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# Segmentectomy for clinically early-stage primary squamous cell carcinoma of the lung

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## Abstract

**Background:** Squamous cell carcinoma of the lung—the second most common subtype of lung cancer—has a poorer prognosis than lung adenocarcinoma. However, in contrast to lobectomy, the oncological outcomes after segmentectomy for primary squamous cell carcinomas remain unknown; hence, this study investigated these outcomes.

**Methods:** Patients who underwent lobectomy or segmentectomy for clinically node-negative primary lung squamous cell carcinoma with a whole tumor size of ≤ 30 mm on preoperative computed tomography scan during April 2010 to December 2020 were included in this study. The cumulative incidence of recurrence (CIR) among all included patients and propensity score-matched patients were compared using the Gray method. Multivariate analysis using propensity scores and surgical procedures was performed using the Fine and Gray method.

**Results:** Overall, 230 patients were included in this study; of these, 172 (74.8%) underwent lobectomy and 58 (25.2%) underwent segmentectomy. No significant differences were observed in the CIR between patients who underwent lobectomy and those who underwent segmentectomy (5-year rate 18.1% vs. 14.2%; $p = 0.787$). Moreover, no significant differences in CIR were observed between the propensity score-matched patients who underwent lobectomy ($n = 43$) and those who underwent segmentectomy ($n = 43$) (8.6% vs. 8.0%; $p = 0.571$). Multivariable analysis was performed for CIR using the propensity score; it revealed that segmentectomy was not a significant predictor of worse CIR (hazard ratio, 0.987; $p = 0.980$).

**Conclusions:** Segmentectomy may be feasible for treating clinically early-stage lung squamous cell carcinoma; its oncological outcomes are similar to those of lobectomy.

**KEYWORDS**
lobectomy, lung cancer, segmentectomy, squamous cell carcinoma

## INTRODUCTION

In the past, lobectomy was known to be the standard treatment for non–small cell lung cancer (NSCLC).[1] However, recent advances in imaging modalities, such as high-resolution computed tomography (CT) and 18-fluorodeoxyglucose positron emission tomography (FDG-PET)/CT, have allowed for more frequent detection of early-stage lung cancer.[2] A randomized trial (JCOG0802/WJOG4607L) assessing prognosis after segmentectomy and lobectomy in patients with NSCLC with a maximum tumor size of ≤ 2 cm and a consolidation tumor ratio of > 50% showed that the overall survival (OS) of patients undergoing segmentectomy was significantly higher than that of those who underwent lobectomy.[3]

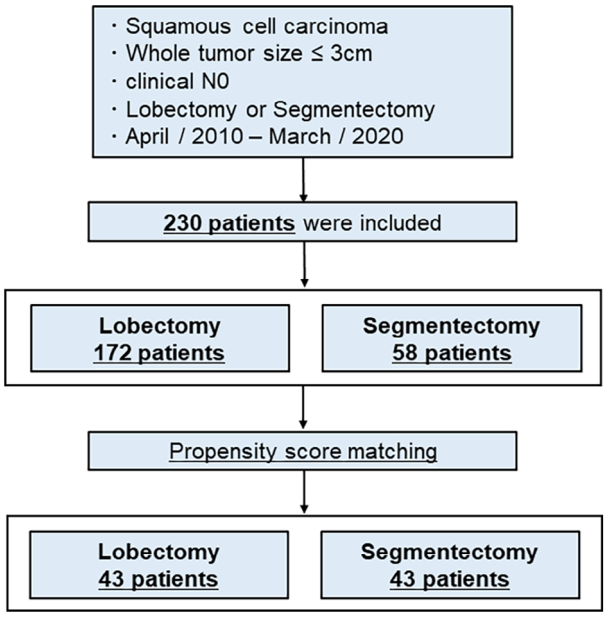


**FIGURE 1** Patient selection flowchart. Patients who underwent lobectomy or segmentectomy for primary lung squamous cell carcinoma with a whole tumor size of ≤ 3 cm (on preoperative computed tomography) were investigated. A total of 230 patients were included in this study

Moreover, several retrospective studies have investigated the outcomes of segmentectomy in NSCLC patients with a whole tumor size of 2.1 to 3 cm,[4] radiologically pure solid appearance,[5] and high FDG accumulation.[6,7] In these studies, the outcomes of segmentectomy were comparable to those of lobectomy. Therefore, segmentectomy is expected to be more commonly performed.

Squamous cell carcinoma (SCC) of the lung, which is known as the second most frequent subtype of NSCLC after lung adenocarcinoma, has a poorer prognosis than lung adenocarcinoma.[8] Previous studies on segmentectomy have merely focused on either lung adenocarcinoma or NSCLC, with many of the included patients having lung adenocarcinoma. We previously showed the feasibility of segmentectomy for treating NSCLC with invasive characteristics, such as lymphatic invasion (LY), vascular invasion (V), and pleural invasion (PL),[9] albeit without analyzing its histological subtypes. Although driver mutations that can serve as therapeutic targets in adenocarcinoma of the lung—such as epidermal growth factor receptor (EGFR) mutations and anaplastic lymphoma kinase (ALK) rearrangement—are known, however, those associated with lung SCC remain unidentified. Therefore, because fewer therapeutic options are available for lung SCC than for lung adenocarcinoma, radical surgical cure of lung SCC assumes greater importance, and it is consequently reasonable to evaluate the outcomes of segmentectomy only in patients with lung SCC. To the best of our knowledge, there are currently no published studies on the feasibility of segmentectomy for treating lung SCC, which is what this study sought to investigate.

# METHODS

## Ethical statement

The Ethical Committee for Epidemiology of Hiroshima University (E1216), Kanagawa Cancer Center Institutional Review Board (2012-EKI-54), and Institutional Review Board of Tokyo Medical University (2017–263) approved this retrospective study using a prospective database, and the informed consent was obtained from patients using the opt-out process.

## Patients

The clinicopathological and prognostic data of patients with clinically node-negative primary lung SCC and a whole tumor size of ≤ 30 mm on preoperative CT who underwent lobectomy or segmentectomy at Hiroshima University Hospital, Kanagawa Cancer Center, or Tokyo Medical University from January 2010 to December 2020 were reviewed. Patients who underwent wedge resection or received induction therapy were excluded. A patient selection flowchart is illustrated in Figure 1.

## Preoperative examinations and operative indications

Preoperative evaluations, including chest CT, whole-body FDG-PET/CT, and brain magnetic resonance imaging, were performed to determine the clinical stage and treatment strategies. Lung cancer staging was undertaken on the basis of the tumor, nodes, and metastases (TNM) Classification of Malignant Tumors, 8th edition.[10]

In our institutions, segmentectomy is performed for patients with peripherally (located in the outer third of the lung field)-located tumors ≤20 mm in size and those considered intolerant to lobectomy. We included SCC with a whole tumor size of ≤ 30 mm on preoperative CT based on the results of the previous study showing comparable results of segmentectomy to lobectomy in NSCLC ≤30 mm in size.[6]

## Histological and pathological evaluations

Pathological staging of lung cancer was conducted based on the TNM Classification of Malignant Tumors, 8th edition,[10] and its histological subtypes were determined according to the World Health Organization classification of lung tumors.[11] Pathological diagnosis of LY was established by immunostaining for D2-40 to locate lymphatic ducts. The presence of V and PL was evaluated using elastic van Gieson staining to determine the tumor invasion beyond the elastic layer of the vessels and visceral pleura.

## Follow-up evaluation

Postoperative follow-up procedures, including physical examination and chest CT every 6 months, were performed for 5 to 10 years after surgical resection. Recurrence was determined based on radiographic features or histological evidence, with the recurrence pattern classified as either local (recurrence in the preserved lobe or surgical stump), locoregional (recurrence within the preserved lung and ipsilateral hilum or mediastinal lymph node metastasis), or distant.

## Statistical analysis

Results are presented as medians and interquartile ranges (IQRs) for continuous variables and as numbers and percentages for categorical variables. Normally and non-normally distributed continuous variables were analyzed using Student's *t*-test and Wilcoxon's rank-sum test, respectively. McNemar's test and paired *t*-tests for categorical and continuous variables, respectively, were used to evaluate propensity score-matched patient pairs. A competing risk analysis was performed for prognosis assessment. The risk of recurrence, which is referred to as the cumulative incidence of recurrence (CIR) in this study and defined as the period from surgery to recurrence, was the main outcome of this study and was estimated using a cumulative incidence function that accounted for mortality without recurrence as a competing event. In the CIR analysis, patients were censored if they were alive and recurrence-free at the last follow-up. The risk of lung cancer-specific death—defined as the cumulative incidence of lung cancer-specific death (CILSD) (i.e., the period from surgery to death from lung cancer)—was estimated using a cumulative incidence function that accounted for death from causes other than lung cancer as a competing event. In CILSD analysis, patients were censored if they were alive with or without recurrence at the last follow-up. Intergroup differences in CIR and CILSD were assessed using the Gray method. The cumulative incidence of all death (CIAD) (i.e., the period from surgery until death from all causes or until the last follow-up visit) was calculated using the Kaplan–Meier method and compared using the log-rank test.

Propensity scores were estimated using a logistic regression model that included solid component size and maximum standardized uptake value ($SUV_{max}$) as variables because they are well-known clinical prognostic factors of early-stage NSCLC and because there were differences between patients who underwent segmentectomy and lobectomy. These propensity scores were then used to create 1:1 matched cohorts; segmentectomy and lobectomy group pairs with an equivalent propensity score were selected using a 1:1 match with a caliper width equal to 0.05 of the standard deviation. Multivariable analysis using the propensity scores and surgical procedures as variables was performed for CIR using the Fine and Gray method to investigate whether the surgical procedure affected prognosis.

In the figures showing the CIR and CILSD of the matched cohort, *p*-values and hazard ratios (HRs) of the Fine and Gray models are shown in figures. In the figures showing the CIAD, *p*-value and HRs of the log-rank test stratified by pairs are shown in figures.

All statistical analyses were performed using EZR version 1.51 (Saitama Medical Center, Jichi Medical University),[12] a graphical user interface for R (The R Foundation for Statistical Computing).

# RESULTS

In total, 230 patients were included in this study. The median follow-up period was 42 months (IQR, 24–62 months). Patient characteristics are shown in Table 1 and the details of the resection are shown in Table S1. Of the 230 patients studied, 172 (74.8%) underwent lobectomy and 58 (25.2%) underwent segmentectomy. The tumor size ($p < 0.001$) was larger in patients who underwent lobectomy, and the $SUV_{max}$, clinical stage, and pathologic stage ($p < 0.001$) were also higher in patients who underwent lobectomy. There were no differences in recurrence patterns ($p = 0.125$) between the patients who underwent lobectomy and those who underwent segmentectomy.

## Prognosis of all included patients

As shown in Figure 2(a), no significant differences were observed in the CIR between patients who underwent lobectomy (5-year CIR rate, 18.1%; 95% confidence interval [CI], 12.1%–25.1%) and those who underwent segmentectomy (5-year CIR rate, 14.2%; 95% CI, 5.1%–27.7%; $p = 0.463$) (Figure 2(a)). Similarly, no significant differences in CIAD were observed between patients who underwent lobectomy (5-year CIAD rate, 18.2%; 95% CI, 13.3%–26.3%) and those who underwent segmentectomy (5-year CIAD rate, 17.1%; 95% CI, 8.8%–31.6%) ($p = 0.693$) (Figure 2(b)). Moreover, CILSD did not significantly differ between patients who underwent lobectomy (5-year CILSD rate, 7.8%; 95% CI, 3.9%–13.3%) and those who underwent segmentectomy (5-year CILSD rate, 2.6%; 95% CI, 0.2%–11.8%) ($p = 0.176$) (Figure 2(c)).

## Prognosis of patients with a whole tumor size of ≤ 20 mm

In patients with a whole tumor size of ≤ 20 mm on preoperative CT scan, no significant differences in CIR were found between the lobectomy (5-year CIR rate, 12.7%; 95% CI, 5.8%–22.5%) and segmentectomy (5-year CIR rate, 12.1%; 95% CI, 3.4%–26.9%) groups ($p = 0.515$) (Figure S1(a)). Similarly, no significant difference in CIAD was observed between the lobectomy (5-year CIAD rate, 10.7%; 95% CI,

**TABLE 1** Characteristics of all included patients

| Variables | Lobectomy $n = 172$ (74.8%) | Segmentectomy $n = 58$ (25.2%) | $p$-value |
|---|---|---|---|
| Age, median (IQR) | 72 (66–76) | 72 (68–77) | 0.215 |
| Sex (%) | | | 0.491 |
| Male | 132 (76.7%) | 47 (81.0%) | |
| Female | 40 (23.3%) | 11 (19.0%) | |
| Brinkman index | 1020 (820–1440) | 1020 (736–1630) | 0.841 |
| Tumor size | | | |
| Whole tumor size (mm), median (IQR) | 21 (15–26) | 15 (13–20) | <0.001 |
| Solid component size (mm), median (IQR) | 21 (15–25) | 14 (12–19) | <0.001 |
| CTR, median (IQR) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 0.988 |
| $SUV_{max}$ | 7.4 (4.6–11.2) | 3.6 (2.6–5.6) | <0.001 |
| Clinical stage (%) | | | <0.001 |
| 0 | 1 (0.6%) | 0 (0%) | |
| IA1 | 9 (5.2%) | 6 (10.3%) | |
| IA2 | 72 (41.9%) | 42 (72.4%) | |
| IA3 | 90 (52.3%) | 10 (17.2%) | |
| LY | 50 (29.1%) | 7 (12.1%) | 0.006 |
| V | 75 (43.6%) | 20 (34.5%) | 0.219 |
| PL | 37 (21.5%) | 6 (10.3%) | 0.047 |
| Lymph node dissection | | | < 0.001 |
| ND1b | 26 (15.1%) | 28 (48.3%) | |
| ND2a-1 | 119 (69.2%) | 30 (51.7%) | |
| ND2a-2 | 27 (15.7%) | 0 (0%) | |
| Pathologic stage (%) | | | <0.001 |
| IA1 | 8 (4.7%) | 8 (13.8%) | |
| IA2 | 50 (29.1%) | 31 (53.5%) | |
| IA3 | 46 (26.7%) | 10 (17.2%) | |
| IB | 39 (22.7%) | 7 (12.1%) | |
| IIA | 1 (0.6%) | 1 (1.7%) | |
| IIB | 23 (13.4%) | 0 (0%) | |
| IIIA | 5 (2.9%) | 1 (1.7%) | |
| Lymph node metastasis | 21 (12.2%) | 0 (0%) | 0.042 |
| Recurrence pattern | | | 0.125 |
| Distant | 6 (3.4%) | 0 (0%) | |
| Locoregional | 18 (11.0%) | 5 (8.6%) | |
| Local | 1 (0.6%) | 0 (0%) | |
| Distant and locoregional | 2 (0.9%) | 0 (0%) | |
| Locoregional and local | 0 (0%) | 1 (1.7%) | |
| Death from any cause | 27 (15.7%) | 9 (15.5%) | 0.974 |
| Death from lung cancer | 12 (7.0%) | 1 (1.7%) | 0.094 |
| Institution | | | <0.001 |
| A | 51 (29.7%) | 25 (43.1%) | |
| B | 66 (38.4%) | 31 (53.4%) | |
| C | 55(32.0%) | 2 (3.4%) | |

Abbreviations: CTR, consolidation tumor ratio; IQR, interquartile range; LY, lymphatic invasion; PL, pleural invasion; SUV, maximum standardized uptake value; V, vascular invasion.

4.9%–23.6%) and segmentectomy (5-year CIAD rate, 16.0%; 95% CI, 7.5%–32.4%) groups ($p = 0.424$) (Figure S1(b)). Additionally, CILSD did not significantly differ between the lobectomy (5-year CILSD rate, 1.5%; 95% CI, 0.1%–7.3%) and segmentectomy (5-year CILSD rate, 3.0%; 95% CI, 0.2%–13.5%) groups ($p = 0.638$) (Figure S1(c)).

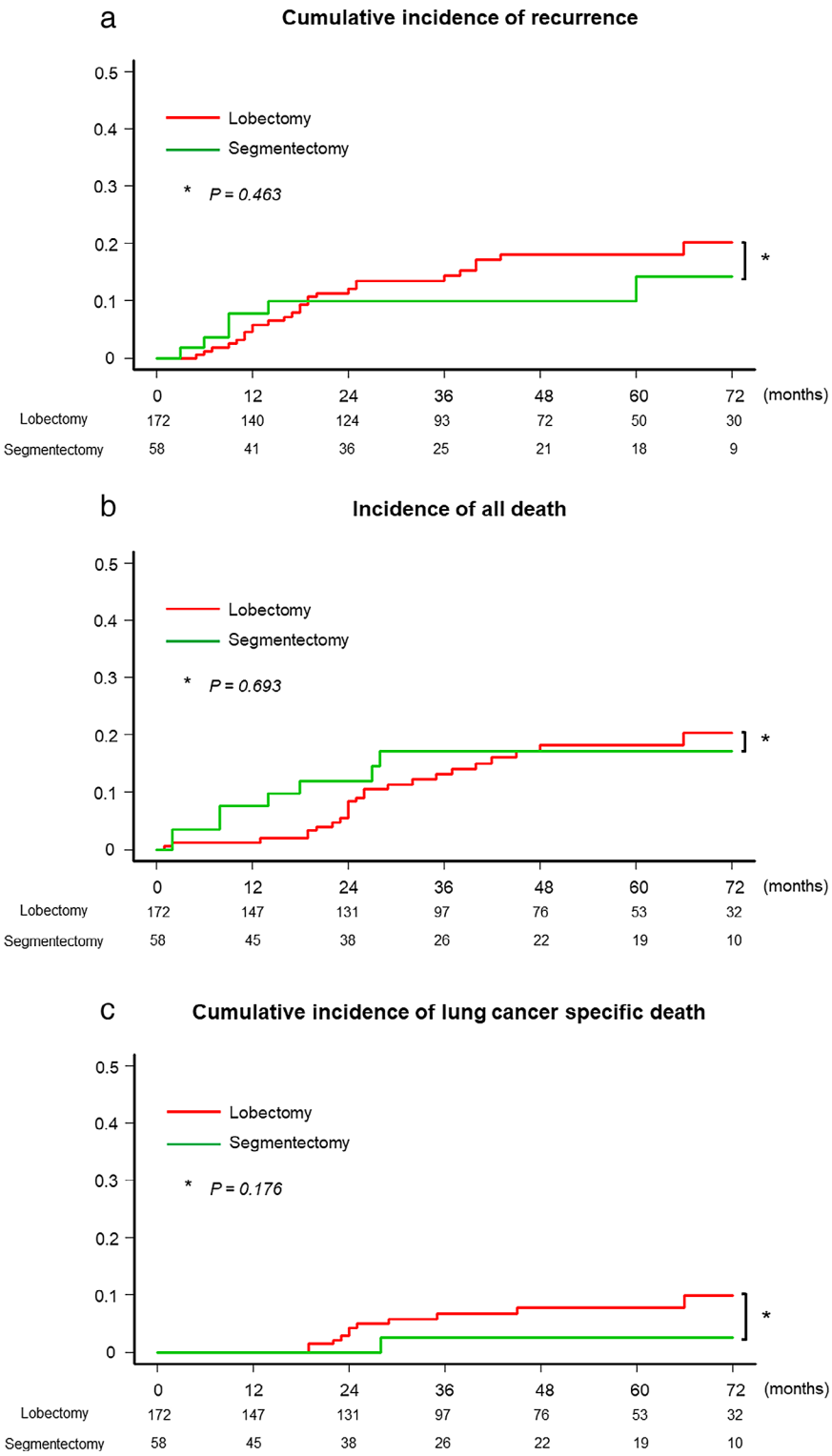


**FIGURE 2** Prognosis of all included patients. (a) No significant differences were observed in the cumulative incidence of recurrence (CIR) between patients who underwent lobectomy (5-year CIR rate, 18.1%; 95% confidence interval [CI], 12.1%–25.1%) and those who underwent segmentectomy (5-year CIR rate, 14.2%; 95% CI, 5.1%–27.7%) ($p = 0.463$). (b) No significant differences were observed in the cumulative incidence of all death (CIAD) between the lobectomy (5-year CIAD rate, 18.2%; 95% CI, 13.3%–26.3%) and segmentectomy (5-year CIAD rate, 17.1%; 95% CI, 8.8%–31.6%) groups ($p = 0.693$). (c) The cumulative incidence of lung cancer-specific death (CILSD) in the lobectomy group (5-year CILSD rate, 7.8%; 95% CI, 3.9%–13.3%) was significantly different from that in the segmentectomy group (5-year CILSD rate, 2.6%; 95% CI, 0.2%–11.8%) ($p = 0.176$)

## Multivariable analysis using propensity score

As shown in Table 2, in the multivariable analysis using propensity scores and surgical procedures as variables, segmentectomy was not identified as a significant predictor of worse CIR (HR, 0.987; 95% CI, 0.393–2.418; $p = 0.980$).

## Prognosis of propensity score-matched patients

The characteristics of the propensity-matched patients are summarized in Table 3 and the details of the resection are shown in Table S2. No differences were found in characteristics between the propensity score-matched patients who underwent lobectomy and those who underwent

**TABLE 2** Multivariable analysis for the cumulative incidence of recurrence using propensity score and procedure as variables by the fine and gray method

| Variables | HR (95% CI) | *p*-value |
|---|---|---|
| Procedure (segmentectomy/ lobectomy [ref]) | 0.987 (0.393–2.418) | 0.980 |

Abbreviations: CI, confidence interval; HR, hazard ratio.

segmentectomy. Similar to the results before propensity score matching, no significant difference in CIR was found between the matched lobectomy (5-year CIR rate, 8.6%; 95% CI, 2.1%–21.1%) and segmentectomy (5-year CIR rate, 8.0%; 95% CI, 2.0%–19.5%) groups (HR, 0.926; 95% CI, 0.219–3.916; $p = 0.920$) (Figure 3(a)). Moreover, CIAD did not significantly differ between the matched lobectomy (5-year CIAD rate, 7.5%; 95% CI, 2.5%–21.5%) and segmentectomy (5-year CIAD rate, 20.0%; 95% CI, 9.1%–37.8%) groups (HR, 2.333; 95% CI, 0.603–9.023; $p = 0.220$) (Figure 3(b)). As shown in Figure 3(c), the CILSD for the propensity score-matched lobectomy group (5-year CILSD rate, 2.5%; 95% CI, 0.2%–11.5%) was not significantly different from that for the propensity score-matched segmentectomy group (5-year CILSD rate, 3.5%; 95% CI, 0.2%–15.4%) (HR, 0.612; 95% CI, 0.059–6.317; $p = 0.680$) (Figure 3(c)).

## DISCUSSION

In this study, there was no difference in the CIR of primary lung SCC between segmentectomy and lobectomy. Similar results were obtained after propensity score matching was performed. Furthermore, segmentectomy was not found to be a significant predictor of CIR in the multivariable analysis. These results suggest that segmentectomy is feasible for treating lung SCC.

Tyrosine kinase inhibitors (TKIs) exert positive therapeutic effects on lung adenocarcinoma patients with EGFR mutations[13–15] or ALK rearrangement.[16,17] Adjuvant therapy with osimertinib, a third-generation EGFR-TKI, has also shown favorable survival.[18] However, therapeutic options for lung SCC are fewer and the prognosis is worse than that of adenocarcinoma. Therefore, it is important to evaluate the outcomes of resection for lung SCC. Because lung SCC occurs in smokers, it may be difficult for some patients to receive adequate pharmacological treatment after recurrence, considering their complex background (e.g., comorbidities and poor cardiopulmonary function). Therefore, we believe that the results of this study are meaningful because they demonstrated that segmentectomy is useful even for early-stage lung SCC.

CIR was set as the primary outcome of our study. Studies on the prognosis of patients undergoing lung cancer resection generally select recurrence-free survival (RFS) or OS as their main outcomes. However, recurrence and death from causes other than lung cancer are treated as the same event in RFS analysis. In OS analysis, all deaths are equally treated as events, regardless of the cause of death. Therefore, we thought that CIR was suitable as the main outcome for oncological analysis—especially in this retrospective study, where bias might have existed in the procedure selection.

Ground-glass opacity on preoperative CT, which is known as a good prognostic factor for NSCLC,[19] is thought to reflect lepidic and other less invasive components of adenocarcinoma.[20] Therefore, SCC is generally considered a radiologically pure solid tumor on preoperative CT. Although the feasibility of segmentectomy for treating radiologically pure solid tumors was investigated in a previous study, histological subtypes other than adenocarcinoma were identified as significant predictors of a poor prognosis in that study.[5] In contrast, it is difficult to establish a preoperative diagnosis in patients with early-stage lung cancer. Hence, an important and novel finding of this study is that segmentectomy may be a feasible treatment option for patients with lung SCC, which is the second most common histological subtype of NSCLC.

In our study, the solid component size and $SUV_{max}$ of patients who underwent lobectomy were smaller and lower in the matched cohort than all patient cohorts because of the small sample size of patients who underwent segmentectomy. The upper quartile of tumor size in the matched cohort was near 20 mm and the segmentectomy outcome was better in patients with tumors smaller than 20 mm. This may mean that segmentectomy is more suitable in patients with tumors smaller than 20 mm, and solid component size and $SUV_{max}$ should be considered when planning segmentectomy for tumors of 20 to 30 mm in size.

This study has several limitations. First, the number of patients was restricted. In contrast, the multivariate analysis for all included patients using the propensity scores and procedures as variables did not show that the procedure was a significantly worse prognostic factor. Moreover, we believe that this study is significant in demonstrating the feasibility of segmentectomy. Second, because this was a retrospective study and the final decision about the procedure was influenced by the preference of the attending surgeon and each patient, selection bias may have affected the results. The proportion of segmentectomy was also different between institutions, but we could not include the institution as a variable for propensity score matching because of the large difference in the proportion of segmentectomy between institutions and the restricted number of included patients. Although we set CIR as a primary endpoint and propensity score matching using solid component size and $SUV_{max}$ as representative clinical oncological factors were performed to investigate oncological outcomes, data on several factors, which could affect prognosis, such as an indication of segmentectomy (intentional or passive), tumor location, comorbid conditions, and lung function, were not available in our database. Patient backgrounds may be different even after propensity score matching. For example, the extent of lymph node dissection is different, and this might affect the incidence of lymph node metastasis. The incidence of LY is

**TABLE 3** Characteristics of the matched patients

| Variables | Lobectomy $n = 43$ | Segmentectomy $n = 43$ | $p$-value |
|---|---|---|---|
| Age, median (IQR) | 72 (66–77) | 73 (69–77) | 0.562 |
| Sex (%) | | | 1.000 |
| Male | 36 (83.7%) | 36 (83.7%) | |
| Female | 7 (16.3%) | 7 (16.3%) | |
| Brinkman index | 1000 (645–1575) | 1040 (800–1580) | 0.580 |
| Tumor size | | | |
| Whole tumor size (mm), median (IQR) | 15 (13–20) | 16 (13–22) | 0.216 |
| Solid component size (mm), median (IQR) | 15 (12–20) | 17 (12–20) | 0.426 |
| CTR, median (IQR) | 1.00 (1.00–1.00) | 1.00 (1.00–1.00) | 0.513 |
| $SUV_{max}$ | 4.5 (3.4–8.0) | 4.0 (3.0–6.2) | 0.217 |
| Clinical stage (%) | | | 0.701 |
| IA1 | 5 (11.6%) | 3 (7.0%) | |
| IA2 | 28 (65.1%) | 31 (72.1%) | |
| IA3 | 10 (23.3%) | 9 (20.9%) | |
| LY | 16 (37.2%) | 5 (11.6%) | 0.005 |
| V | 17 (39.5%) | 17 (39.5%) | 1.000 |
| PL | 6 (14.0%) | 5 (11.6%) | 0.747 |
| Lymph node dissection | | | <0.001 |
| ND1b | 3 (7.0%) | 18 (41.9%) | |
| ND2a-1 | 34 (79.1%) | 25 (58.1%) | |
| ND2a-2 | 6 (14.0%) | 0 (0%) | |
| Pathologic stage (%) | | | 0.569 |
| IA1 | 3 (7.0%) | 3 (7.0%) | |
| IA2 | 24 (55.8%) | 23 (53.5%) | |
| IA3 | 7 (16.3%) | 10 (23.3%) | |
| IB | 6 (14.0%) | 5 (11.6%) | |
| IIB | 2 (4.7%) | 0 (0%) | |
| IIIA | 1 (2.3%) | 1 (2.3%) | |
| Lymph node metastasis | 0 (0%) | 0 (0%) | NA |
| Recurrence pattern | | | 0.244 |
| Distant | 2 (4.7%) | 0 (0%) | |
| Locoregional | 2 (4.7%) | 2 (4.7%) | |
| Local | 0 (0%) | 1 (2.3%) | |
| Death from any cause | 4 (9.3%) | 8 (18.6%) | 0.209 |
| Death from lung cancer | 2 (4.7%) | 1 (2.3%) | 0.553 |
| Institution | | | <0.001 |
| A | 13 (30.2%) | 20 (46.5%) | |
| B | 18 (41.9%) | 23 (53.5%) | |
| C | 12 (27.9%) | 0 (0%) | |

Abbreviations: CTR, consolidation tumor ratio; IQR, interquartile range; LY, lymphatic invasion; PL, pleural invasion; SUV, maximum standardized uptake value; V, vascular invasion.

different even after propensity score matching. Therefore, a large-sized prospective study is needed to overcome these limitations. Third, pathological data, such as spread through air spaces and margin distance were also not included in our database. Finally, patients who were switched to lobectomy were evaluated together with patients in the lobectomy group; there are no data on the patients who were switched to lobectomy. Therefore, a prospective study or subgroup analysis of a prospective trial, such as JCOG0802/WJOG4607L,[3] should be conducted to overcome the above-mentioned limitations of our study. Because the patients included in this study were selected based on the

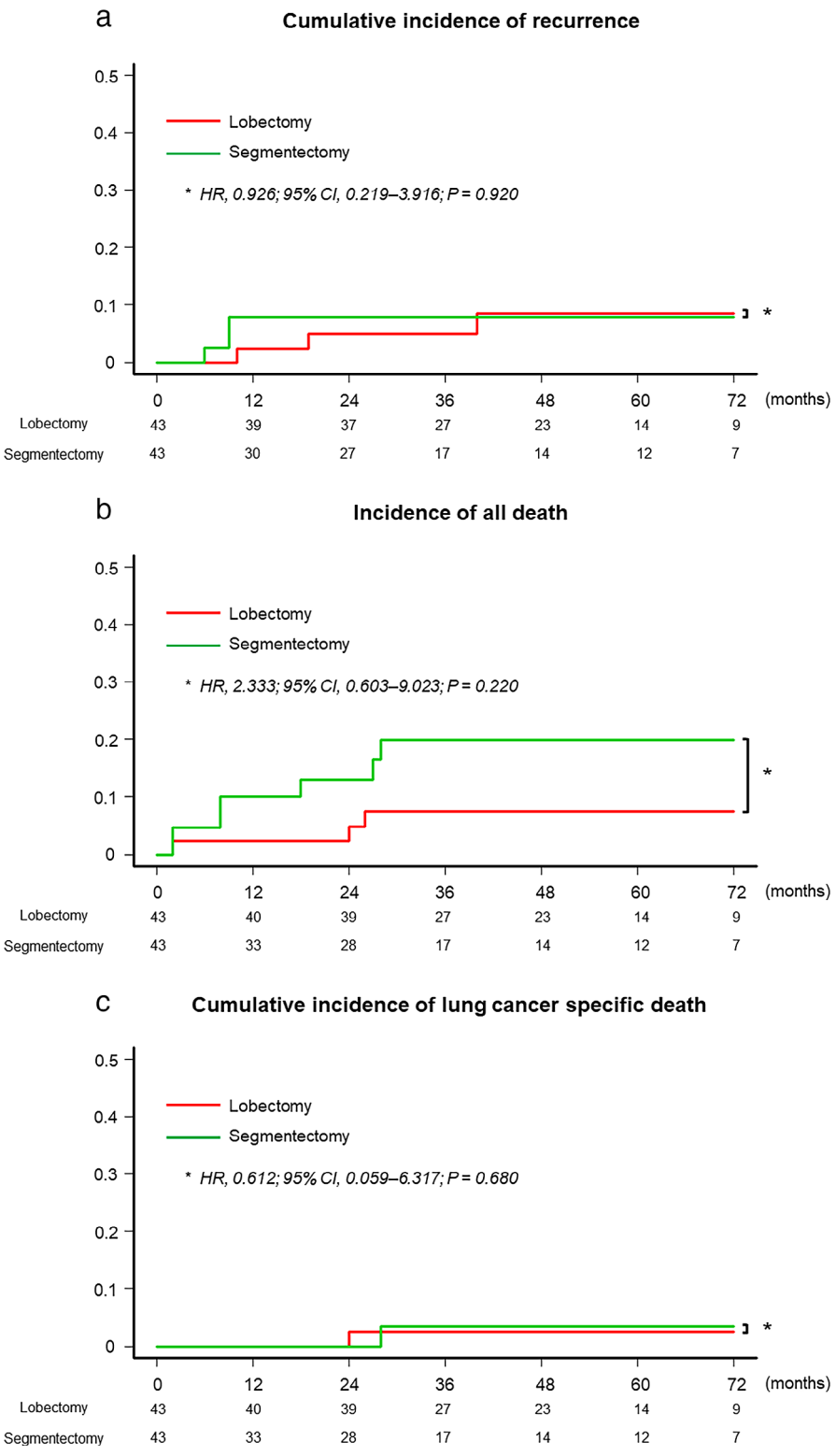


**FIGURE 3** Prognosis of the propensity score-matched patients. (a) The cumulative incidence of recurrence (CIR) for the matched lobectomy group (5-year CIR rate, 8.6%; 95% CI, 2.1%–21.1%) did not significantly differ from that for the matched segmentectomy group (5-year CIR rate, 8.0%; 95% CI, 2.0%–19.5%) (hazard ratio [HR], 0.926; 95% CI, 0.219–3.916; $p = 0.920$). (b) No significant difference was found in the cumulative incidence of all death (CIAD) between the lobectomy (5-year CIAD rate, 7.5%; 95% CI, 2.5%–21.5%) and segmentectomy (5-year CIAD rate, 20.0%; 95% CI, 9.1%–37.8%) groups (HR, 2.333; 95% CI, 0.603–9.023; $p = 0.220$). (c) No significant difference in cancer-specific death (CILSD) was noted between the lobectomy (5-year CILSD rate, 2.5%; 95% CI, 0.2%–11.5%) and segmentectomy (5-year CILSD rate, 3.5%; 95% CI, 0.2%–15.4%) groups (HR, 0.612; 95% CI, 0.059–6.317; $p = 0.680$)

pathological characteristics of the resected tumors, it is difficult to directly adapt the results of our study to the selection of a surgical procedure. However, the results of this study are meaningful and complement the results of JCOG0802/WJOG4607L and previous retrospective studies.

In conclusion, compared with lobectomy, there were no significant differences in CIR after segmentectomy for clinically node-negative lung SCC with a whole tumor size of ≤ 30 mm on preoperative CT scan even in the propensity score-matched cohort. Segmentectomy can be a treatment option for patients with clinically early-stage lung SCC although tumors smaller than 20 mm may be a better indication, and $SUV_{max}$ and solid component size may need to be considered when deciding treatment strategy.

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## FUNDING INFORMATION

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## ETHICS APPROVAL STATEMENT

The Ethical Committee for Epidemiology of Hiroshima University (E1216), Kanagawa Cancer Center Institutional Review Board (2012-EKI-54), and Institutional Review Board of Tokyo Medical University (2017–263) approved this retrospective study and this study was conducted according to the tenets of the Declaration of Helsinki.

## PATIENT CONSENT STATEMENT

Informed Consent was obtained from the patients for publication using the opt-out process.

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## REFERENCES

1. Ginsberg RJ, Rubinstein LV, Lung Cancer Study Group. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Ann Thorac Surg. 1995;60:615–22.
2. Goya T, Asamura H, Yoshimura H, Kato H, Shimokata K, Tsuchiya R, et al. Prognosis of 6644 resected non-small cell lung cancers in Japan: a Japanese lung cancer registry study. Lung Cancer. 2005;50:227–34.
3. Saji H, Okada M, Tsuboi M, Nakajima R, Suzuki K, Aokage K, et al. Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicenter, open-label, phase 3, randomized, controlled, non-inferiority trial. Lancet. 2022;399:1607–17.
4. Kamigaichi A, Tsutani Y, Kagimoto A, Fujiwara M, Mimae T, Miyata Y, et al. Comparing segmentectomy and lobectomy for clinical stage IA solid-dominant lung cancer measuring 2.1 to 3 cm. Clin Lung Cancer. 2020;21:e528–38.
5. Tsubokawa N, Tsutani Y, Miyata Y, Handa Y, Misumi K, Hanaki H, et al. Segmentectomy versus lobectomy for radiologically pure solid clinical T1a-bN0M0 lung cancer. World J Surg. 2018;42:2493–501.
6. Kagimoto A, Tsutani Y, Mimae T, Miyata Y, Okada M. Segmentectomy versus lobectomy for solid predominant cN0 lung cancer: analysis using visual evaluation of positron emission tomography. Eur J Cardiothorac Surg. 2022;61:279–86.
7. Kamigaichi A, Tsutani Y, Mimae T, Miyata Y, Ito H, Nakayama H, et al. Prognosis of segmentectomy and lobectomy for radiologically aggressive small-sized lung cancer. Eur J Cardiothorac Surg. 2020;58:1245–53.
8. Sawabata N, Miyaoka E, Asamura H, Nakanishi Y, Eguchi K, Mori M, et al. Japanese lung cancer registry study of 11,663 surgical cases in 2004: demographic and prognosis changes over decade. J Thorac Oncol. 2011;6:1229–35.
9. Kagimoto A, Tsutani Y, Shimada Y, Mimae T, Miyata Y, Ito H, et al. Oncological outcome of segmentectomy for early-stage non-small-cell lung cancer with invasive characteristics: a multicenter study. Eur J Cardiothorac Surg. 2022;62.
10. Goldstraw P, Chansky K, Crowley J, Rami-Porta R, Asamura H, Eberhardt WE, et al. The IASLC lung cancer staging project: proposals for revision of the TNM stage groupings in the forthcoming (eighth) edition of the TNM classification for lung cancer. J Thorac Oncol. 2016;11:39–51.
11. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 world health organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol. 2015;10:1243–60.
12. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transplant. 2013;48:452–8.
13. Rosell R, Carcereny E, Gervais R, Vergnenegre A, Massuti B, Felip E, et al. Erlotinib versus standard chemotherapy as first-line treatment for European patients with advanced EGFR mutation-positive non-small-cell lung cancer (EURTAC): a multicentre, open-label, randomised phase 3 trial. Lancet Oncol. 2012;13:239–46.
14. Mok TS, Wu Y-L, Thongprasert S, Yang CH, Chu DT, Saijo N, et al. Gefitinib or carboplatin–paclitaxel in pulmonary adenocarcinoma. N Engl J Med. 2009;361:947–57.
15. Sequist LV, Yang JC-H, Yamamoto N, O'Byrne K, Hirsh V, Mok T, et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol. 2013;31:3327–34.
16. Shaw AT, Kim DW, Nakagawa K, Seto T, Crinó L, Ahn MJ, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013;368:2385–94.
17. Hida T, Nokihara H, Kondo M, Kim YH, Azuma K, Seto T, et al. Alectinib versus crizotinib in patients with ALK-positive non-small-cell lung cancer (J-ALEX): an open-label, randomised phase 3 trial. Lancet. 2017;390:29–39.
18. Wu YL, Tsuboi M, He J, John T, Grohe C, Majem M, et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. N Engl J Med. 2020;383:1711–23.
19. Hattori A, Suzuki K, Takamochi K, Wakabayashi M, Aokage K, Saji H, et al. Prognostic impact of a ground-glass opacity component in clinical stage IA non-small cell lung cancer. J Thorac Cardiovasc Surg. 2021;161:1469–80.
20. Travis WD, Brambilla E, Noguchi M, Nicholson AG, Geisinger KR, Yatabe Y, et al. International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society international multidisciplinary classification of lung adenocarcinoma. J Thorac Oncol. 2011;6:244–85.

## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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