Increase in curative treatment and survival of lung cancer in Norway 2001 - 2016

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Introduction

Since the turn of the century there has been a marked improvement in survival for lung cancer patients in several countries [1-3]. The reasons for this may include improved diagnostics, more therapeutic options, better quality of therapy and an increased proportion of patients being treated with intention to cure. Factors as reduced tobacco consumption, public health campaigns and increased awareness may also have contributed.

Due to limited and incomplete data the exact contribution of the different factors on the increase in survival has been difficult to disentangle. A comprehensive overview of the entire group of cancer patients in a complete population is a prerequisite for credible evaluation of incidence, diagnostics, treatment and outcome. Here we present data from Norway, a nation where a universal public health care system, one national cancer registry, and individual, unique identification number for all inhabitants enable merging and cross linking of data from several registers and reports. Access to virtually complete national data offers a good base for evaluation and outcome. The Cancer Registry of Norway (CRN) has a practical complete registration of all cancer patients, and the quality of the registry has been described [4].

In lung cancer, treatment with intention to cure comprises surgery, stereotactic body radiotherapy (SBRT) and conventional fractionated radiotherapy. The aim of this descriptive report, based on nationwide population-based data was to study the whether the proportion of lung cancer patients given curative treatment and the survival rates had changed in the period 2001-2016.

Methods

This material, extracted from CRN comprises data for all patients diagnosed with lung cancer from January 1st 2001 to December 31st 2016 with follow up to December 31st 2017. In this period the Norwegian population increased from 4.5 million to 5.2 million (Table 1).

CRN classifies the lung cancer patients as ‘localized’ (stage I according to TNM7), ‘regional’ (stages II and III), ‘metastatic’ (stage IV) or ‘unknown’. Clinical and pathology reports complement each other to provide complete registration at the CRN when cancers or premalignant conditions are diagnosed. Reporting to CRN is mandatory by law and does not depend on patient consent. For lung cancer this consists of the diagnosis with ICD-10 codes C34.0 – C34.9 (cancer of bronchus and lung). Pathology reports make a basis for identifying those operated and for reminders when reports from the clinicians are lacking. All reporting and exchange of data are based on the unique 11 digit identification number for every inhabitant. The CRN receives patient-identifiable radiotherapy data annually from radiotherapy units across Norway. These data include total dose given, number of fractions, intention of treatment and hospital.

Curative treatment was defined as surgery, SBRT or conventional fractionated radiotherapy. If a patient was given more than one treatment modality (8.8% of the treated patients), he was assigned only to the most intervening. Radiotherapy was defined as SBRT if the patient received one of the following combinations of fractions and total dose: 1) 3 fractions with a total of 45 Gray (Gy), 48Gy or 54Gy, 2) 5 fractions with a total of 50Gy or 55Gy, 3) 7 fractions with a total of 49Gy, 4) 8 fractions with a total of 56Gy or 60Gy, or 5) any combination of fraction and dose where the radiologist has written “stereo” or “SBRT” in a commentary field. Conventional fractionated radiotherapy was identified wherever the radiologist had marked the treatment as curative.

Statistical analyses

Testing for statistical significance in trends of number of new cases and incidence rates were obtained from a likelihood ratio test comparing an unadjusted generalised linear model (glm) with log link and a glm adjusted for calendar year as a categorical variable. Median ages were presented with their respective interquartile intervals. For all testing in proportions and medians, standard RxC chi square test were used [5]. Relative survival (RS) was estimated using the cohort approach for all years where patients have five years of follow up, while a combination of cohort and period approach was used for all subsequent years where there is not enough follow-up time. More details have been described [6]. The estimates were age-standardised according to the lung cancer population in Norway in 2012–2016. All analyses were performed using Stata 15.1 [7].

Results

The group studied comprises a total of 43,137 patients diagnosed with lung cancer, and as shown in Table 1, the absolute numbers diagnosed yearly with lung cancer have had a marked increase to 3205 in 2016. The age adjusted incidence has increased significantly in both sexes ($p < 0.0001$). For men, the number seems to level off in the last five-year period. The age-standardised incidence for the whole group increased from 50.6 per 100,000 in 2001 to 59.5 per 100,000 in 2016 (Norwegian population standard 2014) ($p < 0.0001$). The median age at diagnosis increased in both females and males (Table 1), and the patients given SBRT were older than those given the two other modalities (Table 2).

There was a reduction in the percentage of small cell lung cancer from 19.9% to 15.3% in women ($p < 0.0001$). The change from 15.1% to 13.1% in men did not reach statistical significance.

The percentage diagnosed with localized disease increased from 11.2% to 19.7% in females and from 13.2% to 16.3% in males ($p < 0.0001$ for both). The proportion with metastatic disease was reduced from 52.8% to 38.3% in females and from 47.4% to 37.1% in males ($p < 0.0001$ for both).

In 2001, 16.2% were offered surgical treatment and 6.7% were given conventional fractionated radiotherapy, and none were treated with SBRT, thus 22.9% were treated with intention to cure (Figure 1). In 2016 these figures were 20.6% and 8.5% respectively. In addition, 8.8% were treated with SBRT giving a total of 37.9% treated with curative intent. Thus the percentage of the lung cancer patients given treatment with intention to cure increased significantly from 2001 to 2016 ($p < 0.0001$). SBRT was introduced in 2002, and offered nationwide in 2008 [3]. The percentage of the patients given conventional fractionated radiotherapy varies between 6.2% and 8.9% and show no tendency of change in the period studied.

The 2142 patients diagnosed with lung cancer in 2001 had a median survival of 6.0 (95% CI 5.6–6.7) months and for the 3205 diagnosed in 2016, the median survival was 11.8 (10.9–12.7) months. The 5-year relative survival was 9.4 (8.1–10.8) % in 2001 and estimated to 19.9 (19.2–20.6)% in 2016. Also, the survival after 1 and 2 years have increased significantly from 2001 to 2016 (Figure 1). In the subgroup with localized disease, the 5-year survival increased from 42.6% in 2001 to 64.0% in 2016 in women and from 37.6% to 54.9% in males in the same period (table 3). For those with regional disease the 5-year survival increased from 12.4% to 25.6% in females and from 11.5% to 20.4% in men in the same period. For those with metastatic disease there was a modest increase to 3.2% in females and 2.0% in males in 2016 (Table 3). There has been a centralization of the lung surgery, from 12 hospitals in 2001 to eight hospitals in 2005. The data in CRN show that since 2010 the 30 days mortality after lung cancer surgery has been $\leq 2\%$ and the 90 days mortality $\leq 3\%$.

Discussion

These data from Norway show that the proportion of lung cancer patients treated with intention to cure have had a marked and statistically significant increase from 22.9% in 2001 to 37.9% in 2016. To this 15.0 percent point increase, SBRT contributed with 8.8%. The increase in curatively treated patients was more pronounced than the increase in the proportion of patients diagnosed in localized stage.

In the material presented by Brustugun et al [3], data for SBRT was collected directly from the radiation units, giving 11% treated with this modality in 2016. The treatment data presented here is based merely on the yearly reports to the CRN giving that 8.8% were treated with SBRT that year. Thus, the reported increase in curative treatment may be underestimated. Conventional fractionated radiotherapy was offered also to patients in more advanced stages with a worse prognosis compared to patients offered surgery and SBRT. However, in the period studied, the proportion of the patients given conventional fractionated radiotherapy did not change and probably did not introduce any errors.

It is noteworthy that both median- and 5-year survival have been doubled from 2001 to 2016 (Figure 1). Parts of this improvement in survival may be explained by the reduced percentage diagnosed with small cell lung cancer and increase in patients diagnosed in an earlier stage in 2016 than in 2001. As seen in Table 3, the increase in 5-year survival is mainly explained by increase in those with localized stage, partly also by those with regional disease, but for those with metastatic disease the outcome is practically unaltered and poor. The increase in survival for the whole group of lung cancer patients may be explained by an increased proportion diagnosed at an earlier stage, an increase in curative treatment and improvement in the treatment quality [3]. There has also been a marked reduction in population prevalence of daily smokers [8]. Lung cancer patients are most likely included in this trend which may have positively influenced their co-morbidity, complications related to treatment and survival.

Data from The Norwegian Association of Thoracic Surgeons show that the percentage of the operations where pneumonectomy was performed was 6.2% in 2016. The percentage found inoperable during surgery was 0.9% in 2016. Resection using thoracoscopic technique was done in less than 5% of the operations until 2010. Thereafter there has been an increase, and in 2016, 39% of the operations were done thoracoscopically [9]. These findings reflect improved diagnostics and patient selection which together with the reduced operative mortality may have contributed to the improved long time survival.

The main reason for the improved rate of curative treatment is the advent of SBRT. One consequence of the introduction of SBRT could be a reduction of the use of surgical treatment, but in parallel to the increase in SBRT, surgery has increased from 16.2% in 2001 to 20.6% in 2016.

Despite the positive trends in survival, lung cancer remains a serious disease. Even in the countries with the best surveillance and survival, near 80% of the patients are dead five years after the diagnosis [2] and the disease continues to be a significant cause of death for those who survive the first five years [10].

It is a clear intention that more cancer patients are diagnosed at an early stage, and this has taken place for lung cancer. The present study and the CONCORD material [2] show that the positive trend for lung cancer patients continues. For patients diagnosed with metastatic disease, however, the survival is still poor.

The main finding in this report is a marked increase in the proportion of lung cancer patients offered curative treatment. This tendency is expected to continue and hopefully 40% of the patients diagnosed can be offered curative treatment within a few years. The presented increase in curative treatment and survival may serve as a benchmark for the years to come.

Conflict of interest

PMH has declared that he has received salary and paid travel for giving lecture at Surgical Skills course arranged by Johnson & Johnson. The other authors have declared no conflict of interest.

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