

## Viability of A Donor Lung

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Assessment of viability of a donor lung is required to succeed in lung transplantation. Clinically available methods to assess viability of the lung were experimentally evaluated.

Prior to lung transplantation, the finding of angiogram in a donor lung is of value. The ominous findings to predict losing viability of a donor lung are as follows. 1) the void of pulmonary artery branching at periphery 2) unclearness of the small vessel walls.

The dye-dilution curve drawn by infusion of the dye is also beneficial in assessing viability. It is recommended that the donor lungs with the findings of the mean circulation time of 20msec or more and no appearance of sharp upslope curve be excluded on account of loss of viability.

The pressure monitoring immediately after lung transplantation is one of the valuable means. It is hazardous if the pulmonary artery pressure exceeds 35mmHg and the pressure gradient between the main and the left pulmonary arteries over 5mmHg.

### INTRODUCTION

It is difficult to assess viability of a donor lung prior to lung transplantation. An evaluation of viability of a donor lung is to judge as to whether the donor lung is well functioning or not following transplantation and to ensure the function of the stored donor lung, identifying the degree of ischemic lung injury during a storage period of time.

At present it is necessary to confirm the best way clinically available to assess viability of a donor lung as quickly as possible without giving any tissue damage to the donor lung.

The ultimate purpose of this study is to seek the available means to determine viability of a donor lung prior to lung transplantation.

## MATERIAL AND METHOD

A pair of randomly-selected adult mongrel dogs of both sexes weighing 15 to 20kg were anesthetized and maintained on sodium pentobarbital during surgery. Left thoracotomy was made at the 5th intercostal space. A smaller one of the two dogs was selected (at random) as a donor and the left lung was removed as cephalad as possible at the main pulmonary artery, the left main bronchus and the left atrial wall adjacent to the site of jointing of the pulmonary vein.

After removing the left lung, cannulation to the pulmonary artery was made and infused with a mixture of 5ml heparin with 500ml of 3.6% PVP (polyvinyl pironidone in saline) for the purpose of washing out blood component from the pulmonary vasculature until blood component from the pulmonary vein disappeared, using gravity infusion with a 100cm height and ventilated through tracheal tube with intratracheal pressure of 5 to 7cm H<sub>2</sub>O, less than 10cm H<sub>2</sub>O pressure. A donor lung was stored according to the following procedures and divided into the three groups.

Group I: After removal of the left lung, a donor lung was infused to wash out blood component from the pulmonary vascular beds for 10 to 15 minutes, Group II: After infusion, a donor lung was stored for about 4 hours with use of cooling by which it was packed with plastic bag and immersed into 4°C ice water bath, Group III: A donor lung was continued to infusion during a storage period of 4 hours with 3.6% PVP, adding 0.5g procain amide per 500ml and 20mg methyl predonisolone per 500ml.

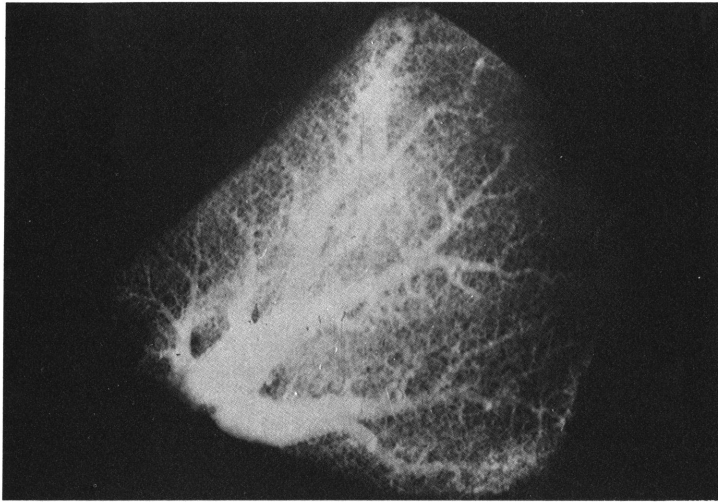
The stored donor lungs were transplanted to the recipient randomly selected and the survival rate was compared.

Prior to transplantation of a donor lung, pulmonary vascular structure was morphologically evaluated by means of pulmonary artery angiogram for which 20ml of contrast medium of 30% urograffin was infused with perfusate as already described. The angiographic findings was analyzed with respect to waning of branching at periphery, clearness of the vessel walls, presence of extravasation and vascular interruption of the small vessels with proximal distension (Fig. 1).

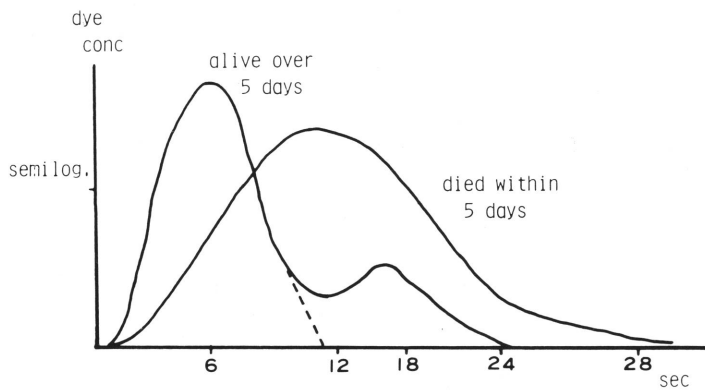
These findings during pulmonary arterial and venous phases were compared with survival and their function following transplantation. Immediately before transplantation of a donor lung, it was ventilated with intratracheal pressure of 7 to 9cm H<sub>2</sub>O to revive a donor lung from atelectasis brought during a stored period.

In this situation, 5ml of cardiogree dye was infused with perfusate and one-second interval samples drained from the pulmonary vein were collected to measure the dye concentration using a spectrophotometer.<sup>1)</sup>

Semilogarithmic replot of dye-dilution curve was drawn to calculate the mean circulation time of a donor lung immediately before transplantation by STEWART' method.



**Fig. 1.** Pulmonary angiogram prior to lung transplantation



**Fig. 2.** dye-dilution curve

The mean circulation time of a donor lung was compared with survival and its function following transplantation (Fig. 2).

Shortly after lung transplantation, the pulmonary artery pressure was measured via the catheters introduced to the main and left pulmonary arteries. The survival after lung transplantation was compared in association with aeration of a donor lung on chest x-ray at least 7 days before rejection response would be predicted not to affect a donor lung.

The dogs with the technical errors at anastomosis of the bronchus, the pulmonary artery and left atrial cuff were excluded from the present study.

## RESULT

The donor lungs dealt with the three methods were transplanted to the recipients randomly selected. These dogs were carefully cared and autopsied at death within 7 days after transplantation. The dogs were excluded from this study in the case that technical failure at surgery was defined as a cause of death at autopsy. All of the dogs that survived more than 6 days following lung transplantation were sacrificed at 7 days and also a dog apparently affected by rejection response with histologic evidence was not eligible for this study.

The deaths within 3 days after transplantation were mainly included in a 4-hour storage group. Those who died within 3 days suffered from difficulty in expectoration of large amount of the sputum (Table 1).

The deaths from 3 days to 5 after transplantation were associated with pulmonary infection which was mostly caused by increasing retention of the bronchial secretion resulting from the wettable transplanted lung. It is no doubt that the function of stored lungs serves as the life-saving. As the transplanted lungs are losing their functions, the recipients have become threatened. Autopsy of the dogs died at 5 days showed less aeration of a donor lung accompanying atelectasis. The longer the survival, the more aeration of a donor lung was aggravated. There was a tendency for a 4-hour storage lung to indicate the high degree of hepatisation as the survival was prolonged. It was a reflection of ischemic tissue damage during a donor lung storage (Table 2).

Table 3 indicates the finding on angiogram during arterial and venous phases. In Group I, the angiographic vessel pattern was satisfactory, demonstrating clearness of vessel margin and abundant branching. Those in Group III were inferior to those in group II which were superior to those in Group I. A finding of extravasation and vascular interruption on angiogram was the most important clue to determine the severe ischemic damage to a donor lung. As a result, moderate ischemic damage to a donor lung was suggested by the findings of waning of branching and unclearness of vessel wall margin. It was suggested that the angiographic patterns of clearness of vessel wall margin and waxing of vessel branching were helpful in determining an excellent viability of a donor lung.

**Table 1.** Survival

	- 3 days	- 5 days	5 days	7 days -sacrificed
G I	1	3	11	
G II	3	4	7	
G III	5	9	4	

**Table 2.** Macroscopic finding of transplanted lung at autopsy

gross finding	survival time	- 3 days	- 5 days	5-7 days
edema		5 (55.5%)	4 (25.0%)	2 (11.2%)
less aeration with atelectasis		4 (44.5%)	8 (50.0%)	7 (38.8%)
hepatisation			4 (25.0%)	9 (50.0%)

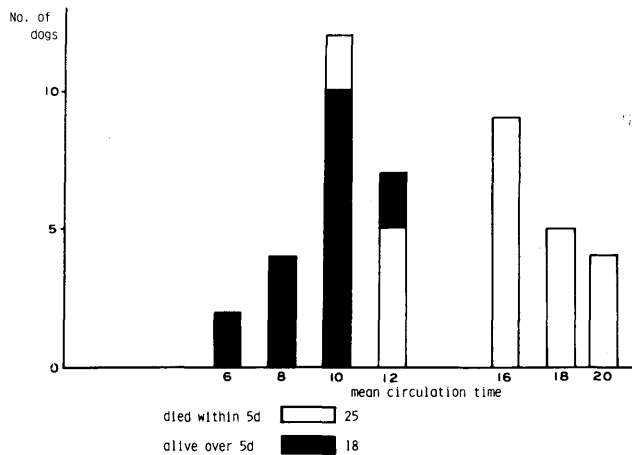
**Table 3.** The finding on angiogram during arterial and venous phase in terms of survival according to the 3 groups in this series

survival	findings	G I			G II			G III		
		~3D	~5D	5D	~3D	~5D	5D	~3D	~5D	5D
arterial phase	clearness of vessel margin			11	3	6		8	4	
	waning of branches		1	1	3	1	1	5	2	
	extravasation	1			3			5	1	
	interruption		1						1	
	proximal distension		1	2		1	1		2	1
venous phase	clearness of vessel margin			5			2		2	2
	waning of branches		1	4	2		1		1	1
	extravasation		1			1	1		1	2
	interruption	1	1		1	2	2		3	1
	proximal distension			3	1	1	1		1	3

Dye-dilution curve of a donor lung was extrapolated as shown in Fig 2. The pulmonary hemodynamics was evaluated with special reference to passage time of dye through the pulmonary vascular structure.

The typical patterns of dye-dilution curves were demonstrated in Fig 2. As shown in Fig 2, the curve obtained from those who survived over 5 days was showing a sharp upslope having slow downslope, although the very flat curve was obtained from those who died within 5 days. The result indicated that prolongation of the mean circulation time proportionated to the duration of survival which related directly to the function of a donor lung immediately after lung transplantation.

Fig 3 showed that when the mean circulation time measured in a donor lung was reduced by less than 10sec, the recipient could survive more than 5 days except in 2 out



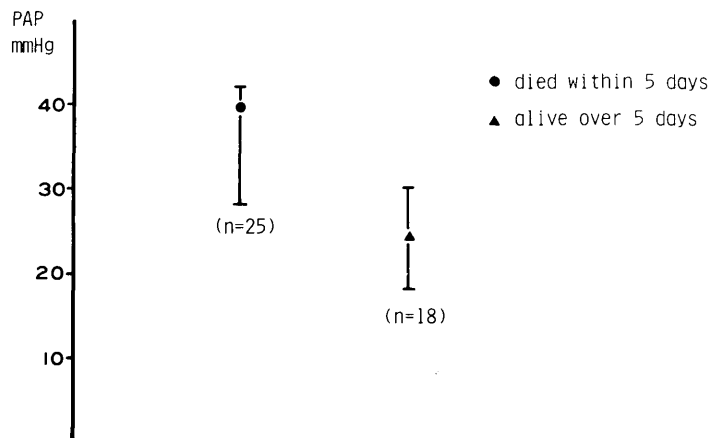
**Fig. 3.** Relationship between survival and mean circulation time of a donor lung

of 24 dogs. In contrast, prolongation of the mean circulation time of more than 16sec did not allow to survive more than 5 days.

It is a reflection that the mean circulation time measured in a donor lung prior to lung transplantation is highly indicative of the degree of viability of a donor lung.

Fig 4 shows the differences in the pressures between main and left pulmonary arteries as compared the dogs alived over 5 days after lung transplantation with those died within 5 days.

Needless to say, the pulmonary artery pressures were influenced by quality of the contralateral lung. The greater the pulmonary artery pressures, the more the mortality rate increased.



**Fig. 4.** The pressure of the pulmonary artery shortly after transplantation

It is assumed that the mean pulmonary artery pressure exceeding 35mmHg indicates to be fatal on account of dysfunction of a donor lung. On the contrary, the mean pulmonary pressure below 30mmHg offers great promise of survival, predicting to be good function of a donor lung.

The pressure gradients between main and left pulmonary arteries were shown in Fig 5. There was no significant difference in the pressure gradient between main and left pulmonary arteries. However, the wider difference of the two pressure gradients between them were demonstrated in those who died within 5 days. There was no statistically significant difference between those who died within 5 days and those who survived over 5 days. It is emphasized that the pressure gradient of more than 5mmHg between main and left pulmonary arteries is so often seen in the dogs who died within 5 days after lung transplantation. In contrast, the pressure gradient of less than 5mmHg probably guarantees the long survival, reflecting better viability of a donor lung.

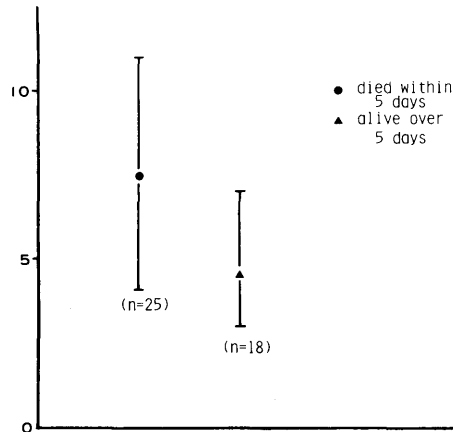


Fig. 5. The pressure gradient between the main pulmonary artery and the left pulmonary artery

## DISCUSSION

There is a great deal of difficulty in extending the clinical use of lung transplantation spite of improved technique for lung transplantation.<sup>2)</sup> One of which is how to assess viability of a donor lung precisely with the use of clinically available means prior to lung transplantation. In the present study, a 4-hour storage method with perfusion of a donor lung was not adequate for expecting a satisfactory result of the survival after transplantation.<sup>3)</sup>

As a matter of fact, a 4-hour preservation method by simple cooling allowed the favorable survival rates rather than that by cooling with perfusion. It is indicated that the influences of the property of perfusate as well as the pressure of perfusion on a donor

lung are complex. Furthermore, it is of doubt if a stored lung be benefited by perfusion, keeping viability of a donor lung from ischemic lung injury.

One must take it into consideration that viability of a donor lung is not necessarily reflected in the survival rates following lung transplantation. Needless to say, the survival rates are the result of the interplay of several factors regarding surgical techniques, viability of a donor lung as well as contralateral lung function, postoperative cares and so on.<sup>4)5)</sup>

Postoperative pulmonary dysfunction is in part based on ischemic lung injury during a storage period. It is well known that poor donor lung function depends on either reimplantation response or pulmonary infection, and occasionally occurrence of acute rejection.<sup>6)</sup> It is clear that ischemic lung injury to a donor lung is liable to lead to retention of a large amount of bronchial secretion following lung transplantation and predisposes a donor lung to postoperative infection. Furthermore, ischemic injury forces a donor lung to cause spasm of the pulmonary artery in addition to denervation caused by transplantation procedure.

The survival rate after lung transplantation is influenced by the function of a donor lung.<sup>7)</sup> It must be emphasized that perfusion procedure is one of the hazardous storage methods. Simple cooling method is reliable for obtaining better results than those by perfusion and/or the other lung storage methods. Continuous or intermittent perfusion of an isolated lung with different type of perfusates generally resulted in immediate edema of the lung. Viewed from the storage method of a donor lung, viability of a donor lung contributes greatly to the survival of lung transplantation. Biochemical assessment of tissue viability and metabolic determinants of the lung seem to be unreliable in predicting the function of the lung after storage. An experimental trial of contralateral pneumonectomy or ligation of the pulmonary artery on the opposite side is made to assess viability and function of a donor lung following lung transplantation.

It has been reported that a limit time for lung storage is a range of 30min to 4 hours. The tolerable time for warm ischemia during storage should be accurately estimated prior to transplantation to improve the survival rate.<sup>8)</sup> It is required that the best way to assess viability of a donor lung prior to lung transplantation is to be detected for a widely clinical use. As the means of assessing viability of a donor lung, various studies on morphological, enzymatic and functional tests are under way.<sup>9)</sup> These are not necessarily adequate for clinical use prior to lung transplantation.

In the present study, angiography of a donor lung was validated prior to transplantation without tissue damage to a donor lung.<sup>10)</sup> The hazardous findings of losing viability of a donor lung on angiogram are the void of the branchings and uncleanness of the image of the pulmonary vessels.

It is emphasized that angiogram for a donor lung is available to assess its viability, predicting the grade of function following transplantation.<sup>11)12)</sup>



Immediately after transplantation the measurement of the pulmonary artery pressure also was useful to predict a function of a donor lung. The higher the main pulmonary artery pressure and the pressure gradient between the main pulmonary artery and the transplanted one, the poorer the function of the transplanted lung is indicating. As another way to assess viability of a donor lung, calculation of the mean circulation time is beneficial in judging as to whether the function of a donor lung is satisfactory or not following transplantation.

On a drawing dye-dilution curve, a hallmark of keeping viability of a donor lung is the appearance of sharp upslope in shape of the curve with shorter mean circulation time although longer time is apparently indicating the loss of viability.

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