Negative Impact of Rurality on Lung Cancer Survival in a Population-based Study

Virginie Westeel, MD, PhD, Alexandre Pitard, MD, Mael Martin, MD, Isabelle Thaon, MD, Alain Depierre, MD, Jean-Charles Dalphin, MD, and Patrick Arveux, MD

Introduction: Several studies have suggested that rurality is a risk factor for worse prognosis in cancer.

Methods: The study population included the 2268 lung cancer cases collected between 1981 and 1996 in the Doubs Cancer Registry (France).

Results: The numbers of patients were 849 (31.8%) in rural areas and 89 (3.3%) in very rural areas. The relative 5-year survival was 15.2% in rural areas and 13.4% in urban areas ($p = 0.5$), and 2.7% in very rural areas and 14.4% in extended urban areas ($p = 0.02$). Multivariate analyses of observed and relative survival showed that patients living in very rural areas ($p < 0.0001$), 65 years of age and older and having small cell carcinoma had a significantly shorter survival.

Conclusions: This study showed that the multidimensional definition of rurality identified a population with unfavorable prognoses.

Key Words: Lung cancer, Rural, Survival, Cancer registry, Prognostic factors.

(*J Thorac Oncol.* 2007;2: 613–618)

Lung cancer is a leading cause of cancer mortality in all developed countries. Lung cancer incidence is high, even still increasing in many countries such as France, with 22,000 new cases every year for a Europe-standardized incidence rate of 35%.[1] The disease remains fatal in a majority of cases, and mortality rates very close to incidence rates are observed. Only modest improvement in prognosis has been demonstrated over the past 20 years, due to therapeutic advances but also to a greater use of cancer treatments.[2–4]

In developed countries, it is of high priority for health care policies to provide everyone with optimal care. Therefore, it is of utmost importance to identify patients with poorer survival and to evaluate the magnitude of the survival difference. Because rural patients might be, for many reasons, at a greater distance from health care services, they constitute a population at risk of poorer prognosis. Several studies focusing on lung cancer have used the distance to the nearest cancer treatment center as the definition of rurality.[5–9] Only one of these studies analyzed survival and showed that patients from outlying areas had poorer survival.[5] Simplicity is the main advantage of this definition. However, only one component of the multidimensional concept of rurality is taken into account. Besides being usually remote from specialized health centers, rural areas also have economic and sociological characteristics. A particular psychological profile was also reported in rural population: rural patients seemed to have less demanding expectations of their care.[10] Therefore, distance may not be the most relevant definition of rurality for every geographic area. Despite the large size of a Canadian province such as British Columbia, a study conducted in the 614 patients included in its registry for a small cell lung cancer (SCLC) in 1990 and 1995 showed no survival difference between patients living within a 2-hour drive from one of the regional cancer centers and those living more than 2 hours to a cancer center.[11] Therefore, this study was performed to test the impact of two other definitions of rurality on survival inequalities in lung cancer. The first definition consisted of a common and simple approach of rurality, based on population density, and the second one offered a multidimensional evaluation of rurality.

MATERIALS AND METHODS

Study Population

The study population included all incident cases of primary lung cancer between January 1, 1981 and December 31, 1996 in the Doubs department. Data were obtained from the Doubs Cancer Registry database. The Doubs is one of the 96 French metropolitan departments. It is located in eastern France and has a surface area of 5234 km^2. All public or private pathological laboratories of the Doubs department systematically send to the registry copies of all histology reports of newly confirmed cancer cases. Data are checked against death certificates and lists of new cancer cases from physicians at public and private institutions. Information collected by the registry includes demographic characteristics (gender, age, residence at the time of diagnosis), date of pathological diagnosis, pathology, and site of cancer within the lung according to the International Classification of Diseases for Oncology (ICD-O), second edition.[12] Patients who were diagnosed at autopsy were excluded from this analysis.

University Hospital of Besançon and University of Franche Comte, Besançon, France.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Jean-Charles Dalphin, MD, Service de Pneumologie, CHU, Hôpital Jean Minjoz, Besançon 25030 France. E-mail: jean-charles.dalphin@univ-fcomte.fr

ISSN: 1556-0864/07/0207-0613

In patients in whom metachronous lung cancers were diagnosed, only the first case was kept. Histology was categorized into five groups using ICD-O codes: small cell (8021, 8041, 8042, 8043, 8044), squamous cell (8033, 8052, 8070, 8071, 8072, 8074), adenocarcinoma (8050, 8140, 8141, 8190, 8201, 8211, 8250, 8251, 8260, 8310, 8480, 8481, 8550), other carcinoma and carcinoma not otherwise specified (8000, 8010, 8012, 8020, 8030, 8031, 8200, 8240, 8246, 8560), and without pathological confirmation (9990).

Main Independent Variables: Rurality

Two variables were constructed to study rurality, using the two official definitions of the French National Institute of Statistics and of Economics Studies and data of the French 1990 census.[13] The residence of patients was the community where patients lived at the date of pathological diagnosis: Variable 1: Rural versus urban areas. Subjects were defined as rural residents if they were not living in a built-up area (housing not more than 200 meters apart) of more than 2000 inhabitants. Other patients were considered as coming from urban areas. Variable 2: Very rural versus extended urban areas. Very rural and extended urban areas were identified by taking into account not only the population density, but also the commercial, industrial, and administrative activities of the community of residence, the proportion of residents working outside the community, the proportion of households living on agriculture and the demographic increase. When the residence was located outside an extended urban area, a patient was considered to be resident of a very rural area. Extended urban areas included not only urban communities, as defined by variable 1, but also communities of fewer than 2000 inhabitants but with one or more of the following conditions: more than 100 employees, proportion of the population working outside the community more than 1.2 × proportion of households living on agriculture, population increase between 1975 and 1982 more than (1.09 × proportion of households living on agriculture) − (0.9 × proportion of the population working outside the community).

Additional Independent Variables

Other variables included in the analysis were gender, age, period of diagnosis, pathology, and mean annual income. Age was dichotomized using the median age of the cohort. The period of diagnosis used two 8-year periods, 1981 to 1988 and 1989 to 1996. Pathology was analyzed as SCLC and non-small cell lung cancer (NSCLC). NSCLC included squamous cell carcinoma, adenocarcinoma, other carcinoma, carcinoma not otherwise specified, and carcinoma without pathological confirmation. Cases were assigned the mean net annual income of all taxable and nontaxable households in their community of residence. This socio-economic variable was based on the 1990 census and was expressed for each subject as the ratio of the annual income in the community to the mean annual income for all the communities in the cohort. This variable was dichotomized using a 15% variation from the mean value of the cohort.

As we used data from the Doubs Cancer Registry database, we did not have information about stage, performance status, and therapy. Retrospectively, we only had these data for our own patients (from the Chest Disease Department of the Besançon University Hospital).

Statistics

Age-standardized (world standard population[14]) incidence rates were calculated for the period 1981 to 1983 using data from the 1982 census and for the period 1984 to 1996 using data from the 1990 census. The Doubs department had a population of 236,144 men and 241,527 women in 1982 and of 236,967 men and 254,861 women in 1990.[15]

Correlation between independent variables was systematically investigated by the χ^2 test. For survival analysis, the endpoint date was July 16, 2001. Beyond 5 years, data were censored. Probability of observed survival ($S_{[t]}$) was estimated using the actuarial method and univariate survival comparisons were performed by the log rank test. Relative survival was calculated using the French mortality tables for the period 1988 to 1990.[16] Univariate comparisons of relative survival used the test of the maximum of likelihood.[17]

Two different Cox models were generated to analyze observed survival. The Cox regression model 1 included rurality variable 1, and, among the other independent variables, those correlated with survival with a p value of less than 0.20 in the univariate analyses of both observed and relative survival. Rurality variable 2 and all other independent variables correlated with survival with a p value of less than 0.20 in the univariate analyses of both observed and relative survival were entered in the Cox model 2. The risk proportionality was checked by the graphic representation of $\ln(-\ln[S_{(t)}])$ over time. In case of nonproportionality of risks, an interaction variable with time was introduced in the model as a time-dependent variable. A multivariate analysis of relative survival was undertaken to assess the effect of the rurality variable that had the most significant prognostic value in the model of observed survival.[18] The regression model by Hakulinen and Tenkanen[18] was used and the same variables kept for the multivariate analysis of observed survival were included. A p value of less than 0.05 was considered as statistically significant. Univariate and observed survival analyses were performed using the SAS software.[19] Relative survival rates were computed with the program by Hakulinen.

RESULTS

Study Population

Between 1981 and 1996, 2690 cases of primary lung cancer were registered in the Doubs Cancer Registry. Fifteen cases diagnosed at autopsy were excluded from the study. The 2675 remaining cases occurred in 2668 patients. World-standardized incidence rates increased in men from 49.9 per 100,000 in 1981 to 58.2 per 100,000 in 1996, and in women from 2.9 per 100,000 in 1981 to 7.6 per 100,000 in 1996. The 2668 first cases were kept for analysis. In 1990, among the 484,770 inhabitants of the Doubs department, 163,488 (33.7%) were living in rural areas (rurality variable 1) and 15,744 (3.3%) in very rural areas (rurality variable 2). Among the 2668 patients, 849 (31.8%) were living in rural areas and 89 (3.3%) in very rural areas. The median age at diagnosis was 64 years (range, 22–94 years). The estimated mean

TABLE 1. Characteristics of Patients Diagnosed with Primary Lung Cancer in the Doubs Department from 1981 to 1996 According to the Rurality Variables

	Rurality Variable 1			Rurality Variable 2			
Characteristics	Rural, No. (%)	Urban, No. (%)	p	Very Rural, No. (%)	Extended Urban, No. (%)	p	Total (%)
Gender			0.10			0.39	
Male	761 (90)	1590 (87)		81 (91)	2270 (88)		2351 (88)
Female	88 (10)	229 (13)		8 (9)	309 (12)		317 (12)
Age, yr			0.50			0.74	
<65	435 (51)	901 (50)		43 (48)	1292 (50)		1335 (50)
≥65	414 (49)	918 (50)		46 (52)	1287 (50)		1333 (50)
Period of diagnosis			0.52			0.82	
1981–1988	365 (43)	806 (44)		38 (43)	1133 (44)		1171 (44)
1989–1996	484 (57)	1013 (56)		51 (57)	1446 (56)		1497 (56)
Pathology			0.12			0.66	
Small cell	135 (16)	267 (15)		14 (16)	388 (15)		402 (15)
Squamous cell	473 (56)	982 (54)		48 (54)	1407 (55)		1455 (55)
Adenocarcinoma	156 (18)	329 (18)		14 (16)	471 (18)		485 (18)
Other and NOS	71 (8)	214 (12)		10 (11)	275 (11)		285 (11)
Not histologically verified	14 (2)	27 (1)		3 (3)	38 (1)		41 (1)
Mean income[a]			$<10^{-4}$			$<10^{-4}$	
<85%	164 (20)	243 (13)		53 (73)	354 (14)		405 (15)
≥85%	659 (80)	1576 (87)		20 (27)	2215 (86)		2235 (85)
Total	849 (32)	1819 (68)		89 (3)	2579 (97)		2668

NOS, not otherwise specified.
[a] Missing data for 17 communities corresponding to 26 patients.

annual income of the 2668 subjects was 12,685 Euros (SD = 1828). Characteristics of the 2668 patients and of their first lung cancer are detailed according to the rurality variables in Table 1. Gender, age, period of diagnosis, and histology did not differ between rural and urban patients or between very rural areas and extended urban areas. The mean annual income was significantly lower in rural and in very rural patients, with a larger difference between patients from very rural areas and extended urban areas than between rural and urban patients.

In the subgroup of 1816 patients from our hospital, 49 were living in very rural areas and 1767 in extended urban areas Therefore, the proportion of patients living in very rural areas was lower in this subgroup (2.7%) than in the subgroup of patients who never came to our department (4.7%). Patients living in very rural areas were less often referred to our hospital: 55% (49/91) versus 68% (1767/2579). However, in our hospital subgroup, age, sex, performance status, standardized cancer treatment (versus best supportive care only), histology, and presence (or absence) of metastases did not differ between patients from very rural areas and extended urban areas.

Survival

As of July 16, 2001, 155 patients (5.8%) were still alive, 2494 (93.5%) had died, and 19 (0.7%) were lost to follow-up. Observed survival of the whole population was 43.4% (SE = 0.010) at 1 year, 24% (SE = 0.008) at 2 years, 16.9% (SE = 0.007) at 3 years, 11.8% (SE = 0.006) at 5 years, and 6.8% (SE = 0.5) at 10 years. Overall relative survival of the cohort was 44.6% (SE = 0.010) at 1 year, 25.5% (SE = 0.009) at 2 years, 18.6% (SE = 0.008) at 3 years, and 14% (SE = 0.007) at 5 years.

Univariate analyses of observed and relative survival are detailed in Table 2. Both observed and relative survival analyses showed that patients living in very rural areas (rurality variable 2), and/or aged 65 years or older and/or who had a small cell type of carcinoma had a significantly shorter survival ($p < 0.05$). There was no survival difference between patients coming from rural areas and those living in an urban environment (rurality variable 1). Correlation of mean annual income and survival was significant for observed survival ($p = 0.01$) but was of borderline significance for relative survival ($p = 0.05$).

Rurality variable 1, age, period of diagnosis, pathology, and mean annual income were entered in the Cox regression model 1. Rurality variable 2, age, period of diagnosis, pathology, and mean annual income were entered in the Cox regression model 2. As risks were not proportional over time for the pathology variable, a pathology x time interaction was introduced in the Cox models. Variables of unfavorable significance on observed survival in the multivariate analysis were very rural residence (rurality variable 2), age of 65 years or older, and SCLC (Table 3). The same variables were shown to be associated with decreased survival in the multivariate analysis of relative survival. There was a trend for improved prognosis of lung cancer over time and in patients with a higher mean annual income. If mean annual income was omitted in the multivariate analysis because of its correlation with rurality variable 2, very rural areas remained highly correlated with survival with a

TABLE 2. Univariate Analyses of Observed and Relative Survival

	5-yr Observed Survival		5-yr Relative Survival	
Characteristics	**% (SE)**	***p***	**% (SE)**	***p***
Rurality variable 1		0.34		0.47
Rural	12.9 (0.005)		15.2 (0.01)	
Urban	11.3 (0.004)		13.4 (0.009)	
Rurality variable 2		0.008		0.02
Very rural areas	2.3 (0.02)		2.7 (0.02)	
Extended urban areas	12.2 (0.006)		14.4 (0.008)	
Gender		0.18		0.36
Male	11.4 (0.007)		13.6 (0.008)	
Female	14.8 (0.02)		16.5 (0.02)	
Age, yr		$<10^{-3}$		$<10^{-3}$
<65	15.3 (0.01)		16.3 (0.01)	
≥65	8.3 (0.008)		11 (0.01)	
Period of diagnosis		0.15		0.17
1981–1988	10.8 (0.009)		12.7 (0.01)	
1989–1996	12.7 (0.009)		15 (0.01)	
Histology		$<10^{-3}$		$<10^{-3}$
Non-small cell	12.9 (0.007)		15.3 (0.008)	
Small cell	6 (0.01)		6.9 (0.01)	
Mean annual income		0.01		0.05
<85%	8.7 (0.01)		10.3 (0.02)	
≥85%	12.5 (0.007)		14.7 (0.008)	

TABLE 3. Multivariate Analyses of Observed and Relative Survival

Variables	Relative Risk (95 % CI)	*p*
Cox model with rurality variable 1		
Age ≥65 yr	1.3 (1.2–1.4)	$<10^{-4}$
Small cell carcinoma	1.2 (1.1–1.4)	0.003
Rural areas	1 (0.9–1.1)	0.5
Mean annual income <85%	1.1 (1–1.3)	0.03
Period 1989–1996	0.9 (0.9–1)	0.1
Interaction pathology × time	0.7 (0.5–0.9)	0.001
Cox model with the rurality variable 2		
Age ≥65 yr	1.3 (1.2–1.4)	$<10^{-4}$
Small cell carcinoma	1.2 (1.1–1.4)	0.004
Very rural areas	1.3 (1.02–1.7)	0.03
Mean annual income <85%	1.1 (1–1.2)	0.1
Period 1989–1996	0.9 (0.9–1)	0.1
Interaction pathology × time	0.7 (0.5–0.9)	0.001
Hakulinen and Tenkanen model		
Age ≥65 yr	1.2 (1.1–1.4)	$<10^{-4}$
Small cell carcinoma	1.4 (1.2–1.5)	$<10^{-4}$
Very rural areas	1.3 (1.02–1.7)	0.04
Mean annual income <85%	1.1 (1–1.3)	0.1
Period 1989–1996	0.9 (0.9–1)	0.08

CI, confidence interval.

hazard ratio of 1.4 (95% confidence interval [CI]: 1.1–1.7; p = 0.004) for observed survival and 1.4 (95% CI: 1.1–1.8; p = 0.004) for relative survival.

DISCUSSION

Both the observed and relative survival analyses of this study showed that the 3.3% of patients living in very rural areas had a risk of death 1.3 times higher than that of subjects from extended urban areas. Using a definition of rurality only based on population density, there was no survival difference in survival between rural and urban residents. Other factors of significant unfavorable prognosis were age of 65 years or older and small cell type. A trend for improved survival was also observed in the 1990s.

The major difficulty when analyzing the influence of rurality on survival is the definition used to distinguish rural from urban areas. In most studies, rurality was estimated by the distance to the nearest treatment center.[5–8] The definition of very rural areas and of extended urban areas, which took into account not only population density but also industries, commuting rates, proportions of households living from agriculture and the demographic increase, offered a better identification of economically isolated populations. These areas also corresponded to deprived areas, which were reported to be associated with decreased cancer survival rates and a significant reduction in chemotherapy delivery (odds ratio = 0.39, 95% CI: 0.16–0.96, p = 0.028).[7,20] In the multivariate analysis of our study, very rural residence had a prognostic implication independently of deprivation. Because this very restrictive definition of rurality concerned a small proportion of the department population, only 3.3% of the 2668 registered cases were in the very rural category. However, considering the high incidence rates of lung cancer and the 11.7% survival difference at 5 years between patients from very rural areas and from extended urban areas, the rate of 3.3% may be worth being identified as well as the reasons for this worse prognosis.

Because very rural areas were also shown to contribute to an unfavorable prognosis in the analysis of relative survival, deaths should be related to the lung cancer. Hypotheses to explain this poorer survival rate of patients living in very rural areas include more advanced disease at the time of diagnosis and at the beginning of treatment and differences in treatments. However, in the subgroup of patients from our department, we did not find any difference for presence of metastases or in the proportion of patients having received standardized cancer treatment between patients living in very rural areas and those living in extended urban areas. Data on tumor stage were not available for this study. Extension of cancer is one of the most powerful prognostic factors of lung cancer.[4,21] Three studies have demonstrated that patients living in remote areas had more advanced lung cancers.[6,8,9] One study was conducted in all cases of colorectal and lung cancer from north and northeast Scotland and collected by the Scottish Cancer Registry in 1995 and 1996.[6] Definition criteria for rural areas used the straight line distance between patients' residence and the nearest cancer center. Proportions of disseminated lung cancers were 42% among the 164 subjects living further than 57 km from the nearest cancer center, 34% in the 143 patients living between 38 and 57 km from the cancer center, and 33% in the 314 patients living within 37 km (p = 0.25; p value for linear trend = 0.098).

Proportions of NSCLC stages I and II were 14% in patients living 58 km or more from the nearest cancer center and 28% in subjects resident within 5 km ($p = 0.025$). Such urban-rural differences have also been shown in 3040 lung cancer cases from the Savannah River Regional Health Information System Registry between 1991 and 1995.[9] Patients living more than 10 miles from a hospital had a risk of having an advanced stage of 1.25 (95% CI: 1.0–1.57) when compared to those living less than 10 miles away ($p = 0.047$). Among the 5407 lung cancer patients collected by the Georgian Cancer Registry between 1978 and 1985, the risk of metastatic disease was compared between residents of metropolitan Atlanta and those of 10 neighboring rural counties. It was 1.14 (95% CI: 0.83–1.57) among whites and 1.89 (95% CI: 1.05–3.39) among blacks.[8]

In France, this geographic variation was studied in colorectal cancer.[22] Of the 1331 new cases collected by the Calvados Digestive Tract Cancer Registry between 1978 and 1984, patients living in very rural areas, with the same definition as that used in the present analysis, were 134 for men and 150 for women. There was no stage difference for men but 18.8% of women in very rural areas had metastatic disease and 12.3% of those living in extended urban areas ($p < 0.05$). Among women, 5-year survival was 30.7% and 40% ($p < 0.02$), respectively. Women living in rural areas had more severe clinical symptoms. Environment still had a significant effect after controlling for symptoms and for disease extension ($p < 0.05$). In a model controlling for symptoms, disease extension, and age, influence of environment was of borderline significance ($p < 0.08$). In a multivariate analysis adjusting for age, symptoms, type of treatment, and tumor extension, environment no longer had a significant prognostic effect. These results suggest that differences in types of treatment might be another explanation for the worse prognosis of cancer in rural areas. The results of another study conducted on 661 new lung cancer cases collected by the Scottish Cancer Registry in 1995 and 1996 favors the stage hypothesis rather than the treatment difference explanation, as it showed no difference in treatment with increasing distance to treatment center or in time between first referral and treatment.[7] This higher proportion of advanced disease in rural areas could result from a delay in diagnosis, which may be explained by both practical and psychological reasons. In a study of 22 colorectal cancer patients and 10 spouses, Bain and Campbell[10] showed that not only longer distances from specialized centers were a limitation, but also that poor coordination between primary and secondary care might be responsible for delayed access to cancer treatment.[10] Psychological profiles were also different whether patients were living in rural or urban areas. Subjects living outside the city boundary had lower expectations of care and were less demanding than their urban counterparts.[10] In our study, we also noted that patients living in very rural areas were less often referred to our hospital (55% versus 68%). Perhaps the distance from all specialized centers (and not only from the university hospital) along with the difference in psychological profiles, as reported by Bain and Campbell, might result in patients from very rural areas, particularly those with advanced stage disease, not being referred to specialized centers.

This study showed that the multidimensional definition of rurality using very rural areas identified lung cancer patients with a significantly reduced prognosis. Although this population only accounts for 3.3% of the whole population of the department, they cannot be considered as marginal with lung cancer being a leading cause of cancer deaths in developed countries and with a survival difference as large as 11.7% at 5 years. Moreover, it is not acceptable to offer suboptimal care to any patient, and development of cancer services must take into account such inequalities to provide uniform quality of care to all patients wherever they live. Therefore, before adapted sanitary measures can be proposed in particular lung cancer care network reorganization, a subsequent study is ongoing to further identify areas of worse prognosis and the reasons for poorer survival, including, performance status, stage, access to cancer care facilities, and treatment differences.

ACKNOWLEDGMENTS

The authors thank the Doubs Cancer Registry staff and Brigitte Depierre for their technical assistance.

REFERENCES

1. Cancer du poumon. In: Ministère de l'Emploi et de la Solidarité et réseau FRANCIM, ed. Le cancer en France: incidence et mortalité. Situation en 1995. Evolution entre 1975 et 1995. Paris, 1998:64–69.
2. Lebitasy MP, Hedelin G, Purohit A, Moreau L, Klinzig F, Quoix E. Progress in the management and outcome of small-cell lung cancer in a French region from 1981 to 1994. *Br J Cancer* 2001;85:808–815.
3. Janssen-Heijnen MLG, Schipper RM, Klinkhamer PJJM, Crommelin MA, Coebergh JWW. Improvement and plateau in survival of small-cell lung cancer since 1975: a population-based study. *Ann Oncol* 1998;9: 543–547.
4. Engeland A, Bjorge T, Haldorsen T, Tretli S. Prognosis of patients with lung cancer diagnosed in Norway, 1954–93. *Cancer Causes Control* 1998;9:57–65.
5. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural factors and survival from cancer: analysis of Scottish cancer registrations. *Br J Cancer* 2000;82:1863–1866.
6. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Rural and urban differences in stage at diagnosis of colorectal and lung cancers. *Br J Cancer* 2001;84:910–914.
7. Campbell NC, Elliott AM, Sharp L, Ritchie LD, Cassidy J, Little J. Impact of deprivation and rural residence on treatment of colorectal and lung cancer. *Br J Cancer* 2002;87:585–590.
8. Liff JM, Chow WH, Greenberg RS. Rural-urban differences in stage at diagnosis. Possible relationship to cancer screening. *Cancer* 1991;67: 1454–1459.
9. Silverstein MD, Nietert PJ, Ye X, Lackland DT. Access to care and stage at diagnosis for patients with lung cancer and oesophageal cancer: analysis of the Savannah River Region Information System Cancer Registry data. *South Med J* 2002;95:900–908.
10. Bain NS, Campbell NC. Treating patients with colorectal cancer in rural and urban areas: a qualitative study of the patients' perspective. *Fam Pract* 2000;17:475–479.
11. Laskin JJ, Erridge SC, Coldman AJ, D'yachkova Y, Speers C, Westeel V, et al. Population-based outcome for small cell lung cancer: impact of standard management policies in British Columbia. *Lung Cancer* 2004; 43:7–16.
12. World Health Organization. *International Classification of Diseases for Oncology. Second Edition.* In: Percy C, Van Holten V, Muir C, eds. Geneva: World Health Organization, 1990.
13. Institut National de la Statistique et des Etudes Economiques. *Composition communale des zones de peuplement industriel ou urbain. Population et délimitation 1990.* Paris: INSEE, 1992.

14. International Agency for Research on Cancer, World Health Organization, International Association of Cancer Registries. *Cancer Incidence in Five Continents. Volume VII*. In: Parkin DM, Whelan SL, Ferlay J, Raymond L, Young J, eds. Lyon, France: IARC Scientific Publications No. 143, 1997.
15. Institut National de la Statistique et des Etudes Economiques. *Recensement de la population de 1999. Evolutions démographiques 1982–1990–1999. Département 25.* Paris: INSEE, 1999.
16. Voutilainen ET, Dickman PW, Hakulinen T. *Surv2: Relative survival analysis Program.* Helsinki: Finnish Cancer Registry, 1998.
17. Hakulinen T, Tenkanen L, Abeywickrama K, Païvärinta L. Testing equality of relative survival patterns based on aggregated data. *Biometrics* 1987;43:313–325.
18. Hakulinen T, Tenkanen L. Regression analysis of relative survival rates. *Appl Stat* 1987;36:306–317.
19. SAS Institute. SAS System. Cary, NC: SAS Institute Inc., 1999.
20. Kogevinas M, Porta M. Socioeconomic differences in cancer survival: a review of the evidence. In: Kogevinas M, Pearce N, Susser M, Boffetta P, eds. *Social Inequalities and Cancer.* Lyon, France: IARC Scientific Publications, 1997:177–206.
21. Ramalingam S, Pawlish K, Gadgeel S, Demers R, Kalemkerian GP. Lung cancer in young patients: analysis of a surveillance, epidemiology, and end results database. *J Clin Oncol* 1998;16:651–657.
22. Launoy G, Le Coutour X, Gignoux M, Pottier D, Dugleux G. Influence of rural environment on diagnosis, treatment, and prognosis of colorectal cancer. *J Epidemiol Community Health* 1992;46:365–367.