Incidence and survival from lung cancer in Greenland is comparable to survival in the Nordic countries

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ABSTRACT

INTRODUCTION: Oncological treatment of lung cancer has been available in Greenland since 2004. We evaluated patient characteristics and survival rates for the first six years of local lung cancer treatment.

METHODS: From September 2004 to August 2010, a total of 173 patients with lung cancer were referred to treatment at Queen Ingrid's Hospital. On 1 February 2014, treatment results, survival, and prognostic variables were analysed.

RESULTS: The mean age at diagnosis was 63 years. Non-small cell lung cancer (NSCLC) was diagnosed in 145 patients (84%); 56% had squamous cell carcinoma, 34% had adenocarcinoma, 2% had large cell carcinoma and 8% had NSCLC not otherwise specified (NOS). In all, 28 (16%) had small cell lung cancer. A total of 142 patients (82%) received treatment; 20 underwent surgery (ten stage Ib, one stage IIa, five stage IIb, four stage IIIa); palliative chemotherapy was given to 122 of the 142 treated patients (86%). Of these, 36 patients (30%) received second-line chemotherapy.The median survival of patients undergoing primary lobectomy/pneumonectomy, palliative chemotherapy, and no treatment was 76.3 months, 11.8 months, and 2.0 months, respectively ($p < 0.0001$).

CONCLUSION: Evaluation of the first six years of lung cancer treatment in Greenland revealed a disease incidence and survival comparable to those found in the Nordic countries. To further decrease mortality from lung cancer, health-care resources should continue to be allocated to the prevention and treatment of lung cancer in Greenland.

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Lung cancer is the most common cause of death from cancer worldwide. In the Inuit population, the incidence has increased remarkably over the past 40 years, and lung cancer is now as frequent as in other Nordic countries with a world population-standardised incidence of 50 per 100,000 [1, 2].

Early detection and rapid initiation of surgical/oncological treatment are issues essential to improved survival rates in patients with lung cancer. Since 2004, oncological treatment of lung cancer has been available in Greenland, and patients are treated according to Danish standards. In Greenland, however, cancer diagnosis and treatment are challenged on several levels: 1. Inadequate recognition by the lay public of the signs and symptoms of possible lung cancer leading to delays in medical attention-seeking. 2. Unavailability of medical services in smaller settlements leading to delays in the provision of medical attention. 3. Issues related to infrastructure, geography and weather conditions, which hamper schedules for diagnostic procedures as well as treatment.

The aim of this study was to evaluate patient characteristics and survival rates from the first six years of lung cancer treatment in Greenland.

METHODS

Patients and diagnostic work-up

Patients diagnosed with lung cancer and referred to Queen Ingrid's Hospital in Nuuk (QIH) during the period from 1 September 2004 to 31 August 2010 were included in the analysis. (QIH is the central hospital facility in Greenland with sole responsibility for local oncological treatment). All patients had permanent residence in Greenland at the time of diagnosis. Data sources were the Registry of the Greenland National Board of Health, the Danish Cancer Registry and patient files from Queen Ingrid's Hospital. Data on residency status at the time of diagnosis as well as mortality data were provided by the Danish National Registry. Histopathological data were generated by the Department of Pathology, Rigshospitalet, Copenhagen, Denmark, as this hospital processes all histological material from Greenland. Staging procedures included computed tomography (CT), positron emission tomography (PET)/CT, mediastinoscopy, oesophagoscopy, bronchoscopy and bronchoscopic ultrasound as well as surgical procedures as needed. Testing for activating epidermal growth factor receptor (EGFR)-mutations or other activating mutations and translocations was not performed routinely during the 2004-2010 period.

Treatment

The treatment strategy at QIH was identical to the strategy employed at the Department of Thoracic Surgery and the Department of Oncology, Rigshospitalet, Copenhagen. Medical treatment was administered at QIH, whereas surgery, radiation therapy, and concomitant chemo-radiation were administered at Rigshospitalet.

ORIGINAL ARTICLE

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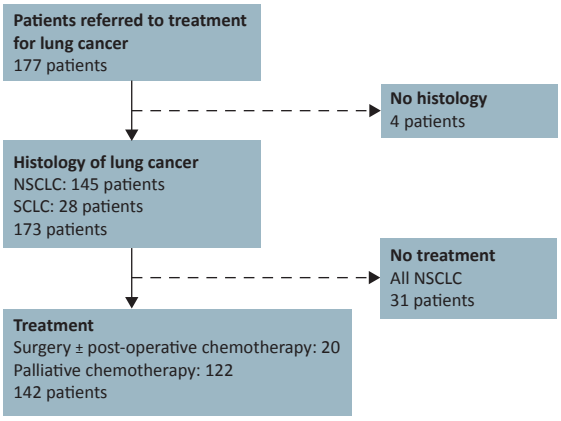
FIGURE 1

Treated lung cancer patients in Greenland from September 2004 to August 2010.



NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer.

TABLE 1

Histological diagnoses and stages in 173 patients with lung cancer.

Diagnosis	Patients, n
Small cell lung cancer	
Limited disease	4
Extensive disease	24
Total	28
Non-small cell lung cancer	
Squamous cell carcinoma, stages:	
I[b]	10
II[a]	1
II[b]	7
III[a]	13
III[b]	27
IV	23
Sum	81
Adenocarcinoma, stages:	
I[b]	2
II[b]	1
III[a]	8
III[b]	19
IV	19
Sum	49
Large cell carcinoma (IIIa, IIIb, IV)	3 (1, 1, 1)
Not otherwise specified (IIIa, IIIb, IV)	12 (2, 3, 7)
Total	145

Inoperable patients with locally advanced non-small cell lung cancer (NSCLC) were offered platinum-based doublet chemotherapy combined with sequential thoracic irradiation 60 Gy in 30 fractions (2004-2009) or concomitant thoracic irradiation 66 Gy in 33 fractions (2009-2010). First-line treatment of patients with advanced disease was a platinum-doublet (cisplatin or carboplatin combined with vinorelbine), and second- or third-line treatment options were docetaxel, erlotinib and pemetrexed. Patients with small cell lung cancer (SCLC) received treatment with cisplatin or carboplatin plus etoposide. In patients with limited stage, chemotherapy was combined with hyperfractionated chest irradiation, i.e. 45 Gy in 30 fractions administered twice daily starting at the first or the second course. Responders with performance status 0-1 were offered prophylactic cranial irradiation, 30 Gy in 10 fractions.

Complications during chemotherapy were treated either at QIH or at local hospitals with professional support from QIH as needed. All patients had optional phone access to the oncology unit at QIH during their cancer treatment.

Ethics

The study was approved by the Ethical Committee of the Greenlandic National Board of Health.

Statistics

Nonparametric analysis was applied to the data. Overall survival was calculated as the interval from the date of diagnosis to the date of death or to 1 February 2014, whichever came first; the minimum follow-up was 30 months. Survival curves were constructed using the method of Kaplan and Meier. The prognostic value of clinical variables was analysed using the log-rank test. Significant variables were fed into a multivariate Cox regression analysis to identify independent variables associated with poor survival. For all tests, $p < 0.05$ was considered the level of significance. The SPSS statistical software system for Windows (SPSS version 19.0, Chicago, IL) was used for the statistical analysis.

Trial registration: not relevant.

RESULTS

Patient characteristics

From September 2004 to August 2010, 177 patients diagnosed with lung cancer were referred to QIH (**Figure 1**). Lung cancer was not histologically verified in four patients, which leaft 173 for analysis; 103 (60%) were men and 70 (40%) were women. The mean age at the time of diagnosis was 63 years for men (range: 45-87 years) and 64 years for women (range: 26-80 years).

NSCLC was diagnosed in 145 patients (84%); 56% had squamous cell carcinoma, 34% had adenocarcinoma, 2% had large cell carcinoma, and 8% had NSCLC not otherwise specified (NOS). A total of 28 (16%) of the patients had SCLC. Histological diagnoses and stages are listed in **Table 1**. Of the 28 patients with SCLC, 24 (86%)

had extensive disease. Of the 145 patients with NSCLC, 61% were diagnosed with stage IIIb-IV disease.

Of the 173 patients with histologically verified lung cancer, 142 patients (82%) received treatment. In all, 20 patients underwent surgery. The pathological stage was: ten stage Ib, one stage IIa, five stage IIb, four stage IIIa. Eleven patients underwent lobectomy and nine patients underwent pneumonectomy (nine patients received post-operative chemotherapy). Palliative chemotherapy was given to 122 of the 142 treated patients (86%). Of these, 36 patients (30%) received second-line chemotherapy.

Thirty-one of the 173 evaluated patients (18%) received no cancer treatment; 18 had performance 3-4, three had poor kidney function, five refrained from treatment and in five patients the reasons were unknown.

Survival

The median survival of patients diagnosed with NSCLC was 10.8 months for men and 10.7 months for women; the median survival for patients diagnosed with SCLC was 14.8 months for men and 11.6 months for women. The gender differences were non-significant, p = 0.78.

Survival analysis of histological subgroups of NSCLC patients showed a median survival of 11.8 months for adenocarcinoma, 12 months for squamous cell carcinoma, and 6.8 months for non-classified NSCLC/large cell carcinomas. The difference in survival between histological subgroups was not statistically significant, p = 0.95. After one year, 41 of 81 patients (51%) with squamous cell carcinoma were alive; 24 of 49 patients (49%) with adenocarcinoma were alive; and 15 of 28 patients (54%) with SCLC were alive.

After two years, 19 of 81 patients (23%) with squamous cell carcinoma were alive; 12 of 24 (24%) with adenocarcinoma were alive; and seven of 28 (25%) with SCLC were alive.

After one year, 39 of 65 treated patients (60%) with squamous cell carcinoma were alive; 23 of 41 patients (56%) with adenocarcinoma were alive; and 15 of 28 patients (54%) with SCLC were alive.

The median survival of patients undergoing primary lobectomy/pneumonectomy, palliative chemotherapy, and no treatment was 76.3 months, 11.8 months and 2.0 months, respectively. The difference between the groups was statistically significant p < 0.0001 (**Figure 2**).

The median survival of NSCLC stage I, II, III and IV patients was 56.5 months, 55.4 months, 12.1 months and 5.8 months, respectively. The difference in survival between stages was statistically significant p < 0.0001 (**Figure 3**).

Multivariate Cox regression analysis showed that stage and treatment were statistically significant predictors of survival, p = 0.0001.

FIGURE 2

Overall survival in 173 patients with lung cancer, 31 patients undergoing no treatment (—), 122 patients undergoing palliative chemotherapy (—), and 20 patients undergoing primary lobectomy/pneumonectomy (—), p < 0.0001.

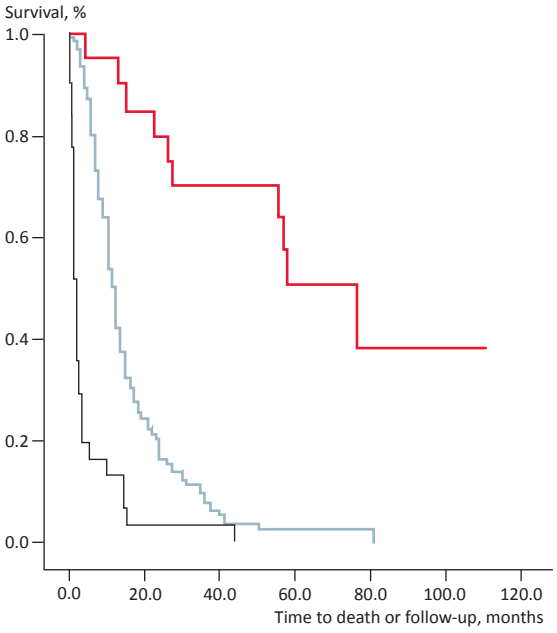
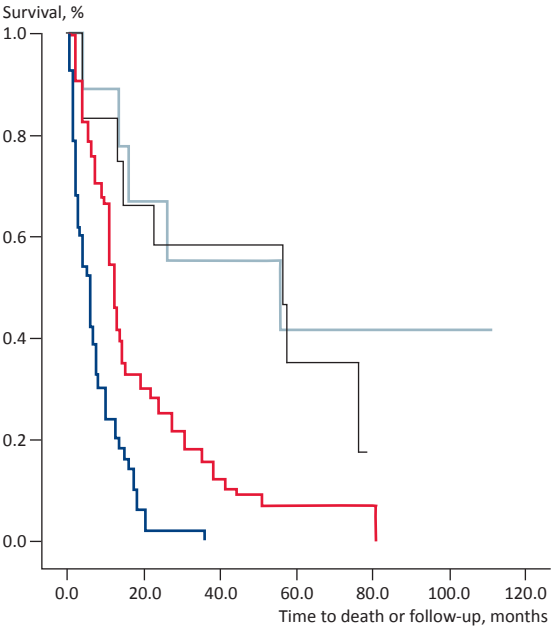


FIGURE 3

Overall survival in 145 patients with non-small cell lung cancer; 12 patients stage I (—), nine patients stage II (—) , 74 patients stage III (—), and 50 patients stage IV(—), p < 0.0001.



Nuuk in winter clothes. Queen Ingrid's Hospital is the yellow complex with the dark roofs situated inland from the third bay on the right.

DISCUSSION

In this study, the mean age at diagnosis of lung cancer was 63 years for men and 64 years for women. In other Nordic countries, the mean age at the time of diagnosis is around 70 years [3]. The age difference may reflect a tendency towards an earlier smoking debut in Greenland than in other Nordic countries.

The histopathological results showed that 56% of the 145 patients with NSCLC had squamous cell carcinoma and 34% had adenocarcinoma. In general, studies of NSCLC have reported an increasing incidence of adenocarcinomas and a relative decrease in squamous cell carcinomas so that adenocarcinomas are becoming more common than squamous cell carcinomas. This trend has been associated with an increasing preference for filter cigarettes among smokers [4]. The high percentage of squamous cell tumours in this study and the early age at diagnosis suggest that smoking habits in Greenland may be different from smoking habits in other countries.

Currently, the lung cancer incidence among Inuit men and women is as high as in the other Nordic countries. The incidence of lung cancer correlates with the prevalence of heavy smokers in Inuit during the past decades. In 2005, 66% of the adult population in Greenland smoked despite widespread anti-smoking campaigns [5]. Although recent surveys suggest a decreasing consumption, a latency period of several decades between smoking and cancer development implies that the lung-cancer epidemic may not have reached its peak [2]. Therefore, it is essential to continue campaigns against smoking and explore smoking behaviours [5]. In patients with lung cancer, smoking cessation is an important means of improving quality of life and increasing the efficacy of treatment; the positive effects of smoking cessation are comparable in power to the effects of established therapeutic interventions. In relation to the interpretation of the histological results and the survival data of this study, it is a limitation that we did not record smoking habits.

Stage IIIb/IV disease was diagnosed in 61% of patients with NSCLC. The percentage of patients with stage IIIb/IV lung cancer at diagnosis seems to be the same in Greenland as in Denmark where 60% of lung cancer patients have stage IIIb/IV at diagnosis [6]. The relative distribution of patients with limited and extended disease stage SCLC also reflects the distribution in Denmark. Hence, the amount of stage IIIb/IV patients in Greenland at diagnosis is not considered a confounder in analysing survival data.

In the present study, 20 of the 173 patients (12%) underwent curatively intended surgery, and their median survival was 76.3 months; 31 of the 173 patients (18%) received no cancer treatment, and their median survival was two months (Figure 2). The difference in survival was statistically significant.

The results stress the importance of diagnosing lung cancer at a curable stage and the benefit of rapid initiation of oncological treatment. In Greenland, the lack of awareness of the disease, relative unavailability of medical services in smaller settlements as well as issues relating to infrastructure and a challenging climate can potentially influence the time of diagnosis and delay initiation of treatment. Thus, patients sometimes have to travel several days and more than 2,000 km to get to the hospital; and appointments at the hospital will often have to be changed due to sudden changes in weather conditions resulting in flight cancellations. To overcome these logistic challenges, treatment information and informed consent are often facilitated by local health-care professionals at the nearest township, and follow-up is often carried out locally.

In this study, 60% of treated patients with squamous cell carcinoma were alive after one year, 56% of treated patients with adenocarcinoma were alive after one year and 54% of patients with SCLC were alive after one year. These results match the results from other urbanised areas, even though wide international inequalities in lung cancer survival remain apparent, even between European countries [3, 7]. However, there is still room for improvement for lung cancer patients in Greenland. A future reduction in lung cancer mortality requires broader education of the public, improved access to health-care and further surveillance on lung cancer incidence and smoking prevalence within subpopulations in various parts of Greenland [7].

CONCLUSION

The establishment of a central oncology unit at QIH in Nuuk, Greenland has been associated with many challenges due to the geographical background, the climate, and the limited health-care resources. Nevertheless, evaluation of the first six years of lung cancer treatment in Greenland showed that treatment according to Danish guidelines is feasible and long-term survivors were seen. In the attempt to further decrease mortality from lung cancer, health-care resources should continue to be allocated to the prevention and treatment of lung cancer in Greenland.

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CONFLICTS OF INTEREST: Disclosure forms provided by the authors are available with the full text of this article at www.danmedj.dk

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