



## Letter

## Epidemiology of unknown primary tumours

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Scanty population-based evidence is available on the epidemiological and clinical characteristics of unknown primary tumours. It is generally reported that unknown primary tumours account for 5–10% of all neoplasms [1], and that they tend to have an unfavourable prognosis [2–4]. In a series of 1285 patients from the South-east Netherlands, unknown primary cancers accounted for 4% of all incident cancers over the period of 1984–1992, and had a median survival of 11 weeks, ranging from over 20 weeks for patients aged under 50 years to 5 weeks only for those aged 70 years or over [5]. To provide additional information on the issue, we considered incident cases registered with unknown primary cancer in the Swiss Cantons of Vaud and Neuchâtel between 1984 and 1993.

The data were abstracted from the two cantonal cancer registry files, which include uniform and standardised information on all incident cases of malignant neoplasms occurring in the resident populations (620 000 inhabitants in Vaud and 166 000 in Neuchâtel in 2000). Information collected by the registries include general demographic characteristics of the patient, site and histological type of the tumour according to the standard International Classification of Diseases for Oncology, 9th edition (ICD-O-9), and time of diagnostic confirmation [6,7]. Information on survival is derived from mortality statistics and, for 'apparently' non-deceased cases, through an active follow-up based on verification of vital status from registries of current

residence. Survival was calculated from the date of diagnosis, which is the date of histological confirmation or that on which clinical diagnosis was established. The vital status of each registered case has been verified up to 31 December 1998. Information on site at diagnosis and on treatment of the unknown primary tumours was not available in the registries' databases.

Of 41 054 neoplasms registered in Vaud and Neuchâtel between 1984 and 1993, 699 (1.7%; 2.3% excluding non-melanomatous skin cancers) were of unknown primary site (ICD-O-9 codes 196–199). The corresponding overall age-standardised (on the world population) incidence rates were 6.2/100 000 males and 4.0/100 000 females. As in the Dutch report [5], biopsy-proven cancer patients were divided into four histological subgroups: adenocarcinomas, poorly differentiated carcinomas (PDC) and poorly differentiated adenocarcinomas (PDA), squamous cell carcinoma and undifferentiated malignant neoplasms.

Table 1 gives the distribution of the 699 patients with unknown primary tumour diagnosed in Vaud ( $n=553$ ) and Neuchâtel ( $n=146$ ) between 1984 and 1993, according to age, gender and histological group, and the corresponding median survival in weeks. Of these, 543 were histologically confirmed. Sixty percent of all of the patients were aged  $\geq 70$  years, and the median age was 73 years. Median age was 71 years for those cases that were histologically confirmed, and 79 years for the non-histologically confirmed patients. The overall median survival rates were 11 and 6 weeks, respectively. Only 15% ( $n=103$ , 9 non-biopsy-proven cases) of the whole series ( $n=699$ ) survived more than 1 year. Survival curves for histologically-confirmed and purely clinical unknown primary cancers are plotted in Fig. 1. Overall

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Table 1

Biopsy-confirmed and clinical unknown primary tumours: distribution according to age, gender and histology: Vaud and Neuchâtel, Switzerland, 1984–1993

Characteristic	Biopsy-confirmed		Clinical diagnosis		Total	
	n (%)	Median survival (weeks)	n (%)	Median survival (weeks)	n (%)	Median survival (weeks)
	543 (100)	11	156 (100)	6	699 (100)	9
Age (years)						
<50	31 (6)	26	3 (2)	3	34 (5)	24
50–59	68 (13)	14	9 (6)	7	77 (11)	14
60–69	150 (28)	10	18 (12)	9	168 (24)	10
70–79	180 (33)	11	51 (33)	7	231 (33)	10
≥80	114 (21)	8	75 (48)	4	189 (27)	7
Gender						
Male	274 (50)	9	82 (53)	4	356 (51)	9
Female	269 (50)	14	74 (47)	7	343 (49)	11
Histological diagnosis						
Adenocarcinoma	336 (62)	11				
PDC/PDA <sup>a</sup>	122 (22)	9				
Squamous cell carcinoma	48 (9)	41				
Undifferentiated malignant neoplasms	37 (7)	7				

<sup>a</sup> Poorly differentiated carcinomas/poorly differentiated adenocarcinomas.

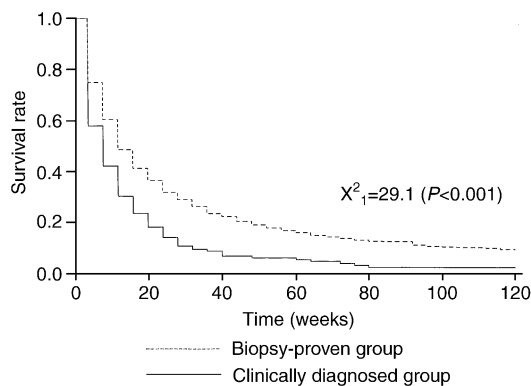


Fig. 1. Survival curves for biopsy-proven ( $n=543$ ) and clinically diagnosed ( $n=156$ ) unknown primary malignant tumours: Vaud and Neuchâtel, Switzerland, 1984–1993.

median survival was 24 months for patients aged <50 years, and declined with age to 8 weeks for those aged ≥70 years. Survival was similar in males (9 weeks) and females (11 weeks). Among the various histological groups, only patients diagnosed with squamous cell cancers had a higher survival rate (median 41 weeks).

In this Swiss population, covered since the early 1970s by a uniform system of cancer registration, which was also able to provide meaningful information on cancer sites that are often inadequately covered by cancer registration systems, such as skin [8] and lymphohaemopoietic tissues [9], 2.3% of all neoplasms (excluding non-melanomatous skin cancers) were of unknown primary site. This is lower than the 5–10% reported from

North America [1,10], and also somewhat lower than the 4% reported from the Southern Netherlands. The overall very poor survival of only 9 weeks compares well with the 11 weeks from the Dutch dataset [5]. Likewise, this study confirms that survival of patients with unknown primary neoplasms, although generally extremely poor, further declines with age, and suggests that it may be somewhat higher for patients with squamous cell carcinomas. Survival was even more unfavourable among the 22% of patients without histological confirmation. These patients were older, but the age-specific median survival was also worse in the non-histologically confirmed patients, indicating that age *per se* cannot totally explain the lower survival in this subgroup.

Although we had no information on the site of the main neoplastic location nor on treatment, this study further quantifies, in a population-based series, the extremely unfavourable prognosis of patients diagnosed with unknown primary tumours.

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