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Original article

Descriptive epidemiology of vulvar and vaginal cancers in Vaud, Switzerland, 1974–1994

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Summary

Background: To analyse trends in incidence, survival and risk of second neoplasms following vaginal and vulvar cancers using data collected by the Swiss Cancer Registry of Vaud over the 21-year period 1974–1994.

Materials and methods: Subjects were 257 vulvo-vaginal cancers. Of these, 69 were vaginal, 153 vulvar cancers, and 35 non-specified lower genital tract neoplasms; 94 *in situ* neoplasms were also registered (85 for the vulva).

Results: Invasive vaginal cancer incidence decreased from 0.8 in 1974–1984 to 0.4/100,000 women in 1985–1994, while invasive vulvar cancer incidence remained approximately stable around 1.2/100,000 (world standard); incidence of *in situ* vulvar cancer increased from 0.8 to 1.3/100,000, the rise being larger in younger women. Significant excesses for second primary neoplasms were observed for oro-pharyngeal and lung cancer, and for non-melanomatous skin neoplasms, as well as for invasive vulvar cancers following *in situ* cancers.

Conclusions: This population-based dataset confirms that the incidence of *in situ* vulvar (but not invasive vulvar or vaginal cancer) has been increasing over the last 20 years. The excess second primary neoplasms supports the hypotheses that human papillomavirus and cigarette smoking are related to vulvo-vaginal neoplasms.

Key words: epidemiology, incidence, multiple tumours, neoplasms, survival, time trends, vagina, vulva

Introduction

Cancers of the vagina and vulva are rare neoplasms, accounting for less than 1% of all cancers in women, and 9% of female genital tract neoplasms [1].

Most information on descriptive epidemiology of these neoplasms comes from the Surveillance Epidemiology and End Results (SEER) Program of the US National Cancer Institute [2, 3]. The SEER data over the period 1973–1987 showed no appreciable change over time for vaginal and invasive vulvar cancer, with age-standardized incidence rates (on the US population) around 1.0 and 1.5/100,000, respectively. In contrast, the incidence rate of *in situ* vulvar cancer nearly doubled between 1973 and 1987, the rise being particularly marked below age 55 [2]. Five-year relative survival was over 90% for vulvar cancers, and less than 50% for vaginal neoplasms [3]. Selected clinical series [4] gave five-year survival of about 60% for vulvar and 50% for vaginal carcinomas. An excess of secondary primary cancers after vulvar and vaginal cancers was found for smoking or human-papillomavirus (HPV) related neoplasms [5]. A significant excess of invasive vulvar cancer following vulvar intra-epithelial neoplasia was also reported [6].

Most other data come from hospital-based series. They confirmed an increase of intra-epithelial vulvar neoplasia, mostly at younger age [7–10]. These trends have been associated to changed sexual habits in most recent cohorts of women, infection with HPV, and smoking [11–13].

To provide further, population-based information on incidence, survival and second neoplasms following vaginal and vulvar cancers, we analysed data from the Cancer Registry of Vaud over the 21-year period 1974–1994.

Materials and methods

Vulvo-vaginal cancer incidence data for the period 1974–1994 were abstracted from the Vaud Cancer Registry file, which includes data concerning incident cases of malignant neoplasms in the Canton (whose population according to the Census 1990 was about 580,000 inhabitants) [1].

Information collected by the register includes general demographic characteristics of the patient (age, sex, municipality of residence), site and histological type of the tumour according to the International Classification of Diseases for Oncology [14], and time of diagnostic confirmation.

The present series comprises 257 invasive vulvo-vaginal cancer primaries (ICD-O T: 184.0, vagina, n = 69; 184.1–184.4, vulva, n = 153; 184.8–184.9, non specified lower genital tract neoplasms, n = 35) registered during the 21 year period from 1974 to 1994. Ninety-five histologically verified *in situ* vulvo-vaginal neoplasms were also registered (85 for the vulva; 56% being labeled as Bowen's disease). Histo-

Table 1. Trends in age-standardized incidence rates[a] of invasive and *in situ* neoplasms of the vagina, vulva and of unspecified neoplams of the lower female genital tract in Vaud, Switzerland, 1974–1994.

Site		Calendar period			
		1974–1984		1985–1994	
		Number	Rate[a]	Number	Rate[a]
Vagina	Invasive	45	0.8	24	0.4
	In situ	3	0.08	6	0.1
Vulva	Invasive	71	1.1	82	1.3
	In situ	33	0.8	52	1.3
Unspecified	Invasive	23	0.3	12	0.1

[a] Rate per 100,000 women, age-standardized on the world population.

Table 2. Trends in age-standardized incidence rates[a] of invasive and *in situ* neoplasms of the vagina, vulva and in separate age groups in Vaud, Switzerland, 1974–1994.

Site		Calendar period					
		1974–1984			1985–1994		
		Rate at age			Rate at age		
		20–44	45–64	⩾65	20–44	45–64	⩾65
Vagina	Invasive	0.2	2.2	4.5	0.2	1.2	1.9
Vulva	Invasive	0.3	1.2	10.7	0.6	2.8	8.0
	In situ	1.0	1.9	1.8	2.2	1.9	3.1

[a] Rate per 100,000 women, age-standardized on the world population.

logical confirmation was performed in over 92% of the invasive neoplasms, and only 2.5% were discovered at death.

Age-standardized incidence rates (by the direct method, world standard population) were computed for the population of all ages and for three separate age groups (20–44, 45–64 and 65 or more years). Mean annual percent changes were derived from standard log-linear regression models.

Information on survival was 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 [14]. Patients who migrated outside the Canton, and were therefore not traceable (2.3%), were censored at the date of emigration. The vital status of each registered case has thus been verified up to June 30th, 1997. One-, three-, five- and 10-year relative survival estimates were computed after allowance for the general lifetables of the Canton [15]

Invasive and *in situ* cases were followed-up to 31 December 1996 for the occurrence of second primary neoplasms, for a total of 1,502 person-years at risk (918 for invasive neoplasms). Calculation of expected numbers of cases were based on site-, age- and calendar period-specific incidence rates, multiplied by the corresponding number of person-years at risk. The significance of the observed: expected ratios (standardized incidence ratio (SIR)) and their corresponding 95% confidence intervals (95% CI) was based on the Poisson distribution [16].

Results

Over the period 1974–1994, 257 vulvo-vaginal invasive cancers were registered. Of these, 69 were vaginal neoplasms (51, 74% squamous cell), 153 vulvar cancers (114, 75% squamous cell) and 35 were non specified lower genital tract neoplasms. A total of 94 *in situ* neoplasms were also registered; of them, 85 were from the vulva.

Table 1 gives the age-standardized (world standard) incidence rates in two separate calendar periods (1974–1984; 1985–1994). Incidence of invasive vaginal cancer decreased from 0.8 to 0.4/100,000 women, while invasive vulvar cancer remained approximately stable (1.1 in 1974–1984; 1.3 in 1985–1994). Other invasive lower female genital tract neoplasms declined from 0.3 to 0.1/100,000. In contrast, some rise was observed for *in situ* vaginal cancers (from 0.08 to 0.1/100,000 women) and for *in situ* vulvar cancers (from 0.8 to 1.3/100,000). The estimated percent annual changes were −3.7% and +2.6% for invasive neoplasms of vagina and vulva,

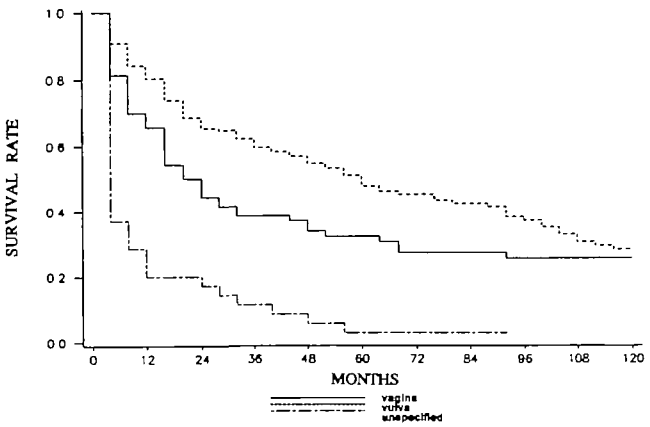

Figure 1. Survival curves of invasive cancers of vagina, vulva and unspecified female lower genital tract neoplasms in Vaud, Switzerland, 1974–1994.

respectively, and +1.2% and +5.1% ($P = 0.05$) for vaginal and vulvar *in situ* neoplasms.

Table 2 gives corresponding figures in three separate age groups (20–44, 45–64, ⩾65 years). While the decline for invasive vaginal cancer was observed both at age 45 to 64 and in elderly women, the rise for *in situ* vulvar cancer was larger below age 45, and under age 65 there was also some increase in invasive vulvar cancers.

Survival rates are plotted in Figure 1 (for invasive neoplasms) and given in Table 3 in terms of relative survival. These were 41% at 10 years for invasive vaginal cancer, 48% for invasive vulvar cancer, and 94% for *in situ* vulvar neoplasms.

Observed and expected numbers of second neoplasms following vaginal and vulvar neoplasms are given in Table 4. Excess rates were observed for oro-pharyngeal cancers following invasive vulvar and vaginal cancers (two observed, 0.2 expected; SIR = 10.3), and for tobacco-related neoplasms (oro-pharyngeal and lung) following combined invasive and *in situ* vulvar and vaginal cancers (seven observed, 0.8 expected; SIR = 9.0; 95% CI: 3.6–18.5). Furthermore, there was a significant excess of invasive vulvar cancer following *in situ* cancer (four observed, 0.03 expected). Rates were also significantly above unity for non-melanomatous skin cancer follow-

Table 3. One-, three-, five- and ten-year relative survival for *in situ* and malignant neoplasms of vagina, vulva and unspecified female lower tract neoplams in Vaud, Switzerland, 1974–1994.

Site		Relative survival at			
		One year	Three years	Five years	Ten years
Vagina	Invasive	0.72	0.45	0.41	0.41
Vulva	*In situ*	0.97	0.95	0.95	0.94
	Invasive	0.84	0.68	0.60	0.48
Unspecified	Invasive	0.27	0.24	0.05	NC

Abbreviation: NC – not computable.

Table 4. Observed and expected cases, and standardized incidence ratios (SIR) of subsequent cancer sites after an initial diagnosis of *in situ* or invasive neoplasm of vagina and vulva, and corresponding 95% CI of the SIR. Vaud, Switzerland, 1974–1994.

Site of second primary	Number of cases		SIR	95% CI
	Observed	Expected		
First vagina, invasive				
Oropharynx	1	0.1	20.3	0.3–112.8
Skin, non-melanoma	3	0.9	3.4	0.7–10.0
Total, all sites[b]	5	3 5	1.4	0.5–3.4
Total, excl. skin[b]	2	2.3	0.9	0.1–3.2
First vulva, invasive				
Oropharynx	1	0.1	7 2	0.1–39.9
Colorectum	4	1.2	3.3	0.9–8.5
Lung	2	0.3	5.8	0.7–21.1
Skin, non-melanoma	7	2.7	2.6	1.0–5.4
Total, all sites[a]	17	9.8	1.7	1.0–2.8
Total, excl. skin[a]	10	7.2	1.4	0.7–2.5
Total invasive[c]				
Oropharynx	2	0.2	10.3	1 2–37.1
Colorectum	5	1.7	3.0	1.0–8.0
Lung	2	0.5	4.1	0.5–15.0
Skin, non-melanoma	10	3.7	2.7	1.3–5.0
Total, all sites[d]	22	13.7	1.6	1.0–2.4
Total, excl. skin[d]	12	9.4	1.3	0.7–2.2
First vulva, *in situ*				
Lung	3	0.2	14.7	3.0–43.0
Skin, non-melanoma	6	1.3	4.5	1.7–9.8
Vulva	4	0.03	139.2	37.5–336.4
Total, all sites[e]	16	5.1	3.1	1.8–5.1
Total, excl. skin[e]	10	3.2	3.1	1.5–5.7

[a] Includes one breast (1.9 expected), one ovarian neoplasm (0.3 expected), and one multiple myeloma (0.1 expected).
[b] Includes one colorectal cancer (0.4 expected).
[c] Includes vulvar, vaginal and unspecified neoplasms.
[d] Includes one breast (2.7 expected), one ovarian neoplasm (0.4 expected), and one multiple myeloma (0.1 expected).
[e] Includes one colorectal (0.5 expectd), one liver (0.02 expected), and one breast neoplasm (1.2 expected).

ing invasive vulvar and vaginal cancers (10 observed, 3.7 expected; SIR = 2.7) as well as *in situ* cancers (six observed, 1.5 expected; SIR = 4.1). A non significant excess was observed for colorectal cancer (five observed, 1.7 expected; SIR = 3.0) following invasive vulvo-vaginal cancer.

Discussion

The incidence rates of invasive and *in situ* vulvar and vaginal neoplasms in this European population were of similar magnitude as those reported from the SEER Program in the United States [2, 3, 18, 19] and also trends in incidence were in the same direction, with some decline in vaginal cancer, but a rise in vulvar cancer, mostly at younger age and for *in situ* neoplasms. Likewise, the five- and 10-year survival rates (over 90% for *in situ* neoplasms, less than 50% for invasive vaginal and vulvar neoplasms) are well comparable with available data from the SEER Program [2, 3, 17, 18] and clinical series [4, 7–10].

The data were derived from a population-based cancer registry system established for over 20 years, and adopting the same criteria of registration for invasive and *in situ* vulvo-vaginal neoplasms [1]. A limitation of the study, however, is given by the small number of cases, particularly for *in situ* vaginal neoplasms.

The main interest and importance of this dataset is therefore in confirming, on the basis of a population-based series from Europe, a number of clinical observations [7–10] suggesting a rise in (*in situ*) vulvar cancers.

This finding has been usually related, as for cervical cancer [19], to the changed sexual habits of younger generations of women, and possibly to infection with HPV [12, 13]. This hypothesis is supported by the excess oral cancer following vulvo-vaginal cancers, since a role of HPV on oral carcinogenesis has also been postulated [20]. HPV has also been related to non-melanomatous skin cancer [21, 22], although the issue remains open to discussion. Likewise, the excess of lung, oral and other tobacco-related neoplasms following vulvo-vaginal neoplasms supports a role for cigarette smoking, as reported in case-control investigations [23–25].

The decline in invasive vaginal cancer, mostly in middle and elderly age, is more difficult to explain, but may be related to the increased frequency of Pap-smear, as reflected by the fall in invasive cervical cancer observed in the same population [26].

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