

# Results of Surgery in Asymptomatic Lung Lesions with Special Emphasis on Lung Cancers

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## Abstract

**Objectives:** Asymptomatic lung lesions are more frequent with screening. We analyzed our surgical results in these patients with special emphasis on lung cancers. **Design:** Retrospective patient series. **Setting:** University Hospital. **Patients and Interventions:** Patients with asymptomatic lung lesions who underwent surgery during 1996-2003 were included. Patients were grouped according to the histologic character and analyzed for age, smoking (pack-years), detection method, surgical procedure and survival. Statistical analysis was performed. **Results:** Thirty-one (8.4%, 6 females) patients were asymptomatic. Twenty-two were malignant (Group 1) and 9 benign (Group 2). Group 1 was older ( $62 \pm 10$  vs  $46 \pm 15$ ;  $p=0.002$ ). Amount of smoking was higher in Group 1, but not significantly ( $38 \pm 29$  vs  $21 \pm 14$ ;  $p=0.09$ ). Lesions were detected on chest X-ray ( $n=26$ ) and CT scan ( $n=5$ ) during check-up ( $n=7$ ); work-up for non-thoracic pathology ( $n=7$ ), cardiovascular disease ( $n=4$ ), and unrelated thoracic disease ( $n=4$ ); preoperative work-up for non-thoracic disease ( $n=5$ ); and during follow-up for non-thoracic malignant disease ( $n=4$ ). Six of the benign lesions were tuberculosis. Nineteen patients had non-small cell lung cancer (NSCLC). Nine were stage I. NSCLC patients ( $n=19$ ) had a two- and five-year survival of 63% and 42%, respectively. In the resected NSCLC patients ( $n=14$ ), survival was 78% at two years and 51% at five years. **Conclusions:** Asymptomatic malignant lung lesions tend to be at an earlier stage. Survival is high and may justify screening.

**Keywords:** asymptomatic, pulmonary lesions, non-small cell lung cancer

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## INTRODUCTION

Ten percent of all lung lesions are asymptomatic and are usually detected during a routine chest X-ray or computerized tomography (CT) scan [1]. The routine use of chest CT scans, which tend to detect smaller lung lesions, has increased the rate of detection of these lesions. Early detection of lung cancer and subsequent surgical resection has been associated with increased long-term survival. Several studies show that stage I lung cancers with tumor size less than 1 cm are associated with an 80-90% five-year survival following surgical resection [2,3]. Lesions less than 2 cm in size were significantly associated with a higher survival rate [4,5]. Some authors even advocate wedge resections for these very early lung cancers [6].

There are a few reports on the results of surgical treatment of asymptomatic lung cancers found in patients undergoing lung volume reduction and vascular surgery [7-9]. In this report, we analyzed our patients with asymptomatic lung lesions that were surgically removed, especially focusing on the lung cancer patients. The aims of this paper were to histopathologically characterize asymptomatic lung lesions and to analyze the outcome of asymptomatic lung cancer patients.

## MATERIALS AND METHODS

At our thoracic surgery clinic, 1212 operations were performed during 1996-2003. Three hundred and seventy patients were operated for pulmonary lesions. Patients undergo routine preoperative assessment with physical examination, chest X-ray, CT scan, pulmonary function tests, electrocardiography, arterial blood gases and ventilation-perfusion scanning and echocardiography as appropriate.

Patients with asymptomatic lung lesions detected with a chest X-ray or CT scan were included in this study. Eventually, all patients had a CT scan prior to their surgical exploration. Patients with any thoracic symptoms related directly to the lung lesion and metastasis-related or paraneoplastic symptoms were excluded. Patients who refused surgery or did not undergo surgery for medical reasons were also excluded. Lesions in patients with unrelated stable lung or cardiac disease detected during routine evaluation were included.

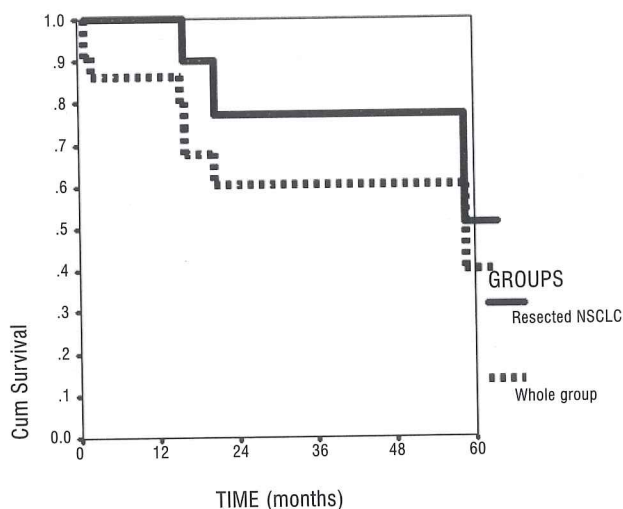
Patient characteristics, smoking history, and lesion characteristics were recorded. Kaplan-Meier survival analysis was performed. Patient characteristics were analyzed with Student's t-test and Mann-Whitney U test.

## RESULTS

Three hundred and seventy patients were operated for pulmonary lesions in 1996-2003. Thirty-one (8.4%) patients had asymptomatic lung lesions, and there was male predominance (25/6). Average age was  $57 \pm 14$  years. Twenty-two patients eventually had a diagnosis of malignancy.

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**Figure 1.** Overall survival of malignant patient group (Dashed line). Two-year and five-year projected survivals are 66% and 44%, respectively. Median survival was 59 months. Survival of surgically resected NSCLC patients (continuous line). Two-year and five-year projected survivals are 77% and 51%, respectively. Median survival was not reached.

Patient characteristics are depicted in Table 1. The average age was significantly lower in the benign lesion group ( $p=0.002$ ). The average amount of smoking was higher in the malignant lesion group; however, this difference did not reach statistical significance ( $p=0.09$ ). The other characteristics were not significant.

Most of the lesions were identified during a routine check-up or work-up of a non-thoracic condition (23/31, 74%). Eight patients had an asymptomatic lung lesion detected during investigation of a cardiovascular disease and thoracic diseases unrelated to malignancy. The situations that led to detection of the lung lesions are listed in Table 2.

Benign lesions were tuberculoma ( $n=6$ ), chondroid hamartoma ( $n=1$ ), hydatid cyst ( $n=1$ ), and fibrotic nodule ( $n=1$ ).

Twenty-two patients had pulmonary malignancy. The histologic diagnoses were adenocarcinoma ( $n=9$ ), and squamous ( $n=8$ ) and large cell carcinoma ( $n=2$ ). The remaining three patients had carcinoid, clear cell, and small cell carcinoma. The stages of the patients with non-small cell lung cancer (NSCLC,  $n=19$ ) are shown in Table 3. Nine patients (47% of NSCLCs) had Stage 1 disease. Fourteen of the pulmonary malignancy patients underwent anatomic lung resections.

Overall survival in the malignancy group was 66% at two years (Figure 1). Projected five-year survival was 44%. Median follow-up was 16.5 months (1-83). In the resected NSCLC patients ( $n=14$ ), survival was 78% at two years and 51% at five years (Figure 1). Median follow-up

**Table 1.** Patient characteristics

	Malignant (n=22)	Benign (n=9)	p-value
Male/Female	18/4	7/2	NS
Average Age	62 $\pm$ 10	46 $\pm$ 15	0.002
History of Smoking	19	7	NS
Never/Current/Ex Smoker	3/9/10	2/5/2	NS
Average Amount of Smoking	38 $\pm$ 29	21 $\pm$ 14	0.09
Detection-Operation Interval (months)	5.3 $\pm$ 10.6	2.8 $\pm$ 5.6	NS

was 19.6 months (4-83). NSCLC patients ( $n=19$ ) had a two- and five-year survival of 63% and 42%, respectively. In patients with stage I disease, only two patients recurred and seven patients are alive without recurrence.

## DISCUSSION

Asymptomatic lung lesions are usually noticed during a routine chest X-ray. It is frequently a nodular lesion in the periphery of the lung. The characteristics of the lesion, such as size, location, infiltrative pattern, presence of calcification, and fat content, and patient characteristics, such as age, and smoking history/amount are all important factors in the clinical evaluation of these lesions. Our study was able to demonstrate a significant difference in average age, with younger age in the case of a benign diagnosis. The average amount of smoking was higher in patients with a malignant diagnosis in our study; however, this can be attributed to the increased age in the malignant group. Eighty-four percent (26/31) of our patients were either current or ex-smokers. We did not have positron emission tomography (PET) scan available until 2003 in our institution; therefore, none of the patients had a preoperative PET scan. Most of the tuberculomas demonstrate a malignant uptake with PET scans, which does not prevent surgical explorations in these patients [10].

In the malignancy group, nine of our patients were stages III and IV. Four patients had T1-2 primary tumor. All of our patients had lesions larger than 1 cm in diameter, which increases the likelihood of lymphatic and distant metastasis. Screening studies in the early 80's have shown that annual chest X-rays were able to detect lung cancers at an early stage in 60% of the patients [11]. Our data is consistent with these findings.

Improved survival figures from surgical treatment series of early-stage lung cancers have stimulated the thoracic teams to carry out screening studies [2,3]. The interest was centered on annual screening of high-risk individuals for lung cancer in order to detect more patients



**Table 2.** Methods of detection of asymptomatic lesions in the lung

	Patients (n=31)	Malignant (n=22)	Benign (n=9)
Check-up, routine screening	7	3	4
Work-up for cardiovascular disease*	4	2	2
Work-up for non-thoracic disease†	7	6	1
Work-up for unrelated thoracic disease‡	4	3	1
Preoperative work-up for non-thoracic diseaseγ	5	5	0
Routine follow-up for non-thoracic malignant diseaseψ	4	3	1
Total	31	22	9

\* History of myocardial infarction or angina (n=4).

† Pharyngitis (n=2), epileptic seizure (n=1), renal colic (n=1), ophthalmic disease (n=1), gastritis (n=1), fibrotic lesion under the clavicle (n=1).

‡ Swelling of xiphoid (n=1), thoracic trauma (n=1), back pain (n=1), interstitial lung disease (n=1).

γ Carotid endarterectomy (n=2), nasal polypectomy (n=1), inguinal hernia repair (n=1), transurethral resection for benign prostate hyperplasia (n=1).

ψ Bladder cancer (n=3), breast cancer (n=1).

with early-stage lung cancer. In the late 90's, the initial report by Henschke and colleagues [12] showed that low-dose helical CT scan was able to detect lung nodules and cancers and was more sensitive than a chest X-ray. Many asymptomatic non-calcified lung nodules less than 1 cm in diameter were found with CT scans. However, only 11.6% of these nodules were found to be lung cancers. The most striking finding of this study was the higher rate (88%) of detection of early-stage lung cancers, when compared with previous studies using chest X-ray as the screening method [12]. Whether this higher rate will lead to a survival advantage remains to be answered.

An annual chest X-ray screening study from Italy showed a baseline lung cancer prevalence of 0.65% (16/2444) [13]. Subsequently, seven patients with asymptomatic lung cancer were detected in the second annual chest X-ray of 1361 subjects. Five of the seven lung cancers were stage I. A Japanese study analyzed 850 patients in relation to the detection of lung cancer and revealed a higher prevalence rate of surgically resectable disease in asymptomatic patients in their forties and fifties [14]. In 2214 patients who had vascular surgery in Germany during 1990-1994, the prevalence of lung cancer was 0.72% (16 patients) [9]. Only two of the patients were amenable for surgical resection. In our series, 14/19 (74%) patients underwent anatomic lung resections. However, our series is retrospective and we did not include patients with asymptomatic lung cancers who did not undergo surgical interventions. Therefore, the high resection rate is probably the result of this sampling bias.

**Table 3.** Stages of resected NSCLC patients (TNM, Mountain 1997)

Stages of the NSCLC Patients (n=19) †	
Stage IA	5
Stage IB	4
Stage IIB	1
Stage IIIA	4
Stage IIIB	1
Stage IV	4*

† 3/22 patients with typical carcinoid, clear cell carcinoma and small cell lung carcinoma were excluded from this group.

\* 2 pleural metastasis, 1 metastatic nodule in a different lobe, 1 multiple lung nodules.

In conclusion, most of the series show that asymptomatic lung cancers tend to be at earlier stages. Annual chest X-ray screening in high-risk populations results in detection of lung cancers at earlier stages in half of the patients. Chest CT scans tend to detect small lung cancers with early stages at higher rates (>80%).

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