Medicine®

OBSERVATIONAL STUDY

OPEN

CT Characteristic of Early Local Recurrence After Resection of the Squamous Cell Carcinoma

Comparison With CT Characteristics of Stump Deformity or Granulation Tissue at Stump Site

Hye Jeon Hwang, MD, Mi Young Kim, MD, PhD, Sung-Soo Kim, PhD, and Chang-Min Choi, MD, PhD

Abstract: The aim of this study is to compare the thin section computed tomography (CT) characteristics of the early local tumor recurrence with those of the stump deformity or granulation tissue after the resection of squamous cell carcinoma (SCC).

Twenty-nine consecutive patients with local recurrence after definitive SCC operation from April 2006 to September 2012 were included in our study. Pre- and postoperative CT findings from these patients were retrospectively reviewed and compared with those in the age- and sex-matched 29 patients with the stump deformity or granulation tissue at stump site after definitive SCC operation, by 2 radiologists. We evaluated the initial tumor stage, tumor size, and tumor location in relation with the bronchus on preoperative CT scan. On postoperative CT scan, we evaluated the size, CT characteristics, and involvement pattern of the suspected soft tissue around the stump site, and the distance between surgical staples and soft tissue at the stump site.

Tumor stage, tumor size, and tumor location in relation with the bronchus on preoperative CT scan were not significantly different between 2 groups, while lymph node stage was more advanced in the local recurrence group. On postoperative CT scan, the size of suspected soft tissue at stump site is significantly larger, and the distance between stump staples and suspected soft tissue was significantly longer in the local recurrence group than control group (median; 19 mm and 3 mm; 18 mm and 0 mm, respectively, $P < 0.001$). The univariate analysis showed that the size of soft tissue and the distance between soft tissue and stump site on postoperative CT scan were associated with the predictive factors of local recurrence ($P < 0.001$). On the receiver-operating characteristic analysis, the optimal cutoffs of the size of soft tissue and the distance between soft tissue and stump staples for determining local tumor recurrence were 6 and 5 mm, respectively.

The proper knowledge CT characteristics of local tumor recurrence including the soft tissue size (cut-off, 6 mm) and the distance (cut-off, 5 mm) between soft tissue and stump site will help us achieve the early diagnosis and higher diagnostic rate of locally recurred SCC.

(*Medicine* 94(41):e1691)

Abbreviations: 18-FDG-PET = 18 F-uorodeoxyglucose positron emission tomography, MaxSUV = maximum standardized uptake value, NSCLC = non-small cell lung cancer, ROC = receiver-operating characteristic, SCC = squamous cell carcinoma.

INTRODUCTION

Surgical resection is the first-line treatment for the early stage non-small cell lung cancer (NSCLC).[1] Reported overall tumor recurrence rates, including local tumor recurrence and distance metastasis after surgical resection, are between 6% and 45% for patients with stage I NSCLC, and between 7% and 55% for patients with stage II NSCLC.[2–11] And local or regional recurrence rate in stage I or II NSCLC after surgical resection has been reported to be between 7% and 27%.[4,9,12–14] Common local recurrence sites are the bronchial stump, adjacent lymphoid tissue, lung parenchyma, and a combination of these.

Squamous cell cancer (SCC) is the predominant histological type of NSCLC, for the locally relapsing lung cancer, followed by adenocarcinoma,[15] and the bronchial stump recurrence was seen only in SCC.[16] Reoperation, chemotherapy, radiotherapy, or combined therapies are used for patients with tumor recurrence. And it was reported that the treatment with reoperation has significantly better postrecurrence survival than no treatment or chemotherapy and/or radiation therapy.[13] Therefore, early detection of local disease recurrence after surgery is important for the proper management including timely reoperation for NSCLC patients during follow-up. Few studies have been reported normal postoperative radiologic findings.[17,18] To the best of our knowledge, the CT characteristics of local tumor recurrence near bronchial stump after surgery of NSCLC have not been well described.

The purpose of this study is to evaluate the thin section CT characteristics of early local recurrence after resection of SCC, and to compare these findings with those of stump deformity or granulation tissue near stump site after surgical resection of SCC.

METHODS

Patients

This retrospective study was approved by the institutional review board of the Asan Medical Center (IRB reference

Editor: Mariusz Adamek.
Received: June 10, 2015; revised: September 3, 2015; accepted: September 4, 2015.
From the Department of Radiology, Hallym University College of Medicine, Hallym University Sacred Heart Hospital, Dongan-gu, Anyang-si, Gyeonggi-do (HJH); Departments of Radiology and Research Institute of Radiology, Asan Medical Center, University of Ulsan College of Medicine, Songpa-Gu, Seoul (MYK); Department of Healthcare Management, Cheongju University, Cheongwon-fu, Cheongju-si, Chungcheongbuk-do (S-SK); and Department of Pulmonary and Critical Care Medicine, and Division of Oncology, University of Ulsan College of Medicine, Asan Medical Center, Songpa-Gu, Seoul, Korea (C-MC).
Correspondence: Mi Young Kim, Department of Radiology and Research Institute of Radiology, University of Ulsan College of Medicine, Asan Medical Center, 86 Asanbyeongwon-Gil, Songpa-Gu, Seoul 138-736, Korea (e-mail: mimowdr@amc.seoul.kr).
The authors have no funding and conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000001691

number 2015-0768), and the informed consent was waived. From April 2006 to September 2012, 29 consecutive patients (mean age 68 years; 29 males and 0 female) with local tumor recurrence after the curative surgical operation for SCC were included in this study. All patients had undergone surgical resection for SCC with pathologic stage I or II or IIIA.

The local tumor recurrence of SCC was defined as the disease recurrence at surgical resection margin, ipsilateral hilum, or mediastinum.[14] The diagnoses of local tumor recurrence were made pathologically by the bronchoscopic biopsy in 24 patients, and 5 patients were diagnosed with the serial follow-up CT and 18 F-fluorodeoxyglucose positron emission tomography (18-FDG-PET) images with hypermetabolism (>2.5 high maximum standardized uptake value).

From the same period, 29 age- and sex-matched patients (mean age 65 years; 29 males and 0 female) without local tumor recurrence at stump site after the curative surgical operation for SCC were included in our study as the control group. The diagnoses of absence of local tumor recurrence were made by bronchoscopic findings and serial follow-up (more than 2 years) CT imaging.

All patients had routine postsurgical surveillance with imaging studies including chest CT. Patients who received preoperative or postoperative chemotherapy and/or radiation therapy or presented with obvious synchronous or metachronous lung cancer were excluded. Medical records of the patients were retrospective reviewed, and clinical characteristics are summarized in Table 1.

CT EXAMINATION

CT Protocol

Chest CT examinations were performed using 16- or 64-detector scanner (Somatom Sensation 16; Siemens Medical Solutions, Forchheim, Germany and Lightspeed VCT; GE Medical, Milwaukee, Wis). Scan parameters were 120 kV and 100 effective mA with dose modulation for the 16-detector row scanner. The images were reconstructed using the B50 algorithm (3 and 5-mm thickness and 3 and 5-mm interval without gap) and B60 algorithm (1-mm reconstruction with 5-mm gap). For the 64-detector raw scanner, CT scan parameters were 120 kV and 100 to 400 mA with dose modulation. The images were reconstructed with the lung algorithm (2.5 and 5-mm thickness and 2.5 and 5-mm interval without gap) and the bone algorithm (1.25-mm reconstruction with 5-mm gap). All CT scans were obtained 50 sec after administration of 100 mL of a 300 mg I/mL IV contrast medium (Iomeron 300, Bracco, Milan, Italy) at a rate of 3.0 mL/sec. All images were viewed at mediastinal (width, 450 HU; level, 50 HU) and lung window (width, 1500 HU; level, −700 HU) settings of axial image using our picture archiving and communication system (Radpia; Hyundai Information Technology, Seoul, Korea).

CT Analysis

Preoperative CT scans from the patients with local recurrence group and control group were selected for the radiologic review. For postoperative CT scan, the CT scan nearest in time to the confirmation of local tumor recurrence in each patient was selected for the CT review in the local recurrence group. In the control group, the CT scan with a disease-free follow-up period of more than 2 years was selected for the CT review for postoperative CT scan. These thin-section CT scans were retrospectively reviewed in consensus by 2 expert chest radiologists (MYK and HJH) who had 18 and 7 years of experience, respectively. These radiologists were blinded to any clinical information.

TABLE 1. Baseline Clinical and Treatment Characteristics of Patients With Local Tumor Recurrence and Patients Without Local Tumor Recurrence

Variables	Local Recur Group (N = 29)	Control Group (N = 29)	P^* Value
Age (y, median)	68 (48–83)	65 (53–78)	0.196
Sex			N/A
Male	29 (100)	29 (100)	
Female	0 (0)	0 (0)	
Smoking history (pack-years, median)	50 (0–112)	40 (0–100)	0.153
Never smoker	2 (6.9)	5 (17.2)	
Past smoker	25 (86.2)	23 (79.3)	
Current smoker	2 (6.9)	1 (3.5)	
Operation			N/A
Segmentectomy	1 (3.5)	0 (0)	
Lobectomy	18 (62.1)	22 (75.9)	
Bilobectomy	5 (17.2)	5 (17.2)	
Pneumonectomy	5 (17.2)	2 (6.9)	
Pathologic T stage			0.514
T1	4 (13.8)	2 (6.9)	
T2	23 (79.3)	25 (86.2)	
T3	2 (6.9)	2 (6.9)	
Pathologic N stage			0.712
N0	13 (44.8)	9 (31.0)	
N1	7 (24.2)	13 (44.8)	
N2	9 (31.0)	7 (24.2)	

Numbers of the data are number of patients (except age and smoking history), and numbers in parentheses are percentages or range.
N = lymph node; T = tumor.
*Statistically significant ($P < 0.05$).

We evaluated initial tumor size, tumor and lymph node stages, and tumor location in relation with the bronchus (endobronchial, bronchial abutting, isolated from bronchus) on preoperative CT scan. On postoperative CT scan, we measured the size of soft tissue which was suspected as local tumor recurrence or granulation tissue at stump site and the distance between surgical staples and suspected soft tissue at stump site. The CT characteristics of these soft tissues, such as shape (round or oval, irregular, flat, and no demonstrable) and enhancement pattern (homogenous, heterogeneous, and no demonstrable), were also evaluated on postoperative CT scan. And we analyzed the involvement pattern of these soft tissues, subdivided into endobronchial, focal bronchial wall thickening, central contour bulging, and peripheral eccentric mass (Fig. 1).

We also evaluated the radiologic diagnostic accuracy of the CT reading in the formal postoperative CT report before the tissue confirmation. The CT reading was regarded as ''misdiagnosis,'' when the correct radiologic diagnosis was within a differential diagnosis rather than first choice. And it was regarded as ''missed diagnosis,'' when the recurrence was not included as a differential diagnosis.

Statistical Analysis

All statistical analyses were performed using statistical software, SPSS (SPSS, release 20.0 for Windows; SPSS Inc, Chicago, IL). Student *t* test was used to evaluate differences in the frequencies of lung lesions on CT and baseline characteristics between 2 groups. Univariate analysis was used to determine the predictive factors for local tumor recurrence. ROC analysis was performed to determine the optimal threshold of the local tumor recurrence size and the distance between surgical staples and local tumor recurrence. A P value <0.05 was considered to indicate statistical significance, and all P values were 2-tailed.

RESULTS

The baseline clinical and treatment characteristics of the local recurrence group and control group were not significantly different (Table 1).

Preoperative tumor stage, size of initial tumor, and tumor location in relation with bronchus were not significantly different between 2 groups, while lymph node stage was more advanced in the local recurrence group ($P < 0.046$) (Table 2).

On the postoperative CT scans, the suspected soft tissues around the stump site were detected in 28 patients of the local recurrence group and in 23 patients of the control group. The size of suspected soft tissue was significantly larger in the local recurrence group than that in the control group (median; 19 and 3 mm, respectively, $P < 0.001$). Measured distance between stump staples and suspected soft tissue was significantly longer in the local recurred group than that in the control group (median; 18 and 0 mm, respectively, $P < 0.001$) (Fig. 2). The recurred tumor was commonly demonstrated as round or oval shape (n = 22, 75.9%) with heterogeneous enhancement (Figures 3 and 4), while the stump site deformity or granulation tissue was commonly demonstrated as flat (n = 10, 34.4%) or irregular shape (n = 12, 41.4%) with heterogeneous enhancement on CT scan (Fig. 5) (Table 3). And recurred tumor commonly showed as the peripheral eccentric lesion (n = 11, 37.9%) or central contour bulging lesion (n = 8, 27.6%) in the relation with stump site (Fig. 4). However, in the control group, the peripheral eccentric lesion or central contour bulging lesion was not observed on CT scan.

TABLE 2. Preoperative CT Characteristics of Patients With Local Tumor Recurrence and Patients Without Local Tumor Recurrence

Variables	Local Recur Group (N = 29)	Control Group (N = 29)	*P* Value
Initial tumor size (mm)	35 (12–50)	36 (0–70)	0.079
CT–T stage			0.708
T1	2 (6.9)	2 (6.9)	
T2	26 (89.7)	25 (86.2)	
T3	1 (3.4)	2 (6.9)	
CT–N stage			0.046*
N0	4 (13.8)	9 (31.0)	
N1	14 (48.3)	14 (48.3)	
N2	11 (37.9)	6 (20.7)	
Tumor location			
Endobronchial	20 (69.0)	18 (62.1)	0.349
Bronchial abutting	3 (10.3)	7 (24.1)	
Peripheral isolated	6 (20.7)	4 (13.8)	

Numbers of the data are number of patients (except initial tumor size), and numbers in parentheses are percentages or range.
N = lymph node; N/A = not available; T = tumor.
*Statistically significant ($P < 0.05$).

The univariate analysis showed that the size of suspected soft tissue and distance between surgical staples and suspected soft tissues were associated with the predictive factors of local recurrence ($P < 0.001$, respectively) (Table 4).

On ROC analysis, the size of suspected soft tissue with the optimal cutoff of 6 mm showed the sensitivity of 96.6% and the

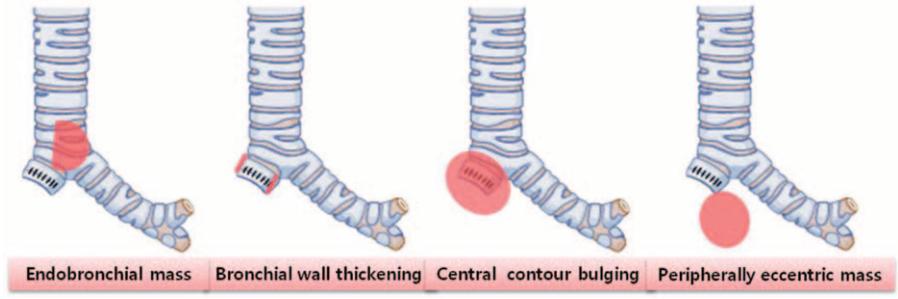

FIGURE 1. Involvement patterns of the suspected soft tissue in relation with stump site.

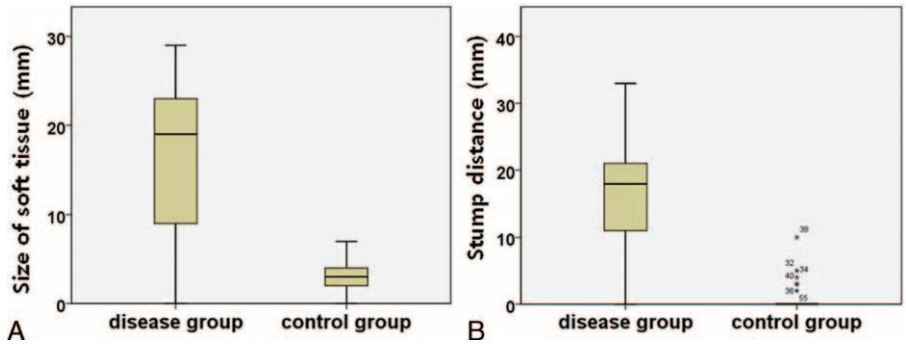

FIGURE 2. Box plots show the distribution of (A) the size of suspected soft tissue and (B) the distance between suspected soft tissue and stump site. Differences in the size and distance were statistically significant ($P < 0.001$).

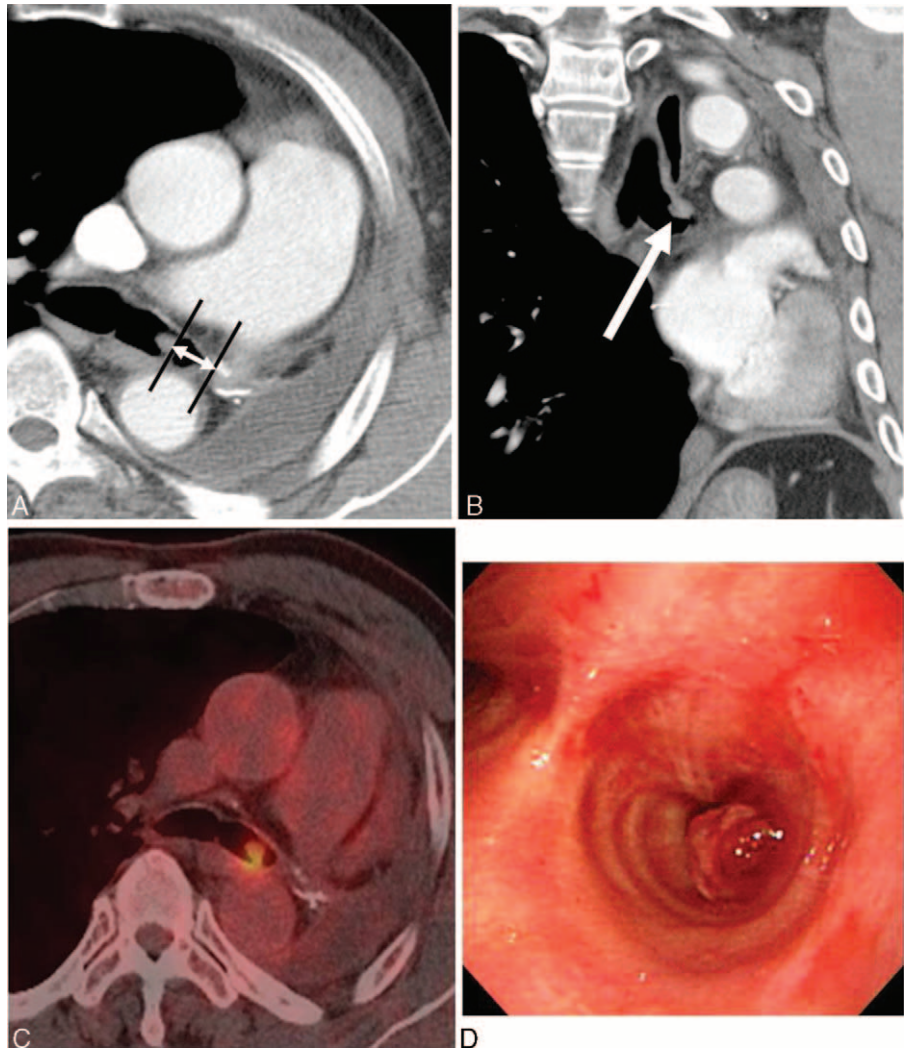

FIGURE 3. A 69-year-old man with tumor recurrence after left pneumonectomy for squamous cell lung cancer (pT1,N1,M0). A, Conventional CT transverse image with mediastinal window (3-mm thickness reconstruction) was obtained at the level of bilateral main stem bronchi. CT image shows round-to-oval shape enhancing endobronchial nodule with 9 mm in long diameter at the left main bronchus and with 20 mm distance from surgical staples (arrow). B, Coronal reformatted lung image (3-mm thickness reconstruction) was obtained at the level of left atrium. Note the nodule abutting the upper wall of the left main bronchus (arrow). C, On 18-FDG-PET, the maximum standardized uptake value of the nodule was 3.6. D, Photograph of bronchoscopy shows endobronchial polypoid nodule. Recurrent cancer was revealed on bronchoscopic biopsy.

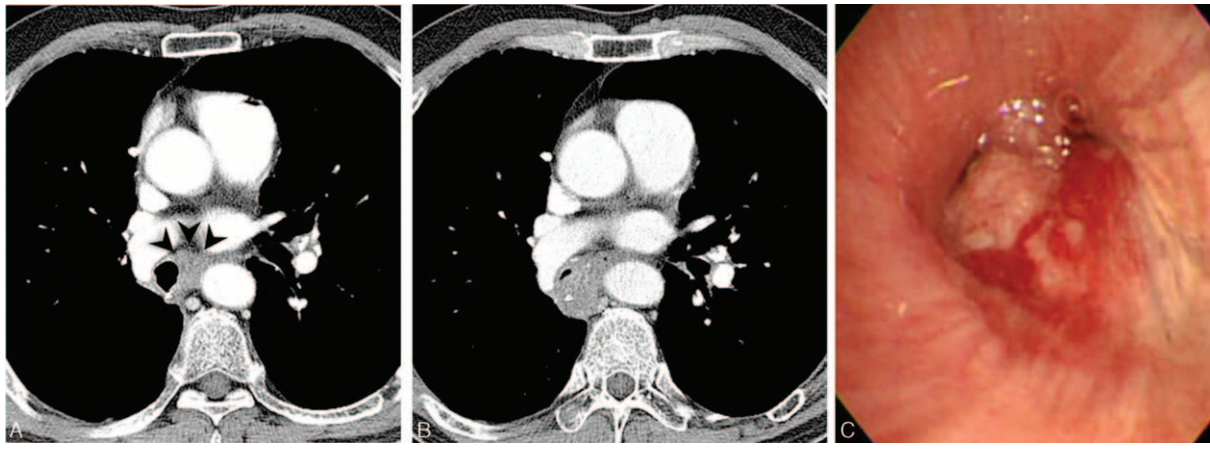

FIGURE 4. A 68-year-old man with tumor recurrence after right lower lobectomy for squamous cell lung in left lower lobe (pT2,N1,M0). A, On postoperative transverse CT image (3-mm thickness reconstruction) shows peripheral eccentric soft tissue with heterogeneous enhancement at the medial side of bronchus intermedius with 15 mm size and 7 mm in the distance between lesion and stump (arrowheads). It was missed on the routine radiologic diagnosis. B, 7 months later, follow-up CT (3-mm thickness reconstruction) at the same level shows the interval growing of the enhancing soft tissue and narrowing of the bronchus intermedius. C, Bronchoscopic image shows endobronchial obstructing mass at bronchus intermedius. Recurrent cancer was revealed on bronchoscopic biopsy.

specificity of 96.6% for the local tumor recurrence. The distance between surgical staples and suspected soft tissue with ideal cutoff of 5 mm has the sensitivity of 96.6% and the specificity of 93.1% for the local tumor recurrence (Fig. 6).

We reviewed the first radiologic diagnosis of the postoperative CT before the diagnosis of tumor recurrence (Table 3). Among the local tumor recurrence group, the ''missed or misdiagnosed'' was made in 8 patients. In these patients, local tumor recurrence was suspected on 18-FDG-PET, which was performed within 1 week after performing of chest CT. The mean size of local tumor recurrence with the correct radiologic diagnosis was larger than that in the ''missed or misdiagnosed'' patients (19.0 and 11.9 mm, respectively). And the distance between local tumor recurrence and surgical staples was shorter in the ''missed or misdiagnosed'' patients than in the patients with the correct diagnosis (12.1 and 18.6 mm, respectively).

DISCUSSION

The most common cause of disease morbidity and mortality for NSCLC after surgical resection is regional and/or distant tumor recurrence, and the risk of disease recurrence is relatively high even in patients with early stage tumor. Reoperation, chemotherapy, radiotherapy, or combined therapies are used as the treatment for patients with tumor recurrence. CT is widely used in the postoperative follow-up after surgery of NSCLC. Various changes in airway stump site, central airway axis, residual lung parenchyma, and mediastinum, which may occur in the postoperative period, can be seen on follow-up CT examination. Early bronchial stump recurrence is easily missed or misdiagnosed as a

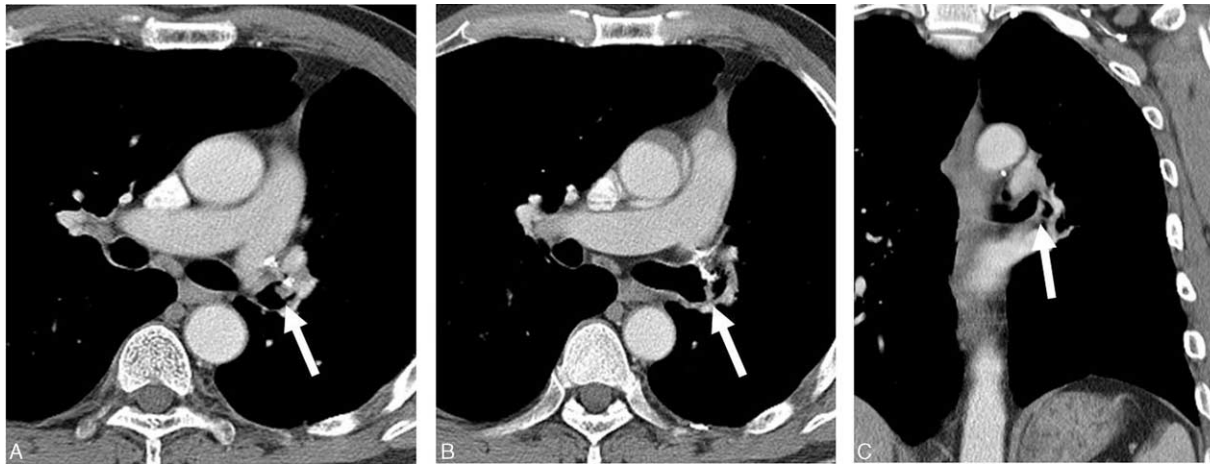

FIGURE 5. A 53-year-old man in control group, who underwent left upper lobectomy for squamous cell carcinoma. A, B, Transverse chest CT images (3-mm thickness reconstruction) with mediastinal setting show continuous endobronchial nodule with lesion size in 9 mm and the distance between lesion and stump in 0 mm (arrows). C, Conventional lung images (3-mm thickness reconstruction) coronal reformations obtained at the level of left upper pulmonary vein. Note the flat shaped focal wall thickening of the upper wall of left main bronchus (arrow). Bronchoscopy and follow-up CT examination revealed chronic granulation tissue at stump site without local tumor recurrence.

TABLE 3. Postoperative CT Characteristics of Patients With Local Tumor Recurrence and Patients Without Local Tumor Recurrence

Variables	Local Recur Group (N = 29)	Control Group (N = 29)	*P* Value
Time interval between Op. date and Postop. CT scan	554 (163–2890)	360 (68–504)	0.007
Involvement pattern of soft tissue			N/A
Endobronchial	6 (20.7)	2 (6.9)	
Focal bronchial wall thickening	3 (10.3)	21 (72.4)	
Central contour bulging	8 (27.6)	0 (0)	
Peripheral eccentric lesion	11 (37.9)	0 (0)	
No demonstrable	1 (3.5)	6 (20.7)	
Shape			N/A
Round or oval	22(75.9)	1 (3.5)	
Irregular	4 (13.8)	12 (41.4)	
Flat	2 (6.9)	10 (34.4)	
No demonstrable	1 (3.5)	6 (20.7)	
Enhancement pattern			N/A
Homogeneous	7 (24.1)	2 (6.9)	
Heterogeneous	21 (72.4)	21 (72.4)	
No demonstrable	1 (3.5)	6 (20.7)	
Size of suspected soft tissue (mm, median)	19 (1–29)	3 (1–7)	<0.001†
Distance between surgical staples and suspected soft tissue (mm, median)	18 (0–33)	0 (0–10)	<0.001†
CT report*			
Correct	21 (72.4)	29 (100)	N/A
Missed or misdiagnosed	8 (27.6)		

Numbers of the data are number of patients (except size of suspected soft tissue and distance between surgical staples and suspected soft tissue). N/A = not available; Op. = operation; Postop = postoperative.

* CT report = misdiagnosis means that the recurrence was included as a differential diagnosis. Missed diagnosis means that the recurrence was not included as a differential diagnosis.

† Statistically significant ($P < 0.05$).

postoperative granulation tissue or plication deformity at stump site on serial follow-up CT due to many causes including anastomotic distortion or surgical artifacts. CT characteristics of early local tumor recurrence including the optimal cut-off value of the size of local tumor recurrence, and the distance between surgical staples and local tumor recurrence, may be helpful for making a decision about the suspected tumor recurrence.

This study showed that the local tumor recurrence after surgery of SCC was significantly larger than that of the granulation tissue with the optimal cutoff of 6 mm, and the local tumor recurrence was located more distantly from the surgical

TABLE 4. Predictive Factors for Local Tumor Recurrence on Postoperative CT Scan

	Univariate analysis			
		CI		
Variables	OR	Lower	*P* Value	Upper
Size of suspected soft tissue	1.746	1.269	2.403	<0.001†
Distance between surgical staples and suspected soft tissue	2.510	1.459	4.316	<0.001†

OR, odds ratio, CI, confidence interval.

† Statistically significant ($P < 0.05$).

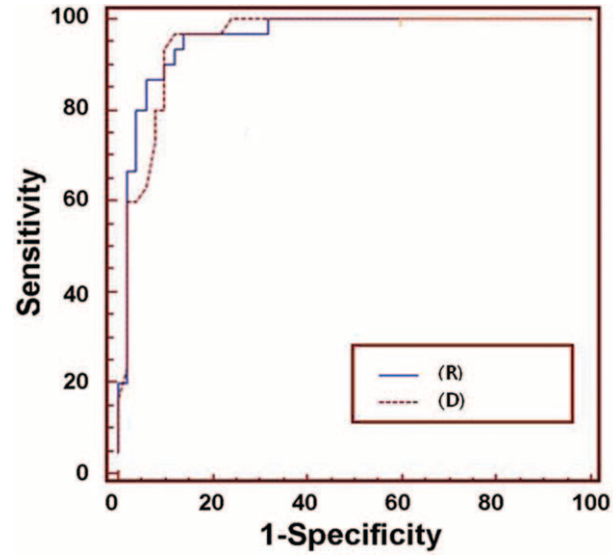

FIGURE 6. Receiver-operating characteristic curve of suspected soft tissue size (R) and distance between surgical staples and suspected soft tissue (D) for curve for distinguishing the recurrence and granulation tissue using chest CT. The optimal cut-off vale of the suspected soft tissue size at 6 mm showed 96.6% sensitivity and 96.6% specificity and the optimal cut-off vale of the distance between surgical staples and suspected soft tissue at 5 mm showed 96.6% sensitivity and 93.1% specificity.

staples than the granulation tissue with the optimal cutoff of 5 mm. The shape of lesion is also important as a round to oval in the recurred tumor (75.9%) rather than a flat or irregular in control group (75.8%). The local recurred tumor was commonly round-to-oval shape with peripheral eccentric location or central contour bulging in relation with the stump site, while the granulation tissue was commonly shown as the flat or irregular shape focal bronchial wall thickening on CT image. With our optimal cut-off values, the correct diagnosis of tumor recurrence can be made in 7 patients among the 8 patients who were ''missed or misdiagnosed'' on the formal CT reports. Although, with our cut-off value regarding the tumor size being 6 mm, one case was not demonstrable on CT image but bronchoscopy only.

Hung et al reported that the treatment method for the initial recurrence is a prognostic predictor for the survival in the resected stage I NSCLC with local recurrence. In that study, patients who were treated by reoperation after local recurrence survived longer than those who received other treatments (chemotherapy and/or radiotherapy) and those who received no treatment.[13] In that study, among the 74 patients with local recurrence after resection of stage I NSCLC, the 8 patients with stump recurrence or lung recurrence without mediastinal recurrence underwent reoperation. There are many factors that may influence to determine the treatment methods after the detection of local tumor recurrence such as previous operation methods, history of radiation treatment, or patients' lung function, but a stump recurrence was more likely to undergo resection in the previous study.[13] In our study, only 4 patients among the local recurrence group had undergone reoperation after confirming of local tumor recurrence. Three patients had undergone pneumonectomy for reoperation, and one patient had underwgone lobectomy for reoperation. And 15 patients had undergone local therapy such as radiation treatment, brachytherapy, or bronchoscopic laser ablation. In our study, mean tumor size tended to be smaller in the patients with reoperation than that in the patients with other treatments (13.8 and 17.5 mm, respectively). The proper diagnosis of early local tumor recurrence on follow-up CT imaging may influence the timely treatment of local tumor recurrence and patients prognosis.

Our hypothesis for the small distance from the stump site (cut-off, 5 mm) of the local tumor recurrence in our study is as in the following. First, SCC could be occurred as metachronous or synchronous cancers with delayed manifestation on postoperative follow-up CT.[19,20] Auerbach et al reported that cigarette smoking causes extensive histological alterations in the bronchial epithelium and multiple altered foci of bronchial epithelium are present throughout the respiratory epithelium.[21] This phenomenon was referred to as ''field of cancerization.'' Recently, many molecular abnormalities, which were also found in carcinoma in situ and SCC, have been detected in the histologically normal epithlia adjacent to SCC.[22–24] And these molecular abnormalities also have been detected in the bronchial epithelia of former smokers without lung cancer.[25,26] Thus, local recurrence after tumor resection can be occurred in the preexisting altered foci of bronchial epithelium or normal epithelia with molecular abnormalities. Second, the tract metastasis is possible in the operation field, especially in the central lung cancer. Insufficient safety margin is also possible. Third, skipped endobronchial metastasis could be possible through submucosal lymphatic channels in certain SCC. In our study, recurrence was relatively high in N2 stage. Fourth, the polypoid tumor with narrow stalk attached to the stump can be unobserved on CT image by a radiologist due to partial volume averaging effect, despite 3-mm reconstruction of slide thickness without gap of volumetric image with coronal reformation. Therefore, it is not easy to make an explanation for the distance issue. Further prospective study is necessary to clarify.

18-FDG-PET imaging also can be used in distinguishing recurrent tumor from post-treatment scarring or granulation tissue. Several studies have been reported that 18-FDG-PET is more sensitive than chest CT in detecting recurrent tumor (sensitivity of 97–100%).[27–29] However, sometimes, 18-FDG-PET yields false-positive results from active inflammation; therefore, the use of 18-FDG-PET for evaluating early tumor recurrence or residual tumor particularly is limited particularly in the acute postoperative stage. Furthermore, early recurrent tumors with small size at or near stump usually show too small to evaluate 18-FDG-PET metabolism in routine practice. Therefore, watchful CT observation is crucial to initial 5 years after cancer resection. Early detection of stump recurrence can give patients a second chance for the definitive therapy such as reoperation or stereotactic radiotherapy rather than systemic chemotherapy.

Our study had several limitations. First, it was a retrospective study performed at a single, tertiary referral center with several thoracic surgeons. Therefore, there could have been patient selection bias. Second, the interval between the 2 CT examinations of each patient was not determined in advance due to the retrospective design of our study, and showed a variable range. At our cancer center, postoperative lung cancer patients undergo CT scanning at approximately 6-month intervals up to 1 year after operation. Third, measuring error regarding size and distance for small lesions can be occurred. However, we measured variables in accordance with routine daily practice. Therefore, this study is radiologically applicable, immediately. Fourth, morphologic evaluation on chest CT can be subjective. Fifth, small numbers of patients in the 2 groups limited the accuracy of our statistical comparisons. Finally, considering all the patients involved in our study are male, the potential sex bias can arise. However, the incidence of squamous cell carcinoma of Korean female is 2 per 100,000, and the smoking rate is significantly lower than Korean male. There is no female stump problem in our study due to very low incidence.

However, it could be useful to combine knowledge of well-focused CT morphological features with the individual clinical characteristics to come up with more detailed assessment, for the decision of the bronchoscopy or 18-FDG-PET and subsequent tissue confirmation, promptly. In addition, 2 experienced chest radiologists analyzed the CT features. We believe that diagnosis and therapeutic plans for early local recurrence should be based on the multidisciplinary inputs from thoracic surgeons, radiologists, pulmonologists, and oncologists. This study could provide an evidence-based approach to dealing with certain overlooked patients during the routine postoperative follow-up using chest CT, despite the limitations of this study.

In conclusion, proper knowledge of CT characteristics of local tumor recurrence including the size (cut-off, 6 mm) and the distance (cut-off, 5 mm) around the stump on CT imaging will help us achieve the early diagnosis and higher diagnostic rate of locally recurred SCC.

REFERENCES

1. Chemotherapy in non-small cell lung cancer: a meta-analysis using updated data on individual patients from 52 randomised clinical trials. Non-small Cell Lung Cancer Collaborative Group. *BMJ*. 1995;311:899–909.

2. Feld R, Rubinstein LV, Weisenberger TH. Sites of recurrence in resected stage I non-small-cell lung cancer: a guide for future studies. *J Clin Oncol.* 1984;2:1352–1358.
3. Feng QF, Wang M, Wang LJ, et al. A study of postoperative radiotherapy in patients with non-small-cell lung cancer: a randomized trial. *Int J Radiat Oncol Biol Phys.* 2000;47:925–929.
4. Harpole DH Jr, Herndon JE 2nd, Young WG Jr et al. Stage I nonsmall cell lung cancer. A multivariate analysis of treatment methods and patterns of recurrence. *Cancer.* 1995;76:787–796.
5. Immerman SC, Vanecko RM, Fry WA, et al. Site of recurrence in patients with stages I and II carcinoma of the lung resected for cure. *Ann Thorac Surg.* 1981;32:23–27.
6. Kato H, Ichinose Y, Ohta M, et al. A randomized trial of adjuvant chemotherapy with uracil-tegafur for adenocarcinoma of the lung. *N Engl J Med.* 2004;350:1713–1721.
7. Kim YT, Kang CH, Sung SW, et al. Local control of disease related to lymph node involvement in non-small cell lung cancer after sleeve lobectomy compared with pneumonectomy. *Ann Thorac Surg.* 2005;79:1153–1161.
8. Lafitte JJ, Ribet ME, Prevost BM, et al. Postresection irradiation for T2 N0 M0 non-small cell carcinoma: a prospective, randomized study. *Ann Thorac Surg.* 1996;62:830–834.
9. Martini N, Bains MS, Burt ME, et al. Incidence of local recurrence and second primary tumors in resected stage I lung cancer. *J Thorac Cardiovasc Surg.* 1995;109:120–129.
10. Sawyer TE, Bonner JA, Gould PM, et al. Factors predicting patterns of recurrence after resection of N1 non-small cell lung carcinoma. *Ann Thorac Surg.* 1999;68:1171–1176.
11. Trodella L, Granone P, Valente S, et al. Adjuvant radiotherapy in non-small cell lung cancer with pathological stage I: definitive results of a phase III randomized trial. *Radiother Oncol.* 2002;62:11–19.
12. al-Kattan K, Sepsas E, Fountain SW, et al. Disease recurrence after resection for stage I lung cancer. *Eur J Cardiothorac Surg.* 1997;12:380–384.
13. Hung JJ, Hsu WH, Hsieh CC, et al. Post-recurrence survival in completely resected stage I non-small cell lung cancer with local recurrence. *Thorax.* 2009;64:192–196.
14. Kelsey CR, Marks LB, Hollis D, et al. Local recurrence after surgery for early stage lung cancer: an 11-year experience with 975 patients. *Cancer.* 2009;115:5218–5227.
15. Stojiljkovic D, Mandaric D, Miletic N, et al. Characteristics of local recurrence of lung cancer and possibilities for surgical management. *J BUON.* 2013;18:169–175.
16. Jang KM, Lee KS, Shim YM, et al. The rates and CT patterns of locoregional recurrence after resection surgery of lung cancer: correlation with histopathology and tumor staging. *J Thorac Imaging.* 2003;18:225–230.
17. Gruden JF, Campagna G, McGuinness G. The normal CT appearances of the second carina and bronchial stump after left upper lobectomy. *J Thorac Imaging.* 2000;15:138–143.
18. Padovani B, Ducreux D, Macario S, et al. [Postoperative chest: normal imaging features]. *J Radiol.* 2009;90 (7–8 Pt 2):991–1000.
19. Kocaturk CI, Cansever L, Kanmaz DZ, et al. Metachronous lung cancer that presented as bilateral synchronous lung cancer. *J Thorac Dis.* 2013;5:E87–89.
20. Saito Y, Sato M, Sagawa M, et al. Multicentricity in resected occult bronchogenic squamous cell carcinoma. *Ann Thorac Surg.* 1994;57:1200–1205.
21. Auerbach O, Stout AP, Hammond EC, et al. Changes in bronchial epithelium in relation to cigarette smoking and in relation to lung cancer. *N Engl J Med.* 1961;265:253–267.
22. Wistuba II, Behrens C, Milchgrub S, et al. Sequential molecular abnormalities are involved in the multistage development of squamous cell lung carcinoma. *Oncogene.* 1999;18:643–650.
23. Wistuba II, Behrens C, Virmani AK, et al. High resolution chromosome 3p allelotyping of human lung cancer and preneoplastic/preinvasive bronchial epithelium reveals multiple, discontinuous sites of 3p allele loss and three regions of frequent breakpoints. *Cancer Res.* 2000;60:1949–1960.
24. Nelson MA, Wymer J, Clements N Jr. Detection of K-ras gene mutations in non-neoplastic lung tissue and lung cancers. *Cancer Lett.* 1996;103:115–121.
25. Mao L, Lee JS, Kurie JM, et al. Clonal genetic alterations in the lungs of current and former smokers. *J Natl Cancer Inst.* 1997;89:857–862.
26. Wistuba II, Lam S, Behrens C, et al. Molecular damage in the bronchial epithelium of current and former smokers. *J Natl Cancer Inst.* 1997;89:1366–1373.
27. Erasmus JJ, McAdams HP, Patz EF Jr. Non-small cell lung cancer: FDG-PET imaging. *J Thorac Imaging.* 1999;14:247–256.
28. Bury T, Corhay JL, Duysinx B, et al. Value of FDG-PET in detecting residual or recurrent nonsmall cell lung cancer. *Eur Respir J.* 1999;14:1376–1380.
29. Hicks RJ, Kalff V, MacManus MP, et al. The utility of (18)FFDG PET for suspected recurrent non-small cell lung cancer after potentially curative therapy: impact on management and prognostic stratification. *J Nucl Med.* 2001;42:1605–1613.