Original Study

Incidental Diagnosis of Asymptomatic Non–Small-Cell Lung Cancer: A Registry-Based Analysis

Florian Kocher,[1,2] Fabian Lunger,[3] Andreas Seeber,[1,2] Arno Amann,[1,2] Andreas Pircher,[1] Wolfgang Hilbe,[1,4] Michael Fiegl[1]

Abstract

There is a paucity of data on non–small-cell lung cancer (NSCLC) patients diagnosed by coincidence in an asymptomatic state. According to this registry-based analysis, 117 of 1279 NSCLC patients had their cancer detected by coincidence. Patients were characterized by lower stage of disease and improved survival compared to patients with symptom-driven detection. Our findings point to the advantage of asymptomatic detection and underline the benefit of screening programs.

Introduction: Clinical manifestation of non–small-cell lung cancer (NSCLC) mainly occurs at advanced stages. Thus, the scientific community is evaluating different screening programs in high-risk patients to detect NSCLC at an earlier stage to improve survival. However, up to now patient selection and modalities have been discussed controversially. In this analysis we aimed to focus on asymptomatic NSCLC patients, whose disease was detected coincidentally and to elaborate the significance and effect of incidentally detected NSCLC on survival. **Patients and Methods:** Medical files of 1279 consecutive NSCLC patients diagnosed between 2001 and 2009 were retrospectively analyzed. Incidentally detected asymptomatic NSCLC patients were compared with patients with tumor-specific symptoms. **Results:** In 117 of 1279 patients an asymptomatic diagnosis was ascertained by coincidence (9.1%). A smoking history of $\geq$ 30 pack-years was documented in 41 (58.6%) of 70 evaluable patients with incidentally detected NSCLC. Patients with incidentally diagnosed NSCLC were characterized by lower stages at diagnosis, a better performance status, and a higher proportion of previous or present other malignancies. Overall survival (OS) was significantly superior in patients with an asymptomatic diagnosis compared with patients with symptoms (median OS, 38.9 months vs. 16.1 months; $P < .001$). In a Cox proportional hazard model, incidental diagnosis proved to be an independent prognostic factor with regard to OS. **Conclusion:** Our findings point to the advantage of asymptomatic detection of NSCLC and might underline the benefit of screening programs. Further research on the detection of lung cancer in asymptomatic patients outside of existing screening criteria is warranted.

Clinical Lung Cancer, Vol. 17, No. 1, 62-7
Keywords: Asymptomatic, Characteristics, Incidental, NSCLC, Outcome

Introduction

Lung cancer accounts for approximately 1.6 million annual deaths worldwide and approximately 85% of these deaths are attributable to non–small-cell lung cancer (NSCLC). Hence, it represents the most common cause of cancer-related death.[1] It is well known that the tumor stage is one of the most important prognosticators in NSCLC and has clinical implications on the specific treatment approach (eg, curative or palliative treatment concept). At diagnosis, most patients are in advanced stages of the disease,[2] and present with symptoms such as coughing, hemoptysis, chest pain, or dyspnea.[3,4] Absence of symptoms in the early stages in combination with aggressive tumor biology certainly contribute to the often late detection of NSCLC.

[1]Medical University Innsbruck, Department of Internal Medicine V (Haematology and Oncology), Innsbruck, Austria
[2]Tyrolean Cancer Research Institute, Innsbruck, Austria
[3]Medical University Innsbruck, Department of Gynaecological Endocrinology and Reproductive Medicine, Innsbruck, Austria
[4]Wilhelminenspital Wien, Department of Internal Medicine I (Haematology and Oncology), Vienna, Austria

Submitted: May 20, 2015; Revised: Jul 31, 2015; Accepted: Aug 11, 2015; Epub: Aug 22, 2015

Address for correspondence: Florian Kocher, MD, Medical University of Innsbruck, Department of Internal Medicine V, Anichstraße 35, A-6020 Innsbruck, Austria
Fax: +43/512504-26303; e-mail contact: florian.kocher@i-med.ac.at

1525-7304/$ - see frontmatter
http://dx.doi.org/10.1016/j.clc.2015.08.006

Nevertheless, some patients are diagnosed with NSCLC by coincidence without symptoms suggestive of the presence of malignancy. The records on such asymptomatically detected patients are sparse. To the best of our knowledge, only 2 studies so far have focused on lung cancer patients diagnosed by coincidence. One single-center study reported on lung cancer patients treated within a time period of 30 years at a university hospital in Japan.[5] The other analysis evaluated the effect of incidental diagnosis in surgically treated NSCLC patients.[6]

Different screening programs have been started over the past decades to detect lung cancer in an asymptomatic state. Within the different screening methods, only computed tomography (CT) proved to be an adequate tool with subsequent mortality reduction.[7-9] However, its use in clinical routine is still discussed controversially.

Over the past decade, our group has established a comprehensive NSCLC registry of patients treated in clinical routine. The aim of this project was to provide a holistic and comprehensive view on the disease with consideration of a multitude of factors that might influence the course of the disease. Consequently, we also evaluated the circumstances leading to diagnosis.[4] Prompted by the paucity of knowledge, we set out to perform a registry-based analysis to elucidate the relevance, clinical characteristics, circumstances leading to diagnosis, and outcome of patients incidentally diagnosed with NSCLC. Herein, we present definitive data regarding the significance of incidental NSCLC diagnosis in a representative cohort of NSCLC patients treated in the delineated region of Tyrol.

Patients and Methods

Between January 2001 and September 2009, 1279 patients were diagnosed with NSCLC at the Medical University of Innsbruck and affiliated hospitals. A prespecified protocol was used for data acquisition and circumstances of diagnosis were investigated and documented in detail. Tumor stage at the time of initial diagnosis was categorized according to the tumor, node, metastases staging system and the corresponding stages (6th edition). In the present study the focus was put on characteristics of NSCLC patients diagnosed incidentally. This cohort of patients was then compared with patients in whom specific symptoms led to the diagnosis of cancer. Patients were documented within our institution's comprehensive lung cancer project "Twenty-Year Retrospective of Lung Cancer (TYROL study)." This registry is focused on longitudinal and comprehensive analyses of lung cancer patients treated in daily routine.[10-14] Relevant data were collected using the hospitals' electronic data base and microfilm documentation. The TYROL study was approved by the ethics committee of the Medical University of Innsbruck.

Definition of Incidental Diagnosis

Medical files of patients were retrospectively reviewed regarding the circumstances of NSCLC diagnosis. Diagnosis in routine examinations (eg, staging of other malignancies, surveillance of previous tumors, preoperative examinations, other nonmalignant diseases, etc) without any lung cancer-specific symptoms was defined as an incidental asymptomatic finding. We used a very stringent definition of incidental diagnosis. Thus, if any symptoms were reported (eg, intermittent cough) it was defined as "symptomatic diagnosis."

Statistical Considerations

Categorical variables were compared using the χ^2 test. Overall survival (OS) was defined as time between diagnosis of NSCLC and death. OS was estimated using the Kaplan–Meier method. A log rank test was used to compare outcomes between different subgroups. Cox regression analysis was performed to depict the effect of different parameters. We conducted a matched-pair analysis in a 1:3 arrangement using a random-pick method. Parameters included in the matched-pair analysis were clinical stage (exact) and sex. In all analyses, a P value $\leq .05$ was considered statistically significant. All analyses were performed using SPSS software version 22 with Fuzzy matching extension plug-in (IBM Corp, Armonk, NY).

Results

Baseline Characteristics

Incidental diagnosis of asymptomatic NSCLC was ascertained in 117 of 1279 consecutively evaluated patients (9.1%). In those 117 patients, the mean age at diagnosis was 66.4 years (range, 41-83) and 77 patients were male (65.8%). The most common histological subtype was adenocarcinoma, which was detected in 74 patients (63.2%). A high proportion of patients were diagnosed in early-stage disease with 54 of the 117 patients (46.2%) diagnosed in stage I. Tumor sizes in node-negative patients without metastases were comparable between the groups (Table 1).

Circumstances Leading to Incidental Diagnosis

Different circumstances led to radiographic evaluations of the thoracic region. In most patients, radiographic examinations for various non-malignant diseases (n = 44; 37.6%) led to the discovery of a lesion suspected to be malignant with subsequent specific examinations and final confirmation of the diagnosis of NSCLC. Notably, examinations within routine medical check-ups in healthy individuals guided toward the diagnosis of NSCLC in 29 patients (24.8%). Surveillance of previous and/or present malignancies other than lung cancer were diagnostic for NSCLC in 25 (21.4%) and 12 (10.3%) patients, respectively. Finally, in 6 patients (5.1%) radiographic examinations after acute trauma led to the incidental detection of NSCLC. In most of the cases, routine chest x-ray (n = 67; 57.3%) was the first examination that guided the way toward the diagnosis of NSCLC. In 50 patients (42.7%), CT scans pointed at the potential occurrence of lung cancer.

Comparison of Incidentally Diagnosed Patients With Patients Who Presented With Symptoms

In a next step we performed a comparison of patients with incidental NSCLC diagnosis with the group of patients who presented with cancer-specific symptoms (n = 1162). Stage I was the most frequent stage in patients with an incidental finding of NSCLC. In comparison, patients with clinical symptoms presented with stage IV disease in most cases. Moreover, the proportion of stage I (incidental vs. symptoms: 46.2% [n = 54] vs. 20.5% [n = 232]; $P < .001$) and IV disease at diagnosis (19.7% [n = 23] vs. 43.0% [n = 487]; $P < .001$) significantly differed between these groups.

Consequently, a greater proportion of incidentally diagnosed patients received curative treatment. In surgically treated patients, 75 of 486 patients (15.4%) were diagnosed incidentally. In patients