Harvesting the lung of a brain-death by international standardizzed methods*

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Abstract: This study was designed to summarize the clinical experience of harvesting the lung of a brain-death donor by international standardized methods so as to establish a set of standards and regulations that are applicable for harvesting the lung of brain-death donors in China. The patient was strictly determined according to international standardized method by two or more advanced neurologists, neurocranial surgeon, anesthetists, and ICU specialists using brain death diagnostic standards and brain death diagnostic technological specification. The family members signed a informed consent of abandoning treatment for brain death and he was a volunteer organ donor. The operation was performed on 1 brain-death donor who had endured 50 hours of mechanical ventilation to evaluate brain death and organ function. The donor was assessed by donor lung function test and international brain death standard. Then the organ was ready for lung transplantation.

INTRODUCTION

On July 19, 2006, we succeed in harvesting the lung from a brain-death voluntary donor according to international standardized method, which is supported by a key grant of National Brain Death Organ Donation, Pro. Chen. Additionally, bilateral sequential lung transplantation was performed on a late pneumonopathy patient based on extracorporeal membrane oxygenation (ECMO). Lung derived from brain-death patient was detailed as follows.

CASE RECOMMEND

A 39-year-old female patient was finally diagnosed as brain death by postoperative relapse of cerebral tumor, deep coma, complete absence of brain stem reflection, non-spontaneous breathing but helped by breathing machine, positive result after breathing holding, straight electroencephalogram, and brain death figure under cranial Doppler ultrasound. A 50-hour mechanical ventilation was performed on the donor, and there was a little of secretory juice. Sputum culture belonged to streptococcal infection, and patients did not receive an examination under fiberoptic bronchoscopy but breath sound without rattle. Pulmonary infiltration and abnormality were not visualized from preoperative sternite. The vital signs showed as preoperative pure arterial oxygen pressure 460 mm Hg, O_2 saturation 100%, heart rate 80 bit/min, and blood pressure 140/90 mm Hg. EB virus, human immunodeficiency virus (HIV), cytomegalovirus, fever blisters virus, and hepatitis B virus were expressed negatively. Furthermore, there were more contributed organs, such as heart, lung, liver, kidney, and cornea.

Operative method

Lung was obtained according to international multi-organ processing; meanwhile, tracheal intubation/mechanical ventilation surgery, cardiothoracic surgery, and abdominal surgery were performed on the patient. Before operation, patient was injected with heparinization (3 mg/kg) into peripheral vein and methylprednisolone (15 mg/kg) into vein.

Pulmonary maintenance of donor

Fraction of inspired oxygen via mechanical ventilation was below 0.5; positive end expiratory pressure 5 cm H_2O; tidal volume (VT) 10 mL/kg. Sometimes, a 30-s positive end expiratory pressure (30 cm H_2O) was needed to prevent from pulmonary atelectasis and alveolar deteleotasis, which were important for patients with respiration ceases. Necessarily, fiberoptic bronchoscopy was performed to completely clear endotracheal endocritic, ensure great pulmonary expanding, and prevent from lobus inferior pulmonis atelectasis.

Selection of heart and lung from donor

Median incision was performed on the chest (from suprasternal notch to inferior appendix ensiformis), and then the chest was sawed from end to top to open bilateral bone, shear arcula cordis and bilateral mediastinal pleura, and expose ascending aorta and main pulmonary artery in which prostaglandin E1 (1 000 μg) was rapidly injected. Aorta and root of pulmonary artery trunk were pocketed and inserted with delivery tube. Meanwhile, ascending aorta was closed; inferior caval vein was sheared; cardiac and pulmonary perfusions were performed on the left auricular appendage (Table 1); HTK cardioplegic solution (1.5 L) was perfused through aorta; modified raffinose-low-potassium dextran solution (4−6 L) was perfused through pulmonary artery[1]. Pulmonary antegrade perfusion of donor: Three bags of low molecular dextran (2 L/bag) added with prostaglandin E1 (125 μg) per liter was hung about 40 cm above operation table to keep pulmonary arterial perfusion pressure at 15 mm Hg to prevent from edema of lung. A total of 4-L low molecular dextran (50−60 mL/kg) was alternatively perfused into two lungs. The machine was ensured ventilation FiO_2 0.5, VT 10 mL/kg, and positive end expiratory pressure 5 cm H_2O.

Meanwhile,ice sheets were used for surface cooling in heart and lung until two lungs were completely white. Lung was re-checked before holding the breath to prevent from pulmonary atelectasis. Air passage was closed at airway pressure 15–20 cm H_2O, and the lung was moderately swelling. Routinely, air tube was closed and sheared off by two one-off air-tube device to fully take heart and lung.

Table 1 Methods for donor lung's perfusion and preservation

Index	Range
Volume of antegrade flush of R-LPD solution	50–60 mL/kg
Volume of retrograde flush	200–250 mL/pulmonary vein
Pulmonary arterial pressure during antegrade flush	10-15 mm Hg
Temperature of flush solution	4–8 ℃
Mechanical ventilation positive end expiratory pressure 5 cm H_2O	Tidal volume 10 mL/kg
Oxygen concentration/FiO_2	≤50%
Airway pressure when tracheal cross clamping	15–20 cm H_2O

Sequestration of the heart and lung

The obtained heart and lung was put on an operation table to separate at 3 cm above aortic annulus and 1 cm above pulmonic ring. Left atrium was cut at 0.5 cm near proximal end of upper and inferior pulmonary veins to separate heart from lung. The two lungs were put at another operation table for pulmonary retroperfusion.

Retroperfusion

A 1-L low molecular dextran was connected to a urethral catheter with sacculus proprius that was engorged 4–5 mL in order to block orifice by a insertion from upper to inferior pulmonary vein. The solution with 250 mL/plasma volume was perfused from upper and inferior pulmonary vein of one lung. A total of 1 000-mL low molecular dextran was used during the perfusion. A small quantity of tiny blood clot was observed during retroperfusion until the solution was clear. Additionally, the sample was maintained in low molecular dextran (3 L, 5 ℃) and covered with iced plastic bag. The temperature was kept at about 1–4 ℃, and the sample was rapidly transported to receptor operating room.

Separation of left and right lungs

Pulmonary artery trunk of free donor lung was far away from heart, and the beginning center of left and right pulmonary artery was mutilated. Posterior wall of left atrium was sheared off between left and right pulmonary vein; left atrium sleeve on the left side was formed along upper and inferior pulmonary vein accompanying with some left atrial posterior wall; left atrium sleeve on the right side was formed along upper and inferior pulmonary vein accompanying with some left atrial posterior wall. Proximal eminence was sheared off along left principal bronchus by cutting stapler to separate left and right donor lung. Bronchial arteries were ligated along the first branch of left and right free pulmonary artery, and connective tissues were kept as many as possible. Moreover, left and right principal bronchien were cut at the two annulus cartilaginous above bilateral superior lobar bronchus. Finally, the samples were covered with cotton mat dipping with low molecular dextran.

DISCUSSION

Brain death means irreversible and permanent loss of entire brain function. This concept has been firstly produced in 1959. Standard of brain death produced by Medical College of Harvard University has been accepted around many countries[2]. The standard is detailed as follows: irreversible deep unconsciousness; spontaneous respiration ceases; brain stem reflex abolition; brain wave disappearance. At present, brain death is mainly determined according to Diagnostic Standard of Brain Death (adult edition) and Diagnostic Technological Specification of Brain Death in China[3-4].

Availability of lung supplied from brain death patients is inferior to heart, liver, and kidney. Injured reasons of donor lung include pulmonary trauma, aspiration (sputum-discharging asthenia from bronchus), and infection; furthermore, norepinephrine may blood plentifully during increased intracranial pressure to cause rapid increased blood pressure and irritable injure of pulmonary arterial endotheliocytes. Neurogenic pulmonary edema is the severest disease among pulmonary edema. Moreover, release of cytokine may activate inflammatory reaction and cause some tissue injuries[5]. Donor with brain stem death may have pulmonary injury to a certain degree[6]. Therefore, about 20% donor lung obtained from brain death patients try to be used after evaluation internationally.

Selective standard of donor lung: PaO_2 value (arterial oxygen pressure) is the best marker to internationally determine donor lung quality at ventilation $F1O_2$ (fraction of inspired oxygen) 1.0 and end-inspiratory positive pressure 5 cm[7].

Standard of donor lung: The donors aged younger than 60 years old, and heart lung transplantation was performed on the subjects who aged younger than 55 years old. They did not have history of primary heart disease (donor heart) and lung disease (donor lung), history of heart lung operation, severe chest trauma, extensive pulmonary contusion, and aspirated pneumonia/pyosis, and the X-ray on the chest was clear. Furthermore, the normal parameters were detailed as follows: F_1O_2 = 1.0, PaO_2 > 40 kPa (300 mm Hg) at positive end expiratory pressure 5 cm H_2O. Pulmonary compliance was normal (tidal volume 15 mL/kg, peak voltage < 30 cm H_2O); bronchoscope was normal; aspiration did not occur in air duct, and inflammation was not found, too; if airway mucous was not found by bronchoscopy, G (+) bacterial sputum and purulent secretion might be ignored.

ABO blood type and size were matched to donor who did not have malignant disease except primary intracranial tumor, human immunodeficiency virus, and hepatitis virus.

Donor lung was finally evaluated after chest open. Arterial blood gas analysis was used to measure pulmonary function. F_1O_2 was ≤ 35%, and PaO_2 was > 12 kPa (90 mm Hg); PaO_2 was ≥ 40 kPa (300 mm Hg) at absorbing pure oxygen. Pulmonary compliance was necessarily closed to normal value to perform donor sputum culture in order to determine pathogen and guide specific treatment after lung transplantation. Therefore, potential deficit of donor was not needed for positive result of sputum culture; however, donor lung in which bacterium and mycetes grew severely should

be excluded. Consolidated evidences were not found in lung parenchyma. Sometimes, bronchofibroscope and physical treatment might improve unsuitable donor lung. Although time of mechanical ventilation was an important factor for incidence of pulmonary infection, it was not be limited especially. Before organ selection, intravenous anti-bacterium drugs, such as cefuroxime, cidomycin, and arilin, might be given to prevent from infection.

Heart and chest surgery and abdominal surgery may operate at the same time or in a certain order during multiple organ selection. Generally speaking, intubation in the heart lung transplantation group and in the abdominal surgery group are finished and tissues are underwent perfusion. Cutting inferior caval vein depends on donor liver and donor heart. Inferior caval vein is generally cut at 0.5 cm above diaphragm. Axle of left auricle is entire during the separation of heart from lung. In a word, close cooperation among different transplantation teams is a key factor to successfully make sure multiple organ obtain and transplantation.

Patient with brain death in this study was strictly determined according to international standards, Diagnostic Standard of Brain Death and Evaluative Specification of Brain Death, by advanced specialists from departments of neurology, cranial surgery, anesthesiology, and ICU. Data were recorded and re-determined after 12 hours. After final diagnosis, the relatives signed the informed consent of treatment discontinued including stopping breathing machine and of organ donation. A receptor was chosen all over the China. After discussion in detail, the receptor underwent the transplantation of heart, lung, liver, kidney, and cornea, suggesting that this method was standard and reliable. Therefore, this method provides evidences for multiple organ transplantation on the basis of international standard and improves legislation of brain death. Although legislation of brain death has not been realized in the China, we believe that usage of brain death donor will be developed on the basis of international standard.

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国际标准化脑死亡供肺获取 1 例*

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摘要：总结国际标准化脑死亡供体肺的获取经验，以形成一套适用于中国临床肺移植的脑死亡供体获取标准和规范。本例脑死亡患者的判定严格按国际通用标准，项目负责人在确认家属捐献意愿后，组织2 位以上的高年资神经内科、颅脑外科、麻醉科或ICU 专家严格按“脑死亡判定标准”及“脑死亡判定技术规范”逐条认真检查患者。脑死亡判定成立后患者家属代表向医院方签署停止一切治疗的知情同意书，签署“脑死亡自愿无偿器官捐献申请书”。对机械通气50 h的志愿捐献者进行脑死亡评估和供体器官功能评估后，严格按照国际标准化多脏器获取流程行供肺获取术。本例供体成功完成了肺的获取。实践证明这项操作流程规范可靠。

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