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Treatment with curative intent of stage III non-small cell lung cancer patients of 75 years: A prospective population-based study

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ABSTRACT

Background: There is little data on the survival of elderly patients with stage III non-small cell lung cancer (NSCLC).

Methods: Patients with stage III NSCLC in the Netherlands Cancer Registry/Limburg from January 1, 2002 to December 31, 2008 were included.

Findings: One thousand and two patients with stage III were diagnosed, of which 237 were 75 years or older. From 228 patients, co-morbidity scores were available. Only 33/237 patients (14.5%) had no co-morbidities, 195 (85.5%) had one or more important co-morbidities, 60 (26.3%) two or more co-morbidities, 18 (7.9%) three or more co-morbidities and 2 patients (0.9%) suffered from four co-morbidities. Forty-eight percent were treated with curative intent. No significant difference in Charlson co-morbidity, age or gender was found between patients receiving curative or palliative intent treatment. Treatment with curative intent was associated with increased overall survival (OS) compared to palliative treatment: median OS 14.2 months (9.6–18.7) versus 5.2 months (4.3–6.0), 2-year OS 35.5% versus 12.1%, for curative versus palliative treatment.

Findings: Patients who received only radiotherapy with curative intent had a median OS of 11.1 months (95% confidence interval [95% CI] 6.4–15.8) and a 5-year OS of 20.3%; for sequential chemotherapy and radiotherapy, the median OS was 18.0 months (95% CI 12.2–23.7), with a 5-year OS of 14.9%. Only four patients received concurrent chemo-radiation.

Interpretation: In this prospective series treating elderly patients with stage III NSCLC with curative intent was associated with significant 5-year survival rates.

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1. Introduction

Non-small cell lung cancer (NSCLC) remains one of the most lethal and frequent cancers world-wide.[1–3] The disease occurs most frequently in the elderly population, with about 50% of the patients being 70 years or older and approximately 25% over the age of 74 years.[1,2,4] With current demographic trends both in Europe, the United States and in major Eastern countries, the absolute number and the proportion of elderly patients with lung cancer will further increase in the coming decades.[1,2] Because of the age distribution and the smoking history of most lung cancer patients, the majority of them present with major co-morbidities at the time of diagnosis, which may render many patients not suitable for aggressive treatments and which will lead to higher non-cancer related deaths in this population.[4,5]

Although concurrent chemo-radiotherapy has become the treatment with the best chance for long-term survival in patients with stage III NSCLC, there are scarce data on the outcome of elderly patients treated with curative intent for stage III NSCLC.[6–13] Elderly patients entered in clinical trials consistently showed more haematological toxicity than the younger group, a finding which was also observed in advanced stage elderly patients.[8,9,12–15] Elderly patients also experienced more non-haematological toxicity, although this varied between trials: In NCCTG 94-24-52, they had more pneumonitis, more oesophagitis in RTOG 94-10, and more renal complications in CALGB 9130.[8,9,13] Despite the increased level of toxicity experienced by the elderly patients, their survival was similar to that observed in younger individuals. The question how to deal with the 75 years and older group with stage III NSLC remains unanswered.[16–19]

In the present study, we investigated in a large prospective population-based registry the outcome of patients treated with curative or palliative intent.

2. Patients and methods

2.1. Netherlands Cancer Registry/ Limburg (NCR/L)

All patients with a pathological diagnosis of NSCLC[20] in south and middle Limburg and with stage III (UICC 6th Edition[21]) from January 1, 2002 to December 31, 2008 were included. Data were obtained from the population-based Netherlands Cancer Registry (NCR) of the Comprehensive Cancer Centre the Netherlands. The NCR/L is a population-based cancer registry, which was established in 1984 and is a department of the Comprehensive Cancer Centre the Netherlands-Location Maastricht. The NCR/L covers the region of mid and southern Limburg, which is situated in the southeast of The Netherlands. On 1 January 2006, the region covered a total of 853,553 inhabitants. The main sources of information are regional hospitals and pathology laboratories from which the NCR/L receives reports on a weekly basis since 1986. After receiving the notification reports, trained registration clerks collect all relevant data of the patients and tumours from the medical records.

Information on topography and morphology was coded according to the International Classification of Diseases for Oncology, 3rd Edition.[21] Tumour stage was recorded in accordance with the tumour–node–metastasis classification system.[21] Completeness of case ascertainment of the NCR/L is very high; for lung cancer, this is estimated to be >95%.[22]

2.2. Co-morbidity

Co-morbidity of all lung cancer patients was scored using the Charlson co-morbidity index (CCI).[23] Co-morbidity was defined as disease that was present at the time of diagnosis and was prospectively retrieved from hospital records.

2.3. Staging and treatment

Only patients without a malignant pleural or cardiac effusion were offered treatment with curative intent. Patients were staged with a whole body ^{18}F-deoxyglucose (FDG)-Positron Emission Tomography (PET) scan and a CT or MRI of the brain unless on a regular CT scan of the chest and the upper abdomen metastases were already visualised. Patients were treated according to standard regional protocols.

According to the regional guidelines, the treatment of choice for patients with stage III (T4 and/or N2-3) NSCLC was concurrent chemo-radiotherapy. Patients with T3N1M0 tumours were treated with a lobectomy and a lobe-specific nodal dissection. Adjuvant chemotherapy was not applied in the studied time period in elderly patients.

In practice, however, the multidisciplinary team, comprising at least a pulmonologist specialised in lung cancer, a thoracic surgeon, a radiation oncologist, a radiologist, a nuclear medicine specialist and a pathologist, was left free to choose the most appropriate treatment for an individual patient. Thus, elderly patients often received sequential chemotherapy and radiotherapy, radiotherapy alone, chemotherapy alone or best supportive care, which could include palliative radiotherapy.

Sequential chemotherapy consisted of cisplatin (75 mg/m^2) or carboplatin (AUC 5) on day 1 and gemcitabine 1250 mg/m^2 on day 1 and 8. Cycles were repeated every 21 days for a total of 3 cycles. The carboplatin dose in milligrams was based on the target AUC (5) × (glomerular filtration rate + 25), with the glomerular filtration rate calculated according to the Cockroft–Gault formula. Standard dose-reduction rules were applied if indicated. In non-progressive patients (RECIST criteria), based on a CT scan of the chest, the primary tumour and the involved lymph nodes were treated with radiotherapy.[24] The dose was specified according to ICRU 50 guidelines.[25] From 2002 to 2005, radiotherapy consisted of a dose of 60 Gy in 30 fractions in 6 weeks. From 2006, individualised accelerated radiotherapy to the primary tumour and the pre-treatment involved lymph nodes on FDG-PET-CT scan was given after induction chemotherapy.[26] The mean radiation dose was 64.8 Gy given in 36 bi-daily fractions of 1.8 Gy with at least 8 h of inter-fraction interval in an overall treatment time of 3.6 weeks.[27] This is a biological