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Time trend in the surgical management of patients with lung carcinoma[1]

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Abstract

Objective: The goal of the study was to analyze the histological and clinical trends in lung carcinoma and their influence upon the preoperative evaluation, surgical procedures and survival. **Methods**: We retrospectively reviewed the charts of 1079 consecutive patients who underwent surgery for primary lung carcinoma between 1977 and 1996 in our institution. Patients were divided into five equal 4-year periods according to the year of surgery (1977–1980; 1981–1984; 1985–1988; 1989–1992; 1993–1996). **Results**: Between 1977–1980 and 1993–1996, the incidence of squamous cell carcinoma significantly declined, whereas the incidence of adenocarcinoma and bronchioloalveolar carcinoma increased. During the same period, the proportion of squamous cell carcinoma visualized at bronchoscopy and the rate of preoperative histological diagnosis significantly decreased. An increasing proportion of lobectomy and less extended resection was associated with an increasing number of patients with stage I carcinoma. Meanwhile, the operative mortality significantly declined from 9 to 4% and the 5-year survival improved from 25 up to 40%. **Conclusion**: Over the last two decades, the shift in histological distribution was associated with an increasing proportion of patients with stage I disease, a lower operative mortality and a better 5-year survival.

Keywords: Lung carcinoma; Operative mortality; Survival; Time trend

1. Introduction

Although a shift in the histologic distribution of primary lung carcinoma has been reported, few studies have analyzed the trends in operative strategy and survival after lung resection [1,2]. Therefore, we retrospectively reviewed all patients who underwent surgery for primary lung carcinoma over the last 20 years at the University Hospital of Geneva, and we analyzed the histological and clinical changes in lung cancer and their influence upon preoperative evaluation, surgical procedures and survival.

2. Materials and methods

Between January 1, 1977 and December 31, 1996, a total of 4245 patients were identified with the diagnosis of primary lung carcinoma in Geneva according to the regional cancer register. Among these patients, 1265 (29.8%) underwent surgery, 1079 (85.6%) in our institution and 186 (14.4%) in other medical centres.

The charts from all patients operated in our institution were retrospectively reviewed and data on patient's age, bronchoscopic findings, tobacco use in pack-year unit (number of tobacco-pack smoked each day times the number of years of smoking), type of surgical procedures, histology and stage of disease were extracted. Patients were subsequently grouped according to the year of surgery into five equal 4-year periods (1977–1980; 1981–1984; 1985–1988; 1989–1992; 1993–1996) (Table 1).

Preoperative diagnostic evaluation included chest X-ray,

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Table 1
Demographic and characteristic patterns of patients operated for primary lung carcinoma at the University Hospital of Geneva between 1977 and 1996

	1977–1980	1981–1984	1985–1988	1989–1992	1993–1996
Patients diagnosed with PLC in Geneva	810	855	881	860	840
Patients undergoing surgery in our Institution (%)	224 (28)	236 (28)	208 (24)	188 (22)	223 (27)
Mean age of patients operated (mean year ± SD)	59.6 ± 8.9	60.3 ± 8.9	60.7 ± 9.1	61.2 ± 9.3	64.6 ± 9.9
Sex ratio among patients operated (male:female)	7.9:1	6.6:1	3.7:1	3.1:1	2.9:1

PLC, primary lung carcinoma.

bronchoscopy, liver function testing, and liver ultrasonography. Since 1984, computed tomographic (CT) of the thorax and upper abdomen was also included in the standard diagnostic work-up. When mediastinal lymph nodes were enlarged on CT (larger than 15 mm in the largest diameter), a mediastinoscopy was performed in order to exclude the patients with N3 disease from surgery. The type of resection was primarily dictated by the local extent of the tumour and secondarily, by the cardiorespiratory function. With regard to pathological staging of the tumour, patients underwent selective sampling of suspicious mediastinal lymph nodes prior to 1992, and systematic mediastinal dissection thereafter. Histologic typ-ing was conducted according to the World Health Organization [3]. Tumour extent was reviewed and determined according to the revised TNM classification for all patients [4].

Adjuvant chemoradiotherapy was administrated to all patients with mediastinal lymph nodes involvement. In addition, radiotherapy was used when the resection was not microscopically complete and, lately, chemotherapy has been randomly assigned to patients with N1 involvement.

Information on follow-up was obtained from hospital charts, phone calls to general practitioners, and review of the regional cancer registry. The cut-off date for the evaluation was at the end of the 5th year following surgery and January 1, 1998 for the patients operated after January 1, 1993. Eighty-seven patients (8%) were lost to follow-up.

2.1. Statistical analysis

Differences in distribution on time-variables were analyzed by Friedman ANOVA-test and chi-square test for trend. Operative mortality included patients deceased within 30 days of surgery and any later deaths occurring during the initial postoperative hospital stay. The 5-year survival, including the operative mortality, was analyzed by the Kaplan–Meier method, and the evaluation of the differences was conducted by the log-rank test for trend. Differences with *P*-values no greater than 0.05, were regarded as statistically significant.

3. Results

There were 877 males and 202 females, aged 61.2 ± 9.2 years (mean ± SD, range 27 to 89 years) and 61.7 ± 10.1 years (range 34 to 82 years), respectively. There were 613 patients with squamous cell carcinoma (57%), 327 with adenocarcinoma (30.3%), 47 with large cell carcinoma (4.3%), 44 with bronchioloalveolar carcinoma (4%), 33 with small cell carcinoma (3%), and 15 with undifferentiated carcinoma (1.4%).

3.1. Trend in histology (Fig. 1)

The incidence of squamous cell carcinoma significantly declined, whereas, that of adenocarcinoma and bronchioloalveolar carcinoma increased. Although this histological shift was observed in both genders, the trend was more significant in females and tended to level off over the last 8 years of our study.

3.2. Trend in smoking habit (Fig. 2)

While the proportion of heavy smokers (>40 pack-year) remained constant at a rate of 50% or higher in males, in females, the incidence of heavy smoker increased significantly from 12% in 1977–1980 up to 40% in 1993–1996. Interestingly, 32% of the patients with bronchioloalveolar

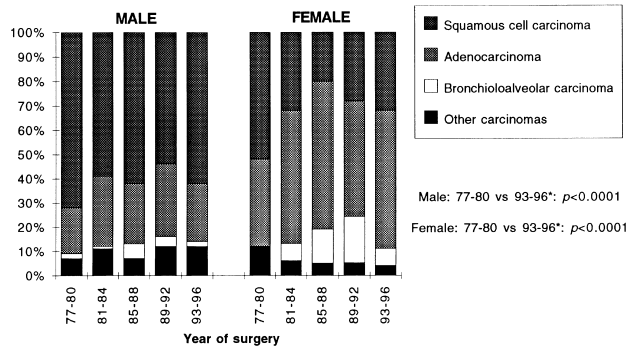

Fig. 1. Trend in histological types among males and females operated between 1977 and 1996 (*chi-square test for trend).

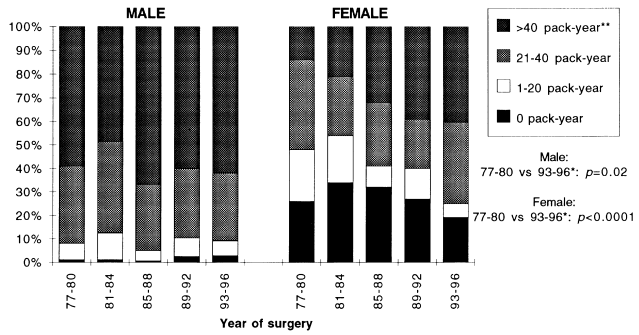

Fig. 2. Smoking habit in males and females operated between 1977 and 1996 (*chi-square test for trend; **pack-year = the number of tobacco-packs smoked per day × the number of years smoking).

carcinoma had never smocked, whereas the rate of non-smoker among other carcinomas ranged from 2% in squamous cell carcinoma to 11% in adenocarcinoma.

3.3. Trend in bronchoscopic findings (Fig. 3)

Bronchoscopy was performed preoperatively in 90–98% of the patients with squamous cell carcinoma and in 80–90% of the patients with adenocarcinoma. While in squamous cell carcinoma, the tumour was usually visualized and a histological diagnosis obtained, this performance progressively decreased over the last 20 years. In contrast, bronchoscopy has remained negative in most patients with adenocarcinoma. Concomitantly, a transthoracic fine needle biopsy was performed more frequently in patients with adenocarcinoma than in those with squamous cell carcinoma.

3.4. Trend in surgical procedures and stage of disease (Table 2)

The proportion of patients with a tumour of stage 1 increased over time. Meanwhile, the number of lobectomy and less extended resection increased, whereas, the rate of larger resection (pneumonectomy and bilobectomy) and exploratory thoracotomy significantly declined.

3.5. Trend in operative mortality and 5-year survival (Table 2 and Fig. 4)

While the operative mortality significantly decreased over the last 20 years, the 5-year survival increased. Although an improvement was observed between each 5-year period, the turning point of survival benefit was situated between the first two and the last three periods of our study (Fig. 4). No differences in the operative mortality and long-term survival was observed between squamous cell carcinoma, adenocarcinoma and the other non-small cell carcinoma. After hospital discharge, lung carcinoma (recurrence, metastasis) was the main cause of death in 79% of the cases (n = 580), 12% died of another cause (n = 87), and the cause remained unknown in 9% (n = 65). Survival was similar in patients who died from their lung carcinoma (34% at 5 years) and in those who died from other diseases (31% at 5 years).

4. Discussion

Over the last 20 years, the proportion of adenocarcinoma and bronchioloalveolar carcinoma significantly increased, whereas the rate of squamous cell carcinoma concomitantly decreased. This histological shift had been previously reported in the US in the 1970s [5,6], and was more recently observed in Europe and Asia [7–10]. Hence, since the University Hospital of Geneva is the single regional referring center, our findings may be considered as a good mirror of the histological trends among the overall population of Geneva.

In accordance with some authors [11,12], but in contrast to previous Swiss studies [8], in our series, the histological shift was more pronounced in females than in males. Indeed, in the last decade, adenocarcinoma predominated in females, whereas squamous cell carcinoma were still diagnosed in the majority of males. This phenomenon could be related to changes in female smoking habits, since heavy smokers largely increased among females in our series, whereas tobacco use remained relatively stable in males. Furthermore, since the beginning of the 1990s, the proportion of heavy smokers and the rate of adenocarcinoma among females concomitantly levelled off in our institution.

The introduction of filter cigarettes could also have contributed to the shift in lung carcinoma cell type. While large particles are selectively removed by cigarette filters, small particles are not and may, thus, promote carcinogenesis and increase the development of adenocarcinoma [6,13]. In addition, the deeper puffs taken because of filter cigarettes may have resulted in the occurrence of tumours located more peripherally in the lung [14]. We found a decreasing number of squamous cell carcinoma visualized at bronchoscopy, and Quinn et al. [15] observed an increasing rate of squamous cell carcinoma in the periphery of the lung on chest X-ray.

Although the mean age of patients undergoing surgery

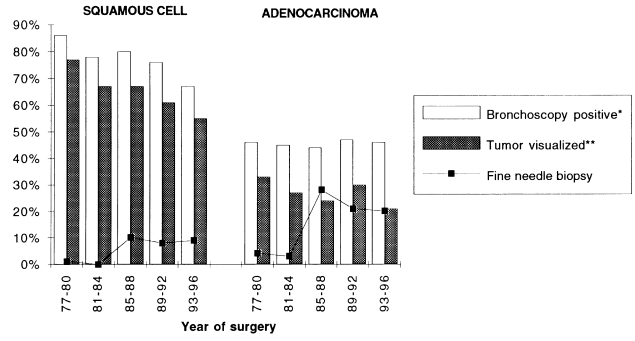

Fig. 3. Histologic diagnosis prior to surgery by bronchoscopy and fine needle biopsy (*histology and/or cytology positive/**within a bronchus).

Table 2
Trend in surgical procedures, stage of disease, operative mortality and survival of 1079 patients who underwent surgery between 1977 and 1996

	1977–1980 (n = 224)	1981–1984 (n = 236)	1985–1988 (n = 208)	1989–1992 (n = 188)	1993–1996 (n = 223)	P-value
Surgical procedures						<0.005*
Thoracotomy only (%)	11	8	6	7	2	
Pneumonectomy and bilobectomy (%)	46	35	31	28	36	
Lobectomy and lesser resection (%)	43	57	63	65	63	
Stage of disease						<0.003*
Stage I (%)	35	44	50	49	50	
Stage II (%)	22	14	21	15	17	
Stage IIIa (%)	27	26	21	25	23	
Stage IIIb (%)	13	13	5	6	7	
Stage IV (%)	3	3	3	4	2	
Operative mortality (%)	9	8	6	5	4	<0.0001**

*Friedman ANOVA-test, **chi-square for trend test.

increased, the overall operative mortality significantly decreased. This finding was likely due to the lowering in the proportion of bilobectomy and pneumonectomy observed during our study [16]. In addition, better preoperative cardiopulmonary evaluation and postoperative management were likely to contributed to the progressive reduction in the operative mortality over the last 20 years.

The 5-year survival rate, significantly improved throughout the period studied. This improvement was associated with a decreasing rate of operation-related death, a decreasing proportion of exploratory thoracotomy and an increasing incidence of stage I carcinoma. Although this improvement was observed between each 5-year period, it seems to have predominated between the first two and the last three periods. Some of these changes may be explained by the introduction of chest CT in the early 1980s and its systematic application for clinical staging since 1984. Indeed, better preoperative evaluation of local tumour extension and the status of mediastinal lymph nodes involvement, certainly helped to improve the patient's selection and thus, survival by excluding the patients with advanced-stage carcinoma. Postoperative chemoradiotherapy in patients with stage III disease, and more recently chemotherapy in patients with stage II disease, may have contributed to increase the long-term survival. However, due to the variety of drugs and type of radiation used over the last two decades, their influence could not be assessed in this study

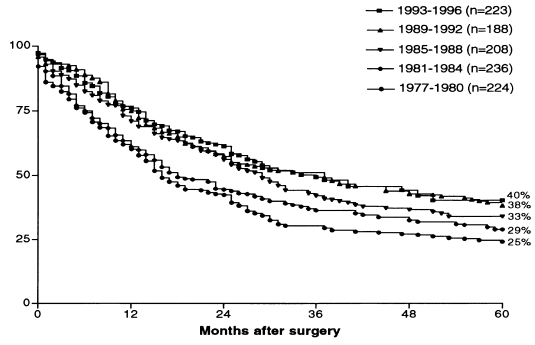

Fig. 4. Five-year survival according to the period of surgery. Log-rank test for trend: 1977–1980 versus 1993–1996, $P < 0.0001$. Log-rank test: 1977–1980 versus 1981–1984, $P = 0.23$; 1981–1984 versus 1985–1988, $P = 0.09$; 1985–1988 versus 1989–1982, $P = 0.3$; 1989–1992 versus 1993–1996, $P = 0.9$.

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Appendix A. Conference discussion

Mr K. Moghissi (*East Yorkshire, UK*): I have had an interest for some time about the resectability rate in Europe. I have found that for the last 40 years it has not moved, and is in the region of 15%. In the UK, for instance, it has been 10–12%. I would like to ask you a question about the resectability rate in the canton of Geneva, as I know that you collect data from there; also a clarification both in your expose and in the abstract. You are dealing with 1079 patients, of which 24% were primary lung cancer. If it is so, were the rest secondary lung cancer? So two questions. Why so many secondary lung cancer, if they are secondary lung cancers, or is there a mistake here? Secondly, what is the resectability rate.

Dr de Perrot: The first question was about resectability rate. We observed an increased resectability rate from 90 to 95% at the beginning of the 1980s with the introduction of the computer tomography scanner in Geneva. Regarding the second question, we called primary lung carcinomas, all non-small-cell lung carcinomas and small-cell lung carcinomas, as opposed to secondary carcinomas which were metastasis and carcinoid tumors, as well as sarcomas which were not included in the study.

Mr P. Goldstraw (*London, UK*): Surely if we are to know whether these changes are merely those of changes in surgical attitude or whether they're truly epidemiological changes, we need to know the denominator. Have you got any evidence that the proportion of patients that you have operated on has not changed? Have you any evidence that the population characteristics of your non-operated cases are the same as your operated cases?

Dr de Perrot: We have looked at that and the proportion is the same. It varies between 22 and 28%, according to the Geneva cancer history which gives the total amount of patients diagnosed in Geneva. However, survival curves may have increased because lung cancers are diagnosed earlier and patient selection is better. Therefore, the 5-year survival would have been increasing because the type of patients have changed but not because the real 5-year survival has increased.

Dr A. End (*Vienna, Austria*): We know the surgeon to be a prognostic factor. Did you look if the variable, 'surgeon', influenced the outcome at your institution?

Dr de Perrot: We have not looked at that, but certainly the quality and expertise of the surgeon plays a role in the operative mortality.

Dr T.F. Molnar (*Pecs, Hungary*): Recently, more and more pathological reports come back to me with the diagnosis adenosquamous carcinoma or mixed-type carcinoma. I am troubled as how to decode this message, maybe it's due to the immunohistochemistry or something else. Do you have similar experiences in your institution with the increasing number of these so-called mixed-type cancers?

Dr de Perrot: Yes, the mixed type have been increasing, but we did not have many of them in our institution, so we don't have so much experience with them.