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Original Article

Lung Cancer Surgery Did Not Show Any Relationship with Survival

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Purpose: There is limited evidence concerning the computed tomography (CT) follow-up interval to detect recurrence and second primary cancers after surgery for non-small-cell lung cancer (NSCLC). In this study, we aimed to investigate the impact of CT interval on survival after surgery.

Methods: This retrospective study analyzed the prognosis of 103 patients who underwent periodic CT after complete resection for pathological stage II–III NSCLC at a single institute between 2015 and 2020. The patients were stratified based on the follow-up CT intervals into the half-year group (Group H) and annual group (Group A). Additionally, the underlying differences in clinical backgrounds between the 2 groups were adjusted by propensity score matching.

Results: A total of 103 patients (Group H, 76 patients; Group A, 27 patients) were included in this study. The 5-year overall survival (OS) rates in the unmatched cohort were 83.5% and 95.2% in groups H and A, respectively ($P = 0.17$). Among the matched cohort, 42 and 21 patients were in groups H and A. The 5-year OS rates of the matched cohort were 89.8% and 94.4% in groups H and A ($P = 0.45$), with no significant difference.

Conclusions: There was no association between CT intervals and postoperative survival.

Keywords: computed tomography surveillance, lung cancer surgery, postoperative follow-up, second primary lung cancer, propensity score matching

Introduction

Patients with localized non-small-cell lung cancer (NSCLC) are treated with radical surgery; however, the current guidelines do not present the optimal timing of postoperative surveillance aimed at detecting cancer recurrence and second primary lung cancers.[1–4] Specifically, there is no definitive evidence for postoperative surveillance after curative lung cancer surgery. Guidelines of the European Society for Medical Oncology fundamentally recommend volume chest computed tomography (CT) scans at least at 12 and 24 months for the first 2 years.[1] By contrast, those of the American

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College of Clinical Pharmacy, American Society of Clinical Oncology, and National Comprehensive Cancer Network suggest arranged CT every 4–6 months for the first 2 years.[2–4] We hypothesized that a curable lung cancer recurrence or second primary lung cancer may be found at a reasonable time and that earlier detection of these events may improve survival outcomes. Conversely, long intervals are preferred to reduce economic costs and physical radiation exposure. Therefore, we aimed to evaluate the prognostic impact of CT frequency after lung cancer surgery, particularly in patients with advanced-stage cancer, and elucidate the optimal postoperative surveillance interval.

Materials and Methods

Study design

We performed a retrospective cohort study to compare the overall survival (OS), recurrence-free survival (RFS), and post-recurrence survival in patients with pathological stage II–III NSCLC who underwent radical surgery and CT surveillance at various intervals. Additionally, we performed a descriptive analysis of recurrence based on detection modalities, treatments, trends (locoregional and distant), and the development of second primary lung cancer.

Patients

All patients who underwent complete resection for preoperative clinical stage I–IIIA NSCLC, pathological stage II–III between January 2015 and December 2020, and who underwent routine postoperative CT surveillance at Kansai Medical University Hospital with or without postoperative adjuvant chemotherapy were included in this study. Patients who underwent incomplete resection, those treated with preoperative chemotherapy and/or radiotherapy, those with histological features, including small-cell carcinoma and carcinoma in situ, and those who did not undergo CT at the optimal timing were excluded. Subsequently, we collected the following clinical data by reviewing a database that retrospectively maintained detailed relevant information and prognoses of surgical cases: age, sex, body mass index (BMI), percentage of forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC), smoking history (pack-years), preoperative carcinoembryonic antigen (CEA) level, comorbidities including diabetes mellitus, chronic obstructive pulmonary disease (COPD), heart failure, and coronary artery disease, history of cancer within 5 years, Charlson comorbidity index,[5] surgical procedure, operation time, bleeding amount, histology, pathological stage, N status, and treatment with adjuvant chemotherapy. Histological tumor type was determined according to the 4th edition of the World Health Organization Classification of Tumors.[6] The tumor stage was determined according to the 8th edition of the UICC for TNM classification.[7] The modality by which the recurrence was first detected was noted. The modalities included chest radiography with X-rays, CT for the chest and abdominal area, symptoms, tumor markers, and brain metastasis were screened using magnetic resonance imaging (MRI) or CT if enhanced imaging was possible.

Recurrence was defined as local lesions if they were found in a previous operative field (resection margin and pulmonary hilum to a mediastinal lymph node on the same side as the primary tumor). In contrast, distant recurrence was defined as tumor recurrence in the contralateral lung/lymph nodes or an area other than the thoracic area. A new pulmonary lesion was considered a second primary tumor rather than a recurrence when it was of a different histologic type, with a time interval of >3 years after resection of the primary tumor, or was judged by the attending doctor.[8–11] The treatment modalities for recurrence include complete surgical resection of a chest or brain lesion, high-dose radiotherapy for locoregional recurrence, and chemotherapy and chemoradiation therapy as systemic therapy for advanced disease. Best supportive care and palliative radiation therapy were included as the treatment options in this study.

Surveillance intensity stratified by CT interval

The half-year or annual cycle interval corresponds to major guideline recommendations (European Society for Medical Oncology, American College of Clinical Pharmacy, American Society of Clinical Oncology, and National Comprehensive Cancer Network).[1–4] The interval until the second postoperative CT scan was used to classify the patients into the following 2 groups:

Group H (half-year): patients who underwent their first CT scan between 3 and 9 months postoperatively and at approximately half-year intervals thereafter.

Group A (annual): patients who underwent at least 1 CT scan at intervals of 10–14 months, that is, patients who underwent their first CT scan at 10–14 months postoperatively or their first CT scan at 6 months postoperatively, followed by a second CT scan at an interval of 10–14 months (**Fig. 1**). During the first 3 years after surgery, follow-up procedures were performed

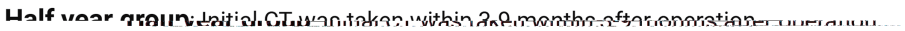

Fig. 1 Definition of the classification of Group H (half-year group) and Group A (annual group)

in both groups. Physical examination, chest radiography with X-rays, and blood tests were performed 2–3 weeks post-operation and every 3 months thereafter. Tumor markers, mainly CEA and squamous cell carcinoma antigen levels, were measured every 3 months at an outpatient clinic. MRI for detecting brain metastasis and F-18 fluorodeoxyglucose-positron emission tomography for detecting local and distant metastases were not performed routinely as stated by the majority of North American guidelines and due to national health insurance limits.

Allocation of CT interval: Half-year or annual interval

There is not a common policy in our department; however, each attending physician determines the follow-up interval for postoperative CT based on major European and North American guidelines.[1–4] The timing of follow-up CT was decided on the preference of 5 outpatient attendant surgeons (TM, HH, TS, YT, and HM) at our institution. When allocating patients into the 2 groups (half-year or annual), the individual recurrence risk per case was not strongly considered; annual CT follow-up was performed solely by TM, while the remaining attending doctors (HH, TS, YT, and HM) conducted the half-year CT follow-up; consequently, patient selection for these groups was not intentional. Since this study received ethical approval from our institution's Ethics Committee and was a retrospective study, patients were not informed of the follow-up policy in advance. However, they were given the opportunity to review detailed study methods, including CT follow-up intervals, and were provided with the option to refuse to provide information through a disclosure document. Consequently, we considered that there was not any disadvantage regarding the CT interval among those patients. When stratifying patients into the H or A groups, one should consider selection bias. In particular, among patients with an

annual CT interval after the first examination at 6 months post-surgery, the minimum recurrence-free period was estimated to be 16 months (**Fig. 1**). Consequently, the recurrence-free period of patients who underwent half-year or annual CT intervals differed by approximately 6 months to 1 year; therefore, all the patients with shorter recurrence-free intervals were inevitably classified into Group H. To address such interval bias, we followed a method outlined in a previous study[12] and accordingly selected only those patients who remained cancer-free for 16 months post-surgery and excluded patients with early recurrence triggered by symptoms or detected by chest X-ray films or the first CT scan.

Analytic methods

Descriptive statistics were reported using the mean (standard deviation [SD]) for variables that were approximately normally distributed, median (interquartile range [IQR] or range) for variables that did not follow a normal distribution, and count (percent) for categorical variables. Continuous variables were compared using the t-test or Mann–Whitney U test. Categorical data were assessed using the chi-square test. All *P*-values were 2-tailed, and values <0.05 were considered significant. Furthermore, propensity score matching for adjusting the background of the 2 groups divided by the CT interval was performed to properly evaluate the prognostic impact of surveillance intensity. The propensity score was calculated using logistic regression. Candidate covariates of interest for propensity score matching were determined based on the literature, clinical significance, and number of cases in the 2 groups and included age, sex, adjuvant chemotherapy, and pathological stage. Spearman's correlation analysis was used to assess the covariance of 2 variables. We used the Optmatch package in R software (version 4.2.2 for Windows) for analysis. Matching was performed by sampling without replacement and using a 0.2 caliper. The matching ratio of Group H to Group A was 2:1 because more patients were included in Group H. The balance between the 2 matched groups was assessed by calculating standardized mean differences (SMD), for which a difference of <0.20 was considered to indicate good balance. OS was calculated as the time from surgery to death or last follow-up. The RFS was calculated from the date of surgery to the date of recurrence, death, or last follow-up. The Kaplan–Meier method was used to assess survival curves, and the log-rank test was used to evaluate the statistical significance of differences between the 2 groups. The Cox proportional hazards model was also used to evaluate the effect of CT interval on survival and post-recurrence survival while adjusting for other related factors. Covariates of interest in the Cox proportional hazard model for OS and post-recurrence survival were CT interval and propensity score. All analyses were performed using EZR (Saitama Medical Center, Jichii Medical University, Saitama, Japan), which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria).[13]

Results

Patients' characteristics

A total of 166 patients underwent surgery for NSCLC pathological stages II or III at our institution between 2015 and 2020. After excluding patients whose conditions were inappropriate for analysis, 103 patients were included in this study: 76 patients in Group H and 27 patients in Group A. In Group A, the first CT scan was performed at 10–14 months post-surgery in 4 patients, and the interval between the first and second CT was at 10–14 months in 23 patients. The clinical characteristics of the patients stratified by the CT interval are listed in **Table 1**. There were no significant differences in age, sex, BMI, smoking history, and preoperative complications that affected prognosis and surgery-related factors, including procedure, bleeding amount, operation time, and N Status. Adjuvant chemotherapy was administered to 42/76 (55.3%) and 8/27 (29.6%) patients in groups H and A, respectively ($P = 0.039$). Additionally, Group H had slightly more patients with stage III (27/76 in stage IIIA vs. 1/76 in stage IIIB) ($P = 0.13$) and adenocarcinoma histology ($P = 0.13$) than Group A.

When selecting covariates of interest for propensity score matching, we performed Spearman's correlation analysis to examine the correlation between N Status and pathological stage. N status could not be incorporated into the propensity score matching as a variable because it was highly correlated with a pathological stage (correlation coefficient: 0.48, $P < 0.01$). After adjusting for clinical background using propensity score matching, 42 patients in Group H and 21 patients in Group A were matched. The clinical characteristics after adjustment are listed in **Table 2**. After matching, each number of patients with chemotherapy was 17/42 (40.5%) vs. 8/21 (38.1%), $P = 1.00$, SMD 0.049), demonstrating that a similar number with chemotherapy was properly matched. The clinical characteristics of the 2 groups did

Table 1

Table 2 Patient characteristics after matching

	Half-year (n = 42)	A year (n = 21)	*P* value	SMD
CT interval (days), median (range)	167 (91–266)	366 (316–413)		
Age, mean (SD)	69.8 (9.8)	71.1 (9.8)	0.59	0.15
Male, n (%)	30 (71.4)	15 (71.4)	1	<0.001
Smoking history (pack-years)				
≤30, n (%)	21 (50.0)	9 (42.9)	0.79	0.14
>30, n (%)	21 (50.0)	12 (57.1)		
CEA, median (IQR)	4.4 (2.3–6.9)	4.7 (3.4–6.4)	0.91	0.037
Body mass index, mean (SD)	22.8 (3.2)	23.3 (3.7)	0.58	0.14
Charlson comorbidity index				
0 or 1, n (%)	33 (78.6)	17 (81.0)	1	0.059
2 or over 2, n (%)	9 (21.4)	4 (19.0)		
COPD, n (%)	8 (19.0)	3 (14.3)	0.74	0.13
Coronary artery disease, n (%)	2 (4.8)	1 (4.8)	1	<0.001
Diabetes mellitus, n (%)	5 (11.9)	6 (28.6)	0.16	0.42
History of cancer within 5 years, n (%)	6 (14.3)	1 (4.8)	0.41	0.33
Heart failure, n (%)	0	0	1	<0.001
FEV1.0/FVC, median (IQR)	71.7 (62.9–79.1)	71.0 (65.9–77.3)	0.83	0.025
Procedure			0.51	0.38
Lobectomy, n (%)	40 (95.2)	19 (90.5)		
Segmentectomy, n (%)	0	0		
Wedge resection, n (%)	1 (2.4)	0		
Pneumonectomy, n (%)	0	0		
Bilobectomy, n (%)	1 (2.4)	2 (9.5)		
Thoracotomy, n (%)	10 (23.8)	4 (19.0)	0.76	0.12
Bleeding amount (mL), median (IQR)	51.0 (10.3–153.5)	30.0 (5.0–100.0)	0.58	0.35
Operation time (min), median (IQR)	121 (96.3–153.3)	129 (109–148)	0.82	0.082
Histology			0.78	0.15
Adenocarcinoma, n (%)	25 (59.5)	11 (52.4)		
Squamous cell carcinoma, n (%)	14 (33.3)	8 (38.1)		
Others, n (%)	3 (7.1)	2 (9.5)		
Pathological stage			0.76	0.12
II, n (%)	32 (76.2)	17 (81.0)		
IIA/IIB	7/25	3/14		
III, n (%)	10 (22.8)	4 (19.0)		
IIIA/IIIB	10/0	4/0		
N status			0.7	0.24
0, n (%)	17 (40.5)	11 (52.4)		
1, n (%)	20 (47.6)	8 (38.1)		
2, n (%)	5 (11.9)	2 (9.5)		
Adjuvant chemotherapy, n (%)	17 (40.5)	8 (38.1)	1	0.049
Death, n (%)	4 (9.5)	1 (4.8)	0.66	
Recurrence, n (%)	12 (28.6)	4 (19.0)	0.54	
Detection of second primary lung tumor, n (%)	0	1 (4.8)	0.66	

CT: computed tomography; CEA: carcinoembryonic antigen; COPD: chronic obstructive pulmonary disease; FEV: forced expiratory volume in one second; FVC: forced vital capacity; SMD: standardized mean difference; IQR: interquartile range; SD: standard deviation

[CI]: 71.0%–90.9%) in Group H and 95.2% (95% CI: 70.7%–99.3%) in Group A, with no significant difference between the groups (P = 0.17) (**Fig. 2A**). Recurrence was observed in 28/76 patients (36.8%) in Group H and 4/27 (14.8%) in Group A (P = 0.06). The 5-year RFS rate was 53.0% (95% CI: 39.4%–64.8%) in Group H and 81.1% (95% CI: 56.5%–92.6%) in Group A, with a significant difference between the groups (P = 0.017) (**Fig. 3A**). In the multivariate analysis of the Cox proportional hazards model of OS, surveillance intensity was

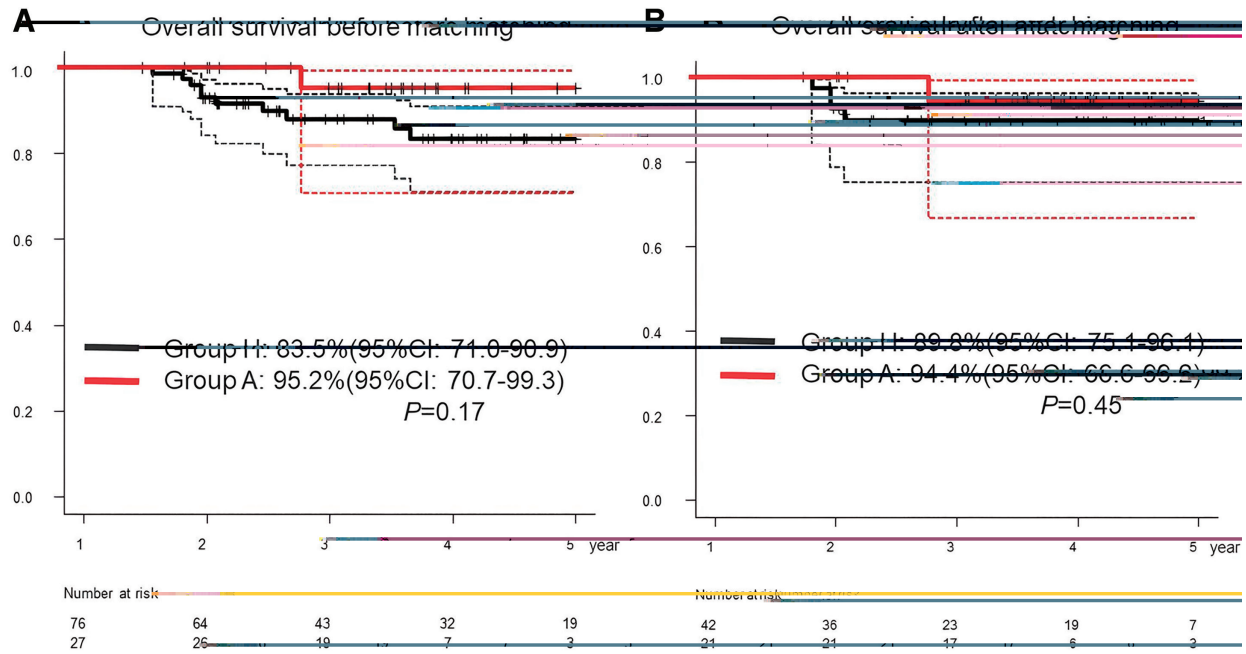

Fig. 2 Five-year OS curves, stratified by CT interval. The 5-year OS curves were not significantly different before and after matching ($P = 0.17$ and $P = 0.45$, respectively). (**A**) OS curves before matching. (**B**) OS curves after matching. OS: overall survival

Table 3 Multivariate analysis for overall survival and post-recurrence survival

Overall survival	Hazard ratio	95% CI	*P* value
Surveillance intensity: Half-year	Reference		
Surveillance intensity: Annual	0.43	0.048–3.9	0.46
Propensity score	2.8	0.00051–15860	0.82
Post-recurrence survival	Hazard ratio	95% CI	*P* value
Surveillance intensity: Half-year	Reference		
Surveillance intensity: Annual	1.1	0.11–10.6	0.94
Propensity score	0.0074	0.00000025–225	0.35

95% CI: 95% confidence interval

not associated with OS (hazard ratio [HR]: 0.43, 95% CI: 0.048–3.9, $P = 0.46$) (**Table 3**).

The median post-recurrence survival time was 317 days in Group H (range, 14–1918 days) and 291.5 days in Group A (range, 70–700 days), which was not significantly different between the groups ($P = 0.41$). In the multivariate analysis of the Cox proportional hazards model, surveillance intensity was not associated with post-recurrence survival either (HR: 1.1, 95% CI: 0.11–10.6, $P = 0.94$) (**Table 3**).

Surveillance intensity and survival in the matched cohort

After adjusting for clinical background using propensity score matching, 4/42 (9.5%) patients in Group H and 1/21 (4.8%) patients in Group A died during the follow-up period ($P = 0.66$). The 5-year OS rate was 89.8% (95% CI: 75.1%–96.1%) in Group H and 94.4% (95% CI: 66.6%–99.2%) in Group A, with no significant difference between the 2 groups ($P = 0.45$) (**Fig. 2B**). Regarding cancer recurrence, 12/42 patients (28.6%) and 4/21 patients (19.0%) in groups H and A, respectively, experienced recurrence during the follow-up period ($P = 0.54$). The 5-year RFS rate was 62.0% (95% CI: 41.6%–77.1%) in Group H and 68.7% (95% CI: 34.0%–87.7%) in Group A, with no significant difference between the 2 groups ($P = 0.43$) (**Fig. 3B**). The median post-recurrence survival time was 181 (range, 14–1918 days) and 291.5 days (range, 70–700 days) in groups H and A, respectively, with no significant difference between the 2 groups ($P = 0.95$).

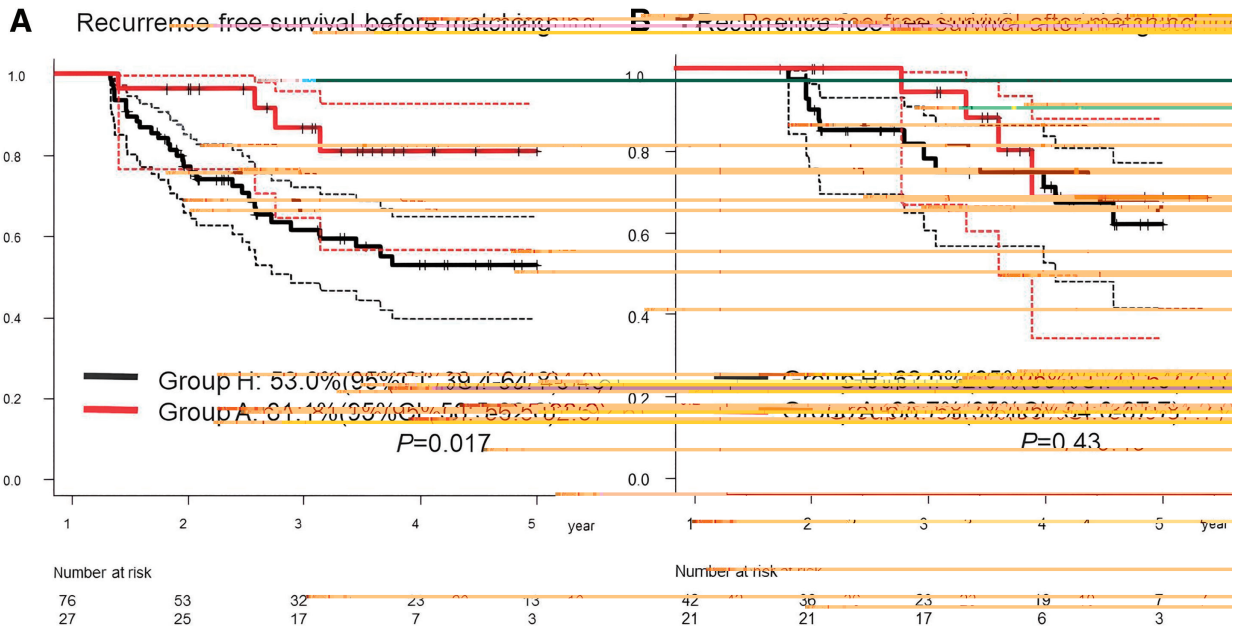

Fig. 3 RFS curves, stratified by CT interval. The RFS curves were significantly different before matching. ($P = 0.017$); however, it was not significantly different after matching ($P = 0.43$). (**A**) Recurrence survival curves before matching. (**B**) RFS curves after matching. RFS: recurrence-free survival

Table 4 Recurrence details

	Before matching			After matching		
	Half-year (n = 28)	Annual (n = 4)	*P* value	Half-year (n = 12)	Annual (n = 4)	*P* value
Recurrence trends			1			1
Locoregional	7 (25.0)	1 (25.0)		4 (33.3)	1 (25.0)	
Distant	21 (75.0)	3 (75.0)		8 (66.6)	3 (75.0)	
Detection modalities			0.09			0.45
CT	20 (71.4)	3 (75.0)		9 (75)	3 (75.0)	
Symptom	6 (21.4)	0		2 (16.7)	0	
Tumor marker	1 (3.6)	0		1 (8.3)	0	
Chest X-ray	0	1 (25.0)		0	1 (25.0)	
Others	1 (3.6)	0		0	0	
Treatment after recurrence			1			0.86
Chemotherapy	15 (53.6)	2 (50.0)		7 (58.3)	2 (50.0)	
Chemoradiation therapy	4 (14.3)	1 (25.0)		1 (8.3)	1 (25.0)	
Palliative radiation	0	0		0	0	
Radiotherapy	2 (7.1)	0		0	0	
Surgery	5 (17.9)	1 (25.0)		2 (16.7)	1 (25.0)	
Best supportive care	2 (7.1)	0		2 (16.7)	0	

CT: computed tomography

Recurrence details

The recurrence details of patients stratified by surveillance intensity before and after matching are listed in **Table 4**. Before matching, 21/28 patients (75.0%) and 3/4 patients (75.0%) in groups H and A, respectively, had distant metastases, with no difference in the trends of recurrence ($P = 1.0$). More than 70% of the recurrences in both groups were detected using CT, and no significant difference was observed in the modalities that detected the recurrences ($P = 0.09$). Moreover, no significant difference was observed in the treatment approach after recurrence between the 2 groups ($P = 1.0$). After

adjusting for clinical backgrounds by propensity score matching, there was no significant difference between the 2 groups in the trends of recurrence ($P = 1.0$), modalities ($P = 0.45$), or treatment after recurrence ($P = 0.86$), demonstrating that the same trend as before matching was ascertained.

Detection of second primary lung cancer

Second primary lung cancer was detected in 1/76 patients (1.3%) in Group H and 1/27 patients (3.7%) in Group A ($P = 1.0$) (**Table 1**). After adjusting for background factors, it was detected in 0/42 patients and 1/21 patients (4.8%) in groups H and A ($P = 0.33$), respectively (**Table 2**). The detection rate of second primary lung cancer was not significantly different between the 2 groups, and these trends did not change before and after propensity score matching.

Discussion

This retrospective study aimed to elucidate the prognostic impact of CT interval for postoperative surveillance in patients who underwent radical surgery for advanced-stage NSCLC using propensity score matching. The results showed that the difference between half-year and annual CT interval was not associated with postoperative OS, RFS, or post-recurrence survival when we assumed that patients remained cancer-free for 16 months post-surgery even in considering the effect of postoperative adjuvant chemotherapy. One of the possible reasons for this result might be associated with recurrence. The varieties of disease recurrence can affect subsequent treatments, which relate to the patient's survival and quality of life. The recurrence type was predominantly distant metastasis in both groups. Locoregional treatments were performed for almost a quarter of the patients with recurrence, regardless of the CT interval, and there was no difference between the 2 groups in systemic therapies that were primarily aimed at prolonging life. There was no outstanding disadvantage in terms of delayed detection followed by a potentially curative or life-prolonging treatment targeted for any recurrence in Group A. Annual CT intervals after advanced lung cancer surgery might be feasible based on our cohort.

The optimal interval of CT surveillance after complete resection for NSCLC could be highly dependent on the patient's condition and clinical factors. In addition to definitive surgical treatment, the development of new anticancer agents, including molecular-targeted drugs and recently developed immune checkpoint inhibitors, has prolonged the survival and improved the quality of life of patients with advanced or recurrent NSCLC.[14] short-interval CT surveillance may be desirable for early detection and treatment, thereby contributing to prolonged post-recurrence survival and improved quality of life. Rather than performing CT surveillance at uniform intervals for all patients with miscellaneous backgrounds of early or advanced cancer staging, planning individualized CT intervals depending on the patient's clinical characteristics and based on the risk of recurrence may be desirable. However, several recent publications have reported that an intensive follow-up with CT after curative treatments did not improve prognosis, which was consistent with our results.[8–10,12,15–18] Although these studies did not focus on individual recurrence risk assessments, they consistently denied an association between CT surveillance and prognosis. The relationship between asymptomatic recurrence detected by CT and prognosis is generally difficult to confirm. An apparently extended survival for asymptomatic patients may not necessarily be ascertained, probably due to "lead time bias."[19] Several studies evaluating the impact of postoperative CT surveillance have found that the detection of asymptomatic recurrence extends post-recurrence survival by approximately 1 year, which seemed to have a positive effect on prognosis.[10,20] In fact, no OS benefit was observed, which was ultimately attributed to "lead time bias" as a confounding factor in these studies.[9,10] Another hypothesis is that the prognosis after lung cancer recurrence is generally poor, regardless of the treatment modality. Even when curative resection is performed for local recurrence, the 5-year survival rate after recurrence is only approximately 15%.[21,22] Therefore, earlier detection of asymptomatic recurrence by postoperative CT surveillance does not always result in prolonged survival, although these results were published before the discovery of new anticancer agents. We need to select individual candidates for close follow-up who will benefit from earlier treatment with newly developed agents in future studies.

Postoperative surveillance after lung cancer surgery is not only aimed at recurrence but also screening for second primary lung cancer. Compared with recurrences, more cases of new primary lung cancer can be curatively treated by early detection.[11,23] The 5-year survival rate after treatment for new primary lung cancer is much better than that after recurrence,

ranging from 25% to 60%.[24,25] According to previous publications, the detection rate of second primary lung cancers was approximately 7.0%–15.3% throughout the observation period.[7,12,16,19,20,23] In this study cohort, the overall detection rate was 1.3% in Group H and 3.7% in Group A before matching (P = 1.0), as well as 0 in Group H and 4.8% in Group A after matching (P = 0.33). It is considered a possible competing risk between the detection of second primary lung cancer and higher recurrence rates with poor prognosis in stage II or III patients in this study. In other words, a higher rate of recurrence and cancer death may cancel out the development of second primary lung cancer and reduce the rate of detection.

Guidelines in the United States recommend surveillance with CT at half-year intervals up to 2 years postoperatively.[2–4] Our retrospective study showed contrary outcomes regarding the non-inferiority of detection of cancer, including second primary lung cancer, when comparing intervals of annual and half-yearly CT examinations. A large cohort prospective study in Japan (Japan Clinical Oncology Group [JCOG] 2012; a randomized phase III trial of postoperative surveillance for pathological stage II–IIIA NSCLC) is currently being conducted. This study was performed prior to the implementation of JCOG2012 and did not include patients who participated in JCOG2012. Therefore, we did not explain the follow-up policy to each patient in advance. Although this was a retrospective study with no prior explanation regarding postoperative CT interval, we believe there was no direct disadvantage to patients because the follow-up methods were chosen based on relevant established guidelines and the study received ethical review. Eventually, the prospective JCOG study may clarify the optimal postoperative CT surveillance in the future.

This study has several limitations. First, the study design was a retrospective analysis conducted at a single institute, and the selection between annual or half-year CT intervals was not randomized. Selection was decided by the outpatient attending staff based on the patient's condition; therefore, an unbalanced patient population was unavoidable, which is a limitation of this study. Second, the study excluded patients with recurrence of up to 16 months, and results regarding the benefit of frequent CT scans in patients with early recurrence are not available. Third, this study did not include a detailed analysis of the individual risk of recurrence in each group and simply evaluated the prognostic impact of the difference in CT intervals between half-year and 1 year. Fourth, relatively fewer patients were treated with postoperative adjuvant chemotherapy due to higher age, renal dysfunction, and multiple comorbidities, which affected postoperative survival and recurrence. Fifth, the study included a small number of patients with recurrence and death in each group which may not provide satisfactory data analyzed for the survival impact of CT interval. However, we gathered data from numerous patients with lung cancer undergoing postoperative periodic CT at annual or half-year intervals, allowing a reasonably robust analysis of the efficiency of annual CT intervals over half-year CT intervals with respect to postoperative OS and post-recurrence survival; annual CT follow-up may be an acceptable follow-up frequency for advanced-stage lung cancer after complete resection. Prospective study designs, such as the JCOG2012 study, which is currently ongoing in Japan, may support our results in the future.

Conclusion

Surveillance with CT at annual intervals after complete resection for NSCLC was comparable to that at a half-year interval, demonstrating that annual CT surveillance may be feasible for detecting and treating postoperative recurrence and second primary lung cancer.

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Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Kansai Medical University Hospital (No: 2022177) and was conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. The requirement for informed consent was waived owing to the retrospective nature of the study.

Consent for publication

Not applicable.

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Data availability

The data that support the findings of this study are available on request from the corresponding author.

Author contributions

NM: Conceptualization, data curation, investigation, writing the original draft. HH: Conceptualization; TU, YT, HM, and TS: Data curation; TM: Conceptualization, supervision. All authors read and approved the final manuscript.

Disclosure statement

The authors have no conflicts of interest to disclose.

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