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The female gender has a positive effect on survival independent of background life expectancy following surgical resection of primary non-small cell lung cancer: a study of absolute and relative survival over 15 years

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Summary Surgical resection is the treatment of choice for non-advanced lung cancer, but is encumbered with an overall relative poor long time prognosis. The purpose of this study was to examine if long time survival for patients operated for non-small cell lung cancer have changed over a 15 years period. We retrospectively studied hospital records of the 351 patients operated, with the intention to cure, for a primary non-small cell carcinoma (NSCLC) in our department between 1 January 1988 and 31 December 2002. Preoperative clinical variables were noted together with variables allowing staging based on pathological examination. Absolute survival and survival relative to expected was studied for the whole group using uni- and multivariate Cox analyses. Early 30 days mortality was 2.0%. The 5-year absolute and relative survivals for all patients were 46.3% and 52.6%, respectively. After 10 years corresponding values were 32.9% and 44.6%. At the end of the study, the 15-year absolute survival was 27.8% with a relative survival of 46.2%. Univariate analysis revealed that age, gender, nodular stage, tumour size, p-stage, type of resection, time of operation and additional cardiovascular disease at the time of operation significantly influenced survival. Multivariate analysis for all patients revealed that low age, female gender, low nodular stage, and operation late in the study period were significant prognostic factors predicting improved survival. When including a population based age- and gender-adjusted median expected life time for every patient as a predictor for survival, only female gender and low nodular stage were additional significant and independent positive prognostic factors.

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1. Introduction

Carcinoma of the lung remains a major health problem with an overall 5-year absolute survival in Norway of 9% for men and 12% for women [1]. Prognosis is generally found to depend on the patient's clinical condition, gender and age, stage of disease at the time of diagnosis and histological type [2—10]. Complete surgical resection is the treatment of choice for non-advanced non-small cell lung cancer, but even this group of patients are encumbered with a relative poor long time prognosis [11—13]. The incidence of lung cancer has declined for men but continues to increase for women, now being the second cause of cancer-related death in the European female population and the most frequent cause of cancer-related death among women in North America [14,15]. This is in parallel to the increase in the prevalence of cigarette smoking among females.

In general, patients that are candidates for lung resection for carcinoma are at a relatively high age. Many previous studies have focused on the late survival without taking into consideration the high comorbidity with regard to age and other diseases. As many as 19—30% of pT1N0M0 NSCLC undergoing surgery die of causes not related to lung cancer [16,17]. Additional cardiovascular disease, in particular, seems to influence the long time survival [18].

The purpose of this study was to examine if long time survival for patients operated for non-small cell lung cancer have changed over a 15 years period.

2. Material and methods

2.1. Patients

In this retrospective study all medical records, but one that was lost, of 466 patients undergoing thoracotomy between 1 January 1988 and 31 December 2002 at Haukeland University Hospital were scrutinised and 109 patients excluded due to non-cancer-related thoracotomy, benign or non-conclusive tumour histology, small cell carcinoma, secondary tumours, secondary operations and explorative operation. Five additional patients undergoing a sub-optimal and limited lung resection, based on per operative macroscopic evaluation, were also excluded. Thus, a total of 351 cases satisfied the inclusion criterion for the present study: patients undergoing their first-time surgical resection, with the intention to cure, for a primary non-small cell carcinoma (NSCLC) of the lung within the study period of 15 years. From the records, preoperative variables were noted with regard to previous cardiovascular disease, medical history leading to diagnosis and preoperative pulmonary function. Throughout the study period, the policy of our unit has been to offer a surgical treatment to patients clinically staged as stage I and II in addition to selected patients in stage IIIa (T3N1M0 or N2-patients) if the patients are judged to have a sufficient cardiac reserve and an adequate predicted residual lung function, based on spirometry and ventilation/perfusion isotopic scan. The clinically staging was based on physical investigation, chest X-ray, electrocardiogram, computerized tomography (CT) of the chest and upper abdomen and bronchoscopy. These standard preoperative examinations have been performed for all the patients in the present study. Supplementary investigations, such as mediastinoscopy and high resolution CT were performed in patients with uncertain staging. Ventilation/perfusion scan examinations were performed in patients with FEV_1 between 1.0 and 1.5 L. All patients studied had been operated with a standard lateral thoracotomy with lung resection along anatomical boundaries for complete clearance of all visible tumour mass with the least possible loss of lung tissue. A formal mediastinal lymph nodal clearance was not performed, but all visible and/or palpable hiliar nodes were dissected free and sampled for evaluation. The retrospective histopathological evaluation of the specimens was the basis for the pathological staging of tumours using the revised international TNM staging for lung cancer [19]. The histological classification of tumours was based on the criteria of the World Health Organisation [20]. Based on this, 292 patients (83.2%) were defined as completely resected. Sixty-three patients did receive postoperative chemotherapy or radiation. Two of these patients were included into ongoing clinical studies (IALT and BLANK), 25 patients were classified as N2/N3 and the remaining 36 patients were treated as a consequence of cancer found in the resection margins or infiltration of mediastinum or chest wall.

2.2. Data collection and follow-up

Patients were seen in the outpatient clinic every 3 months for the first year and every 6 months until 5 years after the operation. One patient, leaving the country, was lost for follow-up 6 months after surgery. All other patients were retrieved through the Norwegian population registry. Median follow-up time was 48.4 months (range 2 days to 186.2 months). Data for expected survival were obtained