

Hyperbaric Lung Preservation with Hypothermia

Masao TOMITA, Hiroyoshi AYABE,
Katsunobu KAWAHARA, Toshiyasu KUGIMIYA
Kaoru IWAMOTO, Satoru HASHIMOTO, Shigehiko ITO

*The First Department of Surgery,
Nagasaki University School of Medicine,
Nagasaki, Japan*

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The tolerable period of ischemia to canine lung were evaluated in preservation at hyperbaria of 3 atmospheres (absolute 3 at.) and 7 at. fed with oxygen or nitrogen gases.

- 1) Three atmospheres (absolute) protect lung transplant from ischemic damage up to 12 hours.
- 2) A 72 hour preservation lung at three atmospheres of nitrogen gas provided lung function after allografting in only one. This led us to know effectiveness of hyperbaria at three atmospheres.

INTRODUCTION

Lung transplantation was an inevitable treatment for relieving respiratory distress which is caused by irreversible damages of the lung.

To enhance the clinical application of lung transplantation, a long-term preservation to minimize ischemic change to the donor lung is also essential for a practical organ transplantation program. The limitation of organ preservation period have been evaluated by means of cooling and perfusion.

This study is to search after an appropriate method to store for a long term using hyperbaria.

METHOD

In 20 young mongrel dogs of median weight of 15 to 20kg in body weight a left pneumonectomy are performed through a lateral thoracotomy incision in the fifth intercostal space. The left pulmonary artery, the bronchus and the left atrium, proximal to the site of draining the left pulmonary veins, are individually transected and the left lung is completely removed.

The donor lungs are prepared for cooling and perfusion. The cannulation to the pulmonary artery and the trachea are performed, as soon after donor lungs are removed as is possible. Perfusion to the pulmonary artery is initiated with perfusate cooled to 4°C using gravity drainage of 40 cmH₂O in height for 15 to 20 minutes, immersing a lung in 4°C ice water. The time was needed until blood is completely flushed from donor lung vasculatures. The flushing time averaged 15 minutes.

Perfusate is composed of 250ml of 10% LMWD, 250ml of saline containing 5000U heparin, 5ml of 10% procaine, 60mg predonine and 30×10⁴ unit penicillin G.

After performing a pretreatment, into the hyperbaric chamber, made by SWENCO co. (USA) which is prepared at 1 atomosphere (at.), 3 at. and 7 at. in either 100% oxygen or nitrogen gases respectively and submerged in a waterbath at 4°C.

After preservation of the donor lung in hyperbarias fed with oxygen and nitrogen gases for 12 and 24 hours, a stored lung was transplanted to unrelated recipient and survivals of within or more than 3 days were compared.

RESULT

Survivals after allotransplantation with stored donor lungs which were kept in cooling to 4°C and hyperbaria, were compared as shown in Table 1.

The stored times of donor lungs were divided into two groups, that is, 12 hours and 24 hours. Survival times were also presented as within 3 days or more.

In storage of the lungs at 1 at of hyperbaria, two out of 12 dogs with a 12 hour storage lung survived over 3 days and only one out of 8 with a 24 hour storage lung was doing well.

In storage of the lungs at 3 at. of 100% oxygen, 12 out of 15 dogs with a 12 hour storage lung survived over 3 days after allotransplantation. Only two out of 12 dogs with a 24 hour storage lung were alive over 3 days. Most of dogs with a 24 hour storage of

Table 1 Survival after allografting with 12 and 24 hour storage lung using hyperbaria combined with hypothermia at 4°C

	storage period	No. of dogs	within 3 days	more than 3 days
Oxygen	12 hours	12	10	2
1 atomosphere	24	8	7	1
Oxygen	12 hours	15	3	12
3 atomospheres	24	12	10	2
Oxygen	12 hours	8	8	0
7 atomospheres	24	5	5	0
Nitrogen	12 hours	9	2	7
3 atomospheres	24	11	10	1

donor lungs had died within 3 days.

In storage of the lungs at 7 at. of 100% oxygen, neither a 12 hour or a 24 hour storage of donor lungs had enabled dogs to survive over 3 days after allotransplantation.

From the result of hyperbaria with 100% oxygen, it is assumed that compression to the lung with as large as 3 at. is adequate for prevention from ischemic damage to a lung.

Compression of 3 at. with 100% nitrogen was then tested as to whether compression to the donor lung is effective in minimizing ischemic damage to a lung for exclusion of O₂ diffusion effect. The donor lungs which was preserved at 3 at. of nitrogen for as long as 12 and 24 hours were prepared for allotransplantation.

In a 12 hour storage of donor lung under nitrogen hyperbaria, seven out of 9 dogs with a 12 hour storage lung survived over 3 days after allotransplantation. In contrast, one out of 11 dogs with a 24 hour storage lung was living over 3 days.

Interesting enough, a 72 hour lung storage by hyperbaria with 100% nitrogen had extricated the lung from ischemic damage in only one after transplantation in our series. Meticulous care was required for keeping air way due to profuse bronchial secretion contributing to wettable donor lung immediately after transplantation.

On the first day of transplantation, transplanted lung on chest xp (Fig. 1) showed cloudy, demonstrating a litter aeration. In elapsing 3 days after transplantation, it was changed to be clear to some extent, showing an improvement of its aeration (Fig. 2).

The dog was survived 5 days despite suffering from profuse bronchial secretion, which necessitated aspiration to remove more frequently. The pulmonary angiography was performed to assess the pulmonary circulation of the lung transplant on day 5 following lung transplantation. On the pulmonary angiography, the lung transplant vasculature

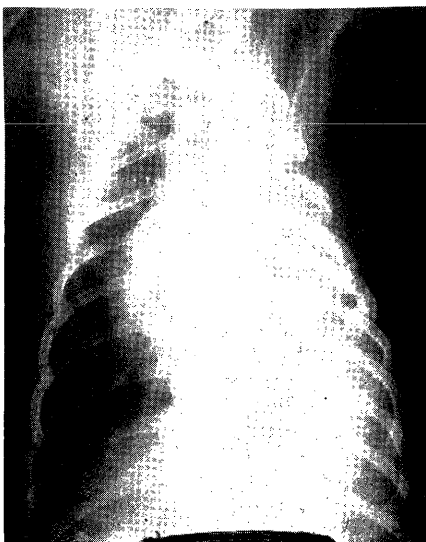


Fig. 1 Chest xp on the first day of lung transplantation with a 72 hour storage in hyperbaria of 3 atmospheres fed with pure nitrogen, showing a finding of lung edema

demonstrated a pattern of good run-off with the intact architecture as shown in Fig. 3, although somewhat narrowing of the pulmonary artery lumens and persistent cloudy shadow in the upper lung field had been revealed.

Soon after the pulmonary angiography was done, the pulmonary edema was induced with a complaint of bloody sputum and the dog expired due to hypotension and hypoxia. At autopsy, macroscopic finding revealed a minimum of aeration of the donor lung.

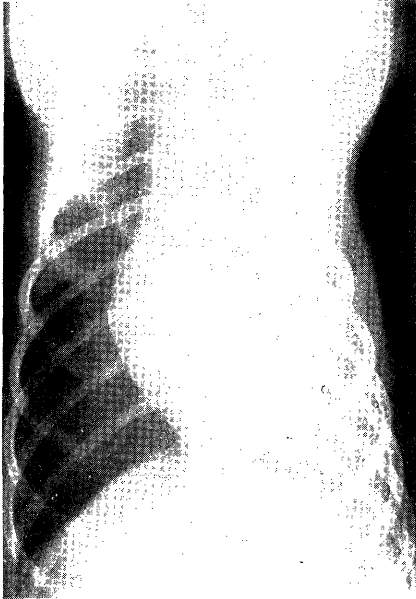


Fig. 2 Chest xp on the 3rd day of lung transplantation on the left, showing a finding of consolidation with less aeration

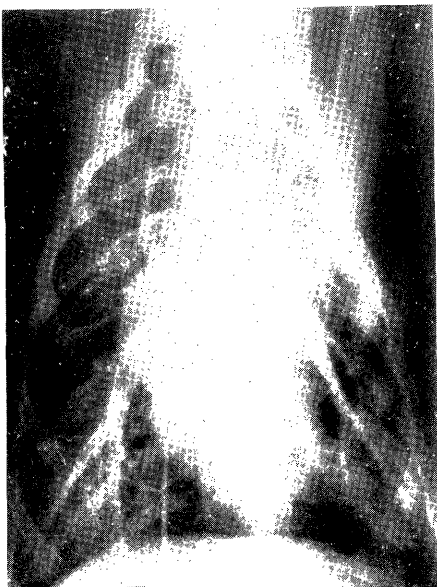


Fig. 3 Pulmonary angiography on day 5, showing a considerably good run-off in the transplant and the findings of narrowing of the pulmonary artery and persistent cloudy shadow in the upper lung field

However, it was congestive on gross appearance and dark in color in comparison with ipsilateral lung (Fig. 4).

Histologic examination showed widened alveolar spaces with interrupted alveolar septa in spite of existing less perivascular edema and bleeding. The inherent architectures of lung parenchyma were reserved (Fig. 5).



Fig. 4 Macroscopic finding at autopsy, showing the congestion with less aeration of transplanted lung (↑)

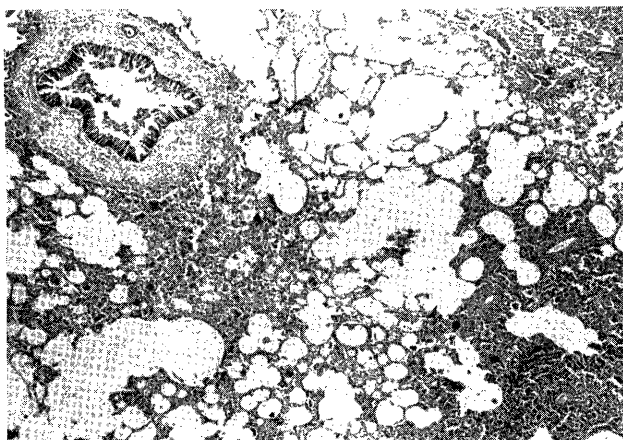


Fig. 5 Histologic findings on transplanted lung at autopsy, showing the widened alveolar space with patchy atelectasis and peribronchial edema

DISCUSSION

Preservation of the donor lung was difficult in maintaining a high quality of the lung for a long time. Lung parenchyma was fragile to various shock which might cause so-called shock lung. Most of donor lungs were damaged to some extent prior to preservation. Then, the length of survival of lung graft was limited. Furthermore, reimplantation response which might be represented as a lung edema after allografting should be avoided.

In normothermia, BLADES¹⁾ and GARZON²⁾ stated that storage time of the lung was restricted for 30 minutes to 4 hours. When the donor lung is inflated during a period of storage, the permissible storage time is shortened to a maximum of 5 hours.^{3,4)}

The methods of storage of the lung are mainly evaluated in two categories, cooling and perfusion. It is defined that cooling alone as a method of lung storage protect lung from ischemic damage up to 24 to 48 hours.

Perfusion is necessary for procuring a good result of lung storage to flush the components of blood corpuscles from the donor lung vasculature.

Various perfusates are used for flushing the blood corpuscles.⁵⁻⁷⁾ It is well known that perfusion of lung transplants may well cause lung edema and selected perfusates analogous to the compositions of physiological intra- or extracellular fluids are appropriate in prevention from subsequent lung edema.

The effects of hyperbaria on relief of ischemic damage to lung transplant are evaluated. Proper compression by hyperbaria play a key role in protection from ischemic damage to the lung transplant.²⁾

Hyperbaria of oxygen is not an effective aid to maintain a viability of donor lung. The compressions of as large as 3 atmospheres of oxygen and nitrogen are most available for protection from ischemic damage to the donor lung. The degrees of the ischemic damage to a preserved lung are estimated in comparison with survivals over 3 days after allotransplantation, excluding a response to ejection and drug toxicity.

Three atmospheres (absolute) of either nitrogen or oxygen produced the best results in our series. It is assumed that hyperbaria by oxygen is not effective in prolonging the tolerable period of ischemia and preservation by hyperbaria provided a acceptable limit of storage period of 12 hours.

However, 72 hour storage at 3 atmospheres of nitrogen succeeded in one lung transplant to protect from ischemic damage. The fact that a 5 day survival had been obtained by management of profuse bronchial secretion due to a resulting lung edema from ischemic damage means that compression of as large as 3 atmospheres is effective in minimizing ischemic damage to a donor lung during a period of storage. Furthermore, increased oxygen pressure used for hyperbaria is not necessary to attain a much more prolonged preservation.

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