Orthotopic heart transplantation in 3 cases*☆

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Abstract: Three cases of terminal stage heart disease received orthotopic heart transplantation at the Department of Cardiothoracic Surgery, the First Hospital of Nanchang University between August 2001 and December 2003. These three cases were all female and died of brain death. Body weight difference between donor and recipient was less than 20%. All three cases underwent superior and inferior vena cave osculation and received immunosuppressive therapy of cyclosporine A, prednisone, and mycophenolate postoperatively. They were successfully discarded. Heart function recovered to grade I-II(NYHA). No infection or serious rejection was found during the surgery. These results indicate that good donor heart preservation, consummate perioperative processing, and proper immunosuppressive therapy are the key measures of successful heart transplantation.

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INTRODUCTION

Heart transplantation is one of the most effective methods to treat end-stage heart disease. The present study retrospectively analyzed 3 cases who had successfully received orthotopic heart transplantation due to end-stage heart disease at the Department of Cardiothoracic Surgery, First Affiliated Hospital of Nanchang University between August 2001 and December 2003.

SUBJECTS AND METHODS

Case data

Case 1 was a 20-year-old male patient who suffered from hypertrophic cardiomyopathy. He complained of tachypnea and chest distress after activity for 7 years and edema of lower limbs for 4 years, and received implantation of heart pacemaker 3 years ago. Physical examination results revealed blood-pressure 110/73 mm Hg (1 mm Hg = 0.133 kPa) and body weight 50 kg. Physical signs showed chronic disease face, without jugular varicosity and and auscultation results revealed clear respiratory sound without crackles in two lungs, apical beat dispersion, feeling of favor in precordium, the realm of heart amphi-expanding, heart rate 60 beats per minute with regular cardiac rhythm, without Traube's murmur, and grade Ⅱ systolic murmur in apical region. In addition, positive sign of ascites and pitting edema in both lower extremities were also found. Electrocardiogram showed sinus rhythm and supervoltage in left ventricle. Ultrasonic cardiography showed pachynsis in both ventricles, left ventricular end-diastolic dimension 76 mm, and ejection fraction 0.38. Mecicin was used to improve heart function before operation.
Case 2 was a 49-year-old female patient who suffered from dilated cardiomyopathy. He complained of tachypnea and cardiopalmus repeatedly for 5 years, edema of lower limbs for 4 years, and diabetes for 3 years. Physical examination results revealed blood pressure 80/50 mm Hg and body weight 53 kg. Her physical signs showed chronic disease face, sit-up position, puffiness of eyelid and face, slight cyanosis of oral lip, and auscultation results revealed coarse respiratory sound without crackles in two lungs, apical beat dispersion, the realm of heart expand to bottom left, heart rate 60 beats per minute with arrhythmia, auscultation of heart showing bearing premature with gallop rhythm, and grade Ⅲ systolic murmur in apical region. Liver was palpated 3 centimeters below ribs, pitting edema in both lower extremities. Electrocardiogram showed sinus rhythm, degree Ⅰ auriculoventricular block, abiogenesis of ventricular premature contraction. Ultrasonic cardiography showed backstreaming of mitral valve and tricuspid valve, left ventricular end-diastolic dimension 72 mm, and ejection fraction 0.38. Blood sugar was 3.3 mmol/L before meal and 10.9 mmol/L two hours after meal. Diabetic diet and Mecicin were used to improve heart function preoperatively.
Case 3 was a 57-year-old male patient who suffered from terminal-stage coronary artery disease. He complained of tachypnea and cardiopalmus after exercise for 10 years and had received medicine treatment for 5 years approximately, but the disease was more severe thereafter. Physical examination results revealed that blood pressure 90/55 mm Hg and body weight 76 kg. His physical signs showed chronic disease face and auscultation results revealed coarse respiratory sound and fine crackles in two lungs, apical beat dispersion, the realm of heart expand to bottom left, heart rate 76 beats per minute with regular cardiac rhythm. Auscultation results revealed grade Ⅱ systolic murmur in apical region. Liver was palpated 3 centimeters below ribs, pitting edema in both lower extremities. Electrocardiogram showed sinus rhythm, degree Ⅰ auriculoventricular block, and obsolete anterior myocardial infarction. In addition, vntricular aneurysm was cued by the change of ST-T. Ultrasonic cardiography showed that atrium sinistrum and left ventricle enlarged apparently, the anterior wall of left ventricle became thin, echo enhancement and flat mobility appear, the wall of Apex of heart became thin and inflated outside,presenting paradoxical motion, left ventricular end-diastolic dimension was 70 mm, and ejection fraction was 0.35. Coronary arteriongraphy

showed diffused stegnosis and left vntricular aneurysm. Mecicin was used to improve heart function preoperatively.

Donor information

All 3 donors were young male, suffering from brain death. They had good health and no history of angiocardiopathy. Their ABO blood types were identical with the recipients. The ratio of lymphocytoxic antibody test was less than 10%. Cytomegalovirus, EB virus, hepatitis virus and HIV in the serum were negative. Body weight difference between donors and recipients was less than 20%.

Methods

Prior to removal of donor heart, 1 000-1 200 mL of 4 ℃ modified St. Thomas liquid was infused into aortic root. Meanwhile, ice was put into the pericardial cavity to keep hypothermy. After taken out, the heart was infused with 4 ℃ UW liquid through the aortic root and preserved in an iced box. Enough length of superior and inferior vena cave should be reserved.

A median incision was made on the sternum to expose the heart. Extracorporeal circulation was established by intubation at the superior and inferior vena cave and ascending aorta after general heparinization. Intubation should be performed remotely. The atriunm sinistrum drainage tube was placed into the right superior pulmonary vein and used for dripping of iced physiological saline during inosculation and for atrium sinistrum drainage after inosculation. The intervals between aorta and pulmonary artery need to be dissociated as well. After aortal blockage, heart was excised along the auriculoventricular groove and semilunar valves with posterior wall of left atrium preserved. Following trimming of the donor heart, atrium sinistrum was over-and-over sutured with 4/0 prolene thread. One stitch started from the root of superior left pulmonary vein until atrial septum, and then the other stitch was sutured to artial septum continuously and knotted with the first stitch. The inferior vena was sutured using 4/0 prolene thread. The location of donor heart was fixed, and the debouchement of aortal and pulmonary artery was properly trimmed. Pulmonary artery was sutured from midpoint of posterior wall firstly. The anterior wall of pulmonary artery was not sutured until aortal opening. Subsequently, the aorta was sutured starting from the posterior wall. Aortal clamp was removed after aortal venting. Atrium sinistrum drainage was performed at the same time, followed by intravenous injection of 500 mg methylprednisolone. Thereafter, the anterior wall of pulmonary artery and subsequent superior vena cava were sutured. Following heart recovery, hemorrhage was carefully examined. Extracorporeal circulation was ceased when powerful heartbeat was felt. Epicardial pacing wire was positioned routinely. Pericardium was interruptedly sutured. Drainage of the mediastinum and pericardium were performed, followed by layer-by-layer closure.

After surgery, patients were asked to stay in the Intensive Care Unit. Electrocardiogram, arterial pressure, O_2 saturation, electrolyte and arterial blood gas analysis were monitored. Breathing machine was used to assist ventilation. Cephalosporin-III was used for one week, and medicine was used to strength heart, diuresis and blood vessel expansion. Meprednisone (500 mg) was used in the process of opening aortal clamp. Ciclosporin-A, prednisone, and mycophenolate were applied to resist rejection. Ciclosporin A dose was regulated according to its serum concentration, maintaining at 200-300 μg/L. Prednisone was administered at 1 mg/kg for one week and then its dose was gradually decreased. Mycophenolate was orally taken 500 mg once, 3 times per day. In case 2, insulin was used to control blood glucose immediately after beginning of post-surgery. Acarbose and diamicron were used to instead of insulin when the patient began to eat. Blood glucose concentration was strictly monitored at the same time.

Main outcome measures

Evidences of acute rejection

Symptoms and signs, electrocardiogram (ECG), ultrasonic cardiography (UCG), cyto-detection, and serological indices.

Main symptoms

Acratia, low-grade fever, lassitude, cardiopalmus, dyspnoea, and anepithymia.

Main monitors of infection

X-ray films of chest, viral antibody in serum, cultivations of sputum, urine, stercus, and eumycete.

RESULTS

Follow-up results

Serious bleeding, malignant arrhythmia, and right heart failure were not found in all 3 patients. No serious infection or rejection occurred during the surgery. Heart function had improved obviously and recovered to grade I-II one month after surgery. Case 1 exhibited epileptic seizure 2 days after surgery, which disappeared after thiopentone and carbamazepine treatment. All of 3 patients were successfully discharged. Case 1 died of malignant arrhythmia 8 months after surgery, case 2 died of serious pulmonary infection 6 months after surgery, and case 3 was followed up for 27 months and found surviving. General condition and follow-up results of 3 patients who underwent orthotopic heart transplantation are shown in Table 1.

Table 1 Baseline material and follow-up results

Case	Gender	Age (yr)	Etiology	Donor	Therapy	Complication	Follow-up Results
1	Male	20	Hypertrophic cardiomyopathy	Brain death	Orthotopic bicaval heart transplantation	None	Died of malignant arrhythmia cordis 8 months after surgery
2	Female	49	Dilated cardiomyopathy	Brain death	Orthotopic bicaval heart transplantation	None	Died of severe lung infection 6 months after surgery
3	Male	57	Terminal-stage coronary artery disease	Brain death	Orthotopic bicaval heart transplantation	None	Surviving

DISCUSSION

Choice of donor and recipient

Suitable recipient is one of the major factors for a successful transplantation. UNOS had enacted detailed criteria for selecting recipient [1]: Patients who suffered from terminal stage heart diseases, such as primary cardiomyopathy, diffused ischemic heart disease, congenital heart disease which can not be cured; the expected survival time was no more than 6-12 months, age was under 55 years, pulmonary vascular resistance was below 6 wood units, without severe structural disease in other organs. The evidences for choosing donors were as follows: the immuno-compatibility between donor and recipient should be identical, including the ABO blood type and lymphocytoxic antibody test be negative; the differences of heart size and body weight between donor and recipient should be no more than 20%. In the present study, all 3 cases were the patients who suffered from terminal stage heart disease, and difference of body weight between donor and recipient was +9%, +15% , and -8%, separately.

Protection of donor's heart

It is important to protect the donor's heart favorable for a successful transplantation. It is considered significant to shorten the warm ischemia and cold ischemia time of heart. However, the ischemia time of heart is closely correlated to the conditions of donor's heart, and operator's preparation and proficiency [2-3]. The specific measures we took were as follows: ①Stablishing artificial respiration as soon as donor suffering from brain death, maintaining a stable hemodynamics as far as possible. ② Infusing cold hypso-kalium liquid into the aortal root to stop the donor heart beating in diastolic phase. ③Shortening the time for donor heart transportation and suturing the donor heart as soon as possible. ④Performing some animal tests and model experiments preoperatively to improve operator's proficiency. The warm ischemia time of three patients was 3, 5, and 6 minutes, separately, and cold ischemia time was 165, 190, and 180 minutes, separately, gaining a favorable effect of myocardial preservation. It's critical to shorten the warm ischemia time for getting a high quality of donor heart.

Transplantation style

There are three methods of inosculation: standard technique, bicaval anastomotic technique, and total orthotopic heart transplantation. The first two methods are frequently used. Wang *et al* [4] thought that bicaval anastomotic technique only left one sinus node, avoiding cardiac arrhythmia and disorder of haemodynamics caused by back flow of atrioventricular valve; bicaval anastomotic technique was also much easier than total orthotopic heart transplantation, decreasing the probability of stomal blood leakage. In the present study, bicaval anastomotic technique was employed in all 3 patients. Results revealed that serious cardiac arrhythmias did not occur postoperatively, and the back flow of tricuspid was slight.

Immunosuppressive therapy and rejection monitoring

Ciclosporin, prednisone and mycophenolate were adopted in the immunosuppressive therapy. Serious rejection, leucocytopenia, or myelosuppression did not occur. At the early period following surgery, valley value of ciclosporin A decreases slightly, and ciclosporin A dose is regulated according to its serum concentration, maintaining at 200-300 μg/L. At the initial stage following surgery, it is better to maintain the valley value of ciclosporin at a relatively high standard, regulating it to the normal level gradually two months later.

Electrocardiogram, ultrasonic cardiography, cyto-detection, X-ray films and serological indices, as well as clinical symptoms and signs were used to monitor rejection. Although myocardial biopsy is thought to be the gold standard of acute rejection [5], two cases did not undergo it in this study. Because myocardial biopsy is an invasive and expensive procedure and can cause mental stress to the patients, it's better not do it repeatedly. Myocardial biopsy is selected when the presence of rejection is suspected.

Prevention of infection

Infection is the second major factor causing death at the early stage following heart transplantation and is the most common factor causing death at the advanced stage. Infection frequently occurs at the early stage of heart transplantation, in particular in the first few weeks [6]. In the present study, severe infection did not occur in all 3 patients because some protective measures were used, including strict sterilization and insulation, chest X-ray monitoring, cultivation of bacterium and eumycete, pulling out various kinds of invasive tubes, tracheal intubation, application of broad-spectrum antibiotic and antiviral drug, and encourage doing activities in patients.

Prevention and management of bleeding

Heart transplantation majors in suturing vessels. It is greatly important to prevent bleeding. Firstly, we need to trim the tissue from donor and recipient to be matched. Secondly, the distance between every tow pins needs to be well-distributed, especially for the back of heart. Thirdly, enough platelet should be prepared prior to surgery. Fourthly, some methods should be applied to stop bleeding during the surgery.

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原位心脏移植 3 例*☆

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摘要：2001-08/2003-12 南昌大学第一附属医院心胸外科分别为 3 例终末期心脏病患者进行了原位心脏移植，3 例供者均为青年男性脑死亡者，供者与受者体质量差异均小于 20%。3 例受者均采用双腔静脉吻合法，移植后采用环孢素 A、强的松及霉酚酸酯联合免疫抑制治疗。3 例患者均顺利出院，心功能恢复至 NYHA Ⅰ~Ⅱ级，围手术期无感染或严重排斥反应发生。提示良好的心肌保护、完善的围手术期处理以及合理的抗排斥治疗是心脏移植成功的关键。

关键词：心脏移植；免疫抑制；心肌保护；器官移植

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CRTER 杂志对研究原著稿件修改的语言描述要求

文题：以准确和特征为重点，可以采用主副标题的形式。

背景：应突出与目的、结论有一致性的呼应关系。

目的：具有创新性结果的文章，以假设为描述用语时，一般不要说对XXX机制的研究，因为许多实验并非真正去研究机制，而只是对作用途径、作用过程的再验证。

以验证为目的的实验，文章应重点描述结果中有特殊意义的内容，切忌应用泛泛的概括性语言。验证的结果可以是阳性的，也可以是阴性的， 阴性的结果可能更有意义。

设计、时间及地点：可以科研设计类型、统计学方法类型、实验方法学水平详细和准确的去描述，地点为实验完成的单位。

结论：重在描述本文结果的创新性意义，本文结果区别与他篇的不同之处。

引言： 描述本文课题的起源、发展过程，以及本文发表的意义，文字可相当于讨论的1/2或1/3。

材料/对象(参与者)和方法 ：这是文章描述的重点，应突出可重复性的原则。

对象：参与者要有自愿原则，知情原则，伦理委员会通过原则，应用符合国际或国内的相关法律或条例，以参考文献注明。

参与者：应有纳入条件，排除条件，分组条件，基线分析。

实验动物：也有伦理原则，应用符合国际或国内的相关法律或条例，以参考文献注明。

相关治疗医生资质：患者的治疗可以是同一个医生，也可以是一个治疗组的几名医生，要有医生及医生组的资质水平描述，应用符合国际或国内的相关法规或条例，以参考文献注明。

材料：描述动物、仪器、试剂、设备、药物、产品，来源，型号，厂家，国家，批号、含量、作用、用途等，要有名称、量，厂家，产地等。

除实验动物外，其他用表描述。

方法/干预：

分自然段的描述用语：实验过程、实验方法、实验造模、实验干预、技术路线、置入过程、移植过程、修复治疗过程等。

实验过程：较复杂的分组、实验程序应以实验流程表显示。

对实验动物造模，组织学、病理学、免疫组化学、影像学、行为学检测步骤应具体描述。一般以客观标准在前，主观标准在后。

实验干预：人为施加的各种因素。

中药应描述制剂类型、服药方法(水煎剂，粉剂，化学淬取，含药血清， 灌胃，腹腔注射，局部外敷等)与效果及偏倚和不足的关系。

针灸应描述部位、针具、时间、深度、强度、频率等与效果及偏倚和不足的关系。

技术路线:

置入过程:

移植过程：

修复治疗过程：

主要观察指标：包括评价方法，评价指标，评价结果。

随访情况：应是具体时间。

设计、实施、评估者：

统计学分析：具体方法，统计者。

结果：合理使用图表，彩图，图表要体现出足够的自明性。

数量分析：参与者/动物，脱落原因，脱落率。

基线资料：

效果分析：统计描述；统计推断。

随访情况：时间要准确，对应到每一个或每一组的参与者。

不良反应：组织工程研究主要的问题表现在生物相容性方面。

可能影响结果的因素：组织工程研究中主要影响生物相容性的表现是材料、宿主、技术操作3者之间的多种影响因素。

结果描述的顺序：由重点、次重点到非重点。

一般为客观结果（金标准，重复时无差异）在前，主观结果（重复时可有差异）在后。

从组织学、病理学、免疫组化学、影像学、行为学检查等结果的角度和顺序描述。

以表说明时不应再重复同样的文字。

多利用三线表、直方图、条图、饼型图，更直观的说明结果。

以细胞图显示时应有箭头指示。

应有对偏倚及不足的描述。

讨论：

不要太多运用他人的理论内容，会影响和冲淡文章结果的分量。

描述文章结果中具有创新性意义的一两个观点，说明文章内容与他人他篇的异同点。

对假设的结果验证为阳性或是阴性时的合理解释。

对偏倚及不足的客观描述，对应用前景的简单描述。

结论：对文章结果的定性和/或定量的描述。

文章辅文：

课题背景：描述文章的内容与基金资助宗旨的关系及意义，基金资助项目名称、项目号，文章反映了基金项目课题设计中哪些方面的成果，体现本文的重要意义。

作者介绍：作者中的院士、博导、国际专家、学科知名专家、学科首席专家在这一研究领域的地位，以及对此课题和对本文章的贡献，体现本文的可信性。

重点实验室：实验完成的单位，如为国家及省部委重点实验室，应介绍本实验室以往完成的实验对本领域的贡献，以及实验室级别和仪器设备水平适应本领域研究的地位，体现文章实验过程的严谨性、科学性。

同行评价：对文章特点简要科学的评价。

偏倚或不足：说明本文作者严肃的科学态度。

注意：文章中尽量少用括号，以语言修饰能力解决语气感，以利于连续阅读。文章中使用缩略语应在 3 个以内，以减少阅读障碍。