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Risk of a new primary cancer among patients with lung cancer of different histological types

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Abstract

The risk of a new primary cancer (NPC) among 77 548 Finnish lung cancer patients from 1953 to 1995 was analysed by the histological type of the lung cancer. The relative risks were expressed as standardised incidence ratios (SIR, ratio of the observed and expected numbers of cases). During the follow-up, 1148 NPCs were observed among men and 152 among women. After exclusion of lung cancers, the risk of NPC was elevated in both males (SIR 1.07; 95% confidence interval (CI) 1.00–1.14) and females (SIR 1.21; 95% CI 1.02–1.42). The excess was larger among lung cancer patients with small-cell carcinoma and adenocarcinoma than those with squamous-cell carcinoma. In all major histological groups of lung cancer, significant excess risks were found for cancers of the larynx (SIRs 2.94–4.25), and bladder (SIRs 2.16–2.86). Significantly elevated SIRs were also found for cancers of the stomach (SIR 1.42; 95% CI 1.12–1.76) and kidney (SIR 2.18; 95% CI 1.56–2.97) in squamous-cell carcinoma; for brain tumours (SIR 3.26; 95% CI 1.20–7.09) in small-cell carcinoma; and for cancers of the prostate (SIR 1.68; 95% CI 1.21–2.27) and thyroid (SIR 3.79; 95% CI 1.23–8.85), and brain tumours (SIR 2.34; 95% CI 1.07–4.43) in adenocarcinoma. The risk of contracting NPC at sites where the majority of tumours are adenocarcinomas was elevated among patients with adenocarcinoma of the lung, but not among squamous-cell or small-cell carcinoma patients. In adenocarcinoma, the excess risks of several smoking-related cancers tended to be somewhat lower than those in the other two histological categories. The relative risk of a NPC among patients diagnosed with lung cancer in 1985–1995 was higher than that of patients from earlier periods in all comparable follow-up categories (up to 10 years), possibly suggesting that the increased use of cytostatic drugs had increased the risk of NPC.

Keywords: Lung cancer; Squamous-cell carcinoma; Small-cell carcinoma; Adenocarcinoma; Second primary cancer

1. Introduction

In Finland, lung cancer is the second most common cancer (after prostate cancer) in males and the fifth most common in females. The age-adjusted ('world standard') incidence rate in 1997 was 39.6 per 100 000 in males, and 9.1 in females [1]. The survival of lung cancer patients has doubled in Finland since the 1960s, but is still rather low: the 5-year relative survival rate among patients diagnosed in 1985–1994 was 10% in males and 13% in females [2]. Younger patients experienced a somewhat more favourable survival than the older ones. Differences exist between histological groups: the 5-year relative survival rate was 16% (males and females) in squamous-cell carcinoma, 16% (males) and 24% (females) in adenocarcinoma, and only 3% (males) and 4% (females) in small-cell carcinoma [2]. Continuous though slow improvement in lung cancer patient survival results in increasing numbers of long-term survivors who are under risk of contracting new primary cancers (NPC).

The treatment of lung cancer has also progressed. Modern chemotherapy for small-cell carcinoma started in the 1970s, and a combination of radiation and chemotherapy is now the standard treatment for small-cell carcinoma. Chemotherapy has occupied an established position also in the treatment of non-small cell lung cancer (NSCLC).

In this study, the risk of a NPC was analysed among lung cancer patients. The motivation for this study

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arose from the following two aspects: (1) Smoking, a well-known risk factor in lung cancer, also increases the risk of many other cancers [3,4]. (2) The increased use of cytostatic drugs is likely to increase the risk of NPC after the diagnosis of lung cancer. Since the proportions of lung cancers attributable to smoking are different for different histological types (being higher for squamous-cell, small-cell and large-cell carcinomas than for adenocarcinoma [5]) and since the treatment of different histological types of lung cancer varies in terms of the use of radiotherapy and chemotherapy, the analyses were conducted separately for the main histological categories of lung cancer.

2. Patients and methods

The Finnish Cancer Registry (FCR) was established in 1952. It is population-based and countrywide, and collects information on cancer patients, e.g. from hospitals, practising physicians, pathology laboratories and death certificates. Today, some 1.5% of the cases are known to the FCR on the basis of death certificate alone. All patients are regularly followed-up for death and emigration through the Population Register. The coding of data has always taken place, or been supervised, by a physician. Special emphasis is given at the FCR on the evaluation of whether two or more primary cancers are diagnosed in one and the same individual. In addition to the direct information obtained on the notifications, the time interval between the diagnoses, histological types of the lesions and general knowledge of the typical clinical behaviour (e.g. sites of metastases) of each cancer are used in this evaluation.

The study population consisted of more than 77 500 lung cancer patients diagnosed in 1953–1995 in Finland (Table 1). In males, squamous-cell carcinoma was the most frequent histological type followed by small-cell carcinoma and adenocarcinoma (including bronchioalveolar carcinoma) (Table 1). Adenocarcinoma was the leading type in females. The category 'other histology' included other specified histological types (e.g. large-cell carcinomas), and unspecified and 'anaplastic' carcinomas. Tumours with a cytological (or any non-microscopic) verification of the diagnosis were included in the category 'no histology' which constituted almost one-third of the total material. The proportion of no histology was almost 60% in the mid-1950s, and diminished to 29% in 1991–1995.

The follow-up of the patients started from the month following lung cancer diagnosis and ended at death, emigration or closing date (31 December 1995), whichever occurred first. It yielded 107 094 person-years at risk, the mean follow-up time being 1.38 years (ranging from less than 1 year for small-cell carcinoma and the no histology group to 2.06 and 2.11 years for squamous-cell and adenocarcinoma, respectively) (Table 1). Approximately 27% of the follow-up time among patients with adenocarcinoma fell within the first year after lung cancer diagnosis, whereas for patients with small-cell carcinoma this proportion was 56% and for those with no histology 55%. In the total material, 12% of the follow-up years were in the category 10+ years (range from 6% in the no histology group to 16% in the adenocarcinoma group).

The expected numbers of a given cancer were calculated by multiplying the gender, age and period-specific numbers of person-years by the corresponding stratum-specific national incidence rates of the cancer in question. The risk of contracting a new primary cancer was estimated using standardised incidence ratios (SIRs) defined as ratios of the observed and expected numbers of cases. Exact 95% confidence intervals (CI) of the SIRs were estimated under the assumption that the observed numbers followed a Poisson distribution.

In addition to individual primary sites of NPC, the analyses were also performed in two larger groups. 'Smoking-related cancers' included cancers of the lip, oral cavity, pharynx, oesophagus, larynx, kidney and urinary bladder; smoking is known to be an important risk factor in these cancers [5]. Another group, 'adenocarcinomas', constituted cancers of the stomach,

Table 1
Numbers of lung cancer patients diagnosed in 1953–1995 in Finland, numbers of person-years at risk for a subsequent new primary cancer by 31 December 1995, and mean follow-up time, by histology of the lung tumour and gender

Histology	Patients (*n*)		Person-years at risk		Mean follow-up time (years)
	Men (%)	Women (%)	Men	Women	
Squamous-cell carcinoma	19 572 (29)	1296 (14)	40 615	2464	2.06
Small-cell carcinoma	8936 (13)	1202 (13)	7301	1281	0.85
Adenocarcinoma	5695 (8)	2301 (25)	11 133	5728	2.11
Other histology[a]	12 216 (18)	1728 (18)	13 997	2631	1.19
No histology[b]	21 753 (32)	2849 (30)	19 322	2622	0.89
All types	68 172 (100)	9376 (100)	92 369	14 726	1.38

[a] Other specified, or unspecified histology, including unspecified carcinoma.
[b] Includes tumours with cytological confirmation (without histology).

colorectum, breast, ovary, corpus uteri, prostate and thyroid; a majority of cancers at these sites are various types of adenocarcinoma.

All analyses were conducted for males and females separately, but if the results were essentially similar, only combined results are shown.

3. Results

3.1. Total material

During the follow-up, 1148 NPC were diagnosed in males and 152 in females (Table 2). The number of new primary lung cancers among males was distinctly lower than expected (SIR 0.36; 95% confidence interval (CI) 0.30–0.42). When lung cancers were excluded from both the observed and expected numbers of cases, the SIR for all remaining cancers taken together was 1.07 (95% CI 1.00–1.14) in men and 1.21 (95% CI 1.02–1.42) in women (Table 2). Significant excess risks were found for cancers of the pharynx (SIR 1.99; 95% CI 1.09–3.34), larynx (2.49; 95% CI 1.87–3.23), kidney (1.60; 95% CI 1.23–2.05), and urinary bladder (1.94; 95% CI 1.63–2.28) in males, and for cancers of the larynx (25.2; 95% CI 8.17–58.7) and ovary (2.09; 95% CI 1.11–3.56) and brain tumours (2.60; 95% CI 1.19–4.93) in females. Cancers of the stomach and colorectum showed significantly low SIRs in males. The risk of leukaemia was significantly elevated for males and females combined (47 cases observed, SIR 1.44, 95% CI 1.06–1.91).

For 'smoking-related cancers', the risk was significantly elevated for both males (1.74; 95% CI 1.56–1.98) and females (1.88; 95% CI 1.13–2.93) (Table 2). For the NPC group of 'adenocarcinomas' the risk was at the expected level in males and slightly (but non-significantly) elevated in females (Table 2).

During the first 5 years of follow-up, the risk of NPC (excluding new lung cancers) was at the expected level; the excess risks in histology-specific categories were balanced by the significantly low SIR among the lung cancer patients with no histology (Table 3). Thereafter, a significant excess risk was seen among both males and females.

The SIR increased by calendar period, being highest in the 1985–1995 period within all follow-up categories up to 10 years for which meaningful comparison was possible (Table 4).

3.2. Squamous-cell carcinoma

In the group of squamous-cell carcinomas, the risk of NPC was slightly increased in both genders (Table 5). A significant excess risk was found for 'smoking-related cancers'; the SIR for males and females taken together was 2.12 (95% CI 1.82–2.44) (Table 6). Elevated relative risks were found for cancers of the larynx (SIR 3.37;

Table 2
Numbers (observed) and SIRs (with their 95% confidence intervals) of selected new primary cancers among lung cancer patients, by gender

Site of new primary cancer	Men		Women	
	Observed	SIR (95% CI)	Observed	SIR (95% CI)
Lung	129	0.36 (0.30–0.42)	10	1.81 (0.87–3.33)
Other 'smoking-related'	326	1.74 (1.56–1.98)	19	1.88 (1.13–2.93)
Lip	24	1.00 (0.64–1.49)	–	– (0.00–7.17)
Oral cavity	7	1.95 (0.79–4.02)	1	2.16 (0.05–12.1)
Pharynx	14	1.99 (1.09–3.34)	1	2.03 (0.05–11.3)
Oesophagus	26	1.23 (0.80–1.79)	2	0.93 (0.11–3.35)
Larynx	55	2.49 (1.87–3.23)	5	25.17 (8.17–58.7)
Kidney	62	1.60 (1.23–2.05)	8	2.08 (0.90–4.10)
Urinary bladder	138	1.94 (1.63–2.28)	2	0.81 (0.10–2.92)
'Adenocarcinomas'	434	0.92 (0.84–1.01)	80	1.22 (0.96–1.51)
Stomach	112	0.84 (0.69–0.99)	7	0.69 (0.28–1.42)
Colorectum	75	0.72 (0.56–0.90)	13	0.94 (0.50–1.60)
Breast	2	1.56 (0.19–5.61)	35	1.33 (0.92–1.84)
Corpus uteri	–		8	1.07 (0.46–2.11)
Ovary	–		13	2.09 (1.11–3.56)
Prostate	240	1.07 (0.94–1.21)	–	
Thyroid	5	1.00 (0.32–2.33)	4	1.88 (0.58–5.45)
Other				
Pancreas	44	0.89 (0.64–1.19)	6	1.03 (0.38–2.25)
Brain	21	1.09 (0.67–1.66)	9	2.60 (1.19–4.93)
Leukaemia	40	1.34 (0.96–1.82)	7	2.45 (0.98–5.04)
All sites[a]	1019	1.07 (1.00–1.14)	142	1.21 (1.02–1.42)

SIRs, standardised incidence ratios.
[a] Lung cancers excluded from both the observed and expected numbers of cases.

Table 3
Numbers (observed) and SIRs (with their 95% confidence intervals) of a new primary cancer among lung cancer patients, by follow-up time (completed years), and histology (men and women taken together); lung cancers excluded from both the observed and expected numbers of cases

Follow-up time (years)	All cancers		Squamous-cell carcinoma		Small-cell carcinoma		Adenocarcinoma		Other histology		No histology	
	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	SIR (95% CI)
< 1	421	1.06 (0.96–1.16)	167	1.34 (1.14–1.55)	61	1.55 (1.18–1.98)	57	1.54 (1.17–1.99)	73	1.40 (1.09–1.75)	63	0.44 (0.34–0.56)
1–4	338	0.97 (0.87–1.08)	158	1.07 (0.91–1.24)	24	1.21 (0.78–1.80)	54	1.10 (0.82–1.43)	45	1.08 (0.79–1.45)	57	0.64 (0.48–0.83)
5–9	203	1.28 (1.11–1.46)	98	1.21 (0.98–1.47)	13	1.68 (0.90–2.88)	45	1.48 (1.08–1.98)	29	1.29 (0.86–1.85)	18	1.05 (0.62–1.65)
10 +	199	1.23 (1.06–1.40)	96	1.25 (1.02–1.53)	12	1.43 (0.74–2.50)	44	1.56 (1.13–2.09)	34	1.14 (0.79–2.09)	13	0.68 (0.36–1.17)
Any	1161	1.09 (1.03–1.15)	519	1.21 (1.10–1.31)	110	1.46 (1.20–1.74)	200	1.38 (1.19–1.58)	181	1.24 (1.06–1.42)	151	0.56 (0.47–0.65)

SIR, standardised incidence ratios.

Table 4
Numbers (observed) and SIRs (with their 95% confidence intervals) of new primary cancer (NPC) among lung cancer patients, by follow-up time (completed years), and period of diagnosis of the lung cancer (men and women taken together); lung cancers excluded from the observed and expected numbers of cases

Follow-up time (years)	Diagnosis of lung cancer					
	1953–1969		1970–1984		1985–1995	
	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	SIR 95% CI
<1	43	0.52 (0.38–0.70)	193	1.09 (0.94–1.25)	185	1.34 (1.16–1.54)
1–4	43	0.75 (0.55–1.01)	165	0.96 (0.82–1.11)	130	1.11 (0.93–1.31)
5–9	41	1.24 (0.89–1.68)	116	1.24 (1.02–1.48)	46	1.42 (1.04–1.89)
10+	79	1.11 (0.88–1.39)	119	1.32 (1.09–1.57)	1	1.18 (0.03–6.55)
Any	206	0.84 (0.73–0.96)	593	1.11 (1.02–1.20)	362	1.26 (1.13–1.39)

SIRs, standardised indicence ratios.

95% CI 2.32–4.72), kidney (2.18; 95% CI 1.56–2.97), and urinary bladder (2.16; 95% CI 1.68–2.73). The risk of 'adenocarcinomas' was close to that expected (SIR 1.07; 95% CI 0.93–1.21) (Table 6). There was a significantly higher than expected number of new stomach cancers (SIR 1.42; 95% CI 1.12–1.76). An excess risk of NPC was seen during the first follow-up year after diagnosis, and also after 5 years (Table 3).

3.3. Small-cell carcinoma

Among patients with small-cell carcinoma the risk of developing a NPC was significantly elevated in both genders; the SIRs for both males (1.42; 95% CI 1.15–1.73) and females (1.76; 95% CI 1.01–2.86) were higher than those in any other histological subcategory (Table 5). As for the individual cancer types, the pattern was similar to that observed for squamous-cell carcinoma: excess risks were found for cancers of the larynx and urinary bladder (SIRs 4.25; 95% CI 1.71–8.76 and 2.86; 95% CI 1.60–4.72, respectively), and for all 'smoking-related cancers' taken together (SIR 2.24; 95% CI 1.54–3.17) (Table 6). In addition, a significantly increased risk was found for brain tumours (SIR 3.26; 95% CI 1.20–7.09). The incidence of 'adenocarcinomas' was at the expected level. An elevated risk of NPC was observed throughout the follow-up period (Table 3).

3.4. Adenocarcinoma

In the group of adenocarcinomas, the relative risk of developing a NPC was elevated among both males (1.33; 95% CI 1.12–1.56) and females (1.50; 95% CI 1.15–1.91) (Table 5). In addition to larynx and bladder cancers (2.94; 95% CI 1.18–6.05 and 2.43; 95% CI 1.53–3.68, respectively), also cancers of the prostate (1.68; 95% CI 1.21–2.27) and thyroid (3.79; 95% CI 1.23–8.85), leukaemia (2.18; 95% CI 1.00–4.13) and brain tumours (2.34; 95% CI 1.07–4.43) were found in excess (Table 6). The risk of 'smoking-related cancers' combined was significantly increased (SIR 1.84; 95% CI 1.35–2.47), as was the risk of 'adenocarcinomas' (SIR 1.39; 95% CI 1.13–1.67) (Table 6). The risk of developing a NPC was increased during the year following lung cancer diagnosis and also after a follow-up of 5 years (Table 3).

3.5. Other histology and no histology

Among lung cancer patients with a histology other than the three main categories considered above the risk of a NPC was slightly elevated (Table 5), the risk pattern resembling that of squamous-cell carcinoma.

In the group of no histology a marked risk deficit was noted among both males and females (Table 5).

Table 5
Numbers (observed) and SIRs (with their 95% confidence intervals) of a new primary cancer (NPC) among lung cancer patients, by histology of the lung tumour and gender; lung cancers excluded from both the observed and expected numbers of cases

Histology of lung cancer	Men		Women	
	Observed	SIR (95% CI)	Observed	SIR (95% CI)
Squamous-cell carcinoma	494	1.20 (1.10–1.31)	25	1.27 (0.82–1.88)
Small-cell carcinoma	94	1.42 (1.15–1.73)	16	1.76 (1.01–2.86)
Adenocarcinoma	137	1.33 (1.12–1.56)	63	1.50 (1.15–1.91)
Other histology	150	1.18 (1.00–1.34)	31	1.63 (1.11–2.32)
No histology	144	0.59 (0.50–0.69)	7	0.25 (0.10–0.52)
All types	1019	1.07 (1.00–1.14)	142	1.21 (1.02–1.42)

Table 6
Numbers (observed) and SIRs (with their 95% confidence intervals) of selected new primary cancers (NPCs) among lung cancer patients, by histology of the lung tumour (men and women taken together)

Site of new primary cancer	Squamous-cell carcinoma		Small-cell carcinoma		Adenocarcinoma	
	Observed	SIR (95% CI)	Observed	SIR (95% CI)	Observed	(SIR 95% CI)
Lung	82	0.52 (0.42–0.64)	7	0.27 (0.11–1.55)	29	0.73 (0.49–1.05)
Lip	10	0.97 (0.47–1.78)	1	0.59 (0.01–3.36)	4	1.56 (0.42–3.98)
Oesophagus	13	1.46 (0.78–2.49)	1	0.65 (0.02–3.62)	2	0.76 (0.09–2.73)
Larynx	33	3.37 (2.32–4.72)	7	4.25 (1.71–8.76)	7	2.94 (1.18–6.05)
Kidney	40	2.18 (1.56–2.97)	6	1.84 (0.68–4.00)	9	1.44 (0.66–2.73)
Urinary bladder	69	2.16 (1.68–2.73)	15	2.86 (1.60–4.72)	22	2.43 (1.53–3.68)
Stomach	78	1.42 (1.12–1.76)	12	1.28 (0.66–2.23)	9	0.60 (0.28–1.14)
Colorectum	36	0.75 (0.52–1.03)	4	0.47 (0.13–1.21)	22	1.32 (0.82–1.99)
Pancreas	24	1.07 (0.68–1.58)	4	1.02 (0.28–2.60)	13	1.77 (0.94–3.02)
Breast	8	1.54 (0.67–3.03)	3	1.30 (0.27–3.80)	16	1.54 (0.88–2.50)
Prostate	101	1.03 (0.84–1.24)	17	1.12 (0.65–1.78)	42	1.68 (1.21–2.27)
Thyroid	1	0.40 (0.01–2.20)	2	3.77 (0.46–13.6)	5	3.79 (1.23–8.85)
Leukaemia	19	1.43 (0.86–2.22)	2	0.87 (0.11–3.13)	9	2.18 (1.00–4.13)
Brain	7	0.73 (0.30–1.51)	6	3.26 (1.20–7.09)	9	2.34 (1.07–4.43)
'Smoking-related'[a]	178	2.12 (1.82–2.44)	32	2.24 (1.54–3.17)	45	1.84 (1.35–2.47)
'Adenocarcinomas'	226	1.07 (0.93–1.21)	41	1.11 (0.79–1.50)	102	1.39 (1.13–1.67)

4. Discussion

The material of this study was population-based and originated in the files of the countrywide Finnish Cancer Registry. From a methodological point of view, it is important that both the observed and expected numbers of cases were obtained from the same database allowing an appropriate assessment of the relative risks. In clinical follow-up studies, the results are often expressed as proportions (percentages) of patients with NPC from the total material. Scientifically, this is misleading or at least not very informative, because the age distributions and follow-up times of the patients vary substantially, and the percentage in question increases continuously with time and is not at all comparable between different studies. We avoided using such estimates.

Sometimes there are problems in cancer registries (as well as in the clinical practice) in defining whether a new cancer is really a new independent primary entity. As a rule, the coding of cases with two or more cancers, suggesting multiple primaries, is always checked by a physician (pathologist). In a large Finnish multiple cancer material (from 1953 to 1991), the percentage of histological or cytological confirmation of those cancers which were followed by a new primary was 98%, and that of subsequent new primaries 92%, compared with 85% in the total registry material [6] which indicates a rather conservative attitude in coding multiple primaries. In other words, histological verification of the two cancers diagnosed in one and the same individual has usually been a prerequisite of coding them as two separate primary cancers.

The lower than expected number of NPC among lung cancer patients without histological verification of the lung tumour is probably, at least in part, due to coding routines: if cancer in the lung has no histological verification, there is a possibility that both the lung cancer and the subsequent new cancer (elsewhere) are in fact manifestations of one and the same cancer process instead of independent entities, and thus the patient may not be coded as having multiple cancer.

A distinctly lower than expected risk was found for contracting a new primary lung cancer after lung cancer diagnosis. This was also observed in a cancer registry-based study in Denmark [4]. In some clinical materials from the USA and Canada, the risk of a non-small cell carcinoma of the lung among small-cell carcinoma patients was greatly increased [7–9]. This discrepancy in the results is obviously due to difficulties, in both clinical work and cancer registration, in the evaluation of whether a new lung tumour in a patient whose lung cancer has been previously treated is a new primary cancer or just a recurrence. From a clinical point of view, a new lung cancer, especially one in the contralateral lung and with a histological type different from that of the first tumour, is a therapeutic challenge and is likely to be considered as a new primary cancer. On the other hand, at a cancer registry where there is no responsibility for the treatment and outcome of the patient, a more restrictive attitude in terms of coding two separate primary lung cancers in 1 patient is understandable although it may lead to an underestimation of the true risks. Currently, there is no routine way to reliably distinguish between a new primary lung cancer and a recurrence of the first tumour. Histology as such is not totally decisive. Various biological cell markers can, in the future, be helpful in this matter. The 50% cumulative actuarial incidence of having a

non-small-cell lung cancer during 8 follow-up years from diagnosis of a small-cell lung cancer as reported by Heyne and colleagues [7] refers to 2-year survivors and cannot thus be generalised.

In this study, the risk of brain tumours among lung cancer patients was elevated. It is difficult if not impossible to deduct whether this is real or whether some metastatic lesions in the brain have been coded as primary brain tumours. It is, however, noteworthy that no excess risk was found for cancers of the liver, another common site of metastases from lung cancer (16 cases observed, 19.7 expected, SIR 0.81, 95% CI: 0.76–1.31).

The prognosis of lung cancer patients is rather unfavourable, and has been even worse in the past. So, even if the original material of lung cancer patients was large, over 77 500, the numbers of long-term survivors and, consequently, NPCs were rather low resulting in instability of many point estimates of relative risk. Two-thirds of the follow-up years fell within the categories of less than 5 years, and an even higher proportion for patients in some of the individual histological categories. The methodology applied (i.e. comparing SIRs of categories with equal length of follow-up) eliminates the possible bias caused by differences in the survival experience of patients with different histologies of lung cancer.

The shortage of long survival times of patients with lung cancer decreases the chance of detecting possible treatment-related excess risks of NPC which are expected to occur after a lengthy latent period. For similar reasons, the long-term effects of the recent changes in the treatment policy of lung cancer on the risk of NPC cannot be evaluated yet. The SIR of NPC increased by calendar period within each follow-up time category up to 10 years which is only partly explained by the slight increase with time in the proportion of adenocarcinoma of the lung (which carries a higher than average risk of NPC). Taken together, this suggests that the increase in the use of cytostatic drugs in the treatment of lung cancer may increase the risk of NPC. In any case, the problem of having a treatment-related NPC after lung cancer is small in terms of absolute numbers of cases.

Lung cancer in men in Finland has been a disease of the lower social strata, while in women, until the mid-1980s, it was more common in the higher social classes [10]. Therefore, cancers of the low social classes (who smoke more than average) were expected to be in excess among male lung cancer patients, and those of affluent people somewhat decreased. From that background, e.g. the SIR of 0.84 for stomach cancer (which has the highest incidences in the poorer socioeconomic classes) might actually represent a larger relative decrease in the risk (due to unduly low expected numbers which are based on the general population) than the SIR of 0.72 for colorectal cancer (a cancer of affluence).

When NPCs at sites where the majority of tumours are adenocarcinomas were combined, the risk was close to that expected for lung cancer patients with squamous-cell or small-cell carcinoma, whereas for patients with adenocarcinoma of the lung, the risk was significantly increased. In terms of absolute numbers of observed cases, this finding was mainly based on excesses of cancers of the prostate, colorectum and breast, i.e. cancers which are known to have a genetic aetiological component. Some observations indicate that lung cancer patients, especially those with adenocarcinoma, with multiple other primary cancers often have a family history of malignant tumours [11]. This refers to a possible role of genetic factors in the occurrence of multiple tumours in patients with adenocarcinoma of the lung.

As expected, 'smoking-related cancers' were found in excess among all the major histological types of lung cancer. Some evidence was obtained suggesting that the risk of contracting adenocarcinomas in different organs is only increased in patients with adenocarcinoma of the lung. It is noteworthy that in this group, the proportion of women and, due to the better general survival, also the proportion of patients with a follow-up time of 5 years or more were higher than in the other histological groups of lung cancer.

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