A new method of segmental resection for primary lung cancer: intermediate results[☆]

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Abstract

Objective: To improve the postoperative results of limited resection for small lung cancer, we have developed a new operative method, pulmonary artery-guided segmentectomy. This resection begins with identification of the pulmonary arterial branches involved in the tumor, then the pulmonary tissue is divided along the pulmonary arteries (i.e. guided by pulmonary arteries) from the hilum toward the periphery by electrocautery. The advantages of this method include the facilitation of securing adequate margin from the tumor, and the feasibility of intralobar lymph node dissection during operation. To examine the efficacy of the new method of segmental resection, we retrospectively reviewed 74 cases of T1N0M0 disease who underwent the pulmonary artery-guided segmentectomy. **Methods**: From 1993 to 2000, 74 patients with pathological T1N0M0 lung cancer were treated by the pulmonary artery-guided segmentectomy. Forty-one patients (55.4%) who underwent the segmentectomy had been considered suitable candidates for lobectomy (intentional resection group). The other 33 patients (44.6%) were considered poor candidates for lobectomy because of poor cardiopulmonary reserve (compromised resection group). **Results**: The overall survival rate at 5 years was 82.0%. The 5-year survivals in the intentional and the compromised resection groups were 81.6 and 77.6%, respectively, and no significant differences were detected between the groups. According to tumor size, the 5-year survival rate for patients with tumors of 20 mm or smaller (92.9%, $n = 53$) was higher than that for the patients with tumors of 21–30 mm (63.0%, $n = 21$), but the difference did not reach statistical significance. Median follow-up time of 27.0 months revealed eight locoregional recurrences and four deaths due to lung cancer. Sixty-three patients (85.1%) are alive with no evidence of disease, and six patients (8.1%) are alive with recurrent disease. Locoregional recurrences occurred in one of 53 patients (1.9%) with tumors 20 mm or smaller and in seven of 21 patients (33.3%) with tumors 21–30 mm, the difference being statistically significant ($P < 0.01$). **Conclusions**: Our intermediate results demonstrated that the new pulmonary artery-guided segmentectomy could be an alternative method for selected patients with small lung cancer, particularly with tumors 20 mm or smaller in diameter. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Segmentectomy; Limited resection; Small lung cancer; Locoregional recurrence

1. Introduction

Small peripheral lung cancers have been detected more frequently as a result of recent developments in diagnostic imaging including high-resolution computed tomography. Limited resection (wedge or segmental resection) for peripheral small bronchogenic carcinomas has been described as a reasonable option for patients with compromised cardiopulmonary reserve [1–4]. However, its application for patients believed to be able to tolerate a lobectomy remains controversial [5,6]. Although there have been some reports showing that lobectomy offered no survival advantage over segmentectomy for the patients with small lung cancer [6–8], a number of studies [7,9], including a prospective randomized trial conducted by the North American Lung Cancer Study Group [5], demonstrated a higher locoregional recurrence rate after a lesser resection as compared with lobectomy. If a lesser resection is actually associated with a higher incidence of locoregional recurrence, it should result from residual cancer in the same lobe that should have been resected by lobectomy. Such residual tumors include intrapulmonary metastasis, intralobar lymph node metastasis, and incomplete resection margin.

In order to compensate for the potential drawbacks in limited resections, we have developed a new type of

segmental resection, pulmonary artery-guided segmentectomy. This resection begins with identification of the pulmonary arterial branches involved in the tumor, then the pulmonary tissue is divided along the pulmonary arteries from the hilum toward the periphery by electrocautery. The advantages of the procedure include the facilitation of securing adequate resection margin from the tumor, as well as the feasibility of segmental and subsegmental lymph nodes dissection. We speculate that this segmentectomy can possibly minimize a risk of residual tumor. To examine whether the segmental resection can be a surgical alternative for small peripheral lung cancer, we retrospectively reviewed 74 cases of pathological T1N0M0 disease who underwent the pulmonary artery-guided segmentectomy at our hospital in the past 8 years.

2. Materials and methods

Between January 1993 and December 2000, 213 patients with primary lung cancer pathologically classified T1N0M0 underwent resections at Kyoto University Hospital. Among these patients, 132 (62.0%) had a standard lobectomy, 74 (34.7%) underwent the pulmonary artery-guided segmentectomy, and seven (3.3%) had a wedge resection. Forty-one of the 74 patients (55.4%) who underwent the segmentectomy had been considered suitable candidates for a standard lobectomy, and were classified as the intentional resection group. The remaining 33 of the 74 patients (44.6%) who had the segmentectomy were considered poor candidates for a lobectomy because of marginal cardiopulmonary reserve, advanced age, or other significant comorbid diseases, and were classified as the compromised resection group.

After selecting a candidate for the segmentectomy based on the preoperative findings (tumor size, location, lymph node status, and cardiopulmonary function), we obtained informed consent from the patient regarding the operative methods, and made the final decision on what type of resection to perform according to the intraoperative findings. Our selection criteria for the intentional resection group were a clinical T1N0M0 peripheral tumor, preferably of 20 mm or smaller in diameter, no lymph node metastasis proven by intraoperative analysis, and a resection margin of greater than 20 mm. Whenever any lymph node or intrapulmonary metastasis was found by intraoperative pathological analysis, lobectomy was completed.

The segmentectomy applied in this study was characterized as follows. The pulmonary arteries were isolated at the hilum, and arterial branches were identified as guides for resection lines that could secure at least 20 mm of resection margin from the tumor. Then the pulmonary tissue was divided along the guiding arterial branches from the hilum to the periphery by electrocautery. When intralobar segmental or subsegmental lymph node was identified during the dissection, the lymph node was analyzed immediately.

When a branch that had been determined the guide for a resection line at the beginning ran too close to the tumor, adequate resection margin from the tumor was secured by changing the guiding pulmonary arterial branch. The small vessels were coagulated by electrocautery. The bronchi, arteries, and veins going to the affected segments that would be eliminated were cut finally. In contrast to the conventional segmentectomy, the resection was not made along the intersegmental plane consequently. In this method, the resection lines constantly secured sufficient resection margin from the tumor (Fig. 1). Complete hilar and mediastinal lymph node dissection was performed in the intentional resection group. The bronchioles in the resection plane were carefully ligated. The resection planes were not plicated but were joined together in order that the lung volume might be preserved as much as possible. When it was anatomically difficult to put the resection planes together, the planes were covered with the mediastinal adipose tissue. As a rule, oral UFT, a 5-fluorouracil derivative chemotherapeutic agent, was administrated for more than 1 year.

Survival was calculated by the Kaplan–Meier method from the day of operation until death or the day of the most recent follow-up (censored), and differences in survival were determined by the log-rank test. To compare the frequencies of the various categorical outcomes in the two groups, data were evaluated by χ^2 test or Fischer's exact test when the sample size was small. Unpaired two-tailed t-test was used for the comparison of mean values. We defined a locoregional recurrence as the development of an additional carcinoma in the ipsilateral hemithorax (lung and mediastinum). Tumors that recurred simultaneously both in the ipsilateral hemithorax and distantly were considered to be distant recurrences.

3. Results

Seventy-four patients aged 45–83 years who underwent the pulmonary artery-guided segmentectomy were retro-
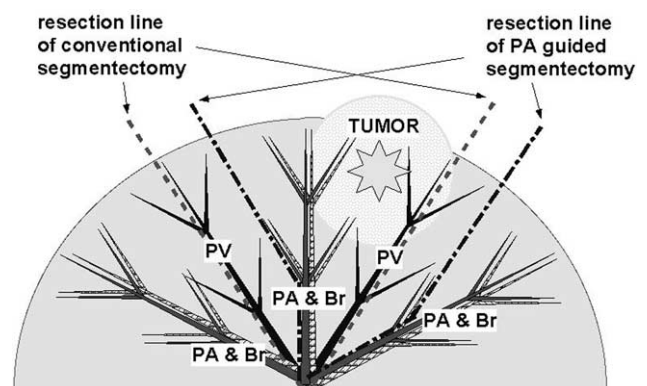

Fig. 1. Schematic comparison of resection lines between a conventional segmentectomy and the pulmonary artery-guided segmentectomy. The resection was not made along the intersegmental plane in the new method.

Table 1
Characteristics of patients

Characteristics	Data
Age (years) (range)	66.1 (45–83)
Gender	
Male	45
Female	29
Histology	
Adenocarcinoma	51
Squamous cell carcinoma	17
Small cell carcinoma	6
Indication	
Intentional	41
Compromised	33
Tumor size (mm) (mean $\pm$ SD)	18.8 ± 5.7
≤ 20	53
21–30	21
Median follow-up (months)	23.5

Fig. 3. Comparison of survival curves between the intentional resection group and the compromise resection group. No significant difference was detected between the two groups.

spectively reviewed. Table 1 summarizes the characteristics of the patients. The average age of the compromised resection group was 69.5 years, and significantly higher than that of the intentional resection group (63.4 years, $P < 0.01$). The median follow-up period was 28.4 months for the intentional resection group and 21.9 months for the compromised resection group. Tumors in the intentional resection group were classified histologically as adenocarcinoma (35 cases), squamous cell carcinoma (three cases), and small cell carcinoma (three cases). Tumors in the compromised resection group were assessed to be adenocarcinoma (16 cases), squamous cell carcinoma (14 cases), and small cell carcinoma (three cases). The high percentage of squamous cell carcinoma was significantly characteristic of the compromised resection group ($P < 0.01$). Of the 41 carcinomas in the intentional resection group, 33 were 20 mm or smaller, and eight were 21–30 mm in diameter. Of the 33 carcinomas in the compromised resection group, 20 were 20 mm or smaller, and 13 were 21–30 mm in diameter. The average diameter of tumors was 17.5 mm in the intentional resection group, and significantly smaller than that in the compro-
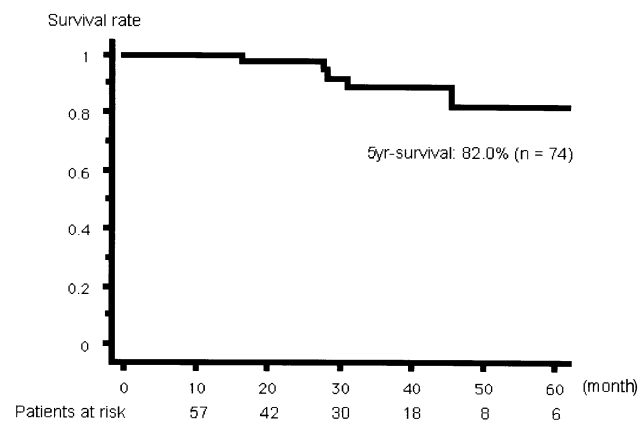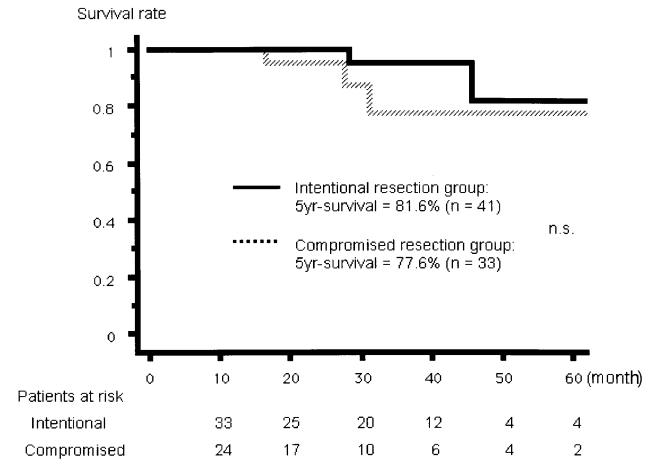
mised resection group (20.6 mm, $P < 0.05$). The tumors were located in the right upper lobe in 15 patients (20.3%), in the right lower lobe in 14 (18.9%), in the left upper lobe in 28 (37.8%), and in the left lower lobe in 17 (23.0%). The mean operative time was 236 ± 46 min, including approximately 30–60 min required for repeated intraoperative pathological examination. The average amount of intraoperative bleeding was 232 ± 163 ml, and blood transfusion was required in only one patient. Of 74 patients, 16 (21.6%) were treated in the intensive care unit postoperatively, and all of the patients returned to the thoracic surgery ward within 24 h. The mean duration of postoperative air leak was 2.2 ± 4.5 days, except in one patient who required reoperation due to prolonged air leak on the 21st day postoperatively.

The overall survival rate at 5 years was 82.0% (Fig. 2). The 5-year survivals in the intentional and the compromised resection groups were 81.6 and 77.6%, respectively, and no significant differences were detected between the groups (Fig. 3). In contrast, the 5-year survival rates were 92.9% for patients with tumors of 20 mm or smaller and 63.0% for the patients with tumors of 21–30 mm (Fig. 4). The difference, however, did not reach statistical significance.

The clinical outcome of the 74 patients is shown in Table 2. There were neither operation-related deaths nor major complications postoperatively except for two patients, who required reoperation because of prolonged air leak and bleeding, respectively. Out of four patients (5.4%) who died of lung cancer recurrence, three had locoregional recurrences, and one died of multiple brain metastasis with no evidence of locoregional recurrence. One patient in the compromised resection group died of interstitial pneumonia. Sixty-three patients (85.1%) are alive with no evidence of disease, and six (8.1%) are alive with recurrent disease. The incidence of lung cancer deaths or recurrences in the two groups was not significantly different. Table 3 presents the clinical outcome of 53 patients with tumors of 20 mm or

Fig. 2. Survival curve of the 74 patients who underwent pulmonary artery-guided segmentectomy for T1N0M0 lung cancer.
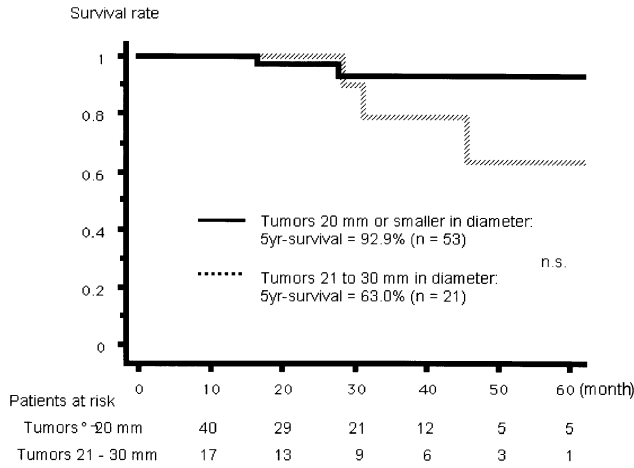
Fig. 4. Comparison of survival curves between the two groups according to tumor diameter. The 5-year survival rate was higher for patients with tumors of 20 mm or smaller than for the patients with tumors of 21–30 mm. The difference, however, did not reach statistical significance.

less in diameter. Only one patient in the compromised resection group died of lung cancer with no evidence of locoregional recurrence. Forty-nine patients (92.5%) are alive without recurrence, and two (3.8%) are alive with recurrent disease. No significant difference in the incidence of lung cancer deaths or recurrences was detected between the two groups.

The incidence of locoregional recurrence was studied according to size of the original tumor (Table 4). Locoregional recurrences occurred in one of 53 patients (1.9%) with tumors 20 mm or smaller and in seven of 21 patients (33.3%) with tumors 21–30 mm, difference in the locoregional recurrence rate being statistically significant ($P < 0.01$).

4. Discussion

The appropriateness of limited resection for a small peripheral lung cancer has been the subject of much controversy. A major criticism of lesser resection particularly for patients considered suitable candidates for a lobectomy is grounded on some reports [5,7,9] describing a higher risk of locoregional recurrence after a limited resection in comparison with a lobectomy. The primary cause of the high inci-

Table 2
Clinical outcome of 74 patients

	Intentional	Compromised	Total
Lung cancer deaths	2 (4.9%)	2 (6.1%)	4 (5.4%)
Non-cancer deaths	0 (0.0%)	1 (3.0%)	1 (1.4%)
Alive			
With locoregional recurrence	1 (2.4%)	3 (9.1%)	4 (5.4%)
With distant recurrence	1 (2.4%)	1 (3.0%)	2 (2.7%)
Without recurrence	37 (90.2%)	26 (78.8%)	63 (85.1%)
Total	41 (100%)	33 (100%)	74 (100%)

Table 3
Clinical outcome of 53 patients with tumor size of 20 mm or smaller

	Intentional	Compromised	Total
Lung cancer deaths	0 (0.0%)	1 (5.0%)	1 (1.9%)
Non-cancer deaths	0 (0.0%)	1 (5.0%)	1 (1.9%)
Alive			
With locoregional recurrence	0 (0.0%)	1 (5.0%)	1 (1.9%)
With distant recurrence	1 (3.0%)	0 (0.0%)	1 (1.9%)
Without recurrence	32 (97.0%)	17 (85.0%)	49 (92.5%)
Total	33 (100%)	20 (100%)	53 (100%)

dence of the recurrence can be considered that remnant tumors of intrapulmonary metastasis, intralobar lymph node metastasis, or at incomplete resection margin are left behind. As many as 10–20% of small peripheral lung cancers were reported to have lymph node metastases [10–12]. A recent pathological study by Yamanaka et al. [12] revealed that 11 of 74 patients (11.7%) with a small peripheral tumor of 3.0 cm or less in diameter had segmental lymph node or intrapulmonary metastases within the same lobe as the main tumor. The authors estimated that six patients (6.4%) or 11 patients (11.7%) would have remnant tumors in the same lobe if segmentectomy or wedge resection was performed, respectively, and commented that segmentectomy seemed to be more preferable than wedge resection. A prospective randomized trial [5] demonstrated that limited resection was associated with a high locoregional recurrence rate; however, in this study, a considerable number (32.8%) of wedge resections in the limited resection group might raise the recurrence rate. Moreover, since conventional methods of segmentectomy invariably divide the lung along the intersegmental planes, there is a great risk of residual cancer cells due to inadequate resection margin when the tumor is adjacent to the intersegmental plane.

We have developed a new method of segmental resection, pulmonary artery-guided segmentectomy, in order to minimize the risk of remnant cancer in limited resections. This segmentectomy enabled a reliable intraoperative analysis of intralobar, hilar, and mediastinal lymph nodes, and constantly secured adequate surgical margin by flexible conversion of the guiding artery. In addition, division by electrocautery could possibly reduce the risk of dissemination of cancer cells. In limited resections, the importance of

Table 4
Locoregional recurrences in the intentional and the compromised resection groups according to tumor diameter

Tumor diameter (mm)	Intentional		Compromised		Totals	
	No.	%	No.	%	No.	%
≤20	0/33	0.0	1/20	5.0	1/53[a]	1.9
21–30	3/8	37.5	4/13	30.8	7/21[a]	33.0

[a] The incidence of locoregional recurrence in the patients with tumors of 21–30 mm was significantly higher than in the patients with tumors of 20 mm or smaller.

aggressive intraoperative pathological examinations on the intralobar, hilar, and mediastinal lymph nodes, and radical lymph node dissection as in a standard lobectomy, has been emphasized repeatedly [5,6,8,12,13]. The pulmonary artery-guided segmentectomy meets these requirements.

From the point of view of postoperative lung function, limited resections are expected to preserve pulmonary function better than a lobectomy and consequently can provide the chance for further resection in the future if a second primary lung cancer develops. In previous studies, postoperative functional advantages of limited resection over lobectomy were demonstrated [5,13,14]. Moreover, we considered it important to avoid a considerable deformity of the residual lobe after segmentectomy to preserve the postoperative lung volume as much as possible. Therefore, it was our principle not to use surgical staplers for division of pulmonary tissue. Unnecessary plication of the resection planes was also avoided for the same reason. As there was no operation-related death, and prolonged air leak that required reoperation occurred only in one patient (1.4%), this segmentectomy was shown to be certainly a safe operative method.

We initially attempted to apply the segmental resection only to compromised patients with limited cardiopulmonary reserve, irrespective of tumor size, and found the postoperative results were acceptable. Subsequently we commenced to apply the segmentectomy with radical dissection of hilar and mediastinal lymph nodes to selected patients with a small tumor who we believed were able to tolerate a lobectomy. Although the median follow-up was 23.5 months and it is premature to draw a definitive conclusion, the overall survival rate at 5 years of the 74 patients was satisfactory (82.0%) and was equivalent to that of standard lobectomy for pathological T1N0M0 disease. Sixty-three patients (85.1%) are alive with no evidence of disease. Locoregional recurrence that has been observed frequently in previous reports [5,7,9] was recognized in eight patients (10.8%), and only in one of 53 patients (1.9%) with tumors 20 mm or less in diameter. Our results, however, revealed a significantly higher locoregional recurrence rate in patients with tumors 21–30 mm; therefore, now we consider a patient with a tumor size of 20 mm or smaller as a candidate for intentional segmentectomy.

Postoperative oral administration of UFT might contribute to the low death rate and locoregional recurrence rate in the present study. The efficacy of postoperative oral UFT was confirmed by a prospective randomized study conducted by the West Japan Study Group for Lung Cancer Surgery [15]. Our recent study [16] suggested that the efficacy of UFT might be associated with incidence of apoptosis and with status of p53 regulating apoptosis, and that the UFT therapy might induce cancer cells in micrometastatic lesions without suppression of patients' immunity, resulting in an improvement in the postoperative prognosis. We think much of postoperative UFT therapy, in particular after a limited resection.

In conclusion, our intermediate results demonstrated that the new pulmonary artery-guided segmentectomy could be an alternative method for selected patients with small lung cancer, particularly with tumors 20 mm or smaller in diameter. As this is not a randomized prospective trial but a retrospective study, a detailed long-term follow-up and a prospective randomized study are necessary to determine the definitive patient criteria for intentional segmentectomy. It is expected that the criteria including the specific radiographic findings based on pathology, genetic information such as p53 status, as well as tumor size, will enable a more reasonable patient selection in the future.

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