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Tolerance and benefits of treatment for elderly patients with limited small-cell lung cancer

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ARTICLE INFO

Article history:
Received 7 December 2012
Received in revised form 29 May 2013
Accepted 30 July 2013
Available online 7 September 2013

Keywords:
Small-cell lung cancer
Elderly
Treatment
Outcome
Survival
Population-based

ABSTRACT

Objectives: Over 20% of all newly diagnosed Dutch patients with small-cell lung cancer (SCLC) are aged ≥75 years. Uncertainties still exist about safety and efficacy of chemotherapy and chemoradiation in elderly patients. We evaluated the association between patient characteristics and (completion of) treatment and also evaluated toxicity, response and survival in elderly patients with SCLC.

Materials and Methods: Population-based data from patients aged 75 years or older and diagnosed with limited SCLC in 1997–2004 in The Netherlands were used (N = 368). Additional data on co-morbidity, motive for deviating from guidelines, grades 3–5 toxicity, response and survival were gathered from medical records.

Results: Although only relatively fit elderly were selected for chemotherapy, almost 70% developed toxicity, leading to early termination of chemotherapy in over half of all patients. Median survival time was 6.7 months, but differed strongly according to type and completion of treatment (13.5 months for chemoradiation, 7.1 months for chemotherapy, 2.9 months for best supportive care, 11.5 months for patients receiving at least 4 cycles of chemotherapy and 3.6 months for less than 4 cycles).

Conclusion: Although toxicity rate was high and many patients could not complete the full chemotherapy, those who received chemotherapy or chemoradiation had a significantly better survival. We hypothesize that a better selection by proper geriatric assessments is needed to achieve a more favourable balance between benefit and harm.

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http://dx.doi.org/10.1016/j.jgo.2013.07.008

1. Introduction

Over twenty percent of all newly diagnosed patients with small-cell lung cancer (SCLC) in The Netherlands are 75 years or older.[1,2] Nowadays, the standard treatment for patients with SCLC limited disease who have a good performance score is concomitant chemoradiation and prophylactic cranial irradiation in case of a good response.[3–5] Elderly patients may experience more toxicities due to serious co-morbidity, polypharmacy, functional limitations or reduced organ functions.[6,7] This is one of the reasons that older patients and those with serious co-morbid conditions are usually underrepresented in clinical trials.[8–11] This means that the results of these studies may not be valid for everyday clinical practice that deals with many elderly patients with serious co-morbidity. Previous population-based studies from our group have shown that 40% of elderly (75+ years) patients with limited disease SCLC did not receive chemotherapy and two-thirds of those receiving chemotherapy could not complete the full treatment.[2,12] In the current study we evaluated the association between patient characteristics and (completion of) treatment on the one hand and treatment outcome on the other hand in elderly Dutch limited disease SCLC patients in everyday clinical practice.

2. Patients and Methods

2.1. Study Population and Data Collection

Population-based data from six of nine regional Dutch cancer registries were used, reflecting the Dutch population and covering about two-thirds of The Netherlands. These registries record data on patients newly diagnosed with cancer in all hospitals in their region. Trained registrars routinely collect data on patient and tumour characteristics, like histology, tumour grade, localisation, morphology, and stage directly from the medical records. The quality of the data is high, due to thorough training of the administrators and computerized consistency checks at regional and national levels. Completeness is estimated to be at least 95%.[13] Data handling of the un-identifiable data from the cancer registry was done according to the specifications of the officially recognized Code of Conduct: Use of Data in Health Research. Follow-up of vital status of all patients was completed up to January 1st, 2009. The information on vital status was actively obtained from the municipal registries. For causes of death, data were merged with the database of Statistics Netherlands.

For the present study, all patients aged 75 years or older with primary limited stage SCLC (C34.0–C34.9 and ICD-O codes 8040–8045), diagnosed in the regions of 6 Dutch comprehensive cancer centres during 1997–2004 were included (n = 368). Clinical stage of limited disease was classified according to the guidelines that were used in the study period as tumours confined to one hemithorax without pleural effusion and no distant metastases. Age was classified as 75–79 years and 80+ years. Recommended treatment for limited disease in this period was cyclophosphamide-doxorubicin-etoposide (CDE) followed by thoracic irradiation (45–50 Gy) or cisplatin-etoposide (CE) with concurrent thoracic irradiation. Treatment of SCLC was classified as combined chemoradiation (sequential or concurrent), chemotherapy alone, radiotherapy alone and best supportive care, including palliative radiotherapy (BSC). Due to the high probability of brain metastases, prophylactic cranial irradiation (PCI) for patients with limited disease (LD) has been recommended since the early 2000s.[14] The implementation of this approach was slow and consequently only 15 patients had received PCI in the study period. Therefore, combined chemoradiation in combination with PCI was not analysed separately. Completion of chemotherapy was classified as: at least 4 cycles of chemotherapy, less than 4 cycles of chemotherapy, and no chemotherapy.

Additional data on co-morbidity (according to the Adult Co-morbidity Evaluation 27 (ACE-27) classification[15]), WHO (World Health Organization) performance status (PS), detailed information on type of treatment, number of cycles, motives for chemotherapy or radiotherapy denial, adaptations of chemotherapy and underlying motives, toxicity and tumour response were gathered from the medical records. For recording toxicity, a list of toxicity based on grades 3–5 toxicity from the CTC (common toxicity criteria) version 3.0[16] was used for recording. As this was a retrospective study, collected data were based on toxicity that was described in the medical files by treating physicians, and toxicity data were therefore gathered less intensively compared to most prospective studies, e.g. weekly blood counts were not routinely performed.

The ACE-27 index is a validated 27-item co-morbidity index for patients with cancer. Twenty-seven co-morbid conditions were gathered from the medical records. Each condition was graded to severity by the registrar and classified as absent, grade 1 (mild decompensation), grade 2 (moderate decompensation) and grade 3 (severe decompensation). In case of two or more co-morbid conditions the highest grade was counted, and two or more grade 2 conditions were counted as grade 3.

2.2. Statistical Analyses

Differences in number of cycles of chemotherapy between groups of patient characteristics were tested with the chi-square test. Toxicity rates and response rates were described as percentages per age group and type or completion of treatment. Crude survival was calculated as time from diagnosis until death (any cause) or the end of the study (January 1, 2009). Patients who were still alive at the end of the study were censored. The log rank test was performed to evaluate differences between survival curves in univariate analyses. Cause of death was described, according to age and pre-existing co-morbidity.

3. Results

3.1. Patient Characteristics

The general characteristics of the patients are shown in Table 1. Three hundred and sixty-eight patients with limited disease were included. Two hundred and forty-eight of these patients (67%) were aged 75–79 years and 120 patients (33%) were diagnosed at age 80 years or older. Eighty-two percent of all patients had co-morbidity at the time of cancer diagnosis (19% grade 1, 35% grade 2, and 28% grade 3). The most