

## Limited Resection for Lung Cancer

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### ABSTRACT

Based on clinical as well as experimental studies, limited operation of choice was evaluated for the management of lung cancer.

From clinical analysis of 39 cases who underwent limited lung resection, our clinical experiences indicated that this operative procedure would be feasible for a large tumors of approximately 4cm in diameter. However, the incidence of lymphnode metastasis is more likely to be high when applied to the tumors of more than 3cm in diameter.

The favorable indication, therefore, is for the cancer less than 3cm in diameter. By careful evaluation of 7 cases with postoperative recurrence, it has become obvious that either the degree of cell differentiation or the existence of lymph nodes metastasis strongly participate in its prognosis.

According to hemodynamic studies immediately after surgery, limited resection of the lung is preferred to conventional radical lobectomy for patients with cardiovascular malfunction because it serves to eliminate a possible left ventricular failure after surgery. An experimental research also demonstrated favorably hemodynamic benefits of limited resection for reducing left ventricular overloading on coronary diseased heart which is experimentally prepared by either creation of stenosis of the main left coronary artery or ligation of the left descending coronary artery.

The immune response in the lymphnodes to a tumor growth also was attested in C<sub>3</sub>H mice with use of MH 134 tumor inoculated, especially in relation to the time of tumor resection.

The results of our experiments confirmed that tumor resection on the 7th and 10th

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day after inoculation of MH 134 tumor cells enabled the immune response in the lymph nodes to remain high when compared with those already inhibited on 17th day. It is of value to note that the immune response in the lymph nodes to PHA remains obviously unchanged by management of earlier tumor resection as compared to that of further delayed resection. Since limited resection is chosen in early cancer of less than 3cm in diameter, it undoubtedly has led to considerably strong immune response of the host without further compromising it. We therefore felt confident that a long term follow-up study after limited resection will afford a better appraisal of the value of this procedure.

## INTRODUCTION

Wide and complete resection has been generally recommended to achieve a better cure rate for patients with various cancers. On the contrary, attention has been focused on the attempts at minimal pulmonary resection for the treatment of lung cancer to reserve the postoperative pulmonary function.

Especially even in patients with lung cancer, the degree of reserved pulmonary function after operation has obviously been implicated as one of the influential factors on its prognosis<sup>1)</sup> and it has become highly important to evaluate a significance of limited operation as an operative procedures of choice<sup>2)3)4)</sup>.

The aim of this study is to certify the advantages of limited operation concerning operative risk, especially in the elderly and the attitudes of the immune response in the lymph nodes.

## ANALYSIS OF CLINICAL MATERIAL

Thirty four patients who underwent limited resection of the lung for the treatment of primary lung cancer were subjected to this study except for 5 patients with metastatic tumor as shown in Table 1.

### 1) Age factors.

According to age distribution undergoing this operation, 5 patients were in their fifties, 15 were in their sixties and 19 were in their seventies. Of them, 5 cases had metastasis; one in fifties and 4 in sixties. From age factors, limited resection is preferably employed in older patients more than 70 years of age.

### 2) The size of tumor resected

In 2 cases, the sizes of tumor in diameter were less than 2cm, in 24 cases less than 3cm and 13 cases less than 4cm

Table 1 Cases undergoing limited resection

	over 70 yrs	under 70 yrs
primary	19	15
metastatic	0	5
tumor size		
2		2
3	6	13
4cm	13	0
histology		( )metastatic
ad well	4	9(1)
ad mod	3	2(3)
ad poor	4	(1)
sq well	5	3
sq poor	2	
undif large	1	
undif small		1
stage I T <sub>1</sub> N <sub>0</sub> M <sub>0</sub>	6	11
stage I T <sub>2</sub> N <sub>0</sub> M <sub>0</sub>	4	2
stage II T <sub>1</sub> N <sub>1</sub> M <sub>0</sub>	2	2
stage II T <sub>2</sub> N <sub>1</sub> M <sub>0</sub>	5	0
stage III T <sub>2</sub> N <sub>2</sub> M <sub>0</sub>	2	0

respectively. Our experiences documented that limited resection enabled us to employ even in those whose tumor sizes in diameter were 4cm, extending its indication widely in the treatment of primary lung cancer.

3) Histological type of tumor resected

Among those who underwent limited lung resection, 22 cases were adenocarcinoma 10 cases squamous cell carcinoma and 2 cases undifferentiated carcinoma. The majority of patients undergoing limited resection showed adenocarcinoma, which most frequently located in the periphery of the lung unlike other histological types. It would seem wise to recommend that adenocarcinoma situated in the periphery of the lung was mostly suitable candidates for limited resection as an operative procedure of choice.

4) Clinical staging

According to staging classification 23 cases were in stage I, 9 cases in stage II and 2 cases in stage III.

Needless to say, the most favorable indication was in stage I cancer. With advancing age over 70 years of age, the less lowering score in either clinical stage or TNM classification is essential in the selection for surgical treatment. Following TNM classification in older patients undergoing limited resection, one case was in T<sub>1</sub>N<sub>0</sub>M<sub>0</sub>, 4 cases in T<sub>2</sub>N<sub>0</sub>M<sub>0</sub>, 2 cases in T<sub>1</sub>N<sub>1</sub>M<sub>0</sub> and 5 cases in T<sub>2</sub>N<sub>1</sub>M<sub>0</sub>. Obviously even in the elderly it was noted that surgical resection for lung cancer was primarily advocated for obtaining as good a cure rate as possible and it was aimed at minimizing functional loss after lung resection. The frequency of metastasis into the hilar and mediastinal lymph nodes was evaluated in relation to tumor size in diameter.

Four cases (21.1%) among 19 cases with tumor size of less than 3cm in diameter had hilar lymph node metastasis, whereas 7 cases (53.8%) among 13 cases with the tumor more than 3cm in diameter had metastasis in the hilum and the mediastinum as indicated in Fig 1. It is logical from this result to assume that the increase of tumor size as well as the

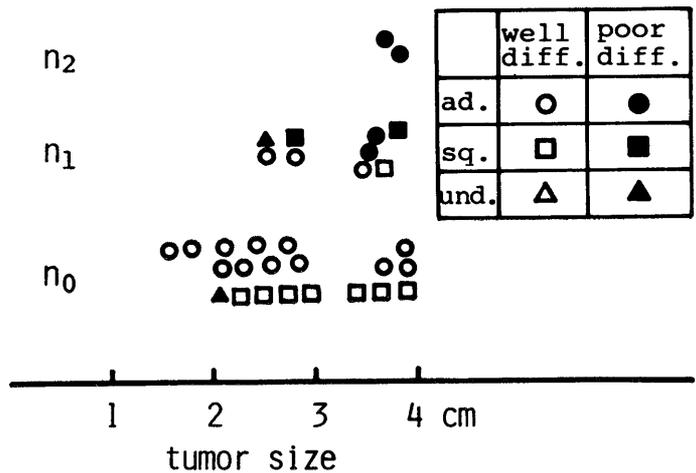


Fig 1 Relationship between the frequency of lymph node metastasis and Tumor size or the grade of cell differentiation

advance of poorly degree of differentiation in histological findings undoubtedly contribute to a higher incidence of lymph node metastasis into the hilum and the mediastinum.

#### 5) Prognosis

According to age distribution, two groups, age 69 and under, age 70 and over, the prognosis in those who underwent limited resection was carefully evaluated. Favorable results have been obtained even in the older patients, which included moderately advanced cases. Postoperative death in the elderly was encountered in 4 cases. It, however, was not inferior to that in the younger. In a follow-up study, it seems that a good cure rate can be expected in those who remained alive well more than 2 years after surgery even in older patients because recurrence tends to occur within at least 2 years after surgery as indicated in Fig 2.

#### 6) Postoperative performance status

The postoperative performance status was expressed as indices of A: not needed rest, B: necessitating rest of less than 50%, C: rest of more than 50% and D: all day rest needed inevitably.

Twelve patients among those 19 cases who underwent limited resection were classified as A group (63.3%) as shown in Fig 3. The remaining 7 cases had B or C grades of rest. It, however, was not a need for ordinary life performance from the view point of cardiopulmonary function.

As compared to the results of those who underwent lobectomy, it apparently was different from the rate of rest-free patients which were classified as 44% in A, 28% in B, 20% in C and 8% in D respectively, whereas 63.3% in A, 31.5% in B and 5.3% in C respectively in those who underwent limited resection.

All but one who belonged to C category in older patients undergoing limited resection presented a satisfactory performance status.

The limited activity in usual life tended to mostly appear in two years or more after lobectomy but its tendency has not become manifest after limited resection, indicating it benefited from the ensuing cardiopulmonary dysfunction.

#### 7) recurrence cases

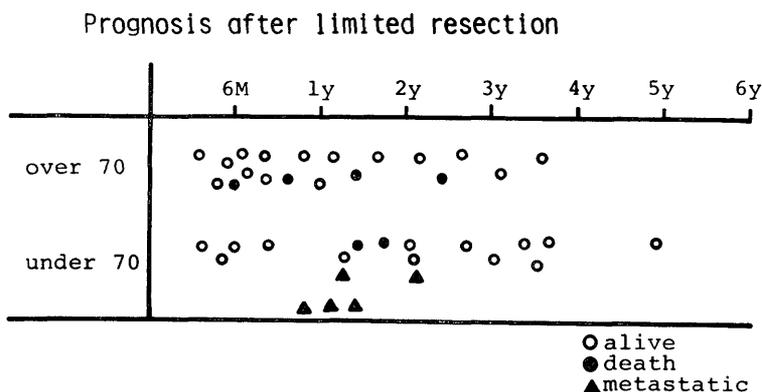


Fig 2 Prognosis in 39 patients after limited resection

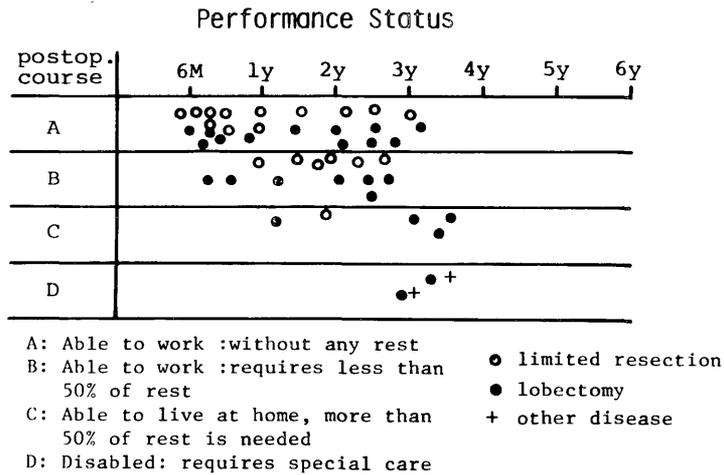


Fig 3 Clinical performance status after limited resection

The patterns of recurrence after limited resection were analyzed in 7 cases with postoperative recurrence, in whom 4 cases were over 70 years of age and the remaining 3 cases were under 70 years of age. These clinical manifestations of recurrence consisted of local recurrence in one, pleural metastasis in one, mediastinal lymphnode metastasis in two and distant metastasis in three cases.

By the findings of chest roentgenogram, preoperative tumor shadows were definitively specialized in 4 cases as malignant patterns with irregular and polygonal shadows in shape as indicated in Fig 4. The connecting shadow with the hilum, otherwise, was revealed in 5 cases and the concomitant pleural thickened shadow associated with lung cancer was confirmed in one with postoperative malignant pleural effusion caused by direct cancer invasion into the pleura rather than metastasis on it.

These findings on chest roentgenogram were in concord with findings of far advanced lung cancer shadows. For many candidates undergoing limited resection, the

Preoperative finding of chest xp shadow in cases with postoperative recurrence  
by Yoshimura

	Tumorous				conglomerating				infiltr	
	round	mulbery	on pleural	irreg. polygonal	nodularly	granularly	pure	with strand		
T1	1/8	0/4	0/2	3/6	1/1					
T2	0/4	1/1	0/3	1/5						
hilar connection										
4/7										

Fig 4 Preoperative finding of chest XD shadow in cases with postoperative recurrence by Yoshimura

authors conjectured that the roediological findings serve either to determine the operative indication or anticipate the resulting prognosis to some extent.

From our clinical experience with postoperative malignant pleural effusion, furthermore, pleurectomy as operative procedure of choice is recommended for the treatment of lung cancer located in the adjacent site to the pleura. It is of value to prevent postoperative malignant pleural effusion.

In the comparative study between the degree of advancing disease and the incidence of postoperative recurrence, there is no close relation with respect to the size of tumors, in which postoperative recurrence were encountered in 5 cases of T<sub>1</sub> and 2 cases of T<sub>2</sub>. All of them, however, had some of lymphnode metastasis, namely all but one with n<sub>2</sub> were n<sub>1</sub>. It is assumed that n-factor is more likely to contribute to its prognosis.

According to histological findings, recurrence was seen in 4 cases in adenocarcinoma, 2 cases in squamous cell carcinoma and 1 cases in undifferentiated carcinoma but all of them showed either moderately or poorly cell differetiation. The degree of histologically cell differentiation is also thought to be a key factor influencing its prognosis.

The indication of limited resection of the lung for the treatment of lung cancer is derived from these clinical experiences as follows 1) at least less than 4cm in diameer of tumor size 2) not detectable lymph node metastasis in the mediastinum except for the hilum of the lung 3) not visible cancer invasion extending on the surface of the lung 4) not noticeable severity of poorly cell differentiation.

#### **Reliability of limited resection with reference to postoperative pulmonary function.**

As compared to the results of postoperative pulmonary function test followed by lobectomy in 15 consecutive cases, those in 12 cases undergoing limited resection were definitively fair. The values of %CV/VC in patients with limited resection were significantly superior to those with conventional lobectomy although there were no remarkable differences between FVC<sub>10</sub>, DLCO and RV/TLC respectively.

Performance status with the elapse of time following surgery was tested during a period of the subsequent 2 or 3 years. A need for rest in normal life had more frequently experienced in cases with lobectomy rather than with limited resection as presented in Fig 3.

In the early stage within 3 days following surgery, the modality of hemodynamic changes was assessed in the elderly with the aid of Swan-Ganz catheter method. The low cardiac output failure occurred preferably in cases with lobectomy rather than with limited resection, accompanying increased pulmonary arterial pressure and its wedge pressure as shown in Fig 5.

From the view point of hemodynamics immediately after surgery, it seems worthwhile to document that limited resection is considered best suitable for operative management of choice, whenever it is indicated for the older patients.

The influence of cardiopulmonary function following pulmonary resection on ischemic heart was experimentally evaluated. This study was undertaken to certify some benefits

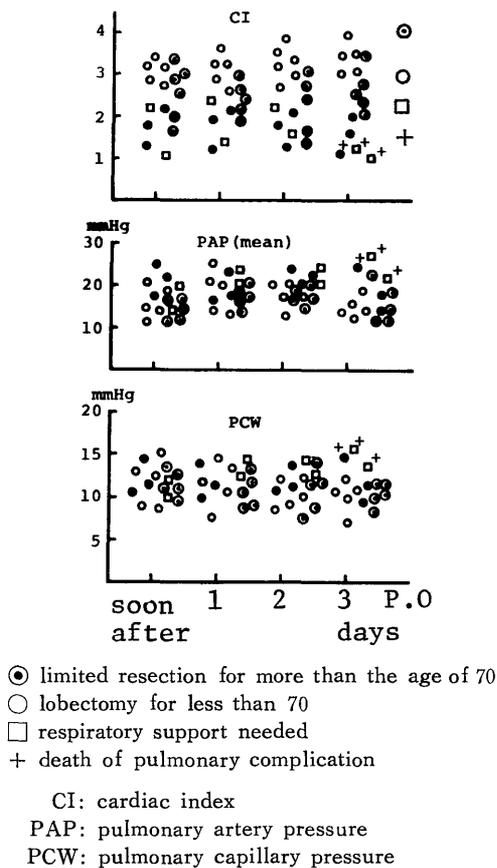


Fig 5 Postoperative hemodynamic study

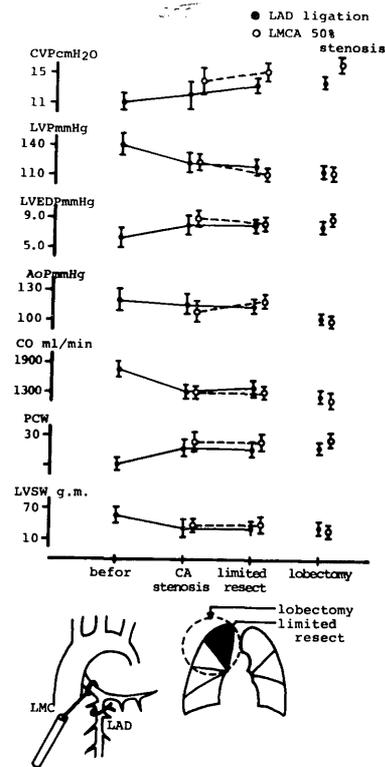


Fig 6 Hemodynamic changes implicated in operative methods of limited resection and lobectomy to experimentally coronary diseased heart

of limited resection for older patients in whom most of aged patients were more likely to suffer from various coronary diseases. The coronary diseased hearts experimentally established were prepared by snearing methods of providing a 50% stenosis either on the descending coronary artery or on the left main coronary artery, adjusting distal flow to a 50% reduction by measurement with the use of electromagnetic flow meter. These dogs underwent either one or two lobe resection in right side respectively as compared to two different ranges of resected pulmonary tissue. The hemodynamic changes were evaluated 5 hours following operative procedures of lobectomy.

In coronary diseased dogs with a 50% stenosis of the left main coronary artery, the decreased left ventricular pressure, the elevated end-diastolic pressure, the low cardiac output, the raised pulmonary wedge pressure and the diminished stroke work were notably demonstrated as hemodynamically deteriorating findings when compared to non-coronary diseased dogs as indicated in Fig 6. It is concluded from this study that limited resection in older patients with coronary diseases of almost any variety contributes to reducing the operative risk when compared to lobectomy. It is of value to note that

limited resection hemodynamically affords a less operative risk rather than conventional lobectomy, especially in older patients.

**An assessment of the immune response of lymphnodes to tumor growth in relation to performing limited resection.**

A great demand for lymph node dissection around the hilum of the lung in the performance of limited resection was clinically evaluated in the aspect of the immune response. It was needed in four cases with lymph node metastasis among 21 cases undergoing limited resection with lung cancer tumor less than 3cm in diameter. Whereas 11 cases were positive of mediastinal lymph node metastasis among 35 cases within 4cm of diameter as already shown in Fig 1. The mediastinal lymph node metastasis proximally beyond the pulmonary hilum occurred in 2 cases (5.7%). Based on the results of clinical experiences the incidence of lymph node metastasis would remain low in those who undergoing limited resection.

Needless to say, the experimental results in regard to the immune response of lymph node were compatible with clinical analysis in studying the survival rate during a period of postoperative course. Response of lymph nodes to tumor growth against PHA was experimentally evaluated on 7th, 10th and 17th day after complete or incomplete tumor resection followed by inoculation of  $2 \times 10^5$  MH 134 tumor at the foodpads of  $C_3H$  mice. The lymph node response was divided into three groups according to their location, namely ipsilaterally popliteal and inguinal lymph nodes ( $Ly_1$ ), ipsilaterally axillar lymphnodes ( $Ly_2$ ) and contralaterally inguinal lymph nodes ( $Ly_1'$ ) respectively. The immune response in the lymph nodes ( $Ly_1$ ,  $Ly_1'$  and  $Ly_2$ ) to PHA was extremely enhanced in moderately early stage after complete or incomplete tumor resection on day 7th or 10 followed by tumor cell inoculation, whereas it was definitively inhibited in the late stage of enhancing tumor growth on day 17 after inoculation as shown in Fig 7.

As conclusion, the data obtained in this study clearly indicate that the immune response in regional lymph nodes close to tumor location is highly enhanced in early stage of tumor growth but it becomes depressed gradually with time as the tumor grows. It also is suggesting that tumor resection as early as possible is beneficial in enhancing the immune response in lymph nodes. As the tumor size increases rapidly, the immune response in lymph nodes has become to be obviously inhibited. As a corollary to these results it is of note, furthermore, that the earlier surgical intervention is compatible with the immunologically suitable status in continuing the enhancing immune response in lymph nodes located even at the different various sites.

Since limited resection undoubtedly tends to be employed in early stage of less than 3cm in tumor size, host resistance is also maintained immunologically without further compromising it by this operative procedure. It, furthermore, is essential to reduce the operative risk without a need for an extended mediastinal lymphnode dissection if it is so early.

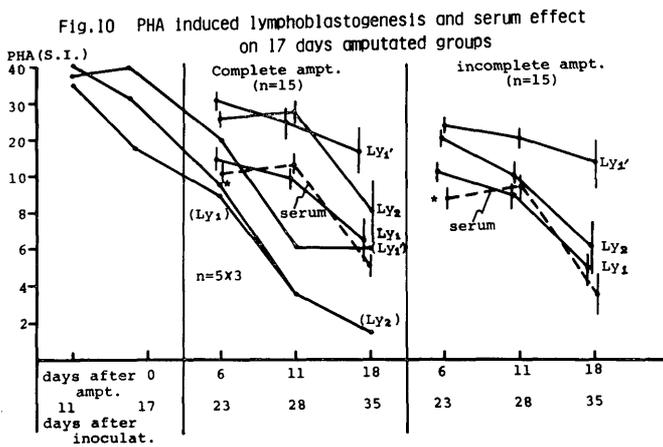
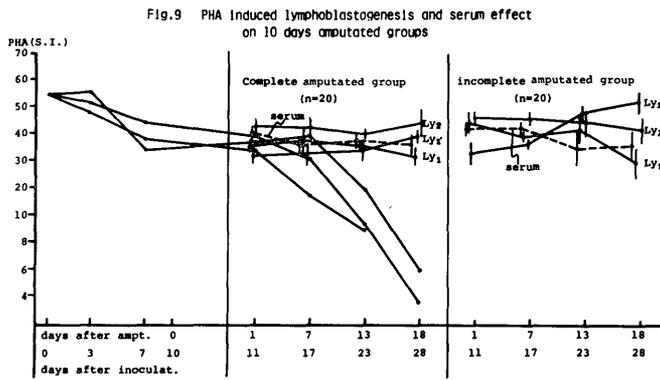
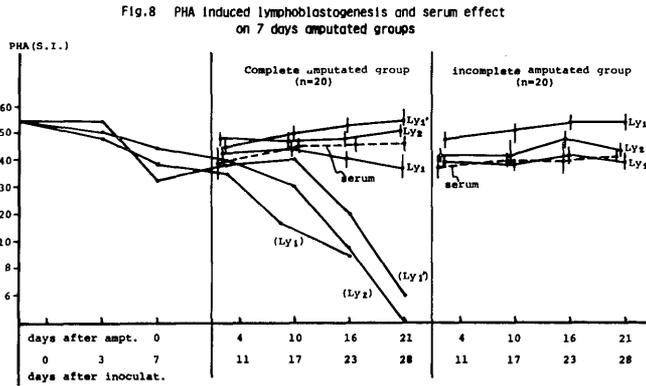


Fig 7 Immune response to regional (Ly<sub>1</sub>) and distant (Ly<sub>1</sub>, Ly<sub>2</sub>) lymph nodes in relation to either the time of tumor resection or the method of complete or incomplete resection

## DISCUSSION

The most favorable results in the treatment of lung cancer have been obtained from an analysis in surgical intervention as compared to those in other treatments<sup>5)</sup>.

The continuing vigorous therapy during a long-term period of time provides a further prolonged survival in patients with surgical resection. It, therefore, seems reasonable to maintain a well-functioning life without any sustained cardiopulmonary dysfunction in the course of postoperation as long as possible. We feel confident that a minimum of pulmonary resection used for this purpose is necessary in avoidance of the subsequent respiratory failure to surgery<sup>3)6)</sup>.

Our clinical experiences support the contention that limited resection in the management of treatment for lung cancer is of some benefits in selected patients for its application. The criteria indicate its use are fulfilled from this study with the mainly following condition, namely 1) tumor size less than 3cm in diameter 2) no mediastinal lymph node involvement. When this operative procedures were used in carefully selected patients, our clinical experiences indicated that the ensuing results either in the maintenance of an adequate cardiopulmonary function or in the prevention from recurrence are encouraging.

Our data in this study also enabled us to conclude that the elective use of limited resection is beneficial in continuing the enhancement of immunological response. Little has been said on the subject of a relation of immunological competence to the modes of surgical procedures. As a rule, surgical stress leads to a somewhat depressed immunological response to the host during the early postoperative period. It, however, is of interest to note that surgical trauma of minimal pulmonary tissue resection intends to keep immunological response unchanged as compared to conventional lobectomy for the treatment of lung cancer.

The role of limited resection in improving its prognosis has remained controversial as parts of a follow up study so far. Concern about limited resection has been raised regarding the appearance of recurrence with high incidence when compared to that after using a conventional operative method<sup>5)</sup>. It is desirable to be substantiated by further clinical experiences. In older patients with lung cancer, great emphasis has been placed upon the reliability of limited resection of choice.

From the view point of experimentally hemodynamic studies, the operative technique of limited resection has a great advantage of permitting the surgeon to preclude left ventricular power failure immediately after operation and progress toward cor pulmonale in the course of long term postoperative period.

It also afforded as good a cure rate as did conventional lobectomy with a less operative risk even in older patients.

Furthermore, it seems worthwhile to document from this study that limited resection of operative procedure of choice is aimed at enlarging its indication and enhancing immunological host response in patients with lung cancer.

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