, right atrium; RV, right ventricle; MVE, mitral Inflow E-wave peak velocity; MVA, mitral Inflow A-wave peak velocity; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation velocity; S', tricuspid annular peak systolic velocity.

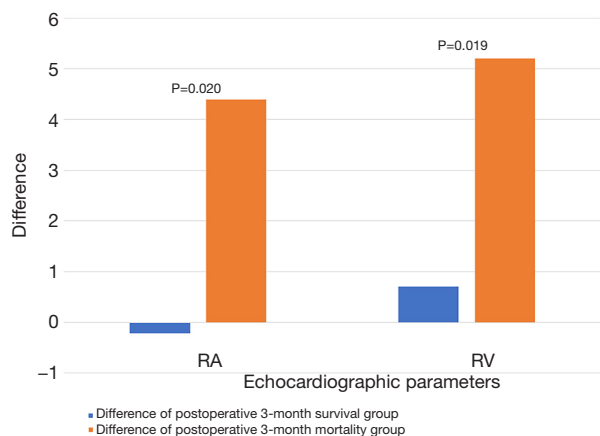


Figure 5 Comparison of changes in echocardiographic parameters (RA, RV) of donor hearts in the survival and death groups at 3 months post-transplant. RA, right atrium; RV, right ventricle.

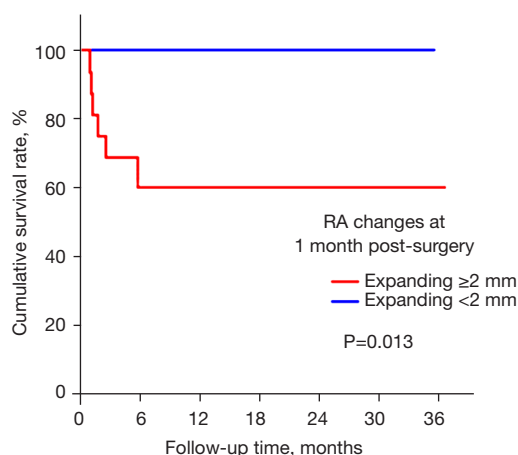


Figure 6 Comparison of survival curves between the RA enlargement ≥ 2 mm group and the RA enlargement < 2 mm group. RA, right atrium.

volume load. However, after heart transplantation, due to the denervation of the heart, the donor's heart loses the regulation of the cardiorenal reflex system in the recipient. Therefore, when the blood volume increases in the body, it cannot effectively achieve diuretic and natriuretic effects through the regulation of the RAAS system. It is not sensitive to the response of diuretics, causing right heart failure with obvious water and sodium retention and increased preload, which is manifested on echocardiography as right heart enlargement (36,37); (VI) "Large pericardium and small heart": in the preoperative long-term heart

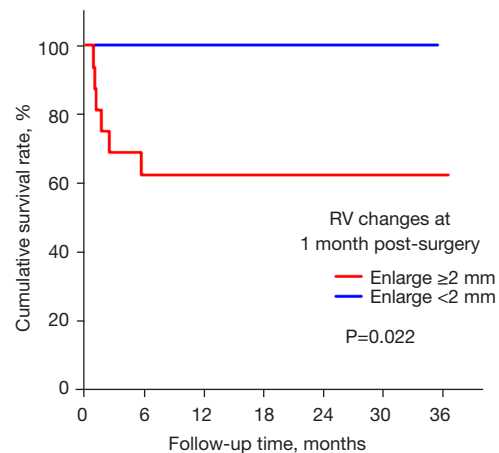


Figure 7 Comparison of survival curves between the RV enlargement ≥ 2 mm group and the RV enlargement < 2 mm group. RV, right ventricle.

failure state of heart transplant patients, the recipient's autologous heart compensates for the enlargement, and the pericardium can limit the overexpansion of the heart cavity; thus, the pericardium also increases accordingly. The right heart system is more prone to enlargement because of better compliance and sensitivity than the left heart (38).

The role of right heart function in the overall circulatory process is also critical. The function of the longitudinal fibers of the right ventricular myocardium is mainly expressed in the motion of the annulus, and TAPSE and S' parameters are easier to obtain and closely related to right heart function (39,40), which can reflect the systolic function of the right ventricle. The American Society of Echocardiography (ASE) states that a TAPSE < 16 mm is indicative of right ventricular systolic insufficiency (41). Reduced systolic function is indicated when S' < 6.5 cm/s (42). Reduced TAPSE often indicates reduced right ventricular systolic function and correlates well with a right heart floating catheter, which can be used as a noninvasive index to assess right heart function and reflect prognosis (43-45). It has been shown that right ventricular systolic function is reduced after heart transplantation, but no significant abnormalities in the function of the left ventricle have been observed (46,47). In our study group, we found that TAPSE and S' were decreased 1 week after transplantation compared with preoperative values, suggesting that there was decompensation of right heart function. TAPSE was still decreased 1 month after surgery compared with preoperative values, suggesting that right heart function was

not fully recovered, which was consistent with the findings of previous studies.

Donor heart echocardiographic parameters and their changes in relation to survival after heart transplant

Data from the International Society for Heart Transplant indicate that right heart dysfunction accounts for 50% of post-transplant complications; 19% of early post-transplant deaths are due to acute right heart failure (33). Patients with end-stage heart disease are mostly associated with varying degrees of pulmonary hypertension, and small pulmonary arteries may have varying degrees of irreversibly increased pulmonary resistance. Pulmonary hypertension and increased pulmonary vascular resistance are important risk factors for right heart failure post-transplant (35,48). Moreover, a study has found that pulmonary hypertension is positively correlated with the development of severe right heart insufficiency after heart transplant (49). The donor's heart is unable to adapt in time to the high pulmonary circulatory resistance of the recipient after transplantation, which leads to the development of acute right heart failure. In addition, to ensure that cardiac function is restored as soon as possible after transplantation in patients with pulmonary hypertension, a large-sized donor heart should be selected as often as possible (50). Pathophysiological changes such as pulmonary hypertension, right heart failure, circulatory insufficiency, and restrictive cardiac failure may occur immediately after transplantation of a donor's heart that is too small (51). The results of our study showed that postoperative survival was higher in transplant recipients when the preoperative donor's heart had a right atrium/ventricle ≥ 32 mm. With increased preoperative pulmonary vascular resistance in the recipient, a larger right heart is better able to adapt to pulmonary circulatory resistance.

To adapt to the high-resistance pulmonary circulation, the transplanted heart must cause compensatory expansion of the right heart volume to increase the right heart output to maintain hemodynamics (52). In a study by Fang *et al.* (28), it was found that elevated pulmonary artery pressure and transient enlargement and hypertrophy of the right heart system occurred early after heart transplantation. Bhatia *et al.* (29) also found that the right heart system enlarged early after heart transplantation. Pulmonary vascular resistance decreases gradually after heart transplantation (53). It has been shown that it takes approximately 2 weeks for the right

ventricle to gradually adapt to the recipient's pulmonary vascular resistance under conditions of post-transplant pulmonary vasodilator therapy (35). The results of our study showed that postoperative survival was lower in heart transplant recipients who had dilation of the right atrium/ventricle ≥ 2 mm at 1 month postoperatively compared with pretransplant values. Moreover, patients who died after transplantation had a significantly higher degree of right atrial/ventricular dilatation at 1 month postoperatively than the surviving patients. The smaller right atrium and right ventricle of the transplanted heart inevitably leads to significant expansion of the right cardiac system to accommodate the high pulmonary resistance of the recipient. However, the overexpanded right heart system may lead to right heart ischemia, which can exacerbate right heart dysfunction (13). Meanwhile, a small right heart system in the transplanted heart that appears significantly dilated post-transplant means that the donor's heart has difficulty adapting to the new recipient environment. Pre- and post-transplant changes in the right heart system of the transplanted heart may be used as an indicator to assess prognosis.

Conclusions

- (I) In the early post-transplant period, ventricular myocardial thickening, right heart enlargement and a decrease in right heart function were observed compared with the pretransplanted heart; postoperative right heart enlargement may indicate a higher pulmonary artery pressure in the recipient than in the donor;
- (II) Postoperative survival was higher among recipients of a heart with right atrium/ventricle ≥ 32 mm; it may suggest that the larger right atrium and right ventricle of the donors are more likely to adapt to the internal environment of recipients;
- (III) Postoperative survival was lower among recipients of a heart with dilation of a right atrium/ventricle ≥ 2 mm at 1 month postoperatively compared with pretransplanted values; it may suggest that those with less right atrium and right ventricle enlargement are more likely to adapt to the internal environment of recipients.

Limitations

This study is a single-center study, and further

investigations with a larger sample size across multiple centers are required. Moreover, this study is retrospective and needs to be further confirmed with prospective studies.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://atm.amegroups.com/article/view/10.21037/atm-22-592/coif>). The authors have no conflicts of interest to declare.

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