



## Letter

## Second primary cancers in laryngeal cancer patients

Fabio Levi<sup>a,b,\*</sup>, Lalao Randimbison<sup>a</sup>, Van-Cong Te<sup>a</sup>, Carlo La Vecchia<sup>c</sup><sup>a</sup>*Vaud Cancer Registry and Cancer Epidemiology Unit, Institute of Social and Preventive Medicine, CHUV-Falaises 1, 1011 Lausanne, Switzerland*<sup>b</sup>*Neuchâtel Cancer Registry, Av. des Cadolles 7, 2000 Neuchâtel, Switzerland*<sup>c</sup>*Istituto di Ricerche Farmacologiche "Mario Negri", and Istituto di Statistica Medica e Biometria, Università degli Studi di Milano, Via Venezian 1, 20133 Milan, Italy*

Received 22 August 2002; accepted 2 September 2002

Quantitative estimates of second primary cancer risk after laryngeal cancer are still open to discussion. Recently published data from the Cancer Registry of Slovenia showed a 2.8-fold excess risk of second primary cancer in patients diagnosed with a laryngeal cancer. Excess risks were observed for lung and other tobacco-related cancers, but also from non-melanoma skin and thyroid cancers [1].

We thus updated to 1998 the follow-up of laryngeal cancer cases from the Vaud Cancer Registry, which had shown a 3.7-fold excess of tobacco-related cancers among cases of laryngeal cancer diagnosed between 1974 and 1994 [2]. To provide additional information on the issue, we have also combined the datasets from the Swiss Registries of the Cantons of Vaud and Neuchâtel whose populations, according to the 31 December, 2000 Census, were 620,294 and 165,731 inhabitants, respectively.

After exclusion of two cases detected at autopsy, five at death or by death certification alone, 19 deceased or followed-up for less than 1 month after diagnosis, or lost to follow-up, and 51 synchronous cancers, the present series comprised 689 (median age: 61.9 years; range: 31.0–93.2 years) male laryngeal cancers, including 323 glottic neoplasms, diagnosed between 1974 and 1998 (rate of histological verifications: 97.2%). These persons were followed-up to the end of 1998 for the occurrence of a second primary neoplasm, emigration or death, for a total of 3825.1 person-years at risk.

Overall, 132 second primary cancers were observed over the 25-year period 1974–1998 versus the 76.8

expected, corresponding to a standardised incidence ratio (SIR) of 1.72 (95% confidence interval (CI): 1.4–2.0) (Table 1). Significant excess risks were observed for oral and pharyngeal, oesophageal, lung and thyroid cancers, and the SIRs were also above unity for pancreas, malignant melanoma, bladder, stomach cancer and leukaemias. No excess risk was observed for colorectal, prostate or skin cancers.

For most sites, the excess risk was greater in relative terms 5 or more years since first diagnosis, in subjects aged <60 years, and for parts of the larynx other than glottis, in agreement with the observations from the Slovenian cancer Registry [1].

The present comprehensive update analysis therefore confirms the existence of a strong excess risk of all major tobacco (and alcohol-) related neoplasms following a diagnosis of laryngeal cancer [2], further stressing the recognised importance of these factors on laryngeal carcinogenesis. It is also of interest that some of the neoplasms less strongly related to tobacco smoking, such as stomach or leukaemias [3], showed some excess risk, although these estimates were non-significant. The excess thyroid cancer risk may be a consequence of radiotherapy on the neck [4], but in the present series should be mainly related to surveillance on the head and neck region, since 2 out of three thyroid neoplasms were diagnosed <3 months after the diagnosis of laryngeal cancer.

Also of interest is the observation that no excess risk was apparent for other most common non-tobacco-related neoplasms, including colorectal, prostate or non-melanoma skin cancer [3,5], indicating that there was no systematic excess surveillance following a diagnosis of laryngeal cancer in this Swiss population.

\* Corresponding author. Tel.: 41-21-314-73-11; fax: +41-21-323-03-03.

E-mail address: fabio.levi@inst.hospvd.ch (F. Levi).

Table 1

Observed cases (O) and standardised incidence ratios (SIR) with corresponding 95% confidence intervals (CI), of selected subsequent cancer sites after an initial diagnosis of laryngeal cancer in strata of selected covariates<sup>a</sup>

Sites		Years since first cancer		Age at first cancer		Laryngeal sub-site		Overall
		< 5	≥ 5	< 60	≥ 60	Glottic	Other part of larynx	
All sites <sup>b</sup>	O	59	73	67	65	53	79	132
	SIR	1.53	1.9	3.29	1.15	1.15	2.58	1.72
	95% CI	(0.2–2.0)	(1.5–2.4)	(2.6–4.2)	(0.9–1.5)	(0.9–1.5)	(2.0–3.2)	(1.4–2.0)
Mouth or pharynx	O	10	12	20	2	9	13	22
	SIR	5.66	8.97	14.1	1.18	5.20	9.49	7.09
	95% CI	(2.7–10.4)	(4.6–14.7)	(8.6–21.8)	(0.1–4.3)	(2.4–9.9)	(5.0–16.2)	(4.4–10.7)
Oesophagus	O	2	5	4	3	3	4	7
	SIR	2.34	6.90	7.60	2.85	3.28	6.02	4.43
	95% CI	(0.3–8.4)	(2.2–16.1)	(2.0–19.5)	(0.6–8.3)	(0.7–9.6)	(1.6–15.4)	(1.8–9.1)
Stomach	O	5	1	1	5	4	2	6
	SIR	3.53	0.83	1.62	2.49	2.59	1.86	2.29
	95% CI	(1.1–8.2)	(0.0–4.6)	(0.0–9.0)	(0.8–5.8)	(0.7–6.6)	(0.2–6.7)	(0.8–5.0)
Colorectum	O	3	4	1	6	4	3	7
	SIR	0.78	1.06	0.54	1.04	0.87	0.99	0.92
	95% CI	(0.2–2.3)	(0.3–2.7)	(0.0–3.0)	(0.4–2.3)	(0.2–2.2)	(0.2–2.9)	(0.4–1.9)
Pancreas	O	1	2	3	0	1	2	3
	SIR	1.09	2.34	6.15		0.95	2.81	1.7
	95% CI	(0.0–6.1)	(0.3–8.5)	(1.2–18.0)		(0.0–5.3)	(0.3–10.2)	(0.3–5.0)
Lung	O	24	26	25	25	17	33	50
	SIR	3.83	4.83	6.74	3.14	2.50	6.80	4.29
	95% CI	(2.5–5.7)	(3.2–7.1)	(4.4–9.9)	(2.0–4.6)	(1.5–4.0)	(4.7–9.5)	(3.2–5.7)
Malignant melanoma	O	0	2	2	0	1	1	2
	SIR		2.74	4.11		1.17	1.73	1.40
	95% CI		(0.3–9.9)	(0.5–14.8)		(0.02–6.5)	(0.0–9.6)	(0.2–5.1)
Non-melanoma skin cancer	O	2	8	6	4	5	5	10
	SIR	0.22	0.81	1.24	0.28	0.43	0.68	0.53
	95% CI	(0.0–0.8)	(0.4–1.6)	(0.5–2.7)	(0.1–0.7)	(0.1–1.0)	(0.2–1.6)	(0.2–1.1) cont'd
Prostate	O	4	3	0	7	3	4	7
	SIR	0.67	0.42		0.64	0.36	0.81	0.53
	95% CI	(0.2–1.7)	(0.1–1.2)		(0.3–1.3)	(0.1–1.1)	(0.2–2.1)	(0.2–1.1)
Bladder	O	3	3	0	6	1	5	6
	SIR	1.74	1.70		2.27	0.47	3.65	1.72
	95% CI	(0.4–5.1)	(0.3–5.0)		(0.8–4.9)	(0.0–2.6)	(1.2–6.5)	(0.6–3.7)
Kidney	O	0	1	1	0	0	1	1
	SIR		1.22	1.85			1.46	0.59
	95% CI		(0.0–6.8)	(0.0–10.3)			(0.0–8.1)	(0.0–3.3)
Thyroid	O	2	1	1	2	2	1	3
	SIR	17.1	10.3	12.7	14.8	16.37	10.9	14.02
	95% CI	(1.9–61.7)	(0.1–57.4)	(0.2–70.4)	(1.7–53.5)	(1.8–59.1)	(0.1–60.6)	(2.8–41.0)
Leukaemia	O	1	2	1	2	1	2	3
	SIR	1.47	3.40	3.01	2.13	1.34	3.84	2.36
	95% CI	(0.0–8.2)	(0.4–12.3)	(0.0–16.7)	(0.2–7.7)	(0.0–7.4)	(0.4–13.9)	(0.5–6.9)

<sup>a</sup> The Swiss Cantons of Vaud and Neuchâtel, 1974–1998.

<sup>b</sup> Sites not included in the table comprise: gall bladder (1), eye (1), brain and nerves (1), multiple myeloma (1), unknown primary site (1).

## References

1. Ecimovic P, Pompe-Kirn V. Second primary cancers in laryngeal cancer patients in Slovenia, 1961–1996. *Eur J Cancer* 2002, **38**, 1254–1260.
2. Levi F, Randimbison L, Te VC, Rolland-Portal I, Franceschi S, La Vecchia C. Multiple primary cancers in the Vaud cancer Registry, Switzerland, 1974–89. *Br J Cancer* 1993, **67**, 391–395.
3. IARC Monographs (Vol. 83) Tobacco Smoke and Involuntary Smoking (Press release June 2002/ [www.iarc.fr](http://www.iarc.fr)).
4. Ron E. Thyroid cancer. In Schottenfeld D, Fraumeni Jr JF, eds. *Cancer Epidemiology and Prevention*. New York, Oxford University Press, 1996, 1000–1021.
5. Levi F, La Vecchia C. Tobacco smoking and prostate cancer: time for an appraisal. *Ann Oncol* 2001, **12**, 733–738.