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Original Research

Changes in treatment patterns and survival in elderly patients with stage I non–small-cell lung cancer with the introduction of stereotactic body radiotherapy and video-assisted thoracic surgery

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Abstract ***Background:*** The optimal treatment of elderly patients with early-stage non–small-cell lung cancer (NSCLC) remains elusive. Still, the introduction of video-assisted thoracic surgery (VATS) and stereotactic body radiotherapy (SBRT) may have led to more elderly receiving treatment and improved median overall survival (OS).
Materials and methods: We analysed data from the Netherlands Cancer Registry of 2168 patients ≥65 years with clinical stage I NSCLC and distinguished two periods: 2004–2008 (A) and 2009–2013 (B). The analyses focussed on treatment patterns and median OS for patients receiving surgery, radiotherapy or neither surgery nor radiotherapy. Furthermore, we explored the influence of the application of VATS and SBRT.
Results: The resection rate did not differ between the periods A and B (51% versus 53%; $p = 0.37$), despite significantly more VATS procedures in the latter period (0% versus 32%; $p < 0.001$). Application of radiotherapy increased (26% versus 33%; $p = 0.001$), especially SBRT (3% versus 63%; $p < 0.001$). The proportion of patients receiving neither therapy decreased (23% versus 14%; $p < 0.001$). Median OS for all patients significantly improved

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(31 versus 42 months; p = 0.001), and also for those receiving radiotherapy (23 versus 33 months; p = 0.02), but not significantly for surgical patients (65 versus 74 months; p = 0.16). Still, in multivariable analysis, surgical patients had an increased risk of death in period A compared with period B (hazard ratio [HR] 1.20; 95% confidence interval [CI], 1.01–1.43); this was not the case for patients receiving radiotherapy (HR 1.19; 95% CI, 0.99–1.43). Five-year OS was 57% for surgical patients and 23% for those receiving radiotherapy.

Conclusion: In elderly patients with stage I NSCLC, the use of surgery remained constant, that of radiotherapy increased and fewer patients received neither treatment over the years. Median OS improved for all patients; surgery was associated with the highest long-term OS.

1. Introduction

Lung cancer is the leading cause of cancer death worldwide [1] and in the Netherlands [2]. The highest incidence rates are found among women aged 65–69 years and among men aged 70–74 years [3]. On the basis of demographic developments, the absolute number of new cases of lung cancer in the Netherlands is expected to increase by 46% for men and 24% for women between 2015 and 2040 [4]. Only small improvements in overall survival (OS) have been reported so far. Driessen *et al.* found that 5-year relative survival for patients ≥70 years in the Netherlands had increased from 12% in 1990–1994 to 16% in 2010–2014 [5].

Surgery offers the best potential cure for early-stage non–small-cell lung cancer (NSCLC). It is not always offered, however, to elderly patients in view of their advanced age and comorbidities [6]. In a study by Palma *et al.*, 38% of 875 patients ≥75 years with stage I NSCLC did not receive any form of treatment [7]. The outcome of surgery can potentially be improved by video-assisted thoracic surgery (VATS) [8]. In previous studies, VATS was superior to thoracotomy in terms of postoperative morbidity, even in octogenarians [9–11]. For patients who are inoperable because of comorbidities, radiotherapy is an alternative treatment with curative intent [8]. Shirvani *et al.* reported that stereotactic body radiotherapy (SBRT) offers better long-term OS than external beam radiotherapy [12]. SBRT makes use of high doses of radiation in a limited number of fractions, thereby avoiding damage to organs close to the tumour [13]. In a study by Haasbeek *et al.*, the application of SBRT in Dutch patients ≥75 years with stage I NSCLC was associated with a 9-month improvement in OS over the period 2001–2009 [8].

New technologies, such as VATS and SBRT, have gained acceptance by now. The question is, however, whether treatment is offered to more elderly patients now and whether the OS has improved. To answer this question, we performed a study evaluating changes in treatment patterns and OS for patients ≥65 years with clinical stage I NSCLC.

2. Materials and methods

Population-based data from the southern region of the Netherlands Cancer Registry (NCR) were used. This region covers 2.4 million inhabitants (15% of the Dutch population). The NCR records data of all patients newly diagnosed with cancer. The NCR automatically receives notifications of all newly diagnosed malignancies from the nationwide network and registry of histopathology and cytopathology in the Netherlands. Additional sources are radiotherapy institutes and the Dutch national registry of hospital discharge. These data are supplemented with data from medical records, including patient characteristics (such as age, sex and comorbidities) and tumour characteristics (such as the date of diagnosis, tumour type, histology, stage and treatment). The type of surgery is recorded in the database, whereas details of radiotherapy such as dose or fraction are missing. We selected data from the southern region because information on comorbidities is routinely collected in this region only. Information on vital status was obtained from the population registries network. Cause of death was not available. Follow-up data were complete until February 2017.

We retrieved data of all patients ≥65 years diagnosed between 2004 and 2013 with clinical stage I NSCLC, according to the International Union Against Cancer tumour-node-metastasis (TNM) edition 6 and 7 (from 2010 onwards). Treatment patterns and median OS were assessed for two periods: 2004–2008 (period A) and 2009–2013 (period B). In 2004, fluorodeoxyglucose positron emission tomography (FDG-PET) scanning has been incorporated in the national guideline for NSCLC in the Netherlands. PET scans were introduced gradually in the Netherlands and became a more common practice between 2005 and 2008. Endoscopic ultrasound/endobronchial ultrasound has become more common in daily clinical practice since 2010 and was incorporated in the national guideline in 2011. In the Netherlands, SBRT became available in 2003 and became widespread after 2007 [8]. In 2006, the first VATS lobectomy was performed in the Netherlands