



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

Steinar Solberg¹ · Yngvar Nilssen² · Odd Terje Brustugun³ · Tom Kristian Grimsrud² · Per Magnus Haram⁴ · Nina Helbekkmo⁵ · Åslaug Helland⁶ · Harald Harris Hjelde⁷ · Bjørn Jakobsen⁸ · Bjørn Møller² · Martin Petersen⁹ · Trond-Eirik Strand² · Sissel Gyrid Freim Wahl¹⁰ · Marianne Aanerud¹¹ · Lars Fjellbirkeland¹²

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Abstract

We have studied the alterations in the use of curative treatment and the outcome for lung cancer patients in Norway 2001–2016. The Cancer Registry of Norway has a practically complete registration of all cancer diagnoses, treatments given and deaths. For the years 2001–2016, 43,137 patients were diagnosed with lung cancer. Stereotactic radiotherapy was established nationwide from 2008 and its use has increased, and in 2016, 8.8% were given this treatment. In addition 20.6% were operated and 8.5% were treated with conventional radiotherapy. Thus 37.9% of those diagnosed were treated with intention to cure, compared to 22.9% in 2001 ($p < 0.0001$). Further, the median survival for the whole group diagnosed with lung cancer increased from 6.0 (95% CI 5.6–6.7) months in 2001 to 11.8 (95% CI 10.9–12.7) in 2016. The 5 year survival increased from 9.4 (95% CI 8.1–10.8)% to 19.9 (95% CI 19.2–20.6)% in the same period. In 2016 the age adjusted incidence rate was 59.5 per 100,000 (Norwegian standard) and had increased significantly in both sexes. There had also been an increase in mean age at diagnosis and the proportion diagnosed in an early stage. The increase in curative treatment has been paralleled with a doubling in both the median and 5-year survival. The present results are used for surveillance and as a benchmark, and we are looking forward to reaching a proportion of 40% of patients given curative treatment.

Keywords Lung cancer · Surgery · Oncology

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.

✉ Steinar Solberg
ssolber@online.no

¹ Department of Cardiothoracic Surgery, Rikshospitalet, Oslo University Hospital, Oslo, Norway

² The Cancer Registry of Norway, Oslo, Norway

³ Section of Oncology, Drammen Hospital, Vestre Viken Hospital Trust, Drammen, Norway

⁴ Department of Cardiothoracic Surgery, St Olavs Hospital, Trondheim, Norway

⁵ Department of Pulmonology and Department of Oncology, University Hospital of North Norway, Tromsø, Norway

⁶ Department of Oncology, Radiumhospitalet, Oslo University Hospital and Faculty of Medicine, University of Oslo, Oslo, Norway

⁷ Department of Thoracic Medicine, St Olavs Hospital, Trondheim, Norway

⁸ Department of Pulmology, Molde Hospital, Molde, Norway

⁹ Department of Pulmology, Stavanger University Hospital, Stavanger, Norway

¹⁰ Department of Pathology, St Olavs Hospital, Trondheim, Norway

¹¹ Department of Pulmology, Haukeland University Hospital, Bergen, Norway

¹² Department of Pulmology, Rikshospitalet, Oslo University Hospital and Faculty of Medicine, University of Oslo, Oslo, Norway

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

Table 1 Background data for the 43,137 patients diagnosed with lung cancer 2001–2016

	2001	2006	2011	2016	<i>p</i> value
Population in Norway*	4,513,751	4,660,677	4,953,088	5,236,151	
New cases of lung cancer					
Females	795	1044	1251	1527	<0.0001
Males	1347	1475	1659	1678	<0.0001
Incidence, age-standardized rates, Norway, 2014 per 100,000 per year					
Total	50.6	56.7	60.2	59.5	<0.0001
Females	35.4	43.8	48.7	53.8	<0.0001
Males	71.5	73.7	75.7	67.9	<0.0001
Age, years median (25, 75 percentile) at diagnosis					
Females	69 (58, 76)	69 (61, 78)	70 (63, 77)	71 (65, 77)	<0.0001
Males	71 (62, 77)	70 (62, 77)	71 (64, 79)	71 (65, 78)	<0.0001
Proportion small cell lung cancer (%)					
Females	19.9	19.2	14.5	15.3	<0.0001
Males	15.1	14.4	12.8	13.1	=0.2003
Stage distribution (%)					<0.0001 [†]
Localized					
Females	11.2	14.7	22.1	19.7	<0.0001
Males	13.2	13.3	19.8	16.3	<0.0001
Regional					
Females	23.5	26.3	25.9	24.2	=0.4005
Males	24.8	30.5	26.8	28.7	=0.0049
Metastatic					
Females	52.8	47.5	43.4	38.3	<0.0001
Males	47.4	44.8	45.0	37.1	<0.0001
Proportion daily smokers in age group 16–74 years (%)*					
Females	31	24	18	11	
Males	30	23	17	13	

*Data from Statistics Norway¹¹. The daily smokers are reported for all inhabitants

[†]Significant differences in stage variable distribution over time in both sexes

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 Gy, 48 Gy or 54 Gy, (2) 5 fractions with a total of 50 Gy or 55 Gy, (3) 7 fractions with a total of 49 Gy, (4) 8 fractions with a total of 56 Gy or 60 Gy, 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 5 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 5-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 statistically 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 (Fig. 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 (Fig. 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

Table 2 Background data for the 5525 patients treated with curative intent 2012–2016

	Surgery	Stereotactic radiation (SBRT)	Conventional radiotherapy
Females, n (%)	1509 (49.0)	595 (53.3)	618 (46.6)
Males, n (%)	1573 (51.0)	521 (46.7)	709 (53.4)
Age, years median (25, 75 percentile) at diagnosis			
Females	68 (61, 72)	73 (68, 79)	67 (60, 72)
Males	68 (63, 73)	74 (69, 80)	68 (62, 73)

Fig. 1 The proportion of lung cancer patients given curative treatment 2001–2016 and the survival for those diagnosed 2001, 2006, 2011 and 2016

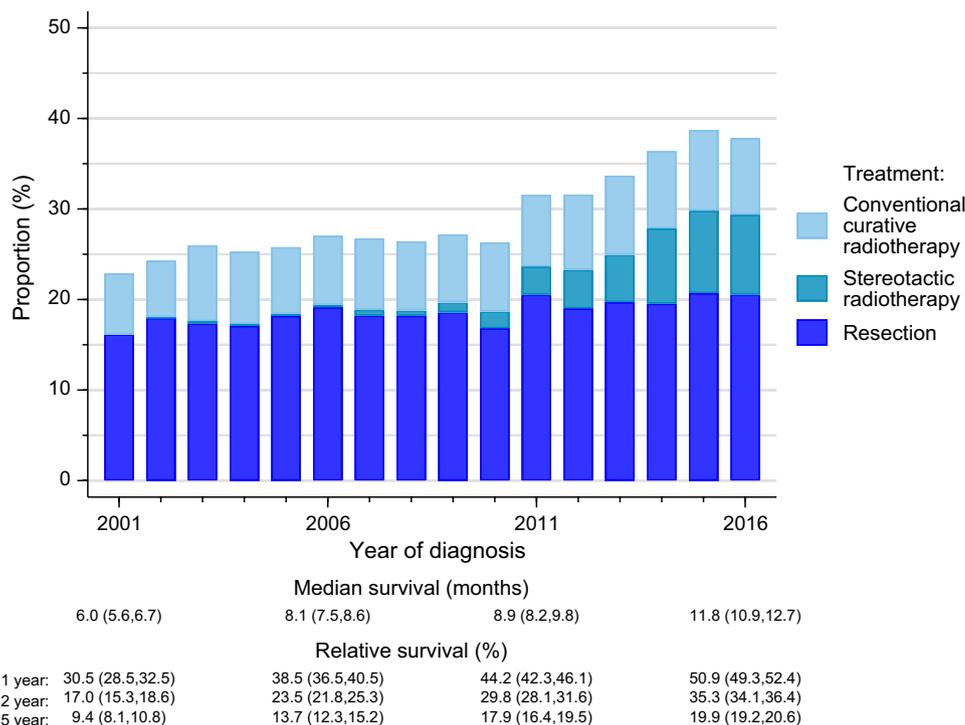


Table 3 Relative, 5 year survival (95% CI) for the subgroups with localized, regional or metastatic stage of lung cancer

	2001	2006	2011	2016
Localized				
Females	42.6 (30.4, 54.2)	50.3 (41.9, 58.1)	54.8 (47.7, 61.5)	64.0 (61.0, 66.9)
Males	37.6 (30.1, 45.1)	48.9 (40.8, 56.5)	48.0 (41.2, 54.4)	54.9 (51.8, 58.0)
Regional				
Females	12.4 (8.0, 17.8)	14.3 (10.5, 18.8)	19.2 (15.1, 23.7)	25.6 (23.5, 27.7)
Males	11.5 (8.0, 15.6)	15.5 (12.1, 19.2)	20.3 (16.3, 24.6)	20.4 (18.7, 22.2)
Metastatic				
Females	0.7 (0.2, 1.9)	2.6 (1.4, 4.4)	2.2 (1.2, 3.9)	3.2 (2.6, 3.8)
Males	1.6 (0.7, 3.0)	1.4 (0.6, 2.7)	2.6 (1.5, 4.0)	2.0 (1.6, 2.4)

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 (Fig. 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 5 years after the diagnosis [2] and the disease continues to be a significant cause of death for those who survive the first 5 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.

Compliance with ethical standards

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.

References

1. Strand TE, Bartnes K, Rostad H. National trends in lung cancer surgery. *Eur J Cardiothorac Surg*. 2012;42(2):355–8. <https://doi.org/10.1093/ejcts/ezs002>.
2. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. 2018. [https://doi.org/10.1016/s0140-6736\(17\)33326-3](https://doi.org/10.1016/s0140-6736(17)33326-3).
3. Brustugun OT, Grønberg BH, Fjellbirkeland L, et al. Substantial nation-wide improvement in lung cancer relative survival in Norway from 2000 to 2016. *Lung Cancer*. 2018;122:138–45. <https://doi.org/10.1016/j.lungcan.2018.06.003>.
4. Larsen IK, Smastuen M, Johannesen TB, et al. Data quality at the Cancer Registry of Norway: an overview of comparability, completeness, validity and timeliness. *Eur J Cancer*. 2009;45(7):1218–31. <https://doi.org/10.1016/j.ejca.2008.10.037>.
5. Cochran WG. The chi square test of goodness of fit. *Ann Math Stat*. 1952;23(3):315–45.
6. The Cancer Registry of Norway. Cancer in Norway, 2017. Technical supplement: statistical methods. Oslo, Norway. 2018. <https://www.kreftregisteret.no/globalassets/cancer-in-norway/2017/cin-2017supmeth.pdf>.
7. StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX; StataCorp LLC2017.
8. Statistics-Norway. Daily smokers. Statistics Norway, Oslo, Norway. <https://www.ssb.no/en/helse/statistikker/royk>. Accessed 10 May 2018.
9. Norwegian Association for Cardiothoracic Surgery. Thoracic surgery in Norway. 2016. <http://legeforeningen.no/Fagmed/Norsk-thoraxkirurgisk-forening/thoraxkirurgiregisteret/>.
10. Bugge AS, Lund MB, Valberg M, Brustugun OT, Solberg S, Kongerud J. Cause-specific death after surgical resection for early-stage non-small-cell lung cancer. *Eur J Cardiothorac Surg*. 2018;53(1):221–7. <https://doi.org/10.1093/ejcts/ezx274>.

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