National trends in lung cancer surgery

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Abstract

OBJECTIVES: Trends in lung cancer surgery may reveal potential for improvement and are important for planning by care providers.

METHODS: Using data from the Cancer Registry of Norway, we analysed the outcomes of lung cancer surgery during the periods of 1994–95, 2000–01 and 2006–07. The Cox regression model was carried out to identify the period effect on survival.

RESULTS: A total of 2201 patients were operated on. Surgery was centralized from 24 hospitals in the first two periods to 13 hospitals in the last. The resection rates varied from 6 to 31% across the counties. From the first to the last period, the national resection rate decreased from 16 to 19% ($P_{\text{trend}}=0.001$), and the 1-year survival rate increased from 73 to 82%. The proportion of resected patients in pathological stage I–II decreased from 87 to 83% ($P_{\text{trend}}=0.048$), the proportion of pneumonectomies from 27 to 15% ($P_{\text{trend}}<0.001$), and the rate of mortality within 30 days of the surgery from 4.8 to 3.0% ($P_{\text{trend}}=0.072$). In the first two periods, 31% of these early deaths were caused by complications directly related to the surgical technique, whereas, in the latter period, no deaths were directly related. The only unfavourable trend was the waiting time between the final diagnostic procedure and surgery, which increased from 29 to 40 days throughout the three periods ($P<0.001$). Survival (excluding those who died within 30 days) was significantly improved in the last period (risk ratio (RR): 0.72 ($P<0.001$)).

CONCLUSIONS: Despite an increased surgical waiting time, important aspects of lung cancer surgery, including resection rates, have improved in recent years.

Keywords: NSCLC • SCLC • Trends

INTRODUCTION

The surgical care of lung cancer patients in the 1990s was suboptimal in Norway and in other countries [1, 2]. In Norway, the postoperative mortality (≤30 days) was high, at 5.0%, and there was a high frequency of fatal surgical complications, such as bleeding or bronchopleural fistulas [3]. Moreover, many patients apparently were not offered potentially curative surgery. Thus, from 1993 to 2000, 16% of Norwegian lung cancer patients underwent surgical treatment but as much as 14% more were considered resectable based on a retrospective evaluation [2]. Waiting times, too, were disappointing, as 43% waited >4 weeks and 8% waited >8 weeks from final diagnosis to surgery [4].

Lung cancer has received increased attention during the last two decades. In parallel, thoracic surgery has been centralized. We have studied trends of important aspects for lung cancer surgery to investigate if care for these patients has improved.

MATERIALS AND METHODS

Using data from the Cancer Registry of Norway, we analysed the surgical treatment of lung cancer patients over three 2-year periods: 1994–95, 2000–01 and 2006–07. The latter period was selected because it was the last period of complete registration when the study was initiated. Furthermore, the registry contains comprehensive data for all of the operated patients since 1993.

All of the lung cancer patients in the registry were identified and included if the diagnosis was confirmed prior to death ($n=12 852$). A total of 236 patients were excluded because the diagnosis was neither clinically certain nor verified by cytology or histology. For the patients with more than one primary lung cancer, each cancer case was included. The registry's data quality and collection criteria have been reported elsewhere [5] (http://www.krefregisteret.no/Global/Publikasjoner%20og%20rapporter/CiN2006_web.pdf).

Patients were regarded as surgically treated only if the malignant tumour was resected. The pathology reports of these patients were reviewed and reclassified according to the seventh version of the tumour-node-metastasis system for lung cancer [6]. Tumours residing in the central third of the lung were classified as centrally located. The number of surgically treated lung cancer patients divided by the national total of lung cancer patients defined the resection rate. Postoperative mortality was defined as death within 30 days of the index operation.

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Differences among the groups were analysed with the Chi-square test, and any variations over time were analysed using a Chi-square trend analysis. For the patients who underwent preoperative cytological or histological sampling, the waiting time was defined as the interval between the last preoperative diagnostic procedure and the surgery. The waiting times in the three periods were compared using a one-way ANOVA. Survival was defined as the time between the date of the index surgery and death. The survival rates were calculated using the life table method. The follow-up ended on 1 September 2010.

Cox regression was used to reveal the relative risks (RRs) for the effect of the various variables on survival. The independent variables of sex, age (<70 vs. ≥70 years old), tumour location (side), surgical procedure (pneumonectomy vs. a less extensive resection), pStage (I–II vs. III–IV), histology (non-small cell lung cancer (NSCLC) vs. 'other' lung cancers) and period (1994–95 vs. 2000–01 vs. 2006–07) were included in the analysis. These variables were chosen from formerly identified prognostic factors and were included using a direct method; thus, entry and exit criteria were not defined [7]. The histological group defined as 'other' lung cancers included all other histologies, such as small cell lung cancer (SCLC) (n = 49), other neuroendocrine tumours (n = 95), sarcomas (n = 7) and unspecified cases (n = 184).

Differences with P-values of ≤0.05 were considered to be statistically significant. Confidence intervals (CIs) are given within 95% limits. SPSS version 18.0 was used for all of the statistical calculations. Institutional review board approval was provided by the Cancer Registry of Norway.

RESULTS

For the three study periods combined, 12,616 cases of newly diagnosed lung cancer were included. A total of 2201 patients underwent resection, seven of whom underwent resection twice. The mean age of resected patients increased from 63.9 years in the first to 64.3 in the second and to 65.2 years in the last period. The age distribution and other characteristics are displayed in Table 1. The proportion of resected patients with adenocarcinoma was 32% (n = 187) in the first period and increased to 44% (n = 305) and 42% (n = 392) in the following periods (Ptrend = 0.001). The diagnosis was based on a clinical investigation (only imaging and/or bronchoscopy without a positive biopsy) in 9%, without significant differences between the study periods. The proportion of centrally localized tumours remained unchanged (37–40%, Ptrend = 0.44).

The surgical procedures were performed in 24 hospitals. In the first two periods, seven and six of these hospitals, respectively, performed fewer than 10 operations per period. In 2006–07, the operations were centralized to 13 institutions, two of which performed fewer than 10 operations per period.

The postoperative mortality gradually decreased from 4.8 to 3.8 to 3.0% over the three periods (Ptrend = 0.072) (Fig. 1). In the first two periods, bleeding and bronchopleural fistulas accounted for 31% of the deaths; however, no patient succumbed to such complications in the last period (Table 2). Postoperative mortality was higher among men (4.8 vs. 1.7% in women, P < 0.001). The proportion of pneumonectomies was almost halved from the first (27%) to the last period (15%) (Ptrend < 0.001).

The proportion of operated patients in pStage IIIA increased from 11% in the first period to 15% in the last two periods

$P_{\text{trend}} = 0.019$ (Table 1). Similarly, the proportion of patients in pStage I–II decreased from 87 to 83% from the first period to the last period ($P_{\text{trend}} = 0.048$) (Fig. 1).

The 1-year survival rate after surgery increased from 73% (CI: 70–77%) in the first period to 76% (CI: 73–79%) in the second and 82% (CI: 80–85%) in the third (Fig. 1). The corresponding 2-year survival rates were 59% (CI: 55–63%), 61% (CI: 58–65%) and 72% (CI: 69–75%), respectively. After excluding deaths within 30 days after surgery, the 1-year survival rates were 77% (CI: 74–81%), 79% (CI: 76–82%) and 85% (CI: 82–87%), respectively, while the 2-year survival rates were 62% (CI: 58–66%), 64% (CI: 60–66%)

Table 1: Characteristics of patients resected for lung cancer in different diagnostic periods

<table>
<thead>
<tr>
<th></th>
<th>1994–95, n (%)</th>
<th>2000–01, n (%)</th>
<th>2006–07, n (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>191 (33)</td>
<td>259 (37)</td>
<td>412 (44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>388 (67)</td>
<td>437 (63)</td>
<td>521 (56)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;50</td>
<td>58 (10)</td>
<td>53 (8)</td>
<td>55 (6)</td>
<td></td>
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<tr>
<td>50–59</td>
<td>105 (18)</td>
<td>176 (25)</td>
<td>190 (20)</td>
<td></td>
</tr>
<tr>
<td>60–69</td>
<td>212 (37)</td>
<td>210 (30)</td>
<td>343 (37)</td>
<td></td>
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<tr>
<td>70–79</td>
<td>196 (34)</td>
<td>237 (34)</td>
<td>298 (32)</td>
<td></td>
</tr>
<tr>
<td>≥80</td>
<td>8 (1)</td>
<td>20 (3)</td>
<td>47 (5)</td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Upper lobectomy</td>
<td>191 (33)</td>
<td>235 (34)</td>
<td>380 (41)</td>
<td></td>
</tr>
<tr>
<td>Lower lobectomy</td>
<td>127 (22)</td>
<td>163 (23)</td>
<td>225 (24)</td>
<td></td>
</tr>
<tr>
<td>Middle lobectomy</td>
<td>13 (2)</td>
<td>15 (2)</td>
<td>41 (4)</td>
<td></td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>47 (8)</td>
<td>63 (9)</td>
<td>71 (8)</td>
<td></td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>157 (27)</td>
<td>165 (24)</td>
<td>135 (15)</td>
<td></td>
</tr>
<tr>
<td>Sublobar resection</td>
<td>44 (8)</td>
<td>55 (8)</td>
<td>81 (9)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: An overview of various quality indicators in different diagnostic periods.
67%) and 75% (CI: 72–77%), respectively. The 2-year survival rates for all lung cancer patients in Norway was 16% (CI: 15–17%) in the first period, 17% (CI: 16–18%) in the second and 23% (CI: 22–24%) in the most recent period.

The lung cancer resection rate (including SCLC) increased from 16.4% (CI: 15.2–17.6%, n = 579) in the first period to 16.8% (CI: 15.7–17.9%, n = 696) in the second period to 19.1% (CI: 18.0–20.2%, n = 933) in the last period (P<0.001) (Fig. 1). Excluding the small number of patients with SCLC (n = 47), the resection rate increased from 19.7% (CI: 18.3–21.1%) to 20.2% (CI: 18.9–21.5%) to 22.5% (CI: 21.2–23.8%) (P<0.003). The resection rates in the various counties ranged from 8 to 26% in the first period, 6 to 22% in the second period and 15 to 31% in the last period. These variations were more pronounced in the first period, in which the standard deviation was 4.8 compared with 3.6 (P = 0.20) in the second period and 3.8 (P = 0.29) in the last period.

A preoperative diagnosis of malignancy was confirmed histologically in 74% (n = 1632) of the cases. The average waiting time from the last conclusive tissue sampling to surgery was 29 days (CI: 27–31 days) in the first period, 33 days (CI: 29–36 days) in the second and 40 days (CI: 36–43 days) in the last (P < 0.001).

The survival (excluding those who died within 30 days) was significantly lower in the last period (RR: 0.72 (P < 0.001)). Advanced age, male gender, an advanced pStage, pneumonectomies and an NSCLC histology (P < 0.001 for all) were identified as risk factors for death (Table 3).

The corresponding results throughout this section for non-small cell cases exclusively were comparable without affecting the conclusions.

**DISCUSSION**

Here, we report substantial improvements in different aspects of lung cancer surgery across three periods from 1994 to 2007. The overall resection rates, the proportion of resected patients in a pStage of ≥I and the 1- and 2-year survival rates were highest in the most recent period, whereas postoperative mortality (not significant) and the proportion of pneumonectomies decreased with time. However, the waiting time for surgery increased.

Several factors may have contributed to the observed positive developments. The first national guideline for the diagnosis and treatment of lung cancer was published in 2000 [8]. Since then, lung cancer care has been centralized, and these patients seem to receive increased attention by care providers. Improvements in multidisciplinary cooperation and postoperative care and more extensive adjuvant treatment are observed.

The higher survival in the most recent period, evident also in the multivariable analyses that adjust for several other independent variables, may reflect improvements in postoperative care, adjuvant therapy or surgical technique. In the last period investigated, adjuvant platinum-based chemotherapy was routinely administered to resected patients who were in stage IIB–IIIA and ≤70 years of age. Such therapy increases postoperative survival by almost 4% after 2 and 5 years [9] and may partly explain the favourable 1- and 2-year survival rates that were observed in the last period. We were not able to assess how the increased use of adjuvant chemotherapy has influenced survival since information about such treatment is not recorded in the Cancer Registry for the periods reported. The effect of the independent variables other than period was not within the scope of this paper to discuss as they have been previously investigated more thoroughly [7].

The argument to include patients with SCLC and other histologies (sarcomas, other neuroendocrine tumours and unspecified lung cancer tumours) in this series was to make the national comparison of lung cancer patients complete and generalizable. This diverse group represents cases with varying prognosis such as SCLC with generally poorer prognosis and low resection rates and carcinoid tumours on the other hand with high resection rates for all lung cancer patients in Norway was 16% (CI: 15–17%) in the first period, 17% (CI: 16–18%) in the second and 23% (CI: 22–24%) in the most recent period.

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rates and favourable outcome. In addition, the group might be more mixed as unpublished data from Norway indicate that a diagnosis of SCLC was changed in >20% of cases by pathologists in retrospect. However, the conclusions generally remained unchanged whether these cases were included or not. In multivariate analysis where NSCLC was analysed in a separate group compared with the group designated as other histologies, the latter demonstrated a poorer outcome.

The increase in the NSCLC resection rate to 23% in the last period is encouraging and parallels a recent Irish study that revealed a significant increase in resection rates from 1994 to 2008 [10]. In Norway, even a modest increase of 3 percentage points (from 16 to 19% for all lung cancer patients) would mean that ~40 more patients could be cured annually. This estimate is based on 2600 new cases per year and a 5-year survival rate of ~50% after resection (http://www.krefregisteret.no/Global/Publikasjoner%20og%20rapporter/CiN2008part1_web.pdf) [7]. To develop a perspective of the impact of augmented resection rates, one might consider the national breast cancer screening programme, which saves ~13 lives in Norway annually [11] (www.ssb.no).

Compared with similar countries, the situation in Norway seems favourable. A resection rate of 13% has been reported in Denmark, whereas 17% of lung cancer patients in Sweden are scheduled for surgery (http://www.lio.se/upload/25976/nat_rapplunga_07.pdf) (http://www.lungecancer.dk/documents/00089.pdf). Reports from the USA and subpopulations in Europe have claimed that the surgical potential may be as high as 25–30%; however, whether the entire lung cancer population was included in these studies is questionable [12, 13].

The tendency towards lower postoperative mortality over time was borderline significant (\(P_{trend} = 0.072\)). In a previous study that exclusively focused on postoperative mortality in the same population for a longer period (1993–2005), there was a significant trend towards a decrease in postoperative mortality in the later years (\(P_{trend} = 0.012\)) [7]. The absence of fatal bleedings and bronchopleural fistulas, although not a significant positive trend in the last period may possibly reflect technical improvements.

Both surgeon speciality and volume could be important for the complication rate and survival opportunities after surgical resection [14, 15]. Such information is not routinely collected in the Cancer Registry and we were not able to compare trends of surgeons’ qualifications with outcomes. On the other hand, the reduction in the proportion of pneumonectomies is believed to result from a change in culture rather than education of the surgeon.

The waiting time for surgery has received increasing attention in Norway before the last study period and therefore it is surprising that patients suffer longer waiting times. Possibly, this reflects a more thorough pretreatment evaluation.

We have indications that mediastinoscopy has been performed less frequently in the last period because of more use of PET, EBUS and EUS, which have been available for all patients in the largest regions. Another limitation with the current study is that we do not have adequate data on pretreatment evaluation. Also the rate of exploratory thoracotomy is not exactly known and thus not reported. Information about the rate of intraoperative lymph node dissection throughout the periods investigated could have given more explanation for why more patients were in advanced pStage during the last two periods. Mortality due to any cause has been used as the endpoint of the survival analysis as we do not regard the data from death certificates to be of a proper quality to provide cancer-specific survival. For patients dying within 30 days, the cause of death is better documented in patient records.

It remains to be seen whether newer guidelines, modern postoperative monitoring and hopefully shorter waiting times will further improve the outcomes of lung cancer patients in the future.

Conflict of interest: none declared.

REFERENCES