*Int Surg* 2019;**104:**297–302
DOI: 10.9738/INTSURG-D-15-00016.1



# Clinicopathologic Characteristics and Prognosis of Patients With Non–Small Cell Lung Cancer Who Undergo Pulmonary Segmentectomy

Akihiro Taira, Takeshi Hanagiri, Shinji Shinohara, Masaru Takenaka, Soich Oka, Yasuhiro Chikaishi, Hidehiko Shimokawa, Hidetaka Uramoto, Tomoko So, Fumihiro Tanaka

*Second Department of Surgery, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan*

**This study retrospectively investigated the clinical characteristics and prognosis of the non–small cell lung cancer (NSCLC) patients who underwent segmentectomy as either intentional or passive limited surgery. The subjects included in this study comprised 72 patients who underwent segmentectomy at our hospital. There were 23 patients who underwent intentional segmentectomy. The histologic type was adenocarcinoma in all of these patients. Regarding the tumor size, 9 tumors were 1 cm or less in diameter, 13 were 1.1 to 2 cm, and 1 was 2.5 cm. All patients who underwent intentional segmentectomy were alive without any recurrence as of the last follow-up examination. A passive segmentectomy was performed for 49 patients. The reasons for passive segmentectomy were due to the presence of metachronous multiple lung cancer in 14 patients, synchronous multiple lung cancer in 9 patients, age above 80 years in 12 patients, reduced pulmonary function in 8 patients, and moderate to severe cardiovascular disease in 4 patients; another 2 patients were receiving treatment for another primary cancer. The 5-year survival rate of the patients who underwent passive segmentectomy was 69.8%. There was no postoperative mortality in either of the groups. This study showed that all of the patients who underwent intentional segmentectomy were alive without any recurrence, thus suggesting that the procedure is associated with sufficient oncologic**

Reprint requests: Takeshi Hanagiri, MD, Second Department of Surgery, School of Medicine, University of Occupational and Environmental Health, Yahatanishi, Kitakyushu 807, Japan.
Tel.: +81 93 691 7442; Fax: +81 93 692 4004; E-mail: Hanagiri@med.uoeh-u.ac.jp

**efficacy, along with preservation of the lung function. The passive segmentectomy was a feasible procedure and was an alternative procedure with an acceptable overall survival rate in high-risk patients with underlying medical comorbidities.**

*Key words:* Non–small cell lung cancer – Surgical resection – Segmentectomy – Limited resection – Postoperative prognosis

Lung cancer remains the most prevalent and lethal cancer worldwide, with non–small cell lung cancer (NSCLC) accounting for approximately 85% of all cases.[1] The current treatment strategy for NSCLC depends on the clinical staging. Surgery remains the mainstay of treatment for early-stage NSCLC because of its long-term survival benefit.[2] The gold standard procedure is a lobectomy and mediastinal lymph node dissection because there is a higher frequency of local/regional recurrence associated with limited operations.[3] However, surgery for lung cancer is a major operation, and the possible complications of surgery depend on the extent of the pulmonary resection and the patient's underlying condition. Recently, acceptable surgical outcomes have been reported for intentional limited operations for peripheral small carcinoma or passive limited resections performed in patients with reduced cardiopulmonary functional reserve, advanced age, and/or decreased physical function.[4–6]

Recent advances in diagnostic imaging technology have enabled the detection of early-stage lung cancer. The widespread use of computed tomography (CT) scans to screen for lung cancer or evaluate patients for other chest diseases appears to be associated with the detection of small peripheral adenocarcinomas with ground-glass opacity (GGO).[7] Recent retrospective studies showed the possibility of a cure by intentional limited surgical resection for small-sized peripheral NSCLCs.[4,5] On the other hand, patients with comorbidities, particularly cardiopulmonary disorders, still have a chance of achieving a cure by limited surgical resection.[6] However, when surgeons perform a segmentectomy, it is necessary to pay closer attention to ensuring that there is an adequate parenchymal surgical margin from the tumor, and to ensure the complete removal of the targeted anatomic segment with its bronchial, vascular, and lymphatic distribution. A segmentectomy is safer for patients with a limited pulmonary function because it helps preserve the lung function. This study retrospectively investigated the clinical characteristics and prognosis of NSCLC patients who underwent segmentectomy as either intentional or passive limited surgery.

## Patients and Methods

The hospital records of 765 consecutive patients who underwent a resection of NSCLC between 2000 and 2009 were reviewed. The subjects included in this study were 72 patients who underwent segmentectomy. The preoperative assessments included chest roentgenography and CT of the chest, upper abdomen, and brain. Clinical N2 status was defined by the presence of a lymph node more than 1 cm in the short-axis diameter. Bone scintigraphy was performed to detect bone metastasis. Magnetic resonance imaging of the brain was routinely employed to assess patients for distant metastasis. We started to use positron emission tomography scans for the assessment of clinical staging in 2005. Bronchoscopy was routinely performed to obtain a pathologic diagnosis by transbronchial lung biopsy, and to evaluate the endobronchial staging. The predictive postoperative lung function was considered to indicate that the patient was operable if his or her forced vital capacity and forced expiratory volume in 1 second as the percent of the forced vital capacity ($FEV_{1.0}$) were greater than 900 mL/$m^2$ and 600 mL/$m^2$, respectively. The patients' records, including their clinical data, preoperative examination results, details of any surgeries, histopathologic findings, and TNM stages, were also reviewed.

Segmentectomy as an intentional limited operation (intentional segmentectomy) was performed for patients who had adenocarcinoma with a diameter of 1.0 cm or less, or who had adenocarcinoma of 1.1 to 2.0 cm in diameter in which the ratio of the GGO was 50% or more. A passive segmentectomy in this study was defined as a limited operation for patients unable to tolerate the standard operation (lobectomy or pneumonectomy) because of their reduced cardiopulmonary functional reserve, advanced age, or other severe disease, or because of a request to help preserve their quality of life. Both intentional

*Table 1 The clinicopathologic characteristics of the patients who underwent segmentectomy as an intentional limited operation*

| | No. |
|---|---|
| Gender | |
| Male | 9 |
| Female | 14 |
| Histology of adenocarcinoma | 23 |
| Tumor size | |
| ≤1 cm | 9 |
| 1–2 cm | 13 |
| >2.1 cm | 1 |
| Proportion of GGO | |
| <50% | 1 |
| 50%–74% | 4 |
| ≥75% | 18 |
| Noguchi classification | |
| Type A | 5 |
| Type B | 15 |
| Type C | 3 |
| Pathologic stage IA | 23 |
| Resected segment | |
| Left upper division | 11 |
| Basal segment | 3 |
| S6 | 3 |
| Lingular segment | 2 |
| Right S1 | 2 |
| Right S2 | 2 |

*Table 2 The clinicopathologic characteristics of the patients who underwent segmentectomy as a passive limited operation*

| | No. |
|---|---|
| Gender | |
| Male | 28 |
| Female | 21 |
| Histology | |
| Adenocarcinoma | 30 |
| Squamous cell carcinoma | 13 |
| Large cell carcinoma | 3 |
| Other | 3 |
| Tumor size | |
| ≤1 cm | 6 |
| 1.1–2 cm | 21 |
| 2.1–5 cm | 20 |
| >5 cm | 2 |
| Pathologic stage | |
| IA | 35 |
| IB | 5 |
| II | 7 |
| IIIA | 2 |
| Resected segment | |
| S6 | 19 |
| Left upper division | 12 |
| Basal segment | 8 |
| Lingular segment | 4 |
| Right S2 | 3 |
| S6 + S10 | 2 |
| S8 | 1 |

segmentectomy and passive segmentectomy were performed through conventional thoracotomy or minithoracotomy. All resected specimens, including the primary tumor and resected hilar and mediastinal lymph nodes, were examined to determine both the tumor histology and the extent of lymph node metastases. Intraoperative frozen sections were examined if invasion of the tumor was suspected at the surgical margins. The histopathologic findings were classified according to the World Health Organization criteria, and the Union for International Cancer Control TNM staging system (7th edition) was employed.[8,9]

Follow-up information was obtained from all patients through office visits or from their primary physicians. In principle, the patients were evaluated every 3 months by chest roentgenography, and chest CT scans and bone scintigraphy were performed every 6 months for the first 2 years after surgery and annually thereafter. Six patients received the best supportive care without regular radiologic examinations being performed by their primary physicians. The mean duration of observation was 42 months (interquartile range, 21–50 months).

The survival curve was calculated by the Kaplan-Meier method, and data were compared using the log rank test for the univariate analysis. The Statview V software package (Abacus Concept, Berkeley, California) was used for all statistical analyses.

## Results

There were 23 patients who underwent intentional segmentectomy for NSCLC. The patients included 9 men and 14 women. The mean age of the patients was 67.3 years (range, 41–81 years). The Eastern Cooperative Oncology Group Performance Status of each patient was evaluated on a scale of 0 to 1. None of the patients had any severe comorbidities. The histologic type of all of these patients was adenocarcinoma. The histologic types based on Noguchi classification included 5 type A (80.5%), 15 type B (13.9%), and 3 type C (5.6%) cases. Regarding the tumor size, 9 tumors were 1 cm or less in diameter, 13 were 1.1 to 2 cm, and 1 tumor was 2.5 cm in diameter. The resected segments were the left upper division in 11, basal segment of the lower lobe in 3, S6 in 3, left lingular segment in 2, right S1 in 2, and right S2 in 2 patients. All of the patients received a diagnosis of stage IA disease (Table 1).

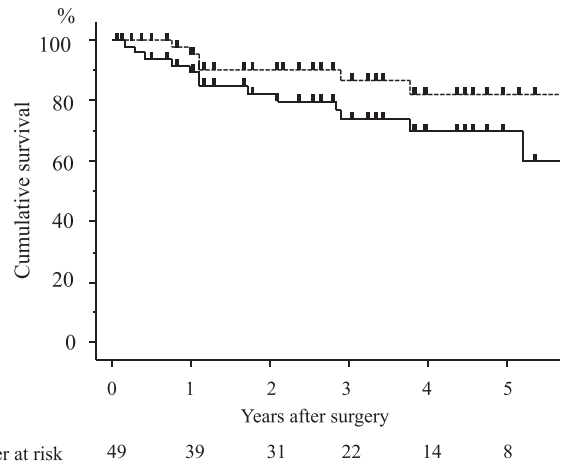
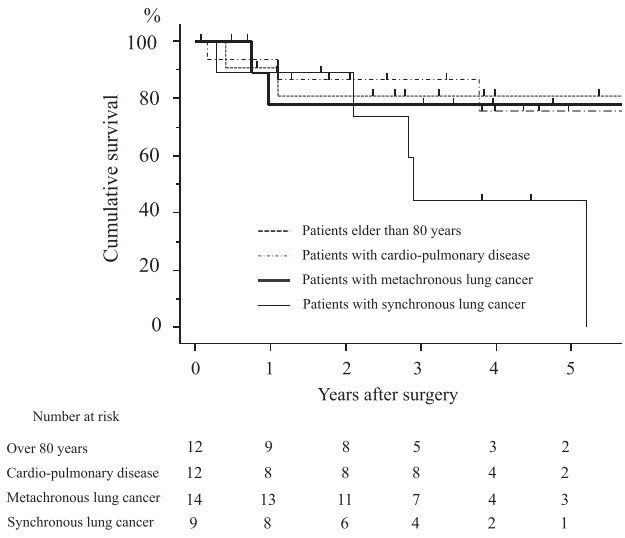



**Fig. 1** The overall and the cancer-specific survival curves in the patients who underwent passive segmentectomy because of their inability to tolerate a standard operation, such as lobectomy and pneumonectomy. The solid line shows the overall survival and the dashed line indicates the cancer-specific survival.




| Number at risk | | | | | | |
|---|---|---|---|---|---|---|
| Over 80 years | 12 | 9 | 8 | 5 | 3 | 2 |
| Cardio-pulmonary disease | 12 | 8 | 8 | 8 | 4 | 2 |
| Metachronous lung cancer | 14 | 13 | 11 | 7 | 4 | 3 |
| Synchronous lung cancer | 9 | 8 | 6 | 4 | 2 | 1 |

**Fig. 2** The overall survival curve in patients according to the reasons for the passive segmentectomy.

A passive segmentectomy was performed for 49 patients (Table 2). The reasons why a passive segmentectomy was selected were metachronous multiple lung cancer in 14 patients, synchronous multiple lung cancer in 9 patients, age over 80 years in 12 patients, reduced pulmonary function in 8 patients, and moderate to severe cardiovascular disease in 4 patients; another 2 patients were under treatment for another primary cancer. The Eastern Cooperative Oncology Group Performance Status of the 12 octogenarians was evaluated on a scale of 1 to 3. There were 28 men and 21 women. The mean age of the patients was 74.2 years (range, 55–85 years). The histologic types included 30 adenocarcinomas (61.2%), 13 squamous cell carcinomas (26.5%), 3 large cell carcinomas (6.1%), and 3 other types of carcinomas (6.1%). There were 6 tumors that were 1 cm or less in diameter, 21 that were 1.1 to 2 cm, 20 that were 2.1 to 5 cm, and 2 that were more than 5 cm in diameter. The pathologic stage was diagnosed as stage IA in 35 patients, stage IB in 5 patients, stage II in 7 patients, and stage IIIA in 2 patients. The resected segments were S6 in 19 patients, the left upper division in 12, the basal segment of the lower lobe in 8, the left lingular segment in 4, right S2 in 3, left S6 + 10 in 2, and left S8 in 1 patient.

All of the patients who underwent intentional segmentectomy were alive without any recurrence as of the last follow-up examination. The 5-year survival rate of the patients who had undergone passive segmentectomy was 69.8% (Fig. 1). The cancer-specific survival rate at 5 years after surgery was 82.1%. The 5-year survival rates were 80.8%, 77.8%, 75.8%, and 44.4% in the patients older than 80 years, those with cardiopulmonary disease, those with metachronous multiple lung cancer, and those with synchronous multiple lung cancer, respectively. Significant differences were observed according to the reasons for the passive segmentectomy (Fig. 2). There was no postoperative mortality in either of the groups. A total of 13 patients died during the follow-up period. Among these patients, 6 died of comorbid diseases and 7 died of recurrence of the cancer. There was 1 patient who developed recurrence in a mediastinal lymph node, and 6 patients developed distant metastasis; however, local recurrence of the affected lobe was not observed in any of these patients.

## Discussion

The standard surgical procedure for NSCLC is a lobectomy. Segmentectomy is a technique used to remove an anatomic division (segment) of a particular lobe of the lung. The procedure is generally performed for patients with two different disease situations. One indication for surgery is an intentional segmentectomy for patients with peripheral small-sized NSCLC, and the other is a passive segmentectomy for patients unable to tolerate the standard operation because of minimal cardiopulmonary reserve or another factor associated with decreased physical performance. Segmentectomy is

a limited pulmonary resection, and it has the theoretical advantage of preserving the pulmonary function over lobectomy, thus reducing the perioperative mortality and morbidity.

As a result of the development of imaging modalities, such as high-resolution CT, small-sized lung cancer is more frequently detected, especially nodules with pure or mixed GGO.[10] Following improvements in imaging technology, new concepts have been introduced, such as adenocarcinoma *in situ* and minimally invasive adenocarcinoma for small solitary adenocarcinomas with either pure lepidic growth or predominant lepidic growth with ≤5-mm invasion.[11] If such patients undergo complete resection, a disease-specific survival rate of nearly 100% is expected.

However, the evidence still remains controversial as to which surgical procedure is the most appropriate for small peripheral adenocarcinoma with GGO, because the disadvantages of segmentectomy include a possibility of increased local recurrence and the complexity of the procedure. However, several studies have demonstrated that intentional segmentectomy in well-selected patients with small-sized peripheral NSCLC is associated with local control and survival rates equivalent to those of lobectomy.[4,5,12,13] These results support the reevaluation of lobectomy as the standard of care for patients with small-sized NSCLC. In the present study, the indications for intentional segmentectomy were adenocarcinoma with a diameter of 1.0 cm or less, or adenocarcinoma of 1.1 to 2.0 cm in diameter in which the ratio of the GGO was 50% or more. There was 1 patient with adenocarcinoma with a diameter of 0.8 cm, and the other 22 patients had adenocarcinoma with a diameter of 11 to 20 mm with 50% or more of the tumor having GGO. The disease-free survival rate at 5 years was 100% in the patients who had undergone intentional segmentectomy according to these criteria.

Based on the progressive aging of society in developed countries, there has been a rapid increase in the number of elderly people undergoing surgery for NSCLC.[14] A number of studies recommend surgical resection even for elderly patients, because of the advances in surgical techniques, perioperative management, and anesthetic management.[15,16] However, carefully evaluating the tolerability of surgery from the viewpoint of important organ function is necessary. A limited life expectancy should be also considered in such patients. In the present study, 12 patients older than 80 years underwent segmentectomy instead of lobectomy because of their advanced age.

If lobectomy is not possible because of severe comorbidities or limited cardiopulmonary function, less invasive surgical resection, such as anatomic segmental resection or broad nonanatomic wedge resection, are alternative procedures. A total of 8 patients underwent segmentectomy in the present study because of their reduced pulmonary function, and 4 patients underwent the procedure because of moderate to severe cardiovascular disease.

The incidence of multiple primary carcinomas has increased because of advances in diagnostic radiographic techniques and the introduction of helical CT in the screening of patients for lung cancer.[17] Several investigators reported that early radiographic detection and surgical resection could yield a favorable prognosis for such patients.[18,19] There were 14 patients in the present study who underwent segmentectomy for metachronous multiple lung cancer, and 9 patients underwent the procedure for synchronous multiple lung cancers. The overall survival rate was 69.8% at 5 years in the patients who had undergone passive segmentectomy, suggesting that segmentectomy should be considered as an acceptable treatment procedure for such high-risk patients.

Sublobular resection includes wedge resection and segmentectomy. Smith *et al*[20] and Sienel *et al*[21] reported that segmentectomy was the preferred technique for the limited resection of patients with stage IA NSCLC, because segmentectomy was associated with significant improvements in the overall and lung cancer–specific survival rates compared with wedge resection. Sawabata *et al*[22] reported that a greater distance from the malignancy-negative margin (larger than the maximum tumor diameter) is necessary to prevent margin relapse.[22] However, the safe surgical margin might depend on the histologic type, such as whether the tumor exhibits pure lepidic growth or predominant lepidic growth, and whether it is another type of solitary adenocarcinoma. Multi-institutional trials are being performed to evaluate the noninferiority of the overall survival rate of segmentectomy compared with lobectomy in patients with small-sized peripheral NSCLC, and the outcomes of these clinical studies are highly anticipated.[23]

The present study showed that all of the patients who underwent intentional segmentectomy were alive without any recurrence at the last follow-up examination, thus suggesting that there was sufficient oncologic efficacy with the preservation of

lung function. Passive segmentectomy is therefore considered to be a feasible procedure, and it represents an alternative procedure with an acceptable overall survival rate in patients who are considered to be at high risk for undergoing lobectomy because of underlying medical comorbidities. Careful assessment of patient background and tumor characteristics will contribute to the selection of the optimal treatment approach.

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