Is the Rate of Pneumonectomy Higher in Right Middle Lobe Lung Cancer Than in Other Right-Sided Locations?

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Background. **Historically, right middle lobe (RML) non-small cell lung cancer (NSCLC) has been reported to be associated with a higher rate of pneumonectomy than other right-sided locations. Because this would discourage minimally invasive approaches in RML-NSCLC, we sought to update this assertion through the study of a large surgical series.**

Methods. **Clinical records of patients who underwent operations for right-sided NSCLC in 2 French surgical centers were prospectively entered and retrospectively reviewed. Demographic and pathologic characteristics of RML NSCLC were compared with other right-sided NSCLC.**

Results. **This study included 3,234 right-sided and 211 RML (6.5%) NSCLC patients. After exclusion of 14 patients who underwent exploratory thoracotomy, patients were a mean age of 61.5 years, most RML resections occurred in men (134 [72.8%]), and most were lobectomies (wedge, n = 4; lobectomy, n = 102; bilobectomy, n = 22; pneumonectomy, n = 56). Pathologic analysis revealed adenocarcinoma in 88 patients (47.8%) and squamous cell carcinoma in 80 (43.5%). pStaging was stage I in 86 patients (46.7%), II in 42 (22.8%), III in 47 (25.5%), and IV in 9 (4.9%). Superior and inferior mediastinal N2 were found in 45.4% and 54.6% of patients, respectively, when 1 station was involved. When compared with other right-sided NSCLC, RML was characterized by higher T status and higher rates of bilobectomy (10.9% vs 5.6%, $p = 0.0017$) and pneumonectomy (30.3% vs 22.3%, $p = 0.0071$) but similar 5-year survival (47.4%).**

Conclusions. **Compared with other right-sided NSCLC, RML location is associated with a higher albeit limited rate of pneumonectomy.**

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The right middle lobe (RML) is characterized by its own peculiar pathology, the RML syndrome, which was initially attributed to bronchial compression by adenopathy [1, 2]. The RML may also be particular by its isolation and less frequent collateral ventilation [3]. Baldry [4] reported 60 years ago that the RML was an uncommon site of carcinoma but that tumors occurring in this site often presented diagnostic difficulties.

More recently, Peleg and colleagues [5] reported that the results of RML operations fell within the lower range of non-small cell lung cancer (NSCLC) generally, whereas Miura and colleagues [6] suggested that the outcome of operations for RML-NSCLC was not worse than in other locations if operability was carefully evaluated. The latest series mentioned that surgical resection of RML cancer required bilobectomy or pneumonectomy in more than 80% of the patients due to specific bronchial and lymphatic extensions.

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This assertion is now commonly accepted in clinical practice, even if the special nature and place of RML-NSCLC has evolved with time and is currently not clearly established. Because the alleged high rate of pneumonectomy in RML-NSCLC tends to discourage minimally invasive approaches in this location, we sought to update this assertion through the study of a large surgical series. We focused on the surgical management of RML-NSCLC to establish the pneumonectomy rate and determining factors in this specific location and compared with other right-sided NSCLC.

Patients and Methods

This study was approved by our Thoracic Surgery Society Ethic Committee, which waived the need for informed consent.

Patients

The clinical records of patients who underwent operations for NSCLC of the right lung from January 1980 to December 2009 in 2 surgery centers were retrospectively reviewed. Data were prospectively entered since April

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1984. The preoperative workup included chest roentgenogram, bronchoscopy, computed tomography since 1983, spirometry, lung-perfusion scan, and a thorough search for metastases, including positron-emission tomography scan since 2004. Mediastinoscopy was performed to exclude N3 disease and to confirm N2 in patients included in various neoadjuvant treatment protocols, depending on referring centers. N3 disease and distant metastases precluded surgical intervention.

Surgical Resection

The resections were performed by posterolateral thoracotomy. Criteria for lung tumors were reclassified by the World Health Organization classification [7] and the recently modified International Staging System for NSCLC [8]. All patients underwent a complete mediastinal lymph node (LN) dissection according to the description by Martini and colleagues [9]. The regional LN classification of Mountain and Dresler [10], modified by the International Association for the Study of Lung Cancer nodal chart with stations and zones [8], established in 2009, was used to define LN stations. The N2 population was divided in single N2 stations, described as 1 station involved in superior mediastinal nodes (stations 2 to 6) or inferior mediastinal nodes (stations 7 to 9), and multiple N2 stations, corresponding to the involvement of 2 or more of any mentioned stations. The 2R and 4R stations were grouped because they form the same anatomic LN chain [11].

Study Design

First, we analyzed the demographic, pathologic, and survival characteristics of patients with right-sided NSCLC according to the location of the primary tumor, divided between RML and other right lobes. We then deciphered RML NSCLC according to the resections performed to establish the factors associated with pneumonectomy. Follow-up information was obtained from the hospital patient records, a questionnaire completed by the chest physician or general practitioner, and from death certificates. Mean follow-up duration was 59.1 ± 62 months, 42.4 ± 49 months for patients who had died and 97.5 ± 70 months for patients who were still alive.

Statistical Analysis

Continuous variables were compared using the Student *t* test and are described as mean ± standard deviation. Categoric variables were compared using χ^2 if more than 5 or the Fisher exact test otherwise and are described as counts and proportions. Actuarial survival curves were estimated by the Kaplan-Meier method. Statistical comparisons between survival distributions were made using the log-rank test. Univariate analysis used the outcome variables of sex, age, type of surgical resection, histology, type of T and N involvement, and perioperative treatments. All data analyses were conducted with the two-sided test, and a p value of less than 0.05 was considered statistically significant. The statistical software used for the analysis was SEM (Anticancer Centre Jean Perrin, Clermont-Ferrand, France) [12].

Results

Right-Sided NSCLC

An operation for right-sided NSCLC was performed in 3,234 patients, including 211 RMLs (6.5%) and 2,807 other lobes with NSCLC (86.8%), after exclusion of 154 tumors (4.7%) located primarily in the intermediate bronchus, 45 (1.3%) in the main bronchus, or 17 (0.5%) involving 2 lobes or more. The surgical management of the RML and other lobes with NSCLC is summarized in Table 1. Compared with other lobes with NSCLC, patients with RML-NSCLC were characterized by a higher rate of induction therapy (15% vs 6.6%, $p = 0.0082$), bilobectomy (10.9% vs 5.6%, $p = 0.0017$), and pneumonectomy (30.3% vs 22.8%, $p = 0.0071$).

After exclusion of patients who underwent induction therapies and exploratory thoracotomies, a first-line surgical resection for right-sided NSCLC was performed in 2,484 patients, including 184 RML-NSCLC (7.4%) and 2,300 other lobes (92.6%) with NSCLC. Their demographic, pathologic, and staging characteristics are reported in Table 2. Compared with other right lobes with NSCLC, patients with RML-NSCLC were characterized by more T2 (52.7% vs 44.5%) and T4 tumors (10.3% vs 4.7%, $p < .001$).

RML-NSCLC Resections

Among the 184 patients who underwent first-line resection for RML-NSCLC, wedge resection, lobectomy, bilobectomy, and pneumonectomy were performed in 4 (2.2%), 102 (55.4%), 22 (12.0%), and 56 patients (30.4%), respectively. After exclusion of the 4 patients who underwent a wedge resection, the pathologic characteristics of the 180 remaining patients are summarized in Tables 3 and 4. The rate of pneumonectomy decreased with periods of time, from 50% in the 1980s to 15.6% in the 2000s ($p = 0.0020$). Compared with lobectomy,

Table 1. Surgical Management of Right-Sided Non-Small Cell Lung Cancer Patients According to the Location of the Primary Tumor in the Right Middle Lobe vs Other Lobes

Treatment	RML (n = 211) No. (%)	Other Lobes (n = 2,807) No. (%)	Right-Sided (n = 3,018) No. (%)	*p* Value
Induction therapy	14 (6.6)	422 (15)	436 (14.4)	0.0082
Exploratory thoracotomy	14 (6.6)	98 (3.5)	112 (3.7)	0.020
Segmentectomy and wedge	4 (1.9)	165 (5.9)	169 (5.6)	0.015
Lobectomy and sleeve	106 (50.2)	1,762 (62.8)	1,868 (61.9)	<0.001
Bilobectomy	23 (10.9)	157 (5.6)	180 (6)	0.0017
Pneumonectomy and completion	64 (30.3)	625 (22.3)	689 (22.8)	0.0071

RML = right middle lobe.