

## Lung Preservation Using Cadaver Perfusion

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Received for publication, September 1, 1984

Cadaver perfusion of in vivo lung storage method is evaluated with respect to time course of ischemic damage to lungs subsequently charged with providing total pulmonary function in comparison with survival and histological derangement of a lung.

It, however, is limited within 2 hours due to failure of extracorporeal circulation with core cooling to 15°C by which splanchnic pooling causes reduced venous return. However, cadaver perfusion is useful to minimize an ischemic damage to a lung as a method of in vivo preservation.

### INTRODUCTION

Detection of the best way of temporary lung storage is necessary for clinical practice of lung transplantation. The longer the permissible storage period of time to minimize ischemic damage to a lung, the easier an access to clinical application of allografting to relieve respiratory distress. Exploration of an effective lung storage method is a major demand for thoracic surgeon.

Experimental studies of lung transplantation have been advanced with technical improvement. Prior to allografting permission of procuring a donor lung from donor's family is needed, holding a lung viable.

For the purpose of development of lung storage to minimize ischemic damage to a donor lung, this study is to evaluate as to whether cadaver perfusion method is effective or not.

## METHOD

Adult mongrel dogs of both sexes, weighing between 10 to 15 kilograms, were anesthetized with 50mg/kg of pentothal sodium for induction and 10mg/kg of intermittent administration for maintenance.

Bilateral thoracotomy was made at the IVth intercostal space through the transverse incision. Cannulations into the vena cava and the ascending aorta were completed to start the cardiopulmonary bypass using perfusate of 5% LMWD cooled at 15°C, adding 5 ml of 10% procaine, 60mg of predonine and 5000 unites of heparine per 250ml of 5% LMWD. The ascending aorta was clamped to make the heart arrested.

Hypothermic perfusion was instituted with high flow of 60 to 70ml/kg/min to maintain an adequate tissue perfusion via the bronchial artery.

Continuous perfusion of extracorporeal circulation has been impeded with reduced venous return by splanchnic pooling. After a 30 minute' perfusion duration, extracorporeal circulation failed to continue on account of extremely reduced venous return.

In this study, low flow perfusion at 15°C with 20 to 30ml/kg/min flow rate was then used to drive a proper extracorporeal circulation continuously. The viabilities of the lungs preserved by cadaver perfusion at 1, 2 and 3 hours were assessed. Survivals after allografting and histologic finding at autopsy on the 3rd day of allografting were compared. It is anticipated that the lung transplant on the 3rd day is more appropriate in assessing the viability of a lung, excluding damage to the lung by drug toxicity and immunoresponse as far as possible.

## RESULT

The lengths of survival of a donor lung by cadaver perfusion at 15°C were compared with survival times after allografting.

The result was shown in Table 1. In 5 dogs with allografting of one hour storage lung, survival more than 3 days was obtained in 4 of 5 dogs. In 5 dogs with 2-hour storage lung, all of 5 dogs had survived more than 3 days. In contrast, in 5 dogs with 3-hour storage lung, three of 5 dogs had died within 3 days and two of them had survived more than 3 days.

**Table 1** Survival after allografting with storage lung by cadaver perfusion

perfusion time (hour)	No of dogs	survival time	
		within 3 days	more than 3 dogs
1	5	1	4
2	5	0	5
3	5	3	2

**Table 2** Causes of death after allografting with storage lung by cadaver perfusion

perfusion time (hour)	No of dogs	Lung edema	Lung necrosis	Lung hepatization	bronchial fistula	sacrificed
1	5				1	4
2	5					5
3	5	1	1	1		2

**Table 3** Microscopically abnormal finding after allografting with storage lung by cadaver perfusion

perfusion time	swelling of alveolar septa	swelling of alveolar epithelium	desquamation	fibrosis with atelectasis
1 hour	+	++	-	+
2 hour	+	+++	+	++
3 hour	++	+++	++	+++

At autopsy in those dogs who survived more than 3 days after allografting, lung transplants were macroscopically and histologically examined.

Causes of death in dogs allografted with storage lung transplant by means of cadaver perfusion were determined on the basis of macroscopic findings as shown in Table 2.

Except for sacrificed dogs, causes of death were lung edema in 1, lung necrosis in 1, lung hepatization in 1 and bronchial fistula in anastomotic site in 1 respectively. For histologic examination, lung tissues were sampled from parts of grossly severe damages selected, fixed in 10% buffered formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin. Abnormal histologic findings were classified according to the following criteria, - : no abnormal finding, + : slight degree, ++ : moderate degree and +++ : severe degree.

Histologic findings of swelling of alveolar septum and alveolar epithelium, desquamation of alveolar epithelium and fibrosis with atelectasis were compared as shown in Table 3. It is shown that the time limit of maintaining viability of the lung transplant by means of cadaver perfusion at 15°C is within 2 hours.

On the basis of the results of survivals after allografting and histologic examinations, the present study has ensured a lung storage method for a short time of 2 hours as an *in vivo* preservation by cadaver perfusion.

## DISCUSSION

Many methods of lung preservation have been used in the past<sup>1)-4)</sup>. The majority of them have been in association with *in vitro* preservations.

However, when we face on a donor in whom brain death occurred accidentally, lung storage in vivo is necessary to ask for permission of procuring a lung from a family of available donor patient.

We attempted to test the effects of hypothermic lung preservation in vivo by using extracorporeal circulation. This method is considered beneficial in maintaining the bronchial blood flow.

An acceptable time limit to exclude warm ischemic damage to a donor lung, however, was limited to 1 hour on account of difficulty in continuity of extracorporeal circulation. Functional loss of vasomotor paralysis results in the development of splanchnic pooling and it causes reduced venous return by which extracorporeal circulation fails to continue. The technical difficulties concerning hypothermic circulation used for cadaver are a major problem to solve.

Lung preservation by means of cadaver perfusion is not acceptable as a routine lung storage. Simple cooling is more suitable with respect to easy and practical techniques of storage of a lung. However, it is necessary to prevent warm ischemia as soon the cardiopulmonary dysfunction would take place on a donor in whom death is recognized as possible. A method of cadaver perfusion benefits from minimizing a ischemic damage to a lung. Even this method has a time limit by which extracorporeal circulation with core cooling to 15°C is disturbed. All efforts to extend the period of an adequate extracorporeal circulation state fail to prolong it. The deeper cooling, the more difficult the continuity of the extracorporeal circulation and the time limit exists within at least 2 hours. The favorable time limit is one hour from the start of extracorporeal circulation on the basis of the results of survival and histological deterioration. Then, this method is available for extension of time course of ischemic damage to a donor lung immediately after the time of recognition of the donor death<sup>5)6)</sup>.

Our goal is the extension of time course of ischemic damage to a lung in lung preservation in vivo.

Little information is available for storage method of cadaver perfusion. It is proved that cadaver perfusion is limited to 2 hours due to difficulty in continuous maintenance of extracorporeal circulation. Cadaver perfusion of lung storage will be practical in extending time course to prevent ischemic damage to a donor lung in vivo.

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